Original article:

A Clinicohematological study of Leucopenia

[1]**Chitra Netare**, [2]**Reshma Mankar,**

[1]Professor, Department of Pathology, SMBTIMRSC, Dhamangaon, Nasik

[2]Assistant Professor, Department of Pathology, SMBTIMRSC, Dhamangaon, Nasik

Correspondence: Dr Chitra Netare

Abstract

A two year cross-sectional study was carried out to ascertain the clinicohematological evaluation of leucopenia at SMBTIMRSC, Dhamangaon, Nasik, Maharashtra. 400 cases of leucopenia were selected with M: F ratio 0.84:1 and age range of 3-70 years. Maximum cases were between 20-40 years age group. Incidence of various etiologies of leucopenia in descending order were typhoid fever(78;19.5%), megaloblastic anemia (65;16.25%), iron deficiency anemia (62;15.5%), dengue fever (62;15.5%), hypersplenism(60;15%), malaria (23;5.75%), acute blood loss(20;5%), tuberculosis(15;3.75%) , HIV(15;3.75%). Low hemoglobin was noted in 88.2% cases in our study and severity of anemia was directly related with leucopenia. Hypersplenism in males and anemia (megaloblastic and iron deficiency anemia) in females had highest incidence of leucopenia in our study. Infectious diseases, anemia, poor sanitation, stagnant water and low socioeconomic status were the factors responsible for leucopenia in our study. Proper education of people at grass root level in rural areas will definitely help to overcome this situation.

Key words: Leucopenia – etiology – clinicohematological study.

Introduction

Leucopenia is an abnormal decrease in the number of leucocytes. Leucopenia with or without anemia or thrombocytopenia is a common problem in clinical practice. The etiology of leucopenia varies from transient self limiting illnesses to serious systemic disease. The present study was done to find the incidence and etiology of leucopenia in rural tertiary care hospital. Identifying the correct etiopathology in a given case is crucial and helps in implementing timely and appropriate treatment.

Materials & Methods

This is a retrospective study done during January 2016 to 2017 in Department of Pathology. A total of 400 cases were selected. Detailed history, clinical examination and hematological investigations were studied in detail. Wherever required, special investigations were done to reach a confirmatory diagnosis. Leucopenia was graded from Grade I to IV: Grade I - WBC count 4000-3000/cu.mm, Grade II - <3000-2000/cu.mm, Grade III- <2000-1000/cu.mm, Grade IV-<1000/cu.mm.

Results

400 cases of leucopenia were studied who had M: F ratio of 0.84:1.0 and age range of presentation was 3-70 years. Low hemoglobin was noted in (88.2%) and thrombocytopenia in (53.0%) cases was noted. Incidence of various etiologies of leucopenia in our study in descending order was as follows: Typhoid fever(78;19.5%), megaloblastic

