Implementation of Bone Marrow Aspiration and Trephine Biopsy Done for Pediatric Patients at Tikur Anbessa Specialized Hospital, A Cross-Sectional Study

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Research Thesis Submission Form

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Abbreviations/Acronyms

AAU	Addis Ababa University
BMA	Bone Marrow Aspiration
BMAT	Bone Marrow Aspiration and Trephine Biopsy
CDT	Contribution to diagnosis and treatment
ETB	Ethiopian Birr
ICSH	Internationa Council for Standardization in Haematology
PCHD	Peadiatric and Child Health Department
TASH	Tikur Anbessa Specialized Hospital

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Summary

Background: Bone marrow is a viscous tissue that resides in the confines of bones and houses the vitally important pluripotent stem cells. [1] The bone marrow aspirate and Trephine biopsy is an important medical procedure for the diagnosis of hematologic malignancies and other

diseases, and for the follow-up evaluation of patients undergoing medical therapy.[2] It is carried out principally to permit cytological assessment but also for immunophenotypic, cytogenetic, molecular genetics, and other specialised investigations.[3] Depending on the type of iatrogenic injury, the procedure may have its side effects and various complications.[4] Individual factors such as age, comorbid conditions, and procedure factors such as aspirate volume significantly affected the yield of BMAT. [5] The final report of bone marrow aspiration and biopsy plays a major role in management planning of each patient.

Objectives: To assess the diagnostic outcome of BMAT and factors affecting outcome of procedure done for paediatrics patients at Tikur Anbessa Specialized Hospital

Methods: The study design was a cross-sectional study with data collection done prospectively; it was be carried out at Addis Ababa University, College of Health Sciences, Paediatrics and Child Health Department. Simple random sampling was used to select patients who fulfilled eligibility criteria. A trained data collector used a questionnaire, and a check list to collect data from chart review, during procedure and collection of pathology report. Data was entered into SPSS version 25.0 and cleaned. Analysis included determining the outcome from the final pathology report by percentage. Fidelity was analyzed and presented with percentage. Factors affecting outcome were analyzed using SPSS software, with multivariate analysis.

Results A total of 108 sample size was included in this study. 49.1% were 5-10 years old, medean age of 6 years. 13% presented with abdominal swelling, followed by cough and neck swelling, each 11%. This study found a 57.5 % fidelity in application of the standard of procedure. The gaps identified are in having a complete blood count before procedure (64%), getting informed consent (86%), explaining the procedure (53.7%), quantity of smear slides (), technique of smear slides (10%), same incision for BMAT (70%), same needles used for BMAT (100%), and biopsy core length (100%). The diagnostic outcome was poor in 12% and good in 88%. In multivariate regression analysis, Duration of illness (1-3 months) increased poor outcome odds by 10.8 times (AOR=10.8, 95%CI=1.94, 24.55). Increased platelet counts increased poor outcome odds by 12.1 times (AOR=12.1,95%CI=1.25, 118.59). Decreased hemoglobin levels reduced poor outcome odds by 84% (AOR=0.15,95%CI=0.012, 0.66).

Conclusion- Significant factors affecting BMAT outcomes included patient age, nutritional status, duration of illness, and pre-procedure hematologic parameters. The lack of a locally

developed Standard Operating Procedure (SOP) contributed to variability in procedural techniques and diagnostic accuracy. This research underscores the need for enhanced training and improved procedural adherence to optimize BMAT effectiveness.

1. Introduction

1.1 Background

Bone marrow aspiration and trephine biopsy is a simple procedure used to take samples from the bone marrow to diagnose several infectious and non-infectious conditions involving the bone marrow. [2] It is performed by trained personnel for patients with specific indications. The sample is then evaluated, and diagnosis settled by a pathologist.

The most common indication for bone marrow evaluation is cytopenia of one or more hematopoietic cell lines. [4] other indications include infectious diseases infiltrating the bone marrow such as tuberculosis, parasitic infections and metastatic deposits [6] BMAT is also indicated in metabolic conditions such as lysosomal storage disorders.[7]

It has high sensitivity and specificity that makes it reliable for diagnosis and management plan. [8] However, the yield could be affected by different factors which could be patient or procedure related. [9] There are also evidence showing that the procedure may have its side effects and complications which could vary according to the type of iatrogenic injury.[4]

It is crucial to thoroughly understand the required personnel, materials and the steps involved in performing a bone marrow aspiration and biopsy.[3] Paediatric age group of patients require differing techniques to avoid complications.[10] Standard of procedure (SOP) helps to standardize it and avoid inter-personnel variation of sampling and complications.[2]

Time is of importance in diagnosing certain conditions such as malignancies as it could adversely affect patient treatment outcome. [7] Optimizing the patient for the procedure is an equally important step to avoid complications. Balancing the urgency to diagnose and the disease related complications, which usually becomes a reason for cancellation of the procedure, is a challenge.

Since the result of bone marrow aspiration and biopsy determines the management plan for certain patients [9], the yield and associated factors should be carefully studied in large centres like Tikur Anbessa Specialized Hospital. The procedure as well as reason for cancellation should also be studied for quality improvement purpose.

1.1 Statement of the problem

BMA and BMB are simple procedures that can be done either in patient or outpatient setting. [3] It can be particularly challenging in paediatrics age group of patients due to need of differing techniques, complications, and inadequacy of samples [10,11]

Cancer is an emerging public health problem. In a study done in Ethiopia, in 2015, leukaemia was the leading cancer diagnosis in the paediatric age group (age 0 to 14 years) [12] most cases are referred to Blacklion hospital for diagnosis and management purpose. BMAT is used for confirmational diagnosis of leukaemia [4] 200 paediatric cancer patients were seen annually in 2010, but the estimated number of cancer patients were increasing [13]

Similarly, time to initiation of treatment can be delayed due to delayed procedure and diagnosis. [14] From observation, procedures are frequently cancelled due to multiple reasons. One of the reasons is thrombocytopenia, which has been proved to be safe to perform BMAT. [15] Studying cancellation rate and other reasons for cancellation would guide in designing evidence-based measures to improve quality of care.

The quality of care and treatment outcome of patients is compromised when our BMAT sample is non diagnostic. Standard of procedure as well as guidelines to perform proper procedure exist [4, 14]; however, to what extent they are used at TASH has not been previously illustrated.

1.2 Rationale

Tikur Anbessa Specialized Hospital is the one of largest referral Hospitals where emerging diseases in Ethiopia, such as malignancies are diagnosed and managed. Bone marrow aspiration and biopsy is done on a regular basis with a well-organized schedule

and facility. Sixty to eighty procedures are done every month. It has an outstanding pathology department for reports of the samples.

Studying the implementation of the SOP [4] as a factor for the diagnostic outcome of BMAT would recognize the gaps and guides the interventions to improve our practice i.e- evidence based intervention

Therefore, it is important to study the effectiveness (diagnostic outcome) of the procedure done in our setup and the barriers (associated factors) to achieving an ideal outcome

2. Literature Review

Introduction

Bone marrow is a viscous tissue that resides in the confines of bones and houses the vitally important pluripotent stem cells. [1] These stem cells can be harvested from bone marrow by a small puncture of the iliac crest of patients.[10] Bone marrow Aspiration is used to withdraw a sample from the liquid potion of the marrow and bone marrow biopsy is used to withdraw sample from solid portion of the marrow [3,4]

Both are important medical procedures for the diagnosis of hematologic malignancies and other diseases, and for the follow-up evaluation of patients undergoing chemotherapy, bone marrow transplantation, and other forms of medical therapy.[7] It allows cytological assessment and other specialised investigations such as immunophenotypic, cytogenetic, molecular genetics. [3,4,16]

Early diagnosis can be made based on the morphological examination of bone marrow aspiration (BMA) within 2 hours until the bone marrow biopsy result is reported within 48 hours. [2, 17] The sensitivity and specificity of bone marrow trephine biopsy test was 84% and 90% respectively in a study done in one centre in India. [8] In addition, BMAT without imaging guidance and reported a diagnostic yield of 95% in a cohort of 1445

patients [19] in addition, another study showed agreement of BMB with BMA was 100% in acute and chronic leukaemia, while BMA was not sufficient for the diagnosis of lymphoma and solid organ metastasis. [17]

