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Comparison of the Hemolysis Rate According to Biochemistry Test Results of Patients Admitted to The Emergency Department with the Results of the Hemcheck Device

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Abstract

Aim: A large proportion (approximately 80%) of medical decisions made by clinicians are based on laboratory test results. The most common cause of sample rejection is hemolysis. The sample must be centrifuged to detect hemolysis. The laboratory of our hospital provides precise hemolytic index measurements. However, since the biochemistry test takes a long time to result, in cases of hemolysis, the sample should be reworked, and the result should be waited. Early detection of hemolysis will provide great convenience to prevent the factors that cause hemolysis.

Materials and Methods: This single-center, prospective study included 983 patients admitted to the emergency department, aged 18 years and over, admitted to the green or yellow area, and required routine biochemistry analysis. To determine whether the Hemcheck device detects hemolysis in advance, the results of the device were compared with those of the laboratory at our hospital.

Results: A total of 1049 samples from patients admitted to the emergency department were evaluated, and 983 of them were included in the study. 628 (63.9%) were female patients, and 325 (33.1%) were male patients. The mean age of the patients was 49.95±19.5 years, 734 (74.7%) were younger than 65 years, and 249 (25.3%) were elderly. In the evaluation according to the application site, 935 (95.1%) patients were antecubital, 18 (1.8%) were forearm, and 30 (3.1%) were overhand. According to the results of our study, the agreement between the device and the laboratory results was good and was found to be statistically significant (kappa statistical value=0.511±0.03 and $p<0.001$).

Conclusions: According to the results of our study, the Hemcheck device successfully detected hemolysis. It has been observed that the negative effects of hemolysis in emergency departments can be reduced by using this device.

Keywords: Hemolysis, hemolytic index, biochemistry analysis, emergency department

Introduction

A large proportion (approximately 80%) of medical decisions made by clinicians are based on the results of laboratory tests (1,2). Therefore, any error in the phlebotomy process can have serious negative consequences for patients, healthcare professionals, and the healthcare system (1). Many studies analyzing major diagnostic errors have shown that approximately 40% of diagnostic errors are associated with the results of services such as imaging or laboratory (3). Laboratory activities can be divided into three main phases: pre-analytical, analytical, and post-analytical (4). The pre-analytical phase includes all procedures before the start of laboratory analysis. Because these procedures involve many non-laboratory healthcare professionals (technicians, nurses, or general practitioners collecting specimens outside the laboratory environment where there is no direct supervision by laboratory personnel), they are responsible for most laboratory errors (1,4,5). At this stage, conditions such as patient preparation, tourniquet application time, blood collection sequence, mixing of blood tubes, and labeling of

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primary blood tubes can lead to changes in laboratory results (6). Problems resulting from improper collection and handling of specimens from patients include inadequate sampling, improper coagulation, contamination of infusion pathways, and, most importantly, specimen hemolysis (6).

Hemolysis is defined as the release of intracellular components into plasma or serum as a result of the breakdown of erythrocytes and other blood cells (6,7). Most hemolysis occurs *in vitro*. *In vitro* hemolysis is caused by inadequate collection or processing of specimens, leading to significant problems in hospitals, including specimen rejection (6,7). It has been shown that the incidence of specimen hemolysis is higher in emergency departments (EDs) than in other clinics (6-9). To reduce the rate of hemolysis, it is important to ensure that the patient adheres to a 12-hour fast, does not exercise for 72 hours prior to blood collection, and rests for at least 15-20 minutes prior to blood collection (6); in addition, knowledge regarding therapeutic drug use should be questioned (4). The assessment of fasting time is an important step prior to diagnostic blood sampling (10). Other factors that may increase the level of hemolysis include the use of venous catheters for blood collection, prolonged centrifugation, sample transport, tourniquet application time, cleanliness of the blood collection site, and distance of the tourniquet from the site of the procedure (6,10).

