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Specimen rejection rate and associated factors among referred specimens through referral network to Debre Markos referral hospital for Laboratory testing, Debre Markos, Ethiopia

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This is to certify that a thesis prepared by **Bewket Mesganaw,** entitled:

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Abbreviations

AAU-Addis Ababa University

APHI- Amhara Public Health Institute

ART- Antiretroviral Therapy

CD4- Cluster of Differentiation 4

DBS- Dried Blood Spot

EID- Early Infant Diagnosis

HIV- Human Immunodeficiency Virus

ISO- International Organization for Standardization

LQMS- Laboratory Quality Management System

NMRL- National Microbiology Reference Laboratory

PHICT- Provider initiated HIV Counselling and Testing

PMTCT- Prevention of Mother-to- Child Transmission

TB- Tuberculosis

VCT- Voluntary counselling and Testing

WHO- World Health Organization

Abstract

Background: Clinical laboratory errors could be classified as pre analytical, analytical and post analytical. The majority of laboratory errors emerge from the manually intensive activities of the pre analytical phase, mainly those related to collection, handling, transportation, preparation and storage of diagnostic specimens.

Objective: The main aim of this study was to assess the specimen rejection rate and associated factors among the referred specimens through referral network to Debre Markos referral hospital for laboratory testing.

Method: Retrospective study was conducted at Debre Markos referral hospital laboratory from January 2016 to December 2019 to evaluate trends of specimen rejection rate. In addition, prospective cross sectional study design was applied from January 2020 to April 2020 to investigate further associated factors of specimen rejection. Data was collected from specimen reception log book and from referring facilities using developed checklist. Finally, statistical analysis was done with excel 2007 and SPSS version 20.0 software.

Result: From the total of 35673 specimens submitted to Debre Markos referral hospital laboratory from January 2016 to December 2019, a total of 560 (1.57%) specimens were rejected. The specimen rejection rates in each year were 2.30%, 1.59%, 1.42% and 1.26 % respectively from 2016 to 2019. Moreover, of 2750 specimens submitted to the laboratory during January 2020 to April 2020, a total of 37 (1.34%) specimens were rejected. Specimen collector training status and experience had significant association with specimen rejection rate (P= 0.01& P=0.04 respectively).

Conclusion: Although specimen rejection rate among referred specimens was improved gradually from 2016 to 2019, still needs more interventions to meet the established target specimen rejection rate (0.3%).Hence, training of health professionals on specimen collection, handling and transportation of requested tests, appropriate preventive and corrective actions could improve the problem in specimen referral network.

Key words: specimen rejection rate, clinical laboratory errors, laboratory quality management system

1. Introduction

1.1. Background

Clinical laboratories are an essential and fundamental part of all health systems and their goal to improve health. Reliable and timely results from laboratory investigations are crucial elements in decision-making in almost all aspects of health services and disease prevention and control programmes. To ensure good treatment for patients, quality laboratory services are mandatory by establishing and maintaining a quality management system for all activities of laboratory services. These include proper arrangement of requests, patient preparation and identification, collection, handling and transportation of specimen, processing and examination with proper interpretation and reporting (1, 2).

Laboratory errors, which are any defect in the all over laboratory testing process (pre analytical, analytical &post analytical), may negatively affect the clinical decision-making process and hence results in poor patient care. Several studies showed that the majority of laboratory errors emerge from the manually intensive activities of the pre analytical phase, mainly those related to collection, handling, transportation, preparation and storage of diagnostic specimens. Therefore the quality of laboratory result is good only if the quality of specimen collection, handling and transportation is appropriate (3, 4, 5).

The international organization for standardization (ISO) defines a sample as "one or more taken from a system and intended to provide information on the system. The term "specimen" is mostly used in the laboratory to indicate a sample taken from the human body. Proper sample collection is a key element for good laboratory practice where as improper sample collection may lead to poor outcomes, such as incorrect diagnosis, inappropriate treatment and death. Due to inadequate materials, financial and trained personnel in most health facilities of resource limited countries like Ethiopia, usually samples are collected outside the laboratory and must be transported for subsequent processing and testing. In such cases, the laboratory shall have a documented procedure for monitoring the transportation of samples to ensure they are transported within a time frame appropriate to the nature of the requested test, within the temperature interval specified for specimen collection, handling and transportation and with appropriate preservatives to ensure the integrity of specimen (2, 6).

As stated in the International Organization for standardization (ISO, 2012), clinical laboratories should set their own specimen rejection and acceptance criteria. Problems with patient or sample identification, sample instability due to delay in transport or inappropriate container(s), insufficient sample volume, clotted sample and hemolyzed sample are some of the example of rejection criteria. The authorized laboratory management should review periodically the number of rejected specimens and reasons for rejection to develop laboratory quality improvement plan and to conduct training on specimen collection, handling and transportation as needed (2, 6).

To increase access of the community with adequate and quality specialized laboratory services, feasible and applicable linkage mechanism among laboratories (laboratory specimen referral network) has been established in Ethiopia since 2008. In the referral system, specimens are collected from any health facility and transported with suitable courier system to referral laboratories where the testing service is available (7, 8).

Debre Markos referral hospital laboratory is one of the referral laboratories to which the surrounding health facilities refer diagnostic specimens for laboratory testing especially for viral load, gene expert for tuberculosis (TB), Early Infant diagnosis (EID) for HIV test and CD4 test. However, there is no study conducted in the area to get detailed information concerning the rate of specimen rejection and the main factors that causes the specimen to be rejected. Therefore, the aim of this study was to determine the specimen rejection rate and the causes of rejection among referred specimens to Debre Markos referral hospital laboratory.

1.2. Statement of the problem

Specimens submitted to the clinical laboratory may be rejected because of many reasons which include improper labelling and poor specimen quality and quantity. Even though rejection of specimen with the aim of proper processing of the specimen and for providing report of high standard considered as good practice of reference laboratories, increase rate of specimen rejection indirectly shows poor pre analytical practice of periphery (referring) laboratories(6, 9).

Improper collection, handling and transportation of specimen may lead to specimen rejection. Specimen rejection may have clinical significant consequences on patients. Patients whose specimens are rejected may be subjected to repeated specimen collection, which results inconvenience and discomfort of repeated phlebotomy. Specimen rejection and the need for specimen recollection or correction also may increase the turnaround time. The prolonged turnaround time especially for referred specimens is clinically most significant for tests ordered with a stat testing priority (10).

