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COMPARATIVE RETROSPECTIVE STUDY OF BONE MARROW ASPIRATE AND TREPHINE BIOPSY

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Abstract:

The present retrospective study entitled "Comparative retrospective study of bone marrow aspiration and bone marrow trephine biopsy" was carried out at Department of Lab Medicine Medanta the Medicity hospital Okhla Phase 2 Delhi, From October 2013 to April 2014. A total of 220 cases out of the 97 cases of Bone Marrow Aspirate (BMA) and 123 cases are of Bone Marrow Aspirate and Bone Marrow Biopsies (BMB) done simultaneously were included in the study. Out of total 220 cases of bone marrow examination, 97(44.09%) cases of BMA done alone and123 (55.9%) cases of BMA and BMB did together. The results of the comparative evaluation were divided into: 1. Number of cases where the diagnosis was given on BMA alone, BMB was non-contributory 2. Number of cases that showed a positive correlation between BMA and BMB 3. The number of cases where a definite opinion could not be given either in BMA or in BMB. 4. In the present study, there was not any case of BMB alone because at the centre of study BMA was preceded or carried out simultaneously BMB. 5. Out of 97 cases of bone marrow aspiration, 66(68.04%) were males and 31(31.95%) as females 6. The age of the patient's at the time of the diagnosis varied from 20 to 83 years. No age below 20 years was found. Depending on their age differences, they are grouped into three categories. The first group consists of Adolescents within 11-20 years. The second's groups consist of adults within 21-30 years and the third group consists of others above 30 years of age. Majority of the patients was above the age of 30 years 7. In a total of 97 cases, 2.1% (2) cases were Adolescents, 7.2% (7) cases were adults and 90.7% (88) cases were above 30 years of age, which show the highest incidence in of BMA diagnosis in patient's above 30 years of age 8. Out of 97 cases of BMA, were 44(46%) case of megaloblastosis,7(7%) cases show Normoblastic reaction 8% cases of Micronormoblastic reaction, 22% cases shows Dimorphic anaemia,2% cases of Sickle – cell anaemia, 3% cases of Eosinophilia 2%cases of Erythroid Hyperplasia and 9.1% cases shows normal morphology. 9. Out of 123 cases, where BMA and BMB both were done together in that case 60.2 % (74) were male and 39.8 % (49) as females, the incidence of increased frequency of diagnosis was more in males than females 10. In a total of 123 cases, 1.62% (2) cases were Adolescents, 3.25% (4) cases were adults and 95.2% (117) cases were above 30 years of age, which show the highest incidence in of BMA diagnosis in patients above 30 years of age. 11. Out of 123 cases, 19.5% (24) were Megakaryocytic Thrombocytopenia, 15.4% (19) cases of Plasmacytoma and 7.3% (9) case of Multiple Myeloma, 12. Out of 123 cases, 0.8% (1) case of Myelofibrosis (MF), 4.8% (6) cases of a Myelodysplastic syndrome and 8.1% (10) cases of Lymphoproliferative disease (LPD). 13. Out of 123 cases, 4.1% (5) case of Acute Leukemia (AL), 3.2% (4) case of Acute Myeloid Leukemia and 1.6% (2) case of Acute Lymphocytic Leukemia (ALL) 14. Out of total

123 cases, 18.6% (23) cases of Non-Hodgkin's Lymphoma(NHL) and 2.4% (3) cases of Hodgkin's Lymphoma(HL) were observed 15. Out of total 123 cases, 2.4% (3) cases of Metastatic Adenocarcinoma, 2.4% (3) cases of Metastatic Malignant Tumor and 4.06% (5) cases of Metastatic Cancer of Breast were observed 16. Out of total 123 cases, were 0.8% (1) case of Erythroleukemia(EL), 1.6% (2) case of Chronic-Lymphoproliferative disease(CLD) and 2.4%(3) cases of Myeloproliferative disease(MPD) observed, 17. Out of the 123 cases studied there was a positive correlation in 85 cases (69.10%). 18. In the present study, we found the highest correlation rate with the diagnosis given as plasmacytoma (94.7%) 18/19. Other cases with a good positive correlation were haematological malignancies such as multiple myeloma where there was (66.6%) correlation. Out of a total of 9 cases diagnosed, 6 cases showed a positive correlation in both BMA and BMB. 19. Non-Hodgkin's Lymphoma showed a positive correlation in 43.4% cases (10/23), Hodgkin's Lymphoma showed a positive correlation in 75% cases 3/4, Leukemia's showed a positive correlation in 81.8% of cases (9/11), those cases diagnosed by BMB alone showed a hypocellular BMA, One case was clinically suspected to be an Erythroleukemia. Megakaryocytic thrombocythaemia showed 70.8% correlation (17/24). 20. Amongst the non-haematological malignancies metastatic to the bone marrow, 63.6% cases (7/11) showed a positive correlation in both BMA and BMB, two of the cases were clinically not suspected for non-hematologic malignancies. A primary tumour could not be ascertained as the patient died before further investigations could be done. The other case was investigated for anaemia. 21. In those cases where a diagnosis of BMA was given, depending on whether macronormoblastic or micronormoblastic, they were further worked up, mostly for anaemia, and accordingly, Perl's stains for iron was studied, biochemical parameters were taken into consideration and the diagnosis was confirmed impression was given. 22. The cases where a definite opinion could not be given either in BMA or in BMB comprised 30.89% (38/123).The reports were varying from an inadequate BMA, where the BMB is hypercellular or reactive, in some cases, BMA appeared to be normal, but with no marrow spaces in the BMB.

INTRODUCTION

Bone marrow aspiration (BMA) and core biopsy have an important role in the investigation and diagnosis of hematological as well as non-hematological malignancies and various other diseases. They are also important in the management of these conditions particularly in the follow-up evaluation of patients undergoing chemotherapy, bone marrow transplantation, typing of anaemia, evaluation of pyrexia of unknown origin and infective diseases and other forms of medical treatment. Involvement of marrow by metastatic tumour, have an effect on clinical treatment and prognosis. Similarly involvement of the marrow by granulomatous lesion especially tuberculous granulomas may be easily identified in bone marrow biopsies. Moreover in cases where malignancies are not clinically suspected, bone marrow aspirations and biopsies have been useful in detecting non-hematologic malignancies. When both the procedures are performed simultaneously, they are complementary to each other there is more material to study the morphology and the pattern of distribution of the cells. **(Riley RS,et,al, 2010)**

Types of bone marrow examination:

There are two types of examination done to evaluate the bone marrow studies

- Bone marrow aspiration (BMA)
- Bone marrow trephine biopsy (BMTB)

Bone marrow aspiration:

Bone marrow aspirations are carried out principally to permit cytological assessment of bone marrow cells. It should be preceded by evaluation of the medical history and clinical features, results of a full blood count, other laboratory tests, and radiological investigations. It should be carried out by trained individuals who are aware of the indications, contraindications, and hazards of the procedure. They should follow a standard operating procedure. The operator should have made an adequate assessment of clinical and haematological features to ensure both that appropriate indications exist and that all relevant tests are performed. For the patient's comfort and safety, the posterior iliac crest is generally the preferred site of aspiration. Films of aspirated marrow and, when appropriate, films of crushed particles should be made and labelled. Once thoroughly dry, films should be fixed and stained. As a minimum, a Romanowsky stain and a Perls' stain are required. A cover slip should be applied. This is essential to ensure that all appropriate tests are performed on the material obtained and to permit an adequate evaluation. It is necessary to know whether the patient is receiving, or has recently been receiving, any medication that may influence the blood count or bone marrow cytology. This includes drugs that may have an adverse effect on the bone marrow and cytokines that have been given to stimulate haematopoiesis**. (B J Bain, 2001)**

