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ASSESSMENT OF SPECIMEN REJECTION RATE AND ASSOCIATED FACTORS AMONG SAMPLES REFERRED TO ADDIS ABABA RESEARCH AND EMERGENCY MANAGEMENT CORE PROCESS LABORATORY, ADDIS ABABA, ETHIOPIA.

By: Berisa Adugna (BSc)

Advisors: Aster Tsegaye (PhD)

Habtamu Molla (MSc, PhD candidate)

Collaborator: Redwan Mohamad (MSc)

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This is to certify that the thesis prepared by BerisaAdugna entitled:

Assessment of Specimen Rejection Rate and Associated Factors Among Samples Referred to Addis Ababa Research and Emergency Management Core Process Laboratory, Addis Ababa, Ethiopia, from June 01, 2018 to May 30, 2020 G.C.and submitted in partial fulfillment of the requirements for Master of Science degree in Clinical Laboratory Sciences (Clinical Laboratory Management and Quality Assurance) complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

Signed by the Examining Committee:

External Examiner_____Signature _____ Date _____

Internal Examiner_____ Signature _____ Date _____

Advisor_____ Signature _____ Date _____

Advisor_____ Signature _____ Date _____

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Chairman of the Department or Graduate Program Coordinator

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Contents

List of Tables **page**

List of figures page

Abbreviations

AAPHREML	**Addis Ababa public health research & emergency management core process laboratory**
CD4	Cluster of differentiation 4
CLSI	Clinical laboratory standard institute
DBS	Dried blood spot
EDTA	Ethylene diamine tetra acetic acid
EID	Early infant diagnosis
EPHI	Ethiopia public health institute
HIV	Human immunodeficiency virus
ISO	International organization for standardization

Abstract

Background: Accurate laboratory results are vital for patient safety and improving the medical diagnosis. Most errors occurred in the pre-analytic phase. Improper collection of samples can lead to sample rejection. In this case laboratory should establish rejection criteria and follow them closely. Specimen rejection may have significant consequences for patients and their clinical management. Thus, understanding the magnitude and taking appropriate action is critical for quality laboratory service provision.

Objective: to assess the Specimen rejection rates and associated factors among samples referred to the laboratory of Addis Ababa Research and Emergency Management core process.

Methods: cross sectional study was conducted using both primary and secondary data which assesses the rate and reason of rejection observed from June 01, 2018 to May 30, 2020 G.C. About 131,909 specimens collected at Addis Ababa Research and Emergency management core process laboratory with in the period of the study was entered and analyzed using SPSS 20.

Result: a total of 131,909 specimens were sent to central reception of the Addis Ababa public health research and Emergence management core processes laboratory. The total rejection rate was 0.69%, 915. The frequencies of rejected specimens were highest in viral load 35.1%, followed by clinical chemistry which was 23.4%. The most common reason of rejection was mislabeling, 27.1%, followed by insufficient 15.8%, and clotted 15.1% specimen. Among rejected specimens, 514 specimens were rejected in the first and 401 Specimens were rejected in the second.

Conclusions: The study demonstrated about 0.7% specimen rejection rate. Alongside of the efforts to minimize laboratory error, this study highlighted a complexity of pre-analytical errors to minimize them. The most commonly rejected specimens were for viral load followed by clinical chemistry samples. The most common pre analytical reason for specimens' rejection was mislabeling, followed by insufficient and clotted specimens.

Key words: *Specimen rejection, Pre-analytic phase, Clinical laboratory, Error*

1. INTRODUCTION

1.1. Background

Clinical laboratories represent an area of health care that has undergone a great deal of improvement in recent years [1]. Its origins may be traced to those early 19th century by French patho clinicians, so called because they were the first to put the practice of medicine on a rational basis by correlating clinical with autopsy findings [2]. Accurate laboratory results are vital for patient safety and improving the medical diagnosis of patients, and many studies have shown that 70% of medical diagnostic decisions depend on the accuracy of laboratory tests. Despite advanced automation in diagnostic labs, there are still considerable error rates at clinical diagnostic laboratory [3].

Quality is the core issue for all laboratories and this requires total quality management in the laboratory process in the pre-analytic, analytic, and post-analytic phases. Promotion of ideal phlebotomy practices and sample transport procedures are a pre-requisite for the effective laboratory functioning. Samples collected outside the laboratory should be transported for test frequently. In this case, transport must be managed carefully in order to maintain sample integrity, temperature, preservation needs, special transport containers, and time limitations. Personnel who package or transport the specimen should be trained about the proper procedures, both for safety and for good maintenance of samples. Keeping record of the errors at all stages of analysis and devising corrective strategies for their future prevention can gradually free a laboratory from errors [4].

The errors anywhere in the laboratory work flow leads to chaos and especially laboratory errors may affect the patient care. The laboratory error has been defined by different bodies in different terms. The term "laboratory error" is defined in International Organization for Standardization (ISO) 22367 as "failure of planned action to be completed as intended, or use a wrong plan to achieve an aim, occurring at any part of the laboratory cycle, from ordering examinations to reporting results and appropriately interpreting and reacting them [5].

