Specimen rejection in laboratory medicine: Necessary for patient safety?

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Abstract

Introduction: The emergency laboratory in Hacettepe University Hospitals receives specimens from emergency departments (EDs), inpatient services and intensive care units (ICUs). The samples are accepted according to the rejection criteria of the laboratory. In this study, we aimed to evaluate the sample rejection ratios according to the types of pre-preanalytical errors and collection areas.

Materials and methods: The samples sent to the emergency laboratory were recorded during 12 months between January to December, 2013 in which 453,171 samples were received and 27,067 specimens were rejected.

Results: Rejection ratios was 2.5% for biochemistry tests, 3.2% for complete blood count (CBC), 9.8% for blood gases, 9.2% for urine analysis, 13.3% for coagulation tests, 12.8% for therapeutic drug monitoring, 3.5% for cardiac markers and 12% for hormone tests. The most frequent rejection reasons were fibrin clots (28%) and inadequate volume (9%) for biochemical tests. Clotted samples (35%) and inadequate volume (13%) were the major causes for coagulation tests, blood gas analyses and CBC. The ratio of rejected specimens was higher in the EDs (40%) compared to ICUs (30%) and inpatient services (28%). The highest rejection ratio was observed in neurology ICU (14%) among the ICUs and internal medicine inpatient service (10%) within inpatient clinics.

Conclusions: We detected an overall specimen rejection rate of 6% in emergency laboratory. By documentation of rejected samples and periodic training of healthcare personnel, we expect to decrease sample rejection ratios below 2%, improve total quality management of the emergency laboratory and promote patient safety.

Key words: clinical laboratory services; total quality management; patient safety; preanalytical phase; preanalytical error

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Introduction

Precision, accuracy, and short turnaround time (TAT) are important in effective emergency laboratory services. The types of laboratory errors are classified as preanalytical, analytical, and postanalytical, depending upon the time of presentation. Laboratory specialists have been demonstrated that 70% of errors occur in the preanalytical phase which is an important component of laboratory medicine (1,2). The International Organization for Standardization (ISO) 15189:2012 standard for laboratory accreditation defines the preanalytical phase as **"**processes that start, in chronological order, from the clinician's request and include the examination request, preparation and identification of the patient, collection of the primary sample(s), and transportation to and within the laboratory, and end when the analytical examination begins" (3).

Plebani *et al*. (4,5) states that the preanalytical phase should be subdivided into pre-preanalytical phase and preanalytical phase. Pre-preanalytical phase includes test request, patient or sample identification, sample collection, handling and transport, whereas preanalytical phase involves the steps of sample preparation for analysis such as centrifugation, aliquoting and sorting. It has

been demonstrated that most errors occur in the pre-preanalytical phase by healthcare personnel who are not under the control of the laboratory, whereas preanalytical phase starts following specimen acceptance by the laboratory staff. For the prevention of preanalytical errors, the most reliable approach is to construct preanalytical standardization (6).

Quality in laboratory medicine has been defined as the guarantee that each single step throughout the total testing process (TTP) is correctly performed (7). Due to the improvements in analytical techniques and instrumentation, a 10-fold reduction in the analytical error rate has been achieved in the past decades. However, the preanalytical errors have been found to be much more vulnerable in the TAT (8). Traditionally, preanalytical phase errors were classified as identification errors and sample problems. The IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) working group of 'Laboratory Errors and Patient Safety' (WG-LEPS) has identified several Quality Indicators (QIs) related with all stages of the TTP; preanalytical phase quality indicators include the appropriateness of test selection, patient/sample identification, samples collected in inappropriate containers or with insufficient volumes, hemolyzed or clotted samples, improperly stored samples or samples damaged in transport (9-11).

Shortening turn-around-time (TAT) is one of the quality indicators in emergency laboratories. We hypothesized that the improvement in TAT is related with correct pre-preanalytical phase procedure; receiving the appropriate sample from the right patient on time is necessary to achieve reliable laboratory results and promote patient safety. Hence, the aim of the study was to evaluate the sample rejection ratios (SRRs) at the emergency laboratory of Hacettepe University hospitals, to determine the types and frequencies of preanalytical errors and plan improvements in patient outcomes.

