

A Narrative Review on the Preanalytical Sample Errors in the Hematology Section of Clinical Laboratory

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ABSTRACT

Background: Various errors may occur during the preanalytical phase of laboratory testing and can introduce inaccuracies that can compromise test findings which creates a significant concern for both clinicians and patients. This narrative review aims to: (1) Determine the sources of the preanalytical error in the haematology section, (2) Identify the impact of these errors and (3) Enumerate the strategies to minimize these errors. **Materials and Methods:** The search for articles and journals was conducted between March 10, 2023 to March 12, 2023 using Google Scholar and PubMed as the database and the SANRA method as the instrumental tool for inclusion and exclusion criteria. Among the 161 total journal studies, 8 journals were considered and analysed in depth. **Results:** The most common preanalytical errors determined in this review are: insufficient blood samples, clotted blood samples, hemolyzed samples and other errors such as transportation delays and wrong patient information. *Insufficient sample* may prolong the clotting time, a low reading of haematocrit and MCV and a high MCHC. Whereas, overfilled samples may produce false positive results for polycythemia, thrombocytopenia, and leukopenia. A *clotted sample* causes damage to the cell and consumption of the coagulation factor which can affect readings on Complete Blood Count, Blood gases, Coagulation, and the Erythrocyte Sedimentation Rate. A *hemolyzed sample* affects tests for hemostasis considerably affecting the results of the Prothromin Time, activated Prothromin Time, D-dimer tests and the levels of antithrombin and fibrinogen. **Conclusion:** Insufficient phlebotomy skills and specimen preparation contribute to the different preanalytical errors that may cause erroneous results in haematology testing. These errors can result in patient misdiagnosis, incorrect treatment plans and poor patient outcomes. Proper specimen collection, handling and transportation should be done to minimize these preanalytic errors.

Keywords: Blood collection, Clotted samples, Hemolyzed samples, Insufficient samples, Phlebotomy.

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INTRODUCTION

Most of the time, clinical decisions on the whole patient workflow in a hospital are based on the results of the

laboratory. With a 60-70 percentage of dependency on laboratory results, a high expectancy of good quality laboratory tests also follows.^[1]

In the Hematology section, analysis of whole blood components may help in the diagnosis of anemia, inflammatory disorders, blood cancer, and bleeding problems; the test results can also be used in monitoring infections, blood loss, and bleeding issues. In terms of the type of anticoagulated tube, the reviewers focused on Ethylenediaminetetraacetic Acid (EDTA) since

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it is the most commonly used anticoagulant in the haematology section.

Hemolyzed blood affects different parameters in different ways and can highly give inaccurate results;^[2] it lowers antithrombin and fibrinogen levels while drastically increasing the Prothrombin Time (PT) and D-dimer tests and also erroneously prolonging or decreasing the aPTT.^[3]

There are other errors that can affect the parameters of whole blood such as: insufficient samples, clotted samples, and hemolyzed samples.^[4] These errors can occur at any point throughout the laboratory phases of testing, including preanalytical, analytical, and post-analytical stages. According to estimates, 70% of all errors in the healthcare system occur during the preanalytical phase.^[5] The same is true in the field of haematology, where mistakes frequently occur during the preanalytical phase.^[6]

Thus, the purpose of this narrative review is to determine the sources of the preanalytical error in the haematology section, identify the impact of these errors, and enumerate the strategies to minimize these errors.

MATERIALS AND METHODS

The reviewers conducted preliminary research using PubMed and Google Scholar. Keywords that were used for searching are “prevalence” AND “preanalytical errors” AND “hematology”. A flow diagram of the process of selecting journal articles to be included in the narrative review is shown in Figure 1. A total of 161 journal articles from Google Scholar and 8 journal articles from PubMed were found. The Scale for the Assessment of Narrative Review articles or SANRA was used to evaluate the journals for the inclusion and exclusion criteria. Reviewers selected journal articles

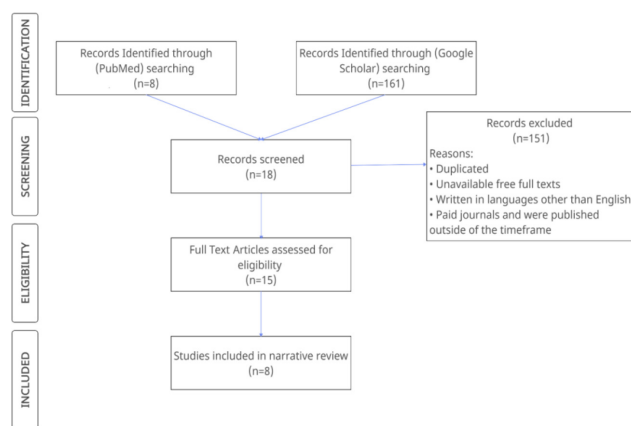


Figure 1: Flow diagram of selecting journal articles to be included in the narrative review.