A retrospective audit that was conducted by Jacbsz LA et al at tertiary laboratory in Cape town to investigate the specimen rejection rate of routine blood specimens received at chemistry and hematology laboratories over a 2-week period, revealed that from the total of 32,910, 481 specimens were rejected giving a rejection rate of 1.46%. About 51.7% of rejected samples were repeated and hence the average time to reach the laboratory was about 5 days. Of the repeated samples 5.1% had results within the critical value. This report shows how much improper sample collection negatively affects patient health outcomes (17)

A study conducted on referred specimens in Ethiopia also, showed that there was problem related to specimen collection, handling and transportation of specimen due to different reasons like wrong package, presence of clots, uncentrifuge, hemolysis and wrong use of tube (5).

However, scientific studies concerning specimen rejection rate and associated factors especially at reference laboratories are limited. That is why this study was designed to assess the specimen rejection rate and associated factors among referred specimen to Debre Markos referral hospital laboratory.

1.3. Significant of the study

- The result of this study may help to the reference laboratory as well as the periphery laboratory to develop laboratory quality improvement plan
- The result obtained in this study may be used as base line data for future studies in other public health laboratories and/or the country at large.
- Finally, this study may help as a bench mark to conduct training on specimen collection, handling and transportation for laboratory personnel so as to produce quality laboratory result.
- Generally, this study may provide great advantage for patients directly, health professionals and the community at large.

2. Literature review

Proper management of specimen during collection, transport and storage must be ensured according to the standard operating procedures. Quality of specimen is monitored through acceptability criteria developed by each laboratory. Hence, those specimens that do not fulfil the acceptability criteria should be rejected (12).

During the first year of implementation of laboratory quality management system a retrospective data analysis was done by Gupta V et al to assess sample rejection rate in the tertiary care medical center laboratory of developing world. The study noted that from the 54603 specimen received during the study period, 3936(7.2%) were rejected. Issues related to request forms and sample accounted for nearly 50% rejections. In the study stated that most common reason for rejection of the sample was "clotted sample" (27.1%) (13).

Though remarkable advances and modern innovations transformed laboratory diagnostics from manual and labor- intensive service to fully automated process, the clinical laboratory still shows a lot of pre analytical errors that may results erroneous patient diagnosis and treatment that follows. A retrospective study conducted by Zaini RG et al at Hera'a Gneral Hospital, Saudi Arabia to investigate the major cause of pre analytical errors that led to sample rejection at clinical biochemistry department noted that samples with hemolysis after centrifugation was the most common cause of rejection which accounts 35% of total rejection. In addition, this study reported a number of different reasons for sample rejection which includes mismatching label on tube and request, incomplete patient's information and clotted samples (14)

K2Specimen rejection varies among different types of laboratory tests. A cross sectional study conducted by Gunnur Dikmen Z et al at Hacettepe university faculty of medicine, department of medical biochemistry Ankara, Turkey to evaluate the sample rejection ratios according to the types of pre analytical errors showed that from 453,171 samples that were received during the study period, 27,067 specimens were rejected. The most commonly reasons were fibrin clots (28%) and insufficient volume (9%) for biochemical tests. Clotted samples (35%) and inadequate volume (3%) were the major causes for coagulation tests, blood gas analyses and CBC (15).

Other retrospective study by Gungoren M et al in Turkey, Konya Necmettin Erbakan university medical faculty hospital biochemistry was carried out to determine specimen rejection rate (SRR) of routine biological samples received. The result of this study showed that from the total number of 852,831 biological specimens collected during the period, the specimen rejection rate was calculated as 1.1%. The reason of specimen rejection was analyzed and it was found that improper specimen (52.1%), inappropriate volume (22.9%), incorrect request (8.5%), improper specimen container (2.9%), inappropriate transport (2.8%) and barcode and labelling errors (0.8%) constitute main categories of specimen rejection. Improper specimen category mainly involves hemolyzed(65%) and clotted samples(23%), incorrect specimen (5.5%), specimen contamination(5%) and lipemic specimen (0.5%). Inappropriate volume category involves mainly mostly inadequate volume (95%) and excess volume (5%). Incorrect requests are mainly due to the mistakes during the usage of laboratory information system (LIS), such as incomplete and repetitive requests. Inappropriate transport, barcode and labelling errors mostly arise from lack of attention of hospital staff (16).

A cross sectional study that was conducted by Mehrotra et al over a period of six months across community health centers (CHC), primary health centers (PHC) district hospitals and government multi-specialty tertiary care hospital and trust autonomously run charity hospital in India revealed that from the total of 2000 samples that were received in the laboratory, 5.3 % were rejected. The rejection rate was higher among the hospitals run by trusts than government. Totally, the rejection rate was higher in blood sample (9.1%) as compared to body fluid (8%) urine (6.8%) stool (5.3) and sputum sample (3.3%). The main reason of rejection was due to inadequacy of specimen collection by paramedical staff (9).

A cross sectional survey that was carried out by Ye Y et al at Beijing hospital, China to determine the frequency and reasons for rejected hematology specimens revealed that from the total sample received during the study period, 0.11% specimens were rejected mainly due to clotted specimen. Rejected specimens were related to department where they were collected, specimen container type and transportation and specimen collector. From the rejected specimens 84% need recollection (18).

Tapper et al conducted a retrospective study at the university hospital of the West Indies to assess the types and frequency of errors and they reported that the most causes for rejection were

unlabelled specimens (37%), inappropriate labeling (23%), inappropriate tube ((14%) and incomplete requisition forms (14%). The rejection ratio for 2015- 2016 was 2.1% (19).

A cross-sectional study done by Chiku C. et al using routine DBS sample data from the National Microbiology Reference laboratory (NMRL) in Harare, Zimbabwe between January and December 2017 showed that from the total of 34,950 DBS samples that were received at the NMRL, 1291 (4%) were rejected. According to this study, reasons for rejection were insufficient specimen volume (72%), specimen without request form (11%), request paper without sample (6%) and contamination (6%). Mismatch of information (4%) and clotted sample (1%). Samples which were collected from rural health facilities were five times more likely to be rejected compared to those which were collected from a central hospital. Specimen rejection rates were above the target set of <2%. The reasons for rejection were 'pre analytical' errors including labeling errors, missing or inconsistent data and insufficient blood collected. Samples collected at primary health care facilities had higher rejection rates (20).