This diagnostic step contributes significantly to diagnosis and treatment in multiple arrays of patients. For instance, a study done to show the contribution to diagnosis and treatment (CDT) of BMA in critically ill patients admitted to ICU, CDT was observed in 40/193 patients (20.7%). [18] another evidence is a study where BMAT results revealed that 60 cases (50%) were malignant in origin, 30 cases (25%) were non-malignant, and 30 cases (25%) were classified as normal. [25]

Another study done to evaluate the diagnostic value of BMA and Triphen biopsy when done simultaneously showed that it helps in making the diagnosis accurately; conditions like tubercular granulomas, haemato-lymphoid neoplasms are better detected by a biopsy.[20]

Indication and contraindications of BMAT

Indications for this procedure can be infectious and non-infectious Conditions. [3] Infectious disease can modify the morphology of the bone marrow by acute or chronic inflammation and by involving the hematopoietic stem cell line hyperplasia or aplasia. [21] Examples of infectious diseases that can involve the bone marrow are mycobacterial infections such as Tuberculosis and Mycobacterium Avium complex, protozoal infections such as Leishmaniasis, and viral infections such as Parvo virus B 19 and cytomegalovirus. [21, 22]

A study done in South Africa showed; Of 327 patients who underwent bone marrow examination, 80 unique diagnoses were obtained in 77 cases (23.5%). The unique diagnoses included the presence of granuloma (n = 49), Mycobacterium tuberculosis (n = 17), Mycobacterium avium complex (n = 3), haematological malignancy (n = 4) and pure red cell aplasia (n = 5). [22]

Other non-infectious indications for bone marrow aspiration and trephin biopsy are nutritional deficiency, cytopenia, metastatic workup of other malignancies. [23] Deficiencies of vitamin B12, folic acid, or iron, or combinations thereof are majority of nutritional deficiencies that affect the bone marrow. [24] Another South African study depicted that the main indications for bone marrow examination were: cytopenias 38 (32%), lymphoma 35 (29%), leukaemia 21 (18%), and multiple myeloma 17 (14%). [25]

In India, a study done in a tertiary Hospital, to show indications for BMAT in infants depicted that the most frequent indication of BME in infants was evaluation of cytopenias, accounting to 82 (27.6%) out of 297 procedures. [26]

Another study done in Pakistan showed of 133 BMA samples, 74 (55.64%) had non-malignant hematological disorders while 40 (30.07%) had hematological malignancies. Out of all 133 cases, 10 patients had single lineage cytopenia, 37 had bicytopenias while 47 presented with pancytopenia. [27]

Systemic conditions, metabolic storage diseases and stromal changes are few of the other indications for BMAT. [28] The utility of BMAT in diagnosing Lysosomal Storage disease was assessed retrospectively with the results depicting that based on BM morphology, 59.4% (n = 19) cases were diagnosed as Neiman Pick/Neiman Pick-like diseases and 40.6% (n = 13) cases as Gaucher Disease. [29] Since Lysosomal Storage Diseases are rare conditions, often marked by unspecific symptoms, in cases of hepatosplenomegaly and cytopenias, a bone marrow examination can also be performed to rule out hematolymphoid disorders. [30].

Contraindications to perform the procedure include severe bleeding diatheses such as severe hemophilia or severe disseminated intravascular coagulopathy. [3] As opposed to the widely accepted belief, thrombocytopenia is not a contraindication. 111 fluoroscopy-guided BMABs were performed on 94 patients including 15 patients with severe thrombocytopenia (platelet less than 20,000 per microliter) and 15 patients with thrombocytopenia (platelets 20,000–50,000 per microliter) and reported no statistically

significant difference in post-procedural hemorrhage or change in hematocrit levels compared to the control group with normal platelet counts. [32]

Factors affecting the diagnostic yield of BMAT

The diagnostic yield of a procedure is of importance as it guides the treatment plan of patients in whom the diagnosis depends on BMAT such as hematologic malignancies. Age, comorbid conditions, and procedure factors such as aspirate volume significantly affected the yield of BMAC [13] Methods for the preparation, processing and reporting of bone marrow aspirates and trephine biopsy specimens can vary considerably resulting in inconsistencies in disease diagnosis or classification. Following Standard of procedure is a major factor affecting the yield of BMAT. [2, 14]

Similarly, inadequacy of biopsy, which happens frequntly, is a major factor affecting the diagnostic outcome. Aspirate adequacy is defined by whether the procedure results in a specimen of sufficient quality for pathologic review. [33] As a standard technique, a 20-mL syringes for aspiration and obtain approximately 0.5 mL of bone marrow aspirate for the preparation of the smears for cytomorphological assessment. [14] The minimum recommended core biopsy length to improve diagnostic yield of BMAB is 2 cm (International Council for Standardization in Hematology) [2] and 1.5 cm (World Health Organization) [14]

In a study done in Europe, trephine biopsies submitted by 25 centres from children with neuroblastoma over a five-year period were reviewed centrally. Of 822 biopsy specimens, 139 (17%) were inadequate. [34] BMAT in neuroblastoma is used for staging purpose as the treatment is largely dictated by the stage of the disease. Sample inadequacy is an avoidable, yet a common challenge as shown in this study.

Other major factor is the indication for which the procedure was done. In a single centre retrospective study done to assess the diagnostic importance of BMAT in 500 patients over 2 years period, the Agreement of BMB with BMA was 100% in acute and

chronic leukaemias, while BMA was not sufficient for the diagnosis of lymphoma and solid organ metastasis. [17]

The BMAT procedure can be done with local anaesthesia or with sedation. [2, 4] The mode of anaesthesia is another factor that could possibly affect the diagnostic yield. The procedure is painful and induces anxiety in both the patient and the physician performing the procedure. Inadequate analgesia could possibly affect the adequacy of the sample and thereof the yield of BMAT.

The factors associated with a Contribution to Diagnosis and Treatment of BMAT in ICU adult patients were haematological malignancy, cancer or non-malignant haematological abnormality known on admission, indication for BMA excluding isolated thrombocytopenia.[18]

Factors related to the operator including anxiety, improper needle location, or experience also affect the quality of samples and thereof diagnostic yield. [35] in the same line, giving regular training and seminars on the standard of procedure has improved outcome as depicted by the experience in Brazil [36]. Similarly, quality control interventions done to improve specimen preparation implementation of a specimen preparation checklist significantly improved core length and frequency of diagnostic samples. [37]

Complications of BMAT

Complications related to the procedure are various and are classified as iatrogenic injuries. Pain is a common post procedure complaint. A nationwide survey y done in Italy to explore current practice of pain management during BMAT procedure, revealed the lack of a standardized approach to procedural pain management. [38]

In addition, physicians and nurses tend to underestimate severe pain and anxiety about the procedure as depicted in a study that showed the proportion of agreement

for occurrence of rated pain during BMA was 73% between patients and registered nurses, and 70% between patients and physicians. [39]

In a south African Study among adults, A total of 182 BMAB procedures were included, and pain was reported in all procedures performed under LA and only in 29.1% of procedures performed with midazolam. [40]

Local procedure site infection is another complication reported by patients who underwent the procedure. It could be as severe as osteomyelitis, sacroiliac septic arthritis, and septicaemia. [41]

Haemorrhage is another complication that can result from internal iliac artery injury, arteriovenous fistulisation, pseudoaneurysm formation. [42,43] gluteal compartment syndrome and sciatica with neurologic deficit, have also been reported. [44]

Standard of Procedure for BMAT

The guideline for standardization of procedure for BMAT was developed by an international Working Party for the Standardization of Bone Marrow Specimens and Reports which was formed by the International Council for Standardization in Hematology (ICSH) to prepare a set of guidelines based on preferred best practices. The guidelines include every detail of the steps that the operator should stick to while performing the procedure. [2]

There is no such guideline or standard of procedure developed in Ethiopia or at Tikur Anbessa Specialized Hospital. Furthermore, there are no data on the diagnostic yield of BMAT performed for paediatric patients in our country Ethiopia. The implementation of this SOP has not been studied and the gaps for evidence-based intervention have not been identified.

