FREQUENCY OF APLASTIC ANEMIA AND MEGALOPLASTIC ANEMIA AS CAUSES OF PANCYTOPENIA IN ADULTS

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ABSTRACT

Introduction: Pancytopenia is a common problem in clinical and hematological practice. The clinical manifestations are usually attributable to anemia, leucopenia or thrombocytopenia, which may manifest clinically as pallor, infections or bleeding problems respectively.

Objective: To determine the frequency of aplastic anemia and megaloblastic anemia in patients with pancytopenia.

Material and Methods: This descriptive cross sectional study was conducted in Medical Department of MTI, LRH from 15th January 2016 to 14th September 2017. We enrolled total of 363 patients. All admitted patients with pancytopenia, age 18-60 years and both gender were included while patients receiving chemotherapy and radiotherapy, genetic or constitutional pancytopenia and history of blood transfusion in recent past (within one week) were excluded.

Results: We enrolled a total of 363 patients among them 138(38%) patients were males while 225(62%) patients were females and mean age was 42 ± 15.84. Forty percent patients had megalobastic anemia while 23% patients had aplastic anemia.

Conclusion: We conclude that the frequency of megaloblastic anemia was 40% and aplastic anemia was 23% in patients with pancytopenia.

Key Words: Pancytopenia, Meglaboblastic anemia, Aplastic anemia

INTRODUCTION

Pancytopenia is critical clinical presentation characterized by decrease in all three formed blood elements (Red Blood Cells, Leukocytes, platelets).[1] Pancytopenia is not a disease entity but a constellation of symptoms and investigations that may be caused by diverse disease processes. The presenting complaints such as pallor, recurrent infections and bleeding tendency are attributed to anemia, thrombocytopenia or leukopenia. These diseases may involve the bone marrow primarily or result in peripheral destruction of blood elements due to hypersplenism, autoimmune process or infection.[2] Various clinical conditions presenting as pancytopenia include Aplastic Anemia (AA), Megaloblastic Anemia (MA), Hypersplenism, Visceral Leishmaniasis, Acute Leukemia, Hairy cell Leukemia, Osteoporosis, Malaria, Myelodysplastic Syndrome etc.[3] Pancytopenia accounts for 3.57-12.6% of hospital admissions in different cities of Pakistan.[4]

AA is haemopoetic stem cell pathology that results in hypocellular bone marrow leading to pancytopenia. Most cases AA are acquired while unusual inherited forms are also reported. The pathogenesis of acquired AA is autoimmune in most cases; activated lymphocytes results in the destruction of haemopoetic stem cells.[5] The immune response is suggested to be triggered by environmental agents like medication e.g. methotrexate, chloramphenicol, and viruses like hepatitis C virus (HCV) and parvovirus 19 still most cases are classified as idiopathic.[6,7,8]

Megaloblastic anemia (MA) includes heterogeneous group of disorders that present with common clinical and pathological features. The etiology of MA is diverse but a common basis is abnormal DNA production. Abnormalities in Vitamin B12 and folic acid metabolism leads to the attenuated synthesis of DNA.[9] Deficiency of either of these vitamins leads to

asynchronized maturation of nucleus and cytoplasm of rapidly regenerating cells, secondary to to abnormal DNA synthesis. The bone marrow becomes hyper cellular as hemopoetic stem cells accumulate while apoptosis of more mature cells results in pancytopenia.[10]

Mussarrat Niazi and Fazl-i-Raziq investigated etiology of 89 cases of pancytopenia and the most common etiologies were reported as A.A (38.3%), M.A (24.7%) hypersplenism (16%) and acute leukemia(13.6%).[2] Another study conducted at Medical Unit II, Holy Family Hospital, Rawalpiandi common causes of pancytopenia found in order of frequency were M.A, hypersplenism and A.A.[11]

The aim of this study was to determine the fre-

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quencies of aplastic anemia and megaloblastic anemia in patients with pancytopenia.