A retrospective study that was conducted by Atao M et al at the Port Moresby General Hospital within the period April 2012 to March 2013 to determine the rate of specimen rejection of blood samples sent to the hematology section in the pathology laboratory noted that rate of sample rejection over the 12 months duration of the study was 1.44%. The areas with the highest rate of rejected specimens were those from the accident and emergency ward (23.19%) followed by children's ward (22.39%). Some of the causes for rejection were clotting of blood specimen (19.24%) followed by requisition forms without specimens (18.32%) and unlabelled specimens (15.65%). Thus, technical errors in the pre-analytical phase of the laboratory testing were among the common reasons for rejection. This includes insufficient volume of blood collection, not inverting the specimen container straight after collecting the blood for effective mixing with the anti-coagulant to prevent clotting, incorrect labelling of samples and request forms, and sending samples unaccompanied by request forms. The investigator also noted that the pre analytical phase is important in ensuring sample integrity and correct patient identification (21).

A descriptive study by Lai X and colleagues reported that among 553,158 samples submitted to laboratory in Hospital of Chongqing Medical University in China, 1,051 unqualified specimens were identified (0.19%). From all these rejected specimens, collected for coagulation tests were the predominant unqualified specimens. They also identified the main causes of generation of

unqualified specimens were insufficient sample volume and improper methods of mixing the samples (22).

A cross sectional retrospective study conducted by Sauramba ML et al on data for specimens submitted Mutare Provincial molecular diagnosis laboratory of Zimbabwe to determine the specimen rejection rate and reasons for sample rejection at Early Infant Diagnosis (EID) laboratory revealed that 10.7% of samples were rejected. The reason for rejection included improper specimen collection, no specimen received, multiple specimen packed in one pack, specimen and requests not labelled correctly (23)

In Ethiopia, a cross sectional study done by Tadesse H. et al at St. Paul's Hospital millennium medical college, Addis Ababa to determine the magnitude of errors in clinical chemistry laboratory tests at different phases of the assay of clinical chemistry unit showed that from the total 1633 clinical chemistry tests done, overall 541errors occurred from which 392 (72.3%), 45 (8.3%), and 104 (19.2%) were pre analytical, analytical and post analytical errors respectively. Incomplete clinical data of patient was observed on 1185 (72.6%) of clinical laboratory tests. Name, gender and age of patients were missed on 8 (0.5%), 190 (11.6%) and 257 (15.7%) forms of the requests respectively. The physician's name existed only on 248 (15.2%) and signature on (1137 (69.6%) of the request forms. In addition, essential patient data were incomplete, which needs emphasis on awareness creation (24).

On the other hand, a cross sectional study conducted by Molla H. et al at St. Paul's Hospital millennium Medical college, Addis Ababa noted that from the total of 8063 specimens submitted to the laboratory during the study period, 116 (1.4%) were rejected. The most frequent reason of specimen rejection was hemolysis (27.6%), followed by clotted specimens (16.4%). Significantly more rejected specimens were occurred in hematology (2.1%) and serology (2.1%) departments. More than twice higher rejections were recorded among specimens collected by non-laboratory personnel (2.8%) compared to specimens collected by laboratory personnel (1.2%). The proportion of specimens that were rejected in emergency department and inpatient service were twice more than the outpatient (1.1%) service (25).

An institution based cross-sectional survey supplemented non participatory type observational study was conducted by Melkie M et al from February 2012 to September 2012 in laboratories of three governmental hospitals of Gamo Gofa zone, southern Ethiopia. They included a total of 19 laboratory professionals working in the three governmental hospitals for survey. The investigators noted that the highest proportion of undesirable practices were related to establishment and adherence to serum/plasma/ whole blood rejection criteria, measures taken when produced serum/plasma is too small for analysis, speed and duration of centrifugation. None of the socio-demographic and background information of participants they assessed was associated with undesirability of venous blood sample processing activities (26).

A study that carried out by Ambachew S et al at Gondar University Hospital to assess errors in the total testing process showed that from the total of 3259 specimens and corresponding laboratory request forms that were received for analysis, 89,9% were pre analytical errors, 2.6% were analytical errors and 7.7 % were post analytical errors. Of the pre analytical errors, incomplete request form filling was the most frequent error observed followed by specimen rejection rate (3.8%) (3).

A retrospective study conducted in Ethiopia by Balew M. et al to assess the magnitude, trend and reasons of rejection among referred specimens through referral network to the Amhara Public Health institute for laboratory testing showed that from the total of 42,923 specimens that were received at APHI for laboratory testing, 221 (0.5%) specimens were rejected. CD4, HIV viral load, gene expert and EID specimen's rejection rates were 0.7%, 0.6% 0.3% and 0.2% respectively. CD4 specimens were rejected due to improper package (84.2%), and the presence of clots (15.85). Un-centrifuge (46.9%), hemolysis (19.8%) and use of inappropriate specimen container (17.7%) were the main rejection reasons for HIV viral load specimens. Although viral load specimen rejection was improved from 1.8 to 0% up to February 2018, the problem reoccurred and continued to the end of May (1.3%) and June (0.3%) 2018. Moreover, CD4 specimen rejection (4.3%) was out of the established target in May, and early infant diagnosis (EID) specimen rejection became increased since March 2018 (5).

The above all literatures confirmed that the problem concerning laboratory specimen collection, handling and transportation is among the major challenges faced in all clinical laboratory settings. In line with the implementation of laboratory quality management system in Ethiopia,

many clinical laboratories are trying to develop their own specimen rejection criteria so as to manage specimen acceptability for the required laboratory testing. But, only limited studies at some health facility laboratories were conducted concerning the specimen rejection rate. Regarding to specimen rejection rate and associated factors especially for referred specimens need further investigation that helps for quality laboratory improvement plan. Therefore, this study filled these gaps and investigates detailed information on referred specimens.