according to inclusion criteria; (1) Journal articles that were related to and specific to preanalytical errors in hematology, (2) Should have available free full texts, (3) Were written in English language, and (4) Published between year 2018 and 2023. For the exclusion criteria, journal articles that were (1) Unrelated, (2) Duplicates of included articles, (3) Unavailable free full texts, (4) Written in languages other than English, (5) Not free-access journals and (6) Journals published outside of the timeframe were not considered. After defining the inclusion and exclusion criteria, 13 out of 161 journal articles matched results from Google Scholar and 5 out of 8 journal articles in PubMed were extracted. However, 3 of the 5 journal articles retrieved from PubMed have duplicates from the results returned by Google Scholar. In total, after removing duplicates, there were only 15 journal articles that could be considered. The reviewers conducted the final filtering of the 15 journal articles. As such, after the final filtering of the articles, the reviewers have been left with 8 journal articles that satisfy all of the inclusion criteria. The search for articles and journals was conducted between March 10, 2023 to March 12, 2023. The list and details of journals included in the narrative review are summarized in Table 1.

RESULTS

Preanalytical testing in Hematology section

The preanalytical phase is considered the most crucial aspect of the overall flow of laboratory testing since this will serve as a basis for a patient’s diagnosis and treatment. A 2022 study found that 70% of total errors encountered in the healthcare setting occur in this phase.^[5] This is due to the phase’s much-needed attention to detail. Errors in the preanalytical phase result in significant effects that affect hospitals’ reputations in terms of accuracy, patient management, and delays in results.^[2] The most common errors found in the Hematology section are: patient misidentification, improper storage and labeling, miscommunication between healthcare professionals and patients, hemolyzed and clotted specimens, inadequate specimens, and wrong choice of anticoagulant.^[6] Other errors mentioned in several studies include insufficient skills in terms of phlebotomy, sample transportation, and physician diagnosis.^[4]

Types of preanalytical errors and their prevalence

Similar studies have shown that there are preanalytical errors found in both outpatient and inpatient blood samples. 513 (0.43%) sample errors out of 118,732 samples were found in a study in 2018.^[1] Out of 95,002 blood samples, Alshaghдали *et al.* (2022) found 8,852

Table 1: List and details of journals included in the narrative review.

Sl. No.	First Author (Year of Publication)	Phenomenon of Interest	Research Design	No. of Sample
1	Alshaghдали, K. (2021)	Review of the Quality Indicators (QI) and the laboratory errors in the preanalytical phase of hematology testing.	Retrospective study	95,002
2	Arul, P. (2018)	Prevalence and types of pre-analytical errors at a tertiary care hospital in South India.	Cross-sectional study	513
3	Gaiki, V. (2022)	Identification of the possible parameters for pre-analytical errors.	Quantitative study	366
4	Gaur, K. (2020)	Evaluation of the types and frequencies of pre-analytical errors occurring in a tertiary care hematology diagnostic center.	Prospective study	189,104
5	Gupta, P. (2021)	To Reduce the percentage of rejected blood samples and enhance specimen acceptability.	Retrospective study	1,001
6	Iqbal, Mohammad Shahid (2023)	Study on the pre-analytical errors in hematology section.	Retrospective study	67,892
7	Keskin, A (2022)	Evaluate the pre-analytical rejection rate and to determine the sources of the error.	Retrospective study	1,307,013
8	Noor, T. (2023)	Identify and reduce the cause of rejection rates.	Cross-sectional study	231,008

(9.3%) sample errors compromising 9.3% of the total number of samples received.^[3] A similar study also observed sample errors in 4,052 (2.14%) samples out of 189,104 samples received.^[7] Recent studies^[2,6] also noted the sample errors they observed compromising 11,897 (5.15%) sample errors out of 231,000 blood samples and 886 (1.3%) sample errors out of 67,892 blood samples respectively. Common sample problems include inadequate blood samples, clotted specimens, and hemolyzed samples, all of which have been found to be common preanalytical errors. Preanalytical errors were discovered in other investigations as well, including the use of incorrect tubes, transportation delays, specimen tube mismatches, and patient misidentification.

