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Clinico Etiological Profile of Pancytopenia with Special Reference to Vitamin B12 and Folic Acid Level

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ABSTRACT

Introduction: Pancytopenia is characterised by reduced in all three hematologic cell lines erythrocytes, lymphocytes and platelets that leads to anemia, leucopenia, and thrombocytopenia. It is not a disease entity by itself but the condition shared a common pathway caused by a wide range of distinct etiologies, including nutritional, autoimmune, infections, neoplastic, and/or hereditary. When a main production defect causes pancytopenia, the bone marrow typically exhibits hypocellularity. Increased utilisation of peripheral cell or destruction are associated with a hypercellular or normocellular marrow. To determine the cause of pancytopenia is a challenge and is important in determining the proper treatment regimen and estimating prognosis. **Aims**: To study the etiology and clinical profile of pancytopenia with special reference to Vit B12 and Folic acid level. **Material and Methods**: This was a hospital based cross sectional study; it was carried out on 50 patients of pancytopenia admitted in department of General Medicine at Jorhat medical college and hospital in the period from March 2023 to February 2024. A total of 50 patients were subjected to Bone marrow examination and Vit B12 and Folic acid level estimation were also done. **Results**: The presents study showed that most common age group affected were between 18 to 30 years. Male were affected more than female. In the present study, majority of cases were diagnosed as megaloblastic anaemia (48%), followed by aplastic anaemia (16%), decompensated chronic liver disease (8%). Multiple myeloma was the least common etiological factor accounting for two cases only. **Conclusion**: Detailed examination of peripheral blood smear along with reticulocyte count reveals important information regarding etiology e.g,macro-ovalocytes with hypersegmented neutrophils in megaloblastic anaemia, absence of any abnormal/immature cell in aplastic anaemia. However, the diagnostic accuracy is increased manifolds when detailed clinical history and examination are combined with complete blood counts and peripheral smear. Although, bone marrow study provides the definitive diagnosis in cases of pancytopenia.

INTRODUCTION

Pancytopenia is characterised by reduced in all three hematologic cell lines platelets, erythrocytes, and lymphocytes and can cause anaemia, leucopenia, and thrombocytopenia. It is not a disease entity by itself but the condition shared a common pathway caused by a wide range of distinct aetiologies, including nutritional, autoimmune, infections, neoplastic, and/or hereditary. To determine the cause of pancytopenia is a challenge and is important in determining the proper treatment regimen and estimating prognosis.[1] Pancytopenia is a condition characterized by a reduced in the quantity of the three primary components of blood red blood cells, white blood cells, and platelets. It is not a single disease, but rather a trio of findings that could arise from several different disease processes that either directly or indirectly affect the bone marrow. In pancytopenia, the relationship between the cellularity and bone marrow composition and the underlying clinical condition varies.

defect causes pancytopenia, the bone marrow typically exhibits hypocellularity. Ineffective haematopoiesis, increased utilisation of peripheral cell or destruction and bone marrow invasive processes are typically linked to a hypercellular or normocellular marrow. Numerous investigations carried out in North and South India have shown that megaloblastic anaemia (MA) is the leading cause of pancytopenia. The incidence of pancytopenia can vary depending on various factors, including regional dispersion, genetics factors, dietary condition, and prevalence of infective disorders. The aetiology of the illness can range from easily curable causes such as infections and megaloblastic anaemia to more severe conditions like leukemia.[2]

Vitamin B12 is a water-soluble form of a vitamin that occurs naturally in certain foods and is also obtainable as a dietary supplement and prescription medication. Cobalamin, a group of chemicals with vitamin B12 action, is characterized by the presence of the metal cobalt. The metabolically active forms of vitamin B12 are methylcobalamin and 5-deoxyadenosylcobalamin.[3]

For DNA formation and maturation require vitamin B12. An imbalance between nuclear and cytoplasmic development characterizes its deficiency, resulting in hypersegmented neutrophils, excessively big platelets, and macrocytic red blood cells [RBCs] with a greater nucleus to cytoplasmic ratio. Dysplastic marrow can also cause pancytopenia, as in the case of a folate or cobalamin deficiency.[4]

Folic acid is a member of the vitamin B complex group. Folate is an essential cofactor necessary for a range of intracellular processes. Folic acid serves as a source of single carbon units and takes part in single carbon transfer mechanisms across different oxidative states. A significant proportion of folate is tightly bound to enzymes, suggesting that there is no excess of this cofactor and that its presence within cells is carefully regulated and protected.

