BJMHR
British Journal of Medical and Health Research
Journal home page: www.bjmhr.com

Evaluation of hematological parameters and bone marrow in Indian patients suffering from pancytopenia

Mahfooz Basha[1], Mehar Aziz[2], S. Manazir Ali[2], Kiran Alam[2], Feroz Alam[2*], Murad Ahmed[2]

1. G. Kuppuswamy Naidu Memorial Hospital, Pappanaickenpalayam, Coimbatore Tamil Nadu India 641037.

2. J.N Medical College, Aligarh Muslim University, Aligarh 202002 ,U.P, India.

ABSTRACT

Pancytopenia is a relatively common hematological disorder manifesting as anemia, leucopenia and thrombocytopenia. Causes of pancytopenia are varied and range from simple drug-induced bone marrow hypoplasia, megaloblastic anemia to fatal bone marrow aplasias and leukemias. Examination of the bone marrow is required in cases for pancytopenia to find out the underlying pathology and hence better patient management. This study was carried out to evaluate hematological and bone marrow findings in patients presenting with pancytopenia. 50 patients in the age group of 6 months- 60 years were included in this prospective study. Detailed history, clinical examination, hematological investigations and bone marrow examination were performed in all the cases. Pancytopenia was more common in second decade of life with slight male preponderance. Fever was the commonest presenting complaint and pallor was the commonest sign. Megaloblastic anemia was the most common cause (58%) of pancytopenia, hypersegmented neutrophils and macro-ovalocyte are very reliable indicators of megaloblastic anemia. Bone- marrow aspiration was diagnostic in majority (80%) of cases, and biopsy is not routinely indicated. Reticulocyte production index is a better indicator of bone-marrow status as compared to reticulocyte count. Nutritional deficiency is the most important cause of megaloblastic anemia, and was the underlying etiology in 58% cases of life-threatening pancytopenia. Findings of automated hematology counter must be correlated with manual peripheral blood smear examination in cases of pancytopenia. Bone- marrow aspiration is highly recommended and reticulocyte production index instead of reticulocyte count must be used to evaluate the actual hematopoietic potential of the bone- marrow.

Keywords: Pancytopenia, megaloblastic anemia, bone marrow examination, reticulocyte production index.

*Corresponding Author Email: ferozalam97@gmail.com
Received 10 March 2016, Accepted 21 March 2016

Please cite this article as: Alam F *et al*., Evaluation of hematological parameters and bone marrow in Indian patients suffering from pancytopenia. British Journal of Medical and Health Research 2016.

INTRODUCTION

Blood is a unique fluid having several important functions which are vital for life. Hippocrates described blood as being one of the "four humors"; the others being phlegm, black bile and yellow bile, and suggested that an imbalance of these can lead to disease.[1] Hematopoiesis is the process by which the various cells present in blood are produced from the hematopoietic stem cells.[2] The organs and tissues of hematopoiesis are bone marrow, thymus, spleen and lymph nodes. Bone marrow is the site of myeloid, erythroid, and megakaryocytic as well as lymphoid cell development.[3] When the counts of all the cell lineages in the peripheral blood are decreased to below normal levels, the condition is called pancytopenia.[4] Pancytopenia is not a disease in itself but a triad of findings that may result from a number of disease processes. These disorders may affect the bone marrow either primarily or secondarily resulting in pancytopenia. Pancytopenia manifests as anemia, leucopenia and thrombocytopenia. Anemia can be of varying severity and cause considerable morbidity. Leucopenia puts the patient at higher risk of infections to which the patient can succumb unless promptly treated. Thrombocytopenia can lead to spontaneous bleeding in the body with a fatal outcome. *The etiology of pancytopenia can vary from treatable disorders such as megaloblastic anemia to more serious conditions such as the myelodysplastic syndromes which increase the likelihood of developing hematological malignancies in future.* Amongst the investigations, the examination of blood and bone marrow play a vital role in the establishment of diagnosis. In addition to the routine hematological investigations, examination of the bone marrow by aspiration and biopsy provides detail that help in understanding the pathogenesis behind pancytopenia in a particular case. The etiology of pancytopenia can thus be established after correlation of the clinical details with the laboratory investigations. This study was an attempt to determine the etiopathogenesis, diagnosis and prognosis in cases of pancytopenia based on hematological indices and bone marrow examination.

