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Table 1. Limitations for each manuscript type.

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Original Article	5000 (Structured)	200	50	6	7 or total of 15 images
Review Article	5000	200	50	6	10 or total of 20 images
Case Report	1500	200	10	No tables	10 or total of 20 images
Letter to the Editor	500	N/A	5	No tables	No media
Scientific letter	900	N/A	10	No tables	2 or total of 4 images
Clinical Imaging/ Visual Diagnosis	400	N/A	5	No tables	3 or total of 6 images
History	900	N/A	10	No tables	3 or total of 6 images
Publication ethics	900	N/A	10	No tables	No media

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Tables should be included in the main document, presented after the reference list and they should be numbered consecutively in the order they are referred to within the main text. A descriptive title must be placed above the tables. Abbreviations used in the tables should be defined below the tables by footnotes (even if they are defined within the main text). Tables should be created using the "insert table" command of the word processing software and they should be arranged clearly to provide an easy reading. Data presented in the tables should not be a repetition of the data presented within the main text but should be supporting the main text.

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Figures, graphics and photographs should be submitted as separate files (in TIFF or JPEG format) through the submission system. The files should not be embedded in a Word document or the main document. When there are figure

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subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system. Images should not be labelled (a, b, c, etc.) to indicate figure subunits. Thick and thin arrows, arrowheads, stars, asterisks and similar marks can be used on the images to support figure legends. Like the rest of the submission, the figures too should be blind. Any information within the images that may indicate an individual or institution should be blinded. The minimum resolution of each submitted figure should be 300DPI. To prevent delays in the evaluation process all submitted figures should be clear in resolution and large in size (minimum dimensions 100x100 mm). Figure legends should be listed at the end of the main document.

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Editorial

Dear Readers,

We are happy to be with you with the first issue of EAJEM in 2016. It is our pleasure to see the manuscripts published in each issue has higher quality than the previous ones. We have seven original articles this month. Two of them points out pneumonia. The first article is about the prognostic power of serum surfactant protein D levels in children. The second one tries to identify whether the Amino-Terminal Fragment of Pro-Brain Natriuretic Peptide in Plasma identifies mortality or not. We have got two articles associated with trauma. The first one will be about one of the lesser evaluated topics in the emergency: Corneal injuries and abuse of topical drugs in workers. The second one will aim preliminary results of one of the untouched areas in Muslim countries: Abusive Head Trauma in Turkey. We hope these published pioneer trauma studies may lead to multicentric prospective studies to enlighten deeper points in the future.

We have also topics about Out-of-Hospital Cardiopulmonary Arrest Cases and Acute Abdominal and Flank Pain. For toxicologic emergencies, writers from far abroad contributed in this issue sharing their experience about Acute Zinc Phosphide Poisoning.

We think the topics and results will be discussed long in the corridors of the hotel that 3rd Intercontinental Emergency Medicine Congress, 3rd International Critical Care and Emergency Medicine Congress will be conducted. Our submit system is more simple now. We are ready to serve you for upcoming prospective manuscripts.

Hope to be with you in the near future issues,

With best regards,

Editor in Chief
Mustafa Serinken

Associate Editor
Mücahit Emet

EURASIAN JOURNAL OF EMERGENCY MEDICINE

Can Serum Surfactant Protein D Levels be used as an Effective Factor Instead of Clinical Severity Scores of Pneumonia in Pediatric Emergency Departments?

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Abstract

Aim: To investigate whether serum surfactant protein D (SP-D) level is an applicable indicator in differentiating bacterial and viral pneumonia and determining clinical severity in cases with community-acquired pneumonia (CAP).

Materials and Methods: A total of 67 subjects were analyzed prospectively; of these, 32 were patients (aged 1 month–18 years) with a diagnosis of CAP and 35 were healthy control subjects.

Results: The median age of the patients was 17.5 months (1.5–156 months). The serum SP-D levels of the patient group were significantly higher than those of the control group ($p<0.001$). Based on the pneumonia clinical severity index, serum SP-D levels in patients with mild (n=7), moderate (n=19), and severe (n=6) pneumonia were significantly higher than those in the control group ($p<0.001$, respectively). The serum SP-D levels in patients with severe pneumonia were much higher than in those with mild and moderate grades based the clinical severity index ($p<0.001$ and $p<0.001$, respectively). Although the serum SP-D levels in the bacterial pneumonia group were higher than those in the viral pneumonia group, the difference was not statistically significant.

Conclusion: Although serum SP-D has limited efficacy in differentiating bacterial and viral pneumonia with respect to CAP in children, it can be used as an effective bioindicator for determining the clinical severity of the disease in emergency services. *(Eurasian J Emerg Med 2016; 15: 1-6)*

Keywords: Community acquired pneumonia, surfactant protein D, pneumonia clinical severity index, pediatric emergency

Introduction

Community-acquired pneumonia (CAP) in children is an important morbidity and mortality factor, especially in developing countries. According to data obtained from the World Health Organization (WHO), 156 million children under the age of five years are diagnosed with pneumonia each year. Twenty million of these children are hospitalized. More than two million are fatally affected (1, 2).

Usually, viral agents (20%–43%) are responsible for CAP etiology in children. Bacterial agents are a less significant factor (10%–40%) (3). However, many studies published in the last ten years have reported that mixed viral/bacterial infections play a role in 45% of pediatric CAP cases (4). Similar signs and symptoms caused by these agents result in the failure of radiological findings to differentiate the agents and difficulties in the routine practice of invasive interventions, such as hemoculture, bronchoalveolar lavage (BAL), and lung needle biopsy. Complications resulting from these interventions have encouraged clinicians to research diagnostic and prognostic biochemical indicators in CAP cases (4, 5). Furthermore, the unnecessary use of antibiotics due to failure to perform invasive interventions based on viral and bacterial pneumonia differentiation leads to financial burdens. Consequently, differentiation is another issue that emphasizes the importance of these bioindicators.

Surfactant protein D (SP-D) is a hydrophilic protein synthesized and secreted by alveolar epithelial type 2 and Clara cells as an acute phase reactant in lung infections (6). SP-D plays an important role in host defense by recognizing the carbohydrate structures in bacteria and viruses (7). According to experimental studies, it is secreted in inflammatory lung diseases, such as lung infection and pneumonitis. SP-D levels also increase due to the deterioration of alveolar cells (8, 9).

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This study aimed to investigate whether serum SP-D levels can be used to determine clinical severity and differentiate bacterial/viral etiology in pediatric CAP cases.

Materials and Methods

Ethical approval for this prospective study was obtained from the Local Ethics Committee of Ondokuz Mayıs University in accordance with the Declaration of Helsinki. Written informed consent was obtained from relatives of the patients. A total of 67 subjects, including 32 patients between one month and 18 years of age, were presented to the Pediatric Emergency Service of the Medical School of Ondokuz Mayıs University due to a CAP diagnosis. Thirty-five age- and gender-matched control subjects were analyzed prospectively. The diagnosis of pneumonia was established according to the criteria determined by the WHO (10). Clinical severity scores were determined using the clinical severity index of Liu et al. (11), which is based on respiratory rate, retraction, the presence of dyspnea, and findings of auscultation (Table 1). To differentiate bacterial and viral pneumonia, modified parameters of the study conducted by Ruuskanen et al. (5) were used as pneumonia etiology prediction scores (Table 2). According to this scoring system, cases with scores <3 were evaluated to have viral etiology. Those with scores ≥3 were evaluated to have bacterial etiology. The criteria of the guidelines of the British Thoracic Society were used in making hospitalization decisions (12). Patients were excluded from the study if they had a medical history of different diseases that may affect serum SP-D levels (including chronic pulmonary diseases such as cystic fibrosis, asthma, bronchiolitis obliterans, and bronchopulmonary dysplasia, as well as hepatic, renal, gastrointestinal, hematological, endocrinological, metabolic, neurological, or cardiovascular disorders). The control group consisted of healthy age- and gender-matched children.

The demographic characteristics, clinical, laboratory and radiological findings, serum SP-D levels, pneumonia clinical severity index results and patient treatment responses were evaluated. The correlation of other variables used for pneumonia clinical severity indexes, pneumonia etiology prediction scores with serum SP-D levels and C-reactive protein (CRP), leukocyte, sedimentation, neutrophil and lymphocyte counts, were analyzed.

Collection of the Serum Samples and Measurement of Serum SP-D levels

Serum samples were allowed to clot spontaneously at room temperature and were centrifuged at 3000 ×g for 10 min. All samples were stored at −80°C pending analysis of serum SP-D. Serum SP-D levels were evaluated using ELISA (catalog no: RD194059101, BioVendor, European Union). Results were recorded in ng/mL.

Table 1. Clinical score for severity of pneumonia (11)

Variables	Clinical score, circle one			
	0 point	1 point	2 points	3 points
		Respiratory rate*		
Age				
<2 m		≤60	61–69	≥70
2–12 m		≤50	51–59	≥60
13 m–2 y		≤40	41–44	≥45
25 m–3 y		≤34	35–39	≥40
37 m–5 y		≤30	31–34	≥35
61 m–12 y		≤26	27–30	≥31
>12 y		≤23	24–27	≥28
Retractions	None	Intercostal	Intercostal and substernal	Intercostal, substernal, and supraclavicular
Dyspnea				
0–2 y	Normal feeding, vocalizations, and activity	Any 1of the following: difficulty in feeding, decreased vocalization, or agitation	Any 2 of the following: difficulty in feeding, decreased vocalization, or agitation	Stops feeding, does not vocalize, or is drowsy or confused
25 m–5 y	Normal feeding, vocalizations, and play	Any 1 of the following: decreased appetite, increased coughing after play, or hyperactivity	Any 2 of the following: decreased appetite, increased coughing after play, and hyperactivity	Stops eating or drinking, stops playing, or is drowsy or confused
≥5 y	Counts till ≥10 in one breath	Counts till 7–9 in one breath	Counts till 4–6 in one breath	Counts till ≤3 in one breath
Wheeze	Normal breathing; no wheezing present	End-expiratory wheeze only	Expiratory wheeze only (greater than end-expiratory wheeze)	Inspiratory and expiratory wheeze, diminished breath sounds, or both

*(breaths/min), count respiratory rate for one full minute while patient is awake; m: months; y: years

Table 2. Clinical and laboratory variables used to distinguish viral pneumonia from bacterial pneumonia (pneumonia etiology prediction score) (5)

Parametres	0 point	1 point
Age	<5 years	≥5 years
Clinical profile	Rhinitis, wheezing	>38.5 °C fever, tachypnea
Total white blood cell count	$<15\times10^9$ cells per L	$\geq15\times10^9$ cells per L
Serum levels of C-reactive protein	<20 mg/L	≥20 mg/L
Chest radiograph findings	Sole interstitial infiltrates, bilaterally	Lobar alveolar infiltrates
Response to antibiotic treatment	Slow or non-responsive	Rapid (in three days)
Total score: ≥3 suspected bacterial, <3 suspected viral		

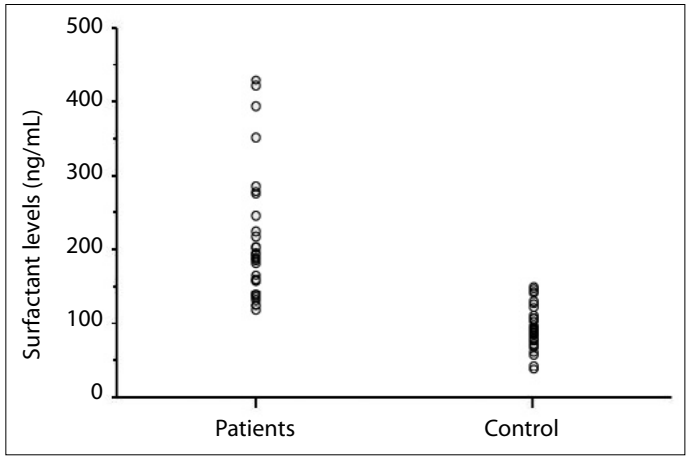

Figure 1. Comparison of serum SP-D levels between patient and control groups

Statistical analysis

All parameters were analyzed using the Statistical Package for the Social Sciences software version 21.0 (IBM SPSS Statistics; New York, USA). Control of normal data distribution was performed using the Shapiro–Wilks test. All categorical variables were represented as numbers and percentages, whereas numerical variables were given as mean±standard deviation and median (minumum–maximum). The normally distributed values of the patients and controls were compared using the independent t test, while non-normally distributed data were analyzed using the Mann–Whitney U and Kruskal–Wallis tests. Pearson's chi-square test was used to analyze categorical data. Correlations between quantitative data were analyzed using the Spearman's correlation test. The accepted value for statistical significance was $p<0.05$.

Results

The study included 67 total subjects, consisting of 35 healthy control subjects and 32 patients who applied to the Pediatric Emergency Service of our hospital with a CAP diagnosis. The median age of the patient group was 17.5 months (1.5 to 156 months), and the median age of the control group was 24 months (1 to 156 months). The female/male ratio of the patient group was 1:13 (17/15), with a 1:18 (19/16) ratio in the control group. No difference was found between the groups with respect to median age value and gender ($p=0.183$ and $p=0.559$, respectively). 24 patients (75%) received oxygen therapy during a follow-up period with a median duration of 2 days (between 0.5 and 27). One patient was intubated and hospitalized in the intensive care unit. 27 total patients applied with fever (84.3%) for a median duration of two days (between one and nine days). All patients received antibiotics for a median duration of five days (between 2 and 42 days). Complications such as parapneumonic pleural effusion requiring no drainage, atelectasis, and respiratory acidosis were detected in 2 (6.2%), 8 (25%), and 11 (34.3%) of the cases, respectively. The mean hospitalization duration of the patients was 11.72±8.25 days (2 to 42 days).

Table 3. Comparison of serum SP-D levels in all study groups

Groups	n	SP-D (ng/mL)*	p
Control	35	93.79 (39.66–154.27)	<0.001
Patients	32	192.92 (120.24–440.81)	
According to the SPS			
LS	7	191.31[A] (143.16–229.64)	0.001
MS	19	169.07[A] (120.24–282.09)	
HS	6	382.67[B] (285.30–440.81)	
According to the PEPS			
Viral	9	132.59 (39.66–282.09)	0.133
Bacterial	23	198.22 (120.24–440.81)	

*median (min-max), SP-D: surfactant protein D; LS: low score; MS: moderate score; HS: high score; SPS: severity of pnemonia score; PEPS: pneumonia etiology prediction score.

Serum SP-D levels were significantly higher in the patient group than in the control group ($p<0.001$) (Figure 1, Table 3). According to the pneumonia clinical severity index, serum SP-D levels in the groups with mild (n=7), moderate (n=19), and severe (n=6) pneumonia were significantly higher than in the control group ($p<0.001$, $p<0.001$, and $p<0.001$, respectively) (Figure 2 and Table 3). While there was no significant difference between serum SP-D levels in cases with mild and moderate clinical severity ($p=0.461$), serum SP-D levels in cases with a severe clinical index were remarkably higher than in cases with mild and moderate clinical severity ($p<0.001$ and $p<0.001$, respectively) (Figure 2 and Table 3). No significant correlation was found between clinical severity index and C-reactive protein (CRP) or thrombocyte and neutrophil counts ($p=0.942$, $p=0.328$, and $p=0.429$, respectively). Serum SP-D levels were higher in the groups with bacterial etiology. However, the difference was not statistically significant ($p=0.133$) (Figure 3 and Table 3). A significant correlation ($r=0.482$, $p<0.001$) was found between serum SP-D level and hospitalization duration in patients with bacterial etiology, whereas no sig-

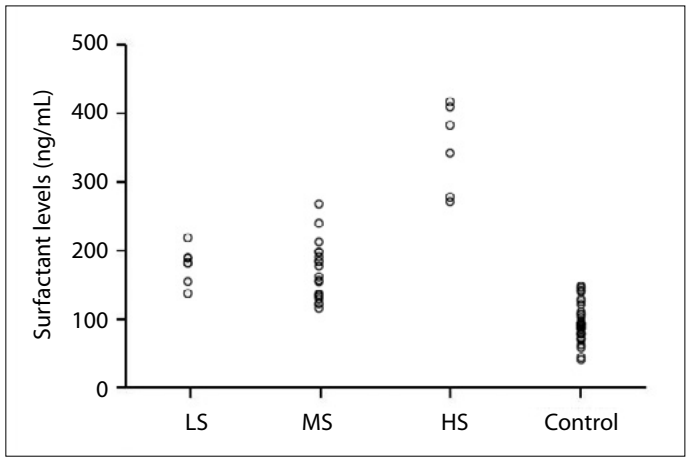

Figure 2. Comparison of serum SP-D levels according to pneumonia severity scores (LS: low score; MS: moderate score; HS: high score)

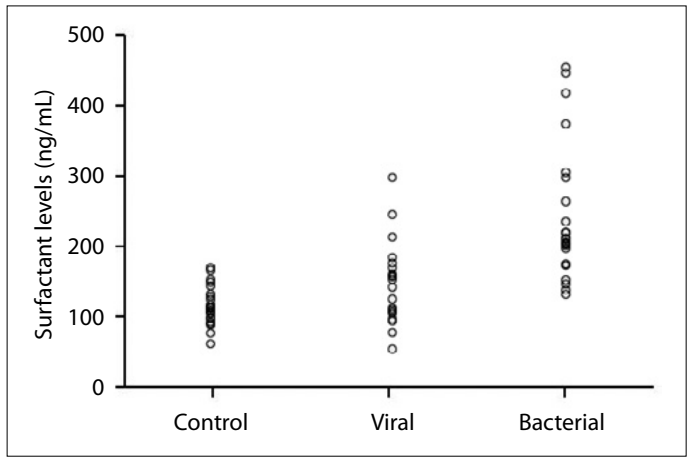

Figure 3. Comparison of serum SP-D levels according to pneumonia etiology prediction scores

Table 4. Comparison of clinical and laboratory findings in all patients according to pneumonia etiology prediction scores

Variables	Bacterial (n=23)	Viral (n=9)	p
Age, median (range)	21 months (1.5–156)	2.5 months (1.5–45)	0.262
Gender			
Male, n (%)	11 (47.8)	4 (44.4)	0.853
Female, n (%)	12 (52.2)	5 (55.6)	
Fever, (mean±SD)	37.10±0.78 °C	36.83±0.45°C	0.331
Total white-blood cell count (mean±SD)	13450±8041 cells/L	14081±7122 cells/L	0.838
Neutrophil count, (mean±SD)	61.7±18.9%	41.0±19.7%	0.114
CRP, median (range)	38.7 mg/L (0.5–270.0)	15.0 mg/L (1.0–29.0)	0.416
Wheezing, n (%)	7 (30.4)	6 (66.7)	0.109
Ral, n (%)	22 (95.7)	8 (88.9)	0.490
Retractions, n (%)	20 (87.0)	7 (77.8)	0.604
Nasal flaring, n (%)	19 (82.6)	6 (66.7)	0.370
Cyanosis, n (%)	5 (21.7)	1 (11.1)	0.648
Oxygen saturation, median (range)	86.2% (43.0–99.6)	82.7% (77.0–97.6)	0.081
Oxygen therapy requirement, n (%)	19 (82.6)	5 (55.6)	0.176
Respiratory acidosis, n (%)	9 (39.1)	4 (44.4)	0.688
Intubation, n (%)	1 (4.3)	-	
Radiological findings			
Sole interstitial infiltrates, bilaterally, n (%)	5 (21.7)	7 (77.8)	0.118
Lobar alveolar infiltrates, n (%)	11 (47.8)	1 (11.1)	0.109
Atelectasia, n (%)	7 (30.4)	1 (11.1)	0.386
Pleural effusion, n (%)	2 (8.7)	-	
Length of hospitalization, median (range)	12 (6–42) days	6 (2–10) days	<0.001

CRP: C-reactive protein; SD: standard deviation

nificant correlation was detected (r=0.183, p=0.638) in patients with viral etiology. When the clinical, radiological, and laboratory findings were compared to pneumonia etiology prediction scores, a significant difference in hospitalization duration was detected between the bacterial and viral etiology groups (p<0.001) (Table 4). No significant correlation was found between serum SP-D level and CRP, total WBC, or neutrophil count (r=0.064, p=0.773; r=0.221, p=0.310; and r=0.339, p=0.114, respectively).

Discussion

This study investigated the efficacy of serum SP-D levels in predicting clinical severity, prognosis, and pneumonia etiology in children with CAP who were presented at our Pediatric Emergency Service.

Serum surfactant protein is a hydrophilic protein from the collectin family, secreted by alveolar epithelial type 2 and Clara cells in the lung tissue (6). SP-D is secreted as an acute phase reactant, especially in the presence of infectious agents; it plays a role in host defense mechanisms via adhesion to micro-organisms due to its hydrophilic nature (6, 7), is important in aggregation, neutralization, and opsonization during phagocytosis, results in direct gram-negative bacterial cell-membrane lysis, inhibiting bacterial/fungal growth in macrophages, and has a aggregation-independent manner (7, 13). Therefore, SP-D is an important biomarker of infectious pulmonary diseases. Studies have shown that it plays an important role in host defense against viral and bacterial CAP agents, such as *Klebsiella pneumoniae* (14, 15), *Haemophilus influenza* (14, 16), *Streptococcus pneumoniae* (14, 17), *Mycoplasma pneumoniae* (14, 18), and influenza A virus (14, 19).

Etiology clarification (bacterial or viral) in CAP cases is important for pneumonia management. Despite advanced diagnostic tests, a clinical algorithm has not yet been developed to clarify etiology in the child age group. Specifically, high coinfection rates (30 to 45%) accompanying viral CAP cases increase the difficulty of this situation (4, 5). Unclarified CAP etiology is critical, since it leads to unnecessary use of antibiotics, elevated resistance, and increased health care expenses. Diagnostic difficulties in CAP cases generally necessitate the evaluation of multiple factors to differentiate viral and bacterial etiology, such as patient age, disease progression, accompanying symptoms, serum biomarkers, serum acute phase reactants, radiological findings, presence of viral epidemics, and clinical response to antibiotics (5). For that purpose, the British Thoracic Society has emphasized that viral pneumonia should be considered in the presence of a fever under 38.5 °C, wheezing, a respiratory rate below 50/min, and striking chest recession for children under five years old (20). In our study, we used the scores of the variables identified by Ruuskanen et al. (5) to differentiate viral and bacterial pneumonia and investigate whether serum SP-D value can be used solely as a marker in this etiological differentiation.

The markers used in biomarker studies of CAP cases include inflammatory indicators such as CRP, WBC, ESR, procalcitonin, IL-6, and TNF-α (5, 21, 22). The conclusions of studies vary with respect to the success of these inflammatory indicators in predicting clinical severity in patients diagnosed with pneumonia. Serum WBC, CRP, and procalcitonin levels are the most widely studied acute phase reactants in child and adult CAP cases (5). The literature has demonstrated significantly higher levels in subjects with bacterial pneumonia, though this indication does not show sufficient specificity or sensitivity when used exclusively (5). Another study conducted by Christ-Crain et al. (23) revealed that C-reactive peptide (CRP) does not show a significant difference in pneumonia cases with different severity degrees assessed by PSI. However, CRP has been identified as a serum marker in predicting bacterial pneumonia in another study conducted by the Pediatric Emergency Service (24). Kolling et al. (25) have shown that IL-1 β levels in CAP patients are not correlated with inflammatory markers, such as WBC and CRP, in contrast to IL-1ra and TNF–α. However, IL-1 β levels are more correlated with clinical pulmonary infection scores. These studies have stated that ESR and WBC, as well as the other acute phase reactants, are most commonly used in clinical practice to demonstrate moderate sensitivity and specificity as well as low diagnostic efficacy (22, 26–28). In this study, no significant correlation was found between the clinical severity index and CRP, WBC, and neutrophil compatibly. However, these markers were observed to be statistically significant in the differentiation of viral and bacterial pneumonia.

In recent years, experimental studies have emphasized that specific pulmonary bioindicators considered to be secreted from deteriorated lung tissue, such as surfactant protein A (SP-A), surfactant protein D (SP-D), Krebs von den Lungren-6 (KL-6), and Clara cell protein (CC-16), are effective in determining lung deterioration severity (29–31).

In a study on adult CAP cases, Leth-Larsen et al. (14) reported that they could only determine the agent in 22 (36%) of 61 CAP cases. Furthermore, they detected that serum SP-D levels were higher in pneumonia cases with atypical etiology than in pneumonia cases associated with *Streptococcus pneumoniae* and *Haemophilus influenza* as etiological agents, in contrast to CRP and WBC, according to etiological detection results in these cases. A study by Ichiyasu et al. (31) on 48 cases of bronchopneumonia with or without chronic asthma in an age group ranging from two to four years revealed that serum SP-D levels were higher in severe cases requiring intensive care. In another study on 53 cases with RSV bronchiolitis with or without chronic heart disease, Mosbah et al. (32) detected that serum SP-D levels were higher in the patient group, which required mechanical ventilation support and oxygen requirements. These two studies indicate that serum SP-D level increases in severe pulmonary infection with either bacterial or viral etiology. In addition, Shu et al. (33) suggest investigating the correlation between lung involvement and serum SP-D levels. Their study on serum SP-D levels in 47 CAP cases attributes this conclusion to the fact that *Mycoplasma pneumoniae* in children correlates to SP-D levels detected by BAL and increases significantly when accompanied by severe lung involvement. This study indicates the validity of using serum SP-D levels rather than interventional diagnostic methods such as BAL to differentiate lung infection etiology. Our research revealed that serum SP-D levels increase according to lung infection severity. This is compatible with the literature concerning viral and bacterial etiology cases. Nevertheless, research has established that the SP-D level increase in CAP cases with bacterial etiology was higher than in cases with viral etiology. However, this difference was not statistically significant.

Study limitations

This study had several limitations. For example, it was conducted at one referral center with a limited number of patients over a short time period.

Conclusion

Serum SP-D levels in children are applicable biomarkers that can help to predict severity in CAP cases applying to pediatric emergency services. Furthermore, prospective studies must be conducted on larger case series. A higher increase in serum SP-D levels in cases of bacterial pneumonia is demonstrated; however, clinical applications related to differentiating bacterial and viral pneumonia are limited.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ondokuz Mayıs University School of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

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Results of Out-of-Hospital Cardiopulmonary Arrest Cases with Intervention by Lay Rescuers and Emergency Health Workers

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Abstract

Aim: In this study, all interventions made by lay rescuers and health professionals and the shortcomings for cardiopulmonary arrest management outside the hospital were examined.

Materials and Methods: The study was conducted between December 2012 and May 2014 in the Emergency Department of Gaziantep University. To ensure orderly and standardized records, a study form was prepared that consisted of 31 questions. The time and location of the cardiac arrest, information regarding the lay rescuers and professional health workers, and the practices followed during transport and at the emergency service were examined. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows software version 22.0, and $p<0.05$ was accepted as statistically significant.

Results: Of the 205 cardiac arrests, 69.8% were male and 30.2% were female. The mean age in all of the cases was 58.34±19.1 years. The cardiac arrests mostly occurred in the home environment (62.4%) and happened between 13.00 and 20.00 hours (43.4%). The most frequent conditions that caused a worsening of the cases were syncope (unresponsiveness) (35.6%). The people who identified the cardiac arrest case and called for help by informing emergency health personnel (EHP) were mostly family members (50.7%). The activation time was 14.27±20.30 min. The time to arrive at the scene was 8.4±6.4 (1–35) min. Lay rescuers performed resuscitation in 19.5% of cases. The most frequent rhythms on the arrival of the EHP were asystole (74.1%). EHP evaluated the glaskow coma scale (GCS) of 88.3% of the cases as ≤7 at the scene. EHP performed basic life support (BLS) on all cases (100%) and endo-tracheal intubation (ETI) on 29.3% of the cases at the scene. The on-scene time and transport time to ED were 8.09±8.82 and 9.02±7.92 (1-50) min, respectively. The average duration of CPR at ED was 35.15±16.9 min. Of all the cases, 7.8% were discharged from intensive care unit (ICU) to homes. Of all the cases, 77.6% died at the ED, and 14.6% died in ICU.

Conclusion: The intervention rate by lay rescuers was far less than the international rates. The survival rates were generally below the internationally reported rates. There is no adequate public awareness in our area for identifying cardiac arrest in patients and for initiating early chest compressions. *(Eurasian J Emerg Med 2016; 15: 7-14)*

Keywords: Out-of-hospital cardiopulmonary arrest, lay rescuer, emergency health staff, emergency department, survive, mortality

Introduction

The prompt identification of cardiac arrest cases, activation of emergency health personnel (EHP), early initiation of chest compressions, early defibrillation, competency in basic life support (BLS) practices, and the correct application of BLS are keys to obtaining significantly positive results in out-of-hospital cardiac arrest (OHCA) (1-4). Chest compressions performed alone by the lay rescuer are an essential basic step for successful resuscitation during cardiac arrest and can increase the rate of survival by two-fold (2-4). However, despite technological improvements and advances in telecommunication tools, the discharge rates of OHCA cases from the hospital are quite low (2.5%–25%) (5).

Even in developed countries, such as the USA and Canada, the estimated intervention incidence in OHCA cases is approximately 50–55/100.00 per year (6). Additionally, the rate of CPR application by lay rescuers in OHCA ranges from 20% to 30% (4). In Turkey, no studies have been conducted to provide exact data regarding intervention in OHCA cases. In general, a very important fraction of OHCA cases cannot receive proper and sufficient CPR intervention from lay rescuers and health workers in the world. This is the reason for the high mortality rates observed in OHCA patients.

The most important step toward solving this problem is to raise awareness in the population with ongoing education for the prompt identification of cardiac arrest, early chest compressions, and the use of an AED to increase the chance of survival without any sequela from increasing perfusion to vital organs in OHCA cases (7).

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Although there are some studies on the outcomes of cardiopulmonary resuscitation (CPR) in hospitals, no prospective study has been conducted regarding the outcomes of CPR in OHCA cases. We aimed to obtain the required data (such as morbidity, mortality) related to OHCA cases in our region. Therefore, we prospectively investigated how lay rescuers identified arrest cases; how they called EMS; the BLS applications with chest compressions performed first; the life-saving interventions performed by emergency medical system (EMS) personnel at the scene, during transportation, and at the emergency service; previous CPR training of the EMS personnel and lay rescuers; and the effects of all of these on mortality and morbidity in OHCA cases in the city of Gaziantep.

Materials and Methods

Before the study

We obtained approval from the Gaziantep University, School of Medicine, Medical Ethics Committee (Ethics Committee decision nr: 19.06.2012/277 Date: 19.06.2012) and complied with the Helsinki Declaration in this study. The study was conducted prospectively from December 1, 2012 to May 31, 2014, in collaboration with the Gaziantep University, School of Medicine, Department of Emergency Medicine, and the Gaziantep Health Board EMS Branch Directorship.