Folate deficiencies can result from a variety of factors, such as decreased intake, elevated metabolism, increased requirements and/or hereditary abnormalities. Megaloblastic anaemia, mood disorders, and hyperhomocysteinemia are among the consequences of a folate deficiency. Neural tube abnormalities have also been linked to folate deficiencies. Several countries have implemented the addition of grain products, such as cereals, as a cost effective method to reduce the occurrence of neural tube abnormalities.[5]

If a patient presents with pallor, a persistent fever, and a tendency to bleed, it is advisable to consider the possibility of pancytopenia. Pancytopenia etiology varies across different populations, influenced by factors including age distribution, gender, nutritional status, geography, lifestyle, exposure to chemicals and medications, and infections. Pancytopenia can occur due to various mechanisms, such as reduced production of hematopoietic cells (as seen in Aplastic anaemia), accumulation of normal cells in the enlarged and overactive reticuloendothelial system (as in hypersplenism), inefficient haematopoiesis (as in Myelodysplastic syndrome), or replacement of bone marrow by abnormal or cancerous tissue. Early detection and treatment of pancytopenia can lead to a cure for most underlying causes. However, in some specific causes where a cure is unattainable, timely recognition, early detection, and adoption of supportive therapy will enhance the quality of life by reducing mortality and morbidity.[1,2]

Finding the correct etiology in a particular case is important since it help in implementation of timely and accurate treatment, as the severity of pancytopenia and its underlying etiology determine the management and prognosis. Since there haven't been many studies conducted in this region of the nation, the goal of this study is to identify the clinical and haematological spectrum of common disorders that can cause pancytopenia.

as conducted in the Department of Medicine, Jorhat Medical College and Hospital, Jorhat.

Duration of Study: One year: March 2023- February 2024

Study Design: Hospital based Cross sectional Study"

Study Population: Patients with pancytopenia admitted in Medicine ward of Jorhat medical college and hospital.

Sample Size:

50 Cases of pancytopenia of adult age group of both sexes who was admitted in the Medicine ward.

Sample Size Calculation: As per the record in the Medical Records Departments of JMCH showed that the total number of pancytopenia patients admitted in the Department of Medicine for the year 2021, 2022 was 92 and 96 respectively (average 7 to 11 cases was admitted per month)

Therefore, the average number of pancytopenia patients admitted per year was,

X= (92+96)/2 =94

Therefore, for a data collection period of 6 months in our study period, number of patients with pancytopenia that were admitted tentatively in JMCH was

n=X/2=47~50

There fore, sample size was taken as 50 for our study.

Sampling Method: Consecutive sample with a diagnosis of "pancytopenia, defined as Hemoglobin <13.5g/dl in male and <11.5g/dl in female

Total leucocyte count<4000/cu.mm. Platelet count < 150,000/cu.mm."

Inclusion Criteria:

All newly detected patients[age>18years] with pancytopenia in both the sexes.

"Exclusion Criteria:

1) Patients who have received or are receiving cancer chemotherapy
2) Patients who have received or are receiving radiotherapy

3) Patient with age < 18 years
4) Recent intake of any drugs which may causes pancytopenia [Chloramphenicol, methotrexate etc]
5) History of recent blood transfusion (within 2 weeks).
6) Patients who are not willing to give consent.

Table 5.1: Age Distribution of Patients with Pancytopenia

Age Group(in years)	Number of Patients(N)	Percentage(%)
≤30	16	32.0
31 - 40	11	22.0
41 - 50	8	16.0
51 - 60	7	14.0
61 - 70	5	10.0
≥71	3	6.0
Total	**50**	**100.0**

Observation: Table 5.1 describes about the age of the patients. Maximum number of cases 16 (32%) were in the age group of 18- 30 yrs. 11 (22%) cases were in the age group of 31- 40 yrs, 8 (16%) were in the age group of 41-50 yrs, 7 (14%) were in the age group of 51-60 yrs, 5 (10%) were in the age group of 61-70 yrs, 3 (6%) cases were in the age group of 71yrs and above. The mean age of the patients was (43.26±12.14), the minimum age of the patients was 19 yrs and the maximum age was 74 years.

