Research Article

Merve Sena Odabasi*, Melahat Dirican, Arzu Yilmaztepe Oral and Guven Ozkaya

Impact of preventive actions on rejection rates in the preanalytical period

Preanalitik dönemde önleyici faaliyetlerin reddetme oranlarına etkisi

https://doi.org/10.1515/tjb-2018-0119
Received March 29, 2018; accepted February 28, 2019; previously published online October 15, 2019

Abstract

Background: It is responsibility of medical laboratories to determine and reject nonconforming samples as well as take preventive actions. In this study, we examined reasons and percentages of rejected samples. We also investigated impact of the preventive actions on decreasing the rejection rates.
Materials and methods: Reasons for rejection were determined by Pareto analysis. Sigma analysis was used for each month to evaluate the ratios and compare with other studies. Some preventive actions were taken to reduce the rejection rates. Pearson's chi square test was used to evaluate effects of preventive actions. Significance level was determined as $p < 0.05$.
Results: Most of the rejected samples consisted of samples not received by the laboratory, haemolysed and insufficient samples. The percentages of samples not received by the laboratory and insufficient samples were reduced from 3.80% to 1.94% and 0.33% to 0.31% respectively, while haemolysed samples percentage was increased from 2.83% to 3.37% after the improvement actions. Also, sigma levels for samples not received by the laboratory and haemolysed samples were at the minimum while insufficient samples were at a reasonable level.
Conclusion: Improvement actions achieved statistically significant decreases for samples not received by the laboratories for a long-term.

Keywords: Sigma level; Pre-analytical error; Rejection rates.

Öz

Amaç: Uygunsuz numuneleri tespit etmek, reddetmek ve önleyici faaliyetlerde bulunmak tıbbi laboratuvarların sorumluluğundadır. Bu çalışmada reddedilen örneklerin nedenlerini ve yüzdelerini inceledik. Ayrıca önleyici faaliyetlerin reddetme oranlarını düşürmedeki etkisini araştırdık.
Gereç ve Yöntem: Reddetme nedenleri Pareto analizi ile belirlendi. Aylık olarak oranları değerlendirmek ve diğer çalışmalarla karşılaştırmak için Sigma analizi kullanıldı. Reddetme oranlarını azaltmak için bazı önleyici önlemler alındı. Önleyici faaliyetlerin etkilerini değerlendirmek için Pearson ki kare testi kullanıldı. Anlamlılık düzeyi $p < 0.05$ olarak belirlendi.
Bulgular: Reddedilen örneklerin çoğu laboratuvara teslim edilmeyen, hemolizli ve yetersiz numunelerden oluşmaktaydı. Düzeltici faaliyetlerle, laboratuvara teslim edilmeyen ve yetersiz numunelerin yüzdeleri sırasıyla % 3.80'den % 1.94'e, % 0.33'den % 0.31'e düşerken, hemolizli numunelerin yüzdesi % 2.83'ten % 3.37'ye yükseldi. Ayrıca, laboratuvara teslim edilmeyen ve hemolizli numuneler için sigma seviyeleri minimum seviyede iken, yetersiz numuneler için kabul edilebilir düzeyde idi.
Sonuç: Düzeltici faaliyetler laboratuvara teslim edilmeyen numunelerde istatistiksel olarak anlamlı düşüş sağladı.

Anahtar kelimeler: Sigma düzeyi; Preanalitik hata; Reddetme oranları.

***Corresponding author: Merve Sena Odabasi,** Department of Medical Biochemistry, Uludag University Medical Faculty, Bursa, Turkey, e-mail: senadur@uludag.edu.tr. https://orcid.org/0000-0003-3774-4241
Melahat Dirican and Arzu Yilmaztepe Oral: Department of Medical Biochemistry, Uludag University Medical Faculty, Bursa, Turkey, e-mail: mdirican@uludag.edu.tr (M. Dirican); arzuy@uludag.edu.tr (A. Y. Oral). https://orcid.org/0000-0002-4956-5278 (M. Dirican); https://orcid.org/0000-0002-8962-9758 (A.Y. Oral)
Guven Ozkaya: Department of Biostatistics, Uludag University Medical Faculty, Bursa, Turkey, e-mail: guvenozkaya@gmail.com