Study area

Gaziantep province covers an area of 6,222 km^2, and it is the sixth most populated city (population of the city center is 1,800,000) in Turkey. Within the body of the City Health Board, there are 33 of 112 Emergency Medicine Service (EMS) stations, with 536 personnel. Of these personnel, 320 are emergency medicine technicians (EMT), 80 are paramedics, 21 are health officers, and 35 are general practitioners. Five of the EMS stations in the city center have a doctor working on the team. There is a 24/7 attending doctor at the head of the 112 Command Control Center (112 CCC). The average daily number of telephone calls to EMS is 15,000. Of these calls, only approximately 300 (2%) are considered emergency cases that require an ambulance team to be sent, whereas the other calls (98%) are recorded as ungrounded cases. There are in total 97 ambulances in service in the EMS Branch: 34 of the ambulances are for emergency aid, 58 are for transportation, two are for transportation with four stretchers, and one is for transporting obese patients. Additionally, there are two motorcycle teams. According to the data provided by the City Health Board, the average time required for an ambulance to reach a patient is 9 min.

Preparation and recording of study forms

To ensure orderly and standardized records, a study form was prepared that consisted of 31 questions. Before the study, all of the 112 emergency health professional (EHP) were informed about the purpose of the study and how to complete the forms. No education was given regarding emergency interventions during cardiac arrest to any of the EHP. We expected that they would practice using their own training. To detect possible faults for completing the forms, a preliminary study was conducted where the forms were filled in for 10 cases of cardiac arrest. All of the EHP were warned about the faults detected in this preliminary study. The cases in the preliminary study were excluded from the actual study. Teams dealing with cardiac arrest cases handed the forms that they had completed to the command and control center (CCC) daily at the end of their shifts. These forms were collected weekly from the CCC by the study conductor, and the data were recorded using a computer.

Information obtained from the form

Time and location of cardiac arrest
- Time of the day and where the cardiac arrest happened.

With regard to lay rescuers:
- Did they quickly identify cardiac arrest?
- Did they activate the EMS system (activation time)?
- Delay before activation of the EMS system
- Did they engage in any life-saving interventions until the arrival of EHP?
- Did they initiate early chest compressions?
- Have they ever been trained for BLS practices (and if so, where)?

With regard to professional health workers
- Did they guide lay rescuers in simple interventions beginning from the moment of the emergency call?
- What was the time for the ambulance to arrive at the scene (response time)?
- What was the condition of the case at the time of arrival of the emergency team, and what was the first detected cardiac rhythm?
- What were the BLS and ACLS interventions that were performed at the scene?
- Did they defibrillate the case at the scene?
- What was the duration of interventions that they performed at the scene (on-scene time)?
- How long have they been practicing in their profession?
- What are their training levels regarding BLS and ACLS, and what courses have they attended?

Practices during transport and in the emergency service
- Interventions performed in the ambulance
- Time to arrive at the emergency service (transport time)
- Interventions performed at the emergency department (ED)
- Duration of CPR performed on the patient at the ED
- Mortality and morbidity of the case at the ED
- Mortality and morbidity of the case in wards and intensive care units (ICU)

Inclusion criteria
- Cardiac arrest taking place outside the hospital
- Adult cases over 16 years old (patients less than 16 years old who received intervention at the scene are not followed up by adult emergency service doctors)
- Patients who had cardiac arrest within 30 min before the arrival of the EHP

Exclusion criteria
- Patients under 16 years old
- Patients who were determined to have had a cardiac arrest more than 30 min before the arrival of EHP
- Patients who had a cardiac arrest at the hospital
- Incomplete completion of the study forms

Table 1. Demographic data of the study

	n	%
Gender		
Male	143	69.8
Female	62	30.2
Witnessed arrest	164	80
Scene of event		
At home	128	62.4
Rural areas (e.g., picnic areas, agricultural fields)	29	14.1
Downtown	26	12.7
Public places (e.g., shopping centers, stadiums)	15	7.3
Miscellaneous*	7	3.4
Timeframe when health condition deteriorated		
08^{00}–12^{00} Hours	44	21.5
13^{00}–20^{00} Hours	89	43.4
21^{00}–07^{00} Hours	72	35.1
Complaint of the case that caused deterioration		
Chest pain	33	16.1
Difficulty in breathing	51	24.9
Syncope (unresponsiveness)	73	35.6
Trauma	27	13.2
Gunshot wound	5	2.4
Miscellaneous	16	7.8
The person who activated EMS		
Family member	104	50.7
A person recognized by the patient	58	28.3
A person unrecognized by the patient	23	11.2
Patient themselves	20	9.8
Intervention by lay rescuer		
Yes	40	19.5
No	165	80.5
First rhythm at scene detected by EHP		
Asystole	152	74.1
VF	15	7.3
PVT	12	5.9
PEA	7	3.4
Sinus bradycardia	10	4.9
Sinus tachycardia	6	2.9
Normal sinus rhythm	3	1.5
Training of lay rescuer		
Yes	20	50
No	20	50
Where did the lay rescuer have his/her training		
Courses in schools and workplaces	4	10
In-service training (health worker)	16	40
No formal training, visual/auditory information (Untrained rescuer)	20	50
EHP performing the intervention		
Doctor	32	15.6
Paramedic	75	36.6
EMT	97	47.3
Health officer	1	0.5
In-service training of EHP who performed interventions		
No training	3	1.5
TRC*	54	26.3
Basic module	58	28.3
ALS**	62	30.2
PALS***	28	13.7

*Miscellaneous: outpatient centers (e.g., health centers medical centers, dialysis units), **ALS: advanced life support, ***PALS: pediatric advanced life support; TRC: trauma resuscitation course; EMT: emergency medical technician; EMS: emergency medicine staff; EHP: emergency health professional; VF: ventricular fibrillation; PVT: pulseless ventricular tachycardia; PEA: pulseless electrical activity

Evaluation of the results

During the 18-month study period, 688 cardiac arrest cases were reported in the records of CCC in the city center of Gaziantep. In total, 483 of the cases were excluded from the study: 4 cases were under 16 years old, 24 cases were determined to have had a cardiac arrest more than 30 min before the initiation of intervention, 51 cases did not need CPR at the scene, 10 cases were included in the preliminary study, and 394 cases had missing information on the forms. The remaining 205 cases (30%) were included in the study.

Statistical analysis

A Kolmogorov–Smirnov test was used to assess the normality of the continuous variables. Student's t test was used to compare the normally distributed variables in two independent groups, and the Mann–Whitney U test was used to compare non-normally distributed variables between two independent groups. A Kruskal–Wallis test and Dunn multiple comparison tests were used to compare more than two independent groups. The correlation between categorical variables was tested using Chi-square analysis. The correlation between numerical variables was tested using a Spearman rank correlation coefficient. Descriptive statistics were given as the frequency, percentage, and mean±std. deviation. Statistical analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS Statistics; New York, USA) for Windows software version 22.0. $p<0.05$ was accepted as statistically significant.

Table 2. Findings at the scene, interventions in the case, and outcomes

	Result				
	Discharged from ward n (%)	**Discharged from ICU n (%)**	**Death at ICU n (%)**	**Death at emergency service n (%)**	**p**
Gender					
Male	5 (3.5)	7 (4.9)	20 (14)	111 (77.6)	
Female	1 (1.6)	3 (4.8)	10 (16.1)	48 (77.4)	0.868
Scene					
At home	4 (3.1)	4 (3.1)	21 (16.4)	99 (77.3)	
Public places (e.g., mall, stadium)	0	2 (13.3)	2 (13.3)	11 (77.3)	
Downtown	2 (7.7)	2 (7.7)	2 (7.7)	20 (77.9)	0.648
Rural areas (e.g., picnic field, agricultural field)	0	1 (3.4)	4 (13.8)	24 (82.8)	
*Miscellaneous	0	1 (14.3)	1 (14.3)	5 (71.4)	
Timeframe of deterioration					
08^{00}–12^{00} Hours	1 (16.7)	2 (20)	3 (10)	38 (23)	
13^{00}–20^{00} Hours	3 (50)	5 (50)	14 (46.7)	67 (42.2)	0.948
21^{00}–07^{00} Hours	2 (33.4)	3 (30)	13 (43.3)	54 (35.9)	
Lay rescuer					
Yes	1 (16.7)	3 (30)	9 (30)	27 (17)	0.360
No	5 (83.3)	7 (70)	21 (70)	132 (83)	
Initial condition of case					
GCS 3–7	4 (2.2)	6 (3.3)	23 (12.7)	148 (81.8)	0.003
GCS 8–11	2 (8.3)	4 (16.7)	7 (29.2)	11 (45.8)	
ACLS					
Yes	2 (33.3)	8 (80)	18 (60)	97 (61)	0.314
No	4 (66.7)	2 (20)	12 (40)	62 (39)	
Defibrillation					
Yes	0	1 (4.8)	1 (4.8)	19 (90.5)	0.280
No	6 (3.3)	9 (4.9)	29 (15.8)	140 (76.1)	
Intervention by lay rescuer trained for BLS					
Yes	0	2 (66.7)	5 (55.6)	13 (48.1)	0.599
No	1 (100)	1 (33.3)	4 (44.4)	14 (51.9)	
Complaint preceding cardiac arrest					
Chest pain	1 (3)	2 (6.1)	5 (15.2)	25 (75.8)	
Difficulty in breathing	4 (7.8)	2 (3.9)	9 (17.6)	36 (70.6)	
Syncope	0	1 (1.4)	7 (9.9)	63 (88.7)	0.277
Trauma	1 (3.7)	2 (7.4)	4 (14.8)	20 (74.1)	
Gunshot wound	0	1 (20)	1 (20)	3 (60)	
*Miscellaneous	0	2 (11.8)	4 (23.5)	11 (64.7)	
Initial rhythm detected by EHP					
Asystole	2 (1.3)	5 (3.3)	20 (13.2)	125 (82.2)	
VF	0	3 (20)	3 (20)	9 (60)	
PVT	0	0	1 (8.3)	11 (91.7)	
PEA	1 (14.3)	0	0	6 (85.7)	0.030
Sinus bradycardia	1 (10)	1 (10)	4 (40)	4 (40)	
Sinus tachycardia	1 (16.7)	1 (16.7)	1 (16.7)	3 (50)	
Normal sinus rhythm	1 (33.3)	0	1 (33.3)	1 (33.3)	

*Miscellaneous: outpatient centers (e.g., health centers medical centers, dialysis units). BLS: basic life support; ACLS: advanced cardiac life support; EHP: emergency health professional; ICU: intensive care unit; PEA: pulseless electrical activity; PVT: pulseless ventricular tachycardia; VF: ventricular fibrillation; GCS: Glasgow coma scale

Results

Of the 205 cardiac arrest cases that were included in the study during the 18-month study period, 143 (69.8%) were male and 62 (30.2%) were female (Table 1). The mean age in all of the cases was 58.34±19.1 (16–95) years. The cardiac arrests mostly occurred in the home environment (n=128, 62.4%) or in suburban streets (n=29, 14.1%) between 13.00 and 20.00 hours (n=89, 43.4%). The exact numbers of witnessed arrests were 164 (80%). The most frequent conditions that caused worsening of the cases were syncope (unresponsiveness) (n=73, 35.6%) and breathing difficulty (n=51, 24.9%). The conditions in 16 (7.8%) cases were grouped as "miscellaneous" and included epileptic seizures, cerebrovascular accidents, anaphylaxis, hanging, foreign object aspiration, massive hemoptysis, epistaxis, substance abuse, smoke inhalation, electric shock, detonation, and stab wound. The people who identified the cardiac arrest case and activated EMS were mostly family members (n=104, 50.7%) and friends (n=58, 28.3%). The activation time of EMS was 14.27±20.30 (1–180) min. (Table 1). EHP arrived at the scene after 8.4±6.4 (1-35) min from the emergency call. In six cases (3%), 112 CCC personnel guided the calling person for emergency intervention over the phone (chest compression in three cases, maintaining the airway in two cases, and emergency bleeding control in one case).

The lay rescuers performed resuscitation in 40 (19.5%) cases. People who had previously received first-aid training made half of these interventions. Sixteen (16%) of them were health workers who were at the scene by chance at that time. Four of the untrained people stated that they had witnessed CPR before, and two of them stated that they had seen a CPR application on TV. The remaining 14 untrained people stated that they performed CPR according to what they had heard before. The most frequent rhythms on the arrival of the EHP were asystole (n=152, 74.1%), VF (n=15, 7.3%), and pulseless VT (n=12, 5.9%) (Table 1). EHP performed BLS on 205 (100%) cases, ACLS on 126 (61%) cases, defibrillation on 21 (10.2%) cases (15 asystole, 5 VF, 1 PEA), and endotracheal intubation (ETI) on 60 (29.3%) cases at the scene. A significant part of these interventions were performed by EMT (n=97, 47.3%) and by paramedics (n=75, 36.6%) (Table 1). The mean experience of the EHP who performed the interventions was 5.72±3.81 (1–20) years. The ratios of the last in-service training of the EMS personnel are given in Table 1. Only three (1.5%) personnel had not completed any training before because they were new hires. The mean duration after the completion of the courses was 1.50±1.50 (0–6) years.

The mean on-scene time (duration between the arrival of the ambulance at the scene and its departure) was 8.09±8.82 (1–77) min. During transport, 180 (87.8%) cases received CPR in the ambulance. The transport time (mean duration to arrive at the hospital starting at departure from the scene) was 9.02±7.92 (1–50) min. According to the evaluation of the GCS of the cases by EHP at the moment of arrival at the scene, 181 (88.3%) cases had GCS ≤7, and the remaining 24 (11.7%) cases had GCS between 8 and 11. At the time of arrival at the hospital, 159 cases (78.7%) had GCS ≤7, 30 cases (14.6%) had GCS between 8 and 10, and six cases (2.9%) had GCS ≥11. In the emergency service, ETI was performed on 93 patients and CPR was performed on 174 patients, with an average duration of 35.15±16.9 (2–113) min. As a result, 10 of the cases who were determined to have GCS ≤7 at the scene (10/181, 5.5%) and six of the cases who were determined to have GCS between 8 and 11 at the scene (6/24, 25%) were discharged after admission to ICU.

Table 3. Performance measures of emergency health professionals

	Application		
	Yes n (%)	**No n (%)**	**p**
Training of the EHP BLS application			
No training	2 (1)	0	0.279
TRC	54 (26.7)	0	
Basic module	56 (27.7)	2 (100)	
ALS	62 (30.7)	0	
PALS	28 (13.9)	0	
Professional distribution BLS application			
Doctor	32 (15.8)	0	0.812
Paramedic	74 (36.6)	1 (50)	
EMT	96 (47.5)	1 (50)	
Training of the EHP ACLS application			
No training	1 (0.8)	1 (1.3)	0.898
TRC	31 (24.8)	23 (29.1)	
Basic module	37 (29.6)	21 (26.6)	
ACLS	40 (32)	22 (27.8)	
PALS	16 (12.8)	12 (15.2)	
Professional distribution ACLS application			
Doctor	16 (50)	16 (50)	0.035
Paramedic	54 (72)	21 (28)	
EMT	54 (55.7)	43 (44.3)	

BLS: basic life support; ALS: advanced life support; PALS: pediatric advanced life support; EMT: emergency medicine technician; TRC: trauma resuscitation course; EHP: emergency health personnel; ACLS: advanced cardiac life support

Table 4. Outcomes depending on durations

	n	Mean	p
Duration of CPR and outcome			
Discharged after admission to ward	6	16.16±8.25	0.006
Discharged after admission to ICU	10	29.6±16.92	
Death in ICU	30	35.83±23.3	
Death in emergency service	159	36.08±15.41	
Duration before activation of EMS and outcome			
Discharged after admission to ward	6	26±24.7	0.342
Discharged after admission to ICU	10	8.9±9.9	
Death in ICU	30	14.1±15.1	
Death in emergency	159	14.1±21.4	

EMS: emergency medicine services; ICU: intensive care unit; CPR: cardiopulmonary resuscitation

Following intervention at the scene, in the ambulance, and at the ED, 159 of the cases (77.6%) died in the emergency service, and 30 of the cases (14.6%) died in the ICU. Sixteen (7.8%) were discharged from the ICU. The general mortality was calculated as 92.2%. The mean duration of CPR for the patients who were resuscitated at the ED and admitted to the ICU was 16.16±8.2 min.

There was no statistically significant association between survival and the location of the cardiac arrest (p=0.648), the timeframe of the event (p=0.948), the condition that caused worsening of the case (p=0.277), whether a lay rescuer intervened (p=0.360), whether the lay rescuer had BLS training or not (p=0.599), the average time for EHP teams to arrive at the scene (p=0.342), and whether BLS (p=0.796) and ACLS (p=0.314) practices were performed at the scene (Table 2). The relationship between the initial conditions of the cases and the airway maintenance type was not statistically significant (p=0.132). The survival and discharge rates of the patients who were determined to have sinus tachycardia and bradycardia at the scene were statistically higher than those who were determined to have fatal rhythms (VF, PVT, asystole, and PEA) (p=0.030) (Table 2). There were no statistically significant correlations between the experience of EMS personnel, their in-service training, and whether they performed BLS (p=0.279) and ACLS (p=0.898). In contrast, paramedics were more active in ACLS practices than were EMTs and doctors (p=0.035) (Table 3). The EMS personnel performed defibrillation for the first 15-asystole rhythms that they identified. However, whether defibrillations were performed correctly or incorrectly did not affect the patient's outcome (p=0.280). Whether lay rescuers called for EMS early or late did not affect survival (p=0.342), whereas the survival rates were higher in patients who received a shorter duration of CPR (p=0.006) (Table 4). Whether cardiac arrests took place near or far from the health centers did not have a statistically significant effect on the outcomes (p=0.648). The mortality among patients with a GCS <7 at scene was statistically significant high (p=0.003) (Table 2).

Discussion

The reason why most of the OHCA events occur at home is because elderly patients who have co-morbidities and are thus at a high risk of mortality spend most of their time at home. The second most likely location was found to be suburban streets. We believe that this is because the population of elderly people is dense and that they do not receive adequate health care in these areas. The most frequently detected conditions preceding cardiac arrest, such as cerebrovascular events chest pain and breathing difficulty, were the same as those found in other studies (8-10). These results support the theory that cardiopulmonary and cerebrovascular events are one of the leading causes of sudden death in elderly patients. The explanation for why 4/5 of our cases were witnessed by someone is that most of the OHCA cases occurred in the family environment. In related studies (8-13), the ratio of witnessed OHCA cases varies from 33%–65%. Those studies have reported that people tend to live alone as the socio-cultural and economical levels rise; one indication of this is the decreasing rate of witnessed cardiac arrest cases at homes. As for our region, older family members of people who have low and moderate incomes live with their children until their death. The finding that most of the witnesses were family members supports this idea. However, the high rates of witnessed cardiac arrests in our study did not result in emergency calls being made quickly. We think that the reason for the late activation time long duration was because witnesses could not comprehend the critical condition of the patient or thought that "they would take the patient to the hospital later." Considering this finding, the family members of patients with a high risk of sudden death might be educated on BLS to increase the awareness of the importance of early interventions in OHCA cases. This education would be valuable because most of the OHCA cases occur at home (8, 14).

Our study showed that 112 CCC personnel could not adequately direct the callers on the phone in the emergent interventions that they had to perform. Their guidance is important to increase the chance of survival of the patient; thus, the failure of this guidance needs to be addressed. In our study, half of the lay rescuers who performed chest compressions on the arrested case did not have any previous training, which may indicate that they were willing to undertake BLS; they should thus be formally trained for correct emergency intervention. Even though their intervention did not have a statistically significant effect on patient outcome, it does not mean that they could not cause harm to the patient.

The results of the studies conducted in Qatar (9), Finland (9), and the U.S. (11) indicate that the mean age of OHCA cases tends to increase going west from the Middle East (57–68 years). The mean age of cases in our study is higher than those found in countries located east of Turkey and lower than those located west of Turkey. Quick arrival at the scene is the most important controllable factor that has an influence on the discharge rates of OHCA. Petrie et al. (12) proposed that CPR and transport to an emergency service is unnecessary when the case is determined to have asystole and when the time required to arrive at the scene is longer than 8 min; they reported 100% mortality rates in these cases. Takei et al. (15) reported that activating EHP within ≤6 min significantly increased the survival rates in all OHCA cases. Moon (11) supported the idea that the prompt calling of emergency teams increases the chance of survival. In contrast, other studies have reported that arriving at the scene sooner does not statistically affect the survival rates (10, 16). Although our results also support this idea, EHP encountered a large number of cases with asystole due to both late calls from the witnesses and late arrival of the EHP team at the scene. We think that these delays play an important role in mortality.

According to studies in Europe and America, such as those conducted by Moon (11), Hiltunen et al. (8), Petrie et al. (12), Van der Hoeven et al. (13), and a meta-analysis by Sasson (14), the rate of BLS interventions performed by lay rescuers varies 35.15±16.9 (2–113) min from 14%–47%. Those studies state that the main reason for the increasing rates is the education of lay rescuers. The results of a study conducted in Sweden (17) prove this statement to be true. In that study, public education regarding BLS practices has been performed for 25 years; as a result, the intervention rates by lay rescuers have risen from 31% to 55%. Another study emphasized that this rate can drop to 6.2% if no education occurs (16). Although the intervention rates by lay rescuers in our study seem to be similar to reports in previous studies, this rate can fall below the reported rates (<%10) when we subtract the interventions performed by health workers who were at the scene at that time by chance. Very few lay rescuers had training for BLS, which indicated that public education is not adequate in our city. There were rescuers who had no training but intervened according to what they had seen in visual media; this finding suggests that media can be used to increase public awareness of OHCA. We think that the reason why the interventions performed by

lay rescuers did not have a statistically significant effect on survival is that those interventions were late and ineffective.

A GCS ≤7 at the initial evaluation of the scene was correlated with a higher mortality rate (p=0.003). In addition, airway control with ETI could be performed only in one-third of the patients with a GCS ≤7. This low rate of ETI intervention could be due to not wanting to lose time at the scene and due to pressures from the patient's relatives to transport the patient as soon as possible. Henlin et al. (18) emphasized that the time spent on performing ETI at the scene causes a delay in chest compressions and decreases the survival rate. In one study by McMullan et al. (19), which included 10,691 cases, although the rate of ETI application at the scene was 52%, the ratio of those who survived was 5.4%.

In our study, the rate of shockable rhythms detected by EHP at the scene was similar to other reports in the literature, but the asystole rate was higher. In various studies and meta-analyses (8, 9, 11, 12, 14), the rates of shockable (VF/PVT) and non-shockable (asystole and PEA) rhythms detected at the scene varied between 13%–38% and 25%–45%, respectively. In one meta-analysis that included seven studies conducted in Europe, North America, Asia, and Australia, the VF rates varied from 11%–40% (20). Although EHP had basic training, such as BLS and ACLS, and had been practicing their profession for an adequate amount of time to gain competency, they performed defibrillation mostly in asystole cases rather than in shockable rhythms. This finding can be explained by their inadequate training. Hiltunen et al. (8) reported that despite a long delay between the detection of a shockable rhythm and defibrillation (9.5–12 min), defibrillation significantly increased patient survival. Fredriksson et al. (21) determined survival rates of 61% and 21% in shockable and non-shockable OHCA cases, respectively.

In studies by Sasson et al. (14) and Hiltunen et al. (8), the rates of BLS practices used for patients were 66.7% and 64%, respectively. Our higher rate is due to the differences in the exclusion criteria applied. However, performing CPR in a greater number of patients did not result in a lower mortality rate. Late activation of the EMS, late arrival at the scene, and fewer interventions performed by lay rescuers could explain this result. In our study, the duration of CPR at the scene was much shorter than the reported durations in the literature (10). However, it did not decrease the need for CPR or shorten the duration of CPR for the same patient at the emergency service. This finding could support the idea that performing CPR at the scene may not be effective. In our study, the duration of CPR performed at the emergency service was longer than the other reported times (16). However, the survival rates were higher in the patients in whom the average CPR durations were shorter (p=0.006). From the reverse perspective, this result indicates that a longer duration of CPR does not increase the chance of resuscitation.

One of the most comprehensive studies related to discharge rates of OHCA cases is a meta-analysis by Sasson et al. (14) that included 143,000 cases. Following CPR, the survival rates (24%) and discharge rates (7.1%) found in that study were similar to our results. In another meta-analysis conducted in Europe (22), the discharge rate was determined to be 10.7%. Aside from these studies, there are also reports of lower (0.3%–1.4%) (23, 24) and higher (28%–33%) (8, 25) discharge rates. In the studies with a higher discharge rate, the most effective factors were determined to be prompt identification of the cardiac arrest case, early chest compression, and early arrival of EHP at the scene.

Study limitations

Inattentive filling of the case forms decreased the number of our study population. Due to the limited time period in our study (18 months), the 6-month and 1-year survival rates of OHCA cases could not be assessed. Because CPR was not performed by the same personnel at the scene and at the emergency service, a standard could not be achieved. Because we could not detect whether the reason for death was late CPR or an important primary cause with a high mortality risk, such as multiple traumas or serious intracranial hemorrhage in the mortal cases, the evaluation of the effectiveness of the CPR interventions was restricted. Different types of arrest patients were also an important limitation in the current study.

Conclusion

Although the number of witnessed cardiac arrests was high, emergency calls were mostly delayed. Also, those who called EMS were not adequately guided by 112 CCC for emergency intervention. The intervention rate by lay rescuers was far lower than the international rates. There is not adequate public awareness in our area for identifying cardiac arrest patients and for initiating early chest compressions. The survival rates in the area are generally below the internationally reported rates.

The in-service training of EHP should be reviewed and inspected. Training programs should be based on modern simulation practices and should include actual scenarios. The relatives of patients who have an especially high mortality risk should be educated on BLS. Public awareness about cardiac arrest cases should be increased via visual and social media tools, and interested parties should be trained.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Gaziantep University School of Medicine.

Informed Consent: It was not able to receive the informed consent because of their arrest.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare that they did not have conflict of interest in current study.

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Metal Workers with Corneal Injuries and Abuse of Topical Drugs

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Abstract

Aim: We evaluated metal workers injured with corneal foreign bodies (FB) in terms of health insurance, use of protective eyeglasses, and unprescribed drug use.

Materials and Methods: Seventy metal workers who were injured with corneal FB were enrolled in the study. We recorded the gender, age, duration of work, use of protective eyeglasses, and health insurance status data of metal workers. In cases of FB existence, the number of FBs and unprescribed drug use were investigated. We examined the presence of corneal scars that could lead to visual impairment.

Results: The mean duration of work was 11.8±10.8 years. Although 29 workers (41.5%) had corneal scars, only three workers (4.3%) had visual impairment due to scars. Also, 29 workers (41.5%) did not report the use of protective glasses; however, 22 (31.4%) workers reported their occasional use and 19 (27.1%) workers reported their routine use. Eighteen workers (25.7%) remarked on topical drug use from time to time. Ten of the 18 patients (55.6%) were using topical Tetrahydrozoline HCL, whereas five (27.8%) were using the topical anesthetic drug 0.5% Proparacaine HCl.

Conclusion: Occupational protective measures are important for metal workers who are at a high risk of eye injuries. Workers must be educated on the prevention and treatment of occupational ophtalmological hazards and be warned about the side effects of taking unprescribed drugs. *(Eurasian J Emerg Med 2016; 15: 15-9)*

Keywords: Abuse topical drug, corneal foreign body injuries, goggles, work-related eye injury

Introduction

Work-related eye injuries (WREI) lead to substantial loss of the workforce as well as increased care and treatment costs and a decreased quality of life (1). Social Security statistics indicate that the incidence of work-related injuries in Turkey is between 70,000 and 80,000 (2). More than 1.3 million work-related injuries that caused at least one day of loss of the workforce were reported in the United States, of which 36,680 of the work-related injuries were eye injuries (3). Eye injuries are generally common among work-related injuries (4). WREI are especially frequent among workers in the metal industry (3-6). Eye injuries have been reported to be more common during machining and plating (4, 5). WREI occur due to exposure to projections or sharp objects, hazardous light, and chemical liquids or gases (1).

Work-related eye injuries among metal workers range from corneal superficial epithelial defects to perforating injuries that can cause blindness (6, 7). The most common and most easily preventible eye injuries are superficial corneal foreign body injuries (CFBI) (5). A study reported the frequency of CFBI among metal workers in Turkey as being 37% (8). Secondary infection may also develop due to CFBI, ranging from keratitis to endopthalmitis (9). Vision loss may develop because of scar development at the visual axis (5). CFBI is an ophtalmological emergency, and the foreign body must be removed from the cornea with a 25-gauge needle in a non-traumatic fasion. Postoperative proliferative antibiotic treatment has also been administered (9).

In Turkey, workers who are exposed to work-related eye injuries may use unprescribed drugs. Serious side effects, especially due to the unprescribed use of drugs, which may result in keratoplasty, have been reported (10-13). It is known that the appropriate use of safety equipment, such as goggles, decreases the risk of eye injuries (1, 3, 9, 14). Workers may be exposed to lights and particles during welding and cutting; therefore, workers must protect their exposed body parts, including their eyes and hands (1). It has been reported that the cost of WREI in terms of lost productivity, covered health care, and compensations exceed 300 million dollars in the United States. It has been stressed that eye injuries can be prevented with protective measures and training (3).

In our study, our aim was to evaluate the health insurance status, use of protective eye wear, and unprescribed drug use among metal workers with superficial cornea injury due to foreign bodies.

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Materials and Methods

Seventy metal workers with a history of eye injury due to a foreign body in their eyes were prospectively evaluated at Fatih University, School of Medicine, ophtalmology outpatient clinic. Participants were informed about the study, and their consent was obtained before the study. This study complies with the tenets of the Declaration of Helsinki and was approved by the local ethics committee of Fatih University. Gender, age, duration of work, use of protective glasses, and the health insurance status of the study metal workers with CFBI were recorded.

The corneal injuries were superficial and none of the eyes required primer suturation surgery. The questionnaires were completed through in-person interviews and through comprehensive ocular examinations. Ophtalmological examination included best corrected visual acuity per Snellen chart, anterior segment, and fundus examinations. In the examination of the anterior segment, corneal scars due to a foreign body, and cataracts that might lead to visual impairment were examined with a slit-lamp biomicroscopy.