Table 5.2: Distribution of Patients with Pancytopenia According to

Sex	Number of patients(N)	Percentage(%)
Male	27	54.0
Female	23	46.0
Total	50	100.0

Observation: Table 5.2 displays about the sex distribution of the patients. Majority, 27 (54%) were male and 23 (46%) were females in the cases. Male: Female ratio was 1.17:1.

Table 5.3: Distribution of Symptoms Associated with Pancytopenia

Symptoms	Number of patients(n)	Percentage(%)
Easy fatigability	50	100.0
Fever	30	60.0
Dyspnea	10	20.0
Palpitation	9	18.0
Bleeding manifestations	12	24.0
Bony pain	7	14.0
Cough	9	18.0
Decreased Appetite	8	16.0
Giddiness	18	36.0
Lower limb swelling	10	20.0

Observation: Table 5.3 describes about the symptoms of the patients in the study. All the cases 50 (100%) in the study had easy fatigability, 30 (60%) had fever, 18 (36%) had giddiness ,12 (24%) had bleeding manifestations, 10 (20%) had dyspnea, 10 (20%) had lower limb swelling, 9 (18%) had palpitation, 9 (18%) had cough, 8 (16%) had decreased appetite and 7 (14%) had bony pain.

Table 5.4: Distribution of Clinical Signs Associated with Pancytopenia

Clinical Sign	Number of Patients(n)	Percentage(%)
Pallor	50	100.0
Splenomegaly	21	42.0
Knuckle Hyperpigmentation	8	16.0

Pedal edema	11	22.0
Glossitis	13	26.0
Icterus	10	20.0
Hepatomegaly	8	16.0
Lymphadenopathy	2	4.0

Observation: Table 5.4 describes the clinical sign of the patients. All the cases in the study had pallor 50 (100%), 21 (42%) had splenomegaly, 13 (26%) had glossitis, 11(22%) had pedal edema, 10 (20%) had icterus, 8 (16%) had hepatomegaly and knuckle hyperpigmentation, 2 (4%) had Lymphadenopathy.

Table 5.5: Peripheral Blood Smear (PBS) Findings

PBS Findings	Number of patients(n)	Percentage(%)
Anisocytosis	48	96.0
Macrocytic	33	66.0
Normocytic Normochromic	10	20.0
Microcytic Hypochromic	2	4.0
Dimorphic Picture	2	4.0
Hypersegmented Neutrophils	20	40.0

Observation: Table 5.5 describes the PBS findings of the patients. It can be seen that 48 (96%) of cases had Anisocytosis and 33 (66%) had Macrocytic, 20 (40%) had Hyper segmental neutrophils, 10 (20%) had Normocytic Normochromic, 2 (4%) cases equally had Microcytic hypochromic and Dimorphic picture.

Table 5.6: Haematological Parameter Associated with Pancytopenia

Statistics	Hemoglobin (g/dl)	TLC(/mm^3)	Platelet count (x10^9/L)	RBC count (millions/mm^3)
Mean	6.1422	2118.4000	55.1000	2.5780
Median	6.3000	2100.0000	54.0000	2.5000
Std. Deviation	1.80771	629.76627	25.68669	.87395
Minimum	1.50	800.00	8.00	1.10
Maximum	9.80	3600.00	102.00	4.30

Observation: Table 5.6 describes the hematological parameter of the patients. It can be seen that the hemoglobin mean was (6.1422 ± 1.80).

Table 5.7: Leucocyte Count Associated with Pancytopenia

Leucocyte Count(/mm^3)	Number of patients(n)	Percentage (%)
< 2000	20	40.0
2000 - <3000	24	48.0
3000 - 4000	6	12.0
Total	50	100.0

Observation: Table 5.7 displays about the Leucocyte count levels of the patients, 20 (40%) cases were having leucocyte count <2000 (/mm^3), cases 24 (48%) were having 2000 - <3000 (mm^3), and 6 (12%) cases had a leucocyte count of 3000 – 4000 (/mm^3).

