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Pre-analytical Errors and Rejection Criteria for Blood Samples in Hematology Laboratory

Muhammad SHOAIB[1*], Iqra MUZAMMIL[2], Zeeshan Ahmad BHUTTA[3], Ishrat YASEEN[1], Huma MUNIR[1], Moazam ALI[2], Muhammad Salman YOUNAS[1], Sarfraz AHMAD[4], Ujala MEHTAB[5]

[1] School of Medical Sciences, Johar Institute of Professional Studies, Lahore, Pakistan
[2] Department of Clinical Medicine & Surgery; Faculty of Veterinary Science, University of Agriculture, Faisalabad, Pakistan
[3] The Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush Campus, Midlothian, EH25 9RG, Scotland, United Kingdom
[4] School of Pharmaceutical Sciences, Johar Institute of Professional Studies, Lahore, Pakistan
[5] Faculty of Veterinary and Animal Sciences, Muhammad Nawaz Shareef University of Agriculture, Multan, Pakistan

[1]: https://orcid.org/0000-0001-8695-1840
[2]: https://orcid.org/0000-0003-2943-0170
[3]: https://orcid.org/0000-0002-0148-425X
[4]: https://orcid.org/0000-0002-8581-6097
[5]: https://orcid.org/0000-0002-4593-8647
[6]: https://orcid.org/0000-0002-1454-3538
[7]: https://orcid.org/0000-0002-9818-4594
[8]: https://orcid.org/0000-0003-4733-5492
[9]: https://orcid.org/0000-0003-4019-8122

*Corresponding author: shoaibsinko8@gmail.com

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ABSTRACT

Pre-analytical errors are the most common types of errors occurring in hematology procedures. These type of errors accounts up to 70% errors of hematology laboratory. Most of the pre-analytical errors occur during sample collection, sample preparation, preparation of patient, sample transportation and storage. However, blood samples are collected and processed in hematology laboratory for various types of tests. Incorrectly collected blood samples are unable for further analysis in hematology laboratory. Each laboratory has developed standard criteria for processing of blood samples. Most of the blood samples are rejected by laboratory due to un-labeling, mislabeling, incorrect container, insufficient volume, incorrect use of preservative, improper storage conditions, clotted, leaked, lipemic, hemolysed and contaminated samples with other fluids. Adaptation of quality control measures not only in analytical procedures is critical but there is a need to provide attention at pre analytical and post analytical phases to ensure the patient interest and to provide quality services for future.

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INTRODUCTION

Quality of laboratory testing is based on handling of specimen during the analytical or laboratory testing phase, which must be standardized by using statistical internal quality control (IQC) and external quality valuation or proficiency testing (EQA/PT) (Lippi and Plebani, 2018). Due to advancement in medical field, the diagnosis of disease is mainly linked and reliable on the data provided by laboratory. Due to automation of laboratory procedures the performance of the laboratory has been improved. Reports from these laboratories help the physician in proper treatment of patient. It's very difficult for the laboratories to work independently and in isolation, so that they work with other departments especially with clinical division for proper sample analysis and filling of requisition. Today's laboratories are very important for diagnosis of disease and clinician depend on the results of laboratories for final diagnosis and for treatment of patient. Now it is duty of diagnostic laboratory to provide quality results. Provision of good quality results is the core issue and this require good management in all stages of procedures including pre-analysis, during analysis and post analysis measures (Naz et al., 2012).