Introduction

The detection, prevention and decrease of unwanted events in laboratories have great importance. So analysing the errors in laboratories has drawn greater attention recently, aiming to detect, prevent or decrease adverse events. Since the beginning of the sixties, analytical quality control has been initiated and focused on issues such as quality management, the use of quality objectives, and the determination of processes, and an approach to quality assurance has been developed [1]. In this respect, the ISO/TS 22367 standard specifies how risk management should be implemented in the structure, organization, and quality management system of clinical laboratories, and it emphasizes the phases before and after analysis [2]. Errors in clinical laboratories are measured and controlled by means of indicators that allow objective evaluation of the problem and comparison with different laboratories [1]. According to ISO 15189, laboratory managers should apply quality indicators systematically to follow the laboratory contribution for clinical evaluation of patients [2].

The analytical phase, which is one of the three basic processes in the clinical laboratory, is the highest standardized process with well-defined indicators and internationally accepted definitions. All studies acknowledge that extra analytical (especially pre-analytical) processes are the most common of the faults. Since these processes involve the participation of various personnel (physicians, medical laboratory specialists, nurses, laboratory technicians, phlebotomists, etc.), the management of this phase is very critical and difficult. The pre-analytical phase errors are responsible for the majority of the total errors (46–68.2%) in laboratory [3]. Various pre-analytical errors are observed, such as the suitability of the test request, patient authentication error, timing errors related to sample retrieval and preparation, haemolytic or lipemic sera, inappropriate transport, insufficient sample, and inappropriate tube usage [4].

The personal impact on sample collection is an important factor, and the pre-analytical error rate for phlebotomists is 2–4 times higher than that of laboratory staff [5]. Due to blood collection errors, sample incompetence is generally more commonly observed in blood sample collection by nurses who do not have adequate experience and training in clinics compared to phlebotomists [6].

The percentages of reasons for rejected samples in laboratories, are also one of the quality indicators. According to the Health Quality Standards (SBL-03), which are prepared by the Turkish Ministry of Health, it is the responsibility of the medical laboratories to identify and reject unsuitable samples for analysis, to evaluate the rejected sample frequency at regular intervals and to initiate preventive actions when necessary [7]. All of these are necessary for clinical laboratories to improve performance and patient safety [6].

In this study, the aim was to analyse the rejected samples in terms of the reasons and the departments they are sent from as well as to evaluate the impact of the improvement actions on the rejection rates.

Materials and methods

All data were obtained from the Uludağ University Health Practice and Research Hospital, which is an 896 bed care centre. The samples rejected in the Biochemistry Laboratory between 01.05.2016 and 01.04.2017 were examined monthly in terms of the reasons and the rejecting departments.

Clinical chemistry, immunochemistry, hematology, glycated hemoglobin (HbA1c), coagulation, erythrocyte sedimentation rate (ESR) and urinalysis tests conducted on these dates were included in the study. Different tubes were used for each assay. Na-citrate vacutainer tubes for coagulation, with gel separator for clinical chemistry and immunoassay, K_2EDTA tubes for hematology, ESR and HbA1c and non-gel separator tubes for urine tests were used. For inpatients, phelobotomist picked up the requisition and generated barcoded labels from the system, properly sticked on pertinent tubes and went to the bedside to check patient's identification. For outpatients, this procedure were done as follows: the barcoded appropriate tubes were given to patients by the staff and then to the phlebotomist. After checking the personal information, the blood is collected by vacutainer. Then, the samples were transferred to the laboratory by the trained staff for processing. Only for chemistry and immunochemistry tests, blood samples were allowed to clot about 20 min, then centrifuged at 2520 g for 7 min. For coagulation tests citrated tubes are immediately centrifugated at 2200 g for 10 min. After centrifugation, all samples were delivered to the analyzers. There is direct spectrophotometric assessment for hemoglobin as haemolysis-index (H-index), triglyceride as lipemia index (L-index) and bilirubin as icteric index (I-index) in our clinical chemistry analysers. This measurement allows us to evaluate large number of serum or plasma samples for interferences mentioned above in a rapid and inexpensive way.

