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Blood specimen rejection rate in clinical laboratory: A systematic review and meta-analysis

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ABSTRACT

Background: Clinical laboratory errors have a great impact on patient safety and treatment. Although specimen rejections result in longer turnaround times and increased health-care costs, different studies present inconsistent findings. Therefore, the study aimed to determine the pooled prevalence of blood specimen rejection in clinical laboratory.

Methods: Electronic databases including MEDLINE, PubMed, EMBASE, HINARI, Cochrane Library, Google Scholar, and Science Direct were comprehensively searched. Articles were screened and the data extracted independently by authors. Publication bias was checked by funnel-plots and Egger's statistical test. Pooled prevalence was estimated using a random-effects model. The I^2 statistical test were performed to assess heterogeneity. The possible sources of heterogeneity were analyzed through subgroup and sensitivity analysis.

Results: Total of 26 articles with 16,118,499 blood sample requests were included in the metaanalysis. The pooled prevalence of blood specimen rejection in the clinical laboratory was 1.99% (95% CI: 1.73, 2.25). Subgroup analysis showed that, the highest prevalence of specimen rejection was observed in Asia [2.82% (95%CI: 2.21, 3.43)] and lowest in America [0.55% (95% CI: 0.27, 0.82)]. The leading cause of blood specimen rejection in clinical laboratories were clotted specimen (32.23% (95%CI: 21.02, 43.43)), hemolysis (22.87% (95%CI: 16.72, 29.02)), insufficient volume (22.81% (95%CI: 16.75, 28.87)), and labelling errors (7.31% (95%CI: 6.12, 8.58)).

Conclusion: The pooled prevalence of blood specimen rejection rate is relatively high especially in developing regions. Therefore, proper training for specimen collectors, compliance with good laboratory practices specific to specimen collection, transportation, and preparation is required to reduce the rejection rate.

1. Introduction

Laboratory medicine plays a vital role in everyday clinical practice as well as in the long term follow-up of patients [1]. The dependence of patient management on laboratory data highlights the need for ensuring the quality of these services [2]. Laboratory

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Abbreviations: TAT:, Turnaround time; CI:, Confidence interval; RBC:, Red blood cell; USA:, United States of America.

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testing is generally classified into pre-analytical, analytical and post-analytical phases [3]. The pre-analytical phase encompasses stages such as test selection, patient identification, sample collection, sample handling, sorting out, pipetting, and centrifugation [1, 4–6]. Approximately 70% of laboratory errors originate in the pre-analytical phase [7]. Pre-analytical issues including missing patient's identification, inappropriate containers, missing samples and labelling errors have been a major challenges faced by the laboratory professionals [8,9].

Specimen collection is one of the initial pre-analytical processes that ensure accurate, reliable and timely results for patients [10]. Specimens are rejected by the laboratory if they do not meet predefined technical requirements for each specific analyte [11]. When samples are rejected, it is important to inform authorized personnel that the sample is unsuitable for testing, and request another sample to be collected [10]. The rejection rate reflects the pre-analytical process of the laboratory path of workflow, which includes sample collection and transport [11].

The main reason for rejection is insufficient specimen collection by the paramedical workers [12]. Some of the pre-analytical errors in the laboratory that lead to sample rejection include labeling errors, no test stated on the request form, illegible requests, clotting, inadequate blood volume, improper sample tube, hemolysis, and incorrect temperature during sample transport or storage [1]. Rejection of specimens has major clinical consequences on the patient management. Re-drawing of blood from a patient is uncomfortable, and complications such as hematoma and iatrogenic anemia are potential risks [13]. Another well-known consequence of specimen rejection is a delay in the performance and reporting of the results of the ordered tests [14]. Reduction of risk associated with the pre-analytical phase is critical for cost effectiveness, total quality improvement and customer satisfaction [15].

Since majority of laboratory errors occurred during the pre-analytical phases, the current systematic review and meta-analysis sought to determine the overall blood specimen rejection rate in the clinical laboratory as well as the causes of specimen rejection in the pre-analytical phase in the global setting.