Materials and methods

In this study, the data about the samples sent to the emergency laboratory during 12 months from January 01 to December 31, 2013 was evaluated. For this study, the laboratory data was retrieved from the intra-institutional laboratory information system (LIS, LAB Asistan 2.0, TENAY) which is connected to HIS (hospital information system).

Laboratory setting

Hacettepe University Hospitals is one of the largest university teaching hospital in Turkey with 1000-bed capacity consisting of the Adult Hospital and Children's Hospital. A total of approximately 980,000 samples were performed *per* year in the clinical pathology laboratory and 45% of these tests were run in the emergency laboratory, which operates with independent staff for 24 hours, 7 days a week, receiving samples from inpatient services, intensive care units (ICUs), adult and pediatric emergency departments (ED). The variable work shift is categorized into 2 groups as day (8:30 AM to 4:30 PM) and night (4:30 PM to 8:30 PM); seven laboratory technician works at day shift and four works at night shift. Additionally, two specialized laboratory secretary for daytime and one for night shift, receive samples and decide to accept or reject samples according to the rejection criteria of our laboratories as given in Table 1. The secretaries were trained 1 week to specialize on rejection criteria and the training program was updated every 6 months by laboratory specialists.

Table 1. The rejection criteria of the emergency laboratory.

Sample rejection criteria of the emergency laboratory
• Improper test requests (incomplete, duplicate, errors in test input, inconsistent information)
• Inappropriate transport (transport temperature, light exposure, delayed transport time)
• Specimens without barcodes or unsuitable barcodes
• Misidentification (unlabeled, mislabeled or mismatched samples)
• Improper container or tube (including precious samples such as cerebrospinal fluid)
• Insufficient specimen volume (inappropriate blood/anticoagulant ratio)
• Incorrect preservation, storage
• Lipemic specimen
• Hemolyzed specimen
• Clotted samples with fibrin

All of the samples are hand delivered to the emergency laboratory in which 23 analyzers are used: 2 clinical chemistry analyzer (Beckman Coulter AU680 chemistry system), 1 immunoassay systems (ADVIA Centaur CP), 2 hemostasis analyzer (Siemens BCS XP system), 2 chemistry analyzers for therapeutic drug monitoring (Roche Integra 400), 2 hematology analyzer (Beckman Coulter LH780), 2 automated sedimentation rate analyzer (ALIFAX), 3 blood gas analyzers (Siemens RAPIDLab 1200), 2 urine chemistry (Beckman Coulter Iris urine analyzer), 1 automated blood culture system (Biomerieux BACT/ALLERT 3D), 1 lithium analyzer (Medica Easy Light Electrolyte Analyzer), 1 osmometer (Advanced Instruments 3320) and 1 spectrophotometer (Schimadzu UVmini-1240). The range of tests performed in emergency laboratory includes biochemical tests, electrolytes, complete blood count (CBC), osmolality (serum, urine), cardiac markers (myoglobin, CK-MB, troponin I, B-type natriuretic peptide), coagulation panel (PT, aPTT, fibrinogen, D-dimer), therapeutic drug monitoring (TDM), hormones (beta-hCG, TSH, free T4 and T3), ethanol, arterial blood gases, urinalysis, anemia panel (ferritin, iron, folate, vitamin B12), ammonia, pyruvate, blood bank laboratory testing (hepatitis markers, HIV) and microbiology cultures (blood, urine, cerebrospinal fluid, body fluids, etc.). All of the emergency tests are available 24 hours a day on a priority basis.

Sample identification

In Hacettepe University Hospitals, the patients are assigned a permanent hospital number and their medical information is entered into the hospital information system (HIS), an electronic version of the Personal Electronic Health Records containing physician notes, pathology diagnoses, radiology, and clinical laboratory results. Each biological sample taken from the patient to be analyzed in the laboratory is labeled with a barcode number; heated barcodes with 9 digits (code 39) are used for internal barcoding system to identify the name, surname, gender, age, the type of the tube, sample type, barcode print time, sample collection time and date, the site of service where the specimens were collected, the list of the requested tests, the name of the doctor who requested the tests and the phlebotomist who collected the blood. Access to the databases is tightly monitored and is restricted to clinical staff and laboratory members. The data related to microbiology cultures and blood bank laboratory testing were not included into the study, as they are under the control of microbiology department.