MATERIALS AND METHOD

The study was conducted in the Dept. of Pathology, J.N.Medical College, Aligarh for a period of two years from November 2008 to November 2010. Patients presenting with features suggestive of pancytopenia, were admitted and detailed history, examination, and various investigations were performed. Criteria for patient inclusion was, hemoglobin <10gm/dL, platelet count <1,00,000/cu.mm and total leucocyte count (TLC) <4,000/cu.mm. Children less than 1 month of age, and patients taking myelotoxic chemotherapy or radiotherapy were excluded from the study. Investigations performed were complete hemogram (performed with lablife H3D premier hematology analyzer**)**, peripheral

blood smear, reticulocyte count, and erythrocyte sedimentation rate. Bone marrow aspiration was done in all the cases and a bone marrow biopsy was performed where ever required. The posterior iliac spine was the preferred site in adult patients however the tibial tuberosity was the ideal site in children under 18 months of age for both bone marrow aspiration and biopsy. Salah's needle and Jamshedi's needle were used for aspiration and biopsy respectively.

RESULTS AND DISCUSSION

A total of 50 patients were included in the study, consisting of 26 males and 24 females with a male-to-female ratio of 1.08:1. The age of patients ranged from 6 months to 60 years (mean age- 22.04 years), and the most common age group involved was between 11-20 yrs of age (38%). Fever was the most common presenting complaint seen in 72% of the cases, followed by generalised weakness (38%), increasing paleness (32%), difficulty in breathing (14%), G.I disturbances (14%), bleeding manifestations (8%) and loss of weight & appetite (8%). On examination pallor was the commonest sign present in all the cases followed by splenomegaly (28%), hepatomegaly (22%), petechiae/rash/ecchymoses (12%), pedal edema (8%), icterus (6%).

After investigations megaloblastic anemia was found to be the most common disease associated with pancytopenia, followed by aplastic anemia. Table-I summarizes the different underlying conditions found in the study.

Table I: Showing different diseases underlying pancytopenia.

Condition	No. of cases	Percentage
Megaloblastic anemia	14	28
Megaloblastic anemia with iron deficiency anemia	15	30
Drug induced aplastic anemia	05	10
Hypersplenism	03	06
Myelodysplastic syndrome	02	04
Tuberculosis	02	04
Leukemia	02	04
Inconclusive	07	14
Total	50	100

Hematological investigations

The patients having hemoglobin level of less than 10 gm/dL were selected. The majority of the cases (46%) had hemoglobin levels between 2.1 to 4.0 gm/dL. The hemoglobin range in different conditions is given in table II. Patients having a WBC count of less than 4000/cu.mm were included in the study and the distribution of cases according to the leucocyte count is shown in the table-II. 70% of the cases had a total leucocyte count in the range of 2000-4000/cu.mm. The inclusion criteria with regards to the platelet count was thrombocytopenia less than 1,00,000/cu.mm, table-II gives the range of platelet count obtained in different conditions of study. 58 % of the cases had a platelet count in the range

20,001 to 60,000/cu.mm. The different hematological indices were obtained by the automated analyzer, along with erythrocyte sedimentation rate and the corrected reticulocyte count. These parameters of all the patients are presented in table- III, the mean value is mentioned for each parameter along with the standard deviation. Peripheral smear was obtained from all the patients and a general blood picture examination was done. *Dimorphic blood picture was the most common type of RBC morphology seen, accounting for 70 % of the total number of cases.* Macrocytic picture was seen in 14% cases, while a normocytic and normochromic blood picture was present in 12% of the cases. *Eight out of the fourteen (57.1%) cases of megaloblastic anemia showed a dimorphic blood picture, as a result of which the MCV was not as high as expected. This finding emphasizes the need to correlate the values of the automated analyzer with the peripheral blood morphology.* Anisopikilocytosis was more pronounced in cases of megaloblastic anemia. Out of the various RBC poikilocytes that can be seen in cases of pancytopenia, the macro-ovalocytes are considered to be a good indicator of megaloblastic anemia. Out of 29 cases of megaloblastic anemia 10 cases (34.4 %) showed the presence of macro-ovalocytes. Hypersegmented neutrophils (Figure-1) are also considered to be good predictors of megaloblastic anemia. They were present in 4 cases (13.7 %) having megaloblastic anemia. Lymphocytosis was a common finding and was present in 34 cases (68 %). All the five patients with aplastic anemia had lymphocytosis. It was present in 17 cases out of the 29 associated with megaloblastic anemia (58.6%).

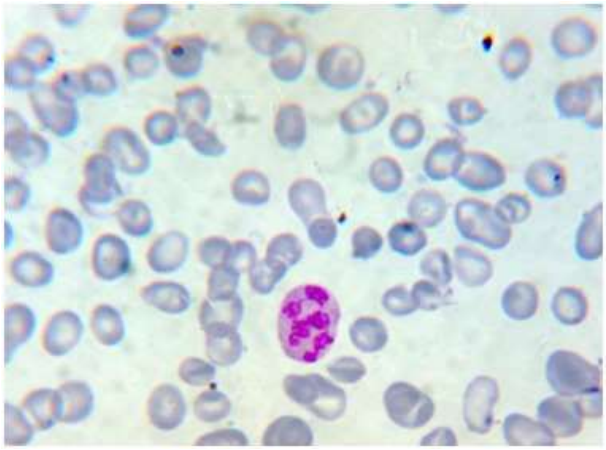

Figure 1 : Photomicrograph of the peripheral blood in a case of megaloblastic anemia showing a hypersegmented neutrophil (Leishman stain x400).

