Research & Reviews: Journal of Medical and Health Sciences

Understanding the Pathophysiological Basis of Alterations of Hematological Picture in Alcohol Abuse Patients

Arjun Maitra[1]* and Chaitali Maitra[2]

[1]Assistant Professor, Department of Physiology, Modern Institute of Medical Sciences, Kanadia Road, Near Kanadia, Indore-452016, Madhya Pradesh, India

[2]Assistant Professor, Department of Biochemistry, Modern Institute of Medical Sciences, Kanadia Road, Near Kanadia, Indore-452016, Madhya Pradesh, India

Research Article

ABSTRACT

Alcohol abuse disorder is a major health related problem. Almost all organs is affected by the alcohol ingestion. Peripheral blood smear usually provides significant information regarding diagnosis and prognosis of a disease. Objective of our study was to determine impairment of hematological system in non cirrhotic alcohol abuse disorder patients compared to the normal subjects. Hematological parameters were investigated in 120 subjects including 30 normal control and 90 alcoholics. Study shows significant changes in WBC status. Total leukocyte count is significantly elevated in heavy drinkers. Significant increase in neutrophil count is observed in moderate (11%) and high (18%) alcohol intake group ($p < 0.05$). Lymphocytes and Monocytes decrease significantly in moderate to heavy drinkers. Our study shows that Eosinophil does not show significant changes among the groups. ESR was found to be increased significantly in alcoholics and shows a strong negative correlation ($r = - 0.89$) with hemoglobin.

INTRODUCTION

Alcohol abuse is a major health problem in North east India, particularly in Sikkim, which has a low socio – economic condition. It is also the major cause of liver cirrhosis among sikkimese population. Relapse to alcohol abuse after de-addiction is also high in the said population [1]. Alcohol abuse is characterized by recurrent performance problems at school or on the job that result either from the after effects of drinking alcohol or from intoxication on the job or at school. Abuse disorders often continue to consume alcohol despite the knowledge that continued consumption possess significant social or interpersonal problem for them. People with alcohol use disorders often consume alcohol despite knowing that they suffer from alcohol related medical problems. Men & women who fulfill criteria for alcohol use disorders decrease their life span by approximately 15 years with abuse and dependence responsible for almost 25% of premature death in men and 15% in women, In 1990, the World Health Organization (WHO) estimated that globally alcohol account for 3.5% of the total days lose to death and disability [2] .

There has been a lot of study of various hematological parameters associated with alcohol use disorders globally but limited studies regarding Indian population has been done. Our study is a basic study to identify the changes in the cellular composition of blood in north eastern population of India, which may be helpful to identify the pathophysiological changes associated with alcoholic assault.

Alcohol causes dysfunction of almost all – major organs including brain liver heart pancreas and adrenal gland and thyroid glands. Absorption of alcohol takes place from both stomach and small intestine and it is most rapid when it is consumed empty stomach and alcohol concentration in the drink is between 20% - 30% [3]. Blood alcohol concentrations vary according to sex, size and body build, previous exposure to alcohol and type of drink.

Alcohol abusers show marked changes in their hematological system. Alcohol abuse may result in mild bone marrow alterations and hematological abnormalities [4]. The hematopoietic tissue cellularity increases and peripheral blood picture changes with the severity of abuse.

Alcoholics show a rise in reticulocyte, a fall in serum iron and a rise or fall in WBC count. Hemoglobin and hematocrit values both fall [4]. Macrocytic anemia is a common feature of alcoholics and non-alcoholic liver cirrhosis patient [5].

There has been very limited study of various hematological parameters associated with alcohol abuse among Sikkimese population.

MATERIALS AND METHOD

Patients were selected from the Outpatient department of Psychiatry and Medicine department of Central Referral Hospital of Sikkim Manipal Institute of Medical Sciences, Gangtok, Sikkim.

CAGE questionnaires and Michigan Alcoholism Screening Test (MAST) were administered for screening purpose of patients. Then detailed alcohol history was taken from the selected patients (alcohol abusers).

The subjects were classified into three groups depending upon their amount of alcohol consumption and duration.

High alcohol intake group (n= 30)

It consists of patients who had been drinking more than 80g of alcohol per day for at least five years.

Moderate alcohol intake group (n= 30)

It consists of patients who had been drinking less than 80g alcohol per day for at least one year.

