ORIGINAL ARTICLE

Evaluation of Blood Sample Rejection in a Clinical Laboratory of an Oncology Institute

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ABSTRACT

Introduction: Error in blood sampling is of one the commonest causes of laboratory sample rejection and poses a great challenge particularly amongst oncology patients due to difficult venous access. This study aims to identify the main causes of blood sample rejection in the haematology and chemical pathology (CP) laboratories of an oncology institute. **Method:** All blood samples received and rejected in the CP and haematology laboratory from 2017 to 2019 were obtained from the laboratory information system (LIS) and sample rejection logbook. The rejection cause for each of the rejected samples was recorded and analysed. **Results:** Out of the total 39 495 blood samples received, 244 (0.6%) were rejected. The rejection rate in the CP was higher compared with that in the haematology laboratory (51.2% vs. 48.8%). The most frequent cause of rejection was haemolysis (49.6%), clotted sample (32.8%), and insufficient sample volume (6.1%). **Conclusion:** Haemolysis, clotted blood and insufficient sample were the main causes of sample rejection in our oncology centre. Effective and multidisciplinary targeted interventions to reduce blood sampling error are important to improve pre-analytical handling of blood samples from oncology patients.

Keywords: Haematology, Biochemistry, Oncology, Pre-analytical, Sample rejection

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INTRODUCTION

A medical laboratory plays a major role in providing accurate and timely laboratory investigation results essential for patient management. About 70% of medical diagnosis is established through the support of laboratory investigation results (1). A laboratory result is generally generated through a series of processes consisting of three phases, namely, pre-analytical, analytical, and post-analytical phases. The pre-analytical phase is the most crucial as it contributes to the majority of laboratory results errors i.e 46%- 70%, compared to the other phases (2,3).

Pre-analytical activities begin from a clinician's request for a laboratory test to sample preparation for analysis. Among pre-analytical errors, blood collection errors are the most frequently observed in most laboratory medicine (4,5). These errors could jeopardize the laboratory test results and have a detrimental effect on patient care such as delay in diagnosis, inappropriate treatment, and prolonged hospital stay. The pre-analytical specimen error costs between 0.23% and 1.2% of total hospital operating costs and is extrapolated to approximately USD 1,199,122 in a 650 beds hospital in the United States (6).

There are patients with difficult venous access such as oncology patients. Most of these patients have received multiple cycles of chemotherapy and are susceptible to vein damage secondary to extravasation of vesicant chemotherapy infusion (7). Previous studies have found that laboratories may differ in terms of their leading cause of blood sample rejection (8,9). Therefore, we have conducted a retrospective study to determine the main causes of blood sample rejection amongst oncology patients in the chemical pathology (CP) and haematology laboratories of Advanced Medical and Dental Institute (AMDI), Universiti Sains Malaysia (USM).

AMDI is a tertiary referral centre for solid cancer in northern Malaysia. Most of the samples received in our medical laboratory are from adult oncology patients. The result of this study provides data for planning of targeted interventions amongst healthcare workers in terms of pre-analytical errors.

MATERIALS AND METHODS

Research location

The study was conducted in the CP and haematology laboratories of Advanced Diagnostic Laboratory (ADL). CP and haematology laboratories were chosen because they received the largest portion of blood samples in ADL. These laboratories have MS ISO 15189 accreditation and well-established procedures for monitoring pre-analytical errors including sample rejection.

Data collection

This study was a retrospective data analysis of sample rejection obtained from the laboratory information system (LIS) and sample rejection logbook from 2017 - 2019. All blood samples registered for the CP and hematology testing within the period were included. Samples without rejection cause documented were excluded. All the rejected samples with documented cause of rejection were recorded and analysed. The percentage of samples rejection in each laboratory was determined. The type of tests requested and the cause of rejection were identified for each rejected sample. The number and percentage for each rejection cause were determined in accordance with the pre-set criteria i.e haemolysis, clotted blood, sample mislabelling, volume overload, sample leakage, double request, missing sample, wrong test requested, insufficient volume, contaminated sample, overnight sample and wrong container.

Statistical analysis

Data were expressed as number and percentage (%). Statistical analysis was performed using IBM SPSS Statistics for Windows (version 24.0 IBM Corporation, Armonk, NY, USA) and Microsoft Excel (Microsoft Corporation, Redmond, WA, USA).

Ethical approval

This study was granted an ethical approval from The Human Research Ethics Committee of USM (JEPeM). Ethical approval number???