Indications for bone marrow aspiration

- Investigation of unexplained microcytosis
- Investigation of unexplained macrocytosis
- Investigation of unexplained anaemia
- Investigation of unexplained thrombocytopenia
- Investigation of pancytopenia (including suspected Aplastic anaemia)
- Investigation of a leucoerythroblastic blood film
- and suspected bone marrow infiltration
- Investigation of suspected acute leukemia
- Assessment of remission status after treatment of
- acute leukemia
- Investigation of suspected MDS or myelodysplastic/ Myeloproliferative disorder
- Investigation of suspected chronic myeloid Leukemia
- Follow up of chronic myeloid leukemia
- Investigation of suspected myeloproliferative disorder (polycythaemia rubra vera, essential thrombocythaemia, idiopathic myelofibrosis, or systemic mastocytosis

MATERIALS AND METHODS

The present retrospective study entitled "Comparative retrospective study of bone marrow aspiration and bone marrow trephine biopsy" was carried out at Department of Lab Medicine, Fortis Escort Heart Institute Okhla Delhi, From October 2011 to April 2012.A total 220 cases out of them 97 cases of Bone Marrow Aspirate (BMA) and 123 cases are of Bone Marrow Aspirate and Bone Marrow Biopsies (BMB) done simultaneously were included in the study. Out of them 79 (35.9%) were female and 141 (64.09%) were male. The age range of patients varied 20 years to 85 years. All relevant data including clinical records concerning, age, sex, cytochemistry immunohistochemistry, cytogenetic, flowcytometry detail and hematological profile taken from laboratory records of the concern department and from Medical records departments of the hospitals. The pathological material for the study were retrieved from laboratory and reviewed in detail. In all the cases bone marrow slide examined and whenever necessary they were restrained.

Criteria for selection of cases:

The following investigation protocol formed the basis of screening for bone marrow aspirate and bone marrow trephine biopsies.

Various modalities used in the diagnosis of bone marrow and classification of the diseases is as follows:

- Bone marrow examination
- Haematological profile (complete blood count by sysmex 1800i).
- General blood picture.
- Cytochemical stain(MPO/PAS/SBB/PERL'S/MGG)
- Histochemical stain (such as H & E)

Fig: 4.1- Commercially available bone marrow procedure kit containing supplies and eauipment for a bone marrow aspirate and biopsy

Site of procedure

Bone marrow aspiration and trephine biopsy are usually performed on the back of the hipbone, or posterior iliac crest. However, an aspirate can also be obtained from the sternum (breastbone). A trephine biopsy should never be performed on the sternum, due to the risk of injury to blood vessels, lun gs or the heart.

Fig: 4.2- showing site bone marrow

Equipment used for sampling of Bone marrrow

- sterile gloves
- sterile drape
- Illinois bone marrow aspiration needle and/or
- Jamshidi biopsy needle (8-,11- or 13-gauge)
- obturator

- 25-gauge 5/8-inch and 22-gauge 1.5-inch needles
- number-11 scalpel blade
- 10-cc Luer slip tip syringes (3)
- Lidocaine 1%
- sodium bicarbonate (1 meq/mL)
- chlorhexadine gluconate 2% or povidone-iodine
- 4-inch x 4-inch gauze sponges
- pressure dressing and tape Optional
- heparinized 10-cc syringe (preservative-free 1000U/mL) for special studies
- 3.5-inch or 5-inch spinal needle
- specimen bottle with formalin
- tube with EDTA anticoagulant

Procedure of bone marrow aspirate and bone marrow trephine biopsies:

A bone marrow biopsy may be done in a health care provider's office or in a hospital. Informed consent for the procedure is typically required. The patient is asked to lie on his or her abdomen (prone position) or on his/her side (lateral decubitus position). The skin is cleansed, and a local anesthetic such as lidocaine is injected to numb the area. Patients may also be pretreated with analgesics and/or anti-anxiety medications, although this is not a routine practice.

Typically, the aspirate is performed first. An aspirate needle is inserted through the skin using manual pressure and force until it abuts the bone. Then, with a twisting motion of clinician's hand and wrist, the needle is advanced through the bony cortex (the hard outer layer of the bone) and into the marrow cavity. Once the needle is in the marrow cavity, a syringe is attached and used to aspirate ("suck out") liquid bone marrow. A twisting motion is performed during the aspiration to avoid excess content of blood in the sample, which might be the case if an excessively large sample from one single point is taken.

Subsequently, the biopsy is performed if indicated. A different, larger trephine needle is inserted and anchored in the bony cortex. The needle is then advanced with a twisting motion and rotated to obtain a solid piece of bone marrow. This piece is then removed along with the needle. The entire procedure, once preparation is complete, typically takes 10–15 minutes.

If several samples are taken, the needle is removed between the samples to avoid blood coagulation.In March 2010, Vidacare Corporation introduced a new technology to facilitate faster and easier insertion when compared to manual insertions with comparable or better core sample quality. The OnControl™ Bone Marrow Biopsy and Aspiration System provides the first advance in bone marrow biopsy and aspiration procedures in over 50 years by combining a specially designed needle with a powered driver to obtain high-quality core samples. Validation testing completed prior to the product's launch on the OnControl™ System showed the following results.Mean length of core sample of 1.32 cm, Median time to core extraction of 81 seconds, Needle insertion success rate of 94%, Biopsy core acquisition success rate of 90%, Zero complications.

After the procedure

After the procedure is complete, the patient is typically asked to lie flat for 5–10 minutes to provide pressure over the procedure site. After that, assuming no bleeding is observed, the patient can get up and go about their normal activities. Paracetamol (acetaminophen) or other simple analgesics can be used to ease soreness, which is common for 2–3 days after the procedure. Any worsening pain, redness, fever, bleeding or swelling may suggest a complication. Patients are also advised to avoid washing the procedure site for at least 24 hours after the procedure is completed.

Complication of procedure:

While mild soreness lasting 12–24 hours is common after a bone marrow examination, serious complications are extremely rare. In a large review, an estimated 55,000 bone marrow examinations were performed, with 26 serious adverse events (0.05%), including one fatality. The same author collected data on over 19,000 bone marrow examinations performed in the United Kingdom in 2003, and found 16 adverse events (0.08% of total procedures), the most common of which was bleeding. In this report, complications, while rare, were serious in individual cases**.(Bain BJ,et,al,2005)**

Complete blood count (by Sysmax 1800i):

The XT-1800i is a compact, high performance, automated hematology analyzer that provides accurate and precise CBC results including a fully automated WBC 5-part differential.

Table: 4.1 show different mode working

Sample Aspiration Mode	Measured Sample	Aspiration Volume	Discrete Mode and Throughput (sample/Hour)		Remarks
			CBC	CBC + DIFF	
Manual Mode	Whole Blood	85 □L	80	80	
CP Sampler Mode	Whole Blood	150 □L	80	80	Sampler Unit is required.
Closed Mode	Whole Blood	150 □L	80	80	It's performed in Sampler Unit.

Preparation of bone marrow slide:

Reagents:

For smear staining and morphology examination, reagents being used include:

- Methanol solution(for fixation of cells on slide)
- Jenner dye(primary stain) (Ranbaxy)
- Geimsa dye(counter stain) (Ranbaxy)

METHODS:

Smear preparation and stain:

Jenner and Geimsa staining:

It is a romonowsky stain, which is basically a mixture of acidic eosin Y(tetra-bromo fluorescein that stain basic groupings if Hb, eosinophil granules), and basic stain of Azur B(Trimethyl thionin, which stain acedic grouping of nucleus, DNA, RNA, neutrophil and basophil granules).