Limited attention is given to extra-laboratory factors while the body of evidence points to the multitude of errors that continue to occur in the pre-analytical phase. Pre analytical errors account for up to 70% of all mistakes made in laboratory diagnosis, most of which arise from

problems in patient preparation, sample collection, transportation, and preparation for analysis and storage. While patient preparation and sample collection (including patient and sample identification, and specimen handling) are widely recognized as frequent sources of errors, greater attention should be paid to sample transportation. This area needs improvement initiatives, as there is an increasing trend towards consolidation of laboratory facilities, with a consequent need for long-distance sample transportation. The most commonly reported types of pre-analytical error are: missing sample and/or test request, wrong or missing identification, contamination from infusion route, hemolysed, clotted, and insufficient samples, inappropriate containers, inappropriate blood to anticoagulant ratio, inappropriate transport and storage conditions [6].

The term “specimen” is very commonly used in the laboratory to indicate a sample taken from the human body and it is useful to note that in some of the existing transport regulations, the term “specimen” continues to be used. Patient samples are sometimes collected by the patient themselves, for example, faecal parasitology samples. It is important that the laboratories have set protocols to ensure that appropriate collection kits with instructions for collection, safety precautions, and labeling are available for their patients. It is suggested that instructions for the patients be in the languages for the community the laboratory is serving or presented as simple easy-to-understand graphics. Improper collection of samples can lead be to sample rejection, in this case laboratory should establish rejection criteria and follow them closely. It is sometimes difficult to reject a sample, but remember that a poor sample will not allow for accurate results. It is the responsibility of the laboratory to enforce its policies on sample rejection so that patient care is not compromised. Management should regularly review the number of rejected samples and reasons for rejections, conduct training on sample collection, and revise written procedures for sample management as needed [7].

Specimen rejection may have significant consequences for patients and their clinical management. Patients whose specimens are rejected are frequently subjected to repeated specimen collection, resulting in inconvenience, the discomfort of repeated phlebotomy or other collection procedures, and/or the potential need for blood transfusion due to excessive iatrogenic blood loss [8].

It is, therefore, important to study and explain the rates and reasons of rejected referral samples, for relevant measures to be undertaken by the laboratories.

1.2. Statement of the Problem

Laboratory diagnostics is pivotal part of clinical decision making but no safer than other areas of health care, with most errors occurring in the manually intensive pre analytical process [9].According to a study, about 10% of patients in countries that make up the European Union are at risk of some kind of error during hospitalization. It cannot be denied that laboratory errors play a significant role to the overall risk of error, because laboratory medicine like any other diagnostic field is susceptible to errors. It is evident that most of the errors occur in the pre-analytical phase of the total testing processes [10].

A review by Julie A et al regarding medical errors in laboratory diagnostics showed that a pre-analytical error rate for in patients was1.9%. The variable receiving the highest frequency rating was specimen hemolysis at 1.10%. For the outpatients, the error rate was 1.2%, and the variable with the highest frequency rating was insufficient volume for testing [11].

The study by Giménez-Marín A. et al at Hospital de Antequera, Antequera, Málaga, Spain on Pre-analytical errors management in the clinical laboratory in2014 showed that the total error rate for the study period was 13.54%, the highest rates corresponded to the indicators “hemolysed sample” 8.76%, and “clotted sample” 1.41% [12].

The survey by Najat D on Prevalence of Pre Analytical Errors in Clinical Chemistry Diagnostic Labs in Suleiman City of Iraqi Kurdistan investigated frequency and types of pre-analytical errors. Delay in sample transportation, expired reagents, hemolyzed and clotted samples were the most common types of errors, presenting 39%, 27%, 26% and 26%, respectively. [2].

There is limited study in Ethiopia regarding specimens’ rejection and their reasons. The rejection rate reported by Ambachew etal at the University of Gondar Hospital, Northwest Ethiopia for clinical chemistry tests were 3.8% [13].A lower rejection rate of 1.4% was reported by Molla etal at St. Paul’s Hospital Millennium Medical College, Addis Ababa Ethiopia [14].For both studies, the most frequently occurring pre-analytical problems were inadequate sample collection ,followed by hemolysis. Sample rejection prevents sample analysis and leads to new sample request, which delay in patient’s diagnosis and treatment.

In Ethiopia, A laboratory specimen referral network is composed of laboratories at each level of the healthcare system that are committed to facilitate the proper diagnosis of diseases, which

have clinical and public health impacts. Until now, both administrative boundaries and geographical proximities were the basis for the laboratory network and referral system in the country. Laboratory specimen referral network is solely based on the geographic proximity, availability of road and testing services so that the referral will be to the geographically closest referral laboratory. The belief is that this arrangement minimizes the turnaround time for obtaining results, reduces transportation costs, and maximizes the benefits of the specimen referral testing services [15].

Therefore, this study is focused on determining a reasons causing sample rejection and immediate actions were taken to improve sample rejection rate at Addis Ababa research and emergency management core process laboratory.

1.3. Significance of the study

Assessing the frequency and identifying the reasons for specimens rejection aid in the planning of the preventive and corrective operations in order to reduce the incidence of these errors. This in turn helps to avoid unnecessary repeated sample collection from patients, and provision of timely result.

Reducing percentage rate of specimen rejection enhances patient care and safety, satisfied clinicians, satisfied referring institutions and regional laboratory since it leads to high quality results and eliminates possibility of redrawing new specimen.

By determining rate of rejected specimens, periodic information will be provided to health care, and this will expect to decrease sample rejection at Addis Ababa research and emergency management core process laboratory. The finding will also serve as reference for future studies.

2. Literature review

The ISO 15189: 2007 standard for laboratory accreditation defines the pre analytical phase as steps starting in chronological order, from the clinician's request, preparation of the patient, collection of the primary sample, and transportation to and within the laboratory, and ending when the analytical examination procedure begins. This clearly recognizes the need to evaluate, monitor and improve all the procedures and processes on specimens [16].