2. Methods

2.1. Study design and search strategy

A systematic review and meta-analysis of published studies were conducted to assess the pooled prevalence of blood specimen rejection in clinical laboratory. In conducting this study, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16] were strictly followed (Supplemental Table 1). The studies were identified by conducting an online search of the databases of MEDLINE, PubMed, EMBASE, HINARI, Cochrane Library, Google Scholar, and Science Direct. The search was done using the following search terms including but not limited to specimen rejection, blood specimen rejection, blood sample rejection, laboratory rejection, sample rejection, analytical error, and clinical laboratory. The search terms were used separately and in combination using Boolean operators like "OR" or "AND". The search strategies for PubMed were (((((Specimen rejection [Title/Abstract])) OR (Blood specimen rejection[Title/Abstract])) OR (Blood specimen rejection[Title/Abstract])) OR (Blood specimen rejection[Title/Abstract])) OR (pre-analytical error[Title/Abstract])) OR (Blood sample rejection [Title/Abstract])) OR (Hematology laboratory[Title/Abstract])) OR (Biochemistry laboratory[Title/Abstract])) OR (Clinical chemistry laboratory[Title/Abstract])) OR (Clinical chemistry laboratory[Title/Abstract])) OR (Molecular biology laboratory[Title/Abstract])). Additional publications were discovered by checking the reference lists of previously recognized articles and conducting a manual search. All published articles before February 30, 2021 were included in this review.

2.2. Eligibility criteria

All prospective and retrospective cohort studies and cross-sectional studies published before to February 30, 2021, that documented the prevalence or rate of blood specimen rejection in clinical biochemistry, hematology and immunology laboratories were included. Studies which report the rate of specimen rejections other than blood specimens and histopathology samples were excluded. Review articles, case-report and case-series studies and duplicated articles published from the same dataset were excluded.

3. Outcome of interest

This review considered studies that include rate of blood specimen rejection in clinical laboratory as an outcome. Specimen rejections are defined as specimens that do not fulfill specimen acceptance criteria of the test(s) requested [13]. The second outcome of interest were determining the major causes of specimen rejection. Samples are rejected on the basis of preset rejection criteria as follows: unlabeled and mislabeled specimen, specimen without request form, wrong choice of sample collection/transportation tube, wrong label/wrong medical record number, insufficient sample, hemolyzed sample, clotted specimens, improper sample transport, and delayed specimen in transit making results invalid [9].

3.1. Data extraction and quality assessment

All the searched articles were imported into EndNote version X7 software and duplicate articles were removed. Two authors (SG and TA) independently reviewed titles and abstract of included studies and reviewed full-text of selected articles according to the eligibility criteria. Moreover, discrepancies between authors were resolved through discussion and consulting a third author (MM). Data extractions were conducted by two authors (SG and MA) independently by using an organized format on Microsoft Excel

Spreadsheet. The following data were extracted for analysis: author's name, publication year, laboratory section, sample size, rate or percentage of rejection, duration of study period and causes of rejection. Quality assessment was conducted by two experts using Joana Brigg's Institute (JBI) critical appraisal checklist for simple prevalence [17]. The checklist consists of 9 items such as [1]: was the sample frame appropriate to address the target population? [2] Were study participants sampled appropriately? [3] Was the sample size adequate? [4] Were the study subjects and the setting described in detail? [5] Was the data analysis conducted with sufficient coverage of the identified sample? [6] Were valid methods used for the identification of the condition? [7] Was the condition measured in a standard, reliable way for all participants? [8] Was there an appropriate statistical analysis? [9] Was the response rate adequate? Based on these, individual studies were assigned a score in line with the review objectives. The responses were scored 0 for "Not appropriate and not reported" and 1 for "Yes". Total scores ranged between 0 and 9. Studies fulfilling 50% of quality assessment were included for analysis (Supplemental Table 2).

3.2. Publication bias and heterogeneity

The existence of heterogeneity of the included studies was assessed using I^2 statistics and its corresponding p-value [18]. A value of 25%, 50%, and 75% was used to declare the heterogeneity test as low, medium and high heterogeneity, respectively. Random effect model was used for results with statistically significant heterogeneity. Funnel plots analysis and Egger weighted regression tests were done to detect publication bias. A p-value <0.05 in Egger's test was considered as evidence of statistically significant publication bias [19,20].