Jenner stain:

0.5 percent solution in methanol, i.e., 0.5 gm in 100 ml of methanol, warm to 50 degree Celsius. Then cool to room temperature and rotate to mix, filter and use. It is the simplest stain.

Geimsa stain:

Stock solution: 1.0 gm Geimsa's powder, mix with 62.5 ml of glycerine; keep at 56 degree Celsius for 3 hours. Once it is cool, add 62.5 ml of methanol. This is a complex stain.

Keep staining reagents in dark brown bottles away from light.

Staining procedure:

Smears from bone marrow or peripheral blood are prepared and stained as described below:

- The smear is properly air dried and fixed by keeping it in methanol for 5 minutes.
- Working solution of jenner dye is made and smear is covered with it for 5 minutes.
- After 5 minutes, Jenner stain is decanted and smear is exposed to workin solution Geimsa dye for 20 minutes.
- The smear is washed under tap water, air dried properly and labeled.

The primary goal of smear preparation and staining is to study the morphology of cells. This method helps in detecting the lineage of cells present in the specimens of the patients(myeloid or lymphoid), sometimes in case of myeloid, blasts in various stages of development are seen which gives a fair idea of the subtype of myeloid leukemia present. The differential leucocyte count is also performed and blast percentage is noted carefully. Based on these findings these findings the doctor decides further diagnosis.

Special staining techniques used for bone marrow aspirate and bone marrow trephine biopsies are discussed below:

Perl's stain (iron stain):

Periodic Acid Schiff (PAS):

SUDAN BLACK B (SBB):(Ranbaxy)

May-Grunwald-Geimsa stain (MGG):(Ranbaxy)

Hematoxylin and Eosin (H&E) Staining:(Ranbaxy)

STATISTICAL ANALYSIS OF DATA

The Data was analyzed using SPSS statistical computer programme. The Pearson correlation were applied to show the spectrum of positive correlation between BMA and BMB and used to find the significance between BMA and BMB which were most significant at the level of 0.01(2-tailed). The

analysis of variance (ANOVA) was used to compare the mean difference for more than two groups.WINDOW-7 was also used somewhere in the distribution of Age and Sex.

OBSERVATION AND RESULTS

The present retrospective study entitled "Comparative retrospective study of bone marrow aspiration and bone marrow trephine biopsy" was carried out at Department of Lab Medicine, Fortis Escort Heart Institute Okhla Delhi, From October 2011 to April 2012.A total 220 cases out of them 97 cases of Bone Marrow Aspirate (BMA) and 123 cases are of Bone Marrow Aspirate and Bone Marrow Biopsies (BMB) done simultaneously were included in the study. Out of them 79 (35.9%) were female and 141 (64.09%) were male. The age range of patients varied 20 years to 85 years All relevant data including clinical records concerning, age, sex, cytochemistry immunohistochemistry, cytogenetic, flowcytometry detail and hematological profile taken from laboratory records of the concern department and from Medical records departments of the hospitals. The pathological material for the study were retrieved from laboratory and reviewed in detail. In all the cases bone marrow slide examined and whenever necessary they were restained.

Out of total 220 cases of bone marrow examination, 97(44.09%) cases of BMA done alone and123 (55.9%) cases of BMA and BMB done together. The results for the comparative evaluation were divided into:

- Number of cases where diagnosis was given on BMA alone, BMB was not required.
- Number of cases that showed positive correlation between BMA and BMB
- Number of cases where a definite opinion could not be given either in BMA or in BMB.
- In present study there was not any cases of BMB alone because at the centre of study BMA was preceded or carried out simultaneously BMB.

Sex distribution on the basis of BMA only

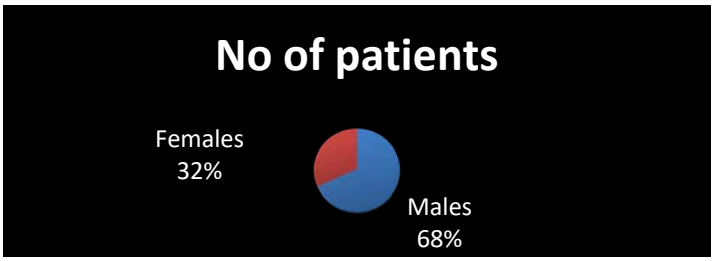
Out of 97 cases of bone marrow aspiration, 66(68.04%) were males and 31(31.95%) as females **(refer to pie-chart no. 5.1 and Table no. 5.1)**

	Males	**Females**
No. of patients	**66**	**31**
Percentage (%)	**68.04%**	**31.95%**

Table: 5.1 Sex distribution of patient's were BMA done only

The analysis of data show increase frequency of BMA in Males.

Pie-Chart: 5.1- show sex distribution in BMA studies,



Age distribution of patients with BMA

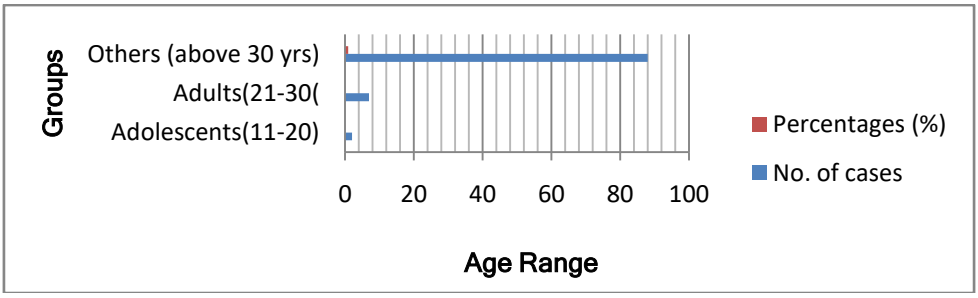
The age of the patient's at time of the diagnosis varied from 20 to 83 years. No age below 20 years was found. Depending on their age differences, they are grouped into three categories. The first group consists of Adolescents within 11-20 years. The second's groups consist of adults within 21-30 years and the third group consists of others above 30 years of age. Majority of the patient's was above the age of 30 years.

Groups	No. of cases(97)	Percentages (%)
Adolescents(11-20)	**2**	**2.1%**
Adults(21-30)	**7**	**7.2%**
Others (above 30 yrs)	**88**	**90.7%**

Table: 5.2- Age distribution of patient's in case of BMA only

In a total of 97 case 2.1% (2) cases were Adolescents, 7.2% (7) cases were adults and 90.7% (88) cases were above 30 years of age, which show highest incidence of BMA diagnosis in patient's above 30 years of age**. (refer to Table no. 5.2 and Bar chart no. 5.1)**

The analysis of data showing increase frequency of patient's above 30 years of age



Bar-Chart: 5.1 Age distribution in case of BMA diagnosis.

