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PANCYTOPENIA;
STUDY OF 40 PATIENTS AT CMC HOSPITAL LARKANA.

DR. AZIZULLAH JALBANI, MCPS, FCPS
Assistant Professor Medicine
Chandka Medical College (CMC) & Hospital Larkana

DR. IMDAD ALI ANSARI, FCPS
Assistant Professor Medicine
Chandka Medical College (CMC) & Hospital Larkana

DR. AFTAB HUSSAIN SHAH, FCPS
Associate Professor Medicine
Chandka Medical College (CMC) & Hospital Larkana

DR. Kouro Mal Gurbakhshani, FCPS
Assistant Professor Medicine
Chandka Medical College (CMC) & Hospital Larkana

DR. Mumtaz Chutto, FCPS
Assistant Professor Medicine
Chandka Medical College (CMC) & Hospital Larkana

DR. Ghulam Akbar Solangi, FCPS
Professor of Medicine
Chandka Medical College (CMC) & Hospital Larkana

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ABSTRACT... Introduction: Pancytopenia is said to exist in an adult when the hemoglobin level is less than 13.5gm/dl in males and 1l.5gm/dl in females, white cell count less than 4xl0^{9}IL and platelet count less than 150x10^9/L^1. The causes of pancytopenia are aplastic anemia, sub-leukemic leukemia, myelodysplasia^2 multiple myeloma, nutritional deficiencies leading to megaloblastic anemia, hypersplenism, paroxysmal nocturnal hemoglobinuria, AIDS, infections such as miliary tuberculosis, leishmaniasis, brucellosis etc. **Objectives:** To determine the frequency of various causes of pancytopenia in gender at Chandka Medical College, Larkana. **Study design:** Cross Sectional Study. **Setting:** OPD & Medical Ward-II, Chandka Medical College Hospital Larkana. **Duration with dates:** 01 years study from February 2007 to February 2008. **Subject and methods:** Patients of either sex, who attended medical ward-II of Chandka Medical College Hospital Larkana, either as inpatient or out patient department, from February 2007 to February 2008 and fulfilled the inclusion criteria, were included in this study. Pancytopenia was considered as hemoglobin value less than 13.5gm/dl in males or 11.5gm/dl in females, a white cell count less than 4x10^9/L and Platelets count less than 150x10^9/L. Patients of less than 12 years and pregnant females were excluded from the study. **Result:** Out of 40 patients, 29 (72.5%) were males and 11 (27.5%) were females. Female to male ratio was 1:2.6. The mean ages of males were 29.10 ± 16.46 years whereas of females 36.14 ± 15.6 years (P = 0.22). Aplastic anemia was the most common pathology encountered and was diagnosed in 13 cases (31.5%), followed by hypersplenism 09 (22.9%), Megaloblastic anemia 06 (15%) and hodgkin's lymphoma in 04 (10%) cases. Other less common causes detected were multiple myeloma 02 (5%), drug induced 02 (5%) and malaria, milliary tuberculosis, myelodysplastic syndrome, hemophagocytic syndrome was 01 (2.5%) case in each. Conclusion: We concluded that aplastic anemia was the most common cause in our patients and more than 2/3rd patients were young males. We think the causes of aplastic anemia in this study may be misuse of drugs, kushtas, exposure to chemicals and viral infections.

Key words: Aplastic anemia; Hypersplenism; Megaloblastic anemia; Hodgkin's lymphoma; Pancytopenia.

INTRODUCTION

Pancytopenia is a laboratory diagnosis characterized by anemia, leucopenia and thrombocytopenia in the peripheral blood. It is a common clinical problem with an extensive differential diagnosis. There are many causes of Pancytopenia, some are curable for which an early and prompt diagnosis is required.

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Correspondence Address:
Dr. Azizullah Jalbani, MCPS, FCPS
Assistant Professor Medicine
Chandka Medical College (CMC) & Hospital Larkana
azizjalbani@yahoo.com

In certain circumstances complete cure is not possible, even in these cases early diagnosis and supportive treatment can improve the quality of life by decreasing morbidity and mortality.

Pancytopenia is said to exist in an adult when the hemoglobin level is less than 13.5gm/dl in males and 1l.5gm/dl in females, white cell count less than $4x10/L^9$ and platelet count less than $150x10^9/l$.

The causes of Pancytopenia are aplastic anemia, sub-leukemic leukemia, myelodysplasia[2] multiple myeloma, nutritional deficiencies leading to Megaloblastic anemia[3], hypersplenism, paroxysmal nocturnal hemoglobinuria, AIDS, infections such as miliary tuberculosis, leishmaniasis, brucellosis etc.