3. Objectives

3.1. General objective

The aim of this study was to determine specimen rejection rate and associated factors among referred specimens through referral network to Debre markos referral hospital for laboratory testing, Debre markos, Ethiopia, 2020

3.2. Specific objectives

- To determine specimen rejection rate among referred specimens through referral network to Debre Markos referral hospital for laboratory testing, Debre Markos, Ethiopia
- To describe the trends of specimen rejection through time among referred specimens through referral network to Debre Markos referral hospital for laboratory testing, Debre Markos, Ethiopia
- To assess factors associated with specimen rejection for referred specimens to Debre Markos referral hospital laboratory, Debre Markos, Ethiopia

4. Methodology

4.1. Study area

The study was conducted at Debre Markos referral hospital and the surrounding specimen referring sites. Debre Markos referral hospital is located at Debre Markos town which is 300 Km from the capital city of Ethiopia, Addis Ababa, and 256 Km from the capital city of Amhara National regional state, Bahirdar. The hospital was built in 1954 E.C and nowadays it provides health service to more than 3.5 million populations in different department services. The hospital laboratory is sub departmentalized in to different testing units. Viral load, Early Infant Diagnosis (EID) for HIV/AIDS, TB gene expert and CD4 count services are not only limited to the patients who comes at hospital but also referred specimens from about 56 health facilities are tested. The reason for selection of the study site was its accessibility and the laboratory has been function as reference laboratory especially for the above four laboratory tests.

4.2. Study period

The study was conducted from October 2019 to June 2020, of which from October 2019 to December2019 was proposal development& proposal defense and from January 2020 to June 2020 was data collection, result analysis& thesis defense period.

4.3. Study design

Retrospective and prospective cross sectional descriptive study design were conducted from January 2016 to December 2019 and from January2020 to April 2020 respectively.

4.4. Population

4.4.1. Source population

The source population was all human clinical specimens referred to Debre Markos referral hospital laboratory for different laboratory testing.

4.4.2. Study population

The study population was all specimens referred for viral load, CD4 count, gene expert and EID to Debre Markos referral hospital laboratory within the period from January 2016 to December 2019 and from January 2020 to April 2020 for retrospective and cross sectional study respectively.

4.5. Inclusion and exclusion criteria

4.5.1. Inclusion criteria

All referred specimens from January 2016 to December 2019 and from January 2020 to April 2020 with all necessarily information and recorded properly in the specimen reception logbook were included in the study.

4.5.1. Exclusion criteria

Specimens with incomplete information and not recorded properly in the specimen reception log book were not included in the study.

4.6. Study variables

Dependent variables: specimen rejection rate

Independent variables: specimen collector characteristics (profession, working experience, training status& educational level), specimen type, requested laboratory test type and reasons for rejections which includes hemolysis, inadequate volume, clotted specimen, unlabelled specimen, samples with no request paper, delayed time, not maintained cold chain, Contaminated specimen, inappropriate specimen container

4.7. Sample size and sampling technique

All specimens referred from the surrounding health facilities and submitted to the Debre Markos referral hospital laboratory within the period from January 2016 to December 2019 and from January 2020 to April 2020 were included. In this study, a total of 35673 and 2750 specimens were included for retrospective and prospective cross sectional study respectively. Convenient sampling technique was used.

4.8. Data collection

Short term training or orientation on data collection checklist was given for data collectors. Informed written consent was obtained from Debre Markos referral hospital laboratory and referring health facilities of responsible body. Then data were retrieved from the specimen record log book by principal investigator and laboratory personnel who are working at Debre Markos referral hospital laboratory for retrospective study. The specimen rejection log book include the variables: specimen type, requested laboratory tests, reasons for rejection and measures taken for rejected specimens. In addition, a developed data collection checklist that incorporates the

specimen collector characteristics like profession, training status and experience was distributed for all referring health facilities and data were also collected for each referred specimens from referring sites so as to get full information about associated factors of specimen rejection.

4.9. Data quality assurance

To maintain the quality of data, at pre analytical phase, the data collection tool was pre tested at Felegehiwot referral hospital laboratory. The collected data were checked by the principal investigator for completeness, clarity and consistency by the performance indicator. At analytical phase, data were entered using double data entry to minimize transcription errors. Data cleansing activities like removing outliers and missing data were done at post analytical phase of data quality assurance.

4.10. Data analysis and interpretation

The overall specimen rejection rate was calculated by the number of rejected specimens per total referred specimens submitted, with excel 2007 & SPSS 20.0 software for retrospective and prospective study respectively. The rejected specimens were analyzed so as to identify the reasons and factors why the specimens were rejected. The percent of rejected specimens were summarized separately by the type of laboratory tests. All statistical tests were done by using Statistical Package for Social Sciences (SPSS) 20.0 software. P values less than 0.05 was taken as statistically significant when looking for association between dependent and independent variables.

4.11. Ethical considerations

Ethical clearance to conduct the study was obtained from the Department Research and Ethics Committee (DREC) from the Department of Medical Laboratory Science, College of health Sciences,Addis Ababa University. The letter of permission also obtained from East gojam zonal health department and Debre Markos referral hospital where the study was conducted. Informed

consent also made with responsible body of Debre Markos referral hospital laboratory and referring health facilities so as to assure the confidentiality of information during data collection.

4.12. Research dissemination

The finding of the study will be submitted to Department of Medical laboratory sciences, Addis Ababa University. Reports will also be presented and submitted to Debre Markos referral hospital. In addition, the finding will also be presented on annual conferences of professional societies. For publication, the manuscript was submitted to peer reviewed journals.

4.13. Operational definitions

Specimen rejection: a judgment by laboratory personnel, that specimens are unsuitable for analysis based on the specimen rejection criteria set by the laboratory.

Specimen rejection rate: the proportion of rejected specimens among the total number of specimens received from the referring laboratories

Insufficient volume: quantity of specimen less than the minimum required volume

Hemolysis: breakdown of red blood cells which is visible as a reddish color in the clear serum/plasma due to the presence of free hemoglobin.

Clotted specimen: a specimen with red cells, white cells, platelets and fibrin strands are forming a clot.

Cold chain: temperature-controlled transportation condition (mostly 2-8 0c)

Delayed time: a specimen is received at laboratory after beyond the minimum specimen storage duration.