Table 1. Distribution of descriptive characteristics

Parameters	
Age (years) (mean±SD)	33.7±8.9
Gender (Male) n (%)	70 (100)
Health Insurance Status (yes)	68 (97.1)
Duration of work (years) (mean±SD)	11.8±10.8
Number of foreign bodies (mean±SD)	10.9±11.2
Corneal scar, n (%)	29 (41.5)
Vision loss, n (%)	3 (4.3)
Goggle use, n (%)	
Occasional	22 (31.4)
Routine	19 (27.1)
Drug use (Yes) n (%)	18 (25.7)
Proparacaine	5 (27.8)
Proparacaine-Diclofenac	1 (5.5)
Tetrahydrozoline	10 (55.6)
Diclofenakc sodium	2 (11.1)

SD: standard deviation; Min-Max: minimum-maximum

Statistical analysis

The Number Cruncher Statistical System (NCSS) 2007 and Power Analysis and Sample Size (PASS) 2008 Statistical Software (Utah, USA) were used for the statistical analysis. Along with the descriptive statistical methods (Mean, Standard Deviation, Median, Frequency, Rate, Minimum, Maximum), the suitability of the data regarding the normal distribution were determined by the Kolmogorov–Smirnov test together with the number of cases. The relevant variables with normal distribution for the two groups were compared with Student's t test, whereas analysis of variance (ANOVA) tests were used in the evaluation of the three groups, and the Bonferroni test was used for post-hoc analysis. When there were three or more groups to compare for variables which did not have a normal distribution, the Kruskal–Wallis test was used. The Mann–Whitney U test was used to determine the group causing differences. Significance was evaluated at the $p<0.05$ level.

Results

This study involved 70 male metal workers. The mean ages were 33.8±8.9 (range 16–53) years. The mean duration of work was 11.8±10.8 (range: 6 months to 40 years) years. The mean estimated number of CFBI was 10.9±11.2, with a range of 1–50 (Table 1).

In anterior segment examination, 29 workers (41.5%) were found to have corneal scars. Three workers with corneal scars had decreased visual acuity (4.3%). Twenty-nine workers (41.5%) did not report the use of protective eye wear during work, whereas 22 (31.4%) workers reported occasional use and 19 (27.1%) workers reported routine use (Table 1). The daytime working hours was the same for the workers occasionally or regularly using goggles. Work-related eye injuries occurring despite the workers using eye protection included photokeratitis, superficial foreign bodies in eyes, corneal abrasion, and blunt injury.

Table 2. Variables in terms of duration and age of the workers

Parameters		**n**	**Duration of work (years) Mean±SD (median)**	**p**	**Age (years) Mean±SD**	**p**
Corneal scar	No	41	11.8±11.0 (8.0)	0.848	33.1±9.0	0.435
	Yes	29	11.9±10.7 (10.0)		34.8±8.9	
Vision loss	No	67	11.6±10.4 (8.0)	-	33.3±8.6 (33.0)	-
	Yes	3	17.7±20.1 (12.0)		45.0±10.6 (49.0)	
Goggles use	No	29	7.1±8.8 (4.0)	0.001	29.3±8.5 (28.0)	0.001*
	Occasional	22	18.5±11.1 (20.0)		37.8±8.7 (37.5)	
	Routine	19	11.3±9.5 (10.0)		35.9±7.1 (37.0)	
Drug use	No	52	13.4±11.6 (10.0)	0.078	34.5±9.2 (35.0)	0.228
	Yes	18	7.2±5.9 (7.0)		31.6±8.1 (31.5)	
Health Insurance Status	No	2	7.5±6.4 (7.5)	-	26.0±9.9 (26.0)	-

*Post-hoc analysis revealed patients who do not use googles significanly differ from patients who use them occasionaly and routinely for the duration of their work and age.

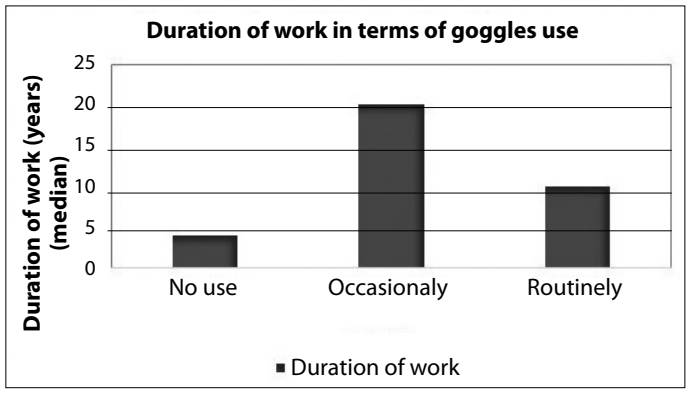

Figure 1. Duration of work in terms of goggles use

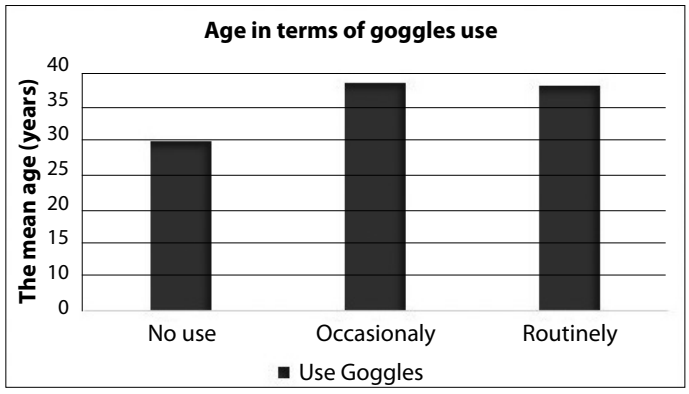

Figure 2. The mean age in terms of goggles use

The unprescribed use of drugs to decrease burning and foreign body sensations in the eyes was investigated. Topical drugs were used to reduce the complaints of injury. It was reported that the drugs were started the same day of the injury and used until the end of the complaints. Eighteen workers (25.7%) remarked on having topical drug use from time to time. Ten of the 18 patients (55.6%) were using topical *Tetrahydrozoline hydrochloride* (HCl), five (27.8%) were using the topical anesthetic drug 0.5% *Proparacaine HCl*, one was using (5.5%) topical *Proparacaine HCl* and *Diclofenac sodium*, and two workers (11.1%) were using *topical Diclofenac sodium* (Table 1). *Tetrahydrozoline HCL* and *Diclofenac sodium* can still be bought from pharmacys without a prescription, whereas *Proparacaine HCL* sales were banned by the Turkısh Goverment a few years ago.

There was no significance difference in the duration of work in terms of corneal scar presence (p=0.848) (Table 2). Because there were only three workers with visual problems due to corneal scars, no statistical comparisons were made.

There was a significant difference in the duration of work regarding the use of protective eyewear (median:4; 20; 10; years, respectively, p=0.001) (Table 2). Post-hoc analysis revealed the median years of working for patients who were not using protective eyewear was significantly different from the remaing two groups, whereas there were no difference between the two groups (Table 2) (Figure 1).

There were no significant difference in the duration of work in terms of drug use [drug users median: 7 years vs non-drug users: 10 years; (p=0.078)]. There was no age difference regarding the presence of corneal scars (p=0.435) Because there were only three workers with visual problems due to corneal scars, no statistical comparisons were made.

There was a significant difference of age regarding the lack of usage of goggles, or occasional or routinel usage [29.3±8.5 vs. 37.8±8.7 vs. 35.9±7.1, years, respectively, (p=0.001)]. Post-hoc analysis revealed that the ages of patients who did not use googles were significantly younger than for the other groups but there were no difference between the patients with occasional or routine google usage (Table 2) (Figure 2).

There were no significant difference of age in terms of drug use (p=0.228). Because there were only two workers without health insurance, no statistical analysis was conducted.

Discussion

In our study, we evaluated metal workers with eye injuries due to corneal foreign bodies in their eyes, in terms of eye health and occupational health and safety. We found that 68 (97.1%) of the metal workers had health insurance, whereas two workers were not insured. The duration of work ranged from 6 months to 40 years, and the mean duration of work was 11.8±10.8 years. All of the metal workers with CFBI were male in our study. The mean age of the workers was 33.8±8.9 years (range 16–53). Similarly, in the study of Ozkurt et al. (5), all the workers with foreign body eye injuries were males and their mean age was 32.5±1.0 (range 14–57) years. WREI have been reported to be more common among young male workers (8, 15).

According to Turkish Social Security Instutition statistical data, there are 18,350,000 active employees with insurance, which is almost 25% of the total population. The percentage of the workforce not registered in the social security instutition corresponds to 36.2% of the total population; 83% of these unregistered workers are employed in agriculture, and the remaining 27% are employed in non-agricultural industries (16). Statistical data indicates that there were 74.871 occupational injuries, of which 1.596 (2.1%) were eye injuries. Work-related injuries are more common among males between 30 and 34 years of age and among workers with a duration of work more than 3 months and less than 1 year (16). A study reported that 15% of work-related injuries consisted of eye injuries in Australia (17).

It has been reported that, in Turkey, WREI are more common among workers in metal work and machinery industries (2). The most common cause of eye injuries are due to corneal foreign bodies (5, 6, 18). Corneal metallic foreign body injury, which is preventible, makes up a substantial part of ophtalmological emergencies (8, 9). It has been known that work-related eye injuries can be significantly reduced and prevented with the use of protective eye wear (4, 19, 20). Besides, being experienced, having occupational safety training before work, and the routine maintainance and care of machineries and tools are reported to decrease eye injuries (1).

In our study, we also evaluated the usage of protective eye wear. Twenty-nine (41.4%) workers were not using glasses during work. Of the 41 workers using goggles, 22 (31.4%) reported occasional and 19 (27.1%) workers reported routine use during work. We found that the mean duration (years) of work was significantly lower in workers who did not use glasses than in workers using goggles. Contrary to our expectations, the duration of work was significantly higher in workers with occasional goggle use than in workers routinely using goggles (18.5±11.1; 11.3±9.5 years, respectively). Ozkurt et al. (5) reported that although 64% of metal workers had been using protective eye wear, among these, patients 57% were not using goggle during

eye injury, and 43% of the injuries occured even though the workers were using protective eye wear (5).

In the present study, the mean number of estimated CFBI in workers was 10.9±11.2 (range: 1–50). Corneal scars due to corneal foreign bodies were found in 29 (41.4%) workers. Three workers with corneal scars had decreased visual acuity because of the scars (4.3%). Ramakrishnan et al. (9) reported that the rate of corneal scar development because of foreign bodies were 88%. In a study from Turkey, Ozkurt et al. (5) reported a 58% rate of corneal scar development. In our study, fewer corneal scar injuries were seen among our study participants. This result may be related to the early arrival of these workes to our ophthalmology clinic.

Some of the metal workers may use unprescribed ophtalmological drugs to reduce redness and pain due to foreign body exposure. Topical anesthetic 0.05% Proparacaine HCl and topical Diclofenac sodium have been used to relieve pain. Tetrahydrozoline HCL 0.05% decreases redness via ophtalmic vasoconstriction (21). Topical Diclofenac drop has anti-inflammatory and corneal hypoaesthetic effects (22). The long-term use of topical Diclofenac following ocular surgery has been reported to cause corneal melting (23). On the other hand, the long-term use of topical 0.05% Proparacaine HCl drop may lead to several eye problems, including superficial punctate keratopathy, persistent epithelial defects, stromal infiltrates, and secondary infectious keratitis (10-13). Keratoplasty may be necessary in cases with corneal abscess due to the abuse of eye drops (13).

When unprescribed ophtalmological drugs, i.e., without physician recommendation, to decrease burning and foreign body sensations in the eyes during metal cutting and foreign body exposure were investigated, it was found that 18 workers (25.7%) had unprescribed drug use. Ten of the 18 patients (55.6%) were using topical Tetrahydrozoline HCl, five (27.8%) were using the topical anesthetic drug 0.5% *Proparacaine HCl*, one was using (5.5%) topical *Proparacaine HCl* and *Diclofenac sodium*, and two workers were on (11.1%) *topical Diclofenac sodium*. No complication due to drug use was detected. The age and duration of work were not significantly associated with drug usage. Workers who were using unprescribed drugs were informed about their effects, side effects, and possible complications. Due to the high reported complications and side effects of *Proparacaine HCl* (10-13), it has been forbidden to be sold without prescription in Turkey.

In order to prevent work-related injuries, training must be provided to workers to improve work skills and knowledge of occupational hazards and the prevention of accidents before beginning active work (1).

The most simple and effective protection for eye injuries is the use of goggles. Unprescribed drug usage without proper medical indication, which may lead to serious side effects, must be avoided. Workers must be informed on the side effects of these drugs, especially during long-term and improper use. It must be kept in mind that health and safety education is important to prevent eye injuries.

Study limitations

There were several limitations in our study. First, the sample size was small in our study; second, the kinds of eye injury were not separated; and third, the study did not assess the working conditions. In addition, the information about injuries was learned from in-person interviews. Workers may not always show an objective attitude to protecting the workplace in terms of the use of glasses and drugs.

Conclusion

Our study concludes that eye injuries may be reduced by better education of the workers about risky behaviors and by persuading them to comply with safety measures. These goggles should be well-fitted, durable, protective eyewear with good visibility, together with strict compliance on their use. Ophthalmologists should inform patients, primary and emergency doctors, and pharmacists about potential permanent visual loss associated with topical anesthetic abuse and other unprescribed drug usage, such as *Tetrahydrozoline HCl* and *Diclofenac sodium*.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Fatih University Clinical Research Ethics Commission.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

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The Utility of a Standardized Evaluation Form for Complaints in Patients with Acute Abdominal and Flank Pain

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Abstract

Aim: In this study, we aimed to assess the diagnostic accuracy and cost effectiveness of a first-step evaluation form, which we improved for patients administrated to the emergency department (ED) with non-traumatic acute abdominal and flank pain.

Materials and Methods: Patients presenting with non-traumatic acute abdominal and flank pain complaints to the ED were included in this prospective cross-sectional cohort study in two consecutive months. Control group patients were evaluated with forms currently in use in our ED in the first month, whereas the evaluation of the test group was perfromed with the standardized evaluation form specifically designed for acute abdominal and flank pain in the second month.

Results: Throughout both sessions, 1224 patients in total presented with non-traumatic abdominal and flank pain. Out of these, 285 of those enrolled in the first session, and 335 enrolled in the second session. Both control and test groups, which were similar demographically and with respect to vital symptoms/findings, did not show any significant difference with respect to the examination/test and treatment. However, we observed a significant decrease in ED patient care expenses in the group evaluated with the new standardized form. Among them, those who were evaluated with the standardized form had relatively fewer complaints than those evaluated with the currently available evaluation form.

Conclusion: Our results showed that utilization of a new standardized form for patients presenting with non-traumatic acute abdominal and flank pain significantly decreased patient care expenses for ED care; furthermore, they experienced relatively fewer complaints after discharge from the ED. *(Eurasian J Emerg Med 2016; 15: 20-3)*

Keywords: Abdominal pain, flank, cost, standardized form, emergency department

Introduction

Acute abdominal pain is defined as an abdominal pain persistent for less than a week. Non-traumatic acute abdominal or flank pain is one of the major reasons for emergency department (ED) visits and accounts for approximately 5%–10% of all ED visits (1-3). However, the rate of undefined abdominal pain is reported to be 41% (4). The elderly account for 20% of ED visits, of which 3%–4% are for acute abdominal pain. Therefore, the approach to acute abdominal pain requires a fast and precise diagnosis in addition to appropriate triage and care.

Taking into account that noting down the history and performing physical examination takes 90%–95% of the patient evaluation time, a standardized method to perform this evaluation may increase the speed of care (5).

The purpose of this study was to evaluate the effectiveness of the use of a standardized complaint evaluation form developed for patients admitted to the ED of a university hospital for non-traumatic abdominal pain and flank pain on diagnostic accuracy and speed as well as on patient care costs.

Materials and Methods

This prospective cross-sectional cohort study was conducted at the ED of a University Hospital. Informed consent was obtained from all participants, and the study was monitored by the local ethical committee of Akdeniz University. Inclusion criteria included patients aged 18 years and above and admitted to the ED of University Hospital for non-traumatic acute abdominal pain. Persons with traumatic abdominal and flank pains, persons aged under 18, persons with

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chronic abdominal and flank pain (abdominal and flank pain complaint persistent for more than 1 week), patients whose history could not be taken due to change of consciousness, and women with third trimester pregnancy were excluded.

The study data were collected within two periods separately. Each period consisted of one month. In the first period of the study (Group 1), patients admitted for abdominal/flank pain were given the ED Patient Evaluation Form, which was already routinely used by triage staff, and also the form entitled "Study on Patients admitted to the ED for Non-traumatic Acute Abdominal and Flank Pain." The assistant doctor who evaluated the patient was asked to fill in the form. In the second period of the study (Group 2), patients admitted for non-traumatic abdominal and flank pain were given the "standardized complaint evaluation form" by the triage staff, and the doctors were informed that they should only use this form for these patients. All doctors in charge of the ED were given a 30-min briefing on how to fill in the form and about the contents of the form.

All patients included in the study in both of these periods were called by telephone approximately 15 days after admission. The patients were asked whether their complaint persisted, and if the complaint disappeared, when it disappeared; whether they had visited another medical institution in 10 days (ED or out-patient clinic), and if they did, whether any additional test or treatment was performed; or whether any surgical intervention or fatality occurred. The patients were called by the evaluating doctors who were not aware of the diagnosis and outcome of the patients between the 15th and 25th days after the discharge.

The hospital cost data for all the patients included in the study that occurred during the ED visits were obtained retrospectively from the MediHasta® software used at our hospital.

Statistical analysis

The data obtained were recorded in the Statistical Package for the Social Sciences 15.0 for Windows (SPSS Inc; Chicago, IL, USA) software and statistical analyses were performed. While continuous variables were expressed as the mean±SD and median (min.-max.), frequency data were expressed as percentages. In comparison of the two cohorts, the Mann–Whitney U test was used for data that was continuous, but did not match normal distribution, and for ordinal data, whereas the chi-square test was used for frequency data. The normal distribution was examined with the Kolmogorow–Smirnov test. All the hypotheses were formed bi-directionally, and the alpha significance value was taken as 0.05.

Results

In the first and second periods of the study, 378 and 474 patients were included, respectively. Overall, 232 of the total 852 patients were excluded from the study due to the exclusion criteria. Data were evaluated over 285 patients for the first period and over 335 patients for the second period.

The mean age of patients evaluated was 39.9±15.4 years, and 242 of them (39%) were male. Overall, 438 (70.6%) patients had abdominal pain, whereas 182 patients (29%) had flank pain. Table 1 shows the patients' demographics and pain type and severity.

The tests required by the doctors were compared between the period in which the form was not used and the period in which the form was used. It was determined that the decision of the doctors to require tests did not change with the use of the standardized complaint form (Table 2).

The diagnoses of the patients at discharge from the ED were classified. Although the abdominal pain rate was 28.1% in the group in which the form was not used, the rate was 27.8% in the group in which the form was used. It was determined that the rate of diagnosing an undefined abdominal pain did not statistically change with the use of the standardized evaluation form (p=1.000).

In this study, 84.9% and 87.8% of the patients in Groups 1 and 2 were discharged, respectively. There was no significant difference between the groups in terms of discharge and hospitalization (p values of 0.706 and 0.820, respectively) (Table 3).

The mean length of stay at the ED for all the patients included in the study was 156±116 min (minimum: 15 min, maximum: 799 min). Although the average length of stay was 162 min in the group in which the form was not used, the average length of stay was 152 min in the group in which the form was used. There was no statistically significant difference between the groups in terms of the length of stay at the ED (p=0.559).

The costs that arose during the ED evaluations of the patients were compared between the patients in Groups 1 and 2. After the discharge, surgical treatment was needed more commonly in Group 1 (Table 4).

Table 1. Demographics characteristics and pain type and severity of patients with abdominal and flank pain

Demographics		Group 1	Group 2	p
Age	Mean±SD	41.1±15.7	38.9±15.1	0.087
	Median	38	37	
	Min-Max	18-84	18-86	
Gender (M/F) no		104/181	138/197	0.248
Abd/flank pain no		206/79	232/100	0.427
Pain severity		6.57	6.69	0.554
M: male; F: female				

Table 2. Required tests for the evaluation of patients admitted to the ED for a complaint of abdominal or flank pain

Tests	Group 1	Group 2	p
Complete blood count	128	135	0.255
Biochemical tests	110	121	0.560
Urinalyses	161	176	0.333
Stool examination	16	14	0.455
Electrocardiography	48	68	0.302
Arterial blood gas	7	4	0.361
Chest X-ray	38	34	0.258
Plain Abd. X-ray	38	40	0.628
Ultrasonography	67	58	0.057
Doppler USG	3	5	0.732
Abdominal CT	4	5	1.000
Other	19	31	0.300
Abd: abdomen; USG: ultrasonography; CT: computer tomography			

Table 3. Results of the evaluation of patients admitted to the ED for an abdominal or flank pain complaint

Conclusion	Group 1 n (%)	Group 2 n (%)
Discharge	242 (84.9)	294 (87.8)
Hospitalization	35 (12.3)	33 (9.8)
Transfers	1 (0.4)	1 (0.3)
Refusal to treatment	7 (2.5)	6 (1.8)
To leave the hospital without permission	0	1 (0.3)
Totality	285	335

Table 4. Telephone follow-up of patients on days 15–25 after discharge from the ED

Conclusion	Group 1 n (%)	Group 2 n (%)	p
Continue of complaint	68 (39.1)	40 (18.1)	<0.001
Extra application	67 (38.5)	53 (24.0)	0.002
Recurrent application	44 (65.8)	45 (84.9)	0.021
Supplement test	55 (82.1)	41 (77.4)	0.647
Operation	9 (5.2)	3 (1.4)	0.038

The average bill amounts for the patients in Group 2 and Group 1 were $54.45 and $65.41, respectively. This difference was shown to be statistically significantly (p=0.002).

When the patient complaints were divided into abdominal pain and flank pain, the average cost for patients with abdominal pain was $68.8 in the group in which the form was not used and $58.5 in the group in which the form was used (p=0.035). For the flank pain complaint, these values were $56.5 and $42.5, respectively (p=0.030).

There was again a significant difference between the groups in terms of cost when the patients were classified as patients diagnosed with undefined abdominal pain complaint and patients with any diagnosis.The average cost of patients diagnosed with undefined abdominal pain complaint was $70.7 in Group 1 and $58.1 in Group 2 (p=0.046). The costs for the group with any diagnosis were found to be $63.4 (Group 1) and $53.0 (Group 2) (p=0.024).

In this study, 395 of the 536 patients discharged from the ED were reached by telephone (73.7%); 174 of the 242 patients (71.9%) in the group in which the form was not used and 221 of the 294 (75.2%) of the patients in the group in which the form was used were reached by telephone. These telephone calls were made between the 15th and 25th days after discharge.

Discussion

Acute undefined abdominal pain is an abdominal pain complaint persistent for less than 7 days and which cannot be defined by physical examination and basic researches. Undefined abdominal pain is a common cause of hospitalization (6). More than 40% of patients with abdominal pain complaint are discharged from the ED without a diagnosis, whereas more than 35% are hospitalized, and approximately 56% are misdiagnosed (7, 8).

Lukens et al. (9) reported that 57% of the patients discharged with undefined abdominal pain diagnosis recovered in 2–3 days after their first visit to the ED. Shesser et al. (10) reported that 82% of the patients discharged from the ED recovered in 2-3 days. Similar results were obtained in our study. These three studies indicate that the first 2–3 days are considerably valuable for following up patients discharged from the ED with undefined abdominal pain complaint and that complaints that persist after the 3rd day justify further evaluation.

There is not yet a sufficient guide in the literature for evidence-based diagnostic imaging options for patients admitted to the ED for abdominal pain.The present diagnostic studies show that the approaches to abdominal pain diagnosis vary considerably between hospitals. Indications for the use of abdominal X-ray, USG, and CT are variable. Compared to the last century, there is a significant increase in the use of CT for patients with abdominal pain complaint. However, new questions have been raised, such as the increase in costs, unnecessary test requests, or failure to request tests despite the existence of an indication (11). In a study where the contribution of helical CT to acute abdominal pain diagnosis was evaluated, it was shown that mortality decreased and the length of stay at the hospital shortened with the use of helical CT. It was also reported that helical CT was beneficial in diagnosing unforeseeable conditions and potentially serious complications (12). In light of these contributions, the frequency of use of CT for patients with undefined abdominal pain complaint should be increased.

Although the requests for tests did not differ between groups in our study, the most required tests included whole blood count, biochemical tests, urinalyses, and USG, respectively. It is remarkable that abdominal X-rays are less preferred by doctors due to poor diagnostic sensitivity and specificity. However, in our study, we noted that CT requests were quite low in the ED. With CT to be required for selected patient groups, re-visits and treatments could be prevented. It should be ascertained for which patients among those who visit the ED for acute abdominal pain that CT is necessary. However, current test options should be selected according to evidence-based pre-determined diagnosis strategies and the patient profile. Despite the performance of numerous and various tests, one quarter of patients are discharged with undefined abdominal pain diagnosis. At this stage, what are the safe discharge criteria should be the question that must be raised. Doctors are inclined to ambulatory follow-up patients due to limited bed capacity at the hospital. In case the complaint persists, the patient may require a re-visit. Is discharge a safe option in undefined acute abdominal pain? Weiner et al. (13) measured the post-discharge follow-up frequency and duration of complaint for patients visiting the ED for abdominal and flank pain complaints. They called all patients in 2-3 weeks after discharge, but could reach only 70% of the patients. They found the median pain duration was 3 days as from the ED visit. In conclusion, they reported that patients with non-traumatic abdominal and flank pain could recover in a few days. In a prospective randomized clinic study, Onur et al. (14) researched whether there was any difference in terms of cost and patient safety between observation at the ED and post-discharge follow-up of patients diagnosed with undefined abdominal pain. In conclusion, they proposed that patients with abdominal pain not considered to be life-threatening could be safely discharged home.

The fact that patients desire to use EDs more intensively to receive medical care leads to crowding and delayed care at EDs (15). Several studies have been designed recently in order to reduce crowding in EDs and to raise the speed of care without compromising quality (16, 17). These studies aim to find out how delays can be prevented. In our study, we determined that the evaluation form developed for abdominal pain complaint did not reduce the length of

stay at the ED compared to the classical manually-completed patient evaluation form. The cause of why this duration did not change may be that they do not only measure the patient evaluation duration.

Guerlain et al. (4) researched the effect of a standardized form on the physical examination and diagnosis of patients admitted to the ED for abdominal pain complaint. They stated that patients with acute abdominal pain were evaluated in an irregular and non-standard manner even within the same institution, and inquired whether a standardized form for abdominal pain would increase the quality and quantity of data collected or not. They showed that the abdominal pain form resulted in a significant increase in the recording of information related to complaint history, background and social history, system review, and physical examination. The form was also beneficial in the long-run for retrospective data analysis.

In the literature, there is no sufficient data about the usefulness of standardized forms in terms of accuracy and the early diagnosis of abdominal pain. It was reported that noting down the history and performing physical examination with a standard data collection method increased the diagnostic accuracy of appendicitis in the ED (18). Korner et al. (19) reported that diagnostic accuracy increased by 5% with structured data records and that the rate of increase in women aged 13–40 years was 13%. In that society-based study, they reported that diagnostic accuracy improved in patients operated on for the suspicion of appendicitis. In our study, it was researched whether a standardized complaint evaluation form would increase the diagnostic accuracy of abdominal pain and the quality of care or not, but no differences could be found in terms of these criteria.

In a study using T-system® in primary care, Mulvehill et al. (20) researched whether the cost would change and reported that the use of a structured form resulted in a significant increase in cost. In our study, however, we determined that the use of a standardized form reduced ED costs. Although there is no difference between the two groups in terms of test and consultation requirement and the result of the care, the difference in cost may be attributed to the existence of several causes in the etiology of abdominal pain, important differences between diagnostic practices of doctors as a whole, and/or the wide distribution of costs. A cost analysis with much more specific diagnoses and between groups with more patients would be appropriate.

Conclusion

The use of a standardized evaluation form for abdominal and flank pain does not change the occurrence of complications, such as urgent surgery or the death of discharged patients due to omitted diagnosis, or the length of stay of the patients at the ED; however, the use of standardized forms may reduce the costs for dealing with patients with abdominal pain.

Ethics Committee Approval: The consent of the General Ethical Board of the Akdeniz University School of Medicine was obtained prior to the study.

Informed Consent: Informed consent was obtained from patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declared no conflict of interest.

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Abusive Head Trauma in Turkey and Impact of Multidisciplinary Team Establishment Efforts on Case Finding and Management: Preliminary Findings

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Abstract

Aim: Abusive head trauma (AHT) is the most common cause of death as the result of child abuse. A task force is planned to provide training on AHT to professionals in different disciplines on clinical presentation, diagnostic workup, and organization of multidisciplinary evaluation at the hospital and community levels. This study reports on the preliminary findings of the pre-intervention phase of a larger study.

Materials and Methods: This is a descriptive, retrospective study exploring the rates of documentation of relevant data in charts, including risk factors for abuse, family demographics, completeness of diagnostic workup, and case finding.

Results: Overall, 345 cases were found in hospital databases that were eligible for the retrospective study from 10 participating hospitals. In total, 305 cases (88.4%) were younger than 2 years of age. The most common documented risk factors were low parental education level in 82 families (23.8%), more than three children under 7 years of age in 76 families (22.0%), and bad child temper in 16 families (4.6%), among others. The rate of complete diagnostic workup in hospitals with a multidisciplinary team (MDT) (25.7%) was statistically significantly higher than in hospitals without an MDT (2.9%) (p=0.001). Etiology was identified as inflicted in 78 cases (22.6%), possibly inflicted in 24 (7.0%), undetermined in 79 (22.9%), and accidental in 164 (47.5%) by the researchers, compared to only three cases (0.8%) diagnosed as inflicted by the treating physicians (p<0.0001). In two of the three cases, the perpetrator was convicted; in one, the prosecutor closed the case without a trial on the basis of "no confession" despite the death of the child and medical evidence.

Conclusion: Clinicians' knowledge of the diagnosis of AHT should be increased to improve case finding, which will allow determination of more accurate incidence/prevalence. This can be accomplished via the establishment of an MDT in teaching hospitals as well as staff training on how to recognize suspicious cases, how to utilize MDT services, and how to report and manage cases on a community level multidisciplinary basis. *(Eurasian J Emerg Med 2016; 15: 24-9)*

Keywords: Abusive head trauma, multidisciplinary team, diagnostic workup

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Introduction

Child abuse and neglect is recognized globally as an important problem from public health, child protection, and child rights perspectives. Physical abuse is a form of child abuse that is highly prevalent worldwide. Violence against children is present in almost all aspects of a child's life: in their home, in school, on the street, at work, in institutions, and in detention centers (1). Children are beaten, tortured, sexually assaulted, or even murdered by the very individuals responsible for their care, and many forms of violence are often viewed as socially acceptable in many societies. The World Report on Violence Against Children provides a global picture of violence against children and proposes recommendations to prevent and respond to this issue. This study reported an estimated homicide rate of 2.04 per 100,000 population in 0–4-year-old males and females in all regions of the United Nations and at all income levels (2).