Low Alcohol intake group (n=30)

It consists of patients who had little or occasional history of alcohol intake.

Control group (n= 30)

It was constituted with normal healthy subjects belonging to sikkimese population.

Subjects of age ranges b 25 to 60, mean age 34.7 years were included in study.

The individual with Diabetes, essential hypertension, thyroid diseases, nephritic diseases, and pregnant women were excluded from the study.

Venous blood samples were taken for the routine biochemical and hematological investigations.

CBC (Complete blood count) was done for the samples, which include Differential leukocyte count (DLC) performed by using Leishaman's Stain method, ESR was determined by using Westergen's Pipette. Total counts were determined manually using Neubauer's Chamber. Hemoglobin estimation was done by the Cynmethaemoglobin method 0.2 ml of blood added to 5 ml of Drabkin's reagent and readings were taken at 540nm after 4 minutes, Cynmethaemoglobin standard had concentration of 15 mg/dL.

Data were analyzed Mean, SD were calculated and ANOVA used to find out the significance among the groups by using SPSS 16.

P < 0.05 was considered as significant. Scatter diagram, bar chart and line diagrams were created to reveal the concept.

RESULTS

A total of 120 participants were included in the study. Subjects were further classified into four different groups according to their alcohol consumption. Total leukocyte count (TLC) appears to be significantly high in High alcohol intake group. Though the TLC apparently decreased with moderate alcohol consumption it was not found to be significant (Table 1).

Results are expressed as mean ± SD, *signifies p<0.05 in comparison to control, @ signifies p<0.05 in comparison to low intake group, #signifies p<0.05 n comparison to moderate intake group

Significant increase in neutrophil count is observed in moderate (11%) and high (18%) alcohol intake group (p < 0.05). Eosinophil count shows no significant alteration among the groups. Lymphocyte and Monocyte count decreases significantly (p < 0.05) in the moderate and high alcohol intake group (Table 1) (Figure 1).

Hemoglobin concentration is significantly reduced in alcoholic groups irrespective of amount of consumption (Table 2) when compared with the control. ESR increases significantly in moderate and high intake group (p < 0.05). It is found that ESR and Hemoglobin concentration show a strong negative correlation (r = -0.89) (Figure 2).

Results are expressed as mean ± SD, *signifies p<0.05 in comparison to control, @ signifies p<0.05 in comparison to low intake group.

Table 1. Values of Total leukocyte count & different Leukocytes and their significance.

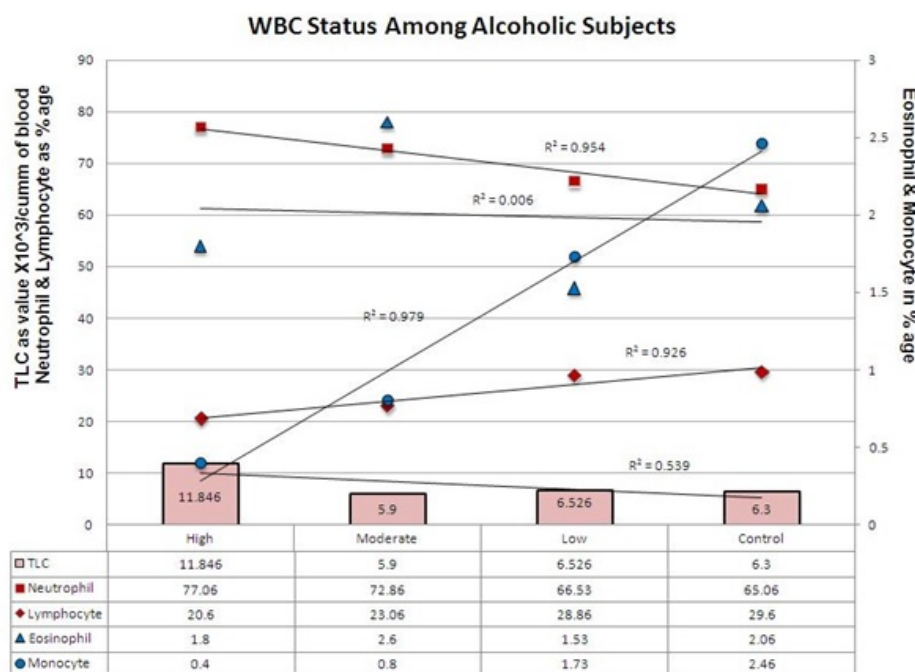| Parameters	Control	Low alcohol intake group	Moderate alcohol intake	High Alcohol intake
TLC (/cumm. Of blood)	6306.66±995.50	6526.66±1940.62	5900±1409.05	11846.67±3577.88 *@#
Neutrophil (%)	65.06±4.58	66.53±7.55	72.86±10.23*@	77.06±11.18 *@
Eosinophil (%)	2.06± 1.57	1.53±1.59	2.6±2.58	1.8±1.61
Lymphocyte (%)	29.6±3.26	28.86±10.01	23.06±8.68 *@	20.6±10.21*@
Monocytes (%)	2.46±1.68	1.73±1.23	0.8±0.86 *	0.4±0.50 *@