3. Conceptual framework

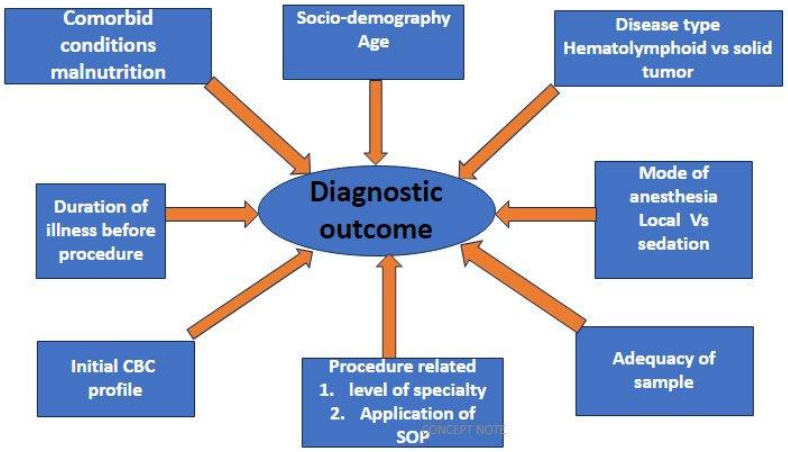

Figure 1: conceptual framework for research thesis on Implementation of Bone Marrow Aspiration and Trephine Biopsy Done for Pediatric patients at Tikur Anbessa Specialized Hospital, a Cross-Sectional Study

4. Research Questions

What is the effectiveness of Bone marrow Aspiration and Trephine biopsy done for pediatric patients at Tikur Anbessa Specialized Hospital?

What are the barriers preventing an ideal diagnostic outcome of bone marrow aspiration and trephine biopsy done for paediatric patients at Tikur Anbessa Specialized Hospital?

What are the pattern of diseases diagnosed by BMAT done for pediatric patients at TASH?

Is there correlation between the clinical diagnoses and BMAT results?

5. Hypothesis

Hypothesis: outcome of anti-tuberculous treatment for tuberculous uveitis

$H1_0$: the diagnostic outcome of bone marrow aspiration and trephine biopsy done for paediatric patients at Tikur Anbessa Specialized Hospital is low <95%

$H1_a$: the diagnostic outcome of bone marrow aspiration and trephine biopsy done for paediatric patients at Tikur Anbessa Specialized Hospital is high >/=95%

6. Objectives

3.1 General objective

- Assess the Implementation of bone marrow aspiration and trephine biopsies done for pediatric patients at Tikur Anbessa Specialized Hospital

3.2 Specific objectives

- Assess the diagnostic outcome of b one marrow aspiration and trephine biopsies done for pediatric patients at Tikur Anbessa Specialized Hospital.
- Determine the factors associated with poor diagnostic outcome of bone marrow aspiration and trephine biopsies done for pediatric patients at Tikur Anbessa Specialized Hospital,
- Describe the pattern of disease diagnosed by bone marrow aspiration and trephine biopsies done for pediatric patients at Tikur Anbessa Specialized Hospital.
- Determine the fidelity to standard of procedure of bone marrow aspiration and trephine biopsies done for pediatric patients at Tikur Anbessa Specialized Hospital.

7. Methods

7.1 Study setting

The study was conducted at Addis Ababa University, College of Medicine, Tikur Anbessa Specialized Hospital in Bole Sub-city, Addis Ababa, Ethiopia. Addis Ababa is the capital city of Ethiopia that is found at 2.3 km above sea level and has an area of over 527 km2. There are 11 sub cities and 99 Woredas.

The department of pediatrics receives referrals from all over the country and is one of the few centers where malignancies are diagnosed and treated. The haemato-oncology unit of the department oversees managing bone marrow aspiration and trephin biopsy procedure that is done 4 days of the week. It provides out-patient service. BMAT procedure is done in the sedation room on the 7th floor. The procedure is done by year two residents with no prior training. It is done either with short sedation, where an anesthetist, a nurse and an assistant are present, or with local anesthesia where residents and interns are present. The samples are collected, specimens are prepared by the nurse, or the residents then taken to the pathology department by the attendant. The nurse at the pathology department fixes the slides and biopsies. The pathology resident examines and consults the most senior pathologist, who signs the result within 48 hours (about 2 days) of the procedure for Aspiration and 1 month for biopsy.

7.2 Study design

The study design is an institution based prospective cross-sectional study

7.3 Study Population

7.3.1 Source Population

The source population for this study Pediatric patients age <14, who had bone marrow aspiration and trephine biopsy was done at Addis Ababa University, Tikur Anbessa Specialized Hospital, Pediatric and Child health Department (PCHD). Patients are sent form various parts of the country as it is tertiary hospital

7.3.2 Study Population

Pediatric patients age <14, who had bone marrow aspiration and trephine Biopsy was done for pediatric patients at Tikur Anbessa Specialized Hospital, during the study period

7.3.3 Study unit/subject

Pediatric patients age <14, who had bone marrow aspiration and trephine Biopsy done for pediatric patients at Tikur Anbessa Specialized Hospital, during the study period and fulfilled the eligibility criteria.

7.4 Eligibility Criteria

7.4.1 Inclusion criteria

1)Complete clinical records of initial clinical condition, CBC profile, clear indications, and complications if any

2) All TASH pediatric patients having BMAT, who have a /verbal or written consent from their parents

3) Final diagnosis settled by a senior pathologist at the department of Pathology of Tikur Anbessa Specialized Hospital

7.4.2Exclusion criteria

1) Subjects who only have the bone marrow aspiration done without having the trephine biopsy

7.5 Sampling procedure

Tikur Anbesa Specialized Hospital was purposefully selected as the patients are representative of the country wide status. The department of paediatrics has an organized haemato-oncology unit who work hand in hand with the pathology department.

All patients that fulfil the inclusion criteria will be included in the study, with in the study period as subjects. Sample size will be calculated with a P value of 50 %, since there are no similar data on paediatric patients. Subjects were selected based on eligibility criteria and included in the study as depicted in Figure 2. All medical records were assigned with a unique study number. Data was collected from the initial medical record of the subject, from the attendant, the physician, pathology result and entered a questionnaire and check list. No identifiable photographs or other materials were entered into the database other than a unique study number.

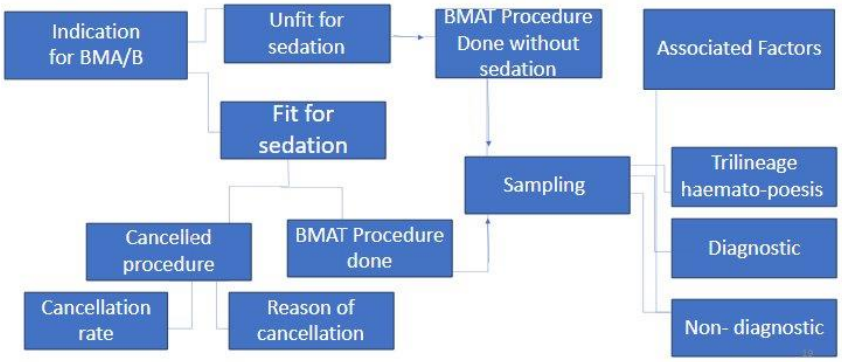

Figure 2: Sampling procedure for the research thesis on Implementation of Bone Marrow Aspiration and Trephine Biopsy Done for Pediatric patients at Tikur Anbessa Specialized Hospital, a Cross-Sectional Study

7.5.1 Sampling technique:

The sampling technique was random sampling. The first subject was selected randomly, then data was collected from every other subject.

7.5.2 Sample size determination

using the simple population formula, Since there is no previous study in similar age group,p value taken is 50 % is taken, margin of error is 5 % Z= 1.96 and d= 0.05

$$n = \frac{Z^2pq}{d^2} = 385$$

Since the source Populaltion is less than ten thousand (10,000), Finite Population Correction Formula is used; Total number of bone marrow done over one year was 450 from the registry at sedation room.s

Using Finit population correction n' = n/ 1+ (n-1/N)

N= 450, n= 385 n'= 385/ 1+ 384/450

n = 385/1.853

n'= 208 accounting for 5 % non-response rate, total sample size was 198

However; due to limitation in time and resources, only 108 samples were collected and analyzed

7.6 Data collection procedures

The data collection tool was questionnaire. All relevant data was collected from the medical records, records at sedation room, results of each patient at pathology department. Qquestionnaire extracted from SOP was completed by the data collector who observed the procedure of BMAT and specimen processing.