MATERIAL AND METHODS

This descriptive cross sectional study was conducted in Medical B Unit MTI LRH from 15th January 2016 to 14th September 2017. Sample size was calculated by applying to WHO software for sample size estimation. Sample size was 363 patients, calculated for 38% estimate for aplastic anemia in total pancytopenia patients, 95% confidence interval and 5% margin of error. Pancytopenia was defined as simultaneous occurrence of Hematocrit of <0.35L/L in female and <0.40in male, Leucopenia, total leukocyte count <3.5 $x10^{-9}$/L, Platelets <150$x10^{-9}$/L.[2] Aplastic anemia was defined as pancytopenia characterized by hypocellular bone marrow (<30%). Magaloblastic Anemia was defined as hyper segmented neutrophils and raised MCV>96fl on blood film, serum B 12 level <100 pg/ml and /or red cell folate level <150ng/ml.[11] We included All admitted patients with pancytopenia to Medical Department of Lady Reading Hospital Peshawar aged 18-60 years. We excluded patients receiving chemotherapy and radiotherapy, genetic and constitutional pancytopenia, History of blood transfusion in recent past (within one week). These factors may act as confounders and make the study results biased if included in study. After taking consent we clinically evaluated the patients. Peripheral smear, bone marrow biopsy, vitamin B12 and serum folate levels were done in pathology department of MTI LRH. Data was recorded in study proforma.

Data was analyzed in SPSS version 18. Frequency and percentages were calculated for categorical variables like aplastic anemia, megalobastic anemia, gender. Aplastic anemia and megalobastic anemia was stratified among age and gender to see the effect modification. Post stratification chi square test was used keeping P≤0.05 as significant value. Date was expressed in the form of tables and Charts.

RESULTS

We enrolled a total of 363 patients in our study among them 138(38%) patients were males while 225(62%) patients were females (Chart No 1) mean age was 42 years with standard deviation as ± 15.84 (table No 1). We diagnosed megalobastic anemia in 145 (40%) patients and 83(23%) patients had aplastic anemia while 37% patients had other diagnosis (Chart No 2).

Stratification of aplastic anemia and megalobastic anemia with respect to age (Table No, 2, 3). And gender (Chart No 3) was not significant.

DISCUSSION

Pancytopenia is not an uncommon hematological problem encountered in clinical practice and should be

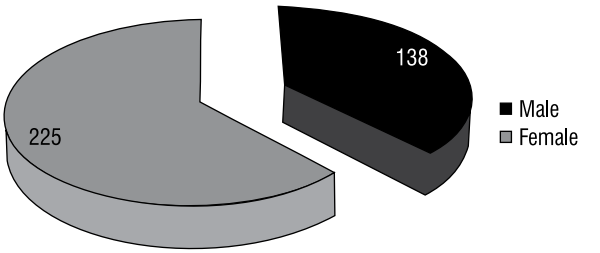

Chart No 1: Gender Distribution (n=363)

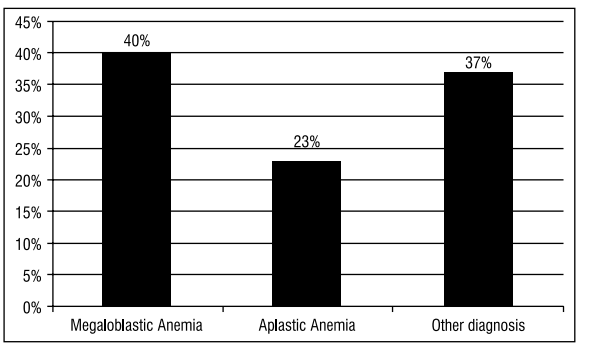

Chart No 2: Frequencies of MEGALOBASTIC ANEMIA and ASPLSTIC ANEMIA in PANCYTOPENIA Cases(n=363)