Patients mostly present with history of bleeding disorders such as epistaxis, hematmesis, melena and bleeding from gums, due to thrombocytopenia. Patient may present with recurrent episodes of chest infection, mouth ulcers, fever or skin infection due to neutropenia or may present with signs and symptoms of anemia.

A detailed history, physical examination, and review of the blood film remain fundamental to diagnosis. Profound neutropenia and thrombocytopenia associated with bleeding and sepsis most often reflect underlying marrow aplasia or leukemia, whereas glossitis, diarrhea, and paresthesiae associated with megaloblastic anemia. In pancytopenic patients with neutrophil hypersegmentation or abnormalities of erythrocyte morphology with low serum Vitamin B_{12} and folate levels confirms megaloblastic anemia. Blasts are seen on blood film of most patients with acute leukemia. Hypogranulated and segmented neutrophils often indicates myelodysplastic syndrome.

In aplastic anemia, spleen, liver, and lymph nodes are usually not palpable if these are found then the diagnosis of aplastic anemia is doubtful. Other laboratory investigations are also helpful such as reticulocyte count, serum B12 or R.B.C folate level and urine for bence Jones proteins but the most important diagnostic investigation is bone marrow aspiration and trephine biopsy[3].

OBJECTIVES

To determine the frequency of various causes of pancytopenia in gender at Chandka Medical College, Larkana.

MATERIAL AND METHODS

Patients of either sex, those attended medical ward-II of Chandka Medical College Hospital Larkana, either as in patient or out-patient department, from February 2007 to February 2008 and fulfilled the inclusion criteria, were included in this randomized, Observational study.

Pancytopenia was considered as hemoglobin value less than 13.5gm/dl in males or 11.5gm/dl in females, a white cell count less than $4x10^9/L$ and Platelets count less than $150x10^9/L$.

Patients less than 12 years of age and pregnant females were excluded from this study.

All patients were thoroughly evaluated and emphasis was given on history of exposure to chemical agents, radiation either by occupational, accidental or by treatment. History of recent viral infection, fever, weight loss, bleeding from gums or else and blood transfusion was also noted.

Relevant points on physical examination were pallor, mouth ulcers, splenomegaly, hepatomegaly, lymphadenopathy and bone tenderness.

Following history and clinical examination protocol, patients were graded into mild, morerate and severe pancytopenia as per severity Criteria:[4].

Mild

Hemoglobin value less than 8gm/dl, polymorphonuclear cell count more than $2.0.5x10^9/L$ and platelets more than $20x10^9/L$.

Moderate

Hemoglobin value less than 7gm/dl. Polymorphonuclear

cell counts less than $0.5x10^9$/L and platelets less than $20x10^9$/L.

Severe

White cell counts less than $0.2x10^9$/L and platelets less than $10x10^9$/L.

Following diagnostic criteria was used for hypersplenism:[5]

1. Presence of anemia, leukopenia and thrombocytopenia in peripheral blood.
2. Increased reticulocyte count.
3. Existence of cellular or hypercellular bone marrow corresponding to peripheral cytopenias.
4. Presence of splenomegaly.
5. Response to splenectomy.

Data Analysis

All data were entered and analyzed by SPSS version 15. Discrete variables like Gender, cause of pancytopenia and severity of pancytopenia were presented in percentages where as age was described as mean ± S.D.

RESULTS

Forty patients were included in this study for analysis of various causes of Pancytopenia in relation to age and gender. The patients included 29 (72.5%) were males and 11(27.5%) were females. Female to male ratio was 1:2.6. (Table no: I).

Table-I. Age and sex distribution (n = 40)

SEX	NO. OF CASES	AGE IN YEARS MEAN ± SD
Males	29(72.5%)	29.10 ± 16.46
Females	11(27.5%)	36.14 ± 15.6
Total	40	37.67 ± 17.76
P-Value	-	P = 0.22 (non significant)

The age of patients ranged from 12-70 years. The mean age of females was 29.10±16.46 years (mean ± SD) whereas of females 36.14 ±15.6 years. The age distributions among sex were found statistically non significant (P = 0.22) (Table no: II).