Table II- Values of hemoglobin, TLC and platelet count in different conditions causing pancytopenia.

Hb in gm/dL	**Meg. Anemia**	**Meg. Anemia with IDA**	**Drug induced AA**	**Hyper-splenism**	**MDS**	**TB**	**Leukemia**	**In conclusive cases**	**Total**
Upto 2.0	3	1	1	0	0	0	0	0	5
2.1-4.0	5	9	2	2	2	0	1	2	23
4.1-6.0	4	3	1	0	0	1	1	4	14
6.1-8.0	1	2	1	1	0	1	0	0	06
8.1-10	1	0	0	0	0	0	0	1	02
TLC/ cumm									
Upto 1000	1	1	1	0	0	1	0	1	5
1001-2000	5	2	1	0	0	0	0	2	10
2001-3000	3	8	2	1	0	0	2	1	17
3001-4000	5	4	1	2	2	1	0	3	18
Plt. Count/cumm									
Upto 20,000	3	1	0	0	0	0	1	1	6
20,001-40,000	3	4	5	2	0	2	0	3	19
40,001-60,000	4	3	0	0	1	0	1	1	10
60,001-80,000	3	2	0	0	0	0	0	1	06
80,001-1,00,000	1	5	0	1	1	0	0	1	09

Bone-marrow examination

Bone marrow aspiration identified the underlying pathology in 40 cases (80%). The procedure failed to identify the cause in 10 cases (20 %). Five of these aspirates were hemorrhagic and aparticulate. Amongst the 40 cases, there were five cases of aplastic anemia, which could be identified on bone marrow aspirate smears. However, a biopsy was obtained in all the five cases for a confirmatory diagnosis. Three out of the 10 failed cases had a poor yield during aspiration and hence a biopsy was performed which helped in the establishment of diagnosis. Bone marrow biopsy was done in eight cases and it helped in the diagnosis of the underlying pathology in all the cases.

74% of the cases had a hypercellular bone marrow with all cases of megaloblastic anemia, leukemia, hypersplenism and myelodysplastic syndrome showing hypercellularity. Aplastic anemia cases were hypocellular (Figure-2). In 10% of cases the bone marrow was hemorrhagic, because of which a diagnosis could not be established. The M:E ratio was normal to decreased in most of the cases. The highest M:E ratio was 3.4:1, seen in case of aplastic anemia. The lowest was 0.3:1 that was observed in a case of megaloblastic anemia with co-existing iron deficiency anemia. The predominant bone marrow reaction was looked for in all the bone marrow smears and megaloblastic change was the most common type of predominant bone marrow response mixed with normoblastic cells, it was seen in 68% of the cases. A mixed megaloblastic and micronormoblastic reaction along with some normoblasts were seen 36% of cases. *Dyserythropoiesis was seen in cases of megaloblastic anemia and myelodysplastic syndromes* (Figures-3&4).Myelodysplastic syndrome was associated with dysplastic features such as the cytoplasmic blebs (Figure-5). Myelopoiesis and erythropoiesis was assessed to look for any maturation arrest, and the results are summarized in table- IV. The maturation of the erythroid and myeloid series could not be assessed in nine cases. Five of these cases were that of aplastic anemia with hypocellular aspirates, two cases of tuberculosis had plenty of lymphoid cells and very little population of other cells, epithelioid cell containing granuloma was also present in a case of tuberculosis (Figure-6). In two cases of leukemia, blast cells had replaced other marrow cell populations.

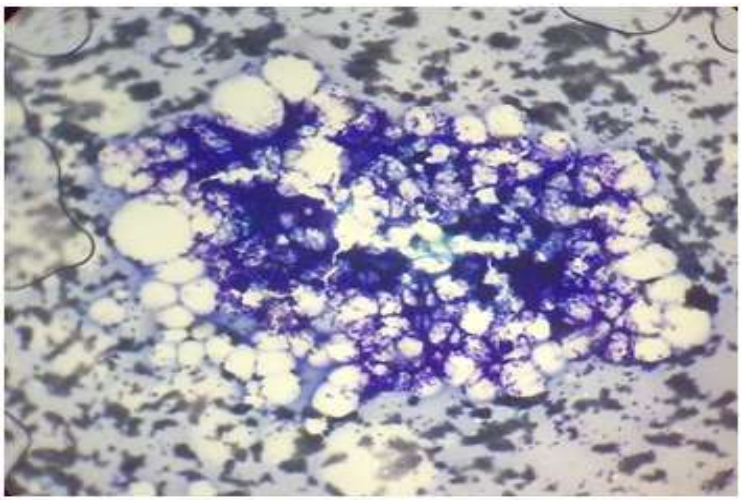

Figure 2: Photomicrograph of bone marrow aspirate smear from a case of aplastic anemia showing a hypocellular bone marrow fragment (Leishman stain x100).