The unsuitable samples were recognized and identified upon their arrival in the laboratory, by a simple visual inspection by the laboratory secretary. Serum indices (hemolysis (H), lipemia (L) and Icterus (I) - LIH) were also measured. Samples that have been rejected are stored in the laboratory for up to 24 hours at 4 °C, a report is immediately issued through the laboratory information system (LIS) stating that the sample has not been processed. When precious specimens such as cerebrospinal fluid (CSF) samples, biopsies (bone marrow etc.) or aspirates are received in unsuitable tubes or transported under inappropriate conditions, the laboratory medicine specialists are responsible for deciding if the sample should be rejected or accepted.

Sample rejection ratios (SRRs) were calculated according to different test groups (biochemistry, CBC, blood gases, coagulation, TDM, cardiac markers, hormones and anemia panel) and analyzed according to the site of services (ED, ICU, inpatient services). The distribution frequencies between the point of collection and the specimen rejections were evaluated by descriptive statistical analyses (Microsoft Excel).

Results

The emergency laboratory of Hacettepe University Hospitals received 453,171 samples and rejected 27,067 samples, and performed 8,979,918 tests in 2013. Out of the total number of rejected samples, 41% of rejected samples were coming from ED (31% from adult ED and 10% from pediatric ED), 31% from ICUs and 28% from inpatient services (Figure 1A).

When all of the services were compared, the highest specimen rejection ratio was observed in adult

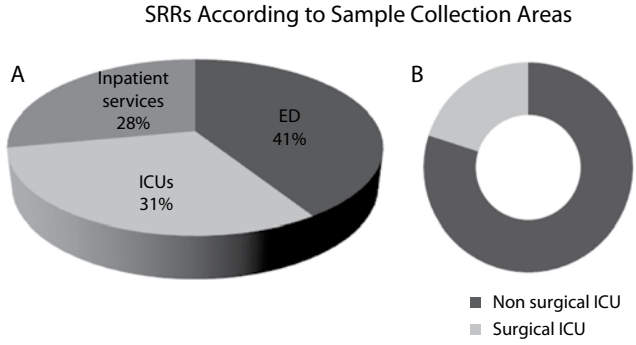

Figure 1. Sample rejection ratios (SRRs) according to sample collection areas A) In emergency departments (ED) (adult ED and pediatric ED, in total), intensive care units (ICUs) and inpatient services B) In non-surgical and surgical intensive care units (ICUs).

emergency department (31%) followed by neurology intensive care unit (14%) and internal medicine inpatient service (10%). To more closely examine this finding, we compared the rejection ratio between ICUs, the nonsurgical ICUs (40%) have significantly higher rejection rate compared with the surgical ICUs (10%) (Figure 1B). The rejection rates for neurology ICU (14%) was 2 fold more than internal medicine ICU (7%) and 3 fold more than surgical ICUs (4.5%), respectively. Evaluation of the pediatric samples received from Hacettepe Children's Hospital has shown that pediatric emergency department (10%) and the newborn service

Table 2. Quality indicators of the preanalytical phase proposed by the IFCC Working Group - Laboratory Errors and Patient Safety (IFCC WG-LEPS) and sample rejection ratios (SRRs) in the emergency laboratory of Hacettepe University.

Quality Indicators of the pre-analytical phase proposed by the IFCC WG-LEPS	SRRs in the emergency laboratory of Hacettepe University (%)
Patient identification	
Number of requests with errors concerning patient identification/Total number of requests	0.1
Data entry of the request	
Number of requests with errors concerning test input (missing or added or misinterpreted) / Total number of requests	1.4
Sample identification	
Number of improperly labeled samples / Total number of samples	0.2
Sample collection	
Number of samples collected in inappropriate container / Total number of samples	3.6
Number of samples with insufficient sample volume / Total number of samples	22
Transport of sample	
Number of damaged samples / Total number of samples	0.2
Number of samples transported at inappropriate time / Total number of samples	3.4
Number of samples transported under inappropriate temperature / Total number of sample	1.2
Number of improperly stored samples / Total number of samples	0.4
Number of samples lost-not received / Total number of samples	0.2
Suitability of sample	
Number of samples with inadequate sample-anticoagulant ratio / Total number of samples	34.9
Number of fibrin clotted samples / Total number of samples	27.9
Number of hemolyzed samples / Total number of samples	2.2
Number of lipemic samples / Total number of samples	0.1
Number of samples contaminated by intravenous infusion / Total number of samples	2.2