Table-II. Age and sex distribution (n = 40)

Cause	Male	Female	Both	%age	95% Confidence Interval
Aplastic anemia	10	3	13	32.5	19.41-48.03
Hypersplenism	4	5	9	22.5	11.56-37.29
Magaloblastic Anemia	6	0	6	15	6.31-28.61
Non-Hodgkin'sl Ymphoma	3	1	4	10	3.25-22.38
Myelodysplastic Syndrome	2	0	2	5	0.84-15.55
Durg Induced	2	0	2	5	0.84-15.55
Multiple Myeloma	1	0	1	2.5	0.12-11.71
Malaria	0	1	1	2.5	0.12-11.71
Military Tuberculosis	0	1	1	2.5	0.12-11.71
Hemophagocytic Syndrome	1	0	1	2.5	0.12-11.71

Overall the most common cause of Pancytopenia was aplastic anemia, which was seen in 13 (32.5%) cases. Hypersplenism was present in 09 (22.9%) cases, Megaloblastic anemia in 06 (15%) cases and non Hodgkin's lymphoma in 04 (10%) cases. Other less common causes were Multiple myeloma 02 (5%), chemotherapy induced 02 (5%), Malaria, Miliary tuberculosis, Myelodysplastic syndrome and

Haemophagocytic syndrome was 01 (2.5%) case each.

Out of 13 patients of aplastic anemic 10 (76.92%) males and 03 (23.08%) were females. The females to male ratio was 1:3.33. Mean age in males was 19.3 years in females was 49 years.

Only 02 (15.4%) patients of aplastic anemia had history of taking drugs from general practitioners or Hakeems. The exact nature of drugs was not known.

Hypersplenism was diagnosed in 09 patients, all had decompensated cirrhosis of liver. Among those 5 (55.55%) cases were females and 4 (44.44%) were males. Male to female ratio was 1:1.25. The mean age in males was 55.5 years and in females 47.6 years. Out of these 09 cases of Cirrhosis, 4 (44.4%) were Hbs Ag reactive, 2 (22.2%) HCV antibody reactive and 01 (11.2%) case had Wilson's disease. But in remaining 2 (22.2%) cases, we were unable to detect the exact cause.

04 (66.66%) out of 06 patients with Megaloblastic anemia had evidence of vitamin B12 deficiency and remaining 02 (33.33%) had folic acid deficiency. The average deficiency level of vitamin B12 was 140 pg per ml, (normal range was 200 to 950 pg per ml) and folic acid was below 120 ng per ml. (normal range was 175 to 700ng per ml). The exact cause of deficiency of these vitamins was not detected but response to treatment with vitamin B 12 and folic acid was documented. All these patients were males. The mean age was 30.16 years.

Among 04 cases of non-Hodgkin's lymphoma, 3 (75%) were males and 01 (25%) was female. Female to male ratio was 1:3. The mean age was 22.5 years.

Regarding the severity of Pancytopenia, in relation to etiology. Among 13 patients of aplastic anemia 06 (46.15%) were severe, 04 (30.76%) were inoderate and 03 (23.07%), were mild in severity.

Out of 09 patients with splenomegaly and hypersplenism, 05 (62.5%) were severe, 01 (12.5%) & 03 (37.5%) were moderate and mild respectively.

All 06 patients of Megaloblastic anemia were males. Out of these, 04 (66.66%) patients had severe Pancytopenia and remaining 02 (33.33%) had of moderate severity. Statistically results are non significant (P > O10, chi-square = 4.5) (Table no: III). The severity of Pancytopenia for a particular cause showed statistically non-significant results. However ignoring the individual causes, the overall severity showed statistically significant results with P < 0.001, chi-square =12.90. (Table no: III).

Table-III. Severity of pancytopenia (n = 40)

SEVERITY	AA	HS	MG	NHL	OTHERS	TOTAL
	n=13	n=9	n=6	n=4	n=8	
Mild	3(23.07%)	3(33.33%)	1(16.7%)	2(50%)	1(12.5%)	10(25%)
Moderate	4(30.76%)	1(11.11%)	1(16.7%)	0%	2(25%)	8(20%)
Severe	6(46.15%)	5(55.56%)	4(66.69%)	2(50%)	6(46.15%)	22(55%)

AA=Aplastic anemia HS=Hypersplenism MG=Megaloblastic anemia NHL= Non-Hodgkin's lymphoma

The clinical presentations of these cases were as follows: Palpitation and weight loss in all cases (100%), fever 28(70%), bleeding manifestations such as epistaxis, hematemesis, melena 28 (70%) and diarrhea 11 (27%) cases and History of repeated episodes of mouth ulcers in (17%) cases, 05 (12.5%) paients had history of sore throat.

All patients were anemic (100%), 28 (70%) were febrile, 15 (37.5%) and 14 (35%) patients had splenomegaly and

hepatomegaly respectively. The other phyical findings were noted as purpuric rashes 08 (17.5%), mouth ulcers 07 (17.5%), lymphadenopathy 06 (15%), jaundice 04 (10%). Gingival hypertrophy were detected in 03 (7.5%) patients.