RESULTS

A total of 244 out of 39495 (0.6%) blood samples were rejected during the study period in both CP and haematology laboratory (Table I). The cause of sample rejection and tests are listed in Table II and III respectively. The number of rejected blood samples in the CP was slightly higher than that in the haematology laboratory [125 (51.2%) vs. 119 (48.8%)]. In the CP laboratory, majority (81%) of sample rejection involve renal function test (RFT) and liver function test (LFT). Haemolysis was the main cause of rejection, followed by wrong blood tube and clotted blood. In the haematology laboratory, almost 90% of sample rejection was for full blood count (FBC). Clotted blood was the leading cause of rejection, followed by haemolysis and insufficient sample volume.

Table 1: Blood specimen received and rejected in CP and Haematology laboratory from 2017 – 2019

	Blood specimen received	Rejection, n (%)
Chemical pathology	25,524	125 (0.5)
Haematology	13,971	119 (0.9)
Total	39,495	244 (0.6)

Table II: Causes of sample rejection from 2017 – 2019

	Chemical Pathology n (%)	Haematology n (%)	Total, n (%)
Haemolysed	107 (85.6)	14 (11.8)	121 (49.6)
Clotted sample	4 (3.2)	76 (63.9)	80 (32.8)
Insufficient volume	2 (1.6)	13 (10.9)	15 (6.1)
Contaminated sample	3 (2.4)	0	3 (1.2)
Overnight sample	3 (2.4)	1 (0.8)	4 (1.6)
Wrong container	6 (4.8)	7 (5.9)	13 (5.3)
Sample mislabelling	0	1 (0.8)	1 (0.4)
Volume overload	0	2 (1.7)	2 (0.8)
Sample leakage	0	1 (0.8)	1 (0.4)
Double request	0	2 (1.7)	2 (0.8)
Missing sample	0	1 (0.8)	1 (0.4)
Wrong test requested	0	1 (0.8)	1 (0.4)
Total	125 (51.2)	119 (48.8)	244 (100)

Table III: Type of tests requested for the rejected samples from 2017 – 2019

Tests	Number, n (%)
Chemical Pathology	
RFT	7(6)
RFT and LFT	75(60)
RFT, LFT and FLP	6(5)
RFT, LFT and FBS	4(3)
RFT, LFT, FLP and FBS	9(7)
Others	24(19)
Haematology	
Full blood count (FBC)	102(88)
Prothrombin time and activated partial thrombin time (PT/ aPTT)	10(8)
Erythrocyte sedimentation rate (ESR)	5(4)

RFT = Renal function test (Sodium, potassium, chloride, urea, creatinine, uric acid, calcium, phosphate).
LFT = Liver function test (Total protein, albumin, globulin, alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, total bilirubin, indirect and indirect bilirubin).
FLP = Fasting Lipid Profile (Triglyceride, total cholesterol, LDL and HDL).
FBS = Fasting blood sugar.
Others = HbA1c, tumor markers and hormones,etc

DISCUSSION

This current study showed that the overall rejection rate in CP and hematology laboratories was 0.6%. This rate is similar to other tertiary hospitals or oncology centres that with reported sample rejection rates between 0.44% and 1.46% (9–11). The major causes of blood sample rejection are similar to those from other studies stating

that clotted blood, haemolysis, and insufficient sample volume are amongst the main cause (12,13).

In this study, we found a remarkable difference in the main cause of blood sample rejection between CP and the haematology laboratories. In the CP, haemolysis is the leading cause of sample rejection, whereas, in the haematology laboratory, clotted blood appeared to be the leading cause. This difference is attributed to the type of tests and testing protocol performed in the laboratories. As haemolysis is well known to interfere with the measurement of many biochemical analytes such as lactate dehydrogenase, aspartate aminotransferase, potassium, and total bilirubin, measurement of sample haemolysis using automated haemolytic index (HI) is therefore routinely performed for all samples (14). Consequently, the haemolysed sample in CP is more commonly encountered compared with that in the haematology laboratory.

By contrast, the detection of sample haemolysis is not routinely practised for testing of FBC or coagulation screening in our haematology laboratory. When sample haemolysis is suspected, the laboratory usually performs the confirmation through visual inspection. Getahun et. al. 2019 showed that the level of agreement between automated serum indices and visual inspection of the sample was only moderate (15). Hence, the visual inspection practice probably has led to the under-reporting of haemolysis, contributing to the lower rate of sample rejection due to haemolysis in the hematology laboratory.

As most oncology patients have small superficial veins, drawing blood samples by using a small-bore needle produces excessive aspiration thus increases the risk of haemolysis (16). Based on a few recent studies, the haemolysis of a mild to a severe degree is also shown to interfere with haematological parameters, causing inaccurate results (17–19). Considering the significant impact on the patient's result, therefore, we recommend that HI examination should also be performed routinely during the sample analysis for haematology testing. This can be done by consolidating a quantitative measurement of HI on the automated haematological measuring platform through the in-vitro diagnostic company, like in most current biochemistry analysers. The automated measurement of HI should be a better option for the detection of sample haemolysis to ensure that accurate and reliable haematology results are delivered for the patient's care.