SRR - sample rejection ratio

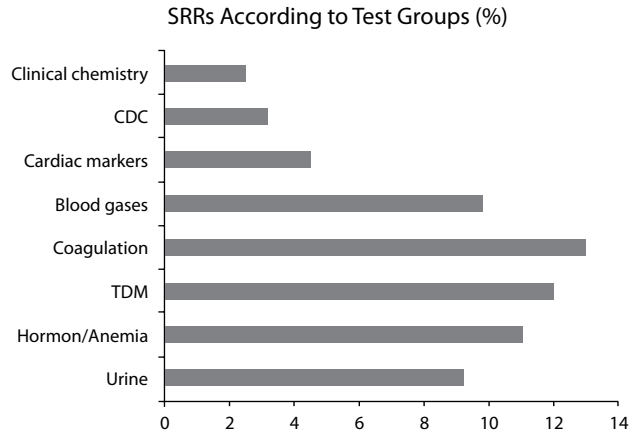

Figure 2. Sample rejection ratios (SRRs) according to test groups.

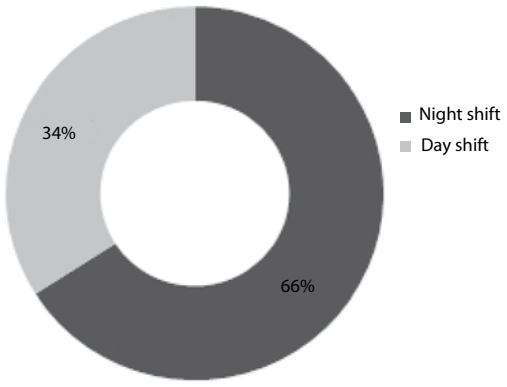

Figure 3. Sample rejection ratios (SRRs) during day shift and night shift.

(5%) have the highest rejection rate. Surprisingly, the rate of rejected samples from pediatric ED (10%) was 3 fold less than adult ED (31%).

The SRRs in our emergency laboratory were grouped according to Quality indicators of the preanalytical phase proposed by the IFCC Working Group - Laboratory Errors and Patient Safety (IFCC WG-LEPS) and given in Table 2.

According to one year follow-up of our emergency laboratory data, the calculated rejection ratios was 2.5% for biochemistry tests, 3.2% for CBC, 9.8% for blood gases, 9.2% for urine analysis, 13.3% for coagulation tests, 12.8% for therapeutic drug monitoring, 4.5% for cardiac markers and 11% for hormone tests as shown in Figure 2.

The most common rejection causes according to the test groups were the presence of fibrin clots (28%) and insufficient volume (9%) were the most frequent causes of rejection of biochemical tests. For coagulation tests, blood gas analyses and CBC; clotted samples (35%) and inadequate volume (13%) were the major causes of rejection.

We also assessed the proportion of rejection by the work shifts of the laboratory personnel; the proportion of specimen rejections was higher during the night shift (66%) compared with the day shift (34%), respectively (Figure 3).

Discussion

Identification and documentation of a problem is a key step for improving the quality of laboratory medicine. We conducted a retrospective study to identify the proportions of rejected specimens at the emergency laboratory. We detected an overall specimen rejection rate of 6% in our emergency laboratory. Our results have shown that the most important rejection cause in our emergency laboratory is fibrin clots (28%) for biochemistry tests, additionally red cell clots (35%) for coagulation tests, CBC and blood gas analyses. We observed that visible clots, either as a red cell clot in whole blood or a fibrin clot in plasma, are usually received from intensive care units, emergency department and newborn premature services. The major cause of clotted samples is probably due to poor mixing after blood collection and leaving the tubes horizontally instead of keeping them vertical. All diagnostic blood specimens collected in vacuum tubes are recommended to be inverted gently several times by all vacuum tubes manufacturers' datasheets and Clinical Laboratory Standards Institute (CLSI) documents to maximize the contact between blood and additives following blood collection (12,13). Parenmark and Landberg (14) have shown that mixing blood samples immediately after collection (for 1 min, inverting 15 times) may not be mandatory and instant mixing may produce hemolysis. Based on their outcomes,