DISCUSSION

This study was conducted on 40 Pancytopenic patients. This risk was more in young people with age ranges from 12 - 45 years. Aplastic anemia and hypersplenism were responsible for more than 50% of causes in this study. The prevalence among males was 29 (72.5%), and females 11 (27.5%), with females to male ratio was 1:2.6. This is comparable with study conducted in Pakistan, in which 58% were males and 42% females and the ratio was 1:1.38.[6] (Table no I).

As in our society the males are the earning members of family, work and uses to fields, industries are more exposed to radiation, agricultural pollution, such as use of insecticides, pesticides or industrial toxins and environmental pollution, that may be the reason, that prevalence of Pancytopenia was more in males. The smaller percentage of females in this study was may be either because total number of patients was small or females are mostly reluctant to take medical advice earlier.

Because of multi system involvement in Pancytopenia, the clinical manifestations are protean. The presenting symptoms and signs are non specific and dominated by infections due to immunocompromised state. The common presenting symptoms in my study were palpitation and weight loss found in all cases (100%). Fever and bleeding manifestations were present in (70%), diarrhea (27%), Mouth ulcers, sore throat was also present. All patients were anemic; (70%) were febrile, hepatosplenomegaly, lymphadenopathy, and jaundice as well as gum hypertrophy were also detected. The results regarding clinical manifestations were statistically significant.

Clinical features are comparable with similar studies conducted in Pakistan by Musrat Niazi and Fazli Razia 2004[6], Waseem Iqbal 1998[8] and Mobina Ahsan Dodhy study[11].

Aplastic anemia

Aplastic anemia was the most common cause of Pancytopenia in our patients which accounted for 32.5%. Among them males were 0l (76.92%) and females were 03 (23.08%) Female: Male ratios were 1:3.33. The incidence of aplastic anemia was 20% in Naeem Khan et al study in 2001[7], Waseem Iqbal 1998[8] had reported 21%. In other studies conducted in Pakistan by Khalid Hussain et a1 1994[9] the female to male was 1: 3.3 and M. Anwar et at 1990[100] the ratio was 1:2.6 these are comparable to our study. An other study carried out in India in 1992[7] by Varm and Dash on 202 Pancytopenic patients, the aplastic anemia accounted for 40.6% 31. It is therefore concluded that in India and Pakistan had more or less similar occurrence of aplastic anemia.

The age in our study ranged between 12-70 years. The mean age of males was 29.10±16.46 years (mean ± S.D), where as females 36.14±15.6 years. Over all age in males ranges between 12-30 years that comprises of 76.92% of aplastic anemia, that means younger patients were more commonly affected in this study. Similar study conducted in Zimbabwe by David et al in1997, showed 62.9% prevalence of aplastic anemia below the age of 21 years. 103 Other studies showed that disease is more common in West in elderly population with equal sex distribution[10].The etiology of aplastic anemia differs according to the prevalence of various factors. In Western countries majority of cases are idiopathic and disease affects older people. In our study out of 13 patients of aplastic anemia only 2 (15.4%) of them had the history of unknown drugs from general practitioner or Hakeems. we think the causes in our population are:

1. Haphazard or misuse of drugs, Kushtas by Hakeems and general practitioners without knowing their side effects.
2. Careless handling and exposure to various chemicals in our industries.
3. Over exposure to hydrocarbons and fuels from motor vehicles. Recently introduced insecticides and pesticides to protect crops may also cause toxic effects.

4. Viral illnesses are a major problem. In this study, patients with aplastic anemia had higher incidence of fever, bleeding disorders and anemia.

CONCLUSION

Pancytopenia basically is a laboratory diagnosis but it may be suspected clinically. We observed that the number of male sufferers were more as compared to females. Majority of our patients were younger or middle aged, although no age is exempted from pancytopenia. In this limited study, aplastic anemia, hypersplenism and megaloblastic anemia comprised about 70% of cases, presented to us.

We concluded that bone marrow aspiration and Trephine biopsy is the hallmark for the diagnosis of cause of pancytopenia. It is easy and safe procedure and can be done even in severe thrombocytopenia without any complications.

RECOMMENDATIONS

1. Treatment of neutropenic patients should be started as soon as possible.
2. Bone marrow examination should be done immediately to find out the cause and treat accordingly.
3. Preventive measures should be encouraged for those who are working in the fields, using pesticides and insecticides or those who are working in Chemical industries.
4. Proper measures should be taken during preparation of food so that over cooking must be avoided and knowledge should be given for balanced diet to prevent nutritional deficiencies.
5. Quackery should be banned so that misuse of drugs can be avoided.
6. Large-scale study should be planned so that exact causes and incidence of Pancytopenia can be identified.

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