Abusive head trauma (AHT) is a subcategory of physical abuse. Incidence of AHT is based on limited studies and hospital records; thus, it makes up a small portion of all abuse cases. Keenan *et al.* studied population-based incidence of AHT in the USA and reported that the incidence of inflicted traumatic brain injury in the first 2 years of life was 17.0 per 100,000 person-years. Infants in the first year of life had a higher incidence than children in the second year of life (29.7 vs. 3.8 per 100,000 person-years) (3). However, this incidence is believed to be much higher than reported because milder forms of AHT may resolve without a hospital visit (4).

Population studies that have studied the use of shaking as a child discipline method propose that actual incidence of AHT in societies where shaking is part of child discipline may range anywhere from 0% to as high as 63.0%. It is concerning that in this study, ≥20% of mothers in 9 communities from 19 communities in Brazil, Chile, Egypt, India, the Philippines, and the United States admitted to shaking children younger than 2 years (5).

Child abuse and neglect is a fairly new clinical field in the Turkish medical community. Many university hospitals have established multidisciplinary teams (MDT) to implement the clinical practice of child protection in Turkey from 1996 on (6, 7). Most of these teams have been collaborating with the University of Iowa Child Protection Program to improve their practice. This collaboration and the implementation of multiple teams across the country improved the response to sexual abuse significantly over the first decade. However, AHT has remained only occasionally recognized, with a handful of cases reported in the literature in Turkey (8-12).

Recognizing this low level of professional awareness, an AHT Task Force was established in Turkey in 2008. The task force planned to provide training on AHT to professionals in pediatrics, forensic medicine, neurosurgery, ophthalmology, radiology, emergency medicine, social work, law enforcement, and prosecution on biomechanics, clinical presentation, diagnostic workup, and organization of multidisciplinary evaluation at the hospital and community levels. This study reports on the preliminary findings of the retrospective pre-intervention phase of the larger study.

Materials and Methods

This is a descriptive, retrospective study exploring the rates of documentation of relevant data in charts, including risk factors for abuse and neglect and family demographics, as these parameters may help physicians with diagnostic workup for AHT and with case-finding. An invitation was extended to 20 teaching hospitals to participate in this study, 10 of which agreed.

Pre-training data from 10 hospitals are included in this report, namely from Gaziantep Children's Hospital, Ankara University, Vakıf Gureba University, Cumhuriyet University, Düzce University, Gazi University, Gaziantep University, Erciyes University, Osmangazi University, and the Ministry of Health Ankara Hospital. Seven of these hospitals are university hospitals, and the rest are teaching hospitals within the network of the Turkish Ministry of Health. Three of the ten hospitals had a hospital-based MDT. No hospital MDT had a neurosurgeon as a team member. The number of head trauma cases enrolled in this study from each hospital and their pediatric emergency department load per year are shown in Table 1. After obtaining permission from the hospital administrations, all pediatric patients admitted for head trauma to the emergency departments during 2008 that met the inclusion criteria as listed below were included in the study.

Inclusion criteria: a) Age: less than 36 months; b) Head CT and/or MRI shows acute SDH (with or without chronic SDH), subarachnoid hemorrhage (SAH), epidural hematoma (EDH), skull fracture, or subgaleal hematoma (SGH) with or without; and c) neurologic compromise (concussion, brain edema, brain infarction, brain contusion, brain laceration, coma, seizures, etc.).

Exclusion criteria: a) Children with coagulopathy due to a known medical condition such as hemophilia, Von Willebrand disease, immune thrombocytopenic purpura, and disseminated intravascular coagulopathy; b) children older than 3 years of age; c) newborns who developed an intracranial hemorrhage while in the newborn unit; and d) secondary intracranial hemorrhage that developed in the hospital during treatment for meningitis/encephalitis/tumor, neurosurgical intervention for non-trauma related causes, etc.

Study data were obtained from the hospital files and judicial records by researchers. The etiology of head trauma in children under three years of age was explored using a scale categorized as accidental, undetermined, possibly inflicted, or inflicted. The algorithm used

Table 1. The number of head trauma cases enrolled from each participating hospital and their pediatric emergency department load per year

Hospital (n)*	GCH (98)	AU (31)	VGU (79)	CU (39)	DU (3)	GU (17)	GAU (20)	EU (20)	OGU (5)	MAH (33)
Pediatric emergency department patient load per year	183,000	43,000	146,000	10,000	18,000	39,500	28,000	57,500	29,000	38,500

*Number of head trauma cases referred to hospitals that were enrolled in this study. GCH: Gaziantep Children's Hospital; AU: Ankara University; VGU: Vakıf Gureba University; CU: Cumhuriyet University; DU: Düzce University; GU: Gazi University; GAU: Gaziantep University; EU: Erciyes University; OGU: Osmangazi University; MAH: Ministry of Health Ankara Hospital

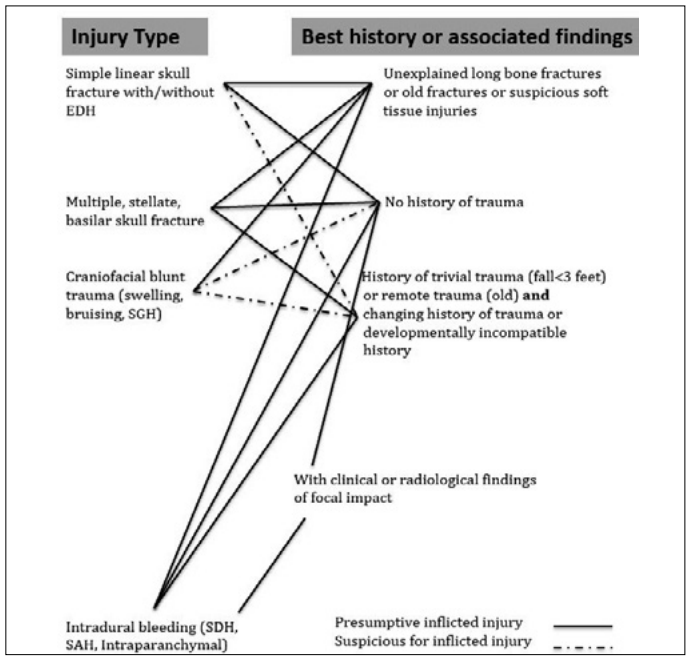

Figure 1. Algorithm to determine the etiology of head trauma in young children (13)

for this purpose is depicted in Figure 1 (13). Cases that were designated to the "undetermined" category had one or more of the below characteristics:

1) Inadequate information that prohibited the utilization of the algorithm

2) Adequate information for the use of the algorithm, but the child is an infant (<12 months of age)

3) Imaging findings are inconsistent with presenting symptoms and length of stay (comatose child or child whose hospital stay is longer than 3 days without fatality, with benign imaging findings reported).

This is a descriptive study exploring the documentation of relevant data in the charts, risk factors for abuse and neglect documented in the charts, demographic characteristics of families in which AHT occurs, rate of case findings, completeness of diagnostic workup, and post-hospital case management.

Nine risk factors were low parental education level, more than three children under 7 years of age in the family, bad child temper, child physical illness, child developmental delay, parental physical illness and admission to the hospital with a similar condition for each, domestic violence, previous abuse history, and sibling abuse history. When there was at least one risk factor, we defined that risk factor (+); if there was more than one risk factor, we measured mean±SD (range) by hospital.

Table 2. The demographic data and distribution of risk factors by hospitals

Hospital (n)	Age (month) Mean±SD	Gender Male (%)*	Risk factor (+) n (%)*	of risk factors Mean±SD (range)
GCH (98)	19.2±10.1	56 (57.1)	91 (92.8)	2.7±1.3 (1–5)
AU (31)	14.5±8.4	18 (58.1)	7 (22.5)	1.3±0.5 (1–2)
VGU (79)	13.9±7.3	45 (56.9)	75 (94.9)	1.8±1.1 (1–6)
CU (39)	20.5±10.5	18 (47.4)	22 (57.9)	1.6±1.3 (1–7)
DU (3)	26.6±7.2	2 (66.6)	1 (33.3)	1.0 (1–1)
GU (17)	17.4±8.6	7 (43.7)	14 (87.5)	2.6±1.3 (1–4)
GAU (20)	9.1±6.9	14 (70)	7 (35)	1.1±0.4 (1–2)
EU (20)	14.0±8.3	11 (57.9)	16 (84.2)	2.1±1.2 (1–5)
OGU (5)	14.4±5.0	1 (20)	2 (40)	1.5±0.7 (1–2)
MAH (33)	13.4±7.9	22 (66.6)	5 (15.1)	2.6±1.1 (1–4)
Total (345)	16.1±9.3	194 (56.3)	240 (69.6)	2.2±1.3 (1–7)

*Percentages were calculated horizontally. GCH: Gaziantep Children's Hospital; AU: Ankara University; VGU: Vakıf Gureba University; CU: Cumhuriyet University; DU: Düzce University; GU: Gazi University; GAU: Gaziantep University; EU: Erciyes University; OGU: Osmangazi University; MAH: Ministry of Health Ankara Hospital

Table 3. Reported abusive head trauma cases

Case	Hospital	Sex	Age (month)	Offender	Comments
1	CU	Female	6	Father	Offender convicted, GCS=3, witnessed by mother, child recovered with handicaps
2	EU	Female	24	Stepmother	Offender convicted, sentenced to life imprisonment, GCS=3, no confession, no witness, child died
3	GU	Female	9	?	Not tried, prosecutor closed case, GCS=3, no confession, child died

GCS: Glasgow Coma Scale; CU: Cumhuriyet University; EU: Erciyes University; GU: Gazi University

Table 4. Post-medical management

Hospital	MDT	Filed to police n (%)	Filed to CPS n (%)	Removed from home n (%)
GCH (98)	-	98 (100)	98 (100)	-
AU (31)	+	31 (100)	-	-
VGU (79)	-	22 (27.8)	-	-
CU (39)	-	37 (97.3)	1 (2.6)	1 (2.6)
DU (3)	-	3 (100)	-	1 (33.3)
GU (17)	+	16 (100)	16 (100)	-
GAU (20)	-	1 (5.0)	-	-
EU (20)	+	7 (36.8)	6 (31.5)	-
OGU (5)	-	-	-	-
MAH (33)	-	29 (87.8)	-	-
Total (345)		244 (70.7)	121 (35.2)	2 (0.6)

GCH: Gaziantep Children's Hospital; AU: Ankara University; VGU: Vakıf Gureba University; CU: Cumhuriyet University; DU: Düzce University; GU: Gazi University; GAU: Gaziantep University; EU: Erciyes University; OGU: Osmangazi University; MAH: Ministry of Health Ankara Hospital; MDT: Multidisciplinary teams; CPS: Child Protective Services

Statistical analysis

All data obtained in the study were recorded in a database and analyzed using the Statistical Package for the Social Sciences (SPSS Inc; Chicago, IL, USA) for Windows, Version 17. Numerical variables were identified as mean and standard deviation (SD), whereas categorical variables were given as frequency (n) and percentage. The chi-square test was used for categorical comparisons. The association between the rate of both skeletal survey and retinal exam practice and the presence of an MDT at a hospital was analyzed via the chi-square test.

Results

Overall, 345 cases that were eligible for this study were found in hospital databases (Table 1). In total, 305 cases (88.4%) were younger than 2 years of age. In addition, 56% of the children were male, and the mean age was 16.1±9.3 months (range: 1–36 months) (Table 2).

The most common documented risk factors were low parental education level in 82 cases (23.8%), more than three children under 7 years of age in the family in 76 (22.0%), bad child temper in 16 (4.6%), child physical illness in 10 (2.9%), child developmental delay in 8 (2.3%), parental physical illness and admission to the hospital with a similar condition for each in 7 (2.0 %), domestic violence in 4 (1.2%), previous child abuse history in 2 (0.6%), and sibling abuse history in 1 (0.3%). The rates of risk factors by hospital are given in (Table 2).

In total, 299 (86.7%) cases presented with a history of trauma on admission; the rest presented with no history of trauma. The Glasgow coma scale (GCS) was not documented in 67 (19.4%) cases, was less than 6 in 33 (9.6%), was between 7 and 12 in 138 (40.0%), and was between 13 and 15 in 107 (31.0%). Etiology was identified as inflicted in 78 cases (22.6%), possibly inflicted in 24 (7.0%), undetermined in 79 (22.9%), and accidental in 164 (47.5%) by the researchers. The difference between the GCS scores among the four etiology groups, when available, was statistically significant ($p<0.001$): When GCS was 6 and less, 30.3% of cases were assigned an etiology code of inflicted compared to 13.8% for GCS 7–12 and 31.8% for GCS 13–15. The length of stay was 5.7+10.4 days in the overall group (range 0–123 days).

In inflicted cases, there was no reported history of trauma in 4 (5.1%), reported history of trauma in 21 (26.9%), and unknown history of trauma in 53 (67.9%) of the cases. In accidental cases, there was no reported history of trauma in 3 (1.8%), reported history of trauma in 87 (53.0%), and unknown history of trauma in 74 (45.1%) of the cases.

The most common chief complaints for the younger than two years age group on presentation were lethargy and change in consciousness in 80 cases (26.2%), scalp swelling, bruising, and bleeding in 49 (16.1%), (no complaint) fall from height in 39 (12.8%), cardio-respiratory arrest in 32 (10.5%), apnea in 29 (9.5%), seizures in 26 (8.5%), vomiting in 18 (5.9%), a combination of the above in 16 (5.2%), irritability in 5 (1.6%), otorhagia in 5 (1.6%), periorbital hematoma in 3 (1.0%), hypotonia in 2 (0.7%), and other in 1 (0.3%). There was a combination of altered mental status, abnormal respiratory status, and seizures in 183/305 (60.0%) cases.

Diagnostic workup, including skeletal survey and ophthalmology exam in children under 2 years of age, in which age group these studies are indicated, was complete in 25 cases (7.2%). Totally, 132 cases (38.2%) had a skeletal survey (20 complete, 112 partial) but not a retinal exam. Seven (2.0%) cases had a retinal exam but not a skeletal survey. Totally, 183 patients had altered mental status, abnormal respiratory status, and seizures. Of 305 cases, only 18 (9.8%) had a full workup including both skeletal survey and retinal exam.

The rate of diagnostic workup, including both skeletal survey and retinal exam, in hospitals with a MDT (25.7%) was statistically significantly higher than in hospitals without a MDT (2.9%) ($p=0.001$). Three cases (0.8%) were diagnosed as inflicted by the treating physicians. Because 78 cases in this study were assessed to be inflicted, 3.4% of AHT cases were recognized as such by the treating teams; hence, the rate of missed diagnosis was 96.6%. A low rate of diagnostic workup including both skeletal survey and retinal exam was associated with the absence of an MDT. In two of the three cases, the perpetrator was convicted; in one, the prosecutor closed the case without a trial on the basis of "no confession" despite the death of the child and medical evidence (Table 3).

A forensic report was filed with the police in 244 cases (70.7%) because all juicidal injuries in Turkey presenting to the emergency department are expected to be routinely reported to police; however, Child Protective Services (CPS) was informed in only 121 cases (35.2%). At the end of assessment, of the 244 children reported to police, 2 (0.8%) were seperated from their family and placed in state custody. A multidisciplinary team approach was established in 3/10 (30.0%) of the hospitals (Table 4).

Discussion

This study revealed that multidisciplinary management of pediatric head injury cases under 3 years of age with a consideration of AHT in differential diagnosis is rarely performed at teaching hospitals in Turkey. Only three of the participating hospitals of this study practiced a multidisciplinary approach. As a result, pediatric head injury cases are not optimally managed from diagnostic workup, etiologic assessment, and post-hospital management perspectives. This study supported the hypothesis that very few pediatric head injury cases are assessed to look for AHT, with subsequent high rates of missed diagnosis (96.2%).

To increase diagnostic ability, a through family interview is of paramount importance to reveal associated risk factors in cases presenting with traumatic injuries. Once suspected, including AHT in differential diagnosis would guide physicians to include retinal examination, skeletal survey, and head CT in diagnostic workup, which will provide all potential data to either confirm or rule out AHT. Especially, emergency department doctors should ascertain and document risk factors for AHT in suspected cases. Assessment of a number of risk factors may permit health professionals to identify parents and children who are at a high risk for child maltreatment, facilitating appropriate implementation of prevention and treatment interventions (14). A study investigating the risk factors for AHT in the Netherlands reported that 40% of the parents had low educational levels (15). In a military cohort study, parental risk factors included younger maternal age, lower sponsor rank or economical status, and current maternal military service (16). Hennes et al. (17) reported risk factors for AHT as single-parent families, mothers younger than 18 years of age, mothers with low education, mothers who did not have prenatal care, and families with a low socioeconomic status.

There are some characteristics of the child that appear to increase the probability of AHT, such as child's age younger than 1 year, male gender, and premature birth or low birth weight (17). The baby's normal pattern of crying has been reported as the main trigger for the occurence of AHT (18). In the current study, the most common risk factors were determined to be families with low parental education level (23.8%) and having a maximum of three children under seven years of age (22%). However, in the majority of cases, risk factors were not explored and documented, impairing the physicians' ability to establish an accurate differential diagnostic list and leading to low rates of appropriate workup and case finding.

Abusive head trauma is the most common cause of death as the result of child abuse. Infants frequently present with nonspecific clinical features without any history of trauma. A groundbreaking study reported that even at a prestigious institution in the USA, as many as 30% of children with AHT may be misdiagnosed at the initial evaluation (19). As shown above, the case series reported here revealed that the absence of a history of trauma was important based on final etiology: In inflicted cases, there was no reported history of trauma in 4 (5.1%) of the cases compared to 3 (1.8%) in accidental cases.

Ascertainment of AHT diagnosis is critical to prevent a potentially fatal recurrence. In order to prevent this form of child abuse and potential fatalities, physicians should recognize that AHT presents with acute encephalopathy, anywhere from somnolence to coma; acute or chronic subdural hematoma with or without subarachnoid hemorrhages; and retinal hemorrhages occurring in the context of an inappropriate, inconsistent, or absent trauma history (20). In this study, of the 78 cases that were assessed to be inflicted, 4 had no history of trauma and 21 had consistent trauma history.

Retinal hemorrhages are noted in 60%–85% of children with AHT in a retrospective series (21). Dilated retinal examinations in infants and children with nonspecific symptoms of illness that raise concern for intracranial processes could increase the recognition of retinal hemorrhages (13). Children under two years of age with suspected AHT should have a fundoscopic examination, preferably by an ophthalmologist, to identify retinal hemorrhages and other eye injuries. Non-ophthalmologists may have difficulty performing an adequate examination and thereby fail to identify injuries that, although not pathognomonic, suggest inflicted injury (22). To accomplish this, every MDT should have an ophthalmologist involved in the team. In this study, evaluation of the retina of the under 2-year-old group was made in extremely few cases (8.2%) that it points to the absence of a structured diagnostic assessment of these cases in the teaching hospitals of Turkey. Extensive intraocular hemorrhage involving multiple layers, extending to the periphery of the eye globe, and presenting with retinal detachment/macular folds in young infants in the setting of acute brain injury and in the absence of a history of severe accidental trauma or underlying medical cause must be considered to be nonaccidental injury until proven otherwise (23).

Distinguishing AHT in young children from other diseases by symptoms is difficult in practice. In one study, physicians missed the diagnosis on initial presentation in one third of cases, and this resulted in repeated trauma, increased morbidity, and death (24). Jenny et al. (19) reported that four factors increased the likelihood of correct diagnosis of AHT, including abnormal respiratory status (by sevenfold), presence of seizures (by sevenfold), presence of facial and/or scalp injury (by fivefold), and parents not living together (by twofold). However, if a child had normal respiration, had no seizures, no facial or scalp injury, and came from an intact family, the probability that AHT would be recognized was less than 1 in 5 (19). In the current study, even when the patients had altered mental status, abnormal respiratory status, and seizures, only 9.8% of 183 such cases had a full workup, indicating the low level of diagnostic care these cases received in the participating hospitals.

Previous studies have reported that over 60% of victims of AHT may have a history and/or clinical evidence of previous child abuse. Physicians assessing children, especially infants, should be alert to indicators of AHT to recognize abuse early on. Including AHT in the differential diagnostic list and taking appropriate steps to rule out or confirm the diagnosis are of paramount importance in establishing child protective services and preventing further abuse and neglect that may at times be fatal (9). In this study, 70.7% of cases were reported to police Because all juicidal trauma cases presenting to the emergency department are by law expected to be reported to law enforcement. However, because professional training of both police forces and prosecutors is not optimal and most trauma cases require social services rather than criminal litigation, most of these reports are

dismissed with little attention paid to the details (6, 7). Child protective services staff are also suboptimally trained on AHT specifically.

Publications on AHT have skyrocketed worldwide and in Turkey alike during the last decades. This can be explained by increased awareness of this issue (25, 26). Clinicians' knowledge on the diagnosis of AHT should be increased to improve case finding, which will allow a more accurate determination of incidence (6). This can be accomplished via establishment of MDT in teaching hospitals, as well as staff training on how to recognize suspicious cases, how to utilize MDT services, and how to report and manage cases on a community based multidisciplinary basis.

Study limitations

This study has several limitations that could impact both the generalizability and interpretability of the findings. Firstly, data were obtained retrospectively. In addition, voluntary hospitals were included in the study; therefore, it can neither be claimed that the study findings reflect the facts on relevant practices in non-participating hospitals nor do they represent the practices in community hospitals.

Conclusion

According to our results, a prospective study should be conducted involving the close to 30 MDTs established in Turkey in teaching hospitals during the last decade. These teams should develop a structured protocol on how to recognize, assess, and manage AHT; train hospital staff at large who might come into contact with suspected AHT cases, including emergency department, pediatrics, neurosurgery, surgery, radiology, ophthalmology, pathology, and nursing staff; develop a child protection consultation system; and focus on prevention efforts. Thus, each child head trauma may be assessed appropriately, leading to increased case finding and prevention of such abuse. Prevention strategies should include parental education on child development, especially on the infant's crying pattern.

Ethics Committee Approval: Ethics committee approval for this study was excluded because it is a retrospective study.

Informed Consent: Patient consent for this retrospective study has not been received.

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Conflict of Interest: No conflict of interest was declared by the authors.

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The Amino-Terminal Fragment of Pro-Brain Natriuretic Peptide in Plasma as a Biological Marker for Predicting Mortality in Community-Acquired Pneumonia: A Cohort Study

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Abstract

Aim: Community-acquired pneumonia (CAP) is an infectious disease that causes the highest mortality rates in developed countries. The primary endpoint of this study was to evaluate the relationship between the plasma concentration of the amino-terminal fragment of pro-brain natriuretic peptide (NT-ProBNP) at the time of CAP diagnosis in a hospital emergency room (HER) and its severity, determined as mortality at 30 days.

Materials and Methods: A prospective, observational cohort study was used to determine NT-ProBNP (ng/L) in patients with CAP, with a follow-up over 30 days and analysis of the mortality rate.

Results: A total of 338 patients were assessed. Thirty patients died within the first 30 days (10.5%). The mean NT-ProBNP values in the deceased patients were 14,035 ng/L (SD: 19,271) compared to 1,711 ng/L (SD: 3,835) in survivors ($p<0.0001$). The cut-off point of 1,769 ng/L showed a negative predictive value (NPV) of 95.3%, whereas 10,808 ng/L showed a positive predictive value (PPV) of 73.3%. The diagnostic performance of NT-ProBNP reached an AUC of 0.783 (95% CI: 0.731–0.829). Entering the potential confounding variables in a logistic regression model revealed that NT-ProBNP behaved like an independent risk factor. Grouping the NT-ProBNP values by every 300, 500, 1,000, and 2,000 ng/L increased the risk of mortality at 30 days by 3%, 5.1%, 10.5%, and 22%, respectively.

Conclusion: The NT-ProBNP values at the time of CAP diagnosis are significantly higher among patients that die than those that survive the first 30 days, and it could be a good predictor of early mortality. NT-ProBNP has good overall accuracy and behaves like an independent risk factor. *(Eurasian J Emerg Med 2016; 15: 30-8)*

Keywords: Amino-terminal fragment of pro-brain natriuretic peptide (NT-ProBNP), community-acquired pneumonia, emergency room, mortality, biomarkers, severity prognostic scales

Introduction

Community-Acquired Pneumonia (CAP) is the most common cause of mortality caused by infectious disease in developed countries. Over the last few years, hospital emergency rooms (HER) have been using severity prognostic scales (predictive scales) that help determine the need for hospitalization. The two most robust, often used, and validated clinical severity scales are PSI and CURB-65 (1, 2). However, these severity indexes have limitations, as shown by the fact that up to 16% of patients admitted to the ICU for CAP belong to PSI risk groups I–III (3).

Over the last few years, Brain Natriuretic Peptide (BNP) has been investigated as a prognosis marker for CAP in emergency rooms, internal medicine, and intensive care units (4-9). Of these studies, few have compared the predictive capacity between biomarkers, and none have compared NT-ProBNP with one of the infectious markers most often used in the HER, procalcitonin (PCT). There are no studies on the capacity of NT-ProBNP to detect severe CAP when associated with other biomarkers.

As there is an established relationship between pneumonia and cardiovascular events and NT-ProBNP is a biomarker for cardiac stress, the purpose of our study was to 1) evaluate the relationship between the plasma concentration of NT-ProBNP at the time of diagnosis of CAP in the emergency room with the severity of CAP, defined as mortality at 30 days; 2) compare the prognostic capacity of NT-ProBNP with predictive scales and biomarkers normally used in

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the emergency room; 3) study the strength of association between NT-ProBNP and severity prognostic scales and biomarkers normally used in the emergency room; 4) evaluate whether the association of NT-ProBNP with predictive scales and biomarkers results in improved predictions; 5) analyze the increased risk of mortality from CAP with the grouped increase of NT-ProBNP levels; and 6) perform survival analysis.

Materials and Methods

Study design

A prospective, longitudinal cohort trial was designed with the inclusion of subjects between February 2012 and 2013 with a clinical diagnosis of pneumonia and radiographic confirmation. Consideration is given to CAP if the process takes place for a patient who has not been hospitalized during the last 14 days; in the event that the patient was already in hospital, it was diagnosed within the first 48 h of the hospital stay.

The inclusion criteria were that the patient must be over 14 years of age and comply with the definition of pneumonia and CAP. The predictor variable was considered to be the result of the determination of NT-ProBNP in blood (in ng/L); the dependent variable was mortality at 30 days.

The case report form should be completed by at least two emergency room physicians. A specialist in radiodiagnosis made a blind a posterior examination of each of the x-rays as he had no clinical knowledge of the patients. A contact interview took place at one month, either in person, by phone, or through the electronic clinical record depending on the patient's final destination, to determine the patient's progress.

This study was designed in accordance with the ethical principles of the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board of our region, Cantabria (IEC/IRB act 8/2012), as well as by the training commission of Laredo Hospital, a public hospital in the north of Spain covering a population of 95,000 people.

Data collection

The following baseline data was obtained from the patients: demographic (age and sex), comorbidity, personal history (alcohol and tobacco use and body mass index), physical examination (heart and respiratory rate, pulsoximetry, and systolic and diastolic blood pressure), laboratory tests (leukocytes, neutrophils, hematocrit, haemoglobin, platelets, glucose, urea, creatinine, sodium, bilirubin, prothrombin time, activated partial thromboplastin time, arterial oxygen and carbon dioxide partial pressure, arterial pH), chest X-ray, and biomarkers (C-reactive protein (CRP), procalcitonin (PCT), lactate, D-dimer (D-D), high-sensitivity troponin T, and NT-ProBNP). The severity of the CAP was assessed using severity prognostic scales (PSI, CURB-65, and ATS/IDSA).

Blood samples

Blood samples were obtained on arrival of the patient in the emergency room. The physicians responsible for the patient requested NT-ProBNP and all determinations considered necessary for correct care of the patient.

Determinations of NT-ProBNP and other biomarkers

The NT-ProBNP sample was collected in a biochemistry tube and analyzed using the proBNP II-Elecsys 2010 kit (Roche Diagnostics GMBH, SandhoferStrasse 116, D-68305 Mannheim, Germany). The analytical technique used was an electrochemiluminescence immunoassay (ECLIA) using the sandwich principle. The measurement range of the assay was between 5 and 35,000 ng/L; however, measurements of up to 70,000 ng/L could be performed using appropriate dilutions.

Statistical analysis

For statistical analysis, categorical variables were described as absolute value and percentage, and continuous variables were described by their means, standard deviations, and 95% confidence intervals (95% CI) and/or medians and interquartile ranges. The analyses were performed using the SPSS Statistics Package for Windows (version 20.0) and MedCalc (version 11.7).

A comparison was made for each variable between the surviving and non-surviving groups. The assessment of differences between the NT-ProBNP concentrations of patients with CAP, survivors, and non-survivors with different biomarkers and SPS as quantitative variables was performed by bivariate analysis using Student's t-test if they followed a normal distribution or the Mann–Whitney non-parametric U test if not. The type of distribution for quantitative variables was first checked using the Kolmogorov–Smirnov Z test. The differences between groups for qualitative variables were evaluated using the Chi-square or Fisher's test.

NT-ProBNP was analysed as a predictor of mortality by calculating the ideal cutoff point optimised by multiplying sensitivity by specificity using mortality at 30 days as a reference and plotting the receiver operating characteristic (ROC) curve. The strength of the relationship between numerical variables was evaluated using Spearman's non-parametric coefficient of correlation test.

Survival was analysed using the Kaplan–Meier method, comparing curves by the Log-Rank test. Logistic regression analysis and the Enter method were then applied to estimate whether the variable of interest, NT-ProBNP, provided any additional predictive improvement to consolidated predictive scales. The personal history of ischaemic cardiopathy, heart and kidney failure, and age were included as categorical confusion variables. Multivariate analysis using NT-ProBNP as a dichotomous variable according to the cutoff point was used to calculate the raw risk after including the confounders in the model. The prediction models were compared using the Hosmer–Lemeshow test.

Results

General characteristics of the patients with pneumonia in cluded to the study

A total of 338 patients were assessed, 287 being included in the study (84.9%). In total, 2% of the rejected patients had nasocomial pneumonias, 8% were pediatric patients, 20% had no request for NT-ProBNP, 22% had a final diagnosis other than CAP, and 48% were rejected by the radiologist as they had no clear radiological condensation.

Overall, 42.2% of patients included in the study were women. The mean age was 66±21 years (min. 14, max. 104). The main demographic characteristics, comorbidity, clinical and radiological variables, prognostic scales, and biomarkers for each group are shown in Tables 1 and 2.