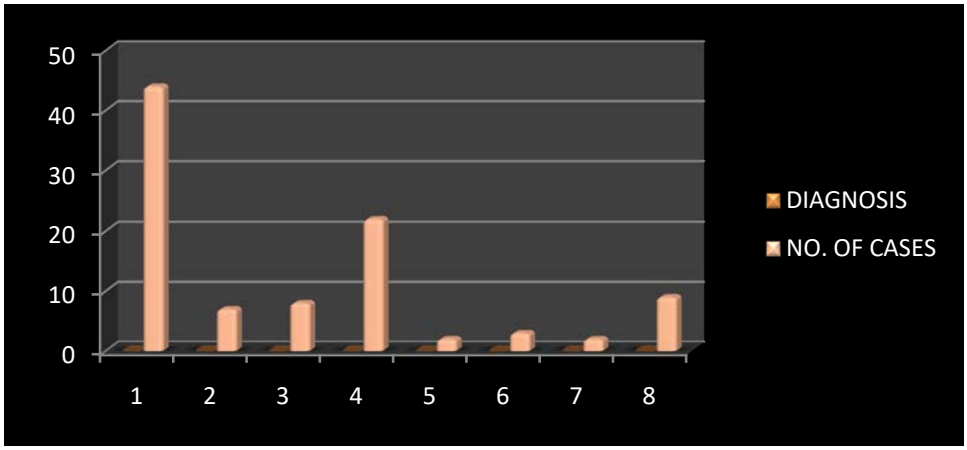
Distribution of diseases on the basis of BMA alone

There were 97 cases which were done on the basis of BMA. Here the BMB was non required as diagnosis was confined on the basis of BMA alone. Table 1 shows the spectrum of cases with BMA.

	DIAGNOSIS	NO. OF CASES
1	Megaloblastosis	44
2	Normoblastic reaction	7
3	Micronormoblastic	8
4	Dimorphic anemia	22
5	Sickle cell anemia	2
6	Eosinophilia	3
7	Erythroid hypoplasia	2
8	Show normal morphology	9

Table: 5.3- Diagnosis on bone marrow aspiration alone

Out of 97 cases of BMA, were 44(46%) case of megaloblastosis,7(7%) cases show Normoblastic reaction,8(8%) cases of Micronormoblastic reaction, 22 (23%) cases shows Dimorphic anemia,2 (2%)cases of Sickle –cell anemia, 3 (3%) cases of Eosinophilia,2 (2%)cases of Erythroid Hypoplasia and 9 cases shows normal morphology**.** The analysis of data show that mainly of cases of megaloblastic anemia was diagnosed on the basis of BMA only followed by 22% can mainly was of micronormoblastic reaction and was confirm also on serum analysis and bone marrow iron stores. **(refer to table no. 5.3 and chart no. 5.2)**



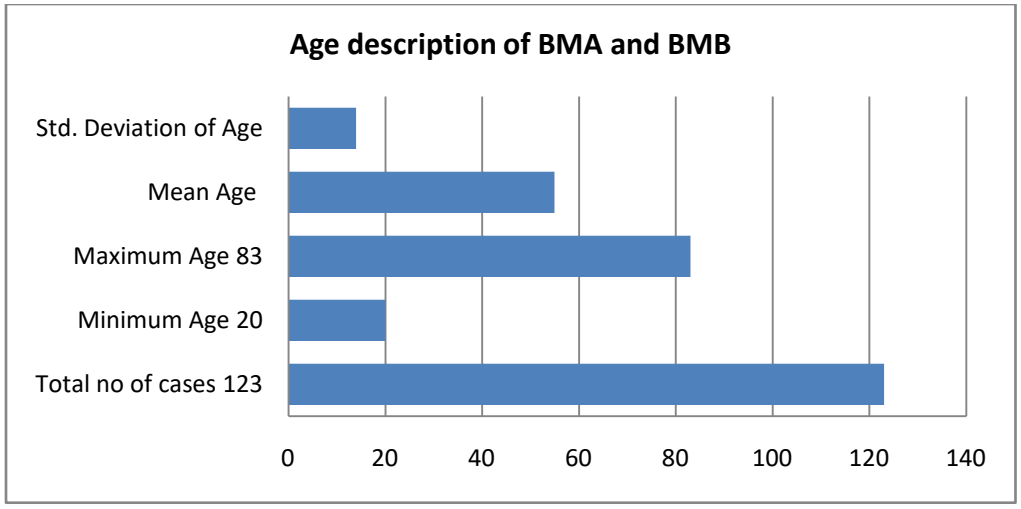
Bar- Chart: 5.2- showing percentage of each case out of total no of cases.

Observation of cases were BMA and BMB both performed

Out of 123 cases, at the time of diagnosis the patient's age range between 20-83 years , the mean of the age was 54.94 years and the std. deviation of the age was 13.97**(refer to table no. 5.4 and Bar chart no.5.3)**

AGE DESCRIPTION	
Total no of cases	**123**
Minimum	**20 years**
Maximum	**83 years**
Mean	**54.94**
Std. Deviation	**13.97**

Table: 5.4- Shows the Age Description of patient's were BMA and BMB both applied.



Bar-Chart: 5.3- Showing Age Description of the patient's on the basis of BMA and BMB

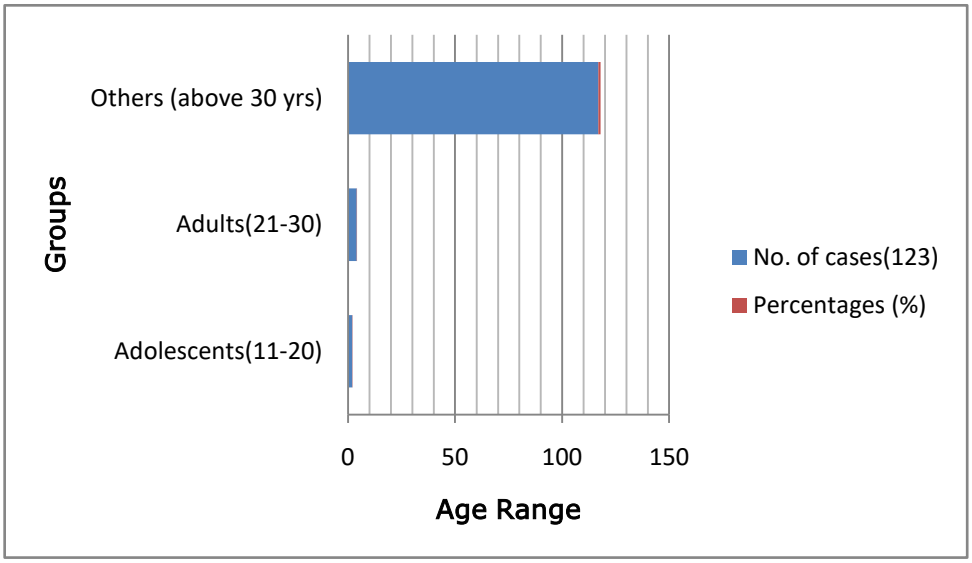
Age distribution of patients on the basis of BMA and BMB

The age of the patient's at time of the diagnosis varied from 20 to 83 years. No age below 20 years was found. Depending on their age differences, they were grouped into three categories. The first group consists of Adolescents within 11-20 years. The second's groups consist of adults within 21-30 years and the third group consists of others above 30 years of age. Majority of the patient's was above the age of 30 years.

Groups	No. of cases(123)	Percentages (%)
Adolescents(11-20)	**2**	**1.62%**
Adults(21-30)	**4**	**3.25%**
Others (above 30 yrs)	**117**	**95.12%**

Table: 5.5- Age distribution of patient's on the basis of BMA and BMB both.