Table 5.8: Hemoglobin Levels in Patients with Pancytopenia

Hemoglobin Level (g/dl)	Number of patients(n)	Percentage(%)
<7g/dl	34	68.0
7 – 9.9 g/dl	16	32.0
Total	50	100.0

Observation: Table-5.8 describes the Hemoglobin levels of the patients in the study. Patients with HB <7 g/dl were 34 (68%) and patients with HB 7-9.9 g/dl were 16 (32%). Majority of the patients in the study were having very low Hemoglobin levels.

Table 5.9: Platelet Count in Patients Associated Pancytopenia

Platelet Count (x10^9/L)	Number of patients(n)	Percentage(%)
< 50000	23	46.0
50000 - 150000	27	54.0
Total	50	100.0

Observation: Table 5.9 shows the platelets count of the patients of the study, 27 (54%) of the cases had platelets count in the range of 50000 – 150000 and 23 (46%) of the cases had platelets count < 50000, there was a risk of bleeding is higher in the samples with platelets count less than 50000. Maximum platelets count was 1.2 lakhs (x10^9/L) and minimum platelets count was 8000 (x10^9/L).

Table 5.10: Bone Marrow Findings

Parameters	Findings	Number of Patients(n)	Percentage(%)
Bone marrow Cellularity	Hypercellular	39	78.0
	Hypocellular	9	18.0
	Normal	2	4.0
Erythroid series	Hyperplastic	38	76.0
	Hypoplastic	8	16.0
	Normal	4	8.0
Myeloid series	Hyperplastic	6	12.0
	Hypoplastic	5	10.0
	Normal	39	78.0
Dyserythropoiesis	Negative	20	40.0
	Positive	30	60.0
Dysmyelopoiesis	Negative	46	92.0
	Positive	4	8.0

Observation: Table 5.10- describes about the "bone marrow findings" of the patients of "pancytopenia", Majority 39 (78%) had Hypercellular, 9 (18%) had hypocellular, only 2 (4%) among the cases had normal cellularity. Regarding Erythroid series 38 (76%) had hyperplastic, 8 (16%) had hypoplastic, and 4 (8%) had normal erythroid series. Cases 39 (78%) had normal Myeloid, 6 (12%) had hyperplastic and 5 (10%) had hypoplastic. Dyserythropoiesis results in the study shows that 30 (60%) were positive and 20 (40%) were negative. Dysmyelopoiesis results among the cases 46 (92%)

Table 5.11 : Vitamin B12 Level in Patients with Pancytopenia

Vitamin B12 level (pg/ml)	Number of patients(n)	Percentage(%)
< 200 pg/ml (Deficient)	17	34.0
200 - 300 pg/ml (Borderline)	9	18.0
> 300 pg/ml (Normal)	24	48.0
Total	50	100.0

Observation: Table 5.11 describes the Vit B12 level among the patients, 17 (34%) had deficient vitamin B12 <200pg/ml, 9 (18%) were in the borderline 200-300pg/ml and 24 (48%) were having normal range >300pg/ml among the patients.

Table 5.12 : Folic Acid Level in Patients with Pancytopenia

Folic acid level (ng/ml)	Number of patients(n)	Percentage(%)
2.1 - 3.9 ng/ml (Border line)	3	6.0
> 4 ng/ml (Normal)	47	94.0
Total	50	100.0

Observation: Table 5.12 describes the folic acid levels among the patients with pancytopenia, 47 (94%) of the patients had normal level folic acid >4ng/ml, whereas 3 (6%) had 2.1 – 3.9 ng/dl that is borderline folic acid level among the patients.

Table 5.13 : Association "Between Vitamin B12 and Folic Acid Level"

Vitamin B12 Level	Folic Acid Level		Total
	2.1 - 3.9 ng/ml	> 4 ng/ml	
< 200 pg/ml	2	22	24
	8.3%	91.7%	100.0%
200 - 300 pg/ml	0	4	4
	0.0%	100.0%	100.0%
> 300 pg/ml	1	21	22
	4.5%	95.5%	100.0%
Total	3	47	50
	6.0%	94.0%	100.0%

$X^2 = .570$ df - 2 $p > .05 = .752$

Observation: Table 5.13 Describes the association between VitB12 and Folic acid level in the cases and there is statistically no significant relation among the samples, as the chi-square results reveal that $X^2 = .570$, df – 2, p > .05 = .752.