There is a wide collection of proof that the rest of the zones for development in laboratory medicine related errors are in the pre analytical and, less significantly, the post analytical stages. In spite of the fact that the general error rate in lab medication is moderately low contrasted with different zones of medication (Lippi and Plebani, 2018). The effect of these errors may be important. If the error is detected before the issuance of result, for instance sample through delta checking or a change in a genetically-determined factor (such as an ABO blood group), it may cause an interruption in diagnosis or treatment, troublesomeness and stress for the patient. Carelessness about preanalytical errors and attention just on quality in the analytical phase has lead to patient damage and all laboratory medicine errors are a groove on healthcare resources. The hole between the magnitudes of analytical and extra-analytical error rates has been termed as an "Iceberg of Errors" which should be noticed to decrease ambiguity (De la Salle, 2019). The occurrence of analytic errors is hard to evaluate and might be underestimated; it has been recommended that 12 million persons yearly in the United States of America endure diagnostic error, half of which are important. Blunders that straightforwardly influence the diagnosis, treatment given to a patient, for instance an erroneous ABO blood group, an inaccurate hereditary test result, a mistakenly recognized infectious agent or an incorrect cell pathology evaluation have a reasonable and conceivably disastrous effect on health safety (Singh et al., 2014). Significantly more hard to identify those errors that bring about a clinically unnoticed quantitative mistake, for instance a patient or sample identification error that prompts the interpretation of one ordinary complete blood count (CBC) result for another, which may not cause harm to patient however will prompt the underestimation of the real

error rate and the loss of opportunity for main cause investigation. This article will review some of the sources of error in the pre-analytical phase as well as rejection criteria for blood samples in hematology laboratory.

TOTAL TESTING PROCESS (TTP)

TTP is the overall process from order of test to results interpretation and divided into different phases such as pre-analytical phase, analytical phase and post-analytical phase (Fig 1). Pre-analytical phase is the phase that rests before the analysis of sample or test. However, there are chances of errors at any stage of processing of blood samples such as pre-analytical errors, analytical errors and post-analytical errors (Stroobants et al., 2003). Lundberg defined the TTP in the form of a "brain-to-brain" loop of 9 phases starting from the brain of the physician through prescribing test, specimen collection, identification of specimen and patient, transportation, preparation, analysis and conclusion given back to the physician. Afterwards, this model was also included by addition of explanation by the laboratory and the concerned physician and describing result in front of patient, and it is known as a post-post analytical stage. Lundberg has also recommended the extension of process to achieve valuation of testing efficiency related to public health (Plebani et al., 2011). Another scientist, Shahangian and Snyder (2009) defined six stages in the TTP including test ordering, patient identification and sample collection, identification, preparation and transport of sample, analysis of sample and explanation, along with total of fourteen potential quality indicators, relevant to health care region of the Institute of Medicine. Due to resemblances in the explanation of TTP stages and the quality indicators, absence of standardization in the terms used in the TTP can produce problems in data collection and observation of errors. Some other major analytical errors in laboratory medicine occur due to unavailability of financial and staff resources, unavailability of standardization and poor arrangement of services.

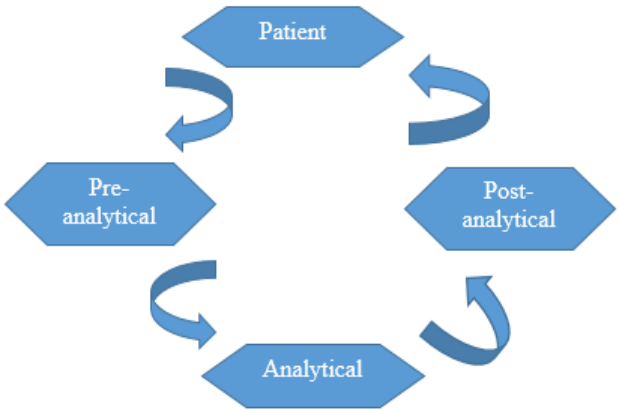

Figure 1. Total Testing Process starts and ends at patient

PRE-ANALYTICAL PHASE AND ERRORS

Errors in test selection and sequence, patient identification, sample labeling, and several other errors are not discussed in this manuscript with special emphasis on hematology errors. The pre-analysis phase includes the process from the doctor's request for lab tests to the preparation of test samples. Patient preparation, sample collection, transport, preparation and storage (up to analysis) are the pre-analysis steps, which are the main causes of laboratory diagnostic errors. Laboratory experts primarily focused on analysis errors and mistakes during diagnosis. However, due to the high frequency of errors, laboratory experts have recently invested more energy in the pre- and post-analysis steps (Sonmez et al., 2020). These errors influence too much safety and health of patient. Pre-analytical errors accounts 70 percent errors of clinical hematology laboratory. A number of process including log in, pipetting, centrifugation, aliquot ting and sorting samples in different batches for introduction into automated samples analyzers are all come in pre-analytical errors. A number of studies showed most of the errors of laboratories occur before and after analysis phase with some mistakes occur during analysis (Bonini et al., 2002).