Table 1. General characteristics of the sample. Comparison between survivors and deaths in the first 30 days

	Survivors n=257				Death n=30				
Personal characteristics	**Mean**	**SD**	**Med**	**IQR**	**Mean**	**SD**	**Med**	**IQR**	**p**
Age	64.1	21.3	67.0	37.0	82.9	14.2	86.0	11.0	<0.001
BMI	25.9	5.5	25.0	7.0	22.9	3.9	23.0	5.0	0.163
Alcohol C. g/week	21.9	62.6	0	0	36.8	130.7	0	0	0.450
Smoker cigarette/day	4.6	9.7	0	2.0	0	0	0	0	0.014
Vital Signs									
HR, bpm	97.5	19.4	97	27.8	97.2	21.9	95	24.0	0.957
RR, rr	20.2	6.0	20.0	8.0	31.1	7.8	30.0	13.3	<0.001
SBP, mm Hg	132.3	24.5	132.0	32.8	119.2	26.1	115.0	34.0	0.004
DBP, mmHg	72.1	12.7	72.0	17.0	60.8	13.0	61.0	20.0	<0.001
Body temperature, ºC	37.7	1.1	37.8	1.7	37.3	1.2	37.2	1.5	0.046
Blood oxygen level, %	93.7	4.4	95.0	6.0	86.1	9.1	88.0	14.3	<0.001
Laboratory values									
Leukocytes per, mm^3	12027	5586	11100	6800	14703	9065	13050	12300	0.158
Neutrophils per, mm^3	9876	5398	8900	6350	12713	8082	10950	11375	0.072
Haematocrit, %	39.5	5.1	40.0	6.0	36.0	7.9	36.5	10.3	0.008
Haemoglobin, g/dL	13.2	2.5	13.1	2.1	11.7	2.5	11.5	3.5	<0.001
Platelets per, $1000/mm^3$	231	89	220	103	277	159	240	171	0.209
Glucose, mg/dL	146	78	124	52	175	70	159	103	0.005
Urea, mg/dL	45.6	30.8	39.0	24.5	106.5	85.6	78.5	54.3	<00001
Creatinine, mg/dL	1.0	0.5	0.9	0.4	2.0	2.6	1.3	0.9	0.005
Sodium, mEq/L	136	5.8	136	5.0	138	9.7	136	9.5	0.483
Bilirubin, mg/dL	0.53	0.29	0.50	0.30	0.64	0.54	0.50	0.30	0.253
Prothrombin time, %	74.9	23.1	81.0	23.3	70.3	17.0	69.0	20.5	0.021
APTT sec.	35.8	3.9	35.5	7.8	33.4	3.3	32.8	6.3	0.480
PO_2 mmHg	63.3	14.7	61.0	15.0	51.5	14.2	50.0	23.0	<0.001
pCO_2 mmHg	37.4	6.6	37.0	8.0	41.1	18.1	34.5	18.3	0.518
Arterial, pH	7.47	0.06	7.46	0.06	7.40	0.13	7.45	0.19	0.047
GFR est. mL/min/1.73 m^2	86.2	34.4	85.4	41.8	73.2	61.3	47.7	55.9	0.049
Biomarkers									
CRP, mg/dL	13.6	13.7	8.9	17.1	16.1	16.4	11.6	17.2	0.333
PCT, ng/mL	1.6	5.6	0.2	0.5	4.8	100	0.4	2.8	0.007
Lactate, mg/dL	14.3	8.4	13.0	10.0	30.6	11.4	36.0	23.8	0.058
D-Dimer, mcg/mL	2.3	2.0	1.9	2.2	4.3	2.2	5.1	4.2	0.082
Troponin T high sensitive, ng/L	58.1	198	11.0	27.0	214.4	321.6	95.0	248	<0.001
NT-ProBNP, ng/L	1711	3835	411	13400	14035	19271	5192	1968	<0.001
Prognostic scales									
PSI	77.4	36.5	78.0	57.5	137.2	38.1	137.2	50.0	<0.001
CURB-65	1.06	1.07	1.0	2.0	3.0	1.2	3.0	2.0	<0.001
ATS/IDSA major criteria	0	0.06	0.0	0.0	0.17	0.46	0	0	<0.001
ATS/IDSA minor criteria	0.77	1.05	0.0	1.0	2.97	1.27	3.0	2.0	<0.001
Progress									
Length of stay	8.7	5.2	7.0	5.0	------	-----	-------	------	------
Days to death	------	------	------	------	7.5	6.4	5.5	6.7	------

Med: median; IQR: inter-quartile range; Alcohol C: alcohol use consumption; Smoker: tobacco use HR: heart rate; RR: respiratory rate; BMI: body mass index; bpm: beats per minute; rr: respiratory rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; ºC: degrees centigrade; GFR: glomerular filtration rate; APTT: activated partial thromboplastin time; CRP: C-reactive protein; PCT: procalcitonin; ATS/IDSA: American Thoracic Society/Infectious Diseases Society of America; PSI: pneumonia severity index; CURB-65: acronym for Confusion; BUN: Blood Urea Nitrogen, Respiratory rate, Blood pressure, age over 65 years

Table 2. General characteristics of the sample. Comparison between survivors and deaths in the first 30 days

	Survivors		Death		
	No	%	No	%	p
Total	257	89.5	30	10.4	
Sex					
Female	106	41.2	15	50	0.358
Male	151	58.8	15	50	
Comorbidity					
Heart failure	20	7.8	3	10	0.719
Ischemic cardiopathy	19	7.4	5	16.7	0.089
Chronic kidney failure	13	5.1	3	10	0.227
Chronic respiratory disease	52	20.2	1	3.3	0.024
Essential HBP	101	39.3	19	6.3	0.012
DM-1	0	0	1	3.3	0.105
DM-2	47	18.3	8	26.7	0.270
Chronic hepatopathy	7	2.7	1	3.3	0.519
Cerebral vascular disease	12	4.7	6	20	0.006
Severe psychiatric disorder	5	1.9	0	0	1.000
Dementia	20	7.8	13	43.3	<0.001
Malignancy	19	7.4	4	13.3	0.279
Immunosuppression	2	0.8	0	0	1.000
Disorder preventing oral treatment	1	0.4	0	0	0.732
Construction work at home or workplace	6	2.3	0	0	0.398
Cohabitation with animals	33	12.8	4	13.3	0.939
Risk Groups					
ATS/IDSA	19	7.4	21	70	<0.001
PSI	257		30		<0.001
I	73	28.4	0	0	
II	40	15.6	0	0	
III	58	22.6	4	13.3	
IV	66	25.7	10	33.3	
V	20	7.8	16	53.3	
CURB-65	257		30		<0.001
1	180	70	3	10	
2	52	20.2	8	26.7	
3	25	9.7	19	63.3	

HER: hospital emergency room; HBP: high blood pressure; DM-1: diabetes mellitus type 1; DM-2: diabetes mellitus type 2; ATS/IDSA: American Thoracic Society/Infectious Diseases Society of America; PSI: pneumonia severity index; CURB-65: acronym for Confusion, BUN: Blood Urea Nitrogen, Respiratory rate, Blood pressure, age over 65 years

Description of the outcome predictor variable

The results interval found was between 8 and 70,000 ng/L, with an arithmetic mean of 3,000 ng/L (SD 8,068 ng/L) and a median of 492 ng/L (IQR: 138–2.003). The values for survivors and death are shown in Figure 1.

There were statistically significant differences between the surviving and deceased patients at 30 days (median 5,192 ng/L; IQR 19,685 vs. median 411; IQR 1,340 ng/L, p<0.001).

Prognostic capacity of NT-ProBNP in CAP

The cutoff points were calculated depending on the mortality at 30 days. The cutoff point was 1,769 ng/L to optimize sensitivity (66.7%; 95% CI: 47.2–82.7), specificity (78.2%; 95% CI: 72.7–83.1), positive predictive value (PPV, 26.3%), and negative predictive value (NPV, 95.3%). For a cutoff point of 232 ng/L, the sensitivity was 93.3% (95% CI: 77.9–99.2), specificity was 39.3% (95% CI: 33.3–45.6), PPV was 15.2%, and NPV was 98.1%. For a cutoff point of 10,808 ng/L, the sensitivity was 36.7% (95% CI: 19.9–56.1), specificity was 98.4% (95% CI: 96.1–99.6), PPV was 73.3%, and NPV was 93% (Figure 2).

When proposing mixed models with demographic variables (age), predictive scales (PSI, CURB-65 and ATS/IDSA 2007), and biomarkers (CRP, PCT, and NT-ProBNP), the most advantageous model combines ATS/IDSA with PCT and NT-ProBNP with an AUC of 0.94.

The diagnostic performance of NT-ProBNP, some other markers such as procalcitonin, and diverse scoring systems used for pneumonia are depicted in Table 3.

Correlation between NT-ProBNP and predictive scales

A study was made of the correlation between NT-ProBNP and the PSI, CURB-65 predictive scales, and minor ATS/IDSA criteria. There was a good association between NT-ProBNP and the PSI scales (Rho 0.71 p=0.0001) and CURB-65 (Rho 0.65 p=0.0001) and a slight association with the ATS/IDSA minor criteria (Rho 0.48 p=0.0001).

Logistic regression model

a. NT-ProBNP as an independent risk factor for early mortality

Initially, a univariate analysis was performed depending on mortality for the following variables as dichotomous variables: age, background of heart failure, ischaemic cardiomyopathy and chronic kidney failure, serum creatinine, NT-ProBNP, PSI score, CURB-65 score, minor ATS/IDSA criteria score, and ATS/IDSA scale. The variables with p<0.25 (age, ischaemic cardiomyopathy, creatinine, NT-ProBNP, PSI, CURB-65, minor ATS/IDSA criteria, and ATS/IDSA as dichotomous variables) were entered into a logistic regression model. Furthermore, forced multivariate analysis was performed on the personal history of heart failure and chronic kidney failure, as these variables have an established relationship with NT-ProBNP levels and therefore could be confusion factors. After adjustment for all these variables, the only ones that maintained statistical significance were age (p=0.002), ATS/IDSA 2007 (p=0.001), and NT-ProBNP (p=0.001).

b. Assess improved outcome prediction by associating NT-ProBNP and other biomarkers

A univariate analysis of NT-ProBNP and the CRP and PCT biomarkers revealed that only PCT (p=0.043) and NT-ProBNP (p<0.0001) showed significant differences between patients that died and survived at 30 days.

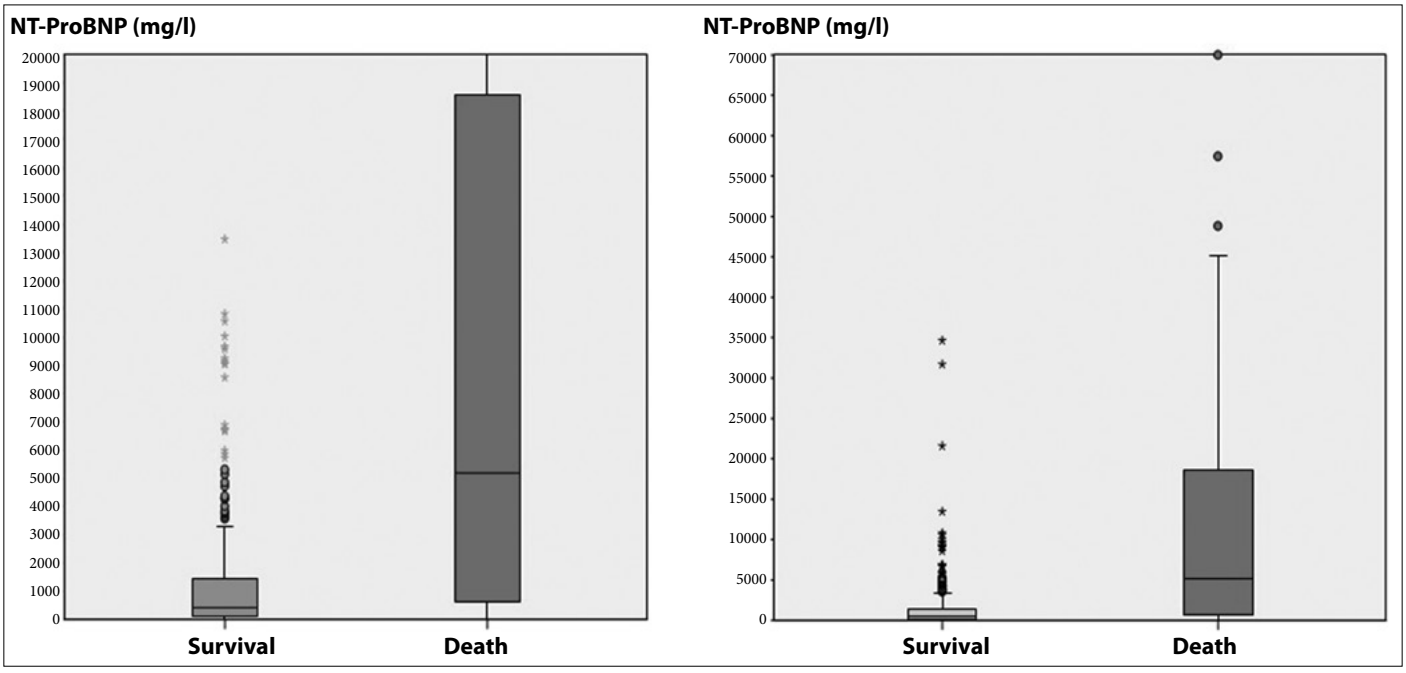

Figure 1. NT-ProBNP values on a scale of 0–20,000 ng/L (left) and on a scale of 0–70,000 ng/L (right)

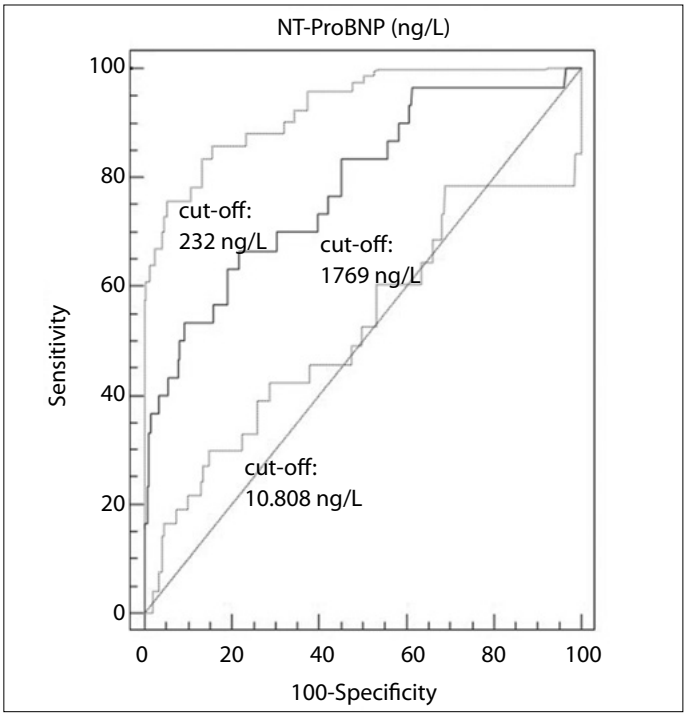

Figure 2. NT-ProBNP ROC curves. AUC 0.783; CI 95%: 0.731–0.829; p<0.001

Survival analysis

It was observed that 20% of patients died within the first 48 hrs and 50% within the first 5 days. Comparison of the survival curves depending on the cutoff point showed significant differences between the patients that died for values over 1,769 ng/L [(hazard ratio 6.2 (CI 2.9-13.2, p=0.0001)], as can be seen in Figure 3.

The survival curves were also compared depending on sex, background of heart failure, ischaemic cardiomyopathy and chronic kidney failure, and creatinine serum levels above and below 1.2 mg/dL.

Table 3. Comparison of diagnosis performance curves

Models	ROC Curves
CRP	0.56
PCT	0.66
NT-ProBNP	0.78
CRP + NT-ProBNP	0.79
PCT + NT-ProBNP	0.85
CRP + PCT + NT-ProBNP	0.82
PSI + NT-ProBNP	0.90
CURB65 + NT-ProBNP	0.91
ATS/IDSA + NT-ProBNP	0.93
PCT + ATS/IDSA + NT-ProBNP	0.94
Age + PCT + NT-ProBNP	0.86
Age + PCT + ATS/IDSA + NT-ProBNP	0.95

ROC: receiver operating characteristic; PCT: procalcitonin; CRP: C-reactive protein; ATS/IDSA: American Thorax Society/Infectious Diseases Society of America; CURB-65: acronym for Confusion, BUN: Blood Urea Nitrogen, Respiratory rate, Blood pressure, age over 65 years

The only significant differences were found for the latter variable (p<0.001).

Discussion

The World Health Organisation estimates that infections of the lower airways are the most common cause of death by infectious disease in the world, with close to 3.5 million deaths a year (10). Early assessment of the severity of pneumonia is crucial to the correct management of these patients. Over the last few years, a multitude

of clinical tools have been designed and developed to predict mortality and help decide the care site, with PSI and CURB-65 being the most reliable and most often used in the HER (1-2). However, these scales are quite often not applied, either because they are simply not used or because objective data such as low blood oxygen level or subjective data such as poor family support recommend admission of the patient (11).

Biological markers and their role in the inflammatory response and relationship to the severity of pneumonia are undering study. Biomarkers may be an alternative to assess the seriousness of pneumonia and predict mortality. These biomarkers include natriuretic peptides (NP) (12-14). The first team to assess NT-ProBNP as a predictor of early mortality at 30 days were Jeong et al. (4), who in 2011 conducted a retrospective study of hospitalized patients, obtaining promising results in their series of 167 patients. According to our information, this NP was recently studied as a prognosis marker for CAP in different scenarios: emergency room (5, 9), hospitalized patients (6), and intensive care units (7, 8).

Description of the outcome predictor variable

We found large differences between NT-proBNP values in survivors and deaths within the first 30 days; there were statistically significant differences between both groups, as in other studies conducted to date.

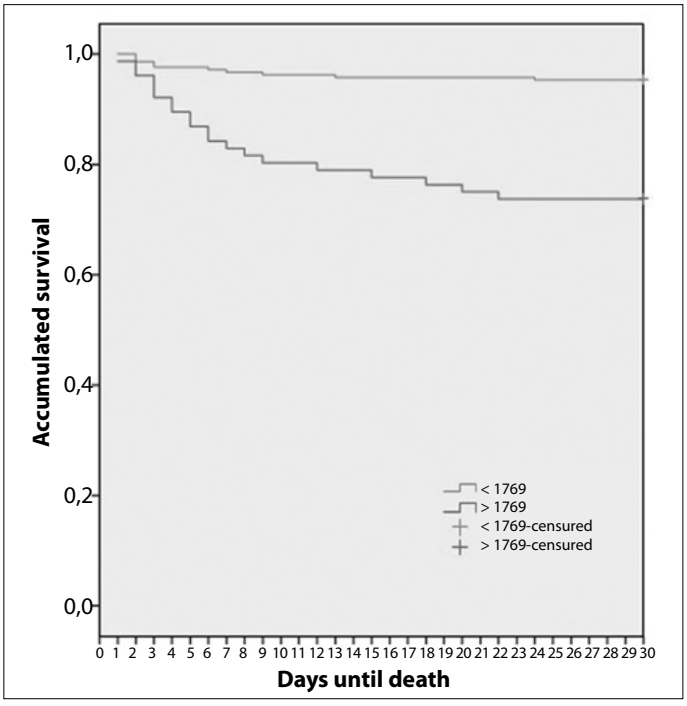

Figure 3. Comparison of the survival curves

Prognostic capacity of NT-ProBNP in CAP

The ideal cutoff point balancing sensitivity and specificity found in our study was 1,769 ng/L. This result is in line with that of studies by Jeong (1,795.5 pg/mL), Nowak (1,935 ng/L), and Chang (1,860 ng/L) in patients diagnosed in the Emergency Room and admitted to a conventional hospital ward (4-6). Our cutoff point differs from that of the cohort by Lin et al. (7) (2,177.5 ng/L). Their patients had more severe CAP, with 83% of patients meeting ATS/IDSA criteria compared to 14% in our series. They also evaluated other types of pneumonia, including hospital-acquired (25%) and that associated with social and health care (40%). We also found differences with the cutoff point established by Xiao et al. (8), almost certainly because this group reduced the cutoff point to obtain a sensitivity of 98.7%.

As severe CAP is a dangerous, but treatable, disease whose severity should be assessed as soon as possible, lowering the cutoff point to 232 ng/L would provide a sensitivity of 93.3% (95% CI: 0.78–0.99), higher than 90% (95% CI: 0.87–0.92), in reference to the Fine's score in the above meta-analysis. This could therefore be useful in the HER to identify patients with non-severe pneumonia and low risk of death who could be safely discharged. Our sensitivity is very close to those of the studies by Jeong and Nowak when they dropped their cutoff points to 235.6 ng/L and 628 ng/L, respectively (4, 5).

A higher cutoff point (10,808 ng/L) would indicate patients requiring a more aggressive initial treatment.

Assessment of the diagnostic performance of NT-ProBNP

After studying the general accuracy of the diagnostic test using ROC curves, NT-ProBNP has good capacity as a diagnostic test to predict mortality at 30 days, with an AUC of 78%. The studies performed to date found an AUC of between 71% and 88% (Table 4).

Comparison of the prognostic capacity of NT-ProBNP compared to a scale to predict severity

The accuracy of these two prediction scales has been compared in various reviews and meta-analyses, resulting in a high NPV in populations with a low prevalence of death, a PSI sensitivity of about 90%, a CURB-65 specificity of close to 80%, and suitable diagnostic capacity with an AUC of around 80% (15-17). However, in spite of the value of these tools, approximately 30%–60% of low risk CAP patients are hospitalized, there being considerable disagreement between the recommendations of the scales and the final destination of the patient (18).

Table 4. Assessment of the predictive capacity of NT-ProBNP and SPS for mortality at 30 days

Studies	NT-ProBNP		PSI		CURB-65		ATS/IDSA	
	AUC	95% CI	AUC	95% CI	AUC	95% CI	AUC	95% CI
Jeong et al. (4)	0.71	0.61–0.81	0.80	0.74–0.85	0.76	0.70–0.83	-	-
Nowak et al. (5)	0.73	0.67–0.77	0.76	0.71–0.81	0.65	0.61–0.70	-	-
Chang et al. (6)	0.88	0.82–0.94	0.87	0.83–0.91	-	-	-	-
Lin et al. (7)	0.72	0.65–0.78	-	-	-	-	0.65	0.58–0.63
Xiao et al. (8)	0.77	0.71–0.84	0.87	0.82–0.92	0.81	0.75–0.87		
Tazón Varela et al. (9)	0.78	0.73–0.83	0.88	0.83–0.91	0.87	0.83–0.91	0.89	0.85–0.92

SPS: Severity Prognostic Scale

In our sample, the two scales to predict severity showed better diagnostic performance than the biomarker. Nevertheless, the AUC obtained in our study for the predictive scales was at the same height of the upper range of the AUC found in systematic reviews and meta-analyses (16, 17). We therefore understand that the diagnostic capacity of NT-ProBNP could be useful in the same terms as the use of PSI and CURB-65 scales.

Comparison of the prognostic capacity of NT-ProBNP compared to other biomarkers

Over the last few years, medical literature has accepted the usefulness of PCT to differentiate acute systemic bacterial infections in CAP to assess the response to treatment or predict hospitalization (19, 20). However, there is still controversy regarding its capacity to predict early mortality. Some studies, such as those by Krüger et al. (21), Horie et al. (22), or Park et al. (23), attribute good capacity to PCT. However, in a systematic review of 30 publications, the ability of PCT to predict early mortality was found to be very similar to our results (24). In our sample, the association of NT-ProBNP with PCT, a combination not used to date, provided high specificity (98%) to detect severe CAP. This combination of infectious and cardiovascular stress biological markers could be useful in the HER or ICU to detect potentially severe patients.

Among the studies that analyze NT-ProBNP and its relationship to CAP, there are very few that study and compare other biomarkers. Only Jeong et al. (4) and Nowak et al. (5) assessed infectious-inflammatory biological markers (leukocytes and CRP); they obtained results very similar to ours, attributing a low predictive capacity to both variables (Table 5).

Correlation between NT-ProBNP and predictive scales

A study was made of the association between NT-ProBNP and predictive scales such as quantitative variables. There was positive and significant interdependence between the severity of pneumonia and the PSI and CURB-65 scales and minor ATS/IDSA 2007 criteria, the strongest association being with Fine's score (Rho 0.71 p<0.0001). These findings are in agreement with Nowak et al. (5), who also found a significant interrelationship between early mortality and the PSI scale (Rho 0.53 p<0.001).

Correlation between NT-ProBNP and other biomarkers

A study was made of the strength of the association between NT-ProBNP and the analyzed biomarkers. Except for troponin T, the correlation was weak with the other inflammatory markers normally used in an emergency room, such as leukocytes (Rho 0.14 p=0.02), CRP (Rho 0.18 p=0.003), and PCT (Rho 0.33 p=0.001). Of special note is the low interrelationship between NT-ProBNP and CRP. Nowak et al. (5) also did not find any correlation between NT-ProBNP, leukocytes, and CRP.

Logistic regression model

a. NT-ProBNP as an independent risk factor for early mortality

A logistic regression analysis was performed, adjusting for possible confusing factors. Only age, the ATS/IDSA scale, and NT-ProBNP maintained statistical significance. However, NT-ProBNP was the only factor maintaining statistical significance in all models. Therefore, age, meeting ATS/IDSA 2007 criteria, and high NT-ProBNP levels are independent predictors of early mortality. These results are consistent with the literature, where NT-ProBNP is also highlighted as an independent risk factor (4-6).

From the evolutionary point of view, an increase of 1 ng/L is not relevant for the clinician; therefore, we grouped the increases of NT-ProBNP as 300, 500, 1,000 and 2,000 ng/L, noting that the risk of death with the first 30 days increased from 3% to 22%. Future studies will be required to determine the solidity of these results and whether this biomarker could be a useful tool in HER and observation units to determine the progress of patients with CAP.

Table 5. Assessment of the predictive capacity of NT-ProBNP and biomarkers for mortality at 30 days

Study	NT-ProBNP		Leukocytes		Neutrophils		D-Dimer	
	AUC	95% CI	AUC	95% CI	AUC	95% CI	AUC	95% CI
Jeong et al. (4)	0.71	0.61–0.81	-	-	-	-	-	-
Nowak et al. (5)	0.73	0.67–0.77	0.52	0.42–0.61	-	-	-	-
Chang et al. (6)	0.88	0.82–0.94	-	-	-	-	-	-
Lin et al. (7)	0.72	0.65–0.78	-	-	-	-	-	-
Xiao et al. (8)	0.77	0.71–0.84	-	-	-	-	-	-
Tazón Varela et al. (9)	0.78	0.73–0.83	0.58	0.51–0.64	0.60	0.54–0.66	0.75	0.56–0.88
Study	**CRP**		**PCT**		**Lactate**		**Troponin T**	
	AUC	95% CI	AUC	95% CI	AUC	95% CI	AUC	95% CI
Jeong et al. (4)	-	-	-	-	-	-	-	-
Nowak et al. (5)	0.55	0.46–0.64	-	-	-	-	-	-
Chang et al. (6)	-	-	-	-	-	-	0.79	0.71–0.87
Lin et al. (7)	-	-	-	-	-	-	-	-
Xiao et al. (8)	-	-	-	-	-	-	-	-
Tazón-Varela et al. (9)	0.56	0.49–0.62	0.66	0.60–0.72	0.80	0.60–0.93	0.85	0.72–0.93

AUC: area under the curve; CI: confidence interval; CRP: C reactive protein; PCT: Procal citonin

b. Assess improved prediction of outcome by associating NT-ProBNP and predictive scales

Some studies are headed in the direction of adding a biomarker to predictive scales to improve the predictive capacity for mortality and the absence of severe complications (25, 26). Several biochemical markers improve the prediction of mortality at 30 days for predictive scales in hospitalized patients, including vitamin D status with PSI (27), CRP with PSI, CURB-65 and CRB-65 (28), CRP and PCT with CURB-65 (29), cortisol with CRB-65 (30), or albumin with PSI and CURB-65 (31).

In our sample, NT-ProBNP improves the prognostic capacity of all three scales. It improves PSI by 3% and CURB-65 by 4%. It is important to note the predictive improvement of the ATS/IDSA scale improved by 11% when associated with NT-ProBNP, reaching an AUC of 93% with a correct classification of 91%. The results in this regard are dissimilar in different studies. When Jeong et al. associated NT-ProBNP with PSI and CURB-65, they found no statistically significant improvement; nor did Lin et al. find an improvement in critical patients when associating NT-ProBNP with the ATS/IDSA scale, although there was an improvement when NT-ProBNP was associated with the APACHE II scale (4, 7). Therefore, this subject is still open to debate.

c. Assess improved outcome prediction by associating NT-ProBNP and other biomarkers

To our knowledge, there is no study using the assessment of diagnostic tests to improve the predictive of a prognosis of mortality by combining NT-ProBNP with another biomarker.

In our study, NT-ProBNP improves the diagnostic performance of classic inflammatory-infectious biomarkers by 24% for CRP and 19% for PCT. It is worthy of note that the PCT model together with NT-ProBNP reaches an AUC of 85%, greater than the AUC provided for PSI (15, 16). Furthermore, in this sample, these two biomarkers had a specificity of 98% in detecting mortality at 30 days, an extremely valuable combination for detecting high risk patients.

d. Assess improved prediction of outcome by associating NT-ProBNP with predictive scales and biomarkers

A study of predictive improvement by associating predictive scales with NT-ProBNP has already been analyzed, with inconsistent results. Jeong et al. did not find that NT-ProBNP improved PSI, CURB-65, or APACHE II (4). Lin et al. (7) did not find that association of NT-ProBNP with minor ATS/IDSA 2007 criteria improved these predictions, although it did do so with APACHE II.

Nowak et al. (5) considered that associating NT-ProBNP with the categorical value of PSI provided additional information. They observed that NT-ProBNP helps detect high or intermediate risk patients when PSI alone marked them as high risk.

In our sample, of all the logistic regression models proposed that included age together with biomarkers and predictive scales, the simplest and most profitable variant would be to use the ATS/IDSA scale and NT-ProBNP, which would give a sensitivity of 80%, a specificity of 92%, good classification of 91% of patients, and an AUC of 93%. That is, in our study, NT-ProBNP combined with the ATS/IDSA 2007 scale is the best combination between biomarkers and predictive scales for detecting severe CAP.

Survival analysis

In the case of CAP, mortality is concentrated within the first few days, with 20% of patients dying in the first 48 h and 50% within the first week. Corrales-Medina et al. (32) detected the majority of cardiovascular complications in the first week. As these complications have a very early onset, the patient may be in the emergency room, observation area, or short stay ward, thus reasserting the importance of early diagnosis and treatment in the HER but also the need for tools that help predict mortality. In our study, survival analysis also revealed that 20% of patients die within the first 48 h and 50% within the first 5 days. Apart from the patients that died, those with NT-ProBNP values above the 1.769 ng/L cutoff point showed statistically significant differences in survival time compared to those that died with values below the cutoff point (Figure 3).