The rejection pattern in our haematology laboratory is similar to that reported by Goswami et. al. 2014. The main causes of sample rejection in their haematology laboratory were clotted blood (78.57%) followed by haemolysis (7.64%), and inadequate sample volume (3.86%) (20). One of the possible factors leading to the high rate of the clotted blood in our haematology laboratory is inadequate blood mixing by the staff during the phlebotomy. According to the Clinical and Laboratory Standards Institute (CLSI) guideline, the blood collected in citrated and ethylenediaminetetraacetic acid (EDTA) tube for coagulation screening and FBC test requires an immediate and adequate mixing by tube inversion (i.e approximately 3 to 4 times for citrated and 8 times for EDTA tube (21). Inadequate blood mixing leads to clot formation, thus rendering it unsuitable for sample analysis. In the biochemistry laboratory, the blood collected in the serum separator plain tubes are allow clotting to separate the serum from the blood cells before centrifugation. Thus, the clotted blood sample is minimally reported in a biochemistry laboratory. Other causes of clotted blood samples are slow blood drawing into the syringe and delay in transferring the blood into the tubes (22). Given that our oncology patients are considered at risk of difficult venous access, prolonged venous manipulation during blood taking is considered as a contributing factor to the increased clotted blood in our haematology laboratory.

Many studies have shown that inappropriate sample collection and sample handling techniques contribute to blood sample rejection in clinical laboratories (23,24). As oncology patients are considered at increased risk of having compromised blood samples due to difficult venous access, a proper phlebotomy technique must be practiced and followed. Unfortunately, not all health institutions have highly skilled phlebotomists. As such, intervention through continuous medical education, seminar, or workshop about phlebotomy techniques and the pre-analytical aspect of testing among clinical staff are important measure to prevent low-quality samples collection from oncology patients. Arslan et. al. 2018 show that training on pre-analytical processes results in a significant decrease in pre-analytical error from 0.6% before training to 0.5% after training (25). Moreover, a local standard guideline about pre-analytical sample handling and sample collection is also needed to reduce heterogeneity in the process. In addition, education and training of laboratory staff on the visual assessment of haemolysis or clotted blood are appropriate measures especially in laboratories that are unable to procure automated HI detection systems due to limited financial resources.

A more specific measure to reduce sample rejection in oncology patients is the use of a chemo port for blood collection to avoid puncturing the smaller superficial veins. If the patient does not have a chemo port, a vein scanner using near-infrared light or ultrasound-guided visualisation should be used to improve venous access visualisation (26). The avoidance of small and superficial veins, and vigilance in drawing blood during phlebotomy, may help to prevent haemolysis and clotted blood, thereby lowering the risk of sample rejection.

Our institution uses a pneumatic transport system (PTS)

to improve laboratory operational efficiency. However, several studies have shown that PTS causes haemolysis of the sample and fragmentation of platelet due to sudden acceleration or deceleration, and vibration of the sample during transportation (27,28). Therefore, placing sample protectors such as sponge rubber or lining the conveyor container with cotton can be done when sending oncology patients' samples.

Considering that both CP and haematology laboratories are accredited under MS ISO 15189, proper sample rejection management and monitoring are essential as it represents one of the laboratory quality indicators (5). Feedback on the rejection rate and its causes need to be communicated to the ordering department. Laboratory comments regarding the compromised samples and the analytes affected should be stated in the laboratory report to alert the staff to be more cautious during blood sampling. Lastly, customer feedback meetings can also be conducted to discuss the appropriate strategy that can be implemented for the improvement of the blood collection activity as well as the patients' care.

Nevertheless, this study has some limitations due to its small sample size. In this study, we are unable to detect other uncommon rejection criteria such as icteric or lipaemic samples. Hence, a big sample population or interventional study is recommended to reduce the bias. Considering that this is a retrospective study of LIS data, we are unable to investigate the clinical consequences of sample rejection in oncology patients. As the information is clinically important especially to the treating clinicians, a prospective study is recommended to evaluate the clinical consequences of sample rejection in oncology patients.

CONCLUSION

Haemolysis, clotted blood and insufficient sample are the main cause of sample rejection in CP and haematology laboratories at our oncology centre. The evaluation of sample rejection is necessary to prevent inaccurate laboratory results related to sample handling error. Effective and multidisciplinary targeted interventions involving both laboratory and clinical staff are important to reduce rejection rate of blood sample, ensure the accuracy and reliability of the test results and subsequently improve oncology patient's care.

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