Aprospective study on Clinical Consequences of Specimen Rejection at College of American Pathologists by Donald S. Karcheretalin 2014 assessed 78 Clinical Laboratories information relating to the rejected specimens. A substantial majority (96.5%) of rejected specimens was blood, with essentially equal numbers of chemistry and hematology specimens. The reason for most rejected specimens 92.4% was inappropriate/inadequate specimen. The remaining 7.6% were rejected owing to improper labeling [8].

Frequency of specimen rejection varies according to the nature of specimens ordered. The type of specimens could be complete blood count (CBC) specimens, coagulation specimens, serum etc. Lai X and colleagues reported that in Hospital of Chongqing Medical University, 0.19 % unqualified samples were identified. From these rejected specimens, samples collected for coagulation tests were the predominant unqualified samples. They also identified the main causes of generation of unqualified samples were insufficient sample volumes and improper methods of mixing the samples [17].

A cross sectional survey by Yuanyuan Y, et al in 2018 investigated Hematology specimen acceptability in a national survey in Chinese laboratories. The study investigated distribution of rejected specimens in Beijing Hospital, National Center of Gerontology, Beijing, China, and the reasons for rejection. Accordingly, about 85% of rejections attributed to the five reasons: specimen clotted 57%, insufficient specimen volume 14%, inappropriate specimen-Anticoagulant volume ratio 6.9%, incorrect container type 4.2% and inadequately labeled (2.9%) [18].

A research done by Soni DS et al from India showed that sample rejection rate of the Microbiology Laboratory of tertiary care hospital in the month of July 2010 was 0.31%. After the training of the nursing staff as well as resident doctors regarding proper collection and

transport of samples based on scientific principles, a decreasing trend in the sample rejection rate was observed, from 0.31% to 0.11 % in the 13 months duration of the study [19].

The effect of point of collection on proportion of specimen rejection was studied, at The Henry Ford Health System, the largest health care provider in south-eastern Michigan, by Stark et al using retrospective study design. The investigators reported that 0.74% specimen were rejected because of errors in the Pre analytical phase of laboratory medicine. Specimens rejected in emergency department and inpatient service were 2-fold and 5-fold higher, respectively, than for the outpatient service [20].

The retrospective study by GokhanCakirca 2018 on ratios of blood sample transfers at Dept. of Biochemistry, Sanliurfa Mehmet AkifInan Training and Research Hospital, Sanliurfa, Turkey determined 1% of samples in the hematology laboratory and 0.6% in the biochemistry laboratory were rejected. The most common cause of rejection in the hematology and biochemistry laboratories was insufficient volume (48.8%) and hemolyzed sample (74.1%), respectively [21].

Descriptive preliminary study was conducted at KatipCelebi University, Ataturk Training and Research Hospital, Department of Clinical Biochemistry, Izmir, Turkey by Atay A.et al 2018to identify rejection rates of blood drawing errors. Common reasons for rejection were hemolysis, clotted specimen and insufficient volume of specimens with a rate of 8%, 24% and 34%, respectively. Among all rejected samples in the study, hemolysis affected the specimens of inpatients in clinical chemistry and coagulation test groups. The clotted specimen error was seen in hematology.

Insufficient volume of specimen error in coagulation was found as the most common rejection cause among other types of errors in the study. The study identified citrated plasma samples used to study for coagulation, exhibited the highest percentage of rejection rate of blood drawing errors that is 71% of the total rejection of all test groups. Whereas the lowest rate had corresponded to serum samples in clinical chemistry [22].

Retrospective study conducted at Prince Hamzah Hospital, Amman/Jordan over a six months period by Abed R; from January 1, 2011 to June 30, 2011 showed that the average rejection rate was 1.5%. The rate of specimen rejection was highest in the medical ward and clotted specimens were the commonest cause for rejection followed by wrong patent identification [23].

Retrospective study conducted at School of Medicine and Health Science by Atan'O M et al. 2017 on rate of rejection of hematology sample in pathology department, University of Papua New Guinea, identified reasons for specimen rejection.The study indicated that the clotted samples for full blood examination were the most common rejection with 19.24%. Other causes of rejection observed were requisition forms without samples, 18.3%, 15.65% unlabelled samples, 13.90% without laboratory request forms, and 12.89% within correct tube /incorrect cap [24].

A retrospective study conducted by Upreti S et al at ChatrapatiShivaji Hospital on a total of 135,808 samples received for testing, 1339 samples were found inappropriate for diagnosis, which approximately constituted 1 % of all samples. Highest numbers of samples were rejected due to misidentification that is 0.35 % and least number were rejected due to dilution of the samples that is 0.04 % [25].

According to a retrospective study conducted by Inalegwu A, et al. 2016 on Active tracking of rejected dried blood samples in a large program in Nigeria,asample rejection rate of 2.4% and repeat rate of 8.8% were established. The major reasons for rejection were improper sample collection (26.3%), improper labeling (16.4%) and insufficient blood (14.8%) [26].

The retrospective audit on Chemistry and hematology sample rejection and clinical impact in a tertiary laboratory in Cape Town by Laurens A.et al. 2016 revealed that the main reasons for rejection of hematology samples were inappropriate clotting (44 %) and insufficient volume or inadequate ratio of sample volume/anticoagulant (21 %). Rejected samples from chemical pathology were mainly due to insufficient volume (31 %) and labeling errors (23 %) [27].