The reasons for rejection were determined by Pareto analysis. According to the Pareto rule, the most important 20% of the causes were responsible for 80% of the

results, and this highlights areas of non-compliance and priority improvement goals. In this study, the reasons for rejection were ranked according to their numerical size and percentages, and afterwards, cumulative percentages were taken. The causes of rejection within a cumulative 90% were identified and assessed. Percent rejection rates for samples not received and insufficient samples were calculated by the rejected sample number × 100/total sample number formula; the percentage rejection rate for the haemolysed samples was calculated by haemolysed samples × 100/total number of samples that could be affected by haemolysis.

The pre- and post-preventative action rates of samples not received by the laboratory and haemolysed and/or insufficient were defined on the basis of the precautions taken. Three preventive actions were taken: (1) written notification of the error to the departments through the chief physician; (2) face-to-face interviews with heads of departments; and (3) corrective and preventive action (CAPA). CAPA is the most formal preventive action by providing information for the hospital quality management. CAPA is a formal process for removing an existing or potential problem. The process begins with filling and sending a special form (CAPA form) to the Quality Management Unit, in which the cause of the problems and necessary steps to achieve the solution are identified by the laboratory manager. The Quality Management Unit, connected to hospital management, evaluates the form and gives information to the related head of the department where the problem is observed. After the advisement by the Quality Management Unit, necessary precautions were taken by the head of department, for example, informing the staff about the problem. The process is ended by giving feedback about the corrective actions performed to the Quality Management Unit.

Each category included different time intervals because the quality meetings held at different time intervals. Data evaluated by dividing them to following five groups: before written notification of error to the departments through the chief physician (May); after written notification of error to the departments through the chief physician (June, July and August); face-to-face interviews with clinicians (September); pre-CAPA period (October and November); and post-CAPA period (December, January, February and March). There was no reference as to how the separation between the categories should be made. To solve the causes of high rejection rates at the end of the August face to face interviews made by the head of departments. The rates of rejected samples, after face to face interviews, decreased in the following month (September) but it was not a permanent solution. The rejection rates returned to the initial levels of study in the next months (November and December). Therefore, only the results of September utilised for estimating the impact of face to face interviews. The results of November and December were used as a pre-CAPA period to evaluate the CAPA effect better. The results belonging September is not included to rule out the effect of low rejection rates caused by face to face interviews.

Pearson's χ^2 test was used to compare data. The significance level was determined as $p < 0.05$.

The data were converted to a six sigma scale using the Westgard calculator to predict the degree of control over the processes and to compare the data given in the literature. For each quality indicator, the rejection number and the total number of samples were entered online at https://www.westgard.com/six-sigma-calculators.htm, and the sigma level was determined. An error rate of 6.68% according to the equivalence table between the Westgard sigma level and the number of defects per million corresponds to a sigma of 3, indicating an unacceptable threshold value; the error rate of 0.62% corresponds to a sigma of 4, indicating that it is well-controlled.

Results

The Pareto analysis was performed to determine the reasons for rejection. In this analysis for any 1 month, it was observed that 91% of the rejected samples were samples not received by the laboratory (52%), haemolysed samples (31%) and insufficient samples (8%), respectively. The vast majority of samples not received by the laboratory were urine samples (Figures 1 and 2).

In May 2016, the total number of samples accepted in the laboratory was 122,232, while the number of samples not received by the laboratory was 4648 (3.80%). Emergency services with 733 (15%) and the paediatric clinics with 471 (10%) numbers were the two most common services responsible for not received samples. The high rejection rates were due to not received urine samples, since urine tests were requested before the samples were collected. In the cardiology clinic, the number of samples not received by the laboratory was 293, whereas in the orthopaedic clinic, this number was 199. In this month, the number of samples that could be affected by haemolysis was 43,946, while the number of haemolysed samples was 1245 (2.83%). The number of insufficient samples was 408 (0.33%). The high rates of insufficient and haemolysed samples were due to same clinics too. Thus, an error declaration was made by the chief physician to these departments to take care of this