7.7 Study variables

7.7.1 Dependent variables

Diagnostic

Nondiagnostic

Trilineage haematopoiesis

7.7.2 Independent variables

Age, Nutritional status, Initial CBC, indication for procedure, duration of illness

Mode of anesthesia, Volume of sample

Experience/Level of specialty of physician performing procedure, and Proper application of the SOP

Prior chemo/radiotherapy

7.8 Operational definition

Diagnostic: A specific diagnosis settled by a senior pathologist after careful assessment of the BMAT sample

Nondiagnostic: inadequate or diluted sample as assessed by by a senior pathologist after careful assessment of the BMAT sample

Trileanage Hematopoesis: normal marrow architecture with normal appearance of production of all three cell lines- red blood cells, white blood cells and platelets- as assessed by a senior pathologist

7.9 Data management

Before data collection

The principal investigator and data collector reviewed the questionnaire for completeness

During data collection

The research conductor and data collector ensured the data collection's completeness during the data collection period by using a check list.

After data collection

The data collected was rechecked for completeness of the information and for avoidance of any errors after which the data was entered correctly into statistical software (Statistical Package for Social Science (SPSS) version 25. Windows software) by the research conductor for further processing and descriptive analysis.

7.10 Data analysis procedures

Data processing was started at the hospital by checking for completeness of the data and performing quality control checks. The collected data was cleaned, edited and subsequently the data w compiled into a computer using Statistical Package for Social Science (SPSS) version 25.0 Windows software. Simple descriptive statistics such as percentages and mean was used to characterize variables. Odds ratio with 95% confidence interval was computed to assess the level of association and statistical significance of the associated factors by multivariate analysis. A p- value of <0.05 was considered statically significant. The analyzed data is presented in tables, graphs and figures accordingly.

7.11 Ethical considerations

Informed consent was taken at first contact of patient from the respective guardian as the subjects were in paediatric age group The information collected in the study was be

treated confidentially and anonymity guaranteed by the principal investigator. The study proposal was submitted to, and clearance obtained from the Research Ethics Committee of Addis Ababa University, College of Medicine. In addition, the research was approved by the Institution Review Board.

7.12 Dissemination of results

The results of this study will be shared with Addis Ababa University, College of Medicine, through hard copy and presentation. Publication of the study in an appropriate journal also will be attempted. It is anticipated that the result would be acceptable to an Ethiopian medical journal or an international journal such as Journal of Pediatric Hemato-oncology.

8. Results

8.1 Sociodemographic and clinical onset related characteristics of the study participants

One-hundred-eight cases were enrolled in this study. Nearly half (49.1%) were in the age group of 5-10 years with the median age of 6 years. Seventy-eight percent of the participants were male. 43% (47) percent of the study participants had <1month duration of illness and 69.4% (73) of them had normal nutritional status. 9.3% had SAM and 21.3 had MAM. Most common chief complaint was abdominall swelling 13% (14), followed by cough 10%(11) and neck swelling 10%(11).

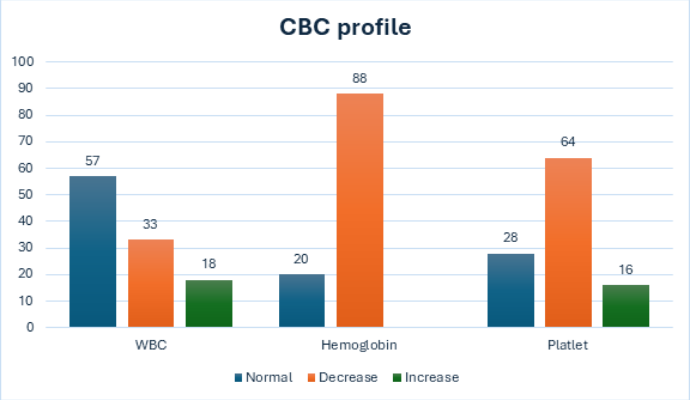

Figure 3. CBC profile of study samples for thesis on Implementation of Bone Marrow Aspiration and Trephine Biopsy Procedure Done for Pediatric patients at Tikur Anbessa Specialized Hospital, a Cross-Sectional Study

8.3 Clinical assessment of the study participants

Thirty-two percent of the children had ALL clinical assessment followed by RMS, AML and NHL as shown in the table below.

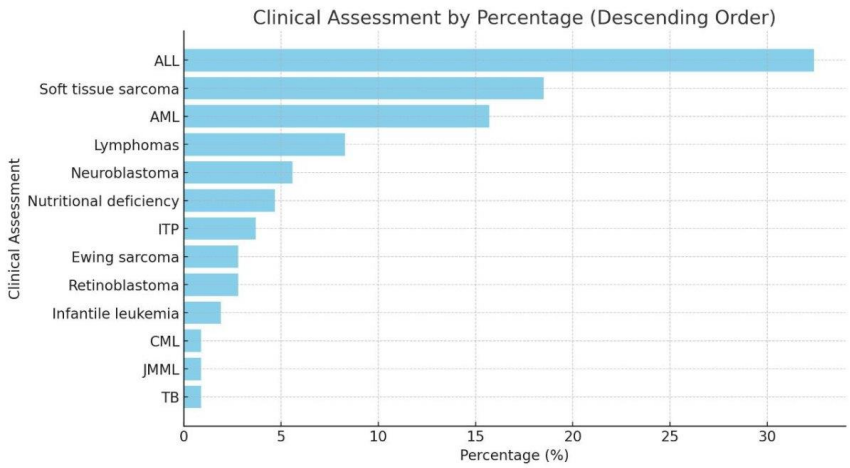

Figure 4: Distribution of clinical assessment for thesis on Implementation of Bone Marrow Aspiration and Trephine Biopsy Procedure Done for Pediatric patients a Tikur Anbessa Specialized Hospital, a Cross-Sectional Study

8.3. Procedural standard related characteristics of the bone marrow aspiration

All the procedure was done by year II resident and unconscious sedation was given for all procedure. 85% of the procedure were finished within less than 15minutes and 61.1% of the procedure were done for an indication of diagnosis, staging and follow up the malignant disorder. For all cases thrombocytopenia and bleeding disorder was seen and 53.7%(58) of the physician explained the procedure to the attendant and CBC was done for 64.8%(70) percent of the participants. Physician obtained written consent after explaining the procedure in 86% (94)of the procedures.

Indications for Bone Marrow Examination	frequency	Percent
Unexplained anemia, abnormal red cell indices, cytopenia or cytoses	38	35.2
Diagnosis, staging and follow-up of malignant hematological disorders	66	61.1
abnormal peripheral blood smear morphology suggestive of bone marrow pathology	1	.9
Investigation of suspected bone marrow metastases Unexplained focal bony lesions on radiological imaging	2	1.9
Unexplained organomegaly or presence of mass lesions in accessible for biopsy	1	.9

Table 1.Distribution of indication of the BMAT for thesis on Implementation of Bone Marrow Aspiration and Trephine Biopsy Procedure Done for Pediatric patients a Tikur Anbessa Specialized Hospital, a Cross-Sectional Study

8.4 Anatomic site related characteristics of the procedure

All the sample were taken from posterior iliac crest and there was no bone lesion on the site of the procedure. Radiotherapy was not given on the area of sampling and 81.5% of the aspiration were taken before biopsy. 70.4% were taken with the same

incision and 19.4% were away from 1 cm from the aspiration site. The aspirate and the trephine were done with different needle in all procedures.

8.4 The Bone Marrow Aspirate and Collection of Aspirate Specimens

All the sample were not drawn with 10-20ml syringe and bed side smear was done with 0.5ml sample. Ninety three percent made squash preparation using more than two slides and eighty nine percent did not make aspirate smears at all.

variable	Frequency	Percent
the sample drawn with 20ml syringe	108	100
bed side smear done with 0.5ml sample	108	100
the rest of the aspirate sample put into EDTA tube		
no	108	100
the number of slides used for aspirate smear		
less than six	15	13.9
more than six	1	.9
six	3	2.8
zero	89	82.4
the number of squash slides made		
less than two	3	2.8
more than two	93	86.1
two	6	5.6
zero	6	5.6
A separate sample taken for flow cytometry cytogenetics and molecular genetics study	8	7.4
stored in a sodium heparin tube (n=8)	8	100

excess aspirate	9	8.3
it kept in EDTA tube for smear	3	2.3

Table 2. The bone marrow aspirate and collection of aspirate specimens for thesis on Implementation of Bone Marrow Aspiration and Trephine Biopsy Procedure Done for Pediatric patients a Tikur Anbessa Specialized Hospital, a Cross-Sectional Study

8.5 Preparation of Aspirate Slides and particle clots related characteristics

Only 17.6% (19/108) used a glass spreader to make smear slide, of which only 10.5 % (2/17) used the right technique. 94.3 % (102/108) prepared squash slides. The fixative used for all samples was air dry and methanol fix with the staining done by wright staining only.