Contaminated specimen: specimen with visible leakage due to breakage or uncapped specimen container

Associated factors – factors that have direct or indirect impact on specimen rejection

5. Results

A total of 35673 specimens were submitted to Debre Markos referral hospital laboratory during January 2016 to December 2019, of which 420 (1.38%) plasma specimens for viral load, 18 (1.61%) DBS specimens for EID, 4 (0.20%) sputum specimens for gene expert, 118 (5.41%) whole blood specimens for CD4 count and totally 560 (1.57%) specimens were rejected because of different pre analytical errors. The majority of the referred specimens, 30429 (85.3%), were for viral load testing to monitor effectiveness of HIV anti-retroviral drugs. Specimen rejection rate varied among requested tests. The highest specimen rejection rate 118 (5.41%) was seen among specimens referred for CD4 count and the least specimen rejection rate 4 (0.20%) was seen among specimens referred for gene expert test (Table 1).

Table1. Specimen rejection rate among referred specimens for each type of requested laboratory tests from January 2016 to December 2019 at Debre Markos referral hospital laboratory

Status of specimen	**Requested laboratory test type**				**Total**
	Viral load	**EID**	**Gene expert**	**CD4 count**	
Total specimens referred	30429	1110	1955	2179	35673
Rejected specimens	420	18	4	118	560
Specimen rejection rate (%)	1.38	1.61	0.20	5.41	1.57

Total specimen rejection rates in each year were 2.30%, 1.59%, 1.42% and 1.26 % respectively from 2016 to 2019 (Table 2).

Table2. Specimen rejection rate among referred specimens in each year from 2016 to 2019 at Debre Markos referral hospital laboratory

Status of specimen	Years				Total
	2016	2017	2018	2019	
Total specimens referred	6009	9477	10143	10044	35673
Rejected specimens	138	151	144	127	560
Specimen rejection rate (%)	2.30	1.59	1.42	1.26	1.57

The trends of specimen rejection were gradually decreased through time from 2016 to 2019 (Figure 1).

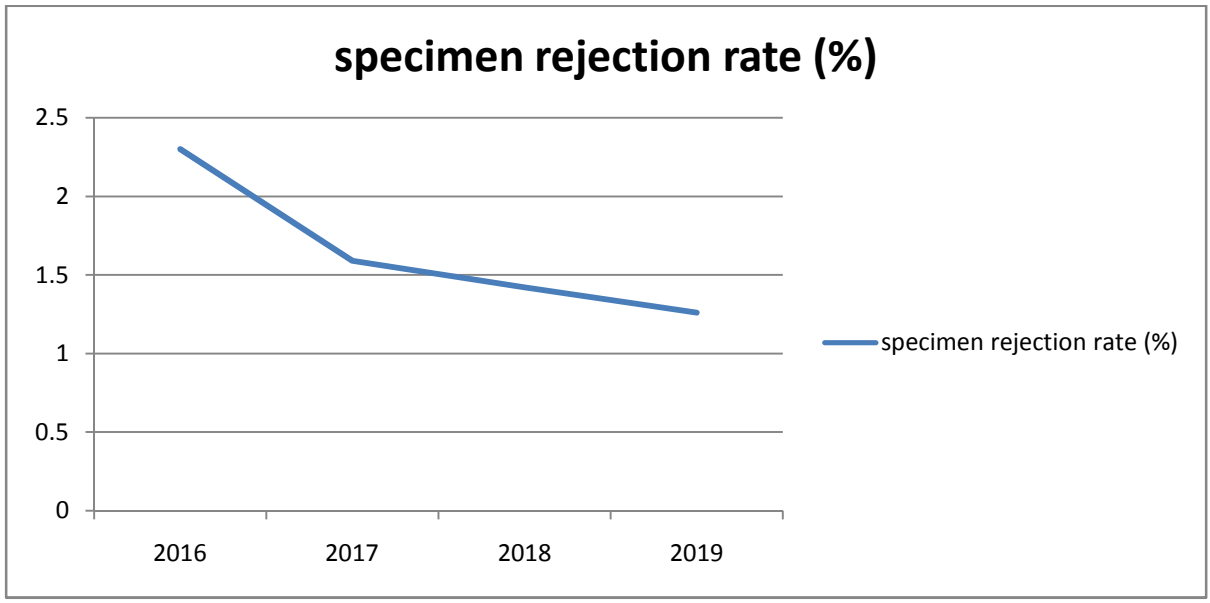

Figure1. Trends of specimen rejection rate among referred specimens from 2016 to 2019 Debre Markos referral hospital laboratory

The main reasons of specimen rejection were hemolysis(28.6%), insufficient volume (22.5%), repeated labeling (9.5%) and clotted specimen (8.0%) (Table3).

Table3. Reasons of specimen rejection among referred specimens from January 2016 to December 2019 at Debre Markos referral hospital laboratory

Reason of rejection	**Years**				**Total specimen rejected**
	2016	**2017**	**2018**	**2019**	
Hemolysis	39(28.3%)	43(28.5%)	41(28.5%)	37(29.1%)	160(28.5%)
Insufficient volume	31(22.5%)	34(22.5%)	32(22.2%)	29(2.3%)	126(22.5%)
Repeated labeling	13(9.4%)	14(9.3%)	14(9.7%)	12(9.4%)	53(9.3%)
Clotted specimen	11(8.0)	12(7.9%)	12(8.3%)	10(7.9%)	45(8.0%)
Delayed time	10(7.2%)	11(7.3%)	11(7.6%)	10(7.9%)	42(7.5%)
Inappropriate specimen container	8(5.8%)	9(6.0%)	8(5.5%)	8(6.3%)	33(5.9%)
Unlabeled specimen	6(4.3%)	7(4.6%)	6(4.1%)	6(4.7%)	25(4.5%)
Requested paper without specimen	6(4.3%)	6(4.0%)	64.1%)	5(3.9%)	23(4.1%)
Not maintain cold chain	5(3.6%)	5(3.3%)	5(3.5%)	4(3.1%)	19(3.4%)
Mismatch label	4(2.9%)	4(2.6%)	4(2.8%)	3(2.4%)	15(2.7%)
Specimen without request paper	3(2.2%)	3(2.0%)	3(2.0%)	3(2.4%)	12(2.1%)
Others	2(1.4%)	2(1.3%)	2(1.4%)	1(0.8%)	7(1.2%)
Total	138(100%)	151(100%)	144(100%)	127(100%)	560(100%)

Moreover in our cross sectional prospective study, a total of 2750 specimens were submitted from 56 health facilities (9 hospitals,46 health centers & 1 private clinic) to Debre Markos referral hospital laboratory within the period January 2020 to April 2020, of which a total of 37 (1.34%) specimens were rejected. For all rejected specimens written feedbacks were given for the respective referring health facilities. Among the total specimens submitted to the reference laboratory, the majority specimens 2581 (93.8%) were plasma specimens referred for viral load testing. The highest specimen rejection among the total referred specimens also were plasma specimens referred for viral load testing (1.24%). (Table 4).