3.3. Synthesis of result and statistical analysis

The data were entered using Microsoft Excel sheet. The meta-analysis was conducted using STATA version 11 software. Forest plots were used to present the pooled effect size and weight of each recruited study with 95% CI to show a graphic summary of the data. The estimated pooled prevalence was computed with 95% CI. Subgroup analysis and sensitivity was done to assess the potential source of heterogeneity.



Fig. 1. Flow chart describing selection of studies on the prevalence of blood specimen rejection.

4. Results

4.1. Search results

We retrieved 2343 possible articles regarding the rate of blood specimen rejection as identified in PubMed, Google Scholar, Scopus, and Science Direct. After duplicate removal, 1408 articles were screened by their title and abstract of which 1359 were excluded. Of the 49 potential full text articles assessed for eligibility, 23 were excluded for major reasons (Fig. 1).

4.2. Description of included studies

In the current study 26 studies published from 2009 to 2020 across the globe were included to estimate the pooled prevalence of blood specimen rejection rate. All of the included studies were carried out in the hematology, clinical chemistry and immunology/ serology laboratory sections. The minimum sample size was 3259 specimens in a study conducted in Ethiopia [21] while the highest sample size was 10,181,036 specimens, in China [22]. Overall, this meta-analysis included a total of 16,118,499 blood specimens. The highest rate of blood specimen rejection was 10.58% in the emergency unit of Sir T General Hospital and Govt. Medical College, Bhavnagar, India [23]. The majority of the laboratories included in these studies serve patients from both inpatient and outpatient settings departments. Furthermore, the majority of the studies retrieved data from the laboratory information system retrospectively. Ten countries were represented in this review. Four of the studies were from Africa [13,15,21,24], 5 from Europe [6,25–28], 13 from Asia [3,9,22,23,29–37] and 4 from America [7,38–40] (Supplemental Table 3).

4.3. Prevalence of blood specimen rejection

A total of 16,118,499 blood specimens in 26 studies were used to estimate the pooled prevalence of blood specimen rejection in clinical laboratories. Of the total blood specimen, 106,984 of them were rejected. The minimum prevalence of specimen rejection rate were 0.11% reported from China [22] while the maximum were 10.58% in New Delhi India from emergency unit of the hospital [23].

| Author, year of publication | | ES (95% CI) | % Weight |
|---|---------|---|-------------|
| Ata'o et al, 2017 | | 1.44 (1.35, 1.53) | 3.61 |
| Atay et al, 2015 | | 0.65 (0.63, 0.67) | 3.62 |
| Goswami et al, 2014 | • | 1.99 (1.89, 2.09) | 3.60 |
| Guimarães et al, 2011 | • | 0.57 (0.52, 0.62) | 3.62 |
| Jandial et al, 2017 | | 1.47 (1.41, 1.53) | 3.62 |
| Sushma et al, 2019 | • | 3.45 (3.19, 3.71) | 3.50 |
| Tesfaw et al, 2015 | | 1.40 (1.14, 1.66) | 3.50 |
| Alavi et al, 2020 | | 1.48 (1.41, 1.55) | 3.61 |
| Ambachew et al, 2018 | | 3.80 (3.14, 4.46) | 2.95 |
| Arul et al, 2018 | | 0.43 (0.39, 0.47) | 3.62 |
| Bhat et al, 2012 | | 0.54 (0.46, 0.62) | 3.61 |
| Jacobsz et al, 2011 | | 1.46 (1.33, 1.59) | 3.59 |
| Kadic et al, 2018 | | 1.70 (1.57, 1.83) | 3.59 |
| Narang et al, 2016 | • | 0.38 (0.36, 0.40) | 3.62 |
| Ruba Abed, 2016 | | 2.02 (1.77, 2.27) | 3.51 |
| Sinici Lay et al, 2014 | • | 2.70 (2.67, 2.73) | 3.62 |
| Ye et al, 2018 | | 0.11 (0.11, 0.11) | 3.62 |
| Agarwal et al, 2012 | | 4.91 (4.70, 5.12) | 3.54 |
| Cakirca, 2018 | | 1.00 (0.96, 1.04) | 3.62 |
| Cakirca, 2018 | | 0.60 (0.57, 0.63) | 3.62 |
| Rooper et al, 2017 | | 0.74 (0.72, 0.76) | 3.62 |
| Cao et al, 2016 | • | 0.26 (0.25, 0.27) | 3.62 |
| Gupta et al, 2015 | | • 7.20 (6.98, 7.42) | 3.54 |
| Bhutani et al, 2020 | | 10.58 (10.46, 10.7) | 0) 3.60 |
| Yenice et al, 2009 | | 1.40 (1.25, 1.55) | 3.58 |
| Yenice et al, 2009 | | 1.20 (1.09, 1.31) | 3.60 |
| Coriolano et al,2016 | | 0.62 (0.59, 0.65) | 3.62 |
| Gaur et al, 2020 | | 2.14 (2.07, 2.21) | 3.61 |
| Overall (I-squared = 100.0%, p = 0.000) | | 1.99 (1.73, 2.25) | 100.00 |
| NOTE: Weights are from random effects and | alysis | | |
| | | 1 | |