Lima-Oliveria *et al.* (15) compared the impact of three different mixing procedures for clinical chemistry, hematology, and coagulation parameters a) Gold standard – all specimens were mixed gently by five-time inversion b) Rest time – all blood specimens remained 5 min at rest in an upright position, followed by gently mixing by 5 inversions; c) No mix- all blood specimens were left in an upright position, without mixing. They observed no fibrin filaments or micro clots in any sample concluding that mixing of blood specimens collected with an evacuated tube system appears to be unnecessary; probably the blood turbulence generated by standard vacuum pressure inside the primary tubes is by itself sufficient to provide solubilization, mixing and stabilization of additives and blood during venipuncture.

The high incidence of fibrin containing samples may be related with the short lag period between the blood collection process and centrifugation step. The mean time between blood collection and centrifugation is usually 10 minutes. To prevent the formation of fibrin, we planned to use rapid serum tubes (RST), which accelerates coagulation, reduces sample processing time and increases serum quality, suitable especially for emergency departments and ICUs. To decrease the ratio of clotted blood gas samples due to long transportation routes, several point of care blood gas analyzers are set up in ICUs and EDs which are under the control of laboratory specialists. Another reason for the high incidence of fibrin clotted samples may be not using evacuated tube system for blood collection. During our visits to inpatient facilities, we observed that collection of blood by the conventional syringe/needle/container system is still used in clinical departments.

Insufficient samples are the second most common reason (22%) for sample rejection in our emergency laboratory. We know the difficulty of collecting sufficient blood sample from newborns, children, oncology and ICU patients. The performance of venipuncture especially in infants and children requires special training and skill. The pediatric population also has a risk for anemia due to frequent blood draws necessitating small specimen volumes (16). Thus, microtainers and microtubes are preferred for blood collection in pediatric, geriatric, oncology, neonatal intensive care unit patients to reduce the sample volume. Additionally, we use advanced automated laboratory instruments with minimized specimen volumes and dead volume in the emergency laboratory. Moreover, insufficient samples cause inappropriate blood to anticoagulant ratio, it has been shown that especially coagulation tests such as PT, aPTT, thrombin time are significantly longer and fibrinogen levels are significantly lower in undefiled samples. Lippi *et al.* (17) have identified a clinically significant bias in test results when tubes are drawn at less than 89% of total fill for activated partial thromboplastin time (aPTT), less than 78% for fibrinogen, and less than 67% for coagulation factor VIII, whereas prothrombin time (PT) and activated protein C resistance remain relatively reliable even in tubes drawn at 67% of the nominal volume. Hence, under-filled citrated tubes containing less than 80% of target volume failed our acceptance criteria.

For TDM, blood samples in the tubes including serum separator gels are not accepted. The barrier gels can absorb some drugs such as phenytoin, phenobarbital, lidocaine and carbamazepine as demonstrated by the recovery of drugs following chemical extraction of the barrier gels with methanol. For this reason, standard blood collection tubes without barrier gels are suggested for TDM (18). For methotrexate measurement, blood samples which are not carried on ice and in the dark are not accepted to the laboratory. For cyclosporine level monitoring, only whole blood samples containing EDTA are accepted.

Patient specimen identification errors have been reported as one of the leading causes of laboratory errors. Misidentification is associated with the worst clinical outcome, due to the potential for misdiagnosis and inappropriate medications or surgery. This is why the Joint Commission and the World Health Organisatin (WHO) Alliance for patient safety have established that the first goal for clinical laboratories should be to **"**improve patient and sample identification**"** (19). In Hacettepe University hospitals, identification wristbands (name and surname, birthdate, and patient identification number) are used at inpatient units to prevent

wrong medication and wrong site surgery. At the same time, electronic barcoding system is used for identification of patients, specimens and laboratory testing and test result reporting. Before a clinical specimen is accepted to emergency laboratory, laboratory secretary make sure that the minimum two criteria for sample identification (name, surname and patient ID) are met, additionally check whether the sample and test requests match correctly. As a result of this, our misidentification ratio is only 0.3%. It has been shown that barcoding practices are effective at reducing patient specimen and laboratory testing identification errors which can cause adverse patient outcomes, therefore recommended as an 'evidence-based best practice' (20). However, from time to time, we observed that barcode scanners may misread patient identification barcodes due to incompatibility between the barcode print area sizes or symbology on patient ID bands or specimen labels with scanner settings.