The analysis of database records for 2014 of early infant diagnosis (EID) sample at KwaZulu-Natal, South Africa by Govender K, et al. (2016) showed that insufficient specimen volume comprised 48.9% of the total number of rejections resulting from pre-analytical problems. Other reasons for rejections included: inadequate information supplied on the test request form; incorrect clinical indication for the test; and poor specimen quality, such as incorrect specimen type, specimens that were too old for analysis and specimen cards that were expired [28].

The cross sectional study by Chiku C, et al. (2019) was the first study in Zimbabwe’s EID-program that assesses the magnitude of and reasons for the rejection of dried blood spot (DBS)

samples sent by five provinces for analysis. The study shows Thirty-four DBS samples for which no reason for rejection was stated on the request form were excluded from their analysis. The major reason for rejection of DBS samples was insufficient specimen volume. If there was insufficient blood on all 5 spots of the DBS card, the volume was considered inadequate and the sample rejected. Other reasons for rejections were missing request form, missing sample, cross contamination, clotted sample, or mismatched information. They also analyzed the number and proportion of rejected DBS samples by province. Rejection rate ranged from 2% to 7% among the 5 provinces. Mashonaland West 7% and Midlands Province 4% showed the highest rejection rates [29].

A cross sectional study was carried out by AmbachewS, et al on errors in the total testing process in the Clinical Chemistry Laboratory at the University of Gondar Hospital, Northwest Ethiopia. The study identified that among the total number of samples submitted to the laboratory for Clinical Chemistry tests, 3.8% were rejected. The most common reason for sample rejection was hemolysis, followed by the request with no sample or sample with no request and mislabeled, 1.1%. Among the pre-analytical errors, incomplete request form filling was the most frequent error observed with sample rejection rate 3.8%. Analytical errors related to internal and external quality control exceeding the target range, 14.4% and 51.4% respectively, were reported [13].

In Ethiopia retrospective study at Amhara Public Health Institute by Shiferaw et al. in 2018 showed that, among the total submitted specimens, 0.5% were rejected due to poor quality of the specimens that did not fulfill the necessary requirements to be tested. The rejection rates varied among specific specimens.Majority of the rejected specimens were Human immune virus (HIV) viral load (0.6%) and CD4 (0.7%). CD4 specimens were rejected due to wrong package, 84.2%, and presence of clots 15.8%.Un-centrifuged specimens 46.9%, hemolyzed specimens 19.8% and use of wrong tube 17.7% were the main rejection reasons for viral load specimens. A total of five EID specimens 0.2% were rejected due to labeling problem and poor packaging (mixed together with icepack) during transportation of the DBS. Similarly, five GeneXpert specimens were rejected due to use of wrong collection tube (2/5) and labeling problems (2/5). Interestingly, there was no rejection for clinical chemistry. Although viral load specimen rejection was improved from 1.8 to 0% up to February 2018, the problem was reoccurred and continued to the

end of May (1.3%) and June (0. 3%). Moreover, EID specimen rejection became increased since March 2018 [30].

The cross sectional study on frequency of specimen rejection and associated factors conduct by Molla H, et al at St. Paul Hospital Millennium Medical College, Addis Ababa showed that a total of 1.4% sample were rejected. From this 54.3% of the rejected specimens were in Hematology department because of specimens clotted, 22.8% because of insufficient quantity of specimens and the remaining 22.8% were rejected because of other reasons. Of the total specimens that were rejected in Serology department, 73.5% were rejected because of hemolysis, 8.8% because of low quantity, 8.8% because of labeling problems, and the remaining 8.8% because of other and unspecified problems. About 87% of rejected specimens were repeated for diagnosis [14].

The other cross sectional study by Tadesse et al. on Errors in the Hematology Laboratory at St.Paul's Hospital Millennium Medical College, Addis Ababa, showed that 25% were rejected because of unlabeled specimens, and the remaining 46.4% were of the specimens rejected in Clinical Chemistry department, 35.7 % were rejected because of hemolysis, 35.7 % because of labelling problems and remaining 28.6% were due to other reasons. The most frequently occurring pre-analytical problems were inadequate sample collection, with a frequency of 48.9% followed by hemolysis 34.5% [31]. As reviewed above various degrees of specimen rejection rates have been reported. Knowing that most errors in the laboratory occurs in the pre analytic phase regular monitoring of rejection rates and reasons for rejection is needed. Identifying the rejection rates with their reasons will help the regional laboratory to design targeted training and other preventive measures.

3. Objectives

3.1. General objective

To assess specimen rejection rate and reasons samples referred to Addis Ababa Public Health Research and Emergency Management Core Process Laboratory from June 01, 2018 to May 30, 2020 G.C.

3.2. Specific objectives

- To measure the specimen rejection rate by the type of test requested at Addis Ababa research and emergency management core process laboratory.
- To identify the reasons for rejection of specimens in Addis Ababa research and emergency management core process laboratory.
- To assess the trend of specimens rejection in Addis Ababa research and emergency management core process laboratory.

4. Materials and methods

4.1. Study area

The Addis Ababa public health research and emergency management core process laboratory (AAPHREM) has been in existence since the year 2004. AAPHREM Laboratory started its operations at Kazanchis area with only 5 laboratory personnel then transferred to Filwuha in 2005 with the name of Addis Ababa regional health laboratory version process. Version process changed to core process and the name becomes Addis Ababa research and Emergency management core process in 2016 with 40 professionals working under three version processes. Those version processes are laboratory and capacity building Version process, public health emergence management version process and research Version process. There are 12 different case teams with eight sections under laboratory and capacity building version process. The central reception used Poly- tech Laboratory Information System (Comp Pro Med, Inc., USA) to transfer requisition and get patient report from the reference laboratories. Then, the specimens were delivered to each laboratory and evidenced with recording in the internal delivery format.