Fig. 2. Forest plot showing the pooled prevalence of blood specimen rejection.

In random-effect model analysis, the pooled prevalence of blood specimen rejection in clinical laboratories was 1.99% (95% CI: 1.73, 2.25). A high level of heterogeneity was observed across the included studies ($I^2 = 100\%$, p < 0.001) (Fig. 2).

4.4. Subgroup analysis

In order to minimize heterogeneity, the pooled prevalence of blood specimen rejection in clinical laboratories, sub-group analysis was done based on WHO-region of the study where conducted. The result showed that the pooled prevalence of blood specimen rejection rate was high in the South-East Asian region [3.19% (95%CI: 2.03, 4.35)], and African region [1.79% (95%CI: 1.43, 2.15)]. However, the pooled prevalence of blood specimen rejection was low in European region [1.32% (95%CI: 0.64, 2.00)] and regions of the Americas [0.55% (95%CI: 0.27, 0.82)]. There was a significant level of heterogeneity between all of the included studies (P \leq 0.001). Furthermore, subgroup analysis by each laboratory section revealed that, the clinical chemistry section (3.05% (95%: 1.74, 4.35) demonstrated the highest number of blood specimen rejection (Table 1).

4.5. Sensitivity analysis

Due to the high heterogeneity of results, a sensitivity analysis was done to evaluate the effect of each study on the pooled estimates by omitting each study stepwise. The analysis revealed that omitted studies have no significant effect on the pooled prevalence of blood specimen rejection in clinical laboratories (Fig. 3).

4.6. Publication bias

The included studies were assessed visually by funnel plot for potential publication bias. The asymmetric funnel plot indicated the presence of publication bias since 100% of the studies fell out of the triangular region (Fig. 4). Besides, the result of Egger's regression test showed evidence of publication bias, P-value ≤ 0.001 . Because of the presence of publication bias, a trim and fill analysis were carried out to reduce the influence of studies that generate asymmetry in the funnel plot and to fill in imputed missing studies using a bias-corrected overall estimate. Accordingly, fifteen additional studies were fitted to the model, and a bias-corrected pooled estimate of blood specimen rejection in the random-effect model was found to be 0.29% (95%CI: 0.02, 0.57). Therefore, it can be concluded that publication bias has a significant impact on the overall effect estimate produced by the remaining studies (Fig. 5).

4.7. Causes of blood specimen rejection

As indicated in (Table 2) clotted specimen [32.23% (95%CI: 21.02, 43.43)] was the major cause of blood specimen rejection followed by hemolysis [22.87% (95%CI: 16.72, 29.02)]. However, insufficient volume of the specimen and labelling errors accounts the least causes of blood specimen rejection [22.81% (95%CI: 16.75, 28.87)] and [7.31% (95%CI: 6.12, 8.58)], respectively. Furthermore, the cause of blood specimen rejection was analyzed for each laboratory section. Accordingly, 40.24% (95%CI: 26.10–54.39) of samples in the hematology laboratory were rejected due to clotting, while 3.56% (95%CI: 0.84–6.28) of samples in the clinical chemistry section were rejected due to clotting. Hemolysis of blood samples was a major cause of specimen rejection in clinical chemistry laboratory section, accounting for 45.05% (95%CI: 21.97–68.14), whereas in the hematology section, it causes for 9.89% (95%CI: 7.57–12.21). Labelling error and insufficient volume of samples were approximately equal causes for sample rejection in both hematology and clinical chemistry laboratory (Table 3).