However, these optimal conditions are often not available in EDs. In addition, delays in the diagnosis and treatment of patients with hemolysis in EDs can lead to serious disruptions. For example, in the case of elevated potassium levels, which are affected by hemolysis and are an important parameter especially for emergency services, clinicians often have to repeat the test to confirm the potassium level, which can lead to prolonged hospital stay, multiple blood samples from the patient, increased use of healthcare resources, and unnecessary additional risk to the patient (11).

To detect hemolysis, the sample must be centrifuged (6). This may prolong the time to detect hemolysis and delay the diagnosis and treatment of patients. The aim of our study was to determine whether we could detect hemolysis in a shorter time compared with the laboratory results using the Hemcheck device, especially to minimize the possibility of incorrect or late diagnosis in patients admitted to the ED. We aim to reduce the length of stay of patients in the ED, avoid the need to draw blood from patients at long intervals to confirm hemolysis, minimize the anxiety of patients due to long waiting times, reduce the workload of nurses and laboratory staff, and reduce hospital costs.

Materials and Methods

The study was prospectively conducted in the ED between 08.01.2021 and 21.12.2021. This study was conducted in accordance with the tenets of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of İstanbul Medeniyet University Göztepe Training and Research Hospital (decision number: 2021/0429, date: 25.08.2021). The Helsinki criteria were fulfilled. The procedure was performed using biochemistry test tubes, which are routinely requested from patients admitted to the ED within the indication. The Hemcheck Point-of-care test device was used to determine the presence of hemolysis in the blood samples collected, and the hemolytic index of the biochemistry analyzers in our hospital were calculated and compared (Figure 1). Informed consent was obtained from all participants who voluntarily participated in the study. Patients aged below 18 years, those with vascular problems, patients on hemodialysis, patients on oral anticoagulant use, and patients with suspected drug intoxication were excluded from the study. Prior to the study, 20 samples were tested to determine whether they were affected by the Hemcheck device. A pair of biochemistry tubes was collected from each patient, and one tube was sent directly to the biochemistry laboratory, the other to the Hemcheck device, and then to the biochemistry laboratory. A study was initiated when no significant difference in the results.

In this study, blood was collected in yellow-capped tubes (approximately 10 mL) from patients admitted to the yellow and green areas of the ED for routine biochemical testing. Blood samples were collected from the antecubital region of the upper extremities using standard syringes or 20G and 22G IV cannula intrakets. Samples were placed into the device without

Figure 1.

waiting. In this study, a blood sample was collected in a 10 mL yellow-capped tube and placed in the Hemcheck device without opening the cap and without clotting. Approximately 100 µL of blood was withdrawn from the sample placed in the Hemcheck device by piercing the cap of the tube with the Hemcheck device needle. The Hemcheck device was determined to be hemolysis present/absent (there are two warning lights on the device; green indicates the absence of hemolysis and red indicates the presence of hemolysis). The same sample was then sent to the laboratory. The hemoglobin concentration is converted to the hemolytic index between 0 and 555 with 1 HI unit equal to 1 mg/dL. The user can define which values are considered positive. In this study, a 100 mg/dL cutoff for hemolysis was considered positive.

The Test Procedure Using The Hemcheck Device:

1. Samples are collected in vacuum tubes and immediately tested for hemolysis.

2. Prepare a V-test I by placing it on a stable flat surface.

3. Open the protective cover of the V-test and insert the dispensing needle into the septum of the vacuum tube without opening the cover.

4. To activate the V-test, the vacuum tube is pressed down toward the dispensing needle by two firm compression in a row. Each compression should be held in the down position for at least 1 second.

5. Once activated, place the V-test in the test chamber of the Reader and press the Start button to begin the hemolysis measurement.

6. When the hemolysis measurement is complete, the results are displayed on the Reader. The result is "hemolysis" (indicator light is solid red) or "no hemolysis" (indicator light is solid green).