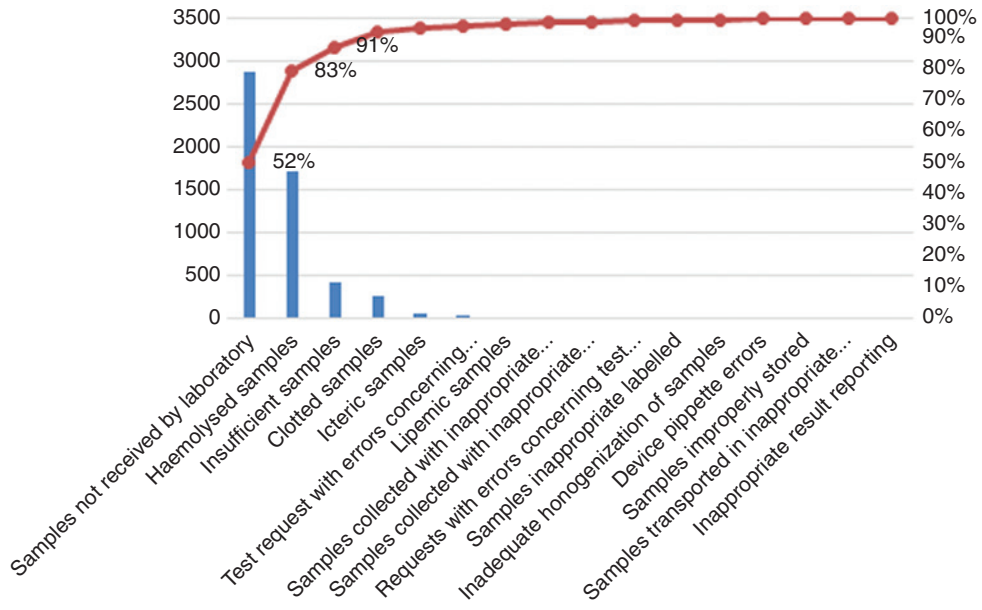


Figure 1: Pareto analysis for a randomly selected month.

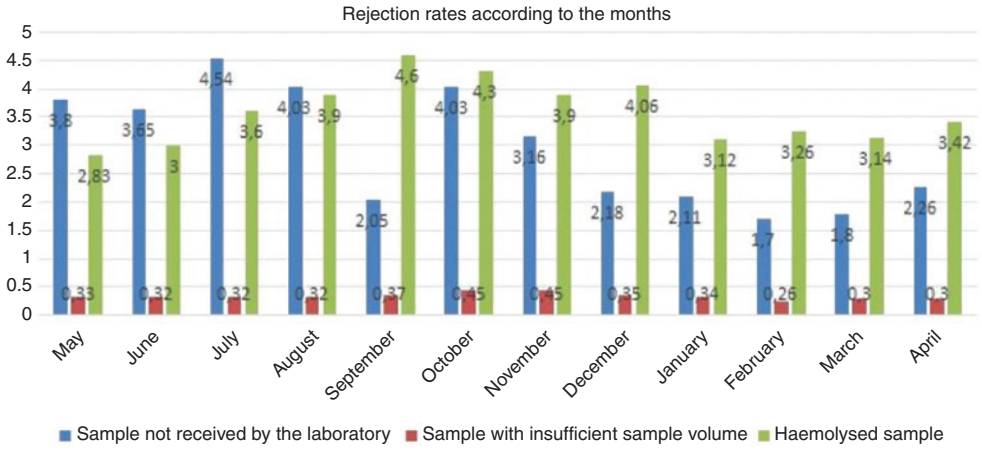


Figure 2: Rejection ratio according to the months.

issue. Therefore, May was evaluated as the period before written notification of the error.

After notification of the departments, the results were analysed in 3 months' time. The total number of accepted samples was 350,456 in June, July and August, and the number of samples not received by the laboratory was 14,205 (4.05%), the number of haemolysed samples was 4532 (3.54%) and the number of insufficient samples was 1137 (0.32%). At the end of August, face-to-face interviews with the heads of emergency services as well as the paediatric, orthopaedic, cardiology, nephrology, oncology, gastroenterology, neurosurgery and general surgery clinics were conducted, and the high rates of samples not received by the laboratory and haemolysed samples were reported. Preventive actions were discussed with heads of these departments to overcome this problem. These 2 months were analysed as the period after written notification of error to the departments through the chief physician.