Table4. Specimen rejection rate among referred specimens from January 2020 to April 2020 at Debre Markos referral hospital laboratory

Status of specimen	**Requested laboratory test type**				**Total**
	Viral load	**EID**	**Gene expert**	**CD4 count**	
Total specimens referred	2581	53	101	15	2750
Rejected specimens	34	1	1	1	37
Specimen rejection rate (%)	1.32	1.89	0.99	6.67	1.34

Insufficient volume (37.8%), hemolysis (21.6%), inappropriate specimen container (13.5%) and uncentrifuge specimen (10.8%) were the main reasons of specimen rejection among the referred specimens (Table 5).

Table5. Reasons of specimen rejection among referred specimens from January 2020 to April 2020 at Debre Markos referral hospital laboratory

Reason of rejection	Number of specimen rejected	Percentage (%)
Insufficient volume	14	37.8
Hemolysis	8	21.6
Inappropriate specimen container	5	13.5
Uncentrifuge	4	10.8
Repeating label	2	5.4
Unlabeled specimen	1	2.7
Specimen without request paper	1	2.7
Clotted specimen	1	2.7
Not maintained cold chain	1	2.7
Total	37	100

Further evaluation of data show that the majorities (41.2%) of the rejected specimens referred for viral load laboratory test were because of insufficient volume. The others main reasons for viral load specimen rejection were hemoysis (23.5), inappropriate specimen container (14.7%) and uncentrifuge specimen (11.8%). On the other hand, 1 specimen due to not maintained cold chain, 1 specimen due to specimen without request paper and 1 specimen due to clotted were rejected referred for EID, gene expert and CD4 count respectively (Table 6).

Table6.Reasons of specimen rejection among in each requested tests from January 2020 to April 2020 at Debre Markos referral hospital laboratory

Reason of rejection	**Requested tests**				**Total**
	Viral load	**EID**	**Gene expert**	**CD4 count**	
Insufficient volume	14(41.2%)	0(0%)	0(0%)	0(0%)	14(37.8%)
Hemolysis	8(23.5%)	0(0%)	0(0%)	0(0%)	8(21.6%)
Inappropriate specimen container	5(14.7%)	0(0%)	0(0%)	0(0%)	5(13.5%)
Uncentrifuge	4(11.8%)	0(0%)	0(0%)	0(0%)	4(10.8%)
Repeating label	2(5.9%)	0(0%)	0(0%)	0(050	2(5.4%)
Unlabeled specimen	1(2.9%)	0(0%)	0(0%)	0(0%0	1(2.7%)
Specimen without request paper	0(0%)	0(0%)	1(100%)	0(0%)	1(2.7%)
Clotted specimen	0(0%)	0(0%)	0(0%)	1(100%)	1(2.7%)
Not maintained cold chain	0(0%)	1(100%)	0(0%)	0(0%)	1(2.7%)
Total	34(100%)	1(100%)	1(100%)	1(100%)	37(100%)

For evaluation of specimen rejection with associated factor we considered different factors like transport conditions, specimen collector profession, educational level, training status and experience. From those factors, only specimen collector training status and experience had significant association with specimen rejection (P= 0.01& P=0.04 respectively). Evaluation of data showed that 1554 specimens were collected by trained personnel from those only 6 (0.38%) specimens were rejected and 1196 specimens were collected by untrained personnel of those 31 (2.59%) specimens were rejected(Table7). In addition, specimen rejection rate was higher in specimens collected by less experienced health personnel (below 1 year) than those specimens collected by more experienced health personnel.

Table7. Specimen rejection rate and training status of specimen collector at Debre Markos referral hospital laboratory

Training status	**Status of specimen**		**Total**	**Specimen rejection rate (%)**
	Accepted	**Rejected**		
Trained	1548	6	1554	0.38
Not trained	1165	31	1196	2.59
Total	2713	37	2750	1.34

In addition, specimen rejection rate was higher in specimens collected by less experienced health personnel (below 1 year) than those specimens collected by more experienced health personnel (Table8).

Table8. Specimen rejection rate and working experience of specimen collector at Debre Markos referral hospital laboratory

Working experience	Status of specimen		Total	Specimen rejection rate (%)
	Accepted	Rejected		
< 1 year	199	15	214	7.0
1-3 years	1296	16	1312	1.2
3-5 years	899	5	904	0.5
>5 years	319	1	320	0.3
Total	2713	37	2750	1.34

However, educational level of specimen collector did not significantly influence the specimen rejection rate (Table9).

Table9.Specimen rejection rate and educational level of specimen collector at Debre Markos referral hospital laboratory

Educational level	Status of specimen		Total	Specimen rejection rate (%)
	Accepted	Rejected		
Diploma	1429	23	1452	1.58
Degree	1284	14	1298	1.08
Total	2713	37	2750	1.34

In this study, the outcome of the binary logistic regression model indicate that training status and experience were have significant association with specimen rejection But, profession and educational level of specimen collector had no significant association with specimen rejection(Table10 a).

Table 10(a). Statistical analysis of associated factors of specimen rejection among referred specimens at Debre Markos referral hospital laboratory

Factors	P-value	Exp(B) (COR)	95% C.I. for EXP(B)	
			Lower	Upper
Profession(1)	0.482	0.782	0.394	1.552
Educational level(1)	0.139	1.038	0.593	32.834
Experience(1)	0.044	8.225	0.967	29.933
Experience(2)	0.399	2.437	0.307	19.340
Experience(3)	0.954	1.068	0.116	9.805
training status(1)	0.006	4.075	1.482	11.204

The outcome of the final multiple logistic regression model indicate that factors like training status and experience were have significant association with specimen rejection(P=0.01& P=0.04 respectively). But educational level of specimen collector had no significant association with specimen rejection (P=0.417) which have P value greater than 0.05(Table10 b).