Statistical Analysis

Descriptive statistics of the obtained data were defined as mean±standard deviation, number, and frequency, depending on the data type. The agreement between the device and laboratory results was evaluated by kappa statistics, and the diagnostic success of the device was explained by the sensitivity, specificity, and false-positive and false-negative rates. The change in hemolysis rates according to sex, age group, and site was evaluated using the Pearson's chi-squared test. $p<=0.05$ was accepted as the level of statistical significance, and SPSS (version 23) was used for the calculations.

Results

A total of 1049 samples from patients admitted to the ED were evaluated. However, when we examined the results of some samples, we found that the biochemical parameters were not included in the content, and some of them were missing the recorded barcode numbers; thus, we excluded a total of 66 (6.3%) samples from the study. The remaining 983 samples were successfully analyzed by our hospital's routine laboratory tests and using the Hemcheck device. When the 983 samples analyzed were separated by sex, 628 (63.9%) belonged to female patients and 325 (33.1%) were male. The mean age of the patients was 49.95±19.5 years, 734 (74.7%) were younger than 65 years, and 249 (25.3%) were elderly. In the evaluation according to the application site, 935 (95.1%) patients were antecubital, 18 (1.8%) were forearm, and 30 (3.1%) were overhand.

To compare the Hemcheck results with the hospital laboratory results and determine the success of the device in detecting hemolysis based on this comparison, the compatibility of these two results was first examined in all patients (Table 1). When the table was examined, 684 (80.7%) of the patients (n=848) who did not have hemolysis according to the hospital laboratory results did not have hemolysis according to the Hemcheck device. This result demonstrates the specificity of the device. In addition, 129 (95.6%) of the patients (n=135) who had hemolysis according to the laboratory results also had hemolysis according to the Hemcheck device. This result demonstrates the device sensitivity. The number of patients who did not have hemolysis according to the laboratory results but had hemolysis according to the Hemcheck device was 164 (19.3%), indicating the false-positive rate of the device. In addition, the number of patients who had hemolysis according to the laboratory test but not according to the Hemcheck device was 6 (4.4%), indicating the false-negative rate of the device. The agreement between the device and laboratory results was good and statistically significant (Kappa=0.511±0.03 and $p<0.001$).

We also evaluated whether the agreement between the Hemcheck device results and the hospital laboratory results varied by sex and age, and the results are shown in Table 2,3.

Table 1. Compatibility between the laboratory result and the Hemcheck device

		Hemolytic index			
	n (%)	**No**	**There is**	**Total**	**p value**
Hemcheck	No	684 (80.7)	6 (4.4)	690	<0.001
	There is	164 (19.3)	129 (95.6)	293	
Total		848	135	983	

Table 2 shows that the agreement between the Hemcheck device and hospital laboratory results was similar in men and women, and significant agreement was found in both. According to the laboratory results, the success (sensitivity) of the Hemcheck device in diagnosing hemolysis was 95% in women and 96.4% in men. In addition, according to the laboratory results, the success (specificity) of the Hemcheck device in diagnosing no hemolysis was 82.1% in women and 78% in men. In addition, the probability of diagnosing hemolysis with the Hemcheck device in patients with positive laboratory results was 5% in women and 3.6% in men, and the probability of diagnosing hemolysis with the Hemcheck device in patients with negative laboratory results was 17.9% in women and 22% in men.

The rate of patients with hemolysis according to laboratory results was 12.7% in women and 15.5% in men, and there was no significant change according to sex (p=0.228, Table 2). In addition, according to the results of the Hemcheck device, the rate of patients with hemolysis was 27.7% in women and 33.5% in men, and significantly more positive results were obtained in men (p=0.050, Table 2).

Table 3 shows that all 734 patients under the age of 65 had no hemolysis according to the laboratory results. However, the Hemcheck device diagnosed 86.6% of these patients as having no hemolysis and 13.2% had hemolysis.

In geriatric patients, the correlation between Hemcheck device and hospital laboratory results was similar and statistically significant. According to the laboratory results in geriatric patients, the success (sensitivity) of the Hemcheck device in diagnosing hemolysis in patients with hemolysis was 95.5%. In addition, the success (specificity) of the Hemcheck device in diagnosing hemolysis in patients without hemolysis was found to be 41.2%. In addition, the probability of the Hemcheck device diagnosing hemolysis was 4.4% in patients with a positive laboratory result, whereas the probability of the Hemcheck device diagnosing hemolysis was 58.8% in patients with a negative laboratory result. These results showed that the false-positive rate was high among geriatric patients. In this case, the device is likely to be positive in elderly patients.