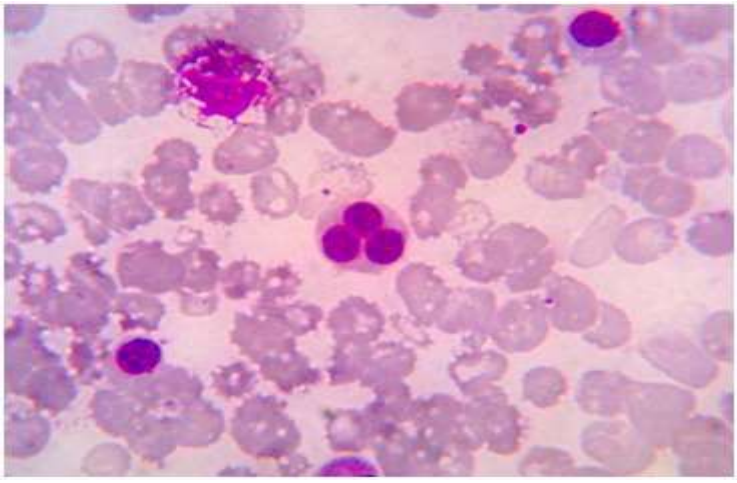

Figure 3: Photomicrograph of the bone marrow aspirate smear showing a multinucleated RBC seen in a case of megaloblastic anemia (Leishman stain x400).

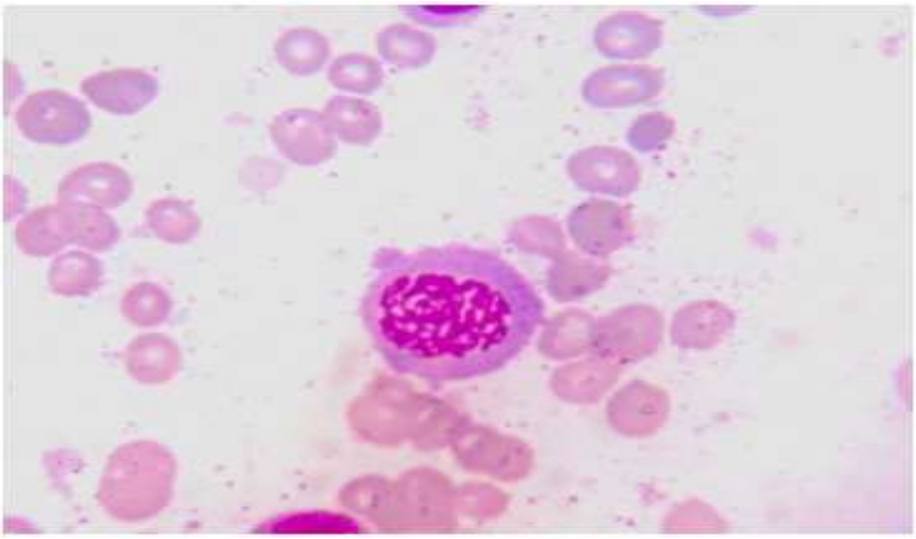

Figure 4: Photomicrograph of the bone marrow aspirate smear showing karyorrhexis in a case of myelodysplastic syndrome (Leishman stain x400).

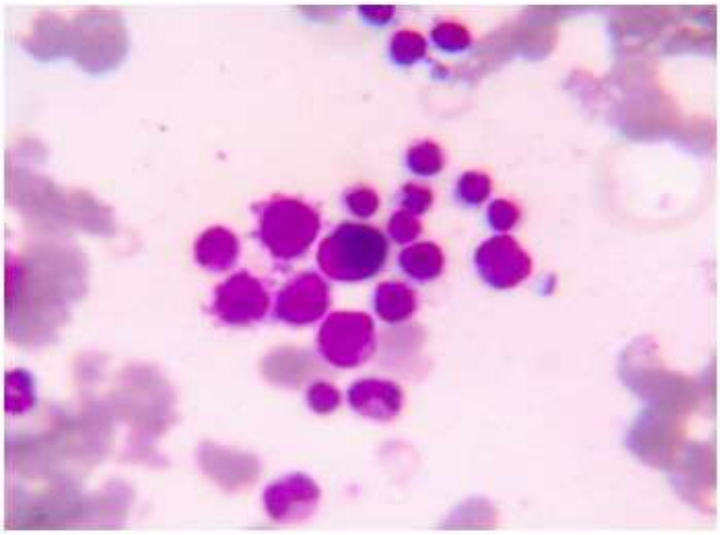

Figure 5: Photomicrograph of the bone marrow aspirate smear showing a myeloblast and other myeloid series cells with cytoplasmic blebs in a case of myelodysplastic syndrome (Leishman stain x400).