4.2. Study design

This cross sectional study using both primary and secondary data was conducted to assess Specimen rejection and reason among referred samples. All samples submitted to the laboratory for analysis during the data collection period were included. In this study a total of 131,909 specimens were included.

4.3. Study period

The study was conducted from June 01, 2018 to May 30, 2020 G.C.

4.4. Population/samples

4.4.1 Source population/samples

All sample referred to Addis Ababa public health research and emergency management core process laboratory.

4.4.2 Study population/samples

All sample referred to Addis Ababa public health Research and Emergency management core process laboratory from June 01, 2018 to May 30, 2020 with no exclusion criteria.

4.5. Study variables

Dependent variable

- Rate of specimen rejection and trend of rejection

Independent variables

Mislabeling of specimens, insufficient specimens, specimens not separated from whole blood, clotting specimens, hemolysis specimens, specimens without request, request without specimens, using inappropriate container, specimens contaminated with food particles (for sputum samples), specimens contaminated with alcohol (for EID specimens), specimens contaminated with blood(for sputum samples) , expired of card (for EID specimens) and referred of un centrifuged specimens.

4.6. Sampling technique and sample size

Information of patients specimens sent from referring sites to the Addis Ababa public health Research and Emergency management core process laboratory investigation was reviewed. In this study a total of 131,909 specimens referred from June 01, 2018 to May 30, 2020 G.C were included.

4.7. Data collection

Data was collected using a structured questionnaire from laboratory information system by the principal investigator and trained laboratory professional. The laboratory was recording all specimens submitted to the laboratory that was unsatisfactory for the analysis during the study period.

4.8. Data quality control

The principal investigator supervised the data collection process. Training was given to the data collectors for collect data in good manner. Completeness of data collected was checked every day by the principal investigator. The questionnaire was pretested using cases of sample rejection that was managed in April 2020. Based on the pretest, questions were revised and edited.

4.9. Data analysis and interpretation

The collected data was coded, cleaned and analyzed using Statistical package for social science (SPSS) version 20 statistical software. Errors related to inconsistency of data were checked and

corrected during data cleaning. Calculations of rejected specimens for each test were presented as frequencies and percentages.

4.10. Ethical considerations

Ethical clearance was obtained from the Ethical Clearance Committee of Addis Ababa University, Department of Medical Laboratory Science. Permission was also be obtained from the Addis Ababa Public health research and emergency management directorate, through formal letter obtained from Department of Medical Laboratory science to use source of information. This study has no direct link with human participants and only coded data was extracted. Data was protected with pass word and hard copies made inaccessible to others through locking.

4.11. Research dissemination

The result of the research will be presented to the Department of Medical Laboratory Sciences Addis Ababa University and Addis Ababa Public Health Research and Emergency Management directorate. As well as, the outcome of the study will be disseminated to concerned body such as service provider, stakeholders, and policy makers and will be presented at conference. It will also be submitted for publication in various Medical Journals.

4.12. Operational definitions

Rejected specimen;-The term specimen rejection refers to specimens that the laboratory determines are unable to be analyzed or must be recollected due to, a wrong or missing patient label, an incompetent specimen container, inadequate specimen volume, hemolysis and failure of the specimen to arrive in the laboratory.

Pre analytic phase;- ‘steps starting in chronological order, from the clinician’s request and including the examination requisition, preparation of the patient, collection of the primary sample, and transportation to and within the laboratory, and ending when the analytical examination procedure begins.

Referral system; -A Laboratory set of connections which indicate the flow (route) of all referring Health Facilities with all their respective referral Laboratories for specimen testing and results delivery system.

5. Results

5.1 Proportion of referred specimens

In this study, a total of 131,909 specimens were sent from both government and private health facilities in Addis Ababa city administration to central reception of the Addis Ababa Public Health Research and Emergency Management Core Processes laboratory. Majority of the specimens 98,922(75%) were for viral load testing to monitor effectiveness of HIV antiretroviral drugs. Followed by CD4 count to measures how strong human's immune system was 15,842 (12%). Hematological test was the least numbers of specimens with 3259 (2.5%) specimens. A total of 6057 specimens were submitted for clinical chemistry tests such as ALT (alanine amino transferase), AST (aspartate aminotransferase), creatinine, cholesterol, glucose, Biluribin and alkaline phosphatase in the laboratory. Gene Xpert for TB drug resistance testing, accounted for (3.3%) of the total specimens received. Specimens for exposed infant diagnosis of HIV were also account for (2.6%) of total specimens. (Showed in table 1 below)

Table 1; proportions of specimen referred to central reception of the AAPRHEML from June 1, 2018 to May 30, 2020. (n=131,909)

Tests	**Number of specimen submitted**	**%**
HIV 1 viral load	98,922	75
EID	3462	2.6
CD4	15,842	12
Clinical chemistry	6057	4.6
TB Gene Xpert	4,367	3.3
Hematology	3259	2.5
Total	131,909	100%

Among the total submitted specimens, 915 (0.7%) were rejected because of errors in the pre analytical phase of laboratory diagnosis. The frequency of rejected specimens were highest in viral load 321/915 (35.1%) followed by clinical chemistry which was 214/915 (23.4%). The rejection was 207/915 (22.6%), 79/915 (8.6%), 63/915 (6.9 %), 31/915 (3.4%) CD4, EID, Gene, Xpert and hematology respectively. The frequency of rejected specimen in viral load were about ten times higher than that of rejected in hematology; the rejection in Clinical chemistry were higher than others, which was more than three times of rejected in Gene Xpert. Frequency of specimen rejection in this institution was showed in Table 2 below.