In September, after the interview, the number of samples not received by the laboratory was 2527 (2.35%). The rates of samples not received by the laboratory decreased by 50%, except for the oncology clinics. The numbers of insufficient samples and haemolysed samples were 406 (0.38%) and 1826 (4.61%), respectively. It was found that the highest rates were mainly due to the samples from the paediatric emergency services as well as paediatric and cardiology clinics. The percentages of this month were used for estimating the impact of face-to-face interviews with the heads of departments.

In October and November, it was noted that all of rates were increased except for that for haemolysed samples. The average rejection rates for these 2 months of samples not received by the laboratory, insufficient samples and haemolysed samples were 3.64%, 0.45% and 4.17%, respectively. Accordingly, improvement action was started by filling out the corrective and preventive activity form for the departments whose rates were determined to be high in the quality meeting held at the beginning of December. The rejection rates of October and November were used as pre-CAPA data. Rejection rates that fell after face-to-face interviews in September were not included in the pre-CAPA data.

After the corrective preventive activity, in December, January, February and March, in particular, the percentage of samples not received by the laboratory decreased. The average rejection rates for these months were 1.94% for samples not received by the laboratory, 3.37% for the haemolysed samples and 0.31% for insufficient samples, which were used as post-CAPA data (Table 1).

When the impacts of the preventive actions were evaluated, there was a significant decrease in only samples not received by the laboratory after the CAPA when compared to the mentioned preventive actions ($p < 0.001$) (Table 2).

Table 1: Rejection rates after corrective and preventive activity.

After corrective preventive activity	Samples not received by laboratory (%)	Insufficient samples (%)	Haemolysed samples (%)
December	2.18	0.35	4.06
January	2.11	0.34	3.12
February	1.70	0.26	3.26
March	1.80	0.30	3.14
Average	1.94	0.31	3.37

Discussion

Pre-analytical errors account for approximately 70% of total laboratory errors and have significant clinical and economic impact in medical care. The pre-analytical stage should be tightly controlled so that the laboratory can attain a sufficient performance level. Quality indicators are useful performance monitoring tools for the pre-analytical phase of the test process [8].

In the literature, Jandial and Gosai found that the main reasons for rejection in a university hospital study in India were insufficient samples (78%), haemolysed samples (18.92%) and lipemic samples (1.81%) [9]. Similarly, Gajjar et al. reported that the most common reason for rejection was insufficient samples (82%) [10]. Similarly, Atay et al. found the most common reason for rejection was insufficient samples (34%), clotted samples (24%) and haemolysed samples (8%) at the İzmir Ataturk Training and Research Hospital [6]. A like Aykal et al. reported that the most frequent cause of rejection was insufficient samples (38%) and the second was haemolysed samples (34%) at the Antalya Training and Research Hospital. They also reported that before preventive actions (face to face interview, clinical staff education, etc.) rejection rate was found 0.25% whereas rejection rate has been found to decrease after preventive actions [11]. Gimenez-Marin et al. reported that the most frequent cause of rejection was haemolysed samples (87%) and that the second most frequent was urine samples not received by the laboratory (1.6%) [1]. Simundic et al. also reported the most common rejection as haemolysed samples (65%) [12]. Grecu et al. reported the main reasons for rejection as haemolysed samples (46.4%), clotted samples (43.2%) and samples not received by the laboratory (6.4%) for the study they carried out for 1 year [8].

Table 2: Changes in the rejection rates of samples not received by the laboratory, haemolysed and insufficient samples with the preventive actions.

Preventive actions	Samples not received by laboratory		Insufficient samples		Haemolysed samples	
	%	Sigma level	%	Sigma level	%	Sigma level
Before a written notification of error to the departments through the chief physician	3.8	3.3	2.83	3.5	0.33	4.3
After a written notification of error to the departments through the chief physician	4.05	3.3	3.54	3.4	0.32	4.3
The first month after face-to-face interviews with clinicians	2.35	3.5	4.61	3.2	0.38	4.2
Pre-CAPA period	3.64	3.3	4.17	3.3	0.45	4.2
Post-CAPA period	1.94	3.6	3.37	3.4	0.31	4.3

CAPA, Corrective and preventive action.