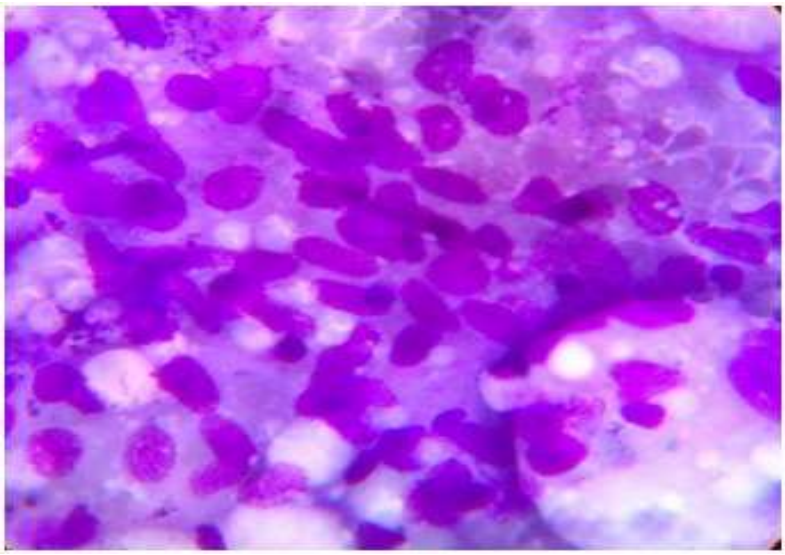

Figure 6: Photomicrograph of bone marrow aspirate showing epithelioid cell clusters in a patient with tuberculosis (Leishman stain x400).

Table III- Hematological parameters in cases of pancytopenia

Parameter	Meg. Anemia	Meg Anemia with IDA	Drug induced AA	Hypersplenism	MDS	TB	Leukemia	Inconclusive cases
Hb	4.05±2.43	3.86±1.48	3.46±2.07	5.00±2.45	3.20±0.56	5.60±2.1	4.35±1.62	5.10±2.34
ESR	50.3±23.43	51.7±12.4	52.8±15.1	68.3±10.4	67.5±4.9	66±2.8	63.5±10.6	53.8±11.2
TLC	2392±1048	2526±749	2140±1059	3133±351	3300±141	1900±1555	2675±388	2571±1249
HCT	14.7±8.7	14.7±6.4	10.4±6.2	15.5±6.5	10.6±0.3	15.9±5.6	16.6±9.6	17.5±8.4
RBC	1.57±0.96	1.58±0.64	1.14±0.76	1.58±0.90	1.19±0.53	1.68±0.40	2.00±0.98	1.92±0.96
MCV	111.1±20.3	92.0±20.6	93.9±8.9	104.7±16.2	98.9±42.4	93.6±11.2	86.4±11.5	93.1±12.7
MCH	33.1±6.0	28.6±8.4	30.5±1.6	32.7±3.0	31.1±18.8	32.6±4.8	23.6±1.9	29.3±4.6
MCHC	30.5±2.7	28.9±5.2	32.8±2.0	31.4±2.0	30.2±6.1	35±0.84	28.2±5.5	31.3±2.5
RDW-CV	17.48±2.51	17.22±3.23	19.38±6.14	20.10±0.45	19.35±3.46	22.50±7.9	15.4±0	18.65±3.76
RDW-SD	64.27±14.41	59.76±13.57	62.3±17.83	64.13±9.04	67.65±37.40	65.75±8.98	52.5±1.62	60.5±7.05
PLATE-LET	46071±26854	59600±27302	32200±5630	47333±34443	76000±28284	27500±4949	30500±16263	47285±27572
MPV	10±1.26	8.98±1.23	8.54±0.87	9.96±1.53	9.25±0.77	7.85±1.48	8.90±1.8	9.25±1.41
PDW	16.98±0.64	16.40±1.32	16.40±2.86	16.93±1.33	16.45±0.21	16.60±2.33	17.8±0.4	17.04±1.36
PCT	0.060±0.026	0.053±0.030	0.028±0.010	0.050±0.04	0.077±0.044	0.020±0	0.03±0.01	0.034±0.023
Reticulocyte	0.54±0.18	0.57±0.27	0.28±0.13	0.83±0.55	0.70±0	0.4±0.28	0.6±0.14	0.35±0.18

Table IV- Assessment of myelopoiesis & erythropoiesis in different cases of pancytopenia.