Study limitations

The limitations are basically those derived from a single-center followup study. This study did not include patients with suspected CAP treated in primary healthcare without being referred to the hospital for assessment.

No analytical controls of NT-ProBNP or any other biomarker were performed during the month of followup, thus limiting our conclusions to assess the evolutionary prognostic capacity. Although we analyzed eight biomarkers, the sample numbers were low for lactate, high-sensitivity troponin T, and D-dimer.

Conclusion

In our sample, elevation of NT-ProBNP at the time of diagnosis in the emergency room was associated with increased short term mortality. This biomarker could be an independent risk factor to predict this mortality. These findings are in agreement with current literature; NT-ProBNP is a prognosis tool that has begun to appear in review articles as an emerging biomarker (33). Until its individual prognostic value is confirmed, this marker could be useful in the initial assessment of CAP patients and be included as a tool in addition to predictive scales; also, it could perhaps be used in the future to design individual treatment strategies.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Cantabria University.

Informed Consent: All the patients who entered in the study fulfilled an informed consent

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE

Aspartate Aminotransferase Level as a Prognostic Marker in Acute Zinc Phosphide Poisoning

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Abstract

Aim: To identify whether hepatic enzyme levels can be used as a clinical predictor for mortality in patients presenting with acute zinc phosphide poisoning.

Materials and Methods: A retrospective analysis of all acute zinc phosphide poisoning cases that had presented to our emergency medicine department within the past 5 years was performed. Statistical significance of the hepatic enzyme value to the outcome of poisoning was investigated.

Results: The average age of the cases was 23.6 years. Overall, 53.3% were females, and 35.5% of the total cases were married. A total of 75% patients developed bleeding manifestations and 53.3% had encephalopathy during the course. Overall, 64.4% patients had hypotension and required inotropic support. Renal failure was seen in 48.8% cases. Within 72 h, 60% cases had high anion gap non-compensated metabolic acidosis. An AST cut-off value of 1061 units/L was identified using an ROC curve, and its association to outcome was calculated and was shown to be significant (p=0.001). The mean ALT level for outcome was calculated and was found to be significant (p=0.001). The mean ALT value at mortality was 982.19±85.2 units/L.

Conclusion: Absence of an antidote and rapid onset of MODS causes high mortality rate in acute zinc phosphide poisoning. From our study, we can suggest that in patients with hepatic involvement due to acute zinc phosphide poisoning, an AST value greater than 1061 units/L on the fifth day post-ingestion of the compound is an independent predictor for mortality. *(Eurasian J Emerg Med 2016; 15: 39-43)*

Keywords: AST, zinc, poisoning, emergency department, hepatic failure

Introduction

It has been documented that some form of poisoning is responsible for more than one million illnesses worldwide annually in one way or the other. This is just an estimate as most cases of poisoning actually go unreported, particularly in Third World countries (1). Self-poisoning has reached epidemic proportions and has become a major public health issue in parts of the developing world (2, 3). Based on the limited data, it is estimated that 220,000 deaths occur worldwide annually, and majority of these deaths are intentional (4).

Zinc phosphide is a dark-grey, crystalline compound and is a highly effective rodenticide that is commonly used in the agricultural sector by mixing with food as bait (3). Phosphides are normally found as powders or pellets, usually as zinc or aluminum phosphide (Zn_3P_2 and AlP); calcium and magnesium phosphide salts are also available. Acute poisoning can be direct (by ingestion of the salt) or indirect [by accidental inhalation of phosphine gas (PH_3) generated during its use]. Because zinc phosphide is cheap and is widely used in our region, its use as a suicidal agent is also increasing (5).

Orally taken zinc phosphide reacts with water and acid in the stomach and produces phosphine gas, which accounts for a large part of the observed toxicity. Being an extremely toxic gas, it irritates the respiratory tract and also causes severe systemic toxicity (6). It disrupts mitochondrial function by blocking the cytochrome C oxidase enzyme and increases free radical generation, resulting in lipid peroxidation and producing energy failure in cells (7). Phosphides produce rapid toxicity within 30 min of ingestion, and death may follow in less than 6 h (8). Phosphide ingestions over 500 mg are often fatal (9).

Zinc phosphide is a potent gastric irritant; profuse vomiting and abdominal pain are often the first symptoms. Respiratory complaints could be tachypnea, dyspnea, and coughing and can even progress to acute lung injury over days (3, 10). Also non-cardiogenic pulmonary edema may develop later and should be managed aggressively by positive end-expiratory pressure ventilation (11). Tachycardia, hypotension and dysrhythmias, like atrial fibrillation, flutter, heart block and ventricular tachycardia, and fibrillation, may develop (12). Nervous system involvement can cause coma, tonic-clonic convulsions,

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and delirium (10). Raised transaminases, hepatic failure, and severe metabolic acidosis with acute distal renal tubular acidosis have been associated with ingestion (13).

Absence of a specific antidote and rapid multi organ failure results in very high mortality. Even though rapid decontamination by the use of activated charcoal or gastric lavage with aggressive resuscitative measures according to various protocols are practiced from center to center, none of these have been proven to be effective in clinical studies.

There are significant numbers of studies detailing the effects, treatment, and prognosis of poisoning with aluminum phosphide and other rodenticides, but zinc phosphide has not been that elaborately studied. The purpose of this study was to identify whether hepatic enzyme levels can be used as a clinical predictor for mortality in patients who present with acute zinc phosphide poisoning.

Materials and Methods

Study design and patients

All cases of acute zinc phosphide poisoning, which had presented to our emergency department (ED) over the past five years (January 1, 2010–June 30, 2015) were retrospectively reviewed and analyzed.

Clinical and laboratory data of 73 patients affected by zinc phosphide and presented to our ED were analyzed. Patient files and electronic records were used to gather data. The cases were diagnosed as zinc phosphide poisoning based on history and laboratory findings. All the patients were transferred to the Critical Care department after initial resuscitation and gastric lavage in our ED. Blood samples for biochemical and hematologic determinations were sent from the ED within 1 h of presentation. Information was collected based on age, gender, nature of poisoning, and any delay in presentation to the hospital. All patients with hepatic involvement were identified, and the severity of poisoning was assessed based on the laboratory and clinical parameters, such as hepatic enzymes [aspartate aminotransferase (AST, normal range: 5–45 U/dL) and alanine aminotransferase (ALT, normal range: 5–40 U/dL)], elevated billirubin levels (>2 mg/dL), deranged INR (>1.5), presence of shock, hypotension [mean arterial pressure (MAP) <60], elevated serum creatinine (>1.4 mg/dL), and alterations in arterial pH level (normal: 7.35–7.45).

Exclusion criteria

Pediatric patients (age <18 years) and patients who had consumed zinc phosphide by mixing with other substances or poisons (alcohol, sedatives etc) were excluded from the study. Also, patients who were diagnosed to have any concomitant liver diseases were also excluded. All chronic poisoning cases and cases presenting after 48 h of zinc phosphide consumption were excluded. Any patient who did not give consent or who got transferred to another facility was also excluded from the study. After applying exclusion criteria, we obtained a sample size of 45 from the initial pool of 73 patients.

Statistical analysis

The study data were analyzed using the Statistical Package for the Social Sciences (SPSS) software. Numeric data were presented as mean±standard deviation, frequent variables as rates. Two group comparisons for numeric variables were performed using the Student-t test, and normality analysis was performed using the Kolmogorov–Smirnov test. Receiver operating characteristic (ROC) analysis was performed for determening sensitivity and specificity. All the hypotheses were constructed as two tailed and an alpha critical value of 0.05 was accepted as significant.

Results

The average age in the study was 23.6 years. 53.3% (n=24) of the total were female subjects and the rest 46.6% (n=21) were male. In total, 88.8% (n=40) subjects ingested the poison in an attempt of suicide. The minimum ICU days was 5, while 15 days was the maximum, and the average ICU stay was 8.9 days.

All subjects had nausea and vomiting as initial symptoms; however, 60% had breathlessness and 48.8% had abdominal pain also as initial symptoms. All the patients had tachycardia as an early sign, whereas 75% also had tachypnea (Figure 1). A total of 75% patients developed bleeding manifestations as the disease progressed, whereas 53.3% also developed altered sensorium. Overall, 64.4% of our study group had hypotension and required inotropic support, and 42.2% of them developed refractory hypotension. A total of 26.6% patients required mechanical ventilation, mainly for severe acidosis and airway protection due to decreased sensorium. On presen-

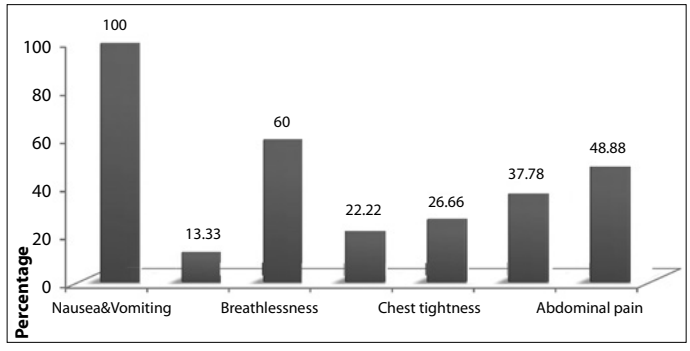

Figure 1. Common presenting symptoms in acute zinc phosphide poisoning
[Frequencies of presenting symptoms are: nausea and vomiting (45); diarrhea (6); breathlessness (27); dyspnea (10); chest tightness (12); palpitation (17); and abdominal pain (22)]

Table 1. Significant factors due to acute zinc phosphide poisoning for the mortality according to univariate analysis test.

Category	Frequency n (%)	Mortality n (%)	p
Tachycardia	45 (100)	21 (46.6)	_
Tachypnea	34 (75)	17 (50)	_
Mechanical ventilation	12 (26.6)	8 (66.6)	_
Hyperbillirubinemia	40 (88.9)	20 (50)	_
Hypoglycemia	25 (55.5)	10 (45.5)	0.059
Hypotension*	29 (64.4)	19 (65.5)	0.001
Coagulopathy*	34 (75)	21 (61.8)	<0.001
Encephalopathy*	24 (53.3)	17 (70.8)	0.001
Metabolic acidosis*	39 (86.6)	21 (53.8)	0.023
Renal failure	22 (48.8)	13 (59.1)	0.139

*Variables that showed significance in the univariate analysis.

tation, 17 (37.7%) had respiratory alkalosis in ABG, but within 72 h, 27 (60%) cases developed non-compensated high anion gap metabolic acidosis (Table 1).

Of the 45 cases, 11.2% had mild, moderate, or severe hepatic failure-each involving 13.3% cases, respectively-and 62.2% developed fatal liver injury in accordance with the Drug Induced Liver Injury Network (DILIN) grading scale. The grade fatal consists of mortality due to liver injury and patients who required transplant. Essentially, all fatal grade patients had developed severe hepatic failure but their outcome was different.

In most patients, derangements in LFT and RFT values were apparent only after 72 h of ingestion. All cases had raised liver function tests by 72 h post-ingestion. Of the 15 (33.3%) who showed elevation of AST/ALT within 24 h of ingestion, 8 (53.3%) dies while the rest 7 (46.6%) had to undergo hepatic transplantation. Renal failure and hyperbillirubinemia were seen by the 5th–6th day of ingestion of poison, while 60% of cases developed acidosis within 72 h.

Mortality in the study was 46.6% (n=21). Of the 53.3% who survived, 29.1% required liver transplant. Also, none who underwent transplantation developed mortality.

On univariate analysis of variables, hypotension, coagulopathy, encephalopathy, and metabolic acidosis were found to be significant factors for mortality (Table 1).

An AST cut-off value of 1061 units/L was identified using the ROC curve; it had a sensitivity of 70.8% and specificity of 80.8% (Figure 2). The association of AST cut-off value and outcome was performed and was found to be significant (p=0.001) (Table 2).

The mean ALT level was calculated and was found to be significant for the outcome. The mean ALT values for survival and mortality were found to be 590.33±475.73 units/L and 982.19±85.2 units/L, respectively (p=0.001) (Table 3).

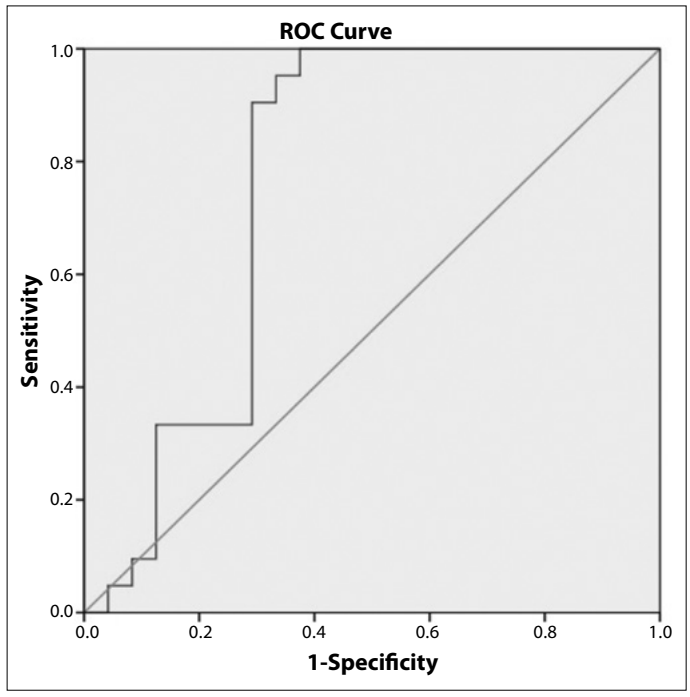

Figure 2. ROC curve of AST cut-off value: 1061 units/L; Sensitivity 70.81%; Specificity 80.95%; Accuracy -75.6% Possitive predictive value -81%; Negative Predicitve Value -70.8%

Table 2. Correlation between AST and the outcome

Factor	Category	Outcome		p
		Mortality n (%)	Survival n (%)	
AST Cut off	<1061 units/L	4 (19)	17 (81)	0.001
Value	>1061 units/L	17 (70.8)	7 (29.2)	

Table 3. Correlation between ALT and the outcome

Factor	Outcome	n	Mean	Standard deviation	p
ALT	Survival	24	590.33	475.73	0.001
	Mortality	21	982.19	85.2	

Discussion

Almost all around the globe, phosphide is commonly used for suicide attempts by the younger productive age group of society (14). In previous studies, the mean age of patients involved have been described as being from 27 years to 40 years; the general notion is that patients in their third decade of life are more prone to suicide (15). In this study, the mean age was 23.6 years, even though lower, it is still comparable to earlier literature. The incidence of attempted suicide in this study was only slightly greater in females than males; while the increased incidence of poisoning in females has been described by various studies, the cause of increased male incidence can be attributed to adaptation issues to social life and financial difficulties, both of which increase the possibility of depression (15–17). Like others, we also found sex to be a non-significant factor for mortality.

The onset of clinical signs and symptoms following ingestion is highly variable, but averages within 4 h (15, 18). Proudfoot et al. (19) reported that, usually systemic toxicity is noticed within a short interval after the ingestion. Phosphine acts as a strong reducing agent capable of inhibiting cellular enzymes involved in several metabolic processes, causing the failure of organ systems (20). Metabolic acidosis indicates a moderate to severe degree of poisoning as per Proudfoot et al.'s study (19). Severe metabolic acidosis alone or in association with acute respiratory alkalosis, is very common (19). In one study by Mathai et al. (14), the mean pH on admission was found to be 7.20±0.14 and the mean bicarbonate concentration was 12.3±5.45 mmol/L. In the present study, five patients (11.1%) had low pH levels at admission and all developed mortality; low pH being the causative factor for deaths in these patients. The mean bicarbonate level in this study was 16.5±4.2 mmol/L. 62.2% of cases were metabolically stable on admission, while 26.66% of patients had acute respiratory alkalosis explained by hyperventilation due to anxiety and 11.1% had compensated metabolic acidosis. Within 24 h of admission, metabolic acidosis increased to 66.7% from the initial 11.1%. Severe metabolic acidosis was found to be a significant factor for mortality in our study, in line with others (15, 18, 19).

Hemodynamic instability and refractory hypotension have been reported in studies (8). In our study, 64.4% of patients had hypotension and 65.5% of them developed mortality. Shock is identified as one of the significant factors for mortality in our study. Central nervous system depression may arise due to hypotension and toxins, as such or due to hepatic or other organ system failure (18, 19, 21). A study by Louriz et al. (22) reported that mortality in acute phosphine

poisoning (APP) correlated with shock and altered consciousness. In our study, 53.3% of patients developed depressed sensorium at some point of treatment; while three of them who had it from presentation itself succumbed to death. 70.8% of those with depressed sensorium died, with refractory state of shock and encephalopathy due to hepatic failure being the cause of high mortality.

It has been proven that the systemic toxicity caused by phosphine is mainly to the heart, lungs, liver, gastrointestinal tract, kidney, and brain since PH_3 molecules targets them particularly (23, 24). The effect of phosphine causing failure of the heart, lungs, and gastrointestinal tract is well studied in cases of aluminum phosphide poisoning, but the effect of it in the liver and renal parenchyma is not well studied (12, 19, 21). Altered liver function tests (LFTs) in non-fatal cases of zinc phosphide poisoning suggest that there is some pathology targeting the liver (24, 25). A study in Iran reported that the liver biopsies from 37 patients who had died of zinc phosphide poisoning showed injury to hepatic parenchyma, which ranged from congestion to necrosis at different stages. The main changes found were fine cytoplasmic vacuolization of the hepatocytes and sinusoidal congestion (26–28).

Saleki et al. (26) stated that PH_3 can cause liver dysfunction, especially after the first day of poisoning. All 45 patients in our study group developed altered liver function tests by the 3rd day (72 h) of admission; 33.3% (15) patients showed altered LFTs within 24 h of admission, of these 53.3% developed mortality. The rate of mortality was twice as high in patients with elevated LFTs within 24 h of admission when compared to those who developed derangement over 72 h. The grading scale developed by the Drug Induced Liver Injury Network (DILIN) was used to grade the severity of liver injury due to poisoning (29). Patients were categorized into four groups of mild, moderate, severe, and fatal liver injury according to the presence of jaundice, hospitalization, signs of hepatic or other organ failure, and the ultimate outcome. According to the grading scale, out of the 45 cases, 24.4% had mild to moderate liver injury, 13.3% had severe, and 62.2% developed fatal liver injury. Clinically, 75% patients had features of severe fulminant hepatic failure like coagulopathy and altered sensorium with rapidly elevating LFTs. Coagulopathy in the form of raised INR was seen in 75% patients-this is a new observation and has not been described in other studies as not many of these have concentrated on the hepatic manifestations of phosphide.

An ROC curve was used to find a cut-off value for AST and ALT. Values from post-ingestion at Day 3 and Day 5 were used to find the cut-off point; as there were absent data from certain patients post the fifth day of ingestion either due to discharge from hospital or death due to poisoning. An AST cut-off value of 1061 units/L was found with a sensitivity of 70.8% and specificity of 80.8%. The association to outcome was calculated and was found to be a significant predictor for mortality with an accuracy of 75.6%. We could not get a similar cut-off value for ALT due to the poor specificity. Hence, the mean ALT levels for survival and mortality were calculated as 590.3±475.7 units/L and 982.1±85.2 units/L, respectively.

Renal failure was present in 48.8% of patients in our study, of which 59% succumbed to death. 81.8% of the patients who had renal failure also had signs of shock too. The cause of renal failure can be due to phosphine or due to severe hypotension.

No antidote is available for poisoning with phosphides. The reported mortality for aluminum phosphine and zinc phosphide greatly varies across different studies, although they are generally high (21). The mortality rate in our study was 46.7%.

Study limitations

Our study group included patients that were admitted to our center, and thus, represented only a small percentage of cases of zinc phosphide poisoning in our state. Unfortunately, we do not have a networked database in our country to provide more comprehensive overview of the topic.

Use of the fifth-day (post-ingestion) AST value as a predictor for mortality can help in the identification of poor prognosis patients and also in decision-making regarding the need for more aggressive treatment strategies for the prevention of mortality (e.g., hepatic transplantation).

Conclusion

Although it is a rare form of suicide attempt, the mortality rate in patients with acute zinc phosphide poisoning is very high. Absence of an antidote and rapid onset of MODS causes high mortality. Even though the presence of metabolic acidosis, refractory hypotension, cardiac failure, and hepatic failure are proven factors for mortality, there is no clear cut-off point to predict mortality. From our study, we can suggest that in patients with hepatic involvement due to acute zinc phosphide poisoning, an AST value greater than 1061 units/L on the fifth day post-ingestion of the compound is an independent predictor for mortality.

Ethics Committee Approval: Ethics committee approval for this study was excluded because it is a retrospective study.

Informed Consent: Patient consent for this retrospective study has not been received.

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

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Two Examples of Nursing Working System in Emergency Medical Services

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Abstract

A nurse who is an indispensable part of the emergency service team should also be aware of her duties, authorities and responsibilities, and skills required for her profession. In this report, the duties and responsibilities of nurses in two different systems have been presented, discussed and compared.
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Keywords: Nursing, emergency medicine, working system

Introduction

Emergency medical service is a special field within healthcare. Emergency units are not only the busiest, most stressful, and complex sections in health institutions but also are the ones where saving lives is a priority, patients requiring attention are evaluated, and treatment and care are provided.

Besides having more distinctive properties and undergoing special training than those in other units, the specification of the nurses' duties, authorities, and expanding roles is essential for the effective management of emergency patients' care and their satisfaction (1). Working long and volatile hours, emergency nurses fall into a risky group in which quick diagnosis and treatment are required. There are patients with malignant diseases and their relatives, forensic cases involved, deaths are commonly encountered, a number of medical devices are being employed (2). The expansion of authority and implementing roles of emergency nurses relieve the pressure in emergency departments, decreasing the waiting time for the patients (3).

In this observational report, topics about nursing services, organization in emergency services, roles, and training have been observed and discussed.

1. First Example of Emergency Units and Emergency Nursing Services

The structure of an emergency unit is like an arena and is modular in shape. For trauma patients, a special trauma unit is carefully appointed. In this organization, emergency nurses are a part of trauma nurses.

a) Departments Assigned to Emergency Nurses:

- Triage
- Units of emergency department A, B, C, D
- Pediatric emergency

b) Hierarchical Structure of Emergency Nurses and their Training

Emergency nurses include charge and training nurses. During the night shift of the charge nurse and assistant and staff nurses, the charge nurse supervises all the work.

It is suggested by the Emergency Nurses Association (ENA) that the certificates given in Table 1 be available. Emergency nurses are required to obtain these certificates and are obliged to renew their certificates at certain intervals (2–4 years). All emergency nurses treating trauma patients have the obligation to obtain the Trauma Nursing Core Course (TNCC) certificate.

In the blue code warning system, emergency nurses are involved in immediate responses in cases of emergency inside the hospital (e.g., to help a patient with syncope in the corridor). They, however, are not a part of the Rapid Response Team. These units have been assigned for quick and urgent responses within the clinic.

c) Duties of Charge Nurses

A charge nurse is the person who is willing to work, has 5 years of experience in emergency services, and possesses all the certificates that emergency nurses are obliged to have; moreover, they are selected by the supervisor and emergency nurses, works in shifts, and is the head of the nurses. A charge nurse is stationed somewhere close to the emergency ambulance entrance. They sit at a desk equipped with a large computer with its monitor and an ambulance

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call device. She receives the first piece of information about the patients (including pediatrics and adults cases) and is responsible for welcoming them, placing them in the patients' module, and making all the decisions. She also organizes the emergency unit and prepares the trauma rooms for good use when on call. She is responsible to emergency charge nurse. While working, she does not provide any patient care service.

During the transfer of patients with the "red" trauma code to the emergency unit, a charge nurse gets the first piece of information. When she receives the red code, she makes sure the entire trauma team gets into action in 2 minutes.

d) Triage: In emergency departments, there are two separate lounges, namely general and triage. The triage nurse receives the story as to the patient's problem and gives the triage code. "Emergency Severity Index' is employed in this service. Triage nurses decide on the appropriate care protocol, thus saving time. It has been reported by the Emergency Nurses Association (ENA) that a triage nurse is required to work at least for 6 months in an emergency unit in order to have strong communication skills and have the ability to work independently and to make quick decisions. A sample application for the triage care protocol is shown in Table 2.

e) Emergency Nursing Applications: An emergency nurse is responsible for five modules and serves five patients at once. After a brief introduction, the emergency nurse gathers information about the patient's story. Before any attempt she makes, she takes spoken and written orders and makes sure they match on the hospital register system and the information form filled out in pen. There is a computer system in which data is immediately recorded and patients can be monitored at any time at the emergency nurse desk. Nurse call buttons are actively used in the emergency patient modules. Within the hospital information system, nurse register headings are as follows:

Clinical Record of Nursing:
1. Triage
2. Medication
3. Surgery
4. History
5. Allergies
6. Interventions
7. Physical Assessment
8. Nursing Progress Notes

Positions and Roles of the Trauma Team

The positions and roles of the trauma team have been summarized in Figure 1.

The duties of the emergency nurses in the trauma team:

1) Primary duties of the nurse:
- Prepares the trauma room
- Keeps a record of all of the resuscitation data and applications
- Assumes the patient's care after the post-trauma.

2) Secondary duties of the nurse:
- Makes sure the IV vein passage is open
- Manages laboratory tests without being warned by the trauma team members
- Provides fluid, blood, and medicine infusion
- Applies NG, OG, and Foley catheter if necessary
- Organizes the trauma room

Each patient admitted to the emergency unit is given care by more than one nurse. One reason for this is that there is an insufficient number of emergency nurses and another is that are too many patients coming.

Some of the emergency nurses have a ''Emergency Nursing Certificate" approved by the Ministry of Health. An emergency nurse receive in-service training and clinic training sessions once a week. In addition to various scientific studies, they attend scientific activities and conventions organized by Emergency Medicine Associate, Emergency Medicine Specialist Associate and Emergency Nursing Associate.

Table 1. Emergency nurse certificate programs

1.	Certified Emergency Nurse
2.	Trauma Nursing Core Curriculum
3.	Emergency Nursing Pediatric Course
4.	Basic Life Support
5.	Advance Cardiac Life Support
6.	Pediatric Advance Life Support

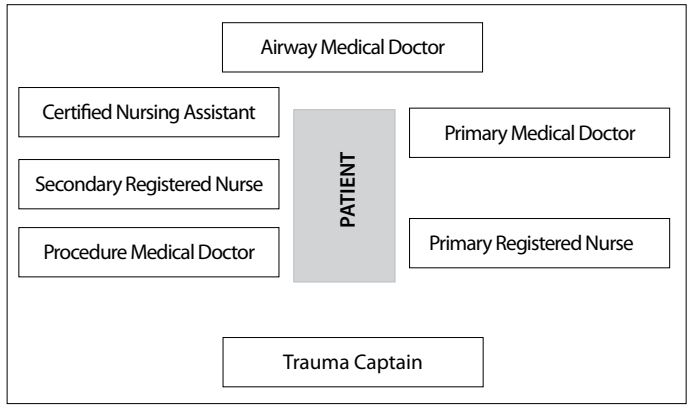

Figure 1. Position and roles of trauma team

Table 2. Adult emergency triage care protocol (for patients aged 18 and over)

Patient complaint	Nursing applications	Laboratory	Drug therapy	Radiological examinations
Chest pain associated with coronary artery disease	Cardiac monitorization, oxygen saturation, electrocardiogram (ECG); start with 2 lt/min through nasal cannula, open the suitable IV way	Na, K, Cl, $paCO_2$, paO_2, BUN, creatinine, glucose, PT, INR, CK, CK-MB, trop, 12-lead ECG	0.4 mg nitroglycerine 5 min × 3 doses	(Chest X-ray)

2. Second Example Emergency Unit and Emergency Nursing Services

The emergency service is a step 3 healthcare service and is an arena and modular system. It has three trauma rooms prepared for trauma patients. However, there is not a planned and appointed trauma team.

a) Units where emergency nurses are employed:

• Rapid care
• Arena

b) Working system and training of emergency nurses

In the emergency arena unit, all the clinical operations and emergency nursing work system are monitored by the most senior nurse appointed by the emergency nurse. There is also a graduate training nurse who works with emergency nurse.

Emergency nurses are not employed in the triage. In the rapid care unit which is an extended part of emergency triage, injection, taking samples for laboratory tests, opening IV vein lines, and ECG can be applied. When there are sick and wounded people because of disasters or terrorist attacks, emergency nurses are given additional duties to watch services. They are responsible for the availability of medical devices and equipment in the emergency arena. In the arena, emergency nurses act according to verbal or written orders, enter manually the nurse part of the emergency patient form used in association with doctors and nurses into the hospital information system.

Discussion

The population growth and the burden of chronic diseases at the present have increased the applications to emergency services. Owing to increased pressure of the services in emergency units, the adoption of new service models seems inevitable (3). In the first emergency service we have observed, a nurse is responsible for five modules and is responsible for treatment of five patients. In fact, she is responsible for the primary treatment of the five patients she observes, immediate treatment and their procedures. In the second emergency service, however, primary nursing applications are employed and at other times, the other emergency patients' procedures are handled. Though not planned, in critical cases, three or four nurses deal with a single patient at the same time. The service organization of the emergency nurses and a careful planning of the work force play an important part in the provision of high quality emergency care services.

Emergency services are the front door of the patient care services. All applications at the emergency services, registration and first nursing evaluation are carried out on the stretcher. Immediate use of the stretcher speeds up the process of acceptance to the emergency services which also includes triage period. Emergency nurses should be responsible for the safety, continuity of care and effective simplification of patient flow (4). In the first emergency service, as individuals pay for their own healthcare, the flow is relatively slower. In the second emergency department, on the other hand, the number of patients flow is higher and a single nurse has to treat more than one patient at once. In both of the emergency departments, the dynamic actions of the emergency nurses facilitate the patient flow.

Opinions of the emergency nurses from Israel have been taken about the notification of the patients and triage. It has been reported that new and broad authorities and increase in practical roles of the nurses will not only decrease the pressure in emergency department but also shortens the waiting period of the patients. Most of the participants in the group asked for authorization and tasks in the triage (5). In the first emergency department observed, the triage nurse is authorized to make a decision in accord with the patients' triage code. All the requests about the emergency patient are given at the outset by the triage nurse, thus saving time. In the other emergency department observed, emergency nurses were not assigned in triage, but they seem to have been employed in the minor care unit.