Figure 1. Showing the relationship of WBC status and different groups of Alcoholic Subjects.Eosinophils and Monocytes are represented in secondary axis (Right hand Side). Actual value of TLC is be read as (X)x10^3/cumm of blood.

Table 2. Values of Erythrocyte Sedimentation Rate (ESR) and Hemoglobin concentration among the groups.

Parameters	Control	Low alcohol intake group	Moderate alcohol intake	High Alcohol intake
Hemoglobin (gm/dL)	14.38±0.85	13.51±1.67 *	11.68±2.04 *@	12.32±1.68 *
ESR(mm/1hr)	3±1.41	4.4±2.58	10.13±8.96*@	12.53±7.19 *@

Correlation coefficient r = -0.89

DISCUSSION AND CONCLUSION

In the present study patient suffering from alcohol abuse are taken care of. In this study basic hematological parameters are evaluated and compared with healthy normal healthy person.

It has been reported that, long term alcohol abuse result in hematological abnormalities. Panasuik A and Kimono A have shown that majority of the patients of alcohol abuse show low hemoglobin concentration level [6]. Macrocytic anemia is also very common among the abusers [7]. Causes of macrocytosis is beyond the scope of our discussion, but Vitamin B6 deficiency in alcoholic patients leads to decreased ALA synthase activity which may lead to decreased production of heme [8].alcohol induced anemia also result in serum G6PD activity [9] . In the present it was seen that the hemoglobin level among the patient significantly decrease in comparison to healthy controls.

Most of the studies are in support that the chronic alcohol uses cause leucopenia [10]. Bone marrow alteration is also found in alcoholic patients. In moderate drinkers mild alterations are reported and the hematopoietic tissue with features of activation moderate myelofibrosis is also reported in long term alcohol abuse [10]. But in chronic alcoholism due to excess load of alcohol metabolism by the hepatocytes initiates a cascade of events evolving protein-aldehyde adducts, lipid peroxidation, immunologic effects and cytokine release (TNF, IL1, IL 6, TGF β) [11] . Release of these cytokines produce alterations in the production of blood cells and may cause leukocytosis [12]. Shaper A et al. (1985) reported that there is positive correlation between alcohol ingestion

and leukocyte count [13]. In the present study we observed that the alteration (increment) in the TLC is significant in high alcohol intake group.
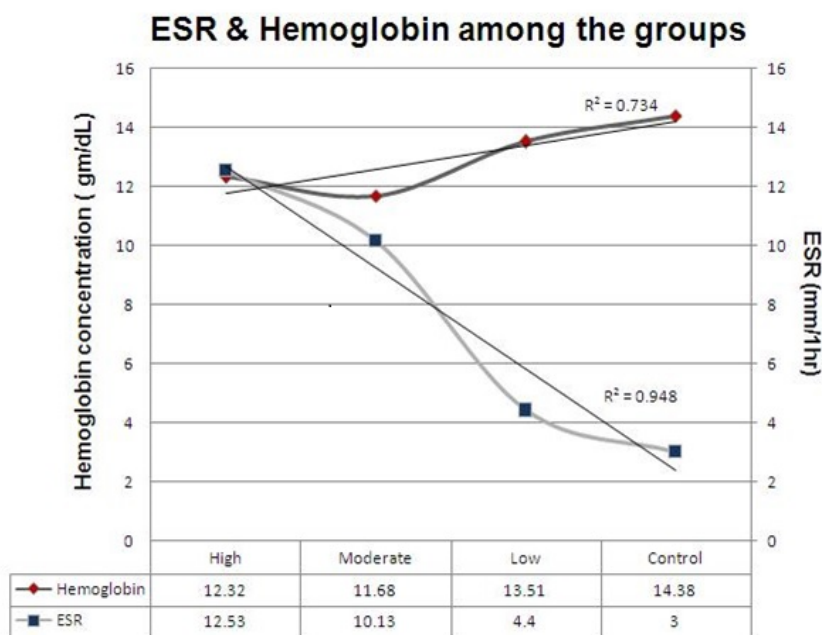