Table 1

Subgroup analysis of the prevalence of blood specimen rejection by region and laboratory section in clinical laboratories globally.

| Subgroup | Number of studies | Prevalence (95% CI) | I^2 | P value |
|---|-------------------|---------------------|-------|--------------|
| WHO- region | | | | |
| South-East Asian | 11 | 3.19 (2.03, 4.35) | 100% | \leq 0.001 |
| African | 4 | 1.79(1.43, 2.15) | 93.9% | ≤ 0.001 |
| European | 7 | 1.32(0.64, 2.00) | 100% | ≤ 0.001 |
| American | 4 | 0.55(0.27, 0.82) | 99.8% | ≤ 0.001 |
| Eastern-Mediterranean | 1 | 1.48(1.41-1.55) | - | - |
| Western-Pacific | 1 | 0.11(0.11-0.11) | - | - |
| Laboratory section | | | | |
| Clinical chemistry | 7 | 3.05(1.74, 4.35) | 100% | ≤ 0.001 |
| Hematology | 10 | 1.22(0.91, 1.53) | 100% | ≤ 0.001 |
| Hematology and clinical chemistry | 8 | 2.45(1.73, 3.17) | 100% | ≤ 0.001 |
| Biochemistry, immunology and hematology | 2 | 0.60(0.55, 0.65) | 62.5% | 0.103 |
| Biochemistry and immunology | 1 | 1.70(1.57, 1.83) | - | - |
| Combined | 28 | 1.99(1.73, 2.25) | 100% | \leq 0.001 |

Abbreviation: CI; Confidence interval.



Fig. 3. Sensitivity analysis of studies included to estimate pooled prevalence of blood specimen rejection.



Fig. 4. Funnel plot of studies included on the prevalence of blood specimen rejection rate.



Fig. 5. Funnel plot showing publication bias after employing trim-fill analysis.

Table 2

Meta-analysis results on the causes of blood specimen rejection.

| Causes of rejection | Number of studies | Prevalence (95% CI) | I^2 | p-value |
|---------------------|-------------------|------------------------------|-------|--------------|
| Clotted specimen | 24 | 32.23% (95%CI:21.02, 43.43) | 100% | ≤ 0.001 |
| Hemolysis | 26 | 22.87% (95%CI: 16.72, 29.02) | 100% | \leq 0.001 |
| Insufficient volume | 25 | 22.81% (95%CI: 16.75, 28.87) | 99.9% | \leq 0.001 |
| Labelling errors | 23 | 7.31% (95%CI: 6.12, 8.58) | 99.5% | ≤ 0.001 |

Abbreviation: CI; Confidence interval.

Table 3

Cause of blood specimen rejection by laboratory section.

| Cause of rejection | Number of studies | Laboratory section | Prevalence (95% CI) | Heterogeneity | |
|---------------------|-------------------|---|---------------------|--------------------|--------------|
| | | | | I ² (%) | P-value |
| Clotting | 10 | Hematology | 40.24(26.10-54.39) | 99.8 | ≤ 0.001 |
| | 4 | Clinical Chemistry | 3.56(0.84-6.28) | 98.3 | \leq 0.001 |
| | 7 | Hematology and clinical chemistry | 36.48(21.85-51.12) | 99.9 | ≤ 0.001 |
| | 2 | Clinical chemistry, immunology and hematology | 30.86(5.17-56.04) | 99.0 | \leq 0.001 |
| | 1 | Clinical chemistry and immunology | 39.87(35.96-43.78) | - | - |
| Hemolysis | 8 | Hematology | 9.89(7.57-12.21) | 98.8 | ≤ 0.001 |
| | 7 | Clinical Chemistry | 45.05(21.97-68.14) | 99.9 | ≤ 0.001 |
| | 8 | Hematology and clinical chemistry | 11.94(6.47-17.42) | 99.8 | ≤ 0.001 |
| | 2 | Clinical chemistry, immunology and hematology | 14.67(8.81-20.53) | 89.2 | 0.002 |
| | 1 | Clinical chemistry and immunology | 48.50(44.51-52.49) | - | - |
| Insufficient volume | 7 | Hematology | 26.12(12.85-39.38) | 99.9 | ≤ 0.001 |
| | 7 | Clinical Chemistry | 23.97(7.54-40.39) | 99.9 | ≤ 0.001 |
| | 8 | Hematology and clinical chemistry | 20.76(9.94-31.57) | 99.9 | ≤ 0.001 |
| | 2 | Clinical chemistry, immunology and hematology | 22.27(20.59-23.95) | 0.00 | 0.349 |
| | 1 | Clinical chemistry and immunology | 22.81(16.75-28.87) | - | - |
| Labelling errors | 10 | Hematology | 5.70(4.27-7.13) | 96.9 | ≤ 0.001 |
| | 6 | Clinical Chemistry | 8.89(5.65-12.13) | 98.2 | ≤ 0.001 |
| | 6 | Hematology and clinical chemistry | 8.17(6.49-9.85) | 99.5 | ≤ 0.001 |
| | 1 | Clinical chemistry and immunology | 1.66(0.64-2.58) | - | - |