Error 1: Insufficient sample

According to various studies, the majority of preanalytical errors in the haematology department of the laboratory were caused by insufficient sample volume. 104 (0.17%) samples out of 513 sample faults reported^[1] had insufficient volume, which is the majority of the preanalytical mistakes discovered in the study. In a study similar to this one, 480 (54.17%) of the 886 sample errors they discovered were caused by insufficient samples.^[2] Insufficient sample amount is another important contributor to preanalytical errors since 52.24% of the total specimens were discarded because of errors. Unskilled phlebotomists, pediatric patients, those with chronic, life-altering illnesses, and chemotherapy patients usually cause this error.^[7] This sampling error is a serious issue since the cells are at risk for shrinking and a low mean corpuscular

volume if the blood volume drawn is less than the amount of Ethylenediaminetetraacetic Acid (EDTA), the anticoagulant found in the purple top.^[1] Overfilling, as opposed to underfilling, also impacts haematological tests, which can result in false positive results for polycythemia, thrombocytopenia, and leukopenia. Insufficient volume will produce low hematocrit, low MCV, and a high MCHC in an automated analyzer.^[2] Underfilled tubes lead to an increase in sample dilution, which may prolong the clotting time due to an increased calcium-binding rate.^[3] Compared to the other studies listed, their study had fewer preanalytical mistakes due to inadequate sample volume. As opposed to outpatient samples, inpatient samples frequently contain this error. This is especially true for critically sick patients, as they are difficult to draw blood from and have a high risk of test rejections for laboratory analysis on hormones, blood gas analysis, coagulation, and ESR types due to insufficient samples.^[5] This situation is also present in the pediatric department because it is challenging to collect venous blood samples from infants and young children.^[2]

Error 2: Clotted sample

The next major error that has been recorded after insufficient blood samples is clotted specimens. It makes up 38.6% of all sample errors making it the most frequent cause of error.^[3] This error was caused by improper mixing or by failing to mix sample tubes after blood collection. The Clinical Laboratory Standards Institute (CLSI) and the vacuum tube manufacturer recommends to gently invert the tubes multiple times

immediately after blood collection, this will increase the contact between the blood and the additives to avoid producing clotted sample. The use of traditional syringe systems and protracted venipuncture is another contributory factor. Improper anticoagulant-to-blood ratios and as well as the delay in blood transfer from the syringe to the vial can cause clotting were reported in a study.^[2] In the investigation, 20.09% of the specimens are clotted, which typically occur in the emergency rooms. On the said department, the staffs are prone to the weariness of constant critical situations and unending high workload, which can impair their work performance, such as doing the phlebotomy procedure. Contrarily, 41.26% of the clotted samples were discovered to be frequent in outpatient clinics because adequate blood sample mixing may be left unnoticed.^[7] Clotted samples were listed as the second-to-highest common error in the hematology section,^[1] compromising 0.12% of the total error. The tiny clots, brought about by an elevated blood-to-additive ratio or inappropriate mixing after the collection, are difficult to notice. This is consistent with Noor's findings from 2023, who discovered that microclots in EDTA or sodium citrate tubes account for 3.88% of clotted specimens.^[6] The reason for the rejected samples in the haematology department may be due to the patient's health.^[5] The clotted samples for complete blood count, blood gases and coagulation testing had the highest rejected sample rate in the emergency patient group. Among the inpatient group, clotted samples were also detected as the second and third highest rejection rates which are both for total blood count and coagulation sample types. The sources of this rejected sample are due to immobility, bed rest, and stagnation seen in hospitalized patients. It has been noted that the reporting or incidence of this inaccuracy varies among studies. The authors compared the preanalytical error rate across all samples in the study,^[3] noting that it was 9.3% overall, which was significantly lower than the researchers' studies in Ethiopia's hematology section. However, studies in Indian hematology laboratories had lower error rates, ranging from 0.38% to 1.34%, and Italy had a 5.5% error rate. Because of this, even though clotted specimens had the second-highest significant error,^[1] it was only recorded as 0.12%. The variation in the rate of errors may also be caused by the various QIs used in the evaluation and the variations in the current policies in sample acceptance and rejection criteria, according to an explanation of this reason provided by Alshaghдали and co-authors.^[3] This error can affect the results, especially for assays that require plasma or whole blood because when the blood clots, this causes damage

to the cell and consumption of the coagulation factors.^[2] Other sample types which are prone to rejection due to clotting are Complete Blood Count, Blood gases, Coagulation, and ESR.^[5]