In a total of 123 case 1.62% (2) cases were Adolescents, 3.25% (4) cases were adults and 95.2% (117) cases were above 30 years of age, which show highest incidence of BMA diagnosis in patient's above 30 years of age**. (refer to Table no. 5.5 and Bar chart no. 5.4)**



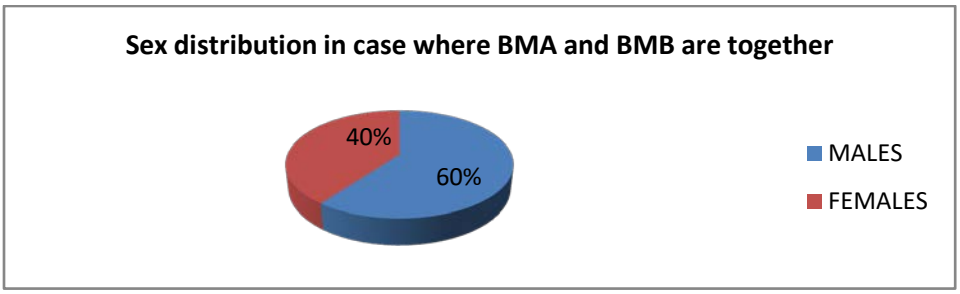
Bar-Chart: 5.4- showing increased frequency of patient's above 30 years.

Sex distribution of patients where BMA and BMB both were performed

Out of 123 cases 60.2 % (74) were male and 39.8 % (49) as females, the incidence of increased frequency of diagnosis were more in males than females**.(refer to Table no. 5.6 and pie-chart no.5.2)**

	MALES	FEMALES
Total No of patients (123)	**74**	**49**
Percentage (%)	**60.2%**	**39.8%**

Table: 5.6- Sex Distribution



Pie-Chart: 5.2- Showing increased percentage of males

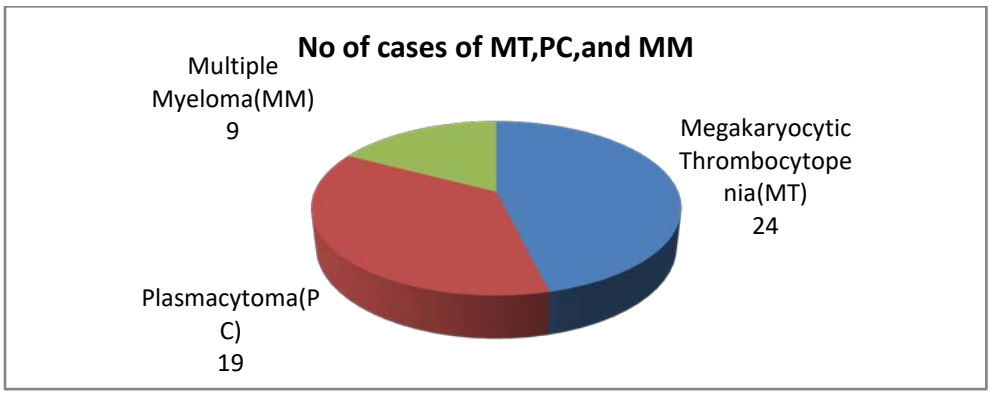
Distribution of various disease on the basis of BMA and BMB

For the convenience of analysis and representation, the disease diagnosed were clubbed in set of three disease and the whole disease distribution is analyzed as under. Out of 123 cases, 19.5% (24) were Megakaryocytic Thrombocytopenia, 15.4% (19) cases of Plasmacytoma and 7.3% (9) case of Multiple Myeloma**, (refer in table no.5.7 and pie-chart no.5.3)**

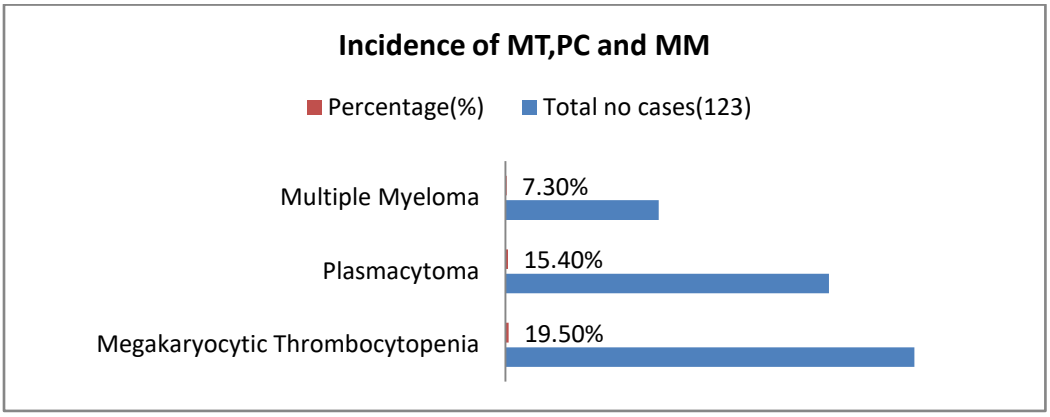
Table: 5.7- showing cases of MT,PC and MM

	Megakaryocytic Thrombocytopenia(MT)	**Plasmacytoma(PC)**	**Multiple Myeloma(MM)**
Total no cases(123)	**24**	**19**	**9**
Percentage (%)	**19.5%**	**15.4%**	**7.3%**

Pie-Chart: 5.3- shows no of cases of MT, PC and MM



The bar chart show that the percentage of MT, PC and MM in out of total 123 cases

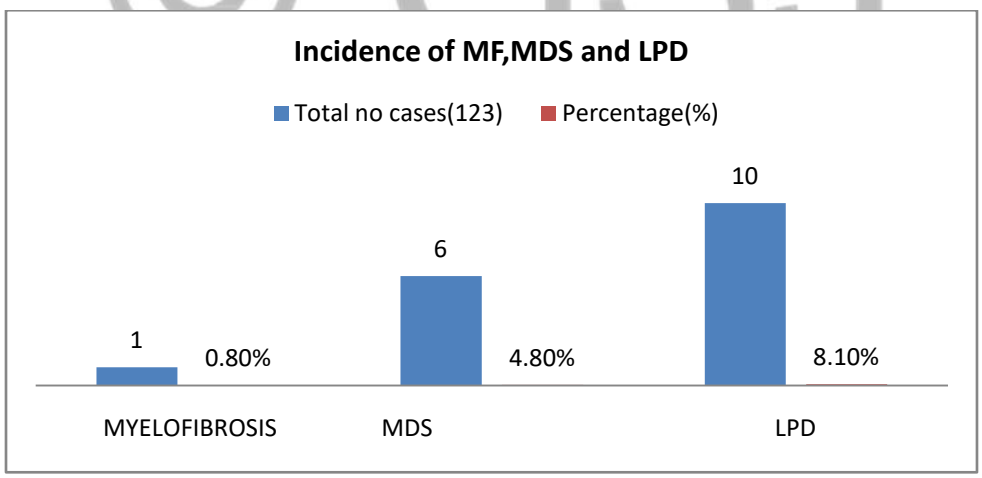


Bar chart: 5.5- shows percentage of MT, PC and MM

Out of 123 cases, 0.8% (1) case of Myelofibrosis(MF), 4.8% (6) cases of Myelodysplastic syndrome and 8.1% (10)cases of Lymphoproliferative disease(LPD**).(refer to table no. 5.8 and bar-chart no. 5.6)**

	MYELOFIBROSIS	MDS	LPD
Total no cases(123)	**1**	**6**	**10**
Percentage(%)	**0.8%**	**4.8%**	**8.1%**

Table: 5.8- showing no cases of MF, MDS and LPD

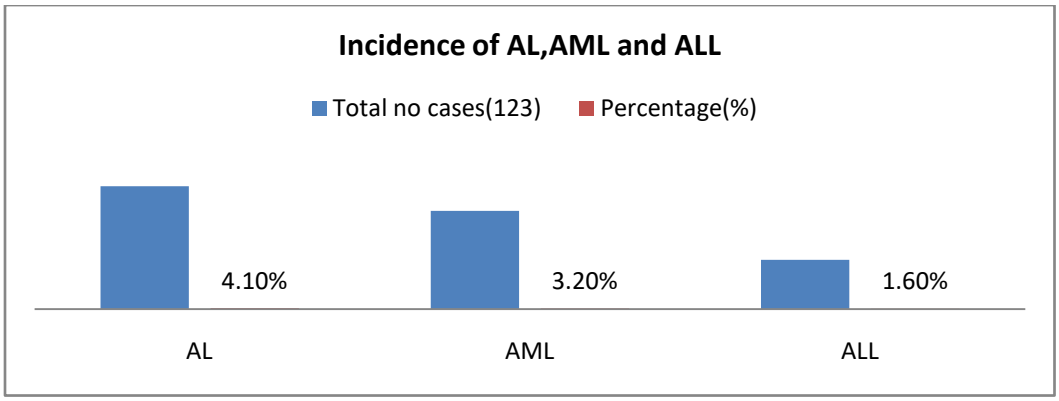


Bar chart: 5.6- shows percentage of MF, MDS and LPD

Out of 123 cases, 4.1% (5) case of Acute Leukemia (AL), 3.2% (4) case of Acute Myeloid Leukemia and 1.6% (2) case of Acute Lymphocytic Leukemia (ALL), which were shown in table

	AL	AML	ALL
Total no cases(123)	**5**	**4**	**2**
Percentage(%)	**4.1%**	**3.2%**	**1.6%**

Table: 5.9- shows the percentage and the cases of AL,AML and ALL

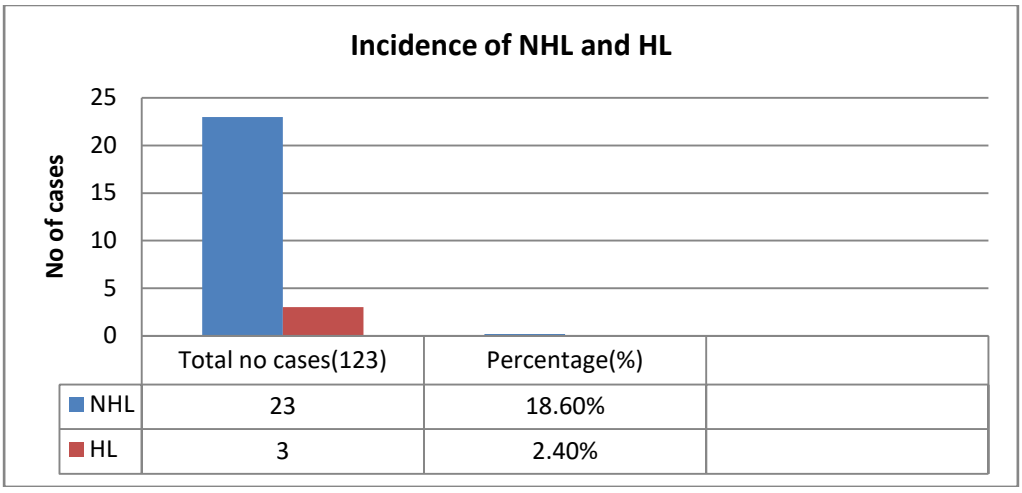


Bar chart: 5.7 showing percentage of AL, AML and ALL in out of total 123 cases

Out of total 123 cases, 18.6% (23) cases of Non-Hodgkin's Lymphoma(NHL) and 2.4% (3) cases of Hodgkin's Lymphoma(HL) were observed, which is refer in table below;

Table: 5.10 showing no. of cases of NHL and HL with their percentage

	NHL	HL
Total no cases(123)	**23**	**3**
Percentage (%)	**18.6%**	**2.4%**

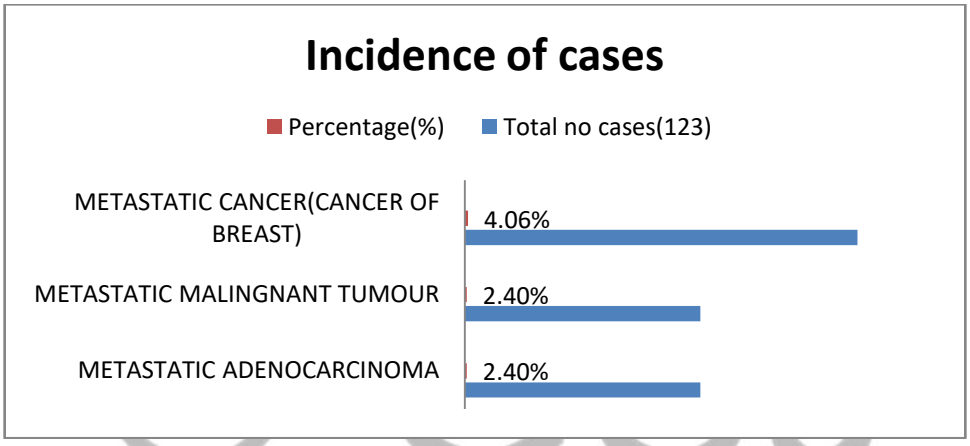


Bar-Chart: 5.8- showing percentage of NHL and HL

Out of total 123 cases, 2.4% (3) cases of Metastatic Adenocarcinoma, 2.4% (3) cases of Metastatic Malignant Tumor and 4.06% (5) cases of Metastatic Cancer of Breast are observed, **(refer in table no. 5.11 and bar-chart no. 5.9)**

Table: 5.11- showing percentage and no of cases of the following disease.

	METASTATIC-ADENOCARCINOMA	**METASTATIC MALINGNANT TUMOUR**	**METASTATIC CANCER OF BREAST**
Total no cases(123)	3	3	5
Percentage (%)	2.4%	2.4%	4.06%



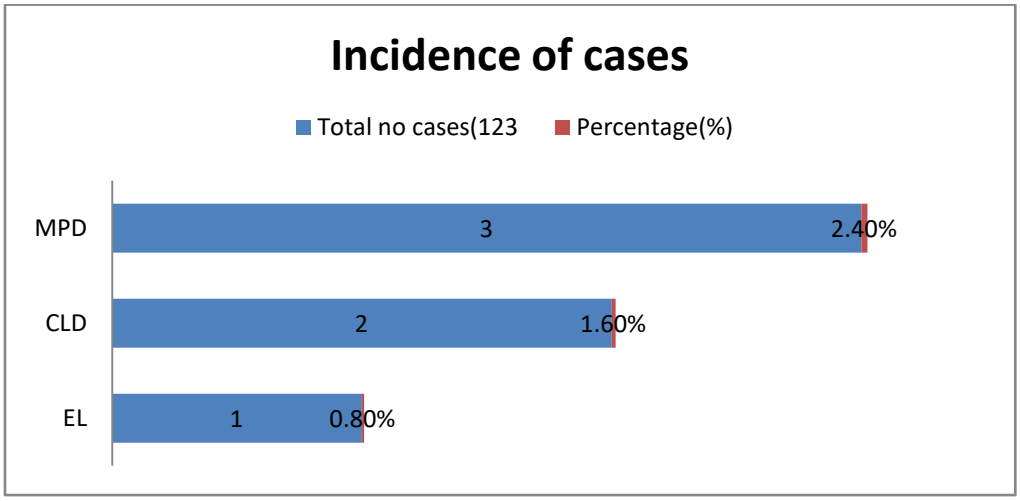
Bar-Chart: 5.9- showing percentage of cases

Out of total 123 cases, were 0.8% (1) case of Erythroleukemia(EL), 1.6% (2) case of Chronic-Lymphoproliferative disease(CLD) and 2.4%(3) cases of Myeloproliferative disease(MPD) observed **(referred in table no. 5.12 and bar-chart no. 5.10)**

Table: 5.12- showing percentage and no. of cases of the disease

	Total no cases(123	**Percentage (%)**
EL	**1**	**0.8%**
CLD	**2**	**1.6%**
MPD	**3**	**2.4%**

There was only one case of erythroleukemia which is finally confirmed by bone marrow biopsy because bone marrow aspiration was not able to give final diagnosis but MPD and CLD both were shows positive correlation in BMA and BMB.



Bar-Chart: 5.10- showing percentage of cases

Out of 123 cases, diagnosis was done on the basis of BMA and BMB together. The data show that the highest cases were of MT i.e. 24 (19.5%) followed by NHL 23(18.6%), plasmacytoma 19 (15.45%) and LPD 10 (8.1%).

Positive correlation in cases of where BMA and BMB both were performed

Out of the 123 cases studied there was a positive correlation in 85 cases (69.10%). Table shows the spectrum of cases with a positive correlation in both BMA and BMB**. (Refer in table no. 5.13)**

Table: 5.13- Positive correlation between bone marrow aspiration and bone marrow biopsy

S.NO	DIAGNOSIS	NO. OF CASES
1	MEGAKARYOCYTIC THROMBOCYTOPENIA	17
2	MYELOFIBROSIS	1
3	LPD	7
4	ALL	2
5	AML	3
6	MDS	4
7	AL	4
8	ERYTHROLUKEMIA	1
9	NHL	10
10	HL	3
11	METASTATIC ADENOCARCINOMA	2
12	METASTATIC MALINGNANT TUMOUR	2
13	METASTATIC CANCER(CANCER OF BREAST)	3
14	CHRONIC LYMPHOPROLIFERATIVE DISORDER	2
15	MYELOPROLIFERATIVE DISORDER	1

16	PLASMACYTOMA	18
17	MM	6

In our study we found that the highest correlation rate with the diagnosis given as plasmacytoma (94.7%) 18/19 and the second highest correlation rate with the diagnosis given as megakaryocytic thrombocytopenia (70.8%) 17/24.

Other cases with a good positive correlation were hematological malignancies such as multiple myeloma where there was (66.6%) correlation. Out of a total of 9 cases diagnosed, 6 cases showed a positive correlation in both BMA and BMB.

There were (70%) 7/10 correlation in lymphoproliferative disorder, (78.9%) 4/5 correlation in acute leukemia, (75.3%) 3/4 cases of AML shows positive correlation and (66.4%) 4/6 cases of Myelodysplastic syndrome shows positive correlation in our study.

In our study we diagnosed all cases (3/3) of Hodgkin's disease by BMB alone. One patient was clinically suspected to have tuberculosis, but BMB showed features of Hodgkin's disease. BMA showed reactive marrow.

Non-Hodgkin's Lymphoma showed a positive correlation in 43.4% cases (10/23),Hodgkin's Lymphoma showed a positive correlation in 75% cases 3/4, Leukemia's showed a positive correlation in 81.8% cases (9/11), those cases diagnosed by BMB alone showed a hypo cellular BMA, One case was clinically suspected to be an Erythrolukemia.

Amongst the non hematological malignancies metastatic to the bone marrow, 63.6% cases (7/11) showed positive correlation in both BMA and BMB, two of the cases were clinically not suspected for non hematologic malignancies. The primary tumor could not be ascertained as the patient died before further investigations could be done. The other case was investigated for anemia. Here the primary malignancy was found in the breast.

Correlations

Descriptive Statistics

Table: 5.14-shows Mean, STD Devi. And total no cases

	Mean	Std. Deviation	Total no. of cases
BMADignosis	2.1707	1.51877	123
BMBDignosis	1.9512	1.53031	123

Out of 123 cases 0f BMA and BMB the mean of the BMA was 2.1707 and the mean of BMB was 1.9512, the std.deviation of BMA and BMB were 1.51877 and 1.53031 respectively.

There were (69.10%) 85/123 positive correlation shown in out of total 123 cases in our studies which shows Pearson correlation i.e. significant at the level of 0.01level (2-tailed), **refer in table no. 5.15**

Correlations

Table: 5.15- shows the spectrum of positive correlation in BMA and BMB

		BMADignosis	BMBDignosis
BMADignosis	Pearson Correlation	1	.875(**)
		.	.000
	Sig. (2-tailed)		
	No. of cases	85	85
BMBDignosis	Pearson Correlation	.875(**)	1
	Sig. (2-tailed)	.000	.
		85	85
	No. of cases		

** Correlation is significant at the 0.01 level (2-tailed).

The Data was analyzed using SPSS statistical computer programme. The Pearson correlation were applied to show the spectrum of positive correlation between BMA and BMB and used to find the significance between BMA and BMB which were most significant at the level of 0.01(2-tailed).

Out of 123 cases studied by both BMA and BMB together in 30.89% (38/123) cases where definite opinion could not be given either in BMA or in BMB and positive correlation could not be established.The reports were varying from an inadequate BMA, where the BMB is hyper cellular or reactive, in some cases BMA appeared to be normal, but with no marrow spaces in the BMB.

In those cases where a diagnosis of BMA were given, depending on whether macronormoblastic or micronormoblastic, they were further worked up, mostly for anemia, and accordingly Perls stains for iron was studied, biochemical parameters were taken into consideration and the impression was given.

SUMMARY AND CONCLUSION

Bone-marrow examination is essential in the investigation of many hematological disorders. It may provide a diagnosis suspected from the clinical features and peripheral blood examination or occasionally gives a previously unsuspected diagnosis. It is also useful in certain diseases for assessing the extent or response to treatment. Bone-marrow fragments may be aspirated and spread on slides, as for a blood film, or a core of bone and marrow may be obtained intact and histological sectioned (trephine biopsy). In

general, aspiration is used to show the morphology of individual haemopoietic cells and to obtain material for ancillary tests, whereas a trephine gives a more representative view of the cellularity of the marrow and allows infiltrations to be recognized. The investigations are limited by the small size of the samples and consequent sampling errors. Infiltrations may be missed, and the cellularity may vary from site to site. Nevertheless, the tests provide a considerable amount of information and should always be considered before a large battery of investigations is requested, particularly if these investigations are time consuming and costly and may prove to have been irrelevant once the marrow appearances are known.**S Knowles, et, al, 2003**

The present retrospective study entitled "Comparative retrospective study of bone marrow aspiration and bone marrow trephine biopsy" was carried out at Department of Lab Medicine, Fortis Escort Heart Institute Okhla Delhi, From October 2011 to April 2012.A total 220 cases out of them 97 cases of Bone Marrow Aspirate (BMA) and 123 cases are of Bone Marrow Aspirate and Bone Marrow Biopsies (BMB) done simultaneously were included in the study.

Out of total 220 cases of bone marrow examination, 97(44.09%) cases of BMA done alone and123 (55.9%) cases of BMA and BMB done together. The results of the comparative evaluation were divided into:

- Number of cases where diagnosis was given on BMA alone, BMB was non contributory
- Number of cases that showed positive correlation between BMA and BMB
- Number of cases where a definite opinion could not be given either in BMA or in BMB.
- In present study there was not any case of BMB alone because at the centre of study BMA was preceded or carried out simultaneously BMB.

- Out of 97 cases of bone marrow aspiration, 66(68.04%) were males and 31(31.95%) as females

- The age of the patient's at time of the diagnosis varied from 20 to 83 years. No age below 20 years was found. Depending on their age differences, they are grouped into three categories. The first group consists of Adolescents within 11-20 years. The second's groups consist of adults within 21-30 years and the third group consists of others above 30 years of age. Majority of the patient's was above the age of 30 years

- In a total of 97 case 2.1% (2) cases were Adolescents, 7.2% (7) cases were adults and 90.7% (88) cases were above 30 years of age, which show highest incidence in of BMA diagnosis in patient's above 30 years of age

- Out of 97 cases of BMA, were 44(46%) case of megaloblastosis,7(7%) cases show Normoblastic reaction 8% cases of Micronormoblastic reaction, 22% cases shows Dimorphic anemia,2% cases of Sickle –cell anemia, 3% cases of Eosinophilia 2%cases of Erythroid Hyperplasia and 9.1% cases shows normal morphology.

- Out of 123 cases, where BMA and BMB both were done together in that case 60.2 % (74) were male and 39.8 % (49) as females, the incidence of increased frequency of diagnosis were more in males than females

- In a total of 123 case 1.62% (2) cases were Adolescents, 3.25% (4) cases were adults and 95.2% (117) cases were above 30 years of age, which show highest incidence in of BMA diagnosis in patient's above 30 years of age**.**

- Out of 123 cases, 19.5% (24) were Megakaryocytic Thrombocytopenia, 15.4% (19) cases of Plasmacytoma and 7.3% (9) case of Multiple Myeloma**,**

- Out of 123 cases, 0.8% (1) case of Myelofibrosis(MF), 4.8% (6) cases of Myelodysplastic syndrome and 8.1% (10)cases of Lymphoproliferative disease(LPD**).**

- Out of 123 cases, 4.1% (5) case of Acute Leukemia (AL), 3.2% (4) case of Acute Myeloid Leukemia and 1.6% (2) case of Acute Lymphocytic Leukemia (ALL)

- Out of total 123 cases, 18.6% (23) cases of Non-Hodgkin's Lymphoma(NHL) and 2.4% (3) cases of Hodgkin's Lymphoma(HL) were observed

- Out of total 123 cases, 2.4% (3) cases of Metastatic Adenocarcinoma, 2.4% (3) cases of Metastatic Malignant Tumor and 4.06% (5) cases of Metastatic Cancer of Breast were observed

- Out of total 123 cases, were 0.8% (1) case of Erythroleukemia(EL), 1.6% (2) case of Chronic-Lymphoproliferative disease(CLD) and 2.4%(3) cases of Myeloproliferative disease(MPD) observed,

- Out of the 123 cases studied there was a positive correlation in 85 cases (69.10%).

- In present study we found the highest correlation rate with the diagnosis given as plasmacytoma (94.7%) 18/19.Other cases with a good positive correlation were hematological malignancies such as multiple myeloma where there was (66.6%) correlation. Out of a total of 9 cases diagnosed, 6 cases showed a positive correlation in both BMA and BMB.

- Non-Hodgkin's Lymphoma showed a positive correlation in 43.4% cases (10/23), Hodgkin's Lymphoma showed a positive correlation in 75% cases 3/4, Leukemia's showed a positive correlation in 81.8% cases (9/11), those cases diagnosed by BMB alone showed a hypo cellular BMA, One case was clinically suspected to be an Erythrolukemia.Megakaryocytic thrombocythemia showed 70.8% correlation (17/24).

- Amongst the non hematological malignancies metastatic to the bone marrow, 63.6% cases (7/11) showed positive correlation in both BMA and BMB, two of the cases were clinically not suspected for non hematologic malignancies. The primary tumor could not be ascertained as the patient died before further investigations could be done. The other case was investigated for anemia.

- In those cases where a diagnosis of BMA were given, depending on whether macronormoblastic or micronormoblastic, they were further worked up, mostly for anemia, and accordingly Perls stains for iron was studied, biochemical parameters were taken into consideration and the diagnosis was confirmed impression was given.

- The cases where a definite opinion could not be given either in BMA or in BMB comprised 30.89% (38/123).The reports were varying from an inadequate BMA, where the BMB is hyper

cellular or reactive, in some cases BMA appeared to be normal, but with no marrow spaces in the BMB.

On clinical analysis of data the following conditions emerged

Bone marrow aspiration and trephine biopsy each have advantages and limitations. The two procedures should therefore be considered as complementary.

- Aspiration is particularly useful, and may well be performed alone, when investigating patients with suspected iron deficiency anemia, anemia of chronic disease, megaloblastic anemia and acute leukemia.

- Trephine biopsy is particularly useful in investigating suspected aplastic or hypo plastic anemia, lymphoma, metastatic carcinoma, myeloproliferative disorders and diseases of the bones.

- The trephine biopsy is generally much more useful than bone marrow aspiration when investigating patients with the advanced stages of Hodgkin's disease in whom hypo cellular, non-diagnostic aspirates are common. It should not be forgotten, however, that trephine biopsy undoubtedly causes more pain to the patient than does aspiration.

- Complications of bone marrow aspiration and trephine biopsy are very rare. Cardiac and great vessel laceration has been common. Otherwise, hemorrhage is uncommon but, when procedures are carried out on patients with a haemostatic defect, prolonged firm pressure is necessary afterwards to ensure that bleeding has stopped.

- Hemorrhage is also occasionally a problem when a biopsy is carried out on bone with an abnormal vasculature, for example in Paget's disease. Severe retroperitoneal hemorrhage has also been observed in patients with osteoporosis and in several patients with normal bones but with hematological disorders.

- Bone marrow aspiration has a minimal role, if any, in detecting involvement of bone marrow by Hodgkin lymphoma. Although bilateral BMAs and BMTBs may increase the chances of detecting solid tumor metastasis and Hodgkin lymphoma in bone marrow. Therefore, abandoning aspirates in these instances might result in missing bone marrow metastasis in only a very small percentage of cases.

The study concludes that all the preparations of aspirate cytology, and trephine biopsy complement each other for evaluating any bone marrow. The assessment of iron status by Perl's stain is although not adequate on biopsy sections in comparison to aspirate smears but trephine biopsy remains the gold standard for diagnosing non hematologic malignancies. Vigilant examination of aspirate smears and meticulously prepared imprint cytology smears are almost equally efficient and more rapid method for diagnosis metastatic solid tumors in comparison to trephine biopsy. Appropriately prepared imprint cytological smears do not only adequately provide cellular composition of marrow but may also define the topographical architecture of marrow. Cytological smears should therefore be standard practice for evaluating any marrow**.**

BMA & BMB are diagnostic procedure used routinely now a days. Both the procedures are complementary to each other. In our experience we felt that for diagnostic purpose both the procedures can be done simultaneously as BMA gives better morphology of the cells and BMB gives a good picture regarding the pattern of distribution of cells. We found that BMB was especially useful in diagnosis of Hodgkin's disease and metastasis of non hematological malignancies. We also found these procedures quite useful in cases where malignancies were not suspected; BMA and BMB are very useful and still an important diagnostic tool. While performing the BMA and BMB simultaneously, employment of proper

technique should be kept in mind so as to yield the maximum material and reduce discomfort to the patient by not repeating the procedure due to inadequate material**.**

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