Bonini *et al*. (21) reported that a higher proportion of specimens that were collected at either inpatient services or emergency department locations were rejected primarily because of hemolysis. Lowe *et al*. (22) have shown that blood draws from indwelling catheters or during IV starts is more prone to hemolysis compared to venipuncture draws. The ratio of hemolytic samples was 2% and samples contaminated with IV infusion 2.2% in our emergency laboratory. We are aware that blood samples collected through an intravenous catheter by some of our medical staff working at the ED and inpatient services increase hemolysis due to flow through the narrow tube. Sheppard *et al*. (23) reported that when the phlebotomy was performed in an emergency department by dedicated laboratory technologists, there was a reduction in overall TAT and blood culture contamination rates. Therefore, the number of professional phlebotomy teams working in shifts needs to be increased in Hacettepe University Hospitals.

Urinalysis is highly susceptible to preanalytical problems as urine samples are collected by patients. To improve the reliability of urine testing, laboratory secretary inform the patients about sampling, container types (sterile, with/without preservatives) and collection of the midstream urine sample. Despite this, incorrect urine collection is still high (9.2%) in our hospital.

Preanalytical errors are largely related with the procedures performed outside the laboratory by healthcare personnel who are not under the control of clinical laboratory but the majority of these errors are preventable. To achieve a high degree of total quality in the preanalytical phase; error prevention, error detection, and error management are the most critical points for laboratory specialists (24-26). Due to continuous staff turnover in services and inadequate training, the ratio of specimen collection into inappropriate containers is 3.6% in our institute. For example, sending cerebrospinal fluid sample in a urine cap instead of special sterile cerebrospinal fluid tube is a common mistake especially observed in neurology ICU. For such situations, an additional biological specimen is requested which threatens patient safety. Lillo R. *et al*. (27) have published that effective improvements in the preanalytical phase can be achieved by periodic educational improvement of the healthcare personnel by laboratory specialists. Thus, we started comprehensive education seminars every 2 months for healthcare personnel (residents, intern doctors, nurses) especially those working in EDs and ICUs related about venipuncture techniques, adequate tourniquet application, use of appropriate tubes with additives, order of tubes, gentle mixing and transport.

The most commonly reported types of preanalytical errors in the stat laboratory were hemolyzed samples (46.4% in biochemistry), clotted samples (43.2% in hematology), lost samples (6.4%), inadequate sample-anticoagulant ratio (2.9%), patient misidentification (0.7%), samples collected in wrong blood collection tubes (0.3%) and missing test requests (0.1%) (11). We have previously reported the sample rejection ratios of our core laboratory; the most frequent reason was the clotted specimen (55.8% of total rejections), followed by inadequate volume (29.3% of total rejections), similar to the emergency laboratory data. Most of the clotted specimens were received from adult hospital inpatient services (54.3%), followed by pediatric hospital inpatient services (26.8%) (28).

Sample rejection prevents sample analysis and leads to new sample request, which prolongs the TAT and cause the delay in diagnosis and treatment of critical patients, leading to adverse patient outcomes (29-31). Unfortunately, it is not easy to standardize all of the preanalytical processes and there are still no universally accepted guidelines for management of unacceptable specimens (32). This study has shown the most frequent causes of pre-preanalytical errors and sample rejection rates that are observed in the emergency laboratory of Hacettepe University Hospitals. We planned to improve the patient outcomes by reducing our SRRs from 6% to below 2%. For this purpose, we started enhanced documentation of rejected samples monthly and organize periodic training for healthcare personnel working in the departments with high rates of rejection. We believe that receiving sufficient amount of the sample collected under appropriate conditions in suitable containers will enhance the reliability of laboratory test results, prevent turnaround delay, and improve the patient outcome. Within 2014, our institution has achieved Joint Commission International (JCI) accreditation which works for improvement in quality and patient safety.

Potential conflict of interest

None declared.

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