Patient Preparation

Physical activity has been identified as an important pre-analytical variable, and the European Federation of Laboratory Medicine (EFLM) recommends that patients avoid excessive or unfamiliar exercise within 24 hours of routine blood loss. According to reports, the number of white blood cells (WBC), neutrophil count, platelet count, red blood cell division, and platelet activation increased after the marathon. Continuous exercise leads to an increase in plasma volume (PV), which reduces the athlete's hemoglobin (Hb), red blood cells (RBC) and hematocrit (Hct) in training events. Therefore, it is necessary to understand the patient's condition when interpreting the results relative to the standard reference interval. Since the physiological response to exercise is affected by an individual's physical health, it is important to distinguish between the effects of continuous training and the onset of vigorous and abnormal movements performed by a sedentary individual. For some time, the patient's posture was associated with changes in CBC. EFLM is the standard method of bleeding surgery and recommends that patients sit and rest for 15 minutes before bleeding.

Sample Collection

Good sample collection is an important part of good laboratory practice. Incorrect sample collection can lead to delayed reporting, unnecessary redrawing/reevaluation, reduced customer satisfaction, increased costs, incorrect diagnosis/treatment, injury, and sometimes death of the patient. Research shows that the applicability of validation samples is a key factor in the accuracy and practicality of test results. Sample loss,

clotting, hemolysis, insufficient or incorrect sample collection and handling are a large part of prior analysis errors.

Quality of Sample

Agglomerated samples are the most common reason for rejecting automatic counting and coagulation. In a large study conducted in China, a total of about 10 million blood samples were collected, 57% of the 11,000 rejection reactions were caused by sample clotting, and the rejection rate was similar (43%) according to the report. In another study, 51% sample size decreased due to condensation. This high blood clot sample rate is primarily the result of poor blood collection and poor sample mixing after blood collection. Bloodletters training and standardization of bleeding methods have been shown to improve sample quality. When taking a sample near the injection site, contamination of the injection may cause anemia and abnormal clotting test results. When the patient died after unnecessary blood transfusions, an incorrect hemoglobin result was performed on a sample taken from the "drop" arm. Venous statis for only 1 to 3 minutes during venipuncture has also been shown to adversely affect CBC results, increasing Hb, Hct, and RBC. The combination of vein mapping or visualization techniques and infrared rays addresses the need for tourniquets to locate veins. The order of extraction of the sample type may not affect the automatic counting results, but there is a risk of contamination of chemical and coagulated samples.

Sample transportation

If transportation conditions are not optimized, significant clinical errors can occur due to delays in transportation to the laboratory. Ideally, all samples should be analyzed within 6 hours of collection, especially if you need blood cell morphology. Long-term preservation of the sample is a recognized asset and will cause morphological changes. Excessive heating or freezing can also make the sample unsuitable for testing. However, in hematology, time-critical outcomes are usually defined by the patient's medical history, for example, the white blood cell and platelet count in cancer patients is Hb after heavy bleeding. There has been controversy over the effect of Pneumatic Tube System (PTS) used for sample transport on the quality of samples in hematology. The hospital pneumatic tube system (PTS) has become a common mode of sample transportation in hospitals. The PTS is a fast automated delivery system that efficiently transports drugs, medical records, patient reports, X-rays, tissues and blood samples to and from laboratories, pharmacies, medical wards, blood banks and emergency rooms. However, transferring blood samples from the site of bleeding to the main laboratory is still the most common application for PTS. Administration of PTS has been shown to have little or no effect on hematology, coagulation, and chemistry results.

Sample preparation

The sample preparation step accounts for about 19% of the total cost of analyzing a single sample and is time consuming (37% of the time it takes to generate results). Manual handling of samples due to infectivity is a perceived risk by laboratory personnel.