8.6 Bone Marrow Trephine Biopsy Specimens related characteristics

All the core length were not at least 1.5cm and Bilateral trephine biopsy was done for 36%(39/108) procedures.

variable	frequency	Percent
blunt stylet is inserted through the distal end of the biopsy needle to expel the core from the proximal end of the biopsy needle onto a glass slide		
yes	108	100
Imprint used before fixation		
yes	23	21.3
the container appropriately labelled at the bedside with the patient surname, first name, unique patient identifier, and date and time of collection,		
yes	108	100

the fixative used a neutral buffered formalin for 6 h		
yes	108	100
Duration of fixation used		
>6hours	108	100
Declaration agent used		
Formic acid	108	100
Duration for take declaration in hours		
1hour	108	100
the specimen embedded in paraffin wax		
yes	108	100
used for staining		
H&E stain only	108	100

Table 3. The trephine biopsy collection and preparation of specimens for thesis on Implementation of Bone Marrow Aspiration and Trephine Biopsy Procedure Done for Pediatric patients a Tikur Anbessa Specialized Hospital, a Cross-Sectional Study

Overall, 19 of 33 pertinent procedures were fulfilled completely. Thus, fidelity to the procedure was 57.7 %

8.7 BMAT results and pattern of Disease diagnosed by BMAT

All the results aspirate specimen were turn with in 48hours of sample submission and with in a month for trephine specimen.

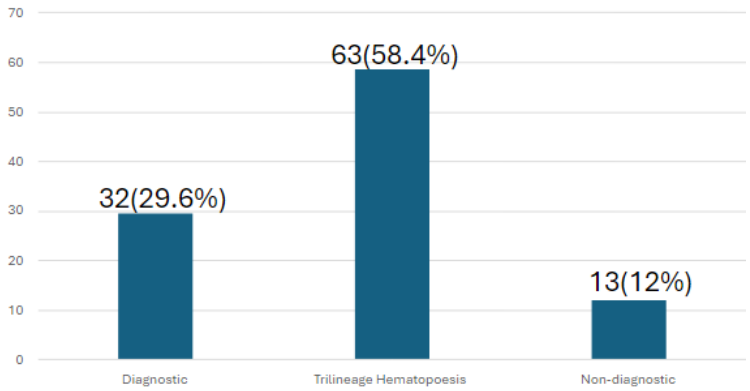

Figure 5: BMAT results for thesis on Implementation of Bone Marrow Aspiration and Trephine Biopsy Procedure Done for Pediatric patients at Tikur Anbessa Specialized Hospital, a Prospective Cross-Sectional

The pattern of diagnosis for those BMAT whose results were diagnostic (n=32) is shown in the figure below.

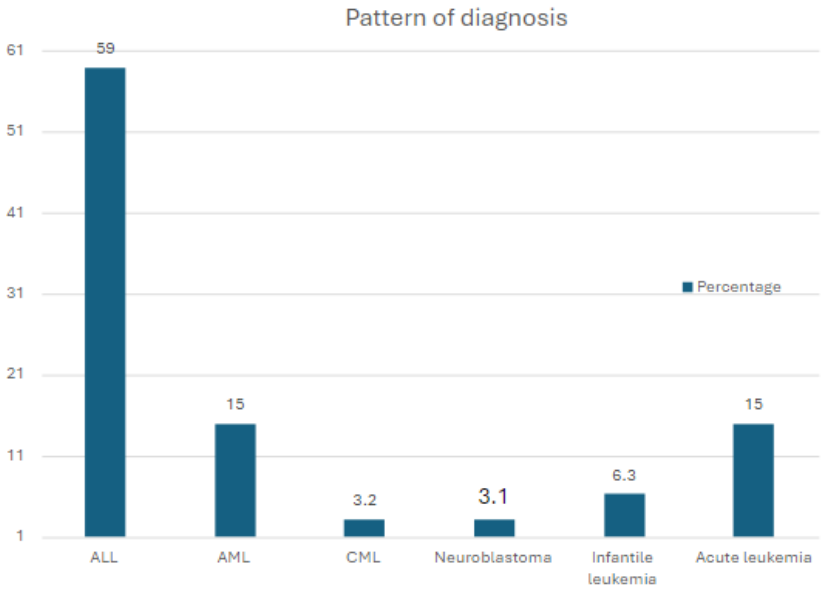

Figure 6: Pattern of disease diagnosed by BMAT for thesis on Implementation of Bone Marrow Aspiration and Trephine Biopsy Procedure Done for Pediatric patients at Tikur Anbessa Specialized Hospital, a Prospective Cross-Sectional

8.8 Diagnostic outcome of BMAT

Here the results that came as diagnostic and trilineage hematopoiesis comprise of 88% whereas, non-diagnostic results were seen in 12 % of the procedures. Thus, we have poor diagnostic outcome in 12% of the samples. This translates, as per the alternate hypothesis, the diagnostic outcome in our institute is low i.e <95%

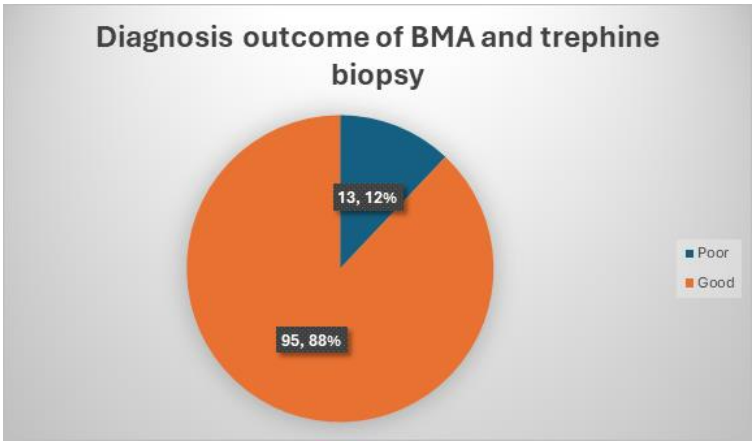

Figure 7: Diagnostic outcome for thesis on Implementation of Bone Marrow Aspiration and Trephine Biopsy Procedure Done for Pediatric patients at Tikur Anbessa Specialized Hospital, Cross-Sectional

8.9 The determinant factors of poor diagnostic outcome of bone marrow aspiration and trephine biopsies

In the bivariate regression increasing platelet level were the only variable of having significant relation with Outcome of BMAT. The multivariate logistic regression revealed that the odds of duration of illness 1-3months were 10.8 times likely to increase poor outcome of BMAT result compared to those of duration of illness <1months (AOR=10.8, 95%CI=1.94, 24.55) the increase platelet counts were 12.1 times increase its poor outcome of BMAT compared to decrease platelet counts (AOR=12.1, 95%CI=1.25, 118.59). On the other hand, the odds of decreased haemoglobin level were 84% less likely of poor outcomes of BMA/BMB compared to those of normal haemoglobin (AOR=0.15, 95%CI=0.012, 0.66).