Table 2; Frequency of rejected laboratory specimens by type of requested laboratory service from June 1, 2018 to May 30, 2020 at AAPHREML.

requested laboratory The service

Type of laboratory service	Frequency	Percent
Viral load	321	35.1
Clinical chemistry	214	23.4
CD4	207	22.6
EID	79	8.6
Gene expert	63	6.9
Hematology	31	3.4
Total	915	100.0

5.2 Proportion of reasons for specimen rejection by requested laboratory service

Among the cause of rejection occurred in this institution, the most common pre analytical reason for sample rejection was mislabeling (0.269 %), followed by insufficient (0.158 %) and clotted specimens (0.151%). Other causes of rejection observed were un-centrifuged samples, (0.11 %), hemolysis specimens (0.081 %), specimens without laboratory request forms (0.0656 %) and the other reasons are shown in Table 3.

Out of the total rejection of specimens of viral load test, 39.6% were rejected because of mislabeling, 13.7% because of plasma not separated from whole blood, 12.1% because of insufficient specimens, 10.9% because of request without sample, 10.3% because of hemolysis and the remaining 13.4% were due to other reasons in Table 3.

The most common cause of rejection in clinical chemistry was un centrifuged specimens (47.2% of total rejections) followed by mislabeling of specimens (20% of total rejections), hemolysis (10.7 % of total rejection) and insufficient volume of specimens (8.6% of total rejection) and the remaining (13.7) were rejected due to other mentioned reasons in Table 3.

Of the total CD4 specimens that were rejected 50.7% of total rejection were rejected because of clotting, 26% because of mislabeling, 13% because of sample without request, 5.8% because of hemolysis and the remaining 4.5% because of other problems mentioned in Table 3

The more common cause of rejection associated with EID specimens were insufficient specimens (57% of total rejections) followed by expired card (21.5% of total rejections), mislabeling (13.9% of total rejection) and the remaining (7.6%) were rejected due to other shown reason in Table 3

Specimens of Gene Xpert rejected (36.5% of total rejection) were because of insufficient of specimens, (19% of total rejection) were rejected because of specimens contaminated with food particles, 17.5% of total rejection were rejected because of specimens mislabeling, 9.5% were rejected because of sample without request and the remaining 17.5% were rejected because of other mentioned reasons in Table 3.

Finally the study showed that 70.6% of specimen a rejected in Hematology department were because of specimens clotted, 17.6% because of specimens hemolysis, 8.8% because of mislabeling of specimens and the remaining 2.9% were rejected because of insufficient specimens

Table 3: Proportion of reasons for specimen rejection by requested laboratory service from June 1 2018 to May 30 2020 at AAPHREML.

The reason of rejection	The requested laboratory service						Total
	Viral load	CD4	EID	Gene xpert	Hematology	Clinical chemistry	
Mislabeling of specimens	127	54	11	11	0	43	246
insufficient specimens	39	9	45	23	1	28	145
specimens not separated from whole blood	44	0	0	0	0	0	44
Clotting specimens	9	105	0	0	24	0	138
Hemolysis specimens	33	12	0	0	6	23	74
Specimens without request	16	27	1	6	0	10	60
Request without specimens	35	0	1	4	0	4	44
Using inappropriate tube	18	0	0	3	0	5	26
Specimens contaminated with food particles	0	0	0	12	0	0	12
Specimens contaminated with alcohol	0	0	4	0	0	0	4
Specimens contaminated with blood	0	0	0	4	0	0	4
Expired of EID card	0	0	17	0	0	0	17
Specimens not centrifuged	0	0	0	0	0	101	101
Total	321	207	79	63	31	214	915

5.3 Trend of specimens rejection

Finally the study analyzed the two years trend in the rate of specimen rejection by test type as depicted in Figure 1. From all the 915 specimens rejected, 514 specimens were rejected in the first year of study and 401 Specimens were rejected in the second year of study. The specimens rejection viral load 181, CD4112, Clinical chemistry 121, EID 46 and Gene Xpert 43, were

higher in the first year (1, June 2018 to 30, May 2019) than second year (1, June 2019 to 30, May 2020) of study but the specimens rejection of hematology specimens (19) were higher in second year (1, June 2019 to 30, May 2020) than the first year (1, June 2018 to 30, May 2019) of study.