Error 3: Hemolyzed sample

Hemolyzed samples were also reported to be a substantial preanalytical error identified in the haematology section.^[1-3,7] These samples contained 0.03%, 6.7%, 4.63%, and 1.83% of these errors (2020). This can be the result of vigorously shaking the tubes and centrifuging the sample before the clotting forms.^[1] Other factors that contribute to this error include using the tourniquet for a long time, not finding the vein, using the wrong needles, using the wrong transportation techniques,^[3] not letting the alcohol in the venipuncture site dry properly, using a syringe system, and forcing blood into a tube with a syringe plunger.^[2] This preanalytical error can have a significant impact on hemostasis tests because the haemoglobin pigment present can interfere with the machine's photo-optical systems, considerably affecting the results of the Prothrombin Time, activated Prothrombin Time, D-dimer tests and the levels of antithrombin and fibrinogen.^[3]

Error 4: Other Cause of Preanalytical Errors

Several studies have mentioned other errors that are often overlooked in the current healthcare setting aside from the previously mentioned. Some examples such as transportation delays and wrong medical records account for 19.45% and 19.16% of a total of 11, 897 rejected samples respectively.^[6] Inadequate information about patients and physicians provided in Laboratory Request Forms (LRFs) results in increased errors in laboratory testing, 30.05% of LRFs did not include the age of the patient, clinical diagnosis was only shown in 39.62% of the forms, and only 8.47% of the LRFs showed the date and time of specimen collection.^[8] Another source of error worth mentioning is the lack of proper training in venipuncture, and clerical errors play a major role in rejected specimens.^[1,7]

As stated in the previously mentioned studies, the enumerated errors are among the most commonly encountered in the pre-analytical phase of the haematology section. In addition to the studies used, an article also identified the following errors as the main source of rejected samples namely, clotted specimen, hemolyzed specimen, insufficient samples, and incorrect labelling.^[9] Similarly, a study conducted in 2019, it was mentioned how clotted samples are obtained due to the incompetent skills performed by a phlebotomist.^[10] This then leads to the idea that most errors encountered

in the pre-analytic phase of the laboratory workflow are because of the insufficient clerical skills of the healthcare workers.

DISCUSSION

The results acquired from each study presented below all contribute to one of the objectives of this paper which is to identify the most prevalent errors in the preanalytical phase of the hematology section. In the studies enumerated, the errors commonly encountered include insufficient samples, clotted samples, and hemolyzed samples. These errors mentioned were then found to be caused by clerical skills. The findings stated in each study, can then be used to determine how the current healthcare setting can surpass such in order to achieve the best possible preanalytical quality. In addition, the results can also be used for further research on the said topic as the reviewers found it difficult to acquire studies mainly focused on the Hematology section.

Strengths and limitations of the method used

In an article entitled Types of Studies and Research from the Indian Journal of Anaesthesia, medical research has two main categories: primary and secondary.^[11] Primary research is divided into three groups: basic research, clinical trials, and Epidemiological trials. Nevertheless, secondary research includes meta-analyses and reviews.^[12] The methods of the references primarily used to complete this narrative review are observational approaches in epidemiological traits type of study under primary research, specifically cohort and cross-sectional study.

Since previously gathered data from primary research are the source of data for narrative reviews,^[13] the biases and accuracy of the references cannot be determined. Issues like unreliability in narrative reviews are straightened out using the Scale for the Assessment of Narrative Review Articles (SANRA). SANRA aids authors and readers in assessing if they are receiving quality information that is necessary for their objectives. On the downside, authors may heavily rely on information gathered from various journals in constructing the paper;^[14] this type of dependency is usually seen in the author's recommendations.

Narrative reviews' findings, in comparison to the other secondary research, are strengthened by the author's real-life experiences, such as in this paper.^[15] Narrative reviews do not specifically answer a specific topic or question,^[16] but they may open doors of opportunities for the readers to comprehend and be more curious

about the topic using pieces of information gathered from different journals.