anemia (65;16.25%), iron deficiency anemia (62;15.5%), dengue fever (62;15.5%), hypersplenism(60;15%), malaria (23;5.75%), acute blood loss(20;5%), tuberculosis(15;3.75%) , HIV(15;3.75%). Typhoid fever (78) with M: F ratio 0.69:1 had Grade I, II, III leucopenia 31, 32, 15 cases respectively who presented as fever, malaise, pain in abdomen, weakness with low hemoglobin in 75.64% cases and thrombocytopenia in 6.4% cases. Blood smear examination showed hypochromic, microcytic anemia in patients with low hemoglobin. Widal test was positive in all cases. Megaloblastic anemia (65) with M: F ratio 0.25:1 had Grade I, II, III leucopenia 24, 20, 21 cases respectively who presented as tingling numbness, weakness. Low hemoglobin was found in all cases and thrombocytopenia in 64.6 % cases. Blood smear examination was diagnostic in 31 cases which showed features of megaloblastic anemia with hypersegmented neutrophils. Vit B12 and folic acid levels were confirmatory. Iron deficiency anemia (62) with M: F ratio 0.29:1 had Grade I, II, III leucopenia 40,22,0 cases respectively who presented as weakness, dysnoea on exertion, easy fatigability, menstrual disturbances. Low hemoglobin was noted in all cases and thrombocytopenia in 38.7% cases. 75 % cases with leucopenia had hemoglobin < 8gm%. Blood smear examination showed hypochromic, microcytic anaemia with anisocytosis and poikilocytosis. Features of hemolysis (polychromasia, nucleated RBC etc.) were noted in those who had Grade III leucopenia. Iron studies were done for confirmation. Dengue fever (62) had M: F ratio 0.67:1 had Grade I,II,II leucopenia 35,26,1 cases respectively who presented as high grade fever , malaise with low hemoglobin in 67.7% cases and thrombocytopenia in all cases. Dengue antigen test was positive in all cases. Hypersplenism (60) with M: F ratio 11:1had Grade I, II, III leucopenia 25,29,6 cases respectively. All cases were males in 30-50 years age group, were chronic alcoholics with decompensated liver disease with low hemoglobin in 91.6% cases and thrombocytopenia in 71.6 % cases. Malaria (23) with M: F ratio 0.64:1 had Grade I,II,II leucopenia 14, 9,0 cases respectively who presented as fever with chills , weakness ,malaise , pain in abdomen with low hemoglobin in 86.9% cases and thrombocytopenia in 52.1% cases. Blood smear examination showed hypochromic, microcytic anemia in patients with low hemoglobin, parasitized RBC were seen in 45 cases. Malaria antigen test was confirmatory. Acute blood loss (20) with M:F ratio 1.5:1 had Grade I,II,II leucopenia in 18,2,0 cases respectively who presented as with post-operative blood loss(8), postpartum hemorrhage (7) and accident (5) with low hemoglobin in all cases and thrombocytopenia (70%). Blood smear examination showed normocytic normochromic anemia. Tuberculosis (15) with M: F ratio 1.8:1 had Grade I, II, III leucopenia 12, 3, 0 cases respectively who presented with low grade fever, weakness, loss of appetite with low hemoglobin in all cases and thrombocytopenia in 53.3% cases. Blood smear examination showed hypochromic, microcytic anemia and chest X-ray and TB antigen test were done for confirmation. HIV (15) with M: F ratio 4:1 had Grade I, II, III leucopenia 10, 4, 1 cases respectively who presented as low grade fever, weakness, loss of appetite, weight loss with low hemoglobin in all cases and thrombocytopenia in 53.0%. Blood smear examination showed hypochromic, microcytic anemia in patient.

Table1: Etiology correlation with incidence and sex distribution.

Etiology of leucopenia	No of cases	Percentage	Males	Females	M:F
Typhoid	78	19.5%	32	46	0.69:1
Megaloblastic anemia	65	16.25%	13	52	0.25:1
Iron deficiency	62	15.5%	14	48	0.29:1
Dengue	62	15.5%	25	37	0.67:1
Hypersplenism	60	15.0%	55	5	11.0:1
Malaria	23	5.75%	9	14	0.64:1
Acute blood loss	20	5.0%	12	8	1.50:1
TB	15	3.75%	11	6	1.80:1
HIV	15	3.75%	12	3	4.0:1

Table 2: Etiology correlation with anemia, thrombocytopenia and grades of leucopenia.

Etiology of leucopenia	Low* Hb	Low Platelet	I (%)	II (%)	III (%)
Typhoid	59(75.64%)	5(6.4%)	31(39.7%)	32(41.02%)	15(19.2%)
Megaloblastic anemia	65(100%)	42(64.6%)	24(36.9%)	20(30.7%)	21(32.3%)
Iron deficiency	62(100%)	24(38.7%)	40(64.5%)	22(35.4%)	-
Dengue	42(67.74%)	62(100%)	35(56.4%)	26(41.9%)	1(1.6%)
Hypersplenism	55(91.6%)	43(71.6%)	25(41.6%)	29(48.3%)	6(10.0%)
Malaria	20(86.9%)	12(52.1%)	14(60.8%)	9(39.1%)	-
Acute blood loss	20(100%)	14(70.0%)	18(90.0%)	2(10.0%)	-
**TB	15(100%)	2(13.3%)	12(80.0%)	3((20%)	-
***HIV	15(100%)	8(53.3%)	10(66.6%)	4(26.6%)	1(6.6%)
Total	353(88.2%)	212(53.0%)	209(52.2%)	147(36.7%)	44(11.0%)