The six sigma scale was used to compare the results with previous studies. Kulkarni et al. [13] indicated that a pre-analytical quality indicator with a sigma value of 4 and above was well controlled, whereas Grecu et al. [8] divided the sigma values into four levels for pre-analytical errors (very good: sigma ≥5; good: sigma of 4–5; minimum: sigma of 3–4; and unacceptable: sigma <3) and suggested that these classifications made it easier to assess improvement in laboratory services.

In this study, sigma values ranged from 3.3 to 3.6 for samples not received by the laboratory. According to the above classification, this sigma value is above the unacceptable limit but is in the position to be improved. In the study conducted by Grecu et al. the sigma value of samples not received by the laboratory was stated as 4.8 [8]. Haemolysed samples had sigma values between 3.2 and 3.5. The sigma value was found to be at the minimum level according to the above classification and was similar to those of other studies. Grecu et al. found the sigma value to be 4.2 in the study they performed [8]. In the study conducted by Sciacovelli et al. the sigma value for haemolysed samples were found to be 3.6 [14]. The sigma value for the insufficient samples ranged from 4.2 to 4.3. According to the classification, the sigma level was at a good level. Sciacovelli et al. [14] reported the sigma level for insufficient samples as 4.8, whereas Gajjar et al. [10] reported it as 3.8. Kulkarni et al. found a sigma level of 4.3 for insufficient samples [13]. Aykal et al. reported that before preventive actions, sigma value of rejected samples was found between 3.5 and 3.65, whereas sigma value of rejected samples was found between 3.75 and 3.87 after interview [11].

International professional laboratory organizations are becoming increasingly interested in performance standards. To reduce laboratory errors, the International Federation of Clinical Chemistry (IFCC) and Laboratory Errors and Laboratory Medicine on Patient Safety have developed a number of specific quality indicators, and they have also defined quality specifications for these indicators. Of the 56 quality indicators, 34 were focused on the pre-analytical phase [15]. Three levels, minimum, desired, and optimum levels, were defined for these quality indicators, and values below the minimum were considered unacceptable [8].

According to IFCC values, post-CAPA rejection rates of samples not received by the laboratory (1.94%) and haemolysed samples (3.37%) were above the unacceptable level and required improvement; the rejection rate of insufficient samples (0.32%) was within the optimum level.

Haemolysis is one of the most common sources of error in clinical laboratories and accounts for approximately 60% of rejected samples during studies [16]. In this study, the haemolysis sigma value was similar to other study data but at the minimum level. It was observed that conformity with the sampling and transport procedures as well as with the centrifuge procedures were important for improving the haemolysed sample rejection rate.

Insufficient samples was the third most common cause of rejection. It is known that it is difficult to collect large enough blood specimens, especially from neonates, children and oncology patients. As expected, in this study, the paediatric clinics were the leading department with the highest number of insufficient samples. Insufficient samples lead to longer coagulation times in tests such as the prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time, and lower fibrinogen level. As a matter of fact, Lippi et al. have found significant differences in outcomes if the citrate tube target volume is less than 89% for aPTT, less than 78% for fibrinogen and less than 67% for coagulation factor VIII. Therefore, citrated tubes with a target volume of less than 80% should be rejected [17]. In this study, it was observed that the insufficient sample rejection rate was similar to the data from other studies and had a good sigma level. However, when insufficient sample rates were analysed according to the clinics, it was observed that the ratio in the paediatric clinics was higher than that of other clinics. It has been concluded that the use of micro-tubes may be beneficial to reduce this rate in paediatric clinics.

It was found that the ratio of samples not received by the laboratory, which is the first reason for rejection, was higher when compared to other study data. When the cause of this high ratio was questioned, it was observed that the clinics had made additional unnecessary test requests at night hours for samples that must be requested in the morning. It was determined that urine specimens not received by the laboratory were responsible for the high rejection rate of emergency and paediatric emergency services. To reduce this rate, it may be suggested that clinics other than emergency and paediatric emergency services should make requests immediately before sampling, while emergency and paediatric emergency services should make urine requests after taking urine samples.