According to the laboratory results, the rate of hemolysis was 0% in people under 65 years of age, whereas it was 54.2% in geriatric patients, and the difference between them was found to be statistically significant (p<0.001, Table 3). In addition, according to the results of the Hemcheck device, the rate of patients with hemolysis was 13.2% in the group under 65 years of age, but it was 78.7% in geriatric patients, and this rate was 78.7% in geriatric patients and was significantly higher (p<0.001, Table). According to these results, the rate of hemolysis was higher in geriatric patients compared with that of both the laboratory and Hemcheck devices.

Table 4 shows that the rate of patients with hemolysis according to laboratory results and the rate of patients with hemolysis according to Hemcheck device results did not show a significant change according to location (p values 0.334 and 0.630 respectively, Table 4).

Discussion

Hemolysis accounts for approximately 40-70% of all unsuitable specimens and is the leading cause of specimen rejection (6).

Table 2. Evaluation of the compatibility between the results of the Hemcheck device and the hospital laboratory results separately in both genders

		Woman			Male			p value
		Hemolytic Index			Hemolytic Index			
		N/A (%)	Was (%)	Total (%)	N/A (%)	Was (%)	Total (%)	
Hemcheck	No	450 (82.1)	4 (5.0)	454	234 (78)	2 (3.6)	236	0.050
		98 (17.9)	76 (95)	174 (27.7)	66 (22)	53 (96.4)	119 (33.5)	
Total	Were	548	80 (12.7)	628	300	55 (15.5)	355	
p				0.228				

Table 3. Evaluation of the compatibility between the results of the Hemcheck device and the hospital laboratory results according to the age group

		Under 65 years old			Geriatric			p value
		Hemolytic Index			Hemolytic Index			
		No (%)	Yes (%)	Total (%)	No (%)	Yes (%)	Total (%)	
Hemcheck	No	637 (86.8)	0	637	47 (41.2)	6 (4.4)	53	<0.001
		97 (13.2)	0	97	67 (58.8)	129 (95.6)	196 (78.7)	
Total	Yes	734		734	114	135 (54.2)	249	
p					<0.001			

This may lead to an increase in patient waiting time and delay in diagnosis. Yilmaz Başer et al. (12) emphasized the importance of early diagnosis and treatment for mortality. The purpose of this study was to evaluate the ability of the Hemcheck device to predict hemolysis-related errors in patients presenting to the ED for biochemistry testing.

In the study by Lippi et al. (9) when hemolyzed specimens were classified by clinic, the highest prevalence was 8.8% for specimens collected in the ED. In a study by Mielke et al. (13) focusing on pediatric patients, the rate of hemolysis in EDs was 14%, and the highest prevalence was reported in infants (0-1 years) (20.1%).

The American Society of Clinical Pathology recommends a hemolysis rate of 2% or less, but this standard may be difficult to achieve in the intensive care unit and ED (14). To reduce the rate of hemolysis in the ED, new studies should be conducted to improve blood collection techniques and apply new methods. As a result of our study, based on the laboratory system of our hospital, the specificity of the Hemcheck device was 80.7% and the sensitivity was 95.6%. In a study conducted by Duhalde et al. (15) using the same device and blood gas analysis, the specificity of the same device was found to be 99%, and the sensitivity was 80% when compared with their own laboratories.

These differences provide important information about how the device performs under different laboratory and testing conditions. The high specificity in the study by Duhalde et al. (15) suggests that the device is very effective at reducing false-positive rates, but the sensitivity of 80% suggests that some hemolyzed samples may be missed. On the other hand, the high sensitivity in our study indicates that the device was more successful in detecting hemolyzed specimens, but the specificity of 80.7% indicates that there may be some false positives.