*Hb: Haemoglobin **TB: Tuberculosis   ***HIV: Human immunodeficiency virus

Table3: Age wise distribution of various etiology of leucopenia

Age in years	0-10	11-20	21-30	31-40	41-50	51-60	61-70	Total
Typhoid	23	21	12	15	4	3	-	78
Megaloblastic anemia	-	23	25	12	2	3	-	65
Iron deficiency	-	18	28	-	2	2	12	62
Dengue	-	14	25	12	5	6	-	62
Hypersplenism	-	-	-	21	24	15	-	60
Malaria		7	4	10	2	-	-	23
Acute blood loss	-	-	7	4	3	5	1	20
TB	-	-	-	7	3	5	-	15
HIV	-	-	3	5	4	3	-	15
Total	23	83	104	86	49	42	13	400

Discussion

Incidence of leucopenia in our study was 0.97% with M: F ratio of 0.84:1. A female preponderance is seen due to more number of female cases of iron deficiency and megaloblastic anemia in our study which showed leucopenia. 88.2% cases of leucopenia were associated with anemia. Anemia was observed in 88.2% cases of leucopenia. Grade I II &III leucopenia was observed in 52.2%, 36.7%& 11.0% respectively. Out of 44 Grade III leucopenia cases, were of megaloblastic anemia-21, typhoid fever-15, hypersplenism -6and HIV-1. Typhoid fever (78), an important public health problemshowed maximum incidence of leucopenia. Poor sanitation, anemia, and malnutrition being contributing factors in our scenario. Most of cases were below 30 years comparable with other studies too[11,15,18]. Leucopenia in typhoid fever is due to bone marrow suppression, hence seen to be associated with suppression of other cell lineage too[15,20]. Megaloblastic anemia was seen in females in our study who mainly were in 20-40 years age group (childbearing age) consistent with other studies[8,19,20]. Chronic inflammatory disorders of gut like parasitic infestations, chronic diarrhea and malabsorption states along with poor nutrition are causes of high incidence of megaloblastic anemia in our study consistent with other studies too. Leucopenia with or without anemia or thrombocytopenia is a known form of clinical presentation of patients. Cytopenias in iron deficiency are seen in earlier studies and incidence increases with degree of anemia especially in those case with hemoglobin < 7gm % [7]. Hypersplenism causes peripheral pooling or trapping and destruction of cells leading to cytopenias. Hypersplenism in our study is seen in males with a history of chronic alcoholism and a decompensated liver disease was found in all cases. Incidence of hypersplenism was 10.4% in our study. Incidence of 29.2% was reported by Arvind Jain et al[15]. A high incidence of hypersplenism could be due to increasing trend of alcoholism in today's society. There are an increasing number of patients with chronic liver disease and subsequent hypersplenism. Dengue fever is associated with thrombocytopenia is a known fact. Severe leucopenia along with thrombocytopenia is seen in patients with Dengue hemorrhagic fever[1,13]. In our study 10% cases had severe or Grade III leucopenia. Leucopenia in malaria

87

especially with other cytopenia is particularly due to impairement of marrow function, hemophagocytosis or direct invasion by parasite[4,9,14]. HIV is known to cause hematological abnormalities affecting one or more cell lineage. Hematological abnormalities may be first clinicohematological manifestation of HIV. Severity of cytopenias increases in advanced stages of the disease. Anemia is most frequent cytopenia, but granulocytopenia with or without lymphopenia and thrombocytopenia is frequently seen in HIV and AIDS[11]. Hematological manifestations in tuberculosis in the form of leucopenia, anemia or even pancytopenia are due to disease itself or due to drugs used for treatment of tuberculosis. Hence regular complete blood counts should be done in patients with tuberculosis[15].

Conclusion:

In present study, hypersplenism (due to chronic alcoholism) in males and anemia (megaloblastic and iron deficiency anemia) in females had highest incidence of leucopenia. Nutritional deficiencies, food habits, poor sanitation, stagnant water, chronic alcoholism and low socioeconomic status are important factors contributing to infectious diseases and nutritional deficiencies in our rural scenario. Low hemoglobin was noted in 88.2% cases and severity of anemia was directly related with grade of leucopenia. Bone marrow suppression, bone marrow necrosis or direct invasion by organism was responsible for suppression of one or more cell lineage. Hence leucopenia is seen associated with anemia or thrombocytopenia or both (pancytopenia). Education of people at grass root level in rural areas will definitely help to overcome this situation in future.