Achieving the best possible preanalytical quality

Preanalytical errors and their consequences are deemed inevitable however, the innovation of various courses of action can alleviate their prevalence. The overall aim of the studies used as references for this review paper was to highlight the importance of recognizing preanalytical errors in laboratory testing. Having constant educational training and interventions among healthcare workers will be of most aid in decreasing specimen rejection rates.^[4] Similar to the 2022 study,^[5] adequate and sufficient training should be provided to phlebotomists in order to perform the procedures without any possible circumstances that may be encountered. As for the errors regarding incomplete patient and physician information, a new format of Laboratory Request Forms (LRFs) must strictly be implemented and described to be more detailed and comprehensive.^[8] The beneficial aspects of reducing the prevalence of preanalytical errors are not only for the healthcare workers but more importantly for the patients. Through the utilization of the aforementioned ways, the turn-around-time of the specimens must be precise as well as the administering of appropriate treatment for the patient. A more tangible approach was stated^[3] wherein Quality Indicators (QIs) were used as an instrument to attain accuracy. These QIs were implemented to contribute to monitoring the overall performance of the laboratory. The all-in-all improvement of the preanalytical phase can be acquired through regular training, constant monitoring and strictly adhering to the standard operating procedures.^[7]

CONCLUSION

The most commonly occurring preanalytical errors determined in this review paper and their impact on different haematological parameters are:

1. *Insufficient blood sample* causes dilution of the sample and increases the calcium-binding rate, which may prolong the clotting time. It can also result in a low hematocrit, a low MCV, and a high MCHC reading on an automated analyzer. Whereas, *overflowing* can impact haematological tests by producing false positive results for polycythemia, thrombocytopenia, and leukopenia.
2. *Clotted blood samples* cause damage to the cell and consumption of the coagulation factors. A clotted blood must be rejected and ordered for another blood collection because it can cause erroneous

results on the determination of Complete Blood Count, Blood gases, Coagulation test and Erythrocyte Sedimentation Rate.

3. *Hemolyzed samples* affect tests for hemostasis that may affect the results of the Prothrombin Time, activated Prothrombin Time, D-dimer tests and the levels of antithrombin and fibrinogen.
4. *Other preanalytical errors* that may affect laboratory readings and are subject to specimen rejection are due to specimen transportation delay and an incomplete or wrong patient's information written in the laboratory request form.

This review also determined that there are few studies on preanalytical errors that focus on the haematological parameters.

Knowing that most of these errors are due to human errors, particularly in performing blood collection, handling and transportation, can be prevented by enhancing the skills of the phlebotomist.

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AUTHORS' CONTRIBUTIONS

AG. P suggested the main topic of the Pre-Analytical Errors in Hematology section for the review paper. LL. L proposed an outline of discussion for the review paper. KA. B and IG. P looked for all the available articles in Google Scholar and PubMed and examined the articles related to the topic. LL. L wrote the background of the study with the help of R.T. LL. L reviewed and revised the first and second drafts of the review paper with the help of KA. B and I.P. MI.P wrote the methodology and R.T provided the flowchart. I.P created the initial summary table of the journal articles with the help of R.M. I.P and KA. B provided all the information in the discussion part. AG. P wrote the conclusion and MI.P wrote the recommendation. KA. B and I.P wrote the abstract for the first and second draft, and was revised by R.M for the final draft. KA. B, LL. L, AG. P, MI. P, and I.P, contributed to the overall review and revision of the final draft of the paper in consultation with R.M.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

aPTT: Activated Partial Thromboplastin Time; **CLSI:** Clinical Laboratory Standards Institute; **EDTA:** Ethylenediaminetetraacetic acid; **ESR:** Erythrocyte Sedimentation Rate; **LRFs:** Laboratory Request Forms; **MCHC:** Mean Corpuscular Hemoglobin Concentration; **MCV:** Mean Corpuscular Volume; **PT:** Prothrombin Time; **QI:** Quality Indicators; **SANRA:** Scale for the Assessment of Narrative Review Articles.

SUMMARY

The practices implemented to reduce the chances of errors in blood testing are included in the pre-analytic phase of the hematology section. In order to gather information on pre-analytical errors that occurred in the hematology section during the study's conduct between March 10 and March 12, 2023, the authors evaluated written works from previously published research. Studies that support the current issue were chosen using the SANRA approach. Insufficient blood sample, clotted blood sample, hemolyzed sample, and other errors such transportation delays and incorrect patient information are the most frequent preanalytical errors identified by this evaluation. An *insufficient blood sample* could result in a slower rate of clotting, a lower haematocrit and MCV value, and a higher MCHC value. On the other hand, samples that are overfilled can result in false-positive tests for leukopenia, thrombocytopenia, and polycythemia. Blood gases, coagulation, and erythrocyte sedimentation rate (ESR) values may all be altered by a *clotted sample* because of cell damage and coagulation factor use. The findings of the Prothrombin Time, activated Prothrombin Time, D-dimer tests, and the levels of antithrombin and fibrinogen are all significantly impacted by *hemolyzed samples* on hemostasis assays. These mistakes are the result of human error, and phlebotomists can avoid them by developing their skills.

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