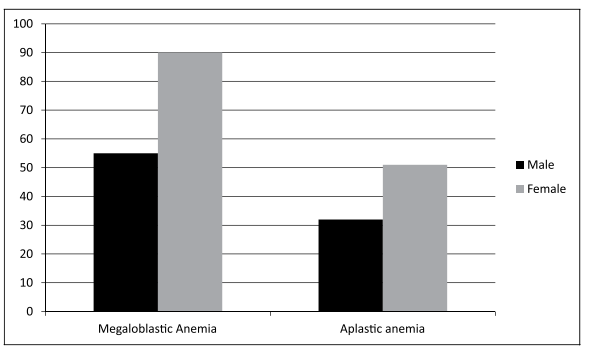

Chart No 3: Stratification of Megaloblastic ANEMIA and ASPLSTIC ANEMIA with Respect to Gender Distribution (n=363)

Table No 1. Age Distribution (n=363)

Age	Frequency	Percentage
18-30 Years	43	12%
31-40 Years	73	20%
41-50 Years	116	32%
51-60 Years	131	36%

suspected on clinical grounds when a patient presents with unexplained pallor, prolonged fever, and tendency to bleed.[4] In our study forty percent patients had megalobastic anemia. Similar results are reported by other local and international researchers i.e. megalobastic anemia accounted for approximately 41.9%, 39%, 30%, and 25% cases of pancytopenia in Makheja KDM et al, Ishtiaq O et al, Jha A et al, and Niazi M et al respective-

Table no 2. Stratification of megalobastic anemia with respect to age distribution (n=363)

MEGALOBASTIC ANEMIA	18-30 Years	31-40 Years	41-50 Years	51-60 Years	Total
Present	17	29	46	53	145
Absent	26	44	70	78	218
Total	43	73	116	131	363

Chi square test was applied in which p value was 0.9990

Table no 3. Stratification of asplstic anemia with respect to age distribution (n=363)

ASPLSTIC ANEMIA	18-30 Years	31-40 Years	41-50 Years	51-60 Years	Total
Present	10	17	26	30	83
Absent	33	56	90	101	280
Total	43	73	116	131	363

Chi square test was applied in which p value was 0.9989

ly.[12,13,14,2] Tariq Aziz et al, Iqbal et al and Qazi et al are comparable series of pancytopenia, all of them reported Megaloblastic anemia to be the most common cause of pancytopenia.[15,16,17] Vitamin B12 and folate deficiency in Pakistan can be explained by poor nutrition and various chronic gastrointestinal diseases like parasitic infections, chronic diarrhea and malabsorption states.[4]

We found that Aplastic Anemia accounted for 23% of cases of pancytopenia. Approximately similar results are reported by Jha A et al, Shazia M et al and Makheja KDM et al stating that Aplastic Anemia caused pancytopenia in 25.47%, 23.9% and 19.4% cases respectively. [13,4,12] Aplastic anemia is more common in eastern population. Environmental factors (exposure to toxic chemicals) rather than genetic factors are thought to be responsible for this increase incidence of AA, this hypothesis is supported by the fact that immigrants to western countries have similar incidence of AA as western population. Studies from Thailand implicated pesticide exposure as cause of AA, same may be true for Pakistani population.[2]

Our study results showed that peak incidence of Megaloblastic anemia in middle age group (41 to 50 years) with an equal gender distribution which is compareable with other national studies.[18,19] Studies from Nepal and Philipines concluded that Aplastic anemia was more commonly diagnosed in males than females, this finding may be due to higher risk of pesticides exposure and occupational exposure to chemicals, both are among the leading causes of Aplastic anemia in these countries.[19,20] This is contrary to our study in which males and females were equally affected with Aplastic anemia. This can be explained in part by the fact that easy availability of over the counter medications to both genders and Pakistan is an agricultural country so both genders are exposed to pesticides.[2] Moreover these variation in the frequency of etiology and other features among the studies can be explained by the wide spectrum of etiologies or disorders behind pancytopenia.

CONCLUSION

We conclude that megaloblastic anemia (40%) was more common than aplastic anemia (23%) in patients presenting with pancytopenia, our results are comparable with national and international studies. So both these entities should be considered while evaluating pancytopenia patients in Pakistan. We recommend nutritional assessment and prompt institution of nutritional supplements especially vitamin B12 and folate to prevent megaloblastic anemia in low socioeconomic population of Pakistan. We also recommend limiting the exposure to toxic chemicals and pesticides to prevent aplastic anemia.

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