Although many preventive actions such as error notification through the chief physician and face-to-face interviews with clinicians were taken in order to decrease the rejection rates, which are important in terms of quality standards in healthcare, it was observed that only CAPA achieved statistically significant decreases in the rejection rates for longer periods. We think that CAPA, which is an official procedure that is linked to hospital management,

is considered seriously by the staff compared to face to face interviews and written notifications, which are carried out through bilateral relations. The rotation of the staff and the lack of knowledge among the entire staff could also be the possible cause of insufficient improvement with face to face interviews and written notifications.

In conclusion, the rejection rates can be improved in cooperation with the hospital management and the laboratory staff as well as all the other employees involved in this process.

Acknowledgements: The authors wish to thank to Prof. Dr. Esma Gür for her assistance in preparing this paper. We also thank the laboratory staff for their technical help.

References

1. Giménez-Marín A, Rivas-Ruiz F, Pérez-Hidalgo MD, Molina-Mendoza P. Pre-analytical errors management in the clinical laboratory: a five-year study. Biochem Medica 2014;24:248–57.
2. International Organization for Standardization. ISO 15189:2012 – Medical laboratories – requirements for quality and competence. n.d. https://www.iso.org/standard/56115.html.
3. Plebani M. Errors in clinical laboratories or errors in laboratory medicine? Clin Chem Lab Med 2006;44:750–9.
4. Carraro P, Zago T, Plebani M. Exploring the initial steps of the testing process: frequency and nature of pre-preanalytic errors. Clin Chem 2012;58:638–42.
5. Çuhadar S. Preanalytical variables and factors that interfere with the biochemical parameters: a review. OA Biotechnol 2013;2:19.
6. Atay A, Demir L, Cuhadar S, Saglam G, Unal H, Aksun S, et al. Clinical biochemistry laboratory rejection rates due to various types of preanalytical errors. Biochem Medica 2014;24:376–82.
7. Sağlıkta Kalite Standartları Hastane. http://dosyamerkez.saglik.gov.tr/Eklenti/3460,skshastanesetiv5r1pdf.pdf?0w (accessed February 27, 2018).
8. Grecu DS, Vlad DC, Dumitrascu V. Quality indicators in the preanalytical phase of testing in a stat laboratory. Lab Med 2014;45:74–81.
9. Jandial S, Gosai V. Sample rejection rate in clinical biochemistry laboratory of a tertiary care centre. Int J Res Med 2017;5:127–31.
10. Gajjar M, Patel A, Jain S. Monitoring of quality indicators in pre analytical phase of testing in the clinical biochemistry laboratory of a tertiary care hospital attached with government medical college. IOSR J Dent Med Sci 2016;15:2279–861.
11. Aykal G, Yegin A, Aydin O, Yilmaz N, Ellidag HY. The impact of educational interventions on reducing the rejection rates in the preanalytical phase. Turk J Biochem 2014;39:562–6.
12. Simundic A-M, Nikolac N, Vukasovic I, Vrkic N. The prevalence of preanalytical errors in a Croatian ISO 15189 accredited laboratory. Clin Chem Lab Med 2010;48:1009–14.
13. Kulkarni S, Ramesh R, Srinivasan AR, Wilma CR, Silvia D. Evaluation of preanalytical quality indicators by six sigma and Pareto's principle. Indian J Clin Biochem 2018;33:102–7.
14. Sciacovelli L, Sonntag O, Padoan A, Zambon CF, Carraro P, Plebani M. Monitoring quality indicators in laboratory medicine does not automatically result in quality improvement. Clin Chem Lab Med 2011;50:463–9.
15. Plebani M, Chiozza ML, Sciacovelli L. Towards harmonization of quality indicators in laboratory medicine. Clin Chem Lab Med 2013;51:187–95.
16. Koseoglu M, Hur A, Atay A, Cuhadar S. Effects of hemolysis interference on routine biochemistry parameters. Biochem Medica 2011;21:79–85.
17. Lippi G, Salvagno G, Montagnana M, Lima-Oliveira G, Guidi G, Favaloro E. Quality standards for sample collection in coagulation testing. Semin Thromb Hemost 2012;38:565–75.