In this dynamic environment, the effective role distribution of the health professionals in emergency services, planning of the building and working system and its continuation are instrumental in overcoming the problems in the information flow. It has been thought that, in order to enhance the quality of the patient care, an emergency team should focus on the interdisciplinary care and the role distribution between nursing and medical jobs should be re-designed. In emergency departments, such matters as technology-based communication system and simultaneous interactions with doctors contribute to the role expansion of the nurse. Cognitive work distribution pattern increases collaboration (6). In the first emergency department observed, the charge nurse can be given as an example for the role expansion of an emergency nurse. Through the technology-based communication system and simultaneous interactions with the doctors, a charge nurse speeds up the transportation of a patient to the emergency treatment and increases the survival chance of the patient. Also, she acts as a coach by providing communication and collaboration among emergency crew. In emergency departments, the presence of emergency nurses experienced, competent and trained as permanent members of the emergency personnel enables a comprehensive evaluation of the patients and the smooth improvement of management skills. In the second emergency department, this task is partly fulfilled by a senior nurse though not formal.

In order to offer better services to patients, emergency nurses should regulate their services with better care and in a more planned way. According to a study, the time that emergency nurse spends with a patient supports the idea of holistic healthcare. Also it is reported that continuous training and further research on the specific patient groups visiting emergency departments (such as pediatrics, mental health, and the aged) are required (7). In the first emergency department, the obligation of obtaining some of the certificates mentioned above and their renewal (2–4 years) will increase the quality of the services. In the second emergency department, there is no such requirement. Besides experience, having received the required education level and attaining clinical approval are among the musts for emergency nurses. In our country, though the importance of certificate programs is being better understood, legal and institutional obligations should be clearly expressed.

Conclusion

In advanced countries, nurses can provide efficient services mainly because of the standardization of the services. Institutional standardization includes nursing services too. The application standardization of emergency nurses who work together with the emergency team and the service organization and planning of the workforce play an important role in the provision of quality healthcare services.

In this review, two distinct nursing applications in emergency departments have been analyzed. In both these departments, the dynamic actions of emergency nurses make the management of the patient flow easier during patient registration and evaluation. The expansion of roles decreases the waiting period of the patients. Clinical authorization of the emergency nurses will increase team dynamics and collaboration.

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Sleep Disorders in Shift Workers in the Emergency Department and Efficacy of Melatonin

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Abstract

No statistical data is available on the number of employees working on night shifts in Turkey. Working on shifts is associated with decreased sleep time, decreased daily sleep quality, and decreased alertness during night shifts. Increased incidences of cardiovascular disorders, peptic ulcers, and some types of cancer in shift workers are well known. Exposure to light at nighttime suppresses melatonin production. In non-synchronized circadian rhythm, disturbed melatonin secretion may lead to excessive sleep, hunger for carbohydrates, and weight gain. Melatonin is the hormone that governs sleep. It seems to be the key regulator of the sleep/wake rhythm. Exposure to light at night and disturbance of the circadian rhythm contribute to the health problems of night shift workers by disturbing melatonin production. In this review, the definitions of social jetlag, delayed sleep phase syndrome, and insomnia will be discussed. Sleep disorders in psychiatric diseases will be reviewed. Melatonergic drugs available on the market will be listed, including their contraindications and side effects. The physiopathology of sleep, sleep disorders, depression, and melatonin will be given with an extended discussion. Two recent reviews about the effect of melatonin on sleep patterns will be discussed. Finally, other treatments for sleep disorders will be summarized. In conclusion, in shift workers, sleep problems are a complex subject in which multiple pathophysiological mechanisms play roles. The double-blind randomized controlled studies, systematic reviews, and meta-analyses that have been conducted can provide only weakly positive data about the beneficial effect of melatonin use in shift workers. In the future, multi-centered and multi-participant studies will shed more light on this issue. *(Eurasian J Emerg Med 2016; 15: 48-53)*

Keywords: Melatonin, sleep, review, shift, night work, emergency medicine, agomelatine, melatonergic drugs

Statistics for night shifts and do night shifts lead to health problems?

In article 69/f.1 of the Republic of Turkey Labor Law no. 4857, the following phrase occurs regarding "night work" and "night work period": "In working life, night is a period that starts latest at 20:00 and lasts until 06:00, with a maximum duration of 11 h." No statistical data are available on the number of employees working on night shifts in Turkey. Studies have revealed that the prevalence of sleep disorders is 5%–11% in day workers and 50%–62% in night workers. The restrictions on social life occur with a frequency of 64% in night workers (1). In the United States, 29% of employees are not regular day workers (2). Working on shifts is associated with decreased sleep time, decreased daily sleep quality, and decreased alertness during night shifts (3).

A relationship of insomnia with obesity and metabolic syndrome has been reported (4). The reason for this was increased activity in the amygdala together with decreased activity in the frontal cortex and insular cortex (5).

Kohyama has suggested that the reason why Japan and Korea have the highest suicide rates might originate from the fact that these are countries where the people sleep less or they do not like to sleep (4). When compared with people who sleep for 6–8 h a day, the suicide rate is 3.5 (HR: 2.0–6.1) times higher in people who sleep for 0–4 h a day, and sleeping for less than 6 h is a risk factor for suicide (6). How much sleep is enough for a person? If a person does not feel sleepless when he/she wakes up, sleep time is considered to be sufficient. If he/she feels sleepy, there is a need for longer sleep time (4).

Sleep problems are not merely specific to shift workers, elderly people, and the population who have psychiatric problems. The United States National Health Interview Survey (NHIS) emphasized that 17.4% of the US population had used products of alternative/integrative medicine within the last 12 months due to insomnia or problems encountered during falling asleep (7). Lentino et al. reported that more than 25% of 14,148 soldiers had poor sleep quality and only 33% stated that they had good-quality sleep (8).

The situation is not different in emergency staff who work at the forefront of the health sector. In a study conducted on female nurses, it has been shown that working in the night shift for a minimum of

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three nights a month for longer than 15 years increased the probability of colon cancer significantly (9). In addition, increased incidences of cardiovascular and metabolic disorders, peptic ulcers, and reproductive dysfunction in shift workers are well known (10–18). A causal link between shift work and cancer has such strong supporting evidence that shift work has been classified as a "probable carcinogen" (19). Besides colorectal cancer, there are many reports about a relation between shift work and endometrial, prostate, and breast cancer (20–22). Exposure to light at nighttime suppresses melatonin production. In non-synchronized circadian rhythm, disturbed melatonin secretion may lead to excessive sleep, hunger for carbohydrates, and weight gain (11, 23).

Definitions and Insomnia

Disorders of biorhythms are known to be mostly associated with changing geographic location (jetlag), aging, and night activity (night shift workers). Jetlag, also known as synchronization disorder, is a status of temporary alterations and irregularities of the 24-h cycle of biologic activity due to sudden changes (1).

In 2006, Wittmann et al. (24) introduced the term of social jetlag in order to describe the undesired physiological and psychological consequences of circadian rhythm that arose from the daily schedule. Then, Randler and Volmer (25) defined this term as an alteration of the sleep pattern during weekdays and holidays and addressed its association with a tendency to physical violence.

Delayed sleep phase syndrome (DSPD) involves a delay in sleep for 2 h or longer after the routine time for going to bed, leading to difficulty in waking up at the desired time (26). DSPD generally affects adolescents, young adults, and insomnia patients. DSPD has been related to various behavioral and cognitive pathologies (Figure 1) (26).

Insomnia is characterized by the presence of one or more of these symptoms: difficulty in falling asleep, multiple awakenings during the nighttime, getting up very early in the morning, a reduction in total sleep time, somnolence together with an additional need for sleep during the daytime, fatigue, irritability, difficulty in concentrating, and difficulty in carrying out daily tasks (27). The prevalence of insomnia varies between 11% and 16% in the community (28–30). Primary insomnia is a difficulty in initiating and maintaining sleep for at least one month (28). Chronic insomnia affects approximately 10% of the population and is difficult to treat (31).

Sleep Disorders and Psychiatric Diseases

Sleep disorders are a well-known risk factor in terms of mood disorders, particularly major depression (32). Major depression is a mental disorder characterized by reduction of self-respect, anhedonia (not getting pleasure from activities that were normally liked and loss of interest), fatigue, anxiety, and changes in sleep and body weight, accompanying low mood (28). Depressed patients often complain of difficulty in falling asleep, frequent awakenings in the nighttime, and waking up early in the morning. Of patients with depression, 90% complain of sleep disorders (33) and 6–29% complain of hypersomnia (34).

Seasonal affective disorder (SAD) or winter depression is characterized by recurrent seasonal major depressive episodes. It is seen during winter and spring in the absence of seasonal psychosocial stressful situations and the symptoms completely disappear during spring and summer. A seasonal pattern may also be observed in major depression and bipolar depressive disorder. Epidemiological studies have revealed that the incidence of SAD is 15–25% in the general population. SAD patients manifest atypical depressive symptoms such as a hunger for carbohydrates, hypersomnia, overeating, and weight gain.

In one study, "the description of a sleep disorder by a patient five weeks prior to the recurrence of a depressive episode" was stated to be a major prodromal symptom (35). Abnormalities of rapid eye movement sleep (REMS) are considered to be specific to major depressive disorder (36). Although unipolar and bipolar depression types can be clearly differentiated, no difference was found between the two disorders in terms of nocturnal sleep patterns (36). Conversely, the sleep patterns seen in major depression are not observed in patients with SAD (37). In patients with unipolar and bipolar depressive disorders, melatonin levels were determined to be significantly lower (38).

There are numerous publications that report lower melatonin levels in major depressive disorder; however, some publications have reported the opposite (39, 40). Although the average melatonin levels were not found to be different in depressed patients when compared with control cases, the nighttime peak secretion was found to be delayed and levels of 6-sulphatoxymelatonin (a melatonin breakdown product in urine) measured in the morning were higher. This shows that in major depression a phase shift occurs in melatonin production (41, 42).

In SAD patients, bright-light therapy is effective in both eliminating the phase anomaly and relieving the depressive symptoms. In a 4-week study, when a bright light of 2500 lux was applied between 06:00 and 08:00, it was demonstrated that the body temperatures, cortisol levels, and moods of the patients returned to those of normal circadian rhythm. When these patients were treated with agomelatine, the relief rate of SAD symptoms was found to be 75.5% and the rate of remission was 70.3% (43–47).

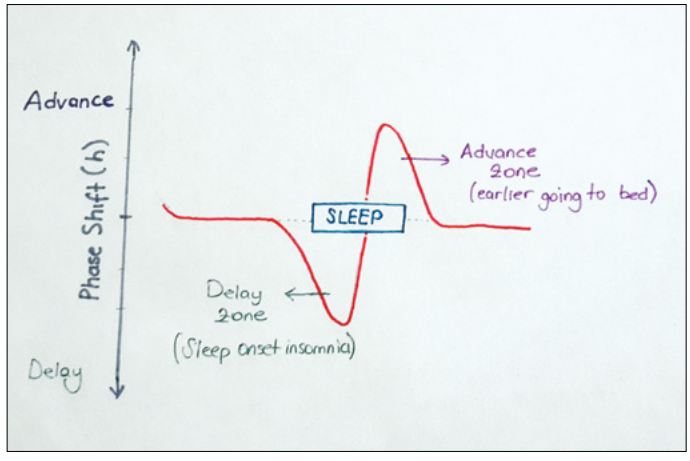

Figure 1. Phase response curve for melatonin: exposure to bright light from just before the time of falling asleep until midnight causes the body clock (and the time of sleepiness) to be delayed. In contrast, bright light in the last couple of hours of the night causes the body clock (and the time of sleepiness) to advance; that is, to shift earlier. Light in the middle of the waking period has no effect on the timing of the body clock. The main symptoms of advanced sleep phase are: 1) falling asleep too early, and 2) waking up too early. Delayed sleep phase is characterized by: 1) falling asleep too late, sometimes after lying in bed awake for many hours, and 2) waking up too late and having trouble getting up on time

What is Melatonin?

Melatonin is the hormone that governs sleep. It seems to be the key regulator of the sleep/wake rhythm (36). The circadian signal, which originates from the suprachiasmatic nucleus (SCN), controls being awake throughout the day and sleeping at night. In all animal species, melatonin is secreted to the greatest extent from the pineal gland at night, regardless of whether the status of the living creature is diurnal, nocturnal, or crepuscular (Figure 2) (48). Melatonin is a soporific (sleep-inducing or sleep-initiating) agent (49). It leads to a phase delay when administered in the daytime and when administered in the nighttime a phase-forwarding function occurs (Figure 3) (50). Exposure to light at night and disturbance of the circadian rhythm contribute to the health problems of night shift workers by disturbing melatonin production (Figure 1) (27).

Melatonin Pharmaceuticals on the Market

For people who have difficulties in falling asleep, short-acting drugs are sufficient. Melatonin reduces sleep latency. Even small doses such as 0.1–0.3 mg/day are sufficient for this purpose (51). All synthetic melatonergic drugs can provide this effect. There are three melatonergic drugs available on the market:

1. Ramelteon (Rozerem©): a non-selective (MT1/MT2) melatonin receptor agonist,
2. Agomelatine (Valdoxan©): a non-selective (MT1/MT2) melatonin receptor agonist and 5-HT_{2c} antagonist, and
3. Circadin©: prolonged-release melatonin.

In a study conducted by the US NHIS, among respondents to the survey, 5.2% reported melatonin use and 27.5% of these gave the reason for using the supplement as insomnia (7).

The drugs that are currently used to treat insomnia are benzodiazepine receptor agonists, antidepressants, antipsychotics, antihistamines and ramelteon, which is a non-selective MT1/MT2 receptor agonist (28, 29). Unfortunately, these hypnotic agents cannot induce physiological sleep and in particular their chronic use is related to the development of drug tolerance, rebound insomnia, physical withdrawal symptoms when quitting, sedation, anorexia, anxiety, agitation, tremors, convulsions, and physical and psychological addiction. Therefore, the MT2 receptor may be the new target for inducing physiological sleep (28).

The time of administration of melatonin is important. Although there is not enough evidence for its effect, the administration of melatonin early in the morning and less exposure to light in the morning are recommended for treating an irregular sleep-wake cycle (32). Exogenous melatonin does not affect the blood levels of prolactin, follicle-stimulating hormone, thyroid-stimulating hormone, and estradiol and does not lead to changes in hematological and biochemical parameters (32). If a benzodiazepine is being used for a sleep disorder, melatonin can replace it or, if they are used together, the benzodiazepine dose can be reduced by 25–66% (32).

Regarding melatonin agonists, liver failure, renal failure, alcohol addiction, and high lipid levels constitute contraindications (52). The side effects of melatonin agonists are nausea, vomiting, headache, elevations in some liver enzyme parameters, rebound insomnia, and, after 6–12 months' use, withdrawal symptoms and addiction (27). There is a risk of hepatotoxicity (53). In experimental animal studies, they are carcinogenic at very high doses (53).

According to a compilation review by Costello et al. (54), no serious side effect was reported for melatonin. The most frequently observed side effects were headache, somnolence, palpitations, and abdominal pain. Rarely reported side effects were nasopharyngitis, arthralgia, tachycardia, dizziness, nausea, vomiting, difficulty in swallowing and breathing, hypnotic activity, heaviness of the head, heartburn, belching, swelling of the arms and legs, sweating, hot flushes, exanthema, sleep problems, depression, and sleepwalking (54).

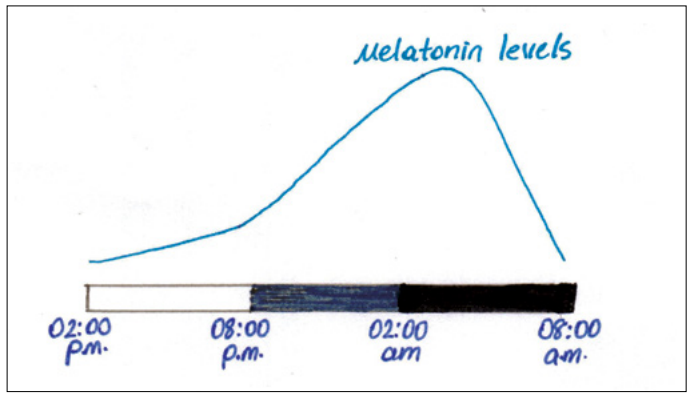

Figure 2. Melatonin levels in a healthy individual during 24 h

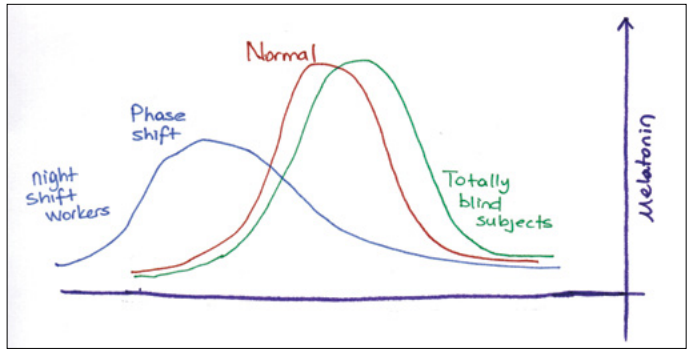

Figure 3. Melatonin levels in normal human, blinded person, and phase shift in a shift worker

The Physiopathology of Sleep, Sleep Disorders, Depression, and Melatonin

In mammals, normal sleep is a transition from alertness to stages of non-rapid eye movement sleep (NREMS), in which slow eye movements are present, and REMS (28). Alertness is characterized by low-voltage rapid electroencephalogram (EEG) activity and high muscle tone together with phasic electromyogram activity (28). NREMS is characterized by high-voltage slow EEG activity, reduced muscle tone, characteristic high-voltage slow waveforms (1–4 Hz, Δ waves), spindles, and K-complexes. REMS or paradoxical sleep is characterized by low-voltage rapid EEG activity together with the absence of muscle tone and a significant θ rhythm (4–9 Hz) (28). The deep stages of NREMS (stages 3 and 4) are also known as slow wave sleep (SWS). This is suggested to be the most restorative stage of sleep (55). Throughout SWS, numerous physiological processes such as memory consolidation, metabolic arrangement, and blood pressure reduction are maintained (28). In patients with major depression, SWS and REMS latency are reduced and REMS density increases (28). Increased REMS density occurs in eating disorders, narcolepsy, pre-senile dementia, and some other neuropsychiatric disorders (28, 56).

The pharmacological activation of MT2 receptors achieved by using selective partial or total agonist drugs improves NREMS without affecting REMS (28).

In healthy young individuals, four non-REM stages are observed during sleep, which last for 70–90 minutes. Stage 1 shows a transition from a status of mild alertness to stages of deep sleep and constitutes less than 5% of total sleep throughout the night. Stage 2 is characterized by sleep K-complexes and sleep spindles. Stages 3 and 4 are the deep stages of sleep and slow waves and unsynchronized delta waves are observed. Then, the individual passes into REMS and NREMS follows this in turn (36).

In depressed patients, a reduction in the number of delta waves during the first NREMS period is observed, together with decreased delta activity throughout the night in polysomnography studies (36). The period from the initiation of sleep to the first REMS period is named REMOL. Whereas the stages of NREMS constitute approximately 80% of total sleep time, REMS constitutes only 20%. The REMS period is prolonged following every successful cycle. Every night, individuals experience five cycles of NREMS and REMS, each lasting for 70–90 minutes (36). The SCN firing rate decreases during the transition from NREMS to REMS (57).

Conventional antidepressants start to improve the sleep patterns of patients 3–4 weeks following initiation of treatment; however, most of their effects are on REMS and their effects on NREMS are less significant (58). Although antidepressants such as tricyclics and selective serotonin reuptake inhibitors suppress REMS, they increase REMOL (59). Most antidepressants increase the amount of MT1 receptor mRNA in hippocampal regions (60).

What do studies tell us about the effect of melatonin on sleep patterns?

In a placebo-controlled multi-center study conducted on 711 patients of different nationalities in Europe, a 25 mg/day dose of agomelatine was found to be very effective for the improvement of depressive symptoms (61). The presence of serotonergic antagonism is considered to be a reason for the therapeutic effectivity of agomelatine in cases of more complex depression (62). The superiority of agomelatine to other antidepressants is the absence of any significant side effects. In general, sexual side effects, constipation, weight gain, orthostatic hypotension, and memory problems are not encountered and withdrawal symptoms do not occur when quitting (26, 63, 64).

Studies on the effect of melatonin for improving sleep irregularities in shift workers are generally conducted on a small number of patients and have durations of one week or less (65). In a meta-analysis of 15 randomized placebo-controlled studies on 718 patients reported in the Cochrane Library in 2014, nine studies were conducted with melatonin, two with hypnotics, two with armodafinil, one with modafinil, and one with "caffeine + nap" (66). Taking melatonin (1–10 mg) after a night shift was found to increase daytime sleep duration (mean difference 24 minutes, 95% CI: 9.8–38.9; seven studies, 263 participants, low level of evidence) and nighttime sleep duration (mean difference 17 minutes, 95% CI: 3.71–30.22; three studies, 234 participants, low level of evidence), when compared with placebo (66). Melatonin did not affect the period of falling asleep in night shift workers, when compared with placebo (mean difference 0.37 min, 95% CI: 1.55–2.29; five studies, 74 participants, low level of evidence) (66).

Armodafinil (150 mg), which is an indirect dopamine receptor agonist, when taken prior to a night shift is associated with being less sleepy and improvement in a simple reaction time test (medium level of evidence). Modafinil is associated with being less sleepy on the Karolinska Sleepiness Scale and increased wakefulness (medium level of evidence). However, in modafinil users (200 mg), headache (34% modafinil vs. 23% placebo) and nausea (11% modafinil vs. 23% placebo) have been determined to be more frequent. In addition, modafinil was shown to be associated with Stevens–Johnson syndrome (66).

Zopiclone (7.5 mg), which is a non-benzodiazepine hypnotic drug, did not lead to an increase in daytime sleep duration when compared with placebo (low level of evidence). Caffeine intake (300 mg) prior to "night shift + nap" was found to be associated with less sleepiness according to the Karolinska Sleepiness Scale (low level of evidence) (66).

In the compilation review by Costello et al. (54) in 2014, 35 randomized clinical studies among 557 articles and a total of 2,356 subjects were included in a study investigating the effect of melatonin on sleep (54). However, in these studies, melatonin dose (0.3–10 mg) and frequency of usage showed great variations among studies (54). In the review, the effects of melatonin in four different kinds of populations were as follows:

1. Shift workers: In an evaluation of the effect of melatonin on falling asleep in eight randomized controlled studies with 300 participants, melatonin was found to be effective in all low-quality studies; however, all high-quality studies reported that there were no satisfactory data for reaching such a conclusion (54). As a result, studies have reported that data that might have enabled any recommendations on melatonin usage in shift workers were not present (54).

2. Jetlag: The efficacy of melatonin usage for jetlag treatment was investigated in eight randomized controlled studies with 972 participants (54). Six out of eight studies found that melatonin usage was effective. In one of the studies, melatonin was found to increase fatigue on the following day (54, 67).

3. Insomnia: The efficacy of melatonin was investigated in insomnia patients in four high-quality studies with 845 participants (54). As in jetlag patients, so also in this group, owing to the small size of the patient population not being able to create sufficient statistical power, melatonin usage remained a low-level recommendation (54).

4. Healthy Volunteers: The investigation of 223 healthy volunteers in 15 randomized controlled studies revealed that melatonin usage may be weakly recommended for falling asleep, owing to the small sample sizes (54). Melatonin usage is also weakly recommended for daytime sleeplessness in healthy individuals (54). Sufficient data are not present about melatonin usage for improving hormonal phase shift in healthy individuals.

According to the results of this study, melatonin prevents phase shifts in jetlag and improves insomnia in healthy individuals. However, there are insufficient data on the effect of melatonin in shift workers (54). At physiological doses (0.1–0.3 mg), melatonin is effective for both the initiation and the maintenance of sleep. For its phase shift effect, higher doses (0.5 mg) of melatonin are needed (54). Oral usage of melatonin at doses of 0.3 mg or less increases daytime melatonin levels to nighttime levels (54).

Daytime oral administration of melatonin in healthy individuals may lead to significant drowsiness, fatigue, and poor performance, particularly at its peak 3–4 h following oral intake (54). If melatonin is used to initiate sleep during the daytime, undesired circadian phase shifts may occur (54).

What are the Other Treatments for Sleep Disorders?

The American Academy of Sleep Medicine recommends melatonin, hypnotic medications, and modafinil in shift workers. It has no specific recommendations regarding the clinical usage of caffeine. It suggests that the benefits of modafinil outweigh its harmful effects. However, a Cochrane meta-analysis study has reported that its benefits are fewer, but adverse effects were frequent (66, 68); because of its slight benefit and the risk of Stevens–Johnson syndrome, the European Medicines Agency canceled the license of modafinil for shift workers (65).

Another treatment of sleep irregularities is light therapy. This treatment is effective, especially in elderly people; the response is at the moderate level in young individuals. For this purpose, the patient is exposed for 1–2 h (between 19:00 and 21:00) to bright blue light (2500–10000 lux) (20). If the patient needs to receive light during the daytime, he/she is exposed to 2500–5000 lux for 2 daytime hours for a duration of 4 weeks (Figure 1). Light therapy was found to be effective in numerous disorders such as sleep disorders due to antisocial personality disorder or aging, major depressive disorder, and seasonal depression (32). Dowling et al. (69) found that light therapy was not effective alone for the treatment of sleep disorders in Alzheimer's disease. They reported that when light therapy and melatonin were used together, daytime wakefulness and activity levels increased and the resting–activity rhythm was enhanced (69). Another beneficial factor that is recommended for sleep disorders is physical exercise.

Conclusion

In shift workers, sleep problems are a complex subject in which multiple pathophysiological mechanisms play roles. The double-blind randomized controlled studies, systematic reviews, and meta-analyses that have been conducted can provide only weakly positive data about the beneficial effect of melatonin use in shift workers. The biggest reason for this is the fact that the effect of melatonin was not studied in a sufficient number of shift workers. In the future, multi-centered and multi-participant studies will shed more light on this issue.

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Cutaneous Anthrax Patients: Evaluation of Four Family Members

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Abstract

Anthrax is a zoonotic infectious disease caused by *B.anthracis*. Declining with each passing day in our country is still an endemic disease. Cutaneous anthrax-(CA) is the most common form and consists of approximately 95% of all cases of anthrax. In this study, we report and discuss with literature 4 skin anthrax diagnosed patients who admitted to emergency service with complaints of no pain and black colored wound on their hands in the same family members. *(Eurasian J Emerg Med 2016; 15: 54-5)*

Keywords: Anthrax, cutaneous anthrax, bacillus anthracis

Introduction

Anthrax is a zoonotic and sometimes fatal infectious disease caused by *Bacillus anthracis*. Contamination occurs when endospores enter the body through skin abrasions, inhalation, or ingestion. Humans are considered as an incidental host and acquire the infection by direct or indirect contact or from animal products (1). Anthrax in humans may present itself in four different clinical pictures: cutaneous, inhalational, gastrointestinal, and oropharyngeal. Infection in humans most often involves the skin, causing cutaneous anthrax (CA), which comprises 95% of all anthrax cases. It mostly affects the hands, arms, face, and neck (1, 2).

A typical history that should raise suspicion for anthrax is a rapidly forming painless ulcer at the center of an edematous region following exposure. Anthrax still remains as an endemic zoonotic disease in Turkey. In this study, 4 family members who presented to the emergency department with painless and black anthrax lesions on their hands 1 week after cutting cattle are presented with a review of related literature.

Case Presentation

Four females from the same family were admitted to the emergency department with a complaint of lesions on their hands and fingers. Obtained their detailed history revealed that they cut cattle 1 week before admission. The appearance of cutaneous lesions was typical of CA (Figure 1). The patients were hospitalized in the Department of Infectious Diseases with the diagnosis of anthrax. On their initial physical examination, they were afebrile and all vital signs were found to be normal. The examination of other organ systems revealed nothing pathological. Blood samples were taken for routine analysis. Table 1 shows demographic features and laboratory results of the patients. Penicillin G 800,000 IU 2×1 iv was commenced in all patients, which resulted in successful resolution of the skin lesions within 10 days.

Discussion

B. anthracis is a disease commonly occurring in tropical regions such as Africa, Asia, and South and Central America (3). In Turkey, although its incidence has been decreasing, it still remains as an endemic problem. In total, 10724 new human anthrax cases were reported between 1960 and 1969. The numbers of reported cases were as follows: 4423 cases between 1980 and 1989, 4220 cases between 1990 and 1999, and 2210 cases between 2000 and 2005. The Turkish Ministry of Health reported the number of new cases as 262, 126, and 132 in 2007, 2008, and 2009, respectively. This downward trend in the incidence of the disease might be due to developments in the economy and social areas, effective animal vaccination programs, and education programs involving farmers (4, 5).

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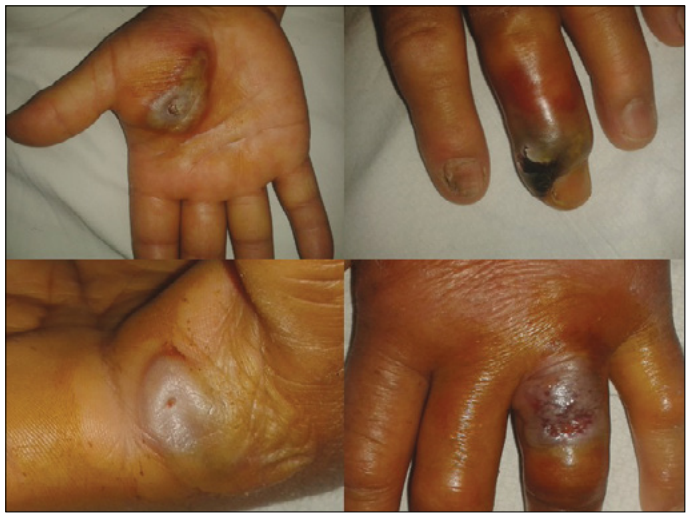

Figure 1. Cutaneous anthrax skin lesion in four family members

Table 1. Demographic and laboratory findings

Patient number	1	2	3	4
Age	32	52	65	73
Gender	Female	Female	Female	Female
WBC count	12,290	9,970	13,030	5,460
Neutrophil (%)	74.2	74.7	78.2	75.8
CRP (mg/L)	7.7	2.4	0.7	1.8

WBC: white blood cell, CRP: C-reactive protein

B. anthracis is a gram-positive, aerobic or facultatively anaerobic, spore-forming, rod-shaped bacterium causing the clinical picture of anthrax. Because anthrax endospores may cease to grow, do not divide, and have no measurable metabolism, they are very resistant to harsh environmental conditions such as drying, heat, ultraviolet light, gamma radiation, and the application of many disinfectants (Dixon). Three types of proteins are present in anthrax toxin: protective antigen, edema factor, and lethal factor. These toxins cause toxic clinical manifestations by inhibiting the action of polymorphonuclear cells (6).

After acquiring CA infection, the clinical picture usually develops following an incubation period of 2–7 days, while it is known that clinical manifestations may be seen anytime between 9 h and 8 weeks after infection (7).