Table 5.14 : Average B12 Level in Patients with Pancytoprnia Based on Etiology

Sr.No.	Etiology	Average B12(pg/ml)	p- value
1	Acute Myeloid Leukemia	457.33	.041
2	Aplastic Anaemia	502	.000
3	Decompensated Chronic Liver Disease	481	.012
4	Dengue Fever	570	.057
5	Megaloblastic Anaemia	166.625	.000
6	Multiple Myeloma	398.5	.053
7	Myelodysplastic Syndrome	401.67	.015
8	Systemic Lupus Erythematosus	535.67	.095, NS

Observation: Table 5.14 describes the average vitamin B12 of the patients as per their Etiology. Patients with Acute Myeloid Leukemia, Vit B12 mean = 457.33, p < .041, Aplastic Anaemia had mean Vit B12 = 502 with p < .05, Decompensated Chronic Liver Disease, Vit B12 Mean = 481, p < .012, patients with Dengue had Vit B12 mean = 570,p = .057, Megaloblastic Anaemia Mean Vit B12 = 166. 625, p < .000, Multiple Myeloma had Vit B12 mean = 398.5, P = 053, Myelodysplastic Syndrome Vit B12 Mean = 401.67, p < .015, Systemic Lupus Erythematosus Vit B12 Mean = 535.67, p > .05, = 095, NS, and there was no statistical significance mean difference in the "vitamin B12" among patients with systemic lupus erythematosus ,Dengue and Multiple myeloma.

Table 5.15: Average Folic Acid Level in Patients Pancytoprnia Based on Etiology

Sr No.	Etiology	Average Folic Acid level (ng/ml)	p- value
1	Acute Myeloid Leukemia	18.33	.060
2	Aplastic Anaemia	17.125	.000
4	Decompensated Chronic Liver Disease	5.35	.018
5	Dengue Fever	25.33	.034
6	Megaloblastic Anaemia	16.27	.000
7	Multiple Myeloma	20.5	.028
8	Myelodysplastic Syndrome	16.33	.197 NS
9	Systemic Lupus Erythematosus	14.67	.073 NS

Observation: Table 5.15 describes about the folic acid levels of the patients as per their etiology. The etiology type and average folic acid, that had significance were Acute Myeloid Leukemia folic acid mean = 18.33 with p > .060, Aplastic Anemia, folic acid mean = 17.125, p < .05, Decom-pensated Chronic Liver Disease had folic acid mean = 5.35. p < .05, Dengue had folic acid Mean = 25.33, p < .034,Megaloblastic Anaemia folic acid mean = 16.27, p <.05, Multiple Myeloma had folic acid Mean = 20.5, p < .028, Myelodysplastic Syndrome folic acid mean = 16.33, p > .05, Systemic Lupus Erythematosus, folic acid mean = 14.67, p > .05. there was significance with 5 etiology findings in this study and others were not relevant.

Table 5.16: Causes of Pancytopenia

Causes	Number of patients(n)	Percentage(%)
Acute Myeloid Leukemia	3	6.0
Aplastic Anaemia	8	16.0
Decompensated Chronic Liver Disease	4	8.0
Dengue	3	6.0
Megaloblastic Anaemia	24	48.0
Multiple Myeloma	2	4.0
Myelodysplastic Syndrome	3	6.0
Systemic Lupus Erythematosus	3	6.0
Total	50	100.0

Observation: Table 5.16 Displays the final diagnosis of the patients. The data showing that 48% had megaloblastic followed by 16% had Aplastic anemia, 8% had Decompensated Chronic Liver disease, 6% each had Acute Myeloid Leukemia, Dengue, Myelodysplastic Syndrome, Systemic Lupus Erythematosus and 4% cases had Multiple Myeloma.

The statistical analysis was done after data cleaning and editing. Data was prepared for analysis. SPSS -26 was used for data analysis. The count and percentage, "mean, standard deviation, minimum and maximum" count of the cases were calculated and presented in form of tables and graphs. Statistical test, chi-square, one sample T

"The present study was a hospital based cross sectional study which was undertaken in the department of Medicine, Jorhat Medical College and Hospital, Jorhat for a period of one year to evaluate the clinico etiological profile of pancytopenia".

A total of 50 cases of Pancytopenia in adults were evaluated. The age, sex, clinical and haematological findings were compared with other similar studies to draw a conclusion.

In our study of 50 patients, 32% were in the age of 18 yrs to 30 yrs. 22% were in the age of 31yrs to 40 yrs, 16% were in the age of 41yrs to 50 yrs, 10% were in the age of 61yrs to 70 yrs, 6% were in the age of 71yrs & above. The mean age of the patients was (43.26±12.14), the minimum age of the patients was 19 yrs and the maximum age was 74 years. the largest number of patients was from 18 to 30 years and the 2nd largest was from 31 to 40 years in our study. "Similar study done by Rao KS et al(2011)" where they found mean age was 41 years .[108] "Another study done by Raphael V et al(2012)" where they found that mean age was 30 years.109 "Similar study done by Mangal S et al(2020) "where they found that most common age between 21-30 years which account for 24% ,22 out of total 44 cases.123 Another study done by Manzoor F et al(2014) they also found that most common age group was between 21 -30 years which account for 32%,16 out of 50 total cases.124 All studies shown that most common age group between 21-30 years which is closely resembled to the present study.

In our study proportion of male and female patients, 54% were males and 46% were females. "Similar study done by Batool Y et al(2021)" where they found that male was 57.81% and female was 42.19%,a total of 237 cases out of which 137 male and 100 female. Another study done by Sharma N et al(2019) where they found that 62% were male 38% were female ,total of 100 cases out of which 62 male and 38 female.[125] Another study done by Cheruka S et al(2019) they also found that male predominance in the study, where total of 150 cases out of which 86 male and 64 were female.[126] All these study shown that there is male predominance which is closely related to our present study.

It was found that in our study that all the patients had easy fatigability (100%), second most common symptoms was fever (60%) and next symptoms after fever was giddiness (36%) followed by Bleeding Manifestations (24%). In the study conducted by Cheruka S et al. (2019), Despande SV et al. (2019), Shah R et al. (2020) , and Periera ADS et al. (2016), the most common symptom associated with pancytopenia was generalised weakness constituting 85%,73.2%, 100%, and 37.5% respectively. The second most common symptom in the studies was fever followed by dyspnea and bleeding manifestations, all of these studies shown similarities to the present study.

In the present study most common clinical sign is that all the patients had Pallor (100%), Splenomegaly (42%) and Hepatomegaly (16%). Lymphadenopathy was seen in only few samples of the study which showed resemblance with the" study conducted by Yadav RK et al. (2020)'' where they found that all sample had pallor (100%), 26.5% had splenomegaly, 17.2% had hepatomegaly. Study conducted by Rao KS et al (2011) found that all sample had pallor(100%),35.57% had splenomegaly,26.92% had hepatomegaly. Study conducted by Despande SV et al. (2019) found 78.7% had pallor,30.69% had splenomegaly and 18.8% had hepatomegaly.

The PBS findings in the study were 96% of the patients had Anisocytosis and 66% had Macrocytosis, which is closely resemblance to the study conducted by Agarwal P et al. (2018), Rao KS et al (2011), and Tilak V et al. (1992) most common PBS finding was anisocytosis with 94%, 60%,and 83.1% respectively. Present study shown 66% had Macro-

cytosis whereas study conducted by Agarwal P *et al.* (2018), Barik S et al (2014)133 found macrocytosis as one of the common PBS findings having 45%, 49% respectively thus showed similarities with the present study.

In the study it was found that 40% of the patients were having leucocyte count <2000, patients 48% were having 2000 - <3000, and 12% had a count of 3000 – 4000. Majority Leucocyte count was between 2000 to 3000. While study conducted by Agarwal P et al. (2018), Mangal S et al. (2020) 42% had leucocyte between 1000-2499/cmm and 56% within 1001-3000/cmm respectively which is closely resemblance to the present study.

Majority of the patients in the study had Hemoglobin level less than 7 g/dl, 68% had Hb below 7g/dl and 32% had HB level between 7 -9.9. Similar study conducted by Islam U *et al.* (2016), the mean hemoglobin was 6.7 +/- 2.3g/dl. Another study conducted by Agarwal P et al. (2018) found 58.75% of cases (total case 80) had hemoglobin within 4- 7 g/dl. Both of the study are closely resemblance to present study. Thus maximum number of cases had severe anemia which reflected in their clinical presentation

The study also found that majority of the patients 54% had platelets count between 50000 -150000($x10^9$/L), whereas < 50000($x10^9$/L) had 46% that is causing a risk of higher bleeding. "In a study conducted by Rohira N et al. (2019) , 24 cases out of 75 (32%) had Platelet Count in the range of 50,000-75,000($x10^9$/L). Study conducted by Rao KS *et al* (2011) showed Platelet Count ranged from 10,000-95, 000($x10^9$/L). In present study platelet counts ranges from 8000 to 1.29($x10^9$/L) lakhs thus the present study had similarities with the study conducted by Rohira N et al. (2019), Rao KS et al (2011) .

In the bone marrow findings, the present study found that majority were having Hypercellular (78%) with 39 cases out of total 50 cases, followed by hypocellular marrow with 9 cases out of total 50 cases (18%), showing resemblance with the study performed by Agarwal P et al.(2018) where they found 78.75% had hypercellular marrow and 10% had hypocellular marrow. Another study done by Gandhi SH *et al*. (2019) where they found that 67.91% had hypercellular marrow and 14.9% had hypocellular marrow.

"In the study conducted by Sahay S et al. (2018) , erythroid hyperplasia" was the significant finding in megaloblastic anemia as well as in combined deficiency (both iron and vit B12) and myelodysplastic syndrome. Dysgranulopoiesis and dysmegakaryopoiesis were observed in megaloblastic anemia and cases of myelodysplastic syndrome. In the present study, erythroid hyperplasia was seen in 38 (76%) cases. Dyserythropoiesis features like nuclear budding, premature nuclear extrusion, internuclear bridging, multinuclearity as well as megaloblastic changes were seen 30 (60%) cases. Thus, the present study showed resemblance with the study conducted by Sahay S et al. (2018)

In other investigations the present study found that none of the patients had HIV infection and a small proportion 6% were having the symptoms of Dengue.

The study found that 34% of the patients had deficiency in vitamin B12 (below 200 pg/ml) and 18% were in borderline (between 200 -300 pg/ml). The average B12 levels were 332.6 (pg/dl) in the study, Majority of the patients in this study had normal levels of folate, only 3 patients (6%) had folate deficiency and 2 patients (4%) had combine deficiency of both cobalamin and folate.

Similar study conducted by Premkumar M et all(2012) found that 81% patients had cobalamin deficiency. In contrast to this, only 7.14% all patients were folate deficient. Combine cobalamin and folate deficiency was seen in 3.51% patients.

In a study by Agarwal P et al. (2018), out of 30 cases of megaloblastic anemia, 19 cases were investigated for vitamin B 12 assay and all 19 cases (100%) showed serum vitamin B12 less than 211pg/ml (211-946 pg/dl as normal range in the study).

In the present study, out of 24 cases of megaloblastic anemia 17 cases showed decrease serum vitamin B12 assay (below 200 pg/ml), and 7 cases shows serum vitamin B12 in borderline level (200-300pg/ml) and thus can be concluded that most common cause of megaloblastic anemia in this part of country is due to nutritional deficiencies mainly vitamin B 12 deficiency or defective absorption which closely resembled to the study done by Agarwal P et al.(2018) and Premkumar M et all(2012).

The statistical test results of the present study show that there was statistically significant mean difference in the vitamin B12 and folic acid among the patients of the study, the study also found that there was statistical relation found between vitamin B12 and folic acid among the patients in the study, mean 316 ± 217, $p < .05$.