One of the most critical measurements in the ED is the change in a patient's potassium level. Evaluation and treatment of hyperkalemia are priorities in the ED. However, many blood samples falsely report high potassium levels during collection because of hemolysis. In the case of high potassium levels due to hemolysis, a repeat sample must be drawn to confirm the test, which can lead to prolonged hospital stay, multiple blood draws, increased use of healthcare resources, and unnecessary risk to patients (16). In a study by Lam et al. (16), potassium levels were shown to be affected even by the use of hand sanitizers (17). Asirvatham et al. (17) found that all types of mechanical factors that cause hemolysis affect potassium levels. Changes in potassium levels are usually expected in critically ill ED patients. However, hemolysis in samples collected and the resulting changes in potassium levels can lead to misdiagnosis (15). Early detection of hemolysis in critically ill patients may help prevent these errors. In conclusion, early detection of hemolysis in the ED plays a critical role in patient safety and healthcare efficiency. The widespread use of hemolysis detection devices and methods can significantly contribute to preventing such errors and improving the quality of healthcare.

In our study, there was no significant difference in the hemolysis rates of blood samples obtained anatomically from the antecubital fossa, forearm, or upper hand. Of course, the fact that most of the samples were obtained from the antecubital fossa may have influenced the results. However, in a study conducted by Barnard et al. (7), blood samples obtained from the distal part of the antecubital fossa were found to be significantly more likely to be hemolyzed than those obtained from the antecubital fossa.

According to the laboratory results of our hospital, the rate of hemolysis was 0% in people under 65 years of age, whereas it was 54.2% in geriatric patients, and the difference between them was found to be statistically significant ($p<0.001$, Table 3). However, according to the results of the Hemcheck device, the rate of hemolysis was 13.2% in the group under 65 years of age, but it was 78.7% in geriatric patients, and this rate was 78.7% in geriatric patients and was significantly higher ($p<0.001$, Table). According to these results, the hemolysis rate was higher in geriatric patients compared with that of both the laboratory and Hemcheck devices. In the study by Jacob E et al. (18), similar to our study, the age of the participant was found to be the only demographic characteristic significantly associated with hemolysis (median age 62 years vs. 70 years, $p=.006$).

Study Limitations

Our study was prospective and included approximately 1000 patients. The entire procedure was recorded by two observing physicians. The limitation of this study was that the Hemcheck device could not detect the rate of hemolysis because it only responded to the presence or absence of hemolysis. In addition,

Table 4. Frequency of hemolysis obtained from the laboratory and obtained from the Hemcheck device by location

		Hemolytic index	Hemcheck conclusion	Total (n)
		+	+	
Location	Antekübital	125 (13.4)	276 (29.5)	935
	Forearm	4 (22.2)	7 (38.9)	18
	Over hand	6 (20)	10 (33.3)	30

the fact that the nurses who draw blood on each shift differed may have affected the hemolysis situation.

Conclusions

According to our study, the success of the Hemcheck device in detecting hemolysis from the front was sufficient. It has been observed that this device can reduce negative effects, such as disruption of patient diagnosis and treatment due to hemolysis in EDs, prolonged patient waiting time, and increased workload of emergency personnel.

Ethics

Ethics Committee Approval: This study was conducted in accordance with the tenets of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of İstanbul Medeniyet University Göztepe Training and Research Hospital (decision number: 2021/0429, date: 25.08.2021).

Informed Consent: Informed consent was obtained from all participants who voluntarily participated in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.A., A.C., M.S.A., F.K.İ., Concept: S.A., M.K., M.S.A., F.K.İ., Design: S.A., A.C., M.S.A., F.K.İ., Data Collection or Processing: S.A., M.K., M.S.A., Analysis or Interpretation: S.A., M.S.A., K.A., F.K.İ., Literature Search: S.A., M.K., K.A., Writing: S.A., A.C., M.S.A., F.K.İ.

Conflict of Interest: The authors declare that they have no conflict of interest.

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