Storage of Samples

If the analysis is delayed, it is best to store the samples at 2-8 °C, but not recommended if the patient is known to have cold agglutinates. The lectin causes erythrocyte aggregation and causes a false increase in MCV. The number of red blood cells increases and the average cellular hemoglobin concentration (MCHC) increases. A blood analyzer equipped with a preheating reagent may reduce the effects of cold agglomerates, but reheating the sample after collection is not recommended, instead replenishing the patient's blood and maintaining the temperature from sample collection to analysis resulting in guaranteed accurate results.

Rejection criteria for Blood Samples

The laboratory has the right to reject the sample before analysis in case of any problem with the sample. Laboratory adopts all measures to maintain the integrity of sample. Laboratory don't discard the sample until the responsible person is not notified (Naz et al., 2012).

GENERAL CRITERIA FOR REJECTION OF SPECIMENS

Unlabeled Samples

Those samples which are not properly labelled are rejected by laboratories because it’s not possible to identify origin of specimen. Sample can be recollected or should consult with the person who collected the sample and ask him to identify the sample and sign a waiver that will provide proof that person have identify this specimen (Plebani, 2012).

Incorrectly labelled samples or mislabeled samples

In this case samples are labelled but they are not providing the sufficient information or labelling is not correct. Sample may be labelled with wrong patient name or compared to requisition or may be labelled with wrong ID number. Minor deficiencies can be accepted and ordered test will be performed but major deficiencies may be rejected. To avoid these type of errors labelling of samples should be done immediately after collection. These type of errors accounts 50% of the identification errors (Plebani, 2012).

Incorrect Container

Use of incorrect containers during sampling may also invalidate the results. Samples with incorrect use of containers should be recollected and proper container should be used. Most common types of containers used are red, yellow, light blue, green, lavender, grey, royal blue and black in colors having different additives and purposes. For example, red containers contain no or silica particles that promotes clot formation and are used for serology, serum testing and blood banks. Yellow containers contain anticoagulant substances such as Sodium Polyanetholsulfonate (SPA) and acid citrate dextrose (ACD) and used for blood and body fluid cultures. Lavender color containers contain EDTA (Ethylenediaminetetraacetic Acid) and are used for hematology testing (CBC, ESR). Similarly, other types of containers contain different additives and used for different purposes. For recollection of sample patients should be contacted (Carraro et al., 2000).

Incorrect use of preservative

Samples having inappropriate preservative for example use of ACD for CBC tests will invalidate the results and should be recollected. The nursing unit and collection staff will be informed for proper use of preservatives (Carraro and Plebani, 2007).

Insufficient sample

If the amount of collected sample is insufficient for the required tests, sample should be recollected. Most of the time 3-5ml blood is collected for hematology tests. Procedure for which the sample is sufficient will be performed (Hollensead et al., 2004).

REJECTION CRITERIA FOR BLOOD SAMPLES

Clotted Samples

The clotting of blood after collection or during collection is found to be major cause of rejection of blood sample. Previous studies reported that 43%-51% of the collected samples are rejected due to clot formation. The main reasons of clot formation mainly the result of poor phlebotomy and improper mixing of sample after collection. The clotting of blood should be avoided by adding proper amount and correct anticoagulant in the sample tubes with the proper training of phlebotomy staff improves the quality of sample (Carraro and Plebani, 2007).

Insufficient blood volume

This is found to be second major cause of rejection of blood samples because of less volume of blood required for different procedures for example collection of 0.5ml blood in 5ml EDTA tube will lead to shrinkage of RBCs. Most of the time 3-5ml blood is

collected for hematology tests. The reasons associated with this type of error may be ignorance of phlebotomist, difficulty in localization of veins, debilitated persons and pediatric patients (Hollensead et al., 2004).

Hemolysed samples

The hemolysis of blood samples during collection will also disturb the results and invalid results will be obtained. Considered as major cause of rejection of samples. Hemolysis of blood due to vigorously shaking of tubes, forcing of blood through fine needle, and centrifugation of samples before clotting. Samples should be collected in such a manner to avoid hemolysis as much as you can. Red color containers without anti-coagulant should not be shaken after collection of blood sample and plasma samples should be kept inverted for few time so that anticoagulant will mixes with blood. These type of errors can reduced by use of vacuum blood collection tubes with closed system that made the blood collection easy and efficient (Lippi et al., 2011).