Table 10(b). Statistical analysis of associated factors of specimen rejection among referred specimens at Debre Markos referral hospital laboratory

Factors	P-value	Exp(B) (AOR)	95% C.I. for EXP(B)	
			Lower	Upper
Training status(1)	0.011	3.528	1.330	9.358
Educational level(1)	0.417	1.328	0.670	2.635
Experience(1)	0.045	8.917	1.055	35.394
Experience(2)	0.467	2.159	0.271	17.177
Experience(3)	0.806	1.313	0.150	11.491

Training status(1)=not trained, educational level(1)=diploma, experience(1)= <1 year, experience(2)= 1-3 years, experience(3)=3-5 years

.

A multiple logistic regression analysis indicate that specimens collected by untrained health personnel have 3.528 chance of rejection compared to specimens collected by trained health personnel (AOR: 3.528, 95%CI: 1.330-9.358, P=0.01). In the same manner, specimens collected by health personnel with experience of below 1 year have 8.917 chances of rejection compared to specimens collected by health personnel with experience of above 5 years(AOR:8.917, 95% CI: 1.055-35.394, P=0.04). Specimens collected by health personnel with experience of 1-3 years have 2.159 chances of rejection compared to specimens collected by health personnel with experience of above 5 years and specimens collected by health personnel with experience of 3-5 years have 1.313 chances of rejection compared to specimens collected by health personnel with experiences of 5 years. This indicates as experiences of specimen collector's increases the rate of specimen rejection is decreased (Table10 b).

6. Discussion

Identifying the technical errors and specimen rejection rate is important in the development of laboratory improvement plan and to ensure quality of laboratory results. We conducted a retrospective study to evaluate the trends of specimen rejection rate whether the problem was improved through time or continued as it was among referred specimens through referral network within the period of four years. We also conducted a cross sectional study separately to identify the reason and association factors of specimen rejection rate. HIV viral load, early infant diagnosis (EID), gene expert for TB and CD4 count were laboratory tests for which specimens were referred from the periphery health facilities.

Our retrospective study finding showed that the overall specimen rejection rate is 1.57% and specimen rejection rate in each year were 2.30%, 1.59%, 1.42% and 1.26% from 2016 to 2019 respectively. Even though no enough similar studies were published to compare the trends of specimen rejection among each year, a four year (2013-2016) retrospective study conducted by Taper MA et al at the university hospital of the West Indies to assess the types and frequency of errors showed that the rejected specimens were increased gradually through time from 2013 to 2016 as 259, 296,331 and 504 respectively. The difference between the previous study and our study may be due to evaluation of trends in specimen rejection rate in our study (19).

Other retrospective study conducted at Amhara puplic health institute by Balew M. et al showed that the rejections were higher in the first five months, rates ranging from 1.3 % to 1.8%, and then it was improved the next three months with zero (0%) specimen rejection rates. However, the rejection reoccurred again in the last four months ranging rates from 0.2% to 1.3% (5). But, the finding of our study showed that the specimen rejection rate has improved through time within four years. The reason of improvement could be corrective actions taken and some training given on specimen collection, handling and transportation of the respective tests. The difference of the previous study and this study could be due to being trends of specimen rejection within one year and trends of specimen rejection within four years respectively (5).

Many national and international programs have reported laboratory rejection rates ranging from 0.3% in outpatient health facilities to 0.83% in hospital based laboratories as quality indicators to

track quality of laboratory (27). Thus, Debre Markos referral hospital laboratory has established target specimen rejection rate as to be below 0.3% as quality indicator. Hence, the overall specimen rejection rate (1.57%) needs to be improved because it has been above the established target specimen rejection rate (0.3%).

On the other hand our cross sectional prospective study revealed that specimen rejection rate among referred specimens was 1.34%. This finding is almost similar with specimen rejection rate determined with a retrospective study that was conducted by Atao M et al at the Port Moresby General Hospital, a retrospective audit that was conducted by Jacbsz LA et al at tertiary laboratory in Cape Town and a cross sectional study conducted by Molla H. et al at St. Paul's Hospital millennium Medical college, Addis Ababa which were 1.46%, 1.44% and 1.4% respectively (17, 21, 25).

But our finding (1.34%) is lower than a retrospective study conducted by Gupta V et al in the laboratory of a tertiary care medical center in the developing world and a cross sectional retrospective study conducted by Sauramba ML et al on data for samples submitted Mutare Provincial molecular diagnosis laboratory which were 7.2% and 10.7% respectively (13, 23). The difference may be due to the study design used, the number of data collection sites and the varieties of specimen types included in the study. For example, the latter study conducted by Sauramba ML et al done only on specimens requested for early infant diagnosis (EID).

In this study, the specimen rejection rate 1.34 % is higher than the specimen rejection rate (0.11%) determined by a cross sectional survey conducted by Ye Y et al at Beijing hospital, China. This difference may be due to the previous study was conducted on only hematology specimens but our study included more than one specific type of specimen. In addition, a similar study on referred specimens conducted at Amhara puplic health institute by Balew M. et al determined specimen rejection rate as 0.5% which is lower than specimen rejection rate determined by our study. This difference may come from the difference in the sample size of the two studies (5, 18).

Our study showed the majority of specimens (almost 38%) were rejected due to insufficient volume. In the same manner, a cross-sectional study done by Chiku C. et al showed that the main

reason of specimen rejection was in sufficient volume which covers 72% of the total rejected specimens (20).

The other main reason of specimen rejection that we investigated in our study is hemolysis which covers about 22% of the total rejected specimens. In the same manner, a retrospective study conducted by Zaini RG et al at Hera'a General Hospital, Saudi Arabia to investigate the major cause of pre analytical errors that results specimen rejection at clinical biochemistry department revealed that samples with hemolysis after centrifugation was the most common cause which accounts 35% of total rejection. In addition, a cross sectional study conducted by Molla H. et al at St. Paul's Hospital millennium Medical College, Addis Ababa also noted that the main reason of specimen rejection was hemolysis (20, 25). Hemolysis may results from inappropriate drawing and transferring of the specimen to collection tubes and also results from transportation of specimen without centrifugation.

Inappropriate specimen container was also revealed as the third main reason of rejection in our study. A retrospective study by Gungoren M et al in Turkey, Konya Necmettin Erbakan university medical faculty hospital biochemistry also noted that improper specimen container was the fourth main reason of rejection next to improper specimen, inappropriate volume, and incorrect request (16).