Variable	Outcome of BMA &BMB		p-value	COR with 95%CI	P-value	AOR with 95%CI
	Poor	Good				
Duration of illness in month						
<1	3	44	1		1	
1-3	6	25	0.093	3.5(0.81, 15.31)	0.046	10.8(1.94, 24.55)
>3	4	26	0.311	2.6(0.47, 10.88)	0.311	3.3(0.33, 33.31)
Nutritional status						
Normal	10	62	1		1	
MAM	2	24	0.116	0.72(0.11, 2.53)	0.319	0.16(0.005, 5.75)
SAM	1	9	0.737	0.69(0.08, 6.04)	0.144	12.7(0.42, 84.71)
WBC						
Decreased	9	24	0.042	6.4(1.74, 55.13)	0.139	9.4(0.48, 83.11)
Normal	3	54	0.962	0.94(0.09, 9.69)	0.351	0.19(0.005, 6.34)
increase	1	15	1		1	
Haemoglobin						
decrease	8	80	0.058	0.3(0.09, 1.04)	0.030	**0.15(0.012, 0.66)**
normal	5	15	1		1	
Platelet						

Decrease	4	60	1		1	
Normal	3	25	0.463	1.8(0.38, 8.63)	0.167	0.06(0.001, 3.211)
increase	6	9	0.002	10(2.36, 42.49)	0.032	**12.1(1.25, 118.59)**
Length of the procedure in minute						
<15	11	74	1		1	
>15	2	21	0.181	0.64(0.13, 3.12)	0.056	12.1(1.25, 65.59)
Excess aspiration						
Yes	2	7	1		1	
no	11	88	0.138	0.44(0.08, 2.38)	0.074	0.04(0.001, 1.37)

Table 4. The bivariate and multivariate association of independent variable with outcome of BMAT among Paediatric Patients at Tikur Anbessa Specialized Hospital, 2024.

9. Discussion

Diagnostic Accuracy and Predictors of Poor Outcomes

The study found that trilineage hematopoiesis was observed in 58.3% of cases, while 29.6% were diagnostic, and 12% were non-diagnostic. Previous studies have reported varying diagnostic yields depending on patient characteristics and procedural techniques. For instance, a study conducted in India showed a sensitivity of 84% and specificity of 90% for trephine biopsy tests [58 45]. Similarly, a retrospective cohort study in South Africa found that 23.5% of bone marrow examinations provided unique diagnoses, including hematological malignancies and infectious diseases [46]. The high percentage of trilineage hematopoiesis among clinical ALL cases suggests that not all

suspected ALL cases underscores the importance of adjunct diagnostic tools such as flow cytometry and cytogenetics [47].

Multivariate logistic regression analysis identified duration of illness (1-3 months) and increased platelet count as significant predictors of poor BMAT outcomes. This aligns with previous studies indicating that prolonged disease duration before diagnosis is associated with adverse outcomes due to disease progression and treatment delay [48]. Conversely, decreased hemoglobin levels were associated with a lower likelihood of poor outcomes, a finding that warrants further investigation.

Procedural Techniques and Standardization

Fidelity to the standard of procedure was 57.5 %. This shows the huge gap in implementing the standard of procedure set on the guideline by the International Council for Standardization in Hematology (ICSH) All procedures in this study were performed under unconscious sedation, ensuring patient comfort and minimizing movement during the procedure. Research has shown that sedation improves procedural success rates and reduces patient anxiety [49]. Additionally, 81.5% of aspirates were taken before biopsies, which aligns with international guidelines recommending aspirates to be collected first to prevent hemodilution [50]. The volume of BMAT taken also aligns with ICSH recommending BMA of 0.5ml for optimal diagnostic yield [51] not that of core biopsy lengths of at least 1.5 cm majority (78.7%) of procedures were completed within 15 minutes, demonstrating procedural efficiency comparable to international guidelines [52].

However, some procedural inconsistencies were noted. For example, 13.9% of procedures lacked proper patient explanation before obtaining consent, and CBC was not performed within 48 hours in 35.2% of cases. Studies suggest that rigorous adherence to pre-procedural protocols improves diagnostic outcomes [53].

Furthermore, the study found that 100% of procedures at TASH were performed by year-two residents, which could contribute to sample variability. A Brazilian study

demonstrated that regular training and quality control measures significantly improved BMAT outcomes [54].

A significant proportion of patients (43.5%) had a disease duration of less than one month, emphasizing the aggressive nature of hematological malignancies and the importance of early diagnosis. Additionally, the nutritional status assessment showed that 69.4% of patients had normal nutritional status, which contrasts with some studies indicating malnutrition as a risk factor for poor treatment outcomes [55].

Diagnostic and Procedural Characteristics

In this study, the most common indications for BMAT included the diagnosis and staging of hematological malignancies (61.1%), unexplained cytopenias (35.2%), and investigation of suspected metastatic involvement (1.9%). These findings are consistent with previous research showing that BMAT is primarily used for diagnosing conditions such as leukemia, lymphoma, and bone marrow failure syndromes [56].

Regarding clinical assessments, acute lymphoblastic leukemia (ALL) was the most frequently diagnosed condition (23.1%), followed by rhabdomyosarcoma (RMS) (11.1%) and acute myeloid leukemia (AML) (10.2%). This distribution is in line with global pediatric oncology statistics, where ALL represents the most common childhood malignancy [57].

A noteworthy finding was that thrombocytopenia and bleeding disorders were assessed in all cases before the procedure, ensuring patient safety. However, only 53.7% of physicians explained the procedure to patient attendants, indicating a need for better communication and informed consent practices, as recommended by the American Society of Hematology [58].

This study provides valuable data on the clinical and procedural aspects of pediatric hematological diagnoses at Tikur Anbessa Specialized Hospital. Future research should explore the integration of immunophenotyping and genetic profiling to enhance diagnostic precision and patient outcomes. Additionally, efforts to strengthen

physician-patient communication and streamline procedural protocols will be crucial in improving pediatric hematology services.

10. Limitations

1. Sample Size: The study initially planned for a larger sample but only analyzed 108 cases due to time and resource constraints, potentially affecting statistical power and generalizability.
2. Single-Center Study: The research was conducted at Tikur Anbessa Specialized Hospital, limiting the applicability of findings to other healthcare settings in Ethiopia or globally.
3. Lack of Longitudinal Data: The study did not follow patients over time to assess long-term outcomes of diagnostic and treatment decisions based on BMAT results.
4. Operator Variability: Since all procedures were performed by Year II residents, variation in technique and experience might have influenced diagnostic yield.
5. Limited Use of Advanced Diagnostics: The study primarily relied on conventional pathology assessments, with minimal incorporation of flow cytometry, cytogenetics, or molecular studies that could improve diagnostic precision.

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11. Conclusion

Significant factors affecting BMAT outcomes included patient age, nutritional status, duration of illness, and pre-procedure hematologic parameters. The lack of a locally developed Standard Operating Procedure (SOP) contributed to variability in procedural techniques and diagnostic accuracy.

This research underscores the need for enhanced training and improved procedural adherence to optimize BMAT effectiveness. Addressing these challenges can improve the quality of pediatric hematological diagnostics and patient management in TASH

12. Recommendations

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Your recommendation is should be based on your finding ONLY!

1. Implementation of Standard Operating Procedures (SOPs):
    a. Develop and enforce hospital-wide SOPs for BMAT to ensure consistency in technique, sample handling, and interpretation.
    b. Regularly update guidelines based on emerging evidence and international best practices.
2. Enhanced Training and Capacity Building:
    a. Conduct regular workshops and hands-on training sessions for residents to improve procedural skills and diagnostic accuracy.
    b. Introduce supervised training programs to minimize variability among operators.
3. Quality Control Measures:
    a. Establish periodic internal audits and quality control checks to assess BMAT adequacy and diagnostic yield.
    b. Implement a feedback mechanism where pathologists provide real-time guidance to residents performing procedures.
4. Pre-Procedural Optimization:
    a. Ensure complete blood count (CBC) testing is performed within 48 hours before BMAT to assess patient suitability.
    b. Improve patient and caregiver education regarding the procedure, risks, and benefits to enhance informed consent processes.
5. Future Research Directions:
    a. Conduct multi-center studies to assess BMAT outcomes across different healthcare settings in Ethiopia.
    b. Perform longitudinal studies to evaluate patient outcomes based on BMAT-based diagnoses and treatment decisions.
    c. Investigate the impact of different anesthetic techniques on patient comfort and procedural success.

By implementing these recommendations, Tikur Anbessa Specialized Hospital can enhance the quality and reliability of BMAT procedures, ultimately improving patient outcomes in pediatric hematological care.