Figure 2. ESR and Hemoglobin among the different groups (r = -0.89).

Previously neutropenia [14] or no significant association [13] were reported in alcoholic subjects, interestingly we observed that the neutrophil is also increased with the severity of abuse. The increase is in the moderate and high intake group is significant. As discussed above increase in the production of IL-1 and IL-6 may be responsible for this effect. IL-1 has stimulatory effect on the stem cells and IL-6 stimulates myeloid proliferation with GM-CSF and G-CSF along with other cytokines[12].

In our study we have found that there is no significant variation in the Eosinophil count in DLC among the various groups. Logical reason behind this could be that there is no alteration in production of IL-10 and IL-13 but there is alteration in TH2 cell activity which can produce mild alteration in production of IL 3 and IL-5 [15, 16].

Kapasi A, Patel G reported that ethanol promotes T cell apoptosis through the activation of intrinsic or mitochondrial pathway [17]. Clinical reports also suggest for acute lymphopenia in acute alcohol intoxication [18]. Phenotypic and functional alteration of lymphocytes, B and NK cells decrease is also reported in alcohol consuming mice [19]. We also found that there is significant decrease in lymphocyte count in DLC in moderate and high alcohol group.

Alcohol abuse has long been known to adversely affect innate immune response and predispose to infections. Alcohol suppresses the activation of monocytes and their progenitor cell by alcohol induced suppression of TNFα. Alcohol inhibits interactions between TNF and its converting enzyme (TACE) [5].

Our result does approve the theory as Monocytes count in DLC decreases significantly moderate and high alcohol intake group.

ESR is though not a diagnostic test but an indicator of bodily reactions to tissue injury and might be independent of age. ESR is raised in almost all pathological conditions in contrast to functional disorders. Fibrinogen, hemoglobin and serum globulin levels are the most important variables that explain most of the variability in the results of ESR [20]. ESR is elevated in the patients of alcoholic liver diseases [21]. In the present study we found that ESR is raised significantly with degree of alcohol abuse.

The limitation of the study was small sample size. In the present study a significant alteration was observed in the basic hematological parameters among alcohol abusers. This may be taken in to account to investigate the degree of impairment in the hematological function during clinical investigation and treatment of at risk alcoholic patient population. More detailed population based studies with larger sample sizes are required to derive conclusive outcome.

CAGE QUESTIONNAIRE

- Have you ever felt you should Cut down on your drinking?

- Have people Annoyed you by criticizing your drinking?

- Have you ever felt bad or Guilty about your drinking?

- Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (Eye opener)?

SCORING

Item responses on the CAGE are scored 0 or 1, with a higher score an indication of alcohol problems. A total score of 2 or greater is considered clinically significant.

REFERENCES

1. Gyatso TR, Bagdas BB (1998) in: Health Status in Sikkim. (Dept. of Health and family welfare, Govt. of Sikkim).

2. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet. 1997 May 24;349(9064):1498-504.

3. Alex Paton. Alcohol in the body. BMJ 2005 Jan 6; 330(7482):330-85.

4. Das SK, Vasudevan DM. Biochemical diagnosis of Alcoholism. IJCB. 2005 Jan; 20(1):35-42.

5. Waluga M, Hartleb M. Alcoholic Liver Disease. Wiad Lek. 2003;56(1-2):61-70.

6. Panasuik A, Kemona A. Bone marrow failure and hematologic abnormalities in alcoholic liver cirrhosis. Rock Akad Med Bialamyst. 2001;46:100-5.