After receiving endospores, skin lesions develop within 3–5 days, and they are usually in the form of nondescript, painless, pruritic papules. Within 24–36 h, the lesion turns to a vesicle with central necrosis and drying, forming the unique black eschar surrounded by edema and few purplish vesicles. Malignant pustules, as common lesions, are not purulent and characteristically painless (1). The most common areas affected by lesions have been reported to be the hands, fingers, and arms, which are exposed to infected animal and animal products (8, 9). Our patients had malignant pustule lesions on their hands and fingers.

The disease mostly affects individuals who work in the fields of animal husbandry and agriculture. Patients working in the field of agriculture comprise most cases in developing countries as it occurs in Turkey. Some studies have reported farmers and housewives as high-risk occupations for the disease (8, 9). All patients in our study were female housewives.

Suspicion is the first step in CA diagnosis. In areas where the disease is not endemic, making the diagnosis may be rather difficult. Brown recluse spider bites, ecthyma, accidental vaccine, ulceroglandular tularemia, and necrotic herpes simplex should be considered in the differential diagnosis of CA. Making the diagnosis may be easier when a typical malignant pustule or extensive edema is present in a patient with a history of contact with animals (5, 8, 9). All patients in our study had a history of direct or indirect contact by infected animals or animal products and lesions typical of the disease.

Penicillin G, an old drug, is still the first choice in treatment; doxycycline or ciprofloxacin are the best alternative options in the treatment of naturally occurring anthrax. Intravenous treatment is required in case of CA with systemic involvement and extensive edema (1). All patients in the present study received penicillin G for treatment. None of our patients developed complications such as secondary infection and toxemic shock, and no mortality occurred.

Conclusion

In conclusion, CA is an infectious disease and is an important cause of morbidity in Turkey. The prognosis is significantly affected by the time and accuracy of the diagnosis. In patients with suspicious skin lesions and a history of contact with animals or animal products, a diagnosis of CA should be considered.

Informed Consent: Written informed consent was obtained from patients who participated in this case.

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Safety Netting through the Prevention and Detection of Child Abuse in Low and Middle Income Countries: Lessons from Pakistan

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Dear Editor,

According to WHO, 6.3 million children died before the age of 5 years in 2013. Five percent of these deaths were due to injury and violence (1). In 2012, it was estimated that around 30,000 childhood deaths were caused due to non-accidental injury (NAI) (2). Child abuse or maltreatment can be physical, emotional, and/or sexual. Even negligence or neglect on the part of the caregiver that may cause harm to the child's physical and mental wellbeing constitutes abuse. Child abuse is most commonly detected is predominantly physical, and there is a large amount of NAIs from high income countries (HICs). In the United States, there is an annual average of 24.6 deaths and disability from child abuse per 100,000 children (3), and in 2013, 3.5 million children were found to have been abused (4). A study conducted in the United Kingdom in 2005 reported that 16% of young adults have experienced maltreatment as a child (5). There is, however, very little published data available on child NAI and intentional violence as it pertains to low and middle income countries (LMICs), and a global review by Mulpuri found such wide incidences of NAI (0.47–2,000 per 100,000) that the differences could only be attributed to differences in detection (6). There is some data available from surveys on accidental trauma and resulting mortality in children in Pakistan (7, 8), but what is the situation actually regarding NAI? Injury, overall, is reported as the third leading cause of death in children in Pakistan, with an annual injury mortality rate of 37 per 100,000 children aged 1-4 years (8). One can assume that much of this is accidental, but because no adequate screening is available for child NAI, there is a high likelihood that abuse is being overlooked.

Therefore, the main purpose of the present paper was to search the available biomedical literature relevant to child NAI in Pakistan and from that to tease out the epidemiology of the problem, especially that pertaining to presentations in the emergency department (ED), as many of the injured children are seen there. We argue that there is a need for the rapid development and implementation of ED-based screening as part of the management of children, with suspected NAI being seen in the EDs of LMICs in general and Pakistan in particular. In tandem with further research in this crucial area, we also make the case for an advocacy-based approach to facilitate health systems-related policy formulation because child safety is at stake.

We searched PubMed and Google Scholar for the following keywords: "Non-Accidental Injury," "Non-Accidental Trauma," "Pediatric," "Child," "Emergency Room," "Intentional Injury," "Pakistan," and "Lower and Middle Income Countries." We used the MeSH term "Child Abuse" in our search. As there are limited articles published on child abuse in Pakistan, we also searched recent newspapers for information on the topic.

As injury is a frequent emergency-related presenting complaint, the pediatric ED is a likely place where child NAI could be detected. According to the U.K.'s National Institute of Health and Care Excellence (NICE) guidelines, it is important for the healthcare provider to be attentive and watchful and to pick up on certain clues from the interaction with the patient and the family, regarding NAI. For example, bruising or ligature marks, especially in a child too young to be moving independently. Also, bites, lacerations, head injury, occult fractures, and retinal hemorrhages may point toward NAI; hence, patients presenting with these should be suspected to have undergone NAI. It may also be suspected if the child is withdrawn or is extremely distressed or agitated (9).

Knowledge of other risk factors for child NAI is important, and such factors may be identified in the history. If risk factors are identified, the child could be evaluated for NAI, as described below. These factors include low socioeconomic conditions, mental health issues in the parent or caregiver, and after a major financial crisis, including a natural disaster. Other risk factors include long-term illness in the child and the caregiver being from outside the family (10). Maguire et al. (11) reported that injuries in younger children (2.5–3.7 years) were more likely to be due to abuse as compared to accidental injuries. Another key risk factor is a previous history of abuse (12). Other known factors include having a teenage parent or a single parent, parents being drug abusers, coming from a crowded household, un-

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employment and poverty, or parents themselves being subjected to child abuse when they were children (13).

A methodical approach is needed in the ED when a suspected case of child NAI is encountered. There are evidence-based guidelines for the proper management of victims of child abuse from places in the U.S., such as Stanford University Hospital. According to these guidelines, the child should be hospitalized, regardless of the extent of injuries, in order to isolate them from the possible source of abuse. Subsequently, it is necessary to treat the injuries, obtain relevant samples for testing, and extract information from the child, if possible, and to diagnose the child based on a proper history, examination, and lab tests. Informing the Children's Protective Services is also important, so that they can intervene and ensure a safer environment for the child (14).

Pakistan's Federal Law prohibits child abuse of any kind, and according to the Charter of Child Rights Act 2009, the child may be separated from the parent in the case of severe abuse or neglect (15). However, there is little implementation of this law, because, unlike in the developed world, there is a lack of formalized programs for screening and managing for child NAI in EDs across Pakistan. There is a need to develop proper protocols and referral services for such cases, in order to ensure protection of the child involved. One hypothetical approach is shown in Figure 1. As per that figure, utilization of a proper referral service, like the Children's Protective Services mentioned above, or maybe even the involvement of the law enforcement agencies, should be necessary next steps when a child with suspected NAI is encountered in the ED. Although it is difficult in principle to isolate the child from potentially abusive parents in LMICs, as the mode of payment for healthcare is out-of-pocket, it might be the only recourse available to ensure the child's safety, and it is permissible under the Federal Law, as stated above. A proper policy regarding the management of these patients needs to be set up that can be followed by the EDs and pediatric departments of hospitals throughout the country, so that proper protection and management of the child can be ensured.

Several preventative programs have been successfully employed in the developed world that can potentially be applicable to LMICs. For example, in one program, parents of newborn children were counseled about the harmful effects of shaking children and were given alternatives to consider if the child was crying, rather than-

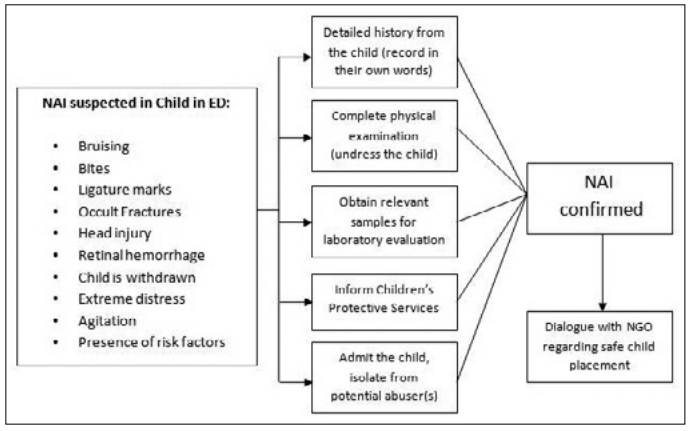

Figure 1. An approach to a child with suspected NAI presenting to the ED of an LMIC. This figure provides a hypothetical model for screening, identifying, and then managing a child suspected to have suffered NAI being encountered in the ED of an LMIC

shaking or beating the child (16). Another prevention model was the Safe Environment for Every Kid (SEEK), in which pediatric residents recognized risk factors for child maltreatment in families and along with social workers, they intervened (17). Such interventions resulted in lower rates of child abuse in both these studies. The Nurse-Family Partnership model is also a good example of a community-based prevention program. In this model, trained nurses visit homes in the community regularly and educate them regarding the harmful effects of child abuse. The study also suggested that pediatricians regularly counsel parents in the clinic regarding child abuse (17).

Preventative programs mentioned above for developed countries might not be too cumbersome for implementation in Pakistan and other LMICs. For instance, pediatricians, pediatric residents and nurses, family physicians, and other healthcare providers involved in caring for children can be trained to identify risk factors for child NAI and to counsel the parents and caregivers accordingly. These counseling sessions regarding the dangers of child maltreatment could also be held during routine visits to the pediatric or family medicine clinics. Awareness sessions regarding child abuse may also be carried out in primary schools, where the children should be provided with various pathways to follow to report abuse, for example, by informing another adult or by calling a helpline like *Madadgaar,* a national telephone helpline that can be accessed by women and children to receive crisis management and legal advice for issues of abuse and intentional violence. According to this helpline, over 5000 cases of child abuse were reported across Pakistan over the span of ten months in 2012, and out of these, 1170 were injuries, according to a recent article in *DAWN*-a major English daily newspaper in Pakistan and one of the most credible sources of information (18). Admittedly, data from newspapers has its limitations as it is not held to the same rigor as that of biomedical publications. However, in a country like Pakistan where research studies on various aspects of child abuse might be hard to implement, epidemiological data that is available from any credible source should be utilized in order to tackle child NAI. It is important to note that data from national helplines might not give a true representation of the actual situation in Pakistan. There is always the possibility that the helpline has not been fully utilized and that many cases simply go unreported. Also, among the cases that are reported, we do not know if they end up receiving proper medical attention. Sahil is an NGO in Pakistan working for the welfare of children subjected to abuse. They organize such trainings and also offer counseling for these children, free of cost (19). An online forum named Laalteyn exists for victims of child abuse. Victims can anonymously post their stories and seek support from other victims (20).

Electronic and print media can be used to spread awareness regarding the issue, and a proper channel can be constructed to report such cases. Print media that is friendly, in the form of story books, can potentially sensitize children and their caregivers to child health-related issues. There is evidence that illustrations contribute a great deal to text coherence, and the presence of colorful pictures increases the child's interest in the text (21). We have attempted this for child literacy in general. We are in the process of piloting this for childhood trauma and injury, such as that from motor vehicle accidents, and its prevention. We are also developing something similar for NAI to engage children with colorful pictorial books to effectively communicate the perils of abuse prevalent in society as well as child NAI prevention information, albeit in a subtle way. Once the material is published and distributed in a local language such as Urdu for

Pakistan and is found to be efficacious, then it can be translated into other languages, such as Hindi for India and Swahili for Africa; thus, the model can be replicated in other LMICs.

Through real advocacy, public and private health care-related partnerships, and national policy making, health systems can be reinforced, and through that, child NAI can holistically be tackled, thus ensuring a safer environment for children in Pakistan and other LMICs. By using similar approaches in the region and through international cooperation among ED-based trauma networks, this can potentially positively impact global child health.

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Imparting Research Ethics in Emergency Medicine-A Perspective from the Developing World

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Dear Editor,

The Emergency Department (ED) is a unique place offering a distinctive clinical practice environment as well as varied moral challenges to healthcare physicians and nursing staff (1). Professional responsibility has been an area of interest to physicians since antiquity (2). The growth of Emergency Medicine (EM) in the developing world has generated both professional and societal attention towards moral issues in healthcare and research (3). As in various other areas of medicine, research has been an integral component of EM with the intention to allow improvement in care that could be critical from the onset. Research ethics in EM is a relevant area for discussion, particularly when the training program is in inception. Our aim is to highlight the current status of EM research in Pakistan and the ethical obligations to be considered when conducting research in such a setting. We also suggest potential solutions to the deficiencies observed in the current research setup of EM in Pakistan.

Emergency department is in its infancy in Pakistan, and therefore, the possibilities of conducting research are limitless. Conducting clinical research in EM exposes many ethical dilemmas for emergency staff personnel and creates an ethical obligation on behalf of the patient (4). At times, they are unable to consent to clinical research, and even if they do, they have patient confidentiality concerns. The family members are so stressed out that they are unable to consent to research in the ED. This puts the emergency physician in a bind regarding EM research involving patients who are in no position to consent themselves. Presently, no universal research ethics standards are being followed in EDs across Pakistan. There are, however, some private institutions that stringently conform to certain research ethics standards; unfortunately, most government institutions till date do not.

Research in areas such as resuscitation and critical care in the ED is most prone to such ethical dilemmas because of rapid turnover, overburdened healthcare staff, overcrowding, less physician–patient interaction, critical presentation of the patient, and less time for making voluntary decisions (5). Most investigators conducting EM research are primarily based in private academic centers where ethical research practice is prevalent. However, there is a paucity of such standards in other places where emergency care is also not up to par. Research and its ethics go hand in hand. Research consent, which is considered the central pillar prior to initiating any study, seems to be an unknown concept for most academic EDs in Pakistan. Research participants are given consent forms mostly in English. Even if they are translated to Urdu, the participants may not be given ample time to read them properly.

Given that the ED deals with a vulnerable population, researchers must carefully conduct research with the voluntary participation of subjects. When faced with such consent problems, researchers may violate ethical standards. Institutional review boards need to be aware of EM-related research proposals; in particular, the protocols must safeguard the rights of clinical research subjects. Formal research ethics training must be provided to data collectors prior to allowing them to initiate clinical research studies in the ED. EM research has immense opportunities in a developing country such as Pakistan. The area can identify possible areas of improvement in research and healthcare. Incorporating public health into EM can create new horizons focusing on basic health issues of the country. Emergency research can identify gaps that occur while managing events such as terrorist attacks and natural disasters. EM services are in infancy with scope for improvement and pre-hospital care. Moreover, EM research has numerous risks. As Pakistan has a low literacy rate with a low understanding about research, participants may be enrolled in studies without properly understanding the rationale of the study and their role in it. As EM research is an area prone to ethical disparities, investigators enrolling patients without paying due attention to the patient autonomy and beneficence; this may create serious issues in violation of patient healthcare rights. Consent importance in EM research must be communicated to the masses of the country through print and electronic media, which are easily accessible.

In conclusion, EM research is a moral endeavor. The moral lapse that has been observed in Pakistan is due to the lack of patient autonomy in EM research principles. EM research, which possesses the potential ground for novel research, could be improved if the focus is toward better training of emergency physicians.

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Primary Epiploic Appendagitis Mimicking Acute Abdomen in Emergency Department

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A 27-year-old man presented to the emergency department of our institution with left lower quadrant pain that started 8 h ago. He did not describe kidney stone, chronic medical problem, or recent trauma in his anamnesis. His vital signs were stable, but physical examination revealed defense and rebond in the left lower quadrant. Laboratory findings were unremarkable except for mildly elevated C-reactive protein (CRP) levels of 6.28 mg/L (reference value: 0–5 mg/L). He was referred to abdominal ultrasonography (USG) following laboratory tests and his written informed consent was obtained before imaging studies. Solid organs were in normal limits in USG, but a significantly increased echogenicity was noted in the pericolic fat tissue adjacent to the sigmoid colon surrounded by a hypoechoic border, which was suspicious for sigmoid diverticulitis (Figure 1).

Following USG, the patient was referred to computed tomography (CT) with the preliminary diagnosis of sigmoid diverticulitis. CT showed a pericolic oval lesion of fat attenuation with a hyperattenuating ring and central dot sign in the same region that was diagnostic for epiploic appendagitis (EA); (Figure 2). However, no diverticula or diverticulitis was observed in the sigmoid colon.

EA is a rare and self-limited condition, mostly seen in middle-aged men, which is caused by either inflammation or ischemic changes related to torsion or venous infarction of the epiploic appendages (1). There are two forms of EA: primary and secondary. Primary EA results from spontaneous torsion of epiploic appendages, with resultant vascular occlusion and ischemia. In contrast, secondary EA is induced by the spread of adjacent inflammation from organs such as gallbladder, appendix, and colon (2).

Primary EA is a diagnostic challenge in emergency medicine; for example, right-sided primary EA is often confused with acute appendicitis or right-sided diverticulitis, whereas left-sided primary EA is often misdiagnosed as sigmoid diverticulitis (1, 3).

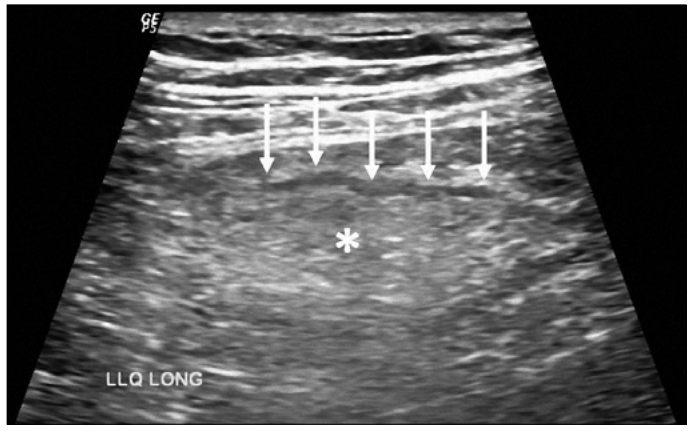

Figure 1. Longitudinal ultrasonographic image from left lower quadrant shows increased pericolic fat echogenicity (asterix) surrounded by a hypoechoic rim (arrows)

EA is seen as a noncompressible hyperechoic small ovoid or round solid mass of adipose tissue between the colon and abdominal wall. The affected epiploic appendage, adherent to the colonic wall, is frequently found to be surrounded by a hypoechoic border during USG (1). CT is the most effective imaging method in EA diagnosis. A hyperattenuating ring sign that represents the inflamed visceral peritoneal covering of the epiploic appendage and central dot sign that corresponds to engorged or thrombosed central vessels or central areas of hemorrhage or fibrosis are the two major CT features of EA (1). In the present case, USG evaluation was first performed by a radiologist in the radiology department. Howev-

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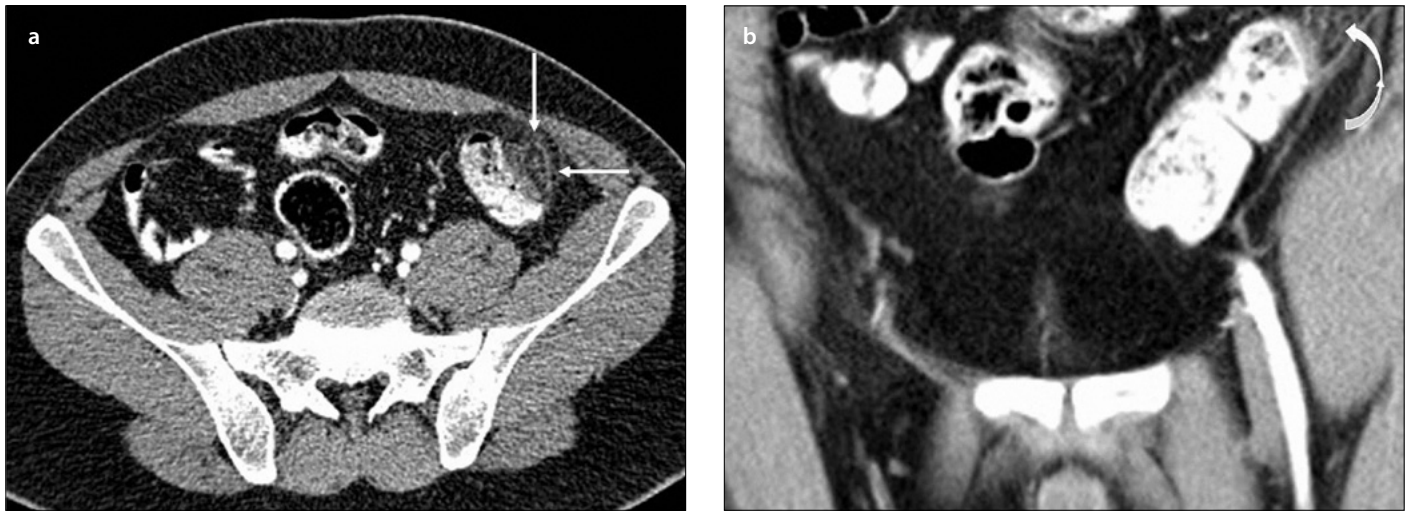

Figure 2. a, b. Axial (a) and coronal reconstruction (b) CT images show hyperattenuating ring sign (arrows) and central dot sign (curved arrow), diagnostic for epiploic appendagitis

er, our experience suggests that if clinicians were familiar with the sonographic features of EA, the same USG features could also be revealed in the emergency department, which would facilitate the diagnosis.

As EA is a self-limited condition, its treatment is conservative in nearly all cases and surgery is not recommended (3). The current patient was treated conservatively as mentioned in the literature, and after treatment his symptoms relieved and CRP level decreased.

In conclusion, EA is a self-limiting benign condition, which may mimic serious abdominal emergencies such as sigmoid diverticulitis. Because the management of EA is different, CT is a more reliable method for diagnosis.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

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Bilateral Shoulder Combined with Unilateral Knee Dislocation After a Fall

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A 54-year-old overweight woman presented to the emergency department (ED) complaining of severe pain and lack of movement in both shoulders and her left knee. Her medical history revealed that the episode began after slipping on the wet floor in the bathroom. The first dislocation of the knee joint occurred during the fall when she lost her balance, and the second occurred when she tried to use her arms to avoid hitting her head on the wet floor. There was no history of connective tissue disease, seizure, or prior dislocations. During clinical examination, there was no evidence of neurovascular deficit for upper extremities and left knee. Radiographs confirmed bilateral anterior glenohumeral dislocation combined with anterior left knee dislocation (Figure 1).

Bilateral anterior shoulder dislocations are reported less often. A recent review of 70 patients demonstrated that the causes of anterior injuries were trauma (50%), muscle contractions (37%) due to seizures or electrocution, and atraumatic events (13%). Because of various etiologies, dislocation mechanisms are different. Lever effect is a type of dislocation mechanism that forces abduction and external rotation of the arm. With the greater tuberosity pressing against the acromion, the humeral head is forced anteriorly out of the glenohumeral joint (1, 2). The patient, in this case, had low-energy trauma as well as left knee dislocation.

Complete dislocation of the knee causes devastating extremity injuries, particularly in the popliteal artery and peroneal nerve. The incidence of nerve and artery injury due to knee dislocation is 10%–40%. Even worse, when a vascular injury secondary to a traumatic knee dislocation cannot be repaired within 8 h, the amputation rate increases to nearly 85%. Therefore, vascular assessment should include examination of both the dorsalis pedis and posterior tibial pulses, ankle-brachial index measurement, and computerized tomography (CT) angiography or arteriography. The patient had no clinical signs of vascular and nerve injury at the time of admission and observation, so she did not urgently need further radiological study such as CT angiography (3, 4).

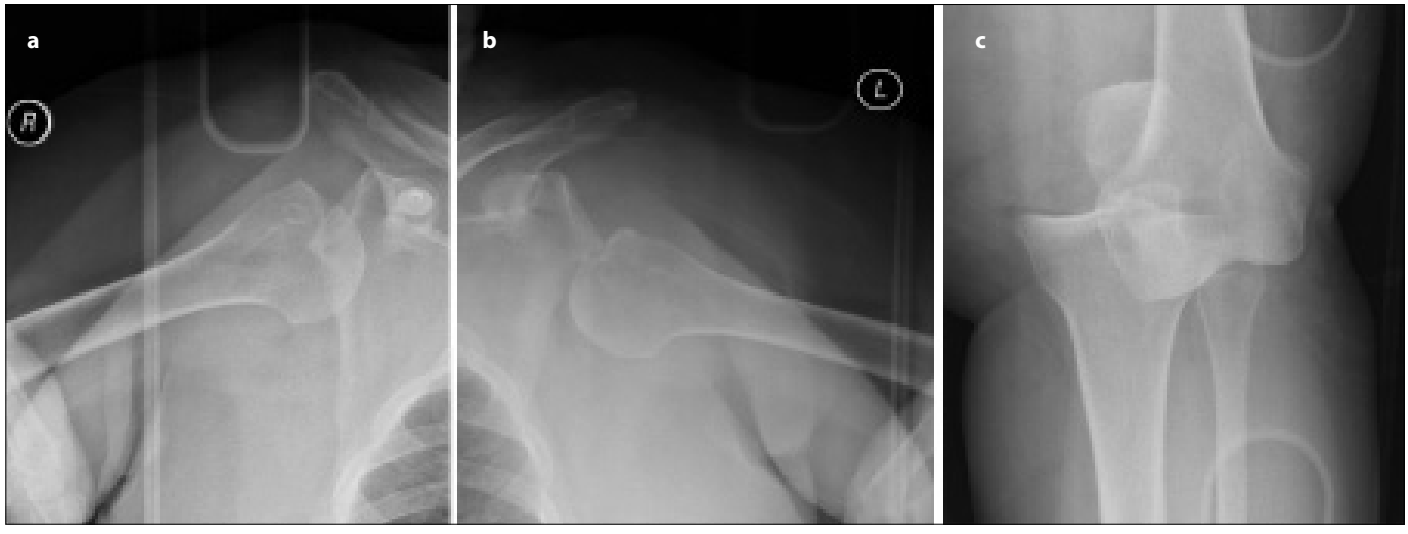

Figure 1. a-c. Anteroposterior X-ray shows bilateral shoulder and left knee dislocation

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In conclusion, multiple large joint dislocations are extremely rare in the ED, and even in cases of low-energy trauma, such situations require urgent intervention, particularly in the case of knee dislocation.

Informed Consent: Written informed consent was obtained from the patient who participated in this case.

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

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Coexistence of Multiple Trauma Diagnoses in One Scene

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A 21-year-old male patient was transferred to the emergency department due to a traffic accident. Flail chest, minor subcutaneus emphysema, tachycardia, and tachypnea were revealed on thoracic physical examination. Pneumothorax, minor hemothorax, multiple rib fractures, traumatic pulmonary lacerations, subcutaneous emphysema, pulmonary contusion, and intrapulmonary hematoma were detected on a thoracic computed tomography (Figure 1). In addition, brain edema and pelvic fractures were seen on another radiologic imaging technique. The patient was intubated due to a low Glasgow Coma Scale score of 8, and tube thoracostomy operation was performed on the left hemithorax.He was then admitted to the intensive care unit where he was connected to a mechanical ventilator. The patient died on the tenth day after hospitalization due to ventilator-associated pneumonia and sepsis.

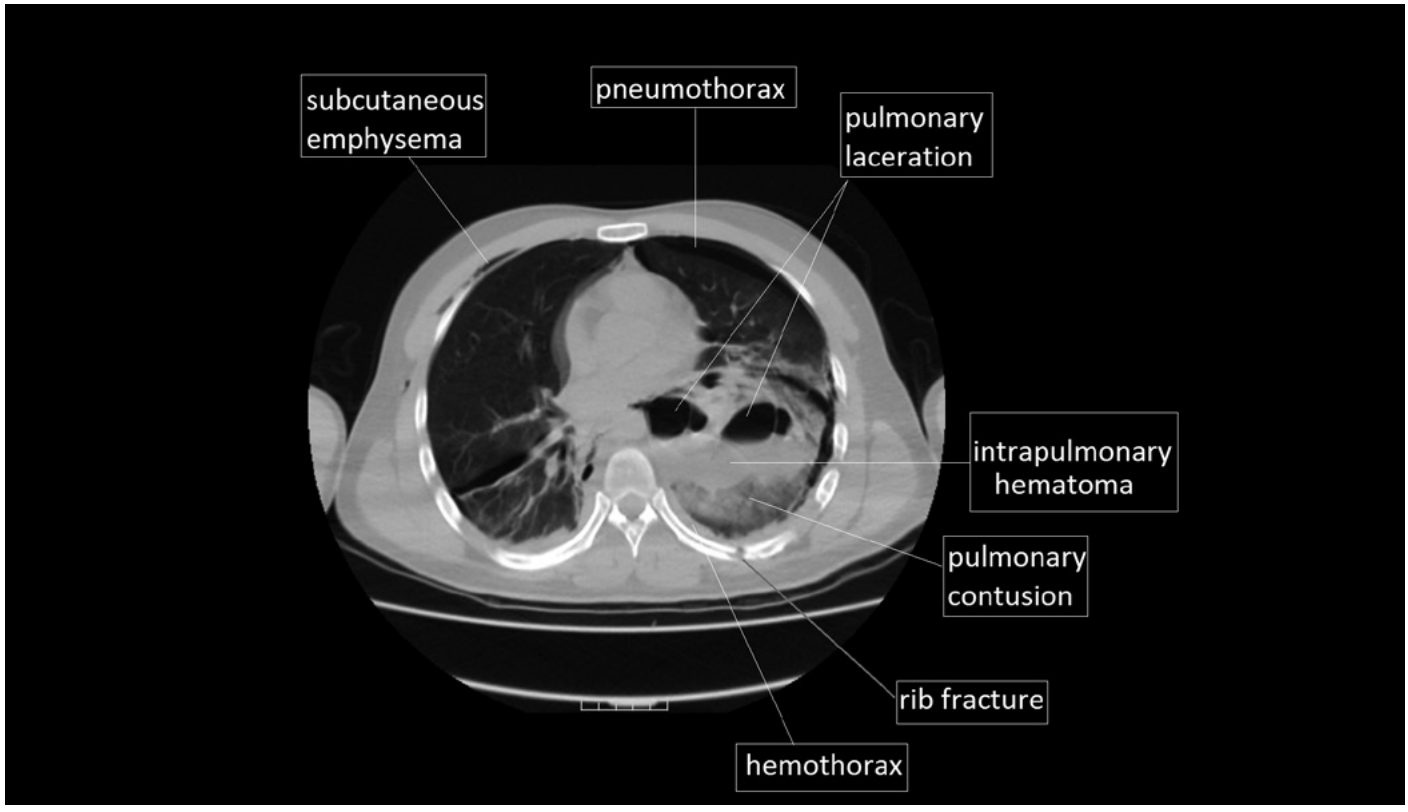

Figure 1. Various types of thoracic trauma seen on thoracic computed tomography

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