13. References

1. **Gurkan, U. A., & Akkus, O. (2008).** The mechanical environment of bone marrow: A review. *Annals of Biomedical Engineering, 36*(11), 1978–1991. https://doi.org/10.1007/s10439-008-9577-x
2. **Lee, S.-H., Enber, W. N., Porwit, A., Tomonaga, M., & Peterson, L. C. (2008).** ICSH guidelines for the standardization of bone marrow specimens and reports. *International Journal of Laboratory Hematology, 30*(5), 349–364. https://doi.org/10.1111/j.1751-553X.2008.01101.x
3. **Schumann, D., Kujat, R., Nerlich, M., & Angele, P. (2006).** Mechanobiological conditioning of stem cells for cartilage tissue engineering. *Biomedical Materials and Engineering, 16*(4 Suppl), S37–S52.
4. **Raskin, R. E., & Messick, J. B. (2012).** Bone marrow cytologic and histologic biopsies: Indications, technique, and evaluation. *Veterinary Clinics of North America: Small Animal Practice, 42*(1), 23–42. https://doi.org/10.1016/j.cvsm.2011.10.001
5. **Muthu, S., Jeyaraman, M., Narula, A., Ravi, V. R., Gandi, A., Khanna, M., Maffulli, N., & Gupta, A. (2023).** Factors influencing the yield of progenitor cells in bone marrow aspiration concentrate: A retrospective analysis of 58 patients. *Biomedicines, 11*(3), 738. https://doi.org/10.3390/biomedicines11030738
6. **Kaur, M., Singh Rana, A. P., Kapoor, S., & Puri, A. (2014).** Diagnostic value of bone marrow aspiration and biopsy in routine hematology practice. *Journal of Clinical and Diagnostic Research, 8*(8), FC13–FC16. https://doi.org/10.7860/JCDR/2014/8994.4704
7. **Riley, R. S., Hogan, T. F., Pavot, D. R., Forysthe, R., Massey, D., Smith, C., & Wright, L. (2004).** A pathologist's perspective on bone marrow aspiration and biopsy: I. Performing a bone marrow examination. *Journal of Clinical Laboratory Analysis, 18*(2), 70–90. https://doi.org/10.1002/jcla.20008
8. **Chauhan, S., Pradhan, S., Mohanty, R., Saini, A., Devi, K., & Sahu, M. C. (2018).** Evaluation of sensitivity and specificity of bone marrow trephine biopsy tests in an Indian teaching hospital. *Alexandria Journal of Medicine, 54*(2), 161–166. https://doi.org/10.1016/j.ajme.2017.06.003
9. **Rindy, L. J., & Chambers, A. R. (2024).** Bone marrow aspiration and biopsy. In *StatPearls*. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK559232/

10. **Abla, O., Friedman, J., & Doyle, J. (2008).** Performing bone marrow aspiration and biopsy in children: Recommended guidelines. *Paediatrics & Child Health, 13*(6), 499–501. https://doi.org/10.1093/pch/13.6.499
11. **Tomasian, A., & Jennings, J. W. (2022).** Bone marrow aspiration and biopsy: Techniques and practice implications. *Skeletal Radiology, 51*(1), 81–88. https://doi.org/10.1007/s00256-021-03882-w
12. **Memirie, S. T., Habtemariam, M. K., Asefa, M., Deressa, B. T., Abayneh, G., Tsegaye, B., Abraha, M. W., Ababi, G., Jemal, A., Rebbeck, T. R., & Verguet, S. (2018).** Estimates of cancer incidence in Ethiopia in 2015 using population-based registry data. *Journal of Global Oncology, 4*, 1–11. https://doi.org/10.1200/JGO.17.00175
13. **Worku, T., Mengistu, Z., Semahegn, A., & Tesfaye, G. (2017).** Rehabilitation for cancer patients at Black Lion Hospital, Addis Ababa, Ethiopia: A cross-sectional study. *BMC Palliative Care, 16*(1), 53. https://doi.org/10.1186/s12904-017-0237-5
14. **Swerdlow, S. H., Campo, E., Harris, N. L., Jaffe, E. S., Pileri, S. A., Stein, H., & Thiele, J. (2008).** *WHO classification of tumours of haematopoietic and lymphoid tissues* (4th ed.). International Agency for Research on Cancer.
15. **Stensby, J. D., Long, J. R., Hillen, T. J., & Jennings, J. W. (2020).** Safety of bone marrow aspiration and biopsy in severely thrombocytopenic patients. *Skeletal Radiology, 49*(5), 769–774. https://doi.org/10.1007/s00256-019-03342-6
16. **Bain, B. J. (2001).** Bone marrow aspiration. *Journal of Clinical Pathology, 54*(9), 657–663. https://doi.org/10.1136/jcp.54.9.657
17. **Dogan, A., & Demircioglu, S. (2022).** Diagnostic importance of bone marrow aspiration evaluation: A single-center study. *Pakistan Journal of Medical Sciences, 38*(4Part-II), 811–815. https://doi.org/10.12669/pjms.38.4.5314
18. **Calvet, L., Pereira, B., Sapin, A. F., Mareynat, G., Lautrette, A., & Souweine, B. (2017).** Contribution to diagnosis and treatment of bone marrow aspirate results in critically ill patients undergoing bone marrow aspiration: A retrospective study of 193 consecutive patients. *Journal of Intensive Care, 5*(1), 67. https://doi.org/10.1186/s40560-017-0261-9
19. **Ellis, L. D., Jensen, W. N., & Westerman, M. P. (1964).** Needle biopsy of bone and marrow: An experience with 1,445 biopsies. *Archives of Internal Medicine, 114*(2), 213–221. https://doi.org/10.1001/archinte.1964.03860080097012
20. **Diebold, J., Molina, T., Camilleri-Broët, S., Le Tourneau, A., & Audouin, J. (2000).** Bone marrow manifestations of infections and systemic diseases

observed in bone marrow trephine biopsy review. *Histopathology, 37*(3), 199–211. https://doi.org/10.1046/j.1365-2559.2000.00964.x

21. **Bharuthram, N., & Feldman, C. (2019).** The diagnostic utility of bone marrow examination in an infectious disease ward. *Southern African Journal of HIV Medicine, 20*(1), 974. https://doi.org/10.4102/sajhivmed.v20i1.974
22. **Letestu, R., & Valensi, F. (2003).** Bone marrow aspiration for diagnostic purposes. *Annales de Biologie Clinique, 61*(6), 655–665.
23. **Krause, J. R. (1988).** The bone marrow in nutritional deficiencies. *Hematology/Oncology Clinics of North America, 2*(4), 557–566.
24. **Tshabalala, W. S., Pillay, S., & Wilson, D. P. K. (2020).** Diagnostic outcomes of bone marrow aspirate and trephine biopsies performed at a hospital in KwaZulu-Natal, South Africa. *African Journal of Laboratory Medicine, 9*(1), 1028. https://doi.org/10.4102/ajlm.v9i1.1028
25. **Unni, S. S., Sachdeva, M. U. S., Kumar, N., et al. (2015).** Spectrum of diseases diagnosed on bone marrow examination of 285 infants in a single tertiary care center. *Hematology, 20*(3), 175–181. https://doi.org/10.1179/1607845414Y.0000000195
26. **Qureshi, H., Farooq, N., Amjid, M., et al. (n.d.).** Pattern of hematological disorders on bone marrow aspirate examination. *Department of Pathology.*
27. **O'Malley, D. P., Smith, L., & Fedoriw, Y. (2018).** Benign causes of bone marrow abnormalities including infections, storage diseases, systemic disorders, and stromal changes. In *Bone Marrow Pathology* (pp. 184–209). Elsevier.
28. **Nishith, N., Siddiqui, S. H., Raja, S. K. R., Agrawal, N., Phadke, S., & Sharma, S. (2023).** Utility of morphologic assessment of bone marrow biopsy in diagnosis of lysosomal storage disorders. *Indian Journal of Pathology and Microbiology, 66*(1), 91–95. https://doi.org/10.4103/ijpm.ijpm_100_22
29. **Hyun, B. H., Gulati, G. L., & Ashton, J. K. (1988).** Bone marrow examination: Techniques and interpretation. *Hematology/Oncology Clinics of North America, 2*(4), 513–523.
30. **Safyan, R. A., Mathew, M., Marchi, E., & Accordino, M. K. (2017).** Bone marrow aspirate quality assessment. *Journal of Clinical Oncology, 35*(8_suppl).
31. **Reid, M. M., & Roald, B. (1997).** Bone marrow trephine biopsy in infants. *Archives of Disease in Childhood, 77*(1), 60–61. https://doi.org/10.1136/adc.77.1.60