References:

1. Tahir Jameel etal. Changing haematological parameters in dengue viral infections.,†Ayub Medical College, Abbottabad, Pakistan. **J** Ayub Med Coll Abbottabad 2012;24(1)

2. Valent P, Horny H-P, Bennett JM, et al. Definitions and standards in the diagnosis and treatment of the myelodysplastic syndromes: consensus statements and report from a workingconference. *Leuk Res.* 2007;31(6):727-736

3. Bawane Vasant. Effect of low count of leucotyes in the rural people. Saint Bahinabai College Shivoor, tq.Vaijapur, India.Department of Zoology, Dr. Bam University, Aurangabad, India. International Journal of Innovative Research & Development

4. Kotepui et al. Effect of malarial infection on haematological parameters in population near Thailand-Myanmar Border. Manas Malaria Journal 2014, 13:218

5. Christopher Gibson and Nancy Berliner. How we evaluate and treat neutropenia in adults. Brigham and Women's Hospital, Boston. BLOOD, 21 August 2014, vol:8

6. Valent P, Bain BJ, Bennett JM, et al. Idiopathic cytopenia of undetermined significance (ICUS) and idiopathic dysplasia of uncertain significance (IDUS), and their distinction from low risk MDS. *Leuk Res.* 2012; 36(1):1-5.

7. Yoojoo Lim etal. Leukopenia in Patients with Iron Deficiency Anemia. Blood 2011 118:5279; The American Society of Hematology

8. Dr. Aditi Raina, Dr. Indu Bhushan. Patterns of Pancytopenia in a Rural Teaching Hospital of Western UP, India. Department of Pathology, Rama Medical College, Ghaziabad, India. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) Volume 14, Issue 8 Ver. VII (Aug. 2015), PP 74-76

9. Ravinder Pal Singh. Plasmodium Vivax Malaria Presenting With Severe Thrombocytopenia. Bhartia Institute of Science and Research, New Delhi, India. The Brazilian Journal of Infectious Diseases 2002; 6(5):263-265.

10. Kyeyune etal . Prevalence and correlates of cytopenias in HIV-infected adults initiating highly active antiretroviral therapy in Uganda.BMC Infectious Diseases 2014, 14:496

11. Sqn Ldr Prateek Kinra. Graded Specialist (Pathology). Prevalence of Haemolysis in Peripheral Blood Smear in Cases of Megaloblastic Anemia. 7 Air Force Hospitals, Kanpur -4. MJAFI, Vol. 62, No. 3, 2006

12. Prevalence of leucopenia among industry workers 2000–2009.Vilma Santana etal, Institute of Collective Health, UFBA, Salvador, Bahia, Brazil; 2Social Service for the Industry, SESI-Bahia, Salvador, Bahia, Brazil 10.1136/oemed-2014-102362.332.

13. Short Report: Severe Neutropenia in Dengue Patients: Prevalence and Significance Tun-Linn Thein etal. Communicable Disease Center, Institute of Infectious Diseases and Epidemiology, Tan Tock Seng Hospital, Singapore; Am. J. Trop.Med.Hyg.90 (6), 2014, pp. 984–987

14. David Dale, Sheldon Wolff. Studies of the neutropenia of acute malaria. Blood. Feb 18 2017

15. Arvind Jain1 and Manjiri Naniwadekar2. An etiological reappraisal of pancytopenia - largest series reported to date from a single tertiary care teaching hospital. Laboratory Department of Pathology, Krishna Institute of Medical Sciences University (KIMSU), Karad, Maharashtra, India BMC hematology2013,13:10

16. Bain BJ, Lewis SM. Preparation and staining methods for blood and bone marrow films. In: Lewis SM, Bain BJ,Bates I, editors. Dacie and Lewis Practical Haematology.10th ed. Philadelphia: Churchill Livingstone; 2006. p. 59-78

17. Latger Cannard V, Bibes B, Dao A, et al. Malaria related cytopenia. Ann Biol Clin2002; 60:213-216. Aouba A, Noguera ME, Clawel JP, et al.

18. MallouhAA, Sa'di AR. White blood cells and bone marrow in typhoid fever. Pediatr Infect Dis J.1987 Jun:6(6):527-9 Pubmed : PMID3615066.

19. Mayo Clinic. Low white blood cell count. Diseases and conditions. www.mayoclinic.com health/low–white-blood cell-count/MY00162.Accessed 11/24/2012.

20. Merck. Neutropenia and lymphocytopenia. Hematology and oncology 2012