Underlying Condition	Myelopoiesis		Erythropoiesis		Could not be assessed
	Normal	Maturation arrest	Normal	Maturation arrest	
Megaloblastic Anemia	0	14	6	8	0
Megaloblastic Anemia With Iron Deficiency	0	15	5	10	0
Drug Induced Aplastic Anemia	0	0	0	0	5
Hypersplenism	3	0	3	0	0
Myelodysplastic Syndrome	0	2	0	2	0
Tuberculosis	0	0	0	0	2
Leukemia	0	0	0	0	2

DISCUSSION

In the present of 50 cases, we had cases ranging from 6 months to 60 years of age. The mean age in our study was 22.04±16.02.The youngest case had pancytopenia secondary to hypersplenism and the eldest 60 yr old patient was a case of myelodysplastic syndrome presenting with pancytopenia. Majority of the patients in our study were in the age group between 11-20 years (38%), the male to female ratio was 1.08:1. Our findings are in concordance with the other studies (Table- V), which also suggested that pancytopenia is more commonly seen in younger age group and is slightly more common in males. Fever was the most common presenting complaint in our study, seen in 72% cases followed by generalised weakness in 38% cases, 32% of the cases also had complaints of increasing paleness (Table-V). Khodke et al. observed that the most common symptom with which patients of pancytopenia presented to them was fever.[5] The second most common complaint was weakness. Niazi and Raziq had patients with pancytopenia presenting to them with generalised weakness (68.2%) in most of the cases, followed by fever and bleeding manifestations.[6] Hamid et al. noted that majority of the patients presented with complaints of fever (86.7%) followed by fatigue and dizziness.[7] Ishtiaq et al. in their study of 100 cases also found that the most common presenting complaint was fever (59%).[8] Bleeding manifestations and diarrhea were the other common presenting complaints. The symptoms in cases of pancytopenia can be attributed to the reduction of blood cells, RBC depletion is the reason for patients presenting with weakness, fatigue and increasing pallor. Leucopenia seen in cases of pancytopenia is the reason for patients presenting with fever as a result of acquiring some infection, deficiency of platelets can lead to bleeding manifestations. Hence, when a patient presents with a combination of symptoms like increasing pallor and fever or weakness with bleeding episodes, one must keep in mind the possibility of pancytopenia and blood counts must be sought for without delay. In our study, pallor was the most common physical finding which was present in all the cases. Splenomegaly was the next most common finding seen in 28% cases, followed by hepatomegaly in 22% cases, our examination findings were in concordance with the other studies (Table-V).

Table V- Comparison of few other studies on pancytopenia with present study.

Study	No. of Cases	Age range	Commonest age group affected	M:f	Most common presenting features	Physical findings
Khodke et al	50	3-69 Years	12-30 Years	1.3 : 1	Fever (40%), Weakness (30%)	Pallor (100%) Splenomegaly (40%) Hepatomegaly (38%)
Ishtiaq et al	100	12-82 Years	-	1.12:1	Fever (59%). Bleeding manifestation (33%), Diarrhea (22%)	Pallor (100%) Splenomegaly (34%) Hepatomegaly (24%)
Niazi and Raziq	89	1-75 Years	21-30 Years	1.7:1	Weakness (68.2%), Fever (47.7%), Bleeding (33.7%)	Pallor (98.8%) Splenomegaly (24.7%) Hepatomegaly (32.5%)
Hamid et al	75	3-85 Years	16-30 Years	1.03:1	Fever (86.7%), Fatigue (76%), Dizziness (64%)	Pallor (100%) Splenomegaly (48%) Hepatomegaly (21.3%)
Tilak and Jain	77	5-70 Years	< 20 Years	1.14 : 1	-	Pallor (100%) Splenomegaly (49.3%) Hepatomegaly (41.5%)
Present study	50	6 months- 60 years	11-20 Years	1.08:1	Fever (72%) Weakness (38%) Increasing paleness (32%)	Pallor (100%) Splenomegaly (28%) Hepatomegaly (20%)