32. **Bain, B. J., & Bailey, K. (2011).** Pitfalls in obtaining and interpreting bone marrow aspirates: To err is human. *Journal of Clinical Pathology, 64*(4), 373–379. https://doi.org/10.1136/jcp.2010.080820
33. **Loureiro, G., Rizzatti, E. G., et al. (2014).** Quality control of bone marrow aspirates: Additional steps toward a safer and more efficient procedure. *Cancer, 120*(9), 1441–1442. https://doi.org/10.1002/cncr.28610
34. **Odejide, O. O., Cronin, A. M., DeAngelo, D. J., Bernazzoli, Z. A., et al. (2013).** Improving the quality of bone marrow assessment: Impact of operator techniques and use of a specimen preparation checklist. *Cancer, 119*(19), 3472–3478. https://doi.org/10.1002/cncr.28215
35. **Liptrott, S. J., Botti, S., Bonifazi, F., et al. (2021).** Management of pain and anxiety during bone marrow aspiration: An Italian national survey. *Pain Management Nursing, 22*(3), 349–355. https://doi.org/10.1016/j.pmn.2021.03.006
36. **Lidén, Y., Olofsson, N., Landgren, O., & Johansson, E. (2012).** Pain and anxiety during bone marrow aspiration/biopsy: Comparison of ratings among patients versus health-care professionals. *European Journal of Oncology Nursing, 16*(3), 323–329. https://doi.org/10.1016/j.ejon.2011.07.006
37. **Alzanad, F., Feyaza, M., & Chapanduka, Z. C. (2022).** A study of patient-reported pain during bone marrow aspiration and biopsy using local anesthesia alone compared with local anesthesia with intravenous midazolam coadministration at a tertiary academic hospital in South Africa. *Health Science Reports, 5*(6), e902. https://doi.org/10.1002/hsr2.902
38. **Khakwani, M., Srinath, S., Pratt, G., & Moss, P. (n.d.).** A rare complication of bone marrow aspiration and trephine biopsy: Staphylococcus aureus.
39. **Berber, I., Erkurt, M., Kuku, I., et al. (2014).** An unexpected complication of bone marrow aspiration and trephine biopsy: Arteriovenous fistula. *Medical Principles and Practice, 23*(4), 380–383. https://doi.org/10.1159/000363233
40. **Chamisa, I. (2007).** Fatal vascular retroperitoneal injury following bone marrow biopsy. *South African Medical Journal, 97*(3), 246.
41. **Roth, J. S., & Newman, E. C. (2002).** Gluteal compartment syndrome and sciatica after bone marrow biopsy: A case report and review of the literature. *American Surgeon, 68*(9), 791–794.
42. **Nishith, N., Siddiqui, S. H., Raja, S. K. R., et al. (2023).** Utility of morphologic assessment of bone marrow biopsy in diagnosis of lysosomal storage disorders. *Indian Journal of Pathology and Microbiology, 66*(1), 91–95. https://doi.org/10.4103/ijpm.ijpm_100_22

43. **Hyun, B. H., Gulati, G. L., & Ashton, J. K. (1988).** Bone marrow examination: Techniques and interpretation. *Hematology/Oncology Clinics of North America, 2*(4), 513–523.
44. **Safyan, R. A., Mathew, M., Marchi, E., & Accordino, M. K. (2017).** Bone marrow aspirate quality assessment. *Journal of Clinical Oncology, 35*(8_suppl).
45. **Chauhan, S., Pradhan, S., Mohanty, R., Saini, A., Devi, K., & Sahu, M. C. (2018).** Evaluation of sensitivity and specificity of bone marrow trephine biopsy tests in an Indian teaching hospital. *Alexandria Journal of Medicine*, *54*(2), 161-166. https://doi.org/10.1016/j.ajme.2017.06.003
46. **Bharuthram, N., & Feldman, C. (2019).** The diagnostic utility of bone marrow examination in an infectious disease ward. *South African Journal of HIV Medicine*, *20*(1), 974. https://doi.org/10.4102/sajhivmed.v20i1.974
47. **Odejide, O. O., Cronin, A. M., DeAngelo, D. J., et al. (2013).** Improving the quality of bone marrow assessment: Impact of operator techniques and use of a specimen preparation checklist. *Cancer*, *119*(19), 3472-3478. https://doi.org/10.1002/cncr.28215
48. **Aladjidi, N., et al. (2013).** Clinical and biological features of childhood acute leukemia. *Pediatric Blood & Cancer*, *60*(5), 799-805. https://doi.org/10.1002/pbc.24423
49. **Lidén, Y., Olofsson, N., Landgren, O., & Johansson, E. (2012).** Pain and anxiety during bone marrow aspiration/biopsy: Comparison of ratings among patients versus health-care professionals. *European Journal of Oncology Nursing*, *16*(3), 323-329. https://doi.org/10.1016/j.ejon.2011.07.006
50. **Lee, S.-H., Enber, W. N., Porwit, A., Tomonaga, M., & Peterson, L. C. (2008).** ICSH guidelines for the standardization of bone marrow specimens and reports. *International Journal of Laboratory Hematology*, *30*(5), 349-364. https://doi.org/10.1111/j.1751-553X.2008.01101.x
51. **Stensby, J. D., Long, J. R., Hillen, T. J., & Jennings, J. W. (2020).** Safety of bone marrow aspiration and biopsy in severely thrombocytopenic patients. *Skeletal Radiology*, *49*(5), 769-774. https://doi.org/10.1007/s00256-019-03342-6
52. **Loureiro, G., Rizzatti, E. G., et al. (2014).** Quality control of bone marrow aspirates: Additional steps toward a safer and more efficient procedure. *Cancer*, *120*(9), 1441-1442. https://doi.org/10.1002/cncr.28610
53. **Swerdlow, S. H., Campo, E., Harris, N. L., et al. (2017).** WHO classification of tumors of hematopoietic and lymphoid tissues. *International Agency for Research on Cancer*. https://publications.iarc.fr/Book-And-Report-Series/Who-Classification-Of-Tumours

54. **Terwilliger, T., & Abdul-Hay, M. (2017).** Acute lymphoblastic leukemia: A comprehensive review and 2017 update. *Blood Cancer Journal*, *7*(6), e577. https://doi.org/10.1038/bcj.2017.53
55. **Bhutta, Z. A., Berkley, J. A., Bandsma, R. H. J., Kerac, M., Trehan, I., & Briend, A. (2017).** Malnutrition and its impact on pediatric oncology outcomes. *The Lancet Child & Adolescent Health*, *1*(1), 15-27. https://doi.org/10.1016/S2352-4642(17)30010-7
56. **Tshabalala, W. S., Pillay, S., & Wilson, D. P. K. (2020).** Diagnostic outcomes of bone marrow aspirate and trephine biopsies performed at a hospital in KwaZulu-Natal, South Africa. *African Journal of Laboratory Medicine*, *9*(1), 1028. https://doi.org/10.4102/ajlm.v9i1.1028
57. **Hunger, S. P., & Mullighan, C. G. (2015).** Acute lymphoblastic leukemia in children. *New England Journal of Medicine*, *373*(16), 1541-1552. https://doi.org/10.1056/NEJMra1400972
58. **American Society of Hematology. (2019).** Guidelines for bone marrow aspiration and biopsy. *Blood Advances*, *3*(19), 2840-2841. https://doi.org/10.1182/bloodadvances.2019000700

Annex I – Information Sheet

Study title

Implementation of Bone Marrow Aspiration and Trephine Biopsy Procedure Done for Pediatric patients at Tikur Anbessa Specialized Hospital, a Cross-Sectional Study

Why is this study important?

The study aims assess the diagnostic outcome (effectiveness) of bone marrow aspiration and trephine biopsy as well as associated factors (barriers) with poor outcome of procedure done for pediatric patients at Tikur Anbessa Specialized Hospital

The result will be used as evidence-based intervention for quality improvement.

Procedures

The data was collected using the questionnaire provided below and analysed by SPSS software

Risks and discomforts

Informed written consent was taken from the patient attendants and the data was kept confidential.

Contact

For additional information please contact the principal investigator.

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