7. Maruyama S, Hiramaya C, Yamamoto S. Red Blood cell status in alcoholic and non alcoholic liver disease. J Lab Clin Med. 2001 Nov;138(5):332-7.

8. Iwama H, Iwase O, Hayashi S. Macrocytic anemia with anisocytosis due to alcohol abuse and Vitamin B6 Deficiency. Rinsho Ketsueki. 1998 Nov;39(11):1127-30.

9. Chaitali Maitra, Arjun Maitra . Serum Glucose-6-Phosphate Dehydrogenase (G6PD): A Marker for Hemolytic Assault in Alcoholic Liver Diseases. Res. Rev.: J. Med. Health Sci . 2014 (Oct – Dec); 3 (4):81-7.

10. Ballard HS. Hematological complications of alcoholism. Alcoholism: Clinical and Experimental Research. 1989 Sep-Oct;13(5):706–720.

11. Crews FT, Bechara R, Brown LA. Cytokines and alcohol. Alcohol Clin Exp Res. 2006 Apr; 30(4):720-30.

12. Gonzalez-Quintela A, Vidal C, Lojo S. Serum cytokines and increased total serum IgE in alcoholics. Ann Allergy asthma Immunol.1999 Jul; 83(1):61-7.

13. Oduola T, Adeosun OG, Oduola TA, Agbaje NR, Raheem ZA. Drinking patterns: biochemical and haematological findings in alcohol consumers in Ile-Ife. Nigeria. Afr. J. Biotechnol. 2005 Nov;4 (11):1304-8.

14. Ballard HS. Alcohol, bone marrow, and blood. Alcohol Health & Research World. 1993;17(4):310–15.

15. Shaw RJ, Walsh GM, Cromwell O, Moqbel R, Spry CJ, Kay AB. Activated Human eosinophil generated SRS-A leukotrienes following physiological (IgG – dependent) stimulation. Nature. 1985 Jul 11-17;316(6024):150-2.

16. Sehmi R1, Wardlaw AJ, Cromwell O, Kurihara K, Waltmann P, Kay AB. IL-5 selectively enhances the chemotactic responses of eosinophils obtained from normal but not eosiniphillic subjects. Blood. 1992 Jun 1;79(11):2952-9.

17. Kapasi AA, Patel G, Goenka A, Nahar N. Ethanol promotes Tcell apoptosis through the mitochondrial pathway. Immunology. 2003 Mar; 108(3):313-20.

18. Padgett EL, Sibley DA. Effect of Adrenalectomy on ethanol associated changes in lymphocyte cell numbers and subpopulation in thymus, spleen and gut associated lymphoid tissues. Int. J Immunopharmacol. 2000 Apr;22(4):285-98.

19. Starekenburg S, Munroo ME, Waltenbaugh C. Early alteration in leukocyte population and Th1/Th2 function in ethanol consuming mice. Alcohol clin Exp Res. 2001 Aug;25(8):1221-30.

20. Dominguez-Santalla MJ, Vidal C , Vinuela J, Perez LF. Increased serum IgE in alcoholic; Relationship with Th1/Th2 cytokine production by stimulated by blood mononuclear cells. Alcohol clin Exp Res. 2001 Aug;25(8):1198-205.

21. Das SK, Mukherjee S, Vasudevan DM, Balakrishnan V. Comparison of haematological parameters in patients with non-alcoholic fatty liver disease and alcoholic liver disease . Singapore Med J. 2011 Mar;52(3):175 – 181.

22. Steinvil A1, Shapira I, Arbel Y, Justo D, Berliner S, Rogowski O. Determinants of the Erythrocyte Sedimentation Rate in the era of microinflammation. Am J Clin Pathol. 2008 Mar;129(3):486-91.

23. Lopez CM, Vallejo NE, Pineiro AE. Alteration of biochemical parameters related with exposure to lead in heavy alcohol drinker. Pharmacol Res. 2002 Jan;45(1):47-50.

24. Myrhed M, Berglund L, Bottiger LE. Alcohol consumption and hematology. Acta Med Scand. 1977;202(1-2)11-5.

25. Zhao XJ, Marrero L. Acute alcohol inhibits TNF-alpha processing in human monocytes by inhibiting TNF/TNF-alpha-converting enzyme interaction in the cell membrane. J Immunol. 2003 Mar 15;170(6):2923-31.