Imbert et al. reviewed 213 adult cases of pancytopenia in France.[9] Malignant myeloid disorders (acute myeloid leukemias, myelodysplastic syndromes, acute myeloid disorders with myelofibrosis) represented 42% of the cases and various malignant lymphoid disorders 18%. Aplastic anemia was diagnosed in 10% of the cases, vitamin deficiencies accounted for 7.5% and non-hematological pathology 10% of the cases. Hamid et al. studied 75 cases of pancytopenia in Yemen, the most common causes of pancytopenia were malaria and hypersplenism in more than 45% of patients, followed by megaloblastic anemia in 14.7%, and aplastic anemia and acute leukemia in 13.3% each.[7] The other causes as determined in the study were myelodysplasia in 8.0%, myelofibrosis in 4.0% and iron deficiency anemia in 1.3%. Khunger et al. in their study of 200 cases of pancytopenia in New Delhi found that megaloblastic anemia was the most common cause of pancytopenia accounting for 74% cases, followed by aplastic anemia (14%), subleukemic leukemia (5%). Myelodysplastic syndrome was found in 2 % of the cases.[10] Tilak and Jain studied 77 cases with pancytopenia in Chandigarh, it was found that the most common cause of pancytopenia as revealed by bone marrow examination was megaloblastic anaemia (68%) followed by aplastic anaemia (7.70%).[11] Khodke et al. carried out a study in 50 patients of pancytopenia and revealed that megaloblastic anemia was the most common cause accounting for 44 % of the cases. Aplastic anemia and kala azar were the next most common causes accounting for 14 % cases each.[5] In our study, megaloblastic anemia was the most common underlying pathology seen in 29 out of 50 cases (58%). *Pancytopenia occurs in severe megaloblastic anemia as the substrates for nuclear synthesis are reduced and there is ineffective hematopoiesis of all the cell lineages.* In fifteen of these cases there was co-existing iron deficiency. The next most common cause was aplastic anemia seen in 10% cases followed by hypersplenism in 6% cases. Leukemia, myelodysplastic syndrome and tuberculosis accounted for 4% each. Our study is in concordance with those of Khunger et al., Tilak and Jain, and Khodke et al. conducted in India. *The high incidence of megaloblastic anemia can be attributed to the high prevalence of vitamin deficiencies in our country. The patients in our study belonged to the lower socio-economic strata, putting them at higher risk of severe nutritional deficiencies.*

Hypersegmented neutrophils and macro-ovalocyte are considered to be strong markers of megaloblastic anemia.[12] In our study they were exclusively seen in cases of megaloblastic anemia and were not found in any other case. Savage et al. also reported in their study that hypersegmented neutrophils were noted in the blood films of 35 (89.7%) out of the 39 patients with megaloblastic anemia but absent in the other patients.[13] They suggested that hypersegmented neutrophils have a high specificity and predictive value for megaloblastic anemia. Hence our study is in concordance with this finding, however the percentage of cases

of megaloblastic anemia showing hypersegmented neutrophils is lower in our study (13.7%). Macroovalocytosis in the peripheral blood smear is also considered to be a marker for megaloblastic anemia. Tilak & Jain and Khodke et al., in their study do not mention this important finding while discussing the peripheral blood picture of pancytopenic patients with megaloblastic anemia. Salvage et al., have said in their study that macroovalocytes are sensitive for megaloblastic anemia but not specific. Our study findings agree with this observation since we had 10 (34.4%) out of 29 cases of megaloblastic anemia having macroovalocytes in the peripheral blood and apart from megaloblastic anemia cases they were also found in one case of myelodysplastic syndrome and one case in which diagnosis could not be established. Nucleated erythroblasts in the peripheral smear were present in 20.7% cases in our study as compared to 9.1% and 24.5% reported by Khodke et al., and Tilak & Jain respectively. Reticulocytosis was reported by Khodke et al., in 9.1 % cases and Tilak & Jain in 9.4% cases. Bain has said that an increased reticulocyte count in cases of anemia can be a misleading indicator of bone marrow output and suggested that a reticulocyte production index is a more accurate predictor of bone marrow regeneration in such cases.[14] *Hence, we used reticulocyte production index in our study and found that no case of megaloblastic anemia has increased reticulocyte production index, even though reticulocytosis was present in 17.2% cases of megaloblastic anemia.*

In our study involving 50 cases of pancytopenia, bone marrow aspirate was representative in 42 cases (84%) of the cases and failed to yield a representative sample in eight (16%) cases. Out of the forty two cases with representative bone marrow aspirates, a diagnosis could be made in forty (95.2%) cases. Hence, the success rate of obtaining a representative sample was comparable to that of Jha et al.,[15] but we had a higher rate of identifying the underlying etiology when a representative sample was obtained. Keeping in mind the high possibility of diagnosis being made from a bone marrow aspirate smear, the importance of obtaining a proper bone marrow sample in cases of pancytopenia can be stressed. Imbert et al., in their study said that a bone marrow aspirate was adequate for diagnosis in 55% of the cases and a bone marrow biopsy was necessary in 30% cases. In our study, bone marrow aspirate was successful in diagnosis of the underlying pathology in 40 (80%) cases. Hence, bone marrow aspirate when properly obtained and examined is sufficient to establish the diagnosis in majority of the cases and a bone marrow biopsy is not required as a routine investigation in cases of pancytopenia. A biopsy must however be obtained in cases where the bone marrow aspirate fails to yield a representative sample, or in cases such as aplastic anemia.