Even though no enough published studies found to compare with our finding regarding to associated factors of specimen rejection like training status and working experience of specimen collector, a cross sectional study that was conducted by Mehrotra A et al at North Indian revealed that the reason of specimen rejection is directly related to the technical errors of specimen collectors. They didn't know how much specimen volume is required for the respective test or they have poor skill to collect enough amounts of specimens for the requested test (9). Our cross sectional prospective study also noted that more specimens were rejected (about 84% of the total rejected specimen) which were collected by untrained health personnel. In the same manner, higher chance of rejection was seen in specimens collected by health personnel with experience of less than one year compared to specimens collected by health personnel with above five years of experience. But this study showed that educational level of specimen collector was not significantly affecting specimen rejection rate.

7. Limitations of the study

In our cross sectional prospective study, some variables like training status of specimen transporter was not included. In addition this study also not evaluated knowledge, attitude and practice of specimen collector which may be considered as factors of specimen rejection. This study also not measured the impacts of specimen rejection on economic, social and health of individuals and the community at large.

8. Conclusions and recommendation

8.1. Conclusions

Our retrospective study shows the overall specimen rejection rate was 1.57% and specimen rejection rate in each year from 2016 to 2019 were 2.30%, 1.59%, 1.42% and 1.26% respectively. The main reasons of specimen rejection were hemolysis, insufficient specimen volume, repeated labeling and clotted specimen. Although specimen rejection rate among referred specimens was improved gradually through time, still needs to be improved until it meets to the established target specimen rejection rate (0.3%).

On the other hand our cross sectional prospective study finding of specimen rejection rate was 1.34%. The major reasons of specimen rejection were insufficient specimen volume, hemolysis, inappropriate specimen container and uncentrifuge specimen. Training status and working experience of specimen collector are the factors that have impact on specimen rejection. When the specimens were collected by trained and more experienced health personnel it was less likely to be rejected. Whenever a specimen is rejected, a new specimen has to be collected which increases turnaround time and thus affects patient care and customer satisfaction. Not only this specimen rejection may have impacts on economic, social and health of individuals and the community at large. Hence, training of health professionals on specimen collection, handling and transportation of requested tests, appropriate preventive and corrective actions could improve the problem of specimen rejection in specimen referral network.

8.2. Recommendations

To minimize specimen rejection rate among referred specimens all laboratory professionals working at the referring health facilities should be trained on collection, handling and transportation of referred tests. In addition, all specimen referring health facilities shall have standard operating procedures of specimen collection, handling and transportation. Moreover, the responsible bodies (the reference hospital itself, zonal health department& non governmental organizations that support the referral network) shall take preventive and corrective actions periodically and make improvement plan so as to improve the identified gaps in specimen referral network. Finally, we recommend that further studies should be done on the impacts of specimen rejection on economic, social and health of individuals and the community at large.

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Annexes

Annex 1. Consent form

Name of the health facility----------

I have been informed about the study which is aimed at assessing the specimen rejection rate and associated factors among referred specimen through referral network to Debre Markos referral hospital for laboratory testing, Debre Markos, Ethiopia. For this study true and direct information is needed to fill the data collection checklist and a document observation will be performed. The aim of the study was 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. I have also been informed that the benefit of the laboratory is identifying factors affecting specimen quality so as to design appropriate intervention strategies to improve the quality of the laboratory service.

Laboratory head name ----------Signature---------- Date----------

Name of data collector----------Signature---------- Date----------

- Please direct any question or problems that you may face during this study:

Name: Bewket Mesganaw

Mobile: +251-9 12-90-92-19

Email: bewketm@gmail.com

Annex 2. Data collection checklist format for cross sectional study

Specimen ID----------

1. Type of specimen
   A. Whole blood
   B. Serum/plasma
   C. sputum
   D. CSF
   E. DBS
   F. Others, specify ----------
2. Specimen collector characteristics

2.1. Profession

A. Laboratory professional
B. Laboratory aid
C. Other health professionals

2.1.Educational level

A. Certificate
B. Diploma
C. Degree
D. Postgraduate

2.2.Working experience on specimen collection or related clinical services

A. < 1 year
B. 1-3 years
C. 3-5 years
D. > 5 years

2.3.Training status on specimen collection, handling & transportation of referred test

A. Yes
B. No

3. Transported by:
    A. Laboratory personnel
    B. Postal service
    C. With others, specify----------
4. For what test the specimen was referred
    A. Viral load
    B. Gene expert
    C. EID for HIV
    D. CD4 count
    E. Others, specify----------
5. Status of specimen
    A. Accepted for analysis
    B. Rejected
6. If rejected,

6.1. Why the specimen was rejected?

    A. Insufficient volume
    B. Unlabeled specimen
    C. Specimen without request paper
    D. Hemolysis
    E. Clotted
    F. Delayed time
    G. Not maintained cold chain
    H. Contaminated
    I. Inappropriate specimen container
    J. Request paper without sample
    K. Repeated labeling
    L. Lipemic specimen
    M. Mismatch labeling
    N. Others, specify……..

6.2.Corrective measures taken at the reference laboratory

A. Written feedback for referring site
B. Phone feedback for referring site
C. No feedback

Annex 3. Data collection checklist format for retrospective study

Specimen ID----------

1. Type of specimen
   A. Whole blood
   B. Serum/plasma
   C. sputum
   D. CSF
   E. DBS
   F. Others, specify ----------
2. For what test the specimen was referred

A. Viral load
B. Gene expert
C. EID for HIV
D. CD4 count
E. Others, specify----------

3. Status of specimen
   A. Accepted for analysis
   B. Rejected
4. If rejected,

4.1. Why the specimen was rejected?

   A. Insufficient volume
   B. Unlabeled specimen
   C. Specimen without request paper
   D. Hemolysis
   E. Clotted
   F. Delayed time
   G. Not maintained cold chain
   H. Contaminated
   I. Inappropriate specimen container
   J. Request paper without sample

K. Repeated labeling

L. Lipemic specimen

M. Mismatch labeling

N. Others, specify……..

Annex 3. 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.

Name: Bewket Mesganaw (BSC, Msc candidate)

Signature: _____

Date of submission: _____

This thesis has been submitted with our approval as advisors.

Advisor: **Fatuma Hassen(BSC,MPH, PhD candidate)**

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia.

Advisor: **Habtamu Molla (BSC, Msc,PhD candidate)**

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia.