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Original Research Article

Evaluation of Bone Marrow Study in Pancytopenia Cases – A Prospective Study for 2 Years at Tertiary Health Centre

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Abstract:

Introduction: Pancytopenia is an important clinico - haematological phenomenon. It is a triad of findings characterised by haemoglobin < 9g/dl, total leucocyte count < 4×10^9/l and platelet count <140×10^9/l. It is a symptom of a primary haematological disease or underlying medical condition. The etiology of pancytopenia varies from decrease in hematopoietic cell production, trapping of normal cells in the hypertrophied and over reactive reticuloendothelial system, ineffective hematopoiesis or replacement of normal bone marrow elements by abnormal or malignant cells. Most common presentation of pancytopenia is anaemia or thrombocytopenia. Most common indication for bone marrow examination is pancytopenia.

Aim and Objectives: To know the preponderance of haematological parameters, the efficacy of bone marrow examination in evaluating various causes of pancytopenia and to do special stains in required cases.

Materials and Methods: The present study is a hospital-based prospective study conducted at Department of Pathology, Government Medical College, Srikakulam, for a period of 2 years from October 2020 to September 2022.

Results: A total of 41 patients were diagnosed as pancytopenia on peripheral smear examination during the study period. To know the exact cause of pancytopenia all the cases underwent bone marrow aspiration and few cases that were inconclusive, further went through bone marrow biopsy and the cause was concluded.

Conclusion: The present study concluded that megaloblastic anaemia is the most common cause of pancytopenia at a young age with a male predilection. Healthy sanitation and hygiene practise, balanced diets, and education about all these could help to reduce pancytopenia's preventable cause.

Keywords: Pancytopenia, Bone Marrow Examination, Perls Stain.

Introduction

A common haematological abnormality called cytopenia arises from the cessation or reduction of one of the major blood-formed elements such as red blood cells, white blood cells, or platelets.[1] Pancytopenia is an important clinical- haematological phenomenon manifested in clinical practice.

Pancytopenia is a triad of findings characterised by haemoglobin less than 9g/dl, total leucocyte counts less than 4×109/l and platelet count less than 140×109/l.32 It is not a diagnosis in and of itself, but rather a symptom of a primary haematological disease or underlying medical condition.[2] Many illnesses that affect the bone marrow either directly or indirectly result in pancytopenia [3]. The causes of pancytopenia range greatly, from a benign course of temporary bone marrow suppression to a more serious and life-threatening illness caused by neoplastic cell infiltration of the marrow. Pancytopenia can be treated and reversed because nutritional inadequacies are the primary cause of the majority of cases.[4] The presenting symptoms of pancytopenia are usually ascribable to anaemia or thrombocytopenia.[4] The Clinical features in patients having pancytopenia are pallor, fatigue, fever, infection, bleeding, weight loss, and organomegaly. The clinical picture and blood analysis clearly show the type of underlying disease. The primary diagnostic challenge arises when there are no specific blood characteristics to support the diagnosis or when the clinical signs are insufficiently specific to identify the underlying aetiology of an associated feature like splenomegaly or lymphadenopathy.

The cornerstone of first-line investigation in pancytopenia patients is a thorough medical history, diligent clinical examination, and careful analysis of complete blood count (CBC) and peripheral blood smear (PBS)[5]. Correlation with bone marrow biopsy is also important in cases where aspirate is hemodiluted or in hypocellular marrows [6] Additional investigations, such as Immunophenotyping, cytogenetics, or molecular tests, are re-

quired when these data are insufficient to make the diagnosis.

As opposed to bone marrow aplasia, the presence of a high serum lysozyme concentration is a sign of an underlying myeloid neoplastic infiltrative process [7]. One of the common indications for bone marrow examination is pancytopenia. Marrow aspiration is evaluated for cytology whereas trephine biopsy provides information on overall cellularity, detection of focal lesion and infiltration [4]. As the underlying pathology dictates the care and prognosis of the patients, bone marrow aspiration is incredibly beneficial to know the cause of pancytopenia by cellularity and cytology to avert serious complications and mortality.

In cases of pancytopenia caused by a primary production defect, the marrow is mostly hypocellular. A normocellular or hypercellular marrow is usually related to the cytopenia caused by inefficient haematopoiesis, increased peripheral cell use or destruction, and invasive processes in bone marrow. Pancytopenia is difficult to diagnose and necessitates the collaboration of both the pathologist and the clinician. Additionally, it makes remarks on the disease's stage, progression, therapy, and prognosis. When utilized in unison for the examination of bone marrow in common haematological diseases, Bone marrow aspiration (BMA) and bone marrow biopsy (BMB) complement one another [8]. Severity of pancytopenia and the treatment provided for the underlying condition determines the health outcome of each patient.[4]

Materials and Methods:

Study Design:

The present study is a hospital-based prospective study conducted in the Department of Pathology, Government Medical College, Srikakulam, for 2 years from October 2020 to September 2022.

Study Subjects:

Peripheral smears of patients from all clinical departments were received in the Department of Pathology and the cases that were reported as pancytopenia and motivated for bone marrow examination after a complete history and examination of the patient about complaints like pallor, fatigue, fever, infection, bleeding, weight loss, organomegaly and lymphadenopathy were taken.

Inclusion Criteria:

In adults and children:

- With clinical complaints of generalised weakness, pallor, bleeding tendencies, fever, bone tenderness, shortness of breath, splenomegaly, hepatomegaly, lymphadenopathy, skin rash
- Hb ≤ 9gm/dl, TLC <4,000 cells/cu.mm, Platelet count <1,00,000 cells/cu.mm.

Exclusion Criteria:

- Follow up cases of leukemia.
- Pregnant women.
- Patients who had not given consent for bone marrow examination.
- Already diagnosed cases of pancytopenia who are taking treatment.

Results:

Table 1: Details of age wise distribution of Pancytopenia cases

S.No	Age	Number	Percentage
1	6 months – 10years	04	9.8
2	11yrs – 20yrs	06	14.6
3	21yrs – 30yrs	08	19.5
4	31yrs – 40yrs	09	22
5	41yrs – 50yrs	08	19.5
6	51yrs – 60yrs	03	7.3
7	61yrs –70yrs	03	7.3
	Total	41	100

As per current study, highest number of pancytopenia cases was noted within age range of 31-40 years (22%). (Table no.1)

Table 2: Sex distribution of Pancytopenia Cases

S. No	Sex	Number	Percentage
1	Male	27	65.9
2	Female	14	34.1
	Total	41	100

In current study of 41 cases, majority were males (65.9%). (Table 2)

Table 3: Clinical features in present study

S.No	Signs And Symptoms	Number	%
1	Generalised weakness	34	82.9
2	Pallor	30	73.1
3	Fever	14	34.1
4	Shortness of breath	12	29.2

5	Bleeding manifestations	04	9.7
6	Bone tenderness	03	7.3
7	Lymphadenopathy	02	4.8
8	Skin rash	01	2.4
9	Jaundice	01	2.4
10	Splenomegaly	01	2.4
11	Hepatomegaly	01	2.4

In current study, the most common clinical presentation was generalised weakness (82.9%) followed by pallor (73.1%) and the least common clinical presentations include Skin rash, Jaundice, Splenomegaly and Hepatomegaly (2.4%). (Table no. 3)

Table 4: Haemoglobin levels in present study

S.No	Hb levels	Number	%
1	≤3g%	04	9.7
2	4-6g%	17	41.5
3	7-9g%	20	48.8
	Total	41	100

In 41 pancytopenia cases, highest number of cases was seen with Hb range of 7- 9g% (48.8%). (Table no.4)

Table 5: Range of Total leucocyte count in present study

S.no	TLC (cells/cu.mm)	Number	%
1	≤1000	0	0
2	1001-2000	03	7.4
3	2001-3000	19	46.3
4	3001-4000	19	46.3
	Total	41	100

In current study of 41 cases, majority of cases were noticed with TLC within range of 2001-4000 cells/cu.mm (92.6%). (Table no. 5)

Table 6: Platelet count in present study

S.No	Platelet count (cells/cu.mm)	Number	%
1	≤50,000	6	15
2	50,001-1,00,000	32	78
3	1,00,001-1,50,000	3	7
	Total	41	100

The majority of cases were observed to be with platelet count range of 50001- 1,00,000 cells/cu.mm (78%) in this study of 41 cases. (Table no.6)

Table 7: Bone marrow aspiration diagnosis of present study

S.No	Diagnosis	Number	%
1	Hypoplastic marrow	09	22
2	Erythroid hyperplasia	06	15
3	Immune thrombocytopenic Purpura	04	9.7
4	Megaloblastic anaemia	15	36.5
5	Acute lymphoblastic leukemia	02	4.8
6	Micronormoblastic marrow with focal megaloblastic change (Mixed Nutritional anaemia)	01	2.4
7	Normoblastic erythropoiesis with marked suppression of megakaryocytes	01	2.4
8	Dry tap	02	4.8
9	Others	01	2.4
	Total	41	100

In present study, most common cause of pancytopenia was found to be megaloblastic anaemia (36.5%) (Fig 1 and 2) on bone marrow aspiration, followed by hypoplastic marrow, erythroid hyperplasia (15%) (Fig. 3), immune thrombocytopenic purpura (9.7%) (Fig 4) and acute lymphoblastic leukemia (4.8%) (Fig 5). Least common cause mixed nutritional anaemia, normoblastic erythropoiesis with marked suppression of megakaryocytes and others (2.4%). (Table no.7)

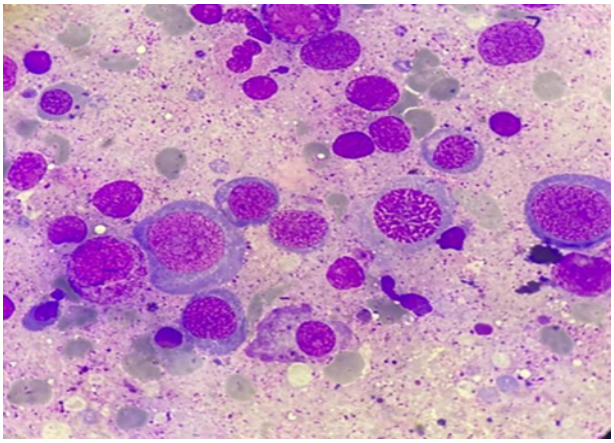

Figure 1: BMA smear of megaloblastic anemia showing megaloblastic erythroid maturation in 100x view with Leishman stain (BMA No. 26/22)

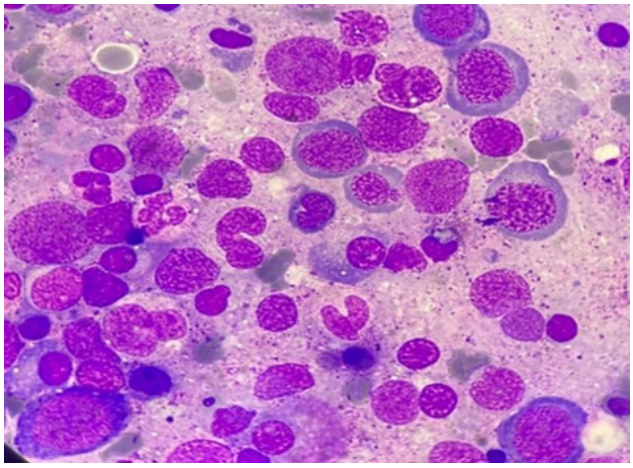

Figure 2: BMA smear of megaloblastic anemia showing megaloblasts with open sieve-like chromatin in 100x view with Leishman stain (BMA No.45/22)

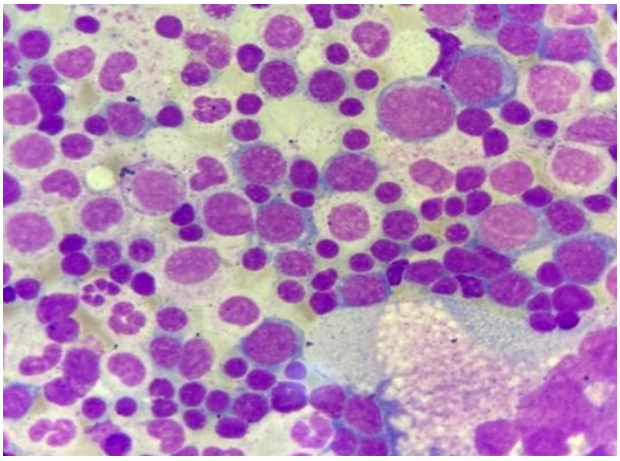

Figure 3: BMA smear of erythroid hyperplasia case showing early, intermediate and late normoblasts with alteration of M:E ratio in 40X view with Leishman stain (BMA No. 28/22)

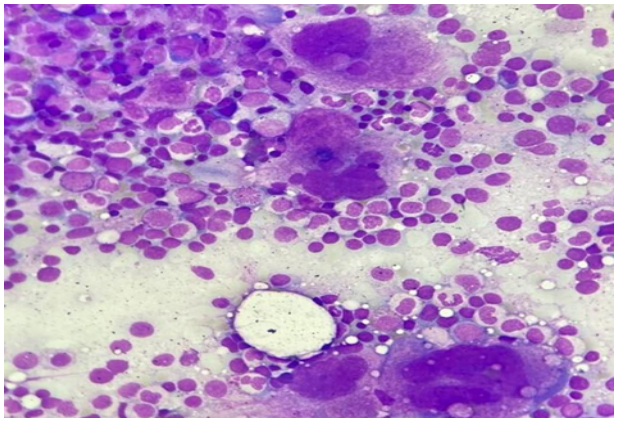

Figure 4: BMA smear of Idiopathic thrombocytopenic purpura showing megakaryocyte hyperplasia in 10X view with Leishman stain (BMA No. 18/21)

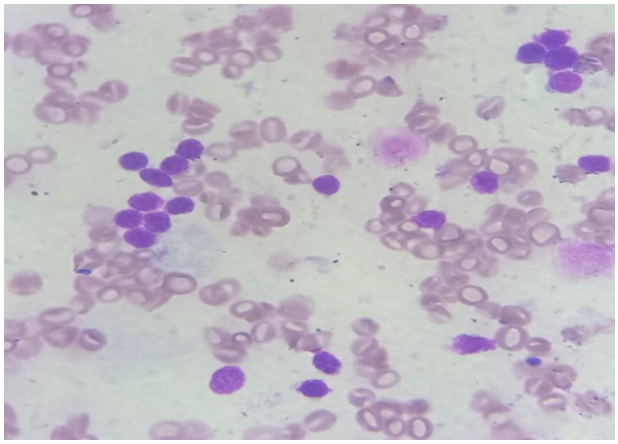

Figure 5: BMA smear of acute lymphoblastic leukemia showing large cells slightly larger than mature lymphocytes, scant agranular cytoplasm, round homogenous nucleus with mild indentation in 40X view with Leishman stain (BMA No. 1/21)

Table 8: Grading of Perl's stain in present study

S. No	Perl's Stain Grade	No. of Cases	Percentage
1	Iron Deficiency	1	2.5
2	Normal Iron stores	40	97.5
3	Increased iron stores	0	0

In Current study of 41 pancytopenia cases, Perls stain on bone marrow aspiration smears (figure 6) depicted normal iron stores in 97.5% and iron deficiency in 2.5%. (Table no.8)

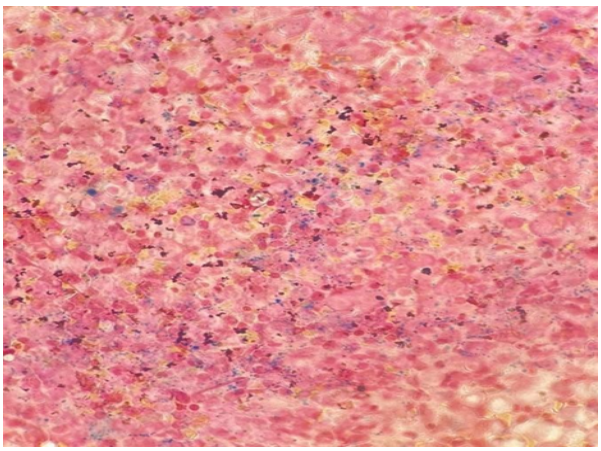

Figure 6: Smear showing few small granules visible in 10X view (grade 2) Normal iron stores with perls stain (BMA No. 46/22)

Discussion

In individuals with pancytopenia, a bone marrow diagnosis is crucial inquiry that needs to be carefully examined to make an accurate diagnosis.

BME can support clinicians in their approach to diagnosis and patient management even in the lack of a definitive diagnosis. [6]

Total of 41 patients (n=41) were studied and their age, gender-wise incidence, clinical complaints, peripheral smear picture, haematological parameters, the bone marrow aspiration smears and various aetiologies of pancytopenia were analysed and the observations made were compared with other studies printed in the articles.

Haemoglobin Range in the Present Study:

Out of 41 cases of this study, the Hb range was between 2.6gm/dl-9gm/dl. The mean Hb value of the current study was 6.18gm/dl. The lowest value of Hb reported was 2.6gm/dl in a female patient of age 65years who was diagnosed with megaloblastic anaemia on bone marrow aspiration. The highest value of Hb reported was 9gm/dl in four female patients of age 20 years and 40years respectively who were diagnosed with erythroid hyperplasia on the bone marrow aspiration, a 2year child diagnosed with a dry tap on bone marrow aspiration and aplastic anaemia on bone marrow biopsy and 24year patient diagnosed as idiopathic thrombocytopenic purpura.

Table 9: Similarities of Haemoglobin Range of Current Study with Other Studies:

Comparative studies	Hb range
Pooja Agarwal et.al (7)	4-7g/dl (58.75%)
Dr. Anzar Ahmad Khan et.al (10)	4-7g/dl (58.75%)
GOVINDARAJ T et.al (11)	5.1-7g% (50%)
Anita P. Javalgi et.al (12)	5.1-8g%
Neeru Singhal et.al (5)	6-7.9gm/dl (46.67%)
Sudha Horakereppa Metikurkea et.al (13)	7.1-10g/dl (48%)
Present study	7-9g/dl (48.7%)

The highest percentage of haemoglobin range in study was between 7-9g/dl accounting for 48.8% which was similar to a study done by Sudha Horakereppa Metikurkea et.al (13) where the Hb value was between 7.1-10g/dl accounting for 48%. (Table no.9)

Table 10: Comparisons of the Total Leucocyte Count Range of This Study with Other Studies:

Comparative studies	Total leucocyte count range
Dr. Anzar Ahmad Khan et.al (10)	1000-2499 cells/mm3 (42%)
Pooja Agarwal et.al (7)	1000-2499 cells/mm3 (42%)
Neeru Singhal et.al (5)	1000-2999 cells/mm3 (70%)
Priti Singh et.al (3)	1100-3000 cells/mm3 (82%)
Sudha Horakereppa Metikurke et.al (13)	2500-4000 cells/mm3 (55%)
Anita P. Javalgi et.al (12)	2501-3900 cells/mm3 (73.58%)
Present study	2001-3000 cells/mm3 (51.2%)

In the present study, there was the highest incidence of 38 cases with a total leucocyte count range of 2001-4000 cells/cu.mm accounting for 92.6%. The present study is showing a high incidence of cases when compared to a study conducted by Anita P. Javalgi et.al (12) where the total leucocyte count range was between 2501- 3900 cells/cu.mm accounting for 73.58% and a study by Sudha Horakereppa Metikurke et.al (13) was showing a total leucocyte range of 2500-4000 cells/cu.mm accounting for 55%. (Table no.10)

Table 11: Comparison of Platelet Count Range in Current Study with Other Studies:

Comparative studies	Incidence
Pooja Agarwal et.al (7)	<50,000 cells/mm3 (57%)
Dr. Anzar Ahmad Khan et.al (10)	50,000-99,999 cells/mm3 (28%)
Sudha Horakereppa Metikurke et.al (13)	50,000-1,00,000 cells/mm3 (78%)
Neeru Singhal et.al (5)	50,000-1,00,000 cells/mm3 (80%)
Priti Singh et.al (3)	76,000-1,00,000 cells/mm3 (41%)
Anita P. Javalgi et.al (12)	1,00,001-1,50,000 cells/mm3 (41.5%)
Present study	50,001-1,00,000 cells/mm3 (78%)

In this study of 41 cases, there was the highest incidence of 32 cases within the range of 50,000-1,00,000 accounting for 78%. This is similar to studies conducted by Sudha Horakereppa Metikurke et.al (13) where platelet range between 50,000- 1,00,000 cells/cu.mm was highest accounting for 78% and Neeru Singhal et.al (5) where platelet range between 50,000-1,00,000 cells/cu.mm was highest accounting for 80%. (Table no.11)

Megaloblastic Anaemia: (15 Cases)

In this study, patients diagnosed as megaloblastic anaemia the age range was from 18-70 years. Mean age was 42.5 years. The majority of patients were in age group of 26-30 years (27%). There was male preponderance and the male-to-female ratio was 4:1. The presenting complaints were generalised weakness and pallor, accounting for 100% and shortness of breath accounting for 46.6% (7/15). Hb range was from 2.6-7gm/dl. The mean Hb value was 5.18g/dl. Total leucocyte count range was from 2,200-3,800 cells/cu.mm. Mean total leucocyte count was 3100 cells/cu.mm. The platelet count range was between 54,000-1,30,000 cells/cu.mm. (Table no.12)

The mean platelet count was 89,933 cells/cu.mm. The bone marrow was hypercellular in 15 cases accounting for 100% of cases.

Table 12: Comparisons of Haematological Parameters of Megaloblastic Anaemia of Current Study with Other Studies:

Haematological parameters	Priti Singh et. al. (3)	Gayathri B N et. al. (14)	Dr Anzar Ahmad Khan et. al. (10)	Jha A et. al. (15)	Kumar et. al. (16)	Present study
Hb range(g/dl)	1-10	1.8-9.2	1.4-8.7	2.3-9.8	2.4-7	2.6-7
TLC(Cells/cu,mm)	500-4000	500-3,900	500-7,600	1200-3900	700-3600	2,200-3,800
Platelet Count(cells/cu.mm)	5000-1,50,000	12,000-95,000	10,000-1,40,000	2000-1,37,000	10,000-1,30,000	54,000-1,30,000

Erythroid Hyperplasia

The age range of the patients with erythroid hyperplasia in this study was 20-50 years. The mean age was 36.1 years. The majority of patients were in age group of 36-40 years of age accounting for 33.3%. There was male preponderance with sex ratio of 2:1. The presenting complaints were generalised weakness (80%), pallor (50%), fever (50%) and shortness of breath (33.3%). The Hb range was 3-9 gm/dl. The mean Hb was 7.08 gm/dl. Total leucocyte count range was 1,900-3,400 cells/cu.mm. Mean total leucocyte count was 2,816 cells/cu.mm. The platelet count range was 50,000-1,00,000 cells/cu.mm (Table no.13).

The mean platelet count was 74,166 cells/cu.mm. The cellularity of bone marrow was hypercellular in 4 cases accounting for 66.7% and normocellular in 2 cases accounting for 33.3%.

Table 13: Comparisons of Haematological Parameters of Erythroid Hyperplasia in the Present Study with Other Studies:

Haematological Parameters	Jha A et. al. (15)	Dr Anzar Ahmad Khan et. al. (10)	Present study
Hb range (gm/dl)	2.2-9.8	2.1-10.8	3-9
TLC (cells/cu.mm)	1000-3700	1000-12,300	1,900-3,400
Platelet count (cells/cu.mm)	2000-1,39,000	20,000-1,60,000	50,000-1,00,000

Idiopathic Thrombocytopenic Purpura (ITP): (4 Cases)

The age range of patients with ITP in current study was 6 to 34 years. Mean age was 22.5 years. The 4 patients were of age 6 years, 24 years, 26years and 34years respectively. There was female preponderance with male to female ratio of 1:3. The presenting complaints were fever (75%), generalised weakness (50%), pallor (25%), and bleeding manifestations (25%).

The Hb range was 6.9-9gm/dl. The mean Hb was 7.9gm/dl. Total leucocyte count range was 2,800-3,800 cells/cu.mm. Mean total leucocyte count was 3,100 cells/cu.mm. The platelet count range was 26,000-60,000 cells/cu.mm. The mean platelet count was 49,750 cells/cu.mm. The cellularity of marrow was normocellular in 3 cases accounting for 75% and hypercellular in 1 case accounting for 25%.

Acute Lymphoblastic Leukemia (ALL): (2 Cases)

The age range of patients with ALL in present study was 7-13 years. Mean age was 10 years. The two patients were of age 7 years, and 13 years respectively. There was male preponderance. The presenting complaints were fever, bone tenderness, lymphadenopathy accounting for 100%, pallor, and generalised weakness accounting for 50%. The Hb range was 7-8gm/dl. The mean Hb was 7.5gm/dl. Total leucocyte count range was 2,800-3.400 cells/cu.mm. Mean total leucocyte count was 3,100cells/cu.mm. The platelet count range was 40,000-80,000 cells/cu.mm. The mean platelet count was 60,000 cells/cu.mm. The cellularity of marrow was hypercellular in 2 cases accounting for 100%.

Conclusion

Pancytopenia is the prominent characteristic of

various serious and life- threatening diseases and may be caused by a variety of conditions, from simple megaloblastic anaemia and the drug-induced bone marrow hypoplasia to a deadly aplastic anaemia and leukemia.

To assess cytopenia, bone marrow aspiration and the biopsy are crucial adjuncts to peripheral smear examination. A simple, risk-free, and minimally invasive outpatient procedure for evaluating pancytopenia cases is bone marrow aspiration. Correlation with a bone marrow biopsy is crucial when the aspirate is haemodiluted or when the marrow is hypocellular.

A comprehensive physical examination, a thorough clinical history, and baseline haematological tests all contribute significantly to the evaluation of pancytopenia patients. This information is crucial for the systematic planning of subsequent investigations to identify the cause and make an appropriate diagnosis. Since many causes of pancytopenia are curable and reversible, prompt diagnosis and treatment could save a patient's life and have a significant impact on their morbidity and mortality. Therefore, knowing the precise aetiology is crucial for prognostication and particular, prompt treatment.

The present study concluded that megaloblastic anaemia is the most common cause of pancytopenia at a young age with a male predilection. Healthy sanitation and hygiene practise, balanced diets, and education about all these could help to reduce pancytopenia's preventable cause.

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