5. Discussion

Clinical laboratory sample analysis is essential in the provision of health care to hospital patients. It is estimated that laboratory results influence 60–70% of all major clinical decisions such as therapy, admission, or discharge [41]. Pre-analytical errors contribute to a number of patient safety risks. Improper sample collection may cause delay patient results to be delayed due to unnecessary specimen redraws and extended remedial and preventive actions. Sample rejection prevents sample analysis, which increases turnaround time (TAT) and cause delays in patient diagnosis and treatment [40–42].

This study found that the overall rate of blood specimen rejection in clinical laboratories was 1.99% (95% CI: 1.73, 2.25). This finding is consistent with studies conducted in Africa (2.0%) [43] and Saudi Arabia (2.07%) [44], and it is higher studies conducted in India (0.54%) [32], Turkey (0.65%) [6], and Brazil (0.62%) [39]. However, it was lower than studies done in India (10.58%) [23] and Turkey (5.97%) [45]. The difference in sample size, clinician and phlebotomist awareness, operational definition of laboratory errors, and laboratory quality requirements could be reasons for this variation.

Due to considerable heterogeneity ($I^2 = 100\%$, $P \le 0.00$) across the included papers, a subgroup analysis by WHO-region was performed. According to the meta-analysis results, the highest rate of blood specimen rejection was found in the South-east Asian region (3.19% (95%CI: 2.03, 4.35)) and African region [1.79% (95%CI: 1.43, 2.15)], while the lowest was found in the European region [1.32% (95%CI: 0.64, 2.00)] and American regions [0.55% (95%CI: 0.27, 0.82)]. The possible explanation for the high prevalence of specimen rejection rate in South-east Asian and African region might be due to the lack of trained phlebotomist for proper sample collection, inadequate infrastructures, increased patient flow or poor-quality management system and poor adherence to follow standard operating procedures. Standardization and monitoring of pre-analytical variables, establishing well-organized laboratories, adequate educational and technological trainings which results reduce operational costs and increased revenues of the laboratories is need [46,47]. Likewise, the subgroup analysis of this study on each laboratory section, the highest pooled prevalence blood specimen rejection was detected in clinical chemistry section (3.05% (95%CI: 1.74, 4.35), followed by the hematology section (1.22% (95%CI: 0.91, 1.53)). The possible reason for the variation could be attributed to the difference in the number of quality indicators, study design, sample size, and laboratory performance.

A trim and fill analysis were performed due to the presence of publication bias in order to reduce the effect of studies that induce asymmetry in the funnel plot and to fill in the imputed missing studies using a bias-corrected overall estimate. As a result, when an additional 15 missing studies are included, the pooled estimate of blood specimen rejection in the random-effect model falls from 1.99% to 0.29%. This indicates that publication bias has an effect on the overall effect estimate, which can affect the validity and

generalization of conclusions [48].