Studies done on cases of pancytopenia have not mentioned the importance of bone marrow imprint smears in the workup of cases. In three cases of pancytopenia in our study where the

aspirate failed to yield any material, a biopsy was obtained and before putting the biopsy sample into the formalin for fixation, it was rolled on a clean glass slide. Hence imprint smears of the biopsy were obtained. They were air dried and stained with hematoxylin and eosin. *Imprint smears were found to be extremely valuable in the absence of a bone marrow aspirate for establishment of diagnosis.* They were helpful in identifying a case of leukemia and megaloblastic anemia within hours of obtaining the sample. The time taken for processing the biopsy requires more than a day because of the time required for fixation and decalcification. In such scenarios, the imprint smears serve as a good alternative for a rapid diagnosis without compromising the diagnostic accuracy. However, it must be kept in mind that imprint smears are only an adjunct and not a substitute for the biopsy.

CONCLUSION

Most important cause of pancytopenia is nutritional deficiency megaloblastic anemia in Indian population (District- Aligarh, State- Uttar Pradesh). This is treatable with folic acid and vitamin B_{12} therapy, hence a life threatening condition of pancytopenia becomes curable with establishment of correct diagnosis after bone marrow examination. Other causes of pancytopenia in children were drug induced aplastic anemia, hypersplenism, leukemia and tuberculosis while in adults myelodysplastic syndrome and leukemia were more common. In adults pancytopenia precedes myelodysplastic syndrome and "smouldering" leukemias (i.e aleukemic or subleukemic leukemia). Reticulocyte production index is a significant and better marker of bone marrow status.

REFERENCES

1. Subbarayappa BV. The roots of ancient medicine: An Historical Outline. J Biosci 2001 Jun; 26:135- 43.
2. Orkin S H. Hematopoiesis: how does it happen? Current Opinion in Cell Biology 1995; 7: 870-7.
3. Shirlyn B. Structure and Function of Haematopoietic System. In: Annette I. Schlueter editors. McKenzie Clinical Laboratory Haematology. New Jersey: Pearson Education publishers; 2004. pp. 43- 6.
4. Kar M and Ghosh A. Pancytopenia. JIACM 2002; 3: 29-34.
5. Khodke K, Marwah S, Buxi G, Yadav RB, Chaturvedi NK. Bone morrow examination in case of pancytopenia. Journal Indian Academy of Clinical Medicine 2001;2:55-9.
6. Niazi M and Raziq F. The incidence of underlying pathology in Pancytopenia - an experience of 89 cases. J Postgrad Med Inst 2004; 18:76-9.

7. Hamid GA, Shukry SAR. Patterns of pancytopenia in Yemen. Turk J Hematol 2008; 25:71-4.
8. Ishtiaq O, Baqai HZ, Anwer F, Hussain N. Patterns of pancytopenia patients in a general medical ward and a proposed diagnostic approach. J Ayub Med Coll Abbottabad 2004 ; 16: 8-13.
9. Imbert M, Scoazec JY, Mary JY, Jouzult H, Rochant H, Sultan C. Adult patients presenting with pancytopenia: a reappraisal of underlying pathology and diagnostic procedures in 213 cases. Hematol Pathol 1989; 3:159-67.
10. Khunger JM, Arulselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia--a clinico haematological study of 200 cases. Indian J Pathol Microbiol 2002;45:375-9.
11. Tilak V and Jain R. Pancytopenia-a clinico-hematologic analysis of 77 cases. Indian J Pathol Microbiol 1999 ;42:399-404.
12. Andres E, Affenberger S, Zimmer J, Vinzio S, Grosu D, Pistol G et al. Current hematological findings in cobalamin deficiency. A study of 201 consecutive patients with documented cobalamin deficiency. Clin Lab Haem 2006; 28:50–6.
13. Savage DG, Allen RH, Gangaidzo IT, Levy LM, Gwanzura C, Moyo A et al. Pancytopenia in Zimbabwe. Am J Med Sci 1999; 317: 22-32.
14. Bain BJ. Blood cells-A Practical Guide. Blackwell Publishing 4th Ed. Quantitative changes in blood cells.Ch.6, Pg. 244.
15. Pathak R, Jha A, Sayami G. Bone marrow examination in cases of pancytopenia. J Nepal Med Assoc 2008; 47:12-17.