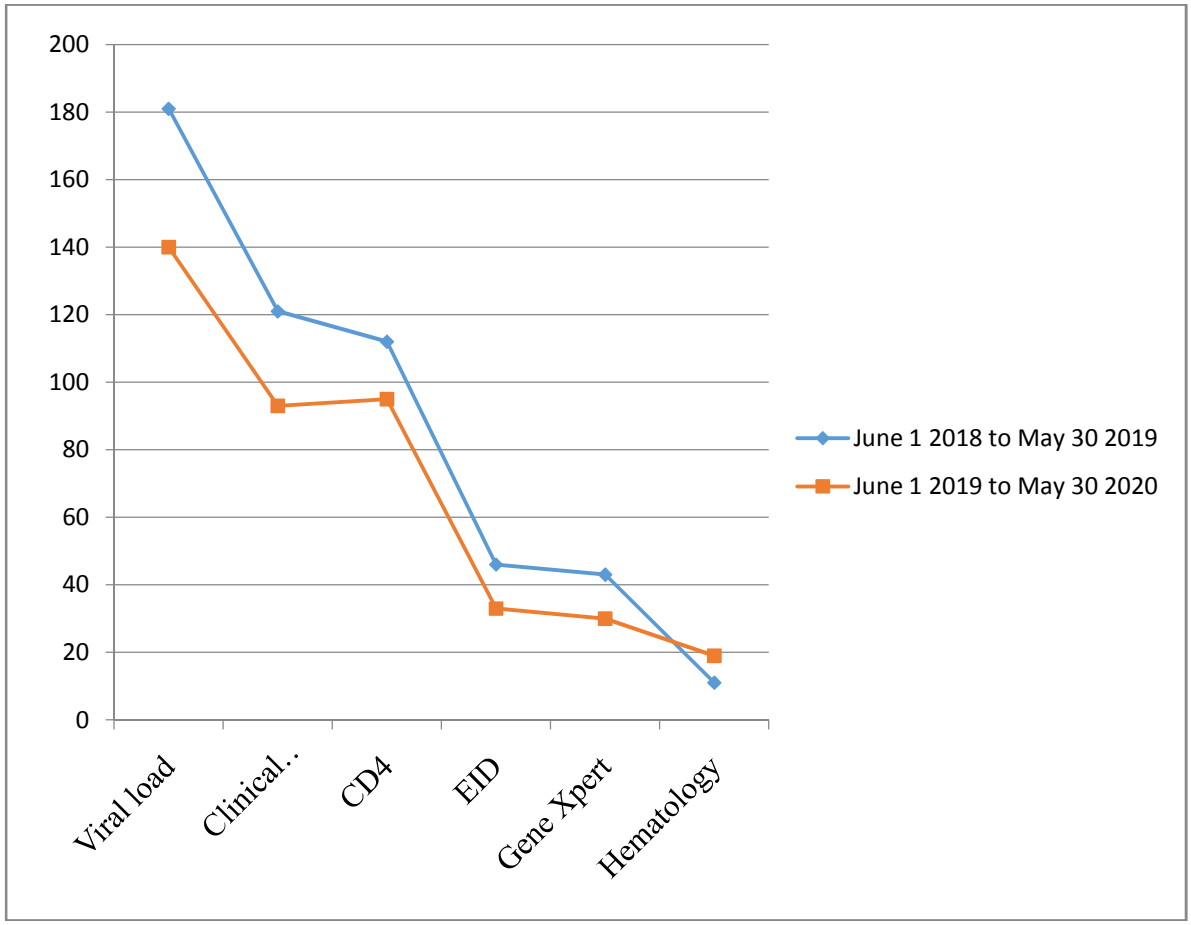

Figure 1; Trend of specimens rejection between two years of study at Addis Ababa Public Health Research And Emergence Management Core Processes Laboratory, Addis Ababa, Ethiopia, 01, June 2019 to 30, May 2020

6. Discussion

This study aimed at determining the rate of specimen rejection and reasons for rejection at Addis Ababa Public Health Research and Emergence Management Core Processes Laboratory. The study also investigated the trend of rejection between two years. The finding showed that among a total of 131,909 specimens through referral linkage 915(0.7%) specimens were rejected due to pre-analytical errors. Pre-analytical errors were more common and a cause for rejection of viral load, CD4, hematology, clinical chemistry, EID and Gene Xpert specimens in this institution.

Laboratory diagnostics is pivotal part of clinical decision making but no safer than other areas of health care, with most errors occurring in the manually intensive pre analytical process [9].The observed rate of rejection in this study is comparable with the rejection of a retrospective study in south-eastern Michigan, which reported a rejection rate of 0.74% [20]. Whereas a study at Amhara Public Health Institute showed that, among the total submitted specimens, 0.5% were rejected [30]. Even though the rate of rejection in this institution seemed somewhat low as also seen in both studies [20, 30], Laboratory have a responsibility to enforce its policies on sample rejection so that patient care is not compromised. Management should regularly review the number of rejected samples and reasons for rejections, conduct training on sample collection, and revise written procedures for sample management as needed [7].

Rate of specimen's rejection varies according to nature of specimens of tests ordered. The frequency of rejected specimens were highest in viral load 321/915 (35.1%) followed by clinical chemistry which was 214/915 (23.4%) and the least rejection rate scored in hematology 31/915 (3.4%).The rejection was 207/915 (22.6%), 79/915 (8.6%) and 63/915 (6.9 %) CD4, EID and Gene Xpert, respectively. In contrary to the current study, a retrospective study in Ethiopia at Amhara Public Health Institute by Shiferaw et al.2018 showed that, among the total submitted specimens, there was no rejection for clinical chemistry [30]. In my study Clinical chemistry samples were highly rejected due to un centrifuged sample referred to institution. Even if it cannot be denied that the laboratory industry like any other diagnostic field is susceptible to errors, the rejection rates scored at clinical chemistry department of this institution in the current study were highest and it needs to apply quality management system in the respective

laboratories to minimize the rejection. Personnel who package or transport the specimen should be trained about the proper procedures, both for safety and for good maintenance of samples.