Collection of lipemic samples

These type of samples are collected after heavy meal and pre-existing problems metabolic disorders such as hyperlipoproteinemia. The fat in the sample effect the values of the test. These type of samples are collected due to negligence of phlebotomist and clinician that not disseminate the information properly and patient preparation is not done accurately. These type of errors can be avoided by collection of sample after overnight fasting and mentioning the metabolic disorders on the requisition slip (Dzik et al., 2003).

Inappropriate patient preparation

Patient activity before sampling is an important criteria for proper results. If the patient had did unnecessary or excessive exercise before sample collection will also affect the results of test. If you take the blood immediately after marathon running then then the parameters of blood such as WBC, neutrophil count and platelet count will be increased. However, sustained exercise for long time will results in the increase of PCV, RBC, Hb, and Hct components of blood. Therefore, the patients status should kept in mind for the interpretation of results. Patient posture also have effect on complete blood count (CBC). It is recommended that patient should rest for 15 minutes in seated position before sample collection or for any phlebotomy procedure (Lau et al., 2000).

Contamination of sample with other fluids

If the sample collection is taken closely from site of infusion of fluids will result in spurious anemia and abnormal coagulation of blood will occur. Venous stasis for short period of time 1-3 minutes results in the adverse effects on the CBC with increase Hb (Hemoglobin), Hct (Hematocrit) and RBC (Red Blood Cells). The proper location

mapping of veins with infra-red light overcomes the need of tourniquet and help in locating the veins (Stainsby et al., 2005).

Inappropriate selection of anti-coagulant or blood-anti-coagulant ratio

The most suitable anti-coagulant for CBC is EDTA with preference of K_2 EDTA while alternatives such as magnesium sulfate to this may be a more suitable for platelet parameters. The most commonly used anti-coagulants used in hematology laboratory are EDTA, sodium fluoride, double oxalate, heparin, and sodium citrate. The CBC vials contain the fixed volume of EDTA for proper profiling of blood, increase and decrease in the volume of EDTA will affect the results of CBC. Overfilling of anticoagulant may result into pseudopolycythaemia, pseudoleucopenia and pseudothrombocytopenia. Under filling of EDTA will disturb the platelet volume and excess of K_3 EDTA will reduce the count of WBC (Plebani, 2012).

Improper storage conditions

Blood samples for CBC analysis should be analyzed as soon as possible within 6 hours of collection. Long time storage of sample can result in increased MCV and also morphological changes in blood cells. Excessive heat and freezing also excel the sample unsuitable for processing. If there is delay in analysis, sample should be stored at proper temperature i.e. 2-8 ^{o}C (Carraro and Plebani, 2007).

Other criteria's for rejection of blood samples

Other criteria's include misidentification of blood samples, use of inappropriate collection tubes, inadequate sample/additive ratio, insignificant icteric samples, sample collected in a syringe, specimen submitted may be incorrect for required test, under filled or overfilled samples tubes, incorrect labelling of sample, broken samples and leaked samples and specimen stored from long time .

CONCLUSION

Pre-analytical errors the major cause of rejection of blood samples in the various sections of hematology laboratory. Among the pre-analytical errors missing of sample, wrong identification of sample, contamination of sample, use of inappropriate containers, wrong identification of patient, improper transport of specimen are considered of higher importance. Blood samples are mainly rejected due to clot formation, insufficient volume of blood and hemolysis of blood. At the end we conclude, laboratory workers require to adopt an integrated process towards lab diagnosis and need to work in close contact with the clinicians to provide effective diagnostic assistance for proper treatment of patients. Adaptation of quality control measures not only in analytical procedures is critical but there is a need to provide

attention at pre analytical and post analytical phases to ensure the patient interest and to provide quality services for future.

Declarations

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Competing Interests

Authors declares no conflict of interest.

Ethical Approval

No ethical approval required.

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