There was significant mean difference in the Vitamin B12 levels of patients with pancytopenia and their etiology, eg with Acute Myeloid Leukemia, Vit B12 mean = 457.33, $p < .041$, Aplastic Anaemia had mean Vit B12 = 502 with $p < .05$, Decompensated Chronic Liver Disease, Vit B12 Mean = 481, $p < .012$, patients with Dengue had Vit B12 mean = 570, $p = .057$, Megaloblastic Anaemia Mean Vit B12 = 166.625, $p < .000$, Multiple Myeloma had Vit B12 mean = 398.5, $P = .053$, Myelodysplastic Syndrome Mean = 401.67, $p < .015$, Systemic lupus erythematosus Mean =535.67, $p > .05$ and there was no statistical significance mean difference in the "vitamin B12" among patients with systemic lupus erythematosus, Dengue and Multiple myeloma. Average folic acid that had significance were Acute Myeloid Leukemia folic acid mean = 18.67 with $p > .060$, Aplastic Anemia, folic acid mean = 17.125, $p < .05$, Decompensated Chronic Liver Disease had folic acid mean = 5.35. $p < .05$, Dengue had folic acid Mean = 25.33, $p < .034$, Megaloblastic Anaemia folic acid mean = 16.29, $p < .05$, Multiple Myeloma had folic acid Mean = 20.5, $p < .028$, Myelodysplastic Syndrome mean = 16.33, $p > .05$, Systemic Lupus Erythematosus mean = 14.67, $p > .05$, there

was significance with 5 etiology findings in this study and others were not relevant.

In a study conducted by Shwetha JH et al. (2021), "most common cause of Pancytopenia was Megaloblastic Anemia (39%) followed by Aplastic Anemia (12.17%)". In other study conducted by Mittal M et al. (2019), Batool Y et al (2021), Barik S et al. (2014) and Rao KS et al. (2011), the most common cause of pancytopenia after proper haematological and biochemical evaluation were Megaloblastic anemia followed by Aplastic Anemia with 33.34%, 27% ,66%, and 77.04% of megaloblastic Anemia and 19.05%, 15.6%,18%, and 18.26% of Aplastic Anemia respectively. In one study conducted by Lakhey A et al (2012), the common cause of "pancytopenia was Hypoplastic Anemia (29.6%)," followed by Haematological Malignancies (27.78%) where was Mangal S et al. (2020) found that Aplastic Anaemia (24.2%) was the most common cause followed by Myelodysplastic Syndrome (17.6%). And Retief FP et al. (1976) concluded Bone Marrow Failure (67.1%) as common cause of Pancytopenia followed by Hypersplenism (17.7%).

In the present study most common cause of "Pancytopenia was Megaloblastic Anemia" with 24 cases out of total 50 cases (48%), followed by "Aplastic Anemia" with 8 scases out of total 50 cases (16%), which is in concordance with study by Shwetha JH et al. (2021), Mittal M et al. (2019), Batool Y et al. (2021), Barik S et al. (2014), Shah R et al. (2014) and Rao KS et al. (2011) but in sharp contrast with the study conducted by Lakhey A et al (2012), Mangal S et al. (2020) and Retief FP et al (1976).

CONCLUSION

From the results and observations of the clinico-etiological study of 50 adult pancytopenia patients which were diagnosed with the aid of hematological invest-igations as well as Bone Marrow Study and serum vit B 12 and folic acid level in Medicine department, Jorhat Medical College and Hospital, Jorhat over the period of 12 months, the following conclusion could be drawn.

In the evaluation of pancytopenia, Megaloblastic Anemia should always be considered as one of the commonest cause in Indian setting as it reflects its higher prevalence due to nutritional deficiency, mainly vit B 12 and folic acid. In the present study Megaloblastic Anemia (48%) was the most common cause associated with pancytopenia. Aplastic Anemia (16%) was the second most common cause of pancytopenia.

The common cause of pancytopenia may vary in different studies due to differences in the time period of the studies conducted, genetic variations among patients, geographical conditions, nutritional status of cases, methodology applied in the various studies, diagnostic criteria applied as well drug history.

Proper clinical history, clinical presentation as well various haematological and biochemical investigations gives important clues to the diagnosis of underlying cause.

Bone Marrow study as well as serum vit B12 and folic acid level play a pivotal role in establishing the diagnosis.

Depending upon the cause and severity of pancytopenia, early treatment can be planned and those treatable causes of pancytopenia carry a better prognosis

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