This meta-analysis also aims at identifying the possible reasons of blood specimen rejection in clinical laboratory. The most frequent cause of specimen rejection was clotted specimen (32.23% (95%CI: 21.02, 43.43)). The result was comparable with studies conducted in China [22], USA [40], and Turkey [28] which reported clotting as the main cause of sample rejection. Clotting is a major cause of samples rejection in hematology laboratory (40.24% (95%CI: 26.10–54.39)), while it less common in clinical chemistry section (3.56% (95%CI: 0.84–6.28)). The finding is consistent with previous studies by Cakirca et al. [27], Goswami et al. [29], and Narang et al. [33]. The probably reason might be due to poor mixing after blood collection [29]. The Clinical Laboratory Standards Institute recommends that all diagnostic blood specimens collected in vacuum tubes are recommended to be inverted gently several times to maximize the contact between blood and additives following blood collection [49,50]. Clotting produce low red cell counts (RBC), aberrant red cell indices, low hematocrit, low white cell counts, and platelet count [51,52]. It also contributed to instrument probe aspiration and clogging, leading to service calls and downtime [53], which prolong TAT of the specimens processing and result reporting.

The second frequent reason for specimen rejection in this study was hemolysis, which is in agreement with the results reported in Brazil [7] and USA [40]. In line with previous studies [27,30], hemolysis of blood samples were a major cause rejection in clinical chemistry laboratory section. Because hemolysis is known to interfere with the measurement of several biochemical analytes such as lactate dehydrogenase, aspartate aminotransferase, potassium, and total bilirubin [54]. In vivo hemolysis occurs as a result of the premature death of RBCs due to antigen-antibody reactions, chemical reaction, toxins and poisonous substance, and mechanical destruction of RBC [55–57]. In vitro hemolysis could be due to pre-analytical errors like incorrect needle size, improper tube mixing, incorrect filling of tubes, excessive suction, prolonged tourniquet, extreme temperature, delayed processing, and prolonged storage [58–60].

This study found that the other cause of sample rejection was due to insufficient or inadequate volume of the specimen which accounts 22.81% (95%CI: 16.75, 28.87) of rejection. This finding was in line with single centered studies conducted in Malaysia [11], South Africa [15], and India [23]. Collection of an inadequate volume may also cause blood clotting. For the anticoagulant to perform the expected action, it is necessary that the proportion of blood/anticoagulant ratio is according to the tube manufacturers' recommendations [39,61]. Studies shows that the incidence of insufficient volume is remarkably high in pediatric, neonatal, and oncology wards, in which peripheral vascular access is difficult [62,63]. Labelling errors (mislabeled and unlabeled specimens) is the less frequently reason for blood specimen rejection in this study. The result was comparable with previous studies done in South Africa and India [15,30]. This may occur at the time of collection where patients are misidentified, the use of illegible handwritten labels and mix-ups occurring before or after collection [64,65]. It can lead to delayed diagnosis, additional laboratory testing being ordered, or the patient being treated for the wrong medical condition.

This review used a comprehensive search strategy and PRISMA guideline was strictly followed during the review process. The limitation of this study was that only articles published in English language were included. Besides, the meta-analysis showed that there was statistical level of heterogeneity and publication bias which may potentially limit the conclusions of the study. All of the criteria for specimen rejection are not included in this study, only hemolysis, clotting, labelling error and insufficient volume were assessed which could potentially limit the study findings.

6. Conclusion and recommendation

In clinical laboratories, the overall prevalence of blood specimen rejection was significant. Clotted specimens, hemolysis, insufficient volume, and labelling errors were the top major reason for specimen rejection. Clotting and hemolysis of blood specimens was a major reason of sample rejection in hematology and clinical chemistry laboratory section, respectively. Specimen rejection has significant consequences including patient discomfort, unnecessary specimen redraws, and delay in diagnosis and treatment of patients. Therefore, targeted training for sample collectors and adherence to policies and procedures specific to specimen collection, transportation, and preparation is necessary. In addition, laboratories themselves should regularly review the specimen rejection rate and related influence factor and take effective actions.

Ethical approval

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Author contribution

All authors involve in literature search, manuscript draft, review, statistical analysis, final approval, and quality assessment. The authors critically revised the paper and agreed to be accountable for all aspects of the work.

Consent for publication

Not applicable.

Declaration of competing interest

The authors declare that they have no competing interests.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.plabm.2022.e00303.

Abbreviations

- TAT Turnaround time,
- CI Confidence interval
- RBC Red blood cell
- USA United States of America

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