The other rejection specimens reported in the institution were EID specimens 79/915 (8.6%). A retrospective study conducted by Inalegwu A, et al. in 2016 on active tracking of rejected dried blood samples in a large program in Nigeria reported sample rejection rate of 2.4% [26].Another cross sectional study by Chiku C, et al. (2019) in Zimbabwe's EID-program that assesses the magnitude of samples sent by five provinces for analysis showed a rejection rate ranging from 2% to 7% among the 5 provinces [29].Whereas a retrospective study in Ethiopia at Amhara Public Health Institute by Shiferaw et al.2018 showed that (0.2%) rejection rate [30].The rate of rejection (8.6%) in this study associated with most occurring insufficient specimens referred to institution were higher than all three studies in Africa and hence it should evaluate all process and procedure of pre analytical stage in the referral linkage.

Among the cause of rejection occurred in this institution, the most common pre analytical reason for specimens rejection was mislabeling, 246/915 (27%), followed by insufficient 145/915(15.8%), and clotted, 138/915(15.1%) specimen. In another, retrospective study conducted by Upreti S et al at Chatrapati Shivaji Hospital the highest numbers of samples were rejected due to misidentification which accounted 0.35 % and least number were rejected due to dilution of the samples that is 0.04 % [25]. To prevent or minimize errors associated with misidentification, there is a need for promotion of ideal phlebotomy practices; and sample transport procedures are a pre-requisite for the effective laboratory functioning.

In this institution the rejection rate of viral load specimens was improved from June 2018 to may 2020 were agree with a retrospective study in Ethiopia at Amhara Public Health Institute by Shiferaw et al.2018 viral load specimen rejection improved from 01 July 2017 to 30 June 2018 . But a need of training of the Laboratory professionals as well as others health professionals regarding proper collection and transport of samples based on scientific principles to decreasing or eliminated a trend in the sample rejection.

7. Strength and Limitations of the study

7.1 Strength of the study

The study collected large number of data referred to Addis Ababa Public Health Research and Emergence Management Core Processes Laboratory to identify reasons for specimen rejection to improve the referral linkage services.

7.2 Limitation of the study

The study depended on the information recorded in specimens tracking sheet and monthly quality indicator at the referral testing site and missed some information associated with sample collection at referring site.

8. Conclusions and Recommendation

8.1 Conclusion

The study demonstrated about 0.7% specimen rejection rate. Alongside of the efforts to reason out to, this study highlighted a complexity of pre-analytical errors to minimize them in Addis Ababa public health research and Emergence management core processes laboratory. The most commonly rejected specimens were for viral load followed by clinical chemistry samples. The most common pre analytical reason for specimens' rejection was mislabeling, followed by insufficient and clotted specimens.

8.2 Recommendation

As quality of the work a laboratory produces is only as good as the quality of the samples it uses for testing. The laboratory must be proactive in ensuring that the samples it receives meet all of the requirements needed to produce accurate test results. Therefore, to the confidence in laboratory diagnosis, the person collecting the sample must accurately identify the patient, the container for the sample is often very important, as it affects volume and any needed additives such as anti-coagulants and preservatives. All requirements for labeling of the sample at the time of collection need to be explained in detail in the instructions for collection. Further study addressing factors at the specimen collection site is recommended to identify the factors responsible for the rejected specimen collection and transportation.

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10. ANNEXS

ANNEX I**: consent form**

Code number _____

Name of the Health facility _____

I have been informed about the study which is aimed at Assessing of specimen rejection rate and associated factors among referred samples to Addis Ababa Public Health Research and Emergency Management core process laboratory, Addis Ababa, Ethiopia. For this study true and direct information is needed to fill the questionnaire and a document observation will be performed. The aims of the study were explained to me.

It is therefore with full understanding of the situation that I gave the informed consent voluntarily to the researcher to use the information gathered within the laboratory regarding specimens. In addition, I have had the opportunity to ask questions about it and received clarification. I have also been informed that the benefit of the laboratory is to identify factors affecting specimen quality and hence design appropriate intervention strategies so as to improve the quality of the laboratory service.

Laboratory head Signature _____

Name of data collector _____ Signature_____ Date _____

Please direct any questions or problems you may encounter during this study to:

Name: BerisaAdugna

Mobile: +251912209308

Email: berisaadugna2557@gmail.com

ANNEX II**: questionnaire format**

Patient code----------

1. Year of test order

A, June 1, 2018 to May 30, 2019 B, June 1, 2019 to May 30, 2020

2. Type of specimen referred

D. Blood

D. sputum

C. Others

3. The requested laboratory service

A. viral load

B. CD4

C. CBC

D. Clinical chemistry

E. EID

F, Gene expert

4. What is the reason for rejection?

A, Mislabeling of specimen B, insufficient specimens

C, specimens not separated from whole blood D, clotting specimens

E, hemolysis specimen F, specimens without request

G, request without specimens H, using inappropriate tube

I, specimens contaminated with food particles J, specimens contaminated with alcohol

K, specimens contaminated with blood L, expired of EID card

M, specimens not centrifuged.

5. What corrective actions or measurements taken on rejected specimens? ----------

Declaration

I, the undersigned, declare that this M.Sc. thesis is my original work, has not been presented for a degree in this or any other university and that all sources of materials used for the thesis have been duly acknowledged.

M.Sc. candidate: BerisaAdugna (B.Sc.)

Signature: _____

Date of submission: _____

This thesis has been submitted with our approval as advisors.

Advisor: Aster Tsegaye (MSc, PhD)

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia.

Advisor: HabtamuMolla (MSc, PhD candidate)

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia.