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Study of Haematological Profile in Patients with Alcohol Dependence Syndrome

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1. Introduction

Alcohol is an organic compound with hydroxyl functional group bound to carbon atom[1]. The American Medical Association considers alcoholism as a disease[2, 3]. Chronic alcohol abuse causes both medical and psychiatric illnesses[4].

Alcoholism is proposed as one of the deadly chronic diseases. Chronic alcohol consumption has significant effects on the haematopoietic system including various blood cells and their progenitors in the bone marrow and clotting components[5]. The most common CNS complication of heavy alcoholics is brain atrophy and it may lead to dementia, even in young drinkers[6].

Alcohol consumption is considered to be the third most important modifiable risk factor for death and disability[7].Alcohol addiction and dependence have become serious health and social problems[8].Heavy alcohol intake increases the risk of stroke[9].
Light to moderate alcohol consumption has a protective role against development of coronary heart disease[10].Alcohol increases the HDL cholesterol level and reduces the risk of coronary heart disease[11].

The effect of alcohol on public health is complex and multidimensional[12]

Overall third-most popular drink is alcohol, after water and tea [13,14].

Alcohol consumption has been associated with significant financial burden, unemployment, loss of family, accidental injury or death [15].

Chronic alcohol intake can lead to deficiency of iron and other vital micronutrients such as vitamin B12 and folate required for erythropoietic activities [16].

Alcohol intake has been associated with both advantages and disadvantages[17]. Alcohol is associated with decreased risk of myocardial infarction, if the person is having low to moderate consumption[18], sudden cardiac death can occur with heavy drinking[19].

Alcohol dependence syndrome is associated with increased risk of pneumococcal bacteremia especially if patient is having leucopenia [20,21,22]. Because of less gastric alcohol dehydrogenase activity in women compared to men resulting in higher blood ethanol levels in women[23].

According to the American Heart Association/American Stroke Association guidelines, the maximum alcohol intake should not be more than 2 drinks per day in men and not more than 1 drink per day in non pregnant women[24].

2. Aims and Objectives of Study

To study the Haematological changes in Alcohol Dependenc e Patients.

3. Review of Literature

Alcohol Dependence syndrome (According to ICD-10 classification of Mental and Behavioural disorders) [25]. A cluster of physiological, behavioural, and cognitive phenomena in which the use of a substance or a class of substances takes on a much higher priority for a given individual than other behaviours that once had greater value. A central descriptive characteristic of the dependence syndrome is the desire (often strong, sometimes overpowering) to take psychoactive drugs (which may or may not have been medically prescribed), alcohol, or tobacco. There is evidence that return to substance use after a period of abstinence leads to a more rapid reappearance of other features of the syndrome than occurs with non-dependent individuals.

Diagnostic Guidelines
A definite diagnosis of dependence should usually be made only if three or more of the following have been present together at some time during the previous year:

a) A strong desire or sense of compulsion to take the alcohol;
b) Difficulties in controlling alcohol-taking behaviour in terms of its onset, termination, or levels of use;
c) A physiological withdrawal state when alcohol use has ceased or been reduced, as evidenced by: the characteristic withdrawal syndrome for the alcohol; or use of the same (or a closely related) substance with the intention of relieving or avoiding withdrawal symptoms;
d) Evidence of tolerance, such that increased doses of the alcohol are required in order to achieve effects originally produced by lower doses.
e) Progressive neglect of alternative pleasures or interests because of alcohol use, increased amount of time necessary to obtain or take it or to recover from its effects;
f) Persisting with alcohol use despite clear evidence of overtly harmful consequences, such as harm to the liver through excessive drinking, depressive mood states consequent to periods of heavy alcohol consumption, or

impairment of cognitive functioning; efforts should be made to determine that the user was actually, or could be expected to be, aware of the nature and extent of the harm.

Epidemiology

There are 140 million people with history of alcohol intake world wide as per WHO[26]. Risk of development of alcohol dependence is 2 to 3 times higher in individuals who started drinking at the age of 12 compared with those who started at the age of 19 years[27].

Different Patterns of Drinking[28]

a) Moderate alcohol consumption:
   Women <65 years of age: <2 drinks per day
   Men <65 years of age: <3 drinks per day
   People >65 years age: <2 drinks per day
b) Heavy alcohol consumption:
   Women: > 7 drinks per week or three drinks per occasion
   Men : >14 drinks per week or four drinks per occasion
c) Binge drinking:
   Women: 4 or more drinks in one drinking occasion
   Men: 5 or more drinks in one drinking occasion

Effects of Alcohol on the Body

A. Cardiovascular effects:

1. Coronary heart disease

Moderate alcohol consumption reduces the risk of Coronary Heart Disease by 40-70% when compared with persons with no alcohol consumption or with heavy alcohol intake both in Men and Women.[29] Light to moderate alcohol consumption has protective effect against development of coronary Heart Disease and risk of cardiovascular deaths in diabetic patients[30,31].

2. Hypertension:

People taking more than two drinks per day have 1.5 to 2 fold increase incidence of development of Hypertension compared with nondrinkers[32].

3. Heart failure:

Light to moderate alcohol consumption may protect against development of Heart failure[33]. Chronic excess alcohol consumption can lead to development of secondary dilated cardiomyopathy[34]. Prevalence of developing alcoholic cardiomyopathy is similar in both men and women. Women develop alcoholic cardiomyopathy at a lower dose of ethanol when compared to men; this sex difference is due to delayed gastric metabolism of ethanol in women[35].

4. Stroke risk:

Heavy drinking of alcohol more than 60 gm/day is associated with increased risk of all types of strokes. Moderate alcohol consumption of 12-24 gm/day (around 1-2 drinks per day) is associated with significant reduction in ischemic stroke and there is no effect on hemorrhagic stroke. Light alcohol consumption of less than 12 gm/day(around one drink per day) is associated lowest risk of all types of strokes[36,37].

5. Peripheral vascular disease:

Alcohol reduces the risk of peripheral vascular disease. Moderate alcohol intake in Men and Light drinking in women decreases the risk of intermittent claudication[38].

6. Anti thrombotic effects:

Alcohol consumption at light to moderate exhibits antithrombotic effects by inhibiting platelet aggregation and reduces the risk of Coronary Heart Disease[39].

B. Neurological complications:

1. Wernicke Encephalopathy:

It is an acute neurologic complication caused by thiamine deficiency secondary to chronic alcohol intoxication[40].

2. Korsakoff syndrome:

Korsakoff syndrome is a late manifestation of Wernicke encephalopathy. It is characterized by anterograde and retrograde amnesia with relative preservation of long-term memory, apathy and intact sensorium. Confabulation is not seen in all cases[41].

3. Cerebellar degeneration:

Chronic alcohol use results in degeneration of purkinje cells in the cerebellar cortex. [42].

4. Marchiafava-Bignami Disease:

It is most commonly seen in malnourished alcoholics. It is a disorder of demyelination or necrosis of the corpus callosum and adjacent subcortical white matter[43].It is characterized by dementia, dysarthria, spasticity and inability to walk[44].

5. Peripheral neuropathy: Alcohol abuse associated with symmetric polyneuropathy, autonomic neuropathy and mononeuropathies[45,46].

6. Myopathy:

Alcoholic myopathy can be acute or chronic. Acute myopathy develops after binge drinking of alcohol[47,48,49].

C. Cancer:

1. Breast cancer:

When compared to abstainers, women who consumes low to high levels of alcohol had risk of developing breast carcinoma[50].

2. Gastrointestinal cancer:

Alcohol consumption is associated with increased risk of malignancies mainly squamous cell carcinoma of esophagus, however adenocarcinoma of esophagus is not associated with alcohol consumption[51].There is no causal relationship between alcohol consumption and development of colon cancer[52]. Pancreatic carcinoma is associated with heavy consumption of alcohol[53]. Hepatocellular carcinoma is associated with alcohol intake. Even with low levels alcohol intake there is increased risk of hepatocellular carcinoma in hepatitis B and hepatitis C carriers[54].

D. Gastrointestinal system:

1. Cholelithiasis:

Moderate alcohol intake causes reduction in the biliary cholesterol saturation index and lowers the risk of gallstones[55].

2. Pancreatitis:

Excess alcohol consumption is associated with pancreatitis in both men and women[56].

3. Alcoholic liver disease[57]:

Liver pathology due to alcoholism ranges from fatty liver to hepatic inflammation and from necrosis to progressive fibrosis.

Nyblom H, et al[58] published a study in 2004 to assess the importance of AST/ALT ratio in medical population.Results showed that AST/ALT ratio of more than 1 was not seen in most of the patients with heavy alcohol use, even though high AST/ALT ratio was associated with advanced alcoholic liver disease.

E. Haematological Complications of Alcoholism[59]:

Excess alcohol intake produces adverse effects on bone marrow. The generation of mature red blood cells and white blood cells and platelets are diminished.

Need for Study

Alcoholism is a global socio-economic problem affecting the public health of people.It accounts for about 10%-15% of all patients admitted into general hospitals. Hence it is necessary to conduct more studies for better understanding of the role of haematological parameters in alcohol dependent patients, which will be useful for therapeutic intervention.

4. Materials and Methods

Study design:

Hospital Based, Time Bound, Observational Case study.

Study site: Justice K.S.Hegde Charitable Hospital unit of K.S.Hedge Medical Academy, Nitte University, Deralakatte, Mangalore- 575018.

Sample size:

100 Consenting Patients of Alcohol dependence Syndrome.

Sample size n = [DEFF*Np(1-p)]/ [$(d^2/Z^2_{1-\alpha/2}$*(N-1)+p*(1-p)]

Population size(N)	: 1000
Hypothesized % frequency of outcome factor in the population (p)	: 80%+/-5
Confidence limits (d)	: 5%
DEEF Design effect	: 0.5

Duration of study: The study was conducted over a period of one and a half year from January 2016 to June 2017, after ethical clearance.

Method of collection of data: Venous blood samples of patients who were diagnosed with Alcohol dependence syndrome were collected under aseptic conditions and sent for haematological analysis for estimation of Hb, TLC Platelet count. Peripheral smear, Serum Iron and Serum Ferritin were done for patients with haemoglobin < 12 gm/dl in women and haemoglobin < 13gm/dl in men, accordingly anaemia was classified. LFT and USG abdomen was done in all patients.

Inclusion Criteria:

Patients in the age group of ≥18 years who had come to Justice K.S Hegde Charitable Hospital,unit of K.S Hegde Medical Academy, Nitte university and who were diagnosed as alcohol dependence syndrome according to ICD-10 classification of mental and behavioural disorders and consented for present study were included.

Exclusion Criteria:

- Chronic liver disease.
- Pregnancy.

History of Haematological malignancies, Tuberculosis and Hypothyroidism.

- Patients who were not consenting for the study.

Statistical Analysis:

Descriptive statistics for data collected like mean and standard deviations were calculated and presented. Proportions were used to determine the hematological variations in the study subjects SPSS Version 22 (statistical packages for social sciences) was used for analyzing the obtained data

5. Results

Table 1: Age Distribution of the Subjects in the Study

Age group (years)	No.of ADS Patients (n=100)	Percentage
15-30	15	15%
31-45	43	43%
46-60	28	28%
>60	14	14%

In this study, majority of the patients were in the age group of 31- 45 years (43%).The maximum age was 80 years and minimum age was 19 years. The mean age was 44.73 years with standard deviation of 13.8.

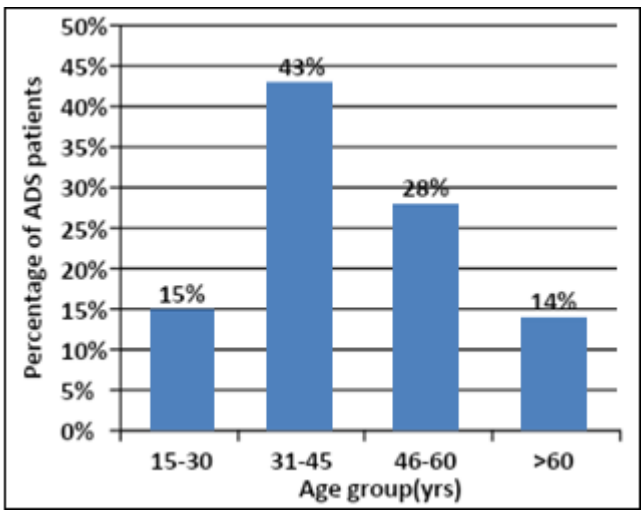

Figure 3: Age Distribution of the Subjects in the Study

Table 2: Gender Distribution in the Study

Gender	Frequency (n=100)	Percent
Female	2	2.0
Male	98	98.0
Total	100	100.0

In our study 98 were male and 2 were female. Majority were male, accounting for 98% of the total population.

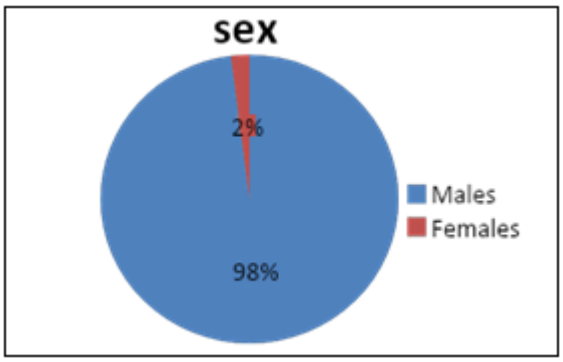

Figure 4: Gender distribution of the Subjects in the Study

Table 3: Duration of alcohol intake of ads patients

Duration of Alcohol Intake Years)	No. of ADS Patients (n=100)	Percentage
0 to 5	7	7%
6 to 10	18	18%
11 to 15	18	18%
16 to20	25	25%
21 to 25	9	9%
26 to 30	13	13%
31 to 35	3	3%
>35	7	7%

In this study, minimum duration of alcohol intake of less than 5 years included 7 patients and maximum duration of alcohol intake for more than 35 years included 7 patients. Majority of the patients (25%) consumed alcohol for a duration of 16 to 20 years with a mean of 19.45 years and standard deviation of 10.45

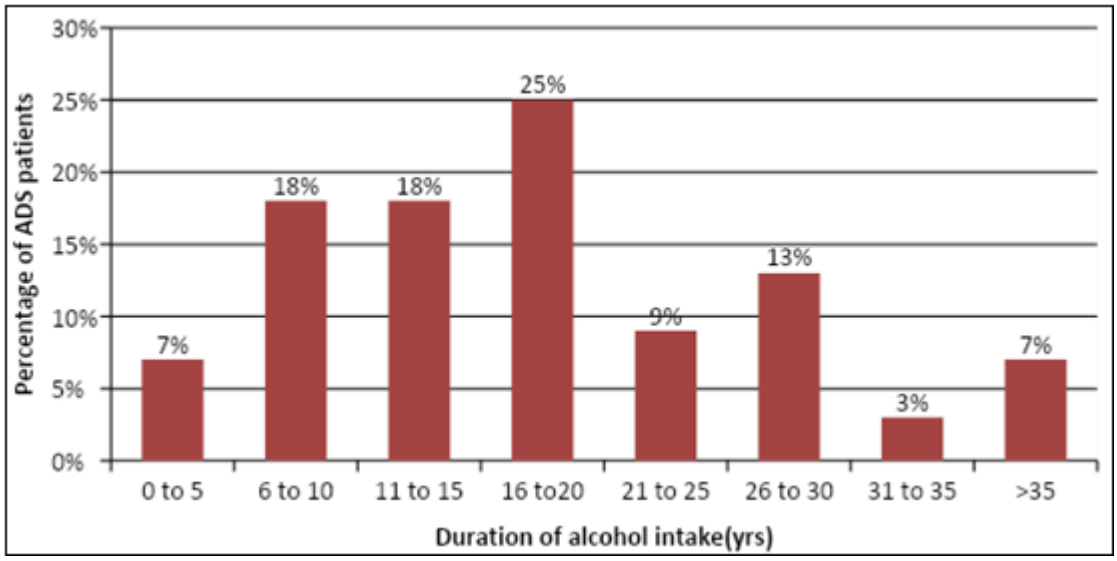

Figure 5: Duration of alcohol intake of ads patients

Table 4: Haemoglobin in Ads Patients

Hb(gm/dl)	No. of ADS Patients(n=100)	Percentage
13-17	52	52%
<13	44	44%
>17	4	4%

In this study 52% patients had normal haemoglobin, 44% had Haemoglobin of less than 13gm/dl and 4% had haemoglobin of more than 17 gm/dl also minimum Hb observed was 6.5 gm/dl and maximum Hb observed was 18.1 gm/dl and mean Hb was13.136 with a standard deviation of 2.41.

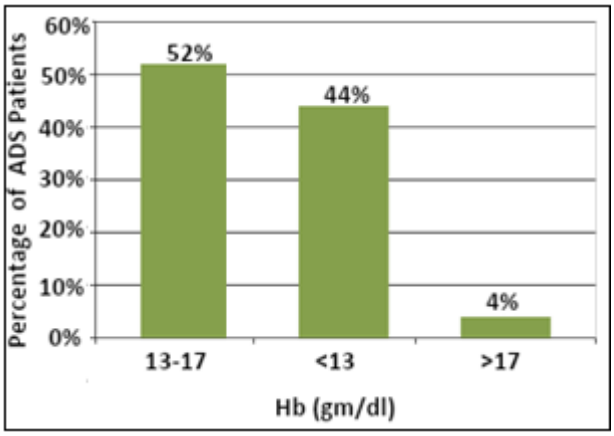

Figure 6: Haemoglobin in Ads Patients

Table 5: Grading of Severity of Anaemia

		No. of ADS Patients(n=44)	percentage
Hb (gm/dl)	Mild(11 - 12.9)	27	61.36%
	Moderate (8-10.9)	14	31.82%
	Severe(< 8)	3	6.82%

In this study, total subjects were 100.Out of which 44% had anaemia. These anaemic subjects were further classified according to severity of anaemia. Mild anaemia was observed in 27 patients (61.36%) , moderate anaemia in 14 patients (31.82%) and 3 patients(6.82%) had severe anaemia. These anaemic patients(44%) were further evaluated for serum iron, serum ferritin, peripheral smear.

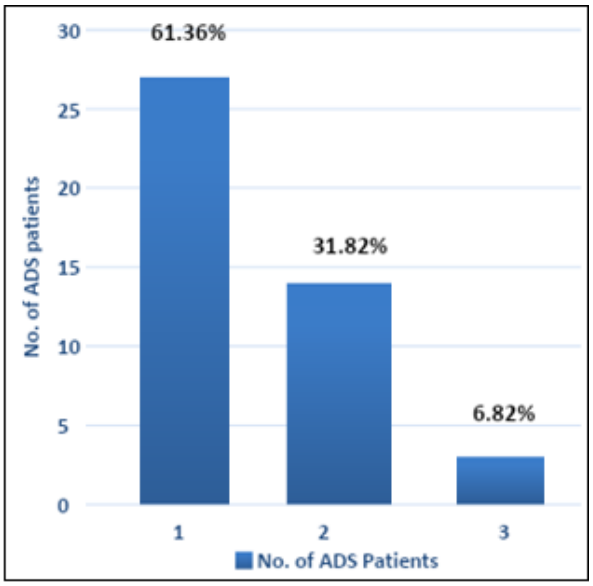

Figure 7: Grading of Severity of Anaemia

Table 6: Serum Iron in Ads Patients with Anaemia

		No. of ADS Patients (n=44)	Percentage
Serum Iron (micro gram/dl)	60 - 170	10	22.72%
	< 60	32	72.72%
	> 170	2	4.54%

In this study 44 anaemic patients were evaluated for serum iron. Majority of these patients (72.72%) had low serum iron. Minimum serum iron observed was 12mcg/dl, maximum serum iron observed was 207 mcg/dl with a mean vale of 51.325 and standard deviation was 37.0370.

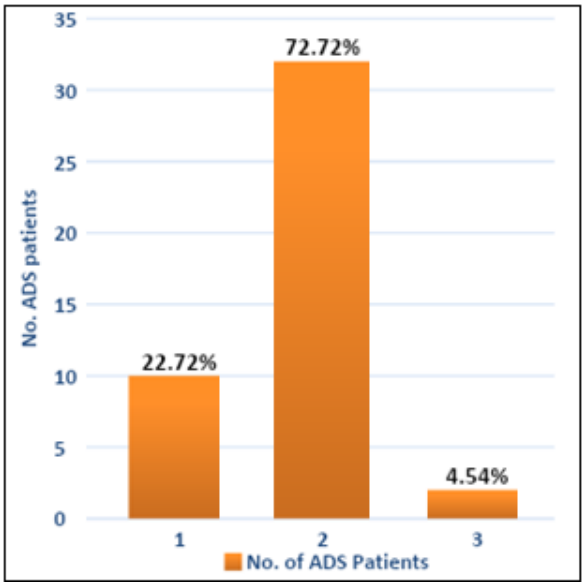

Figure 8: Serum Iron in Ads Patients with Anaemia

Table 7: Serum Ferritin in Ads Patients with Anaemia

		No. of ADS Patients(n=44)	percentage
Serum Ferritin (nano gram/ml)	50 - 300	16	36.36%
	< 50	8	18.18%
	> 300	20	45.45%

In this study serum ferritin was done in 44 anaemic patients. Majority of these patients (45.45%) had high serum ferritin. The minimum ferritin observed was 2.34 ng/ml and maximum observed was 1,172 ng/ml with a mean ferritin of 373.47 ng/ml and standard deviation was 315.89.

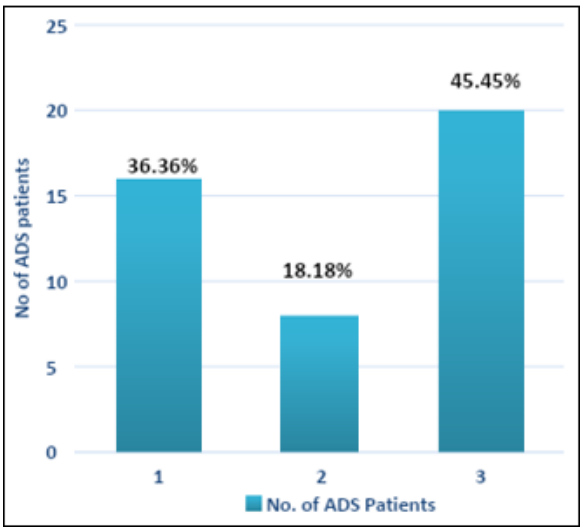

Figure 9: Serum Ferritin in Ads Patients with Anaemia

Table 8: Peripheral Smear in Ads Patients with Anaemia

		No. of Ads Patients (n=100)	Percentage
Peripheral Smear	Microcytic Hypochromic Anaemia	8	18.18%
	Macrocytic Hypochromic Anaemia	2	4.54%
	Normocytic Normochromic Anaemia	22	50%
	Dimorphic Anaemia	12	27.27%

In this study all anaemic patients (n=44) were evaluated for peripheral smear. It was observed that majority of patients (50%) had normocytic normochromic anaemia.

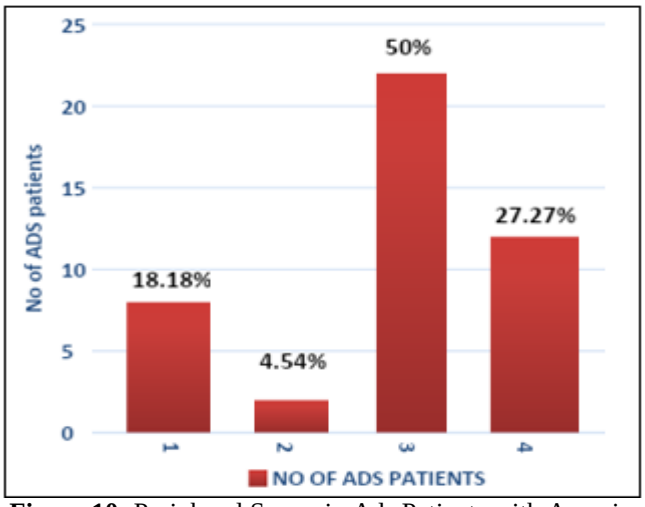

Figure 10: Peripheral Smear in Ads Patients with Anamia

Table 9: Total Leucocyte Count in Ads Patients

		No. of ADS Patients (n=100)	Percentage
Leucocyte count (cells/mm3)	4000 - 10000	77	77%
	<4000	6	6%
	>10000	17	17%

In this study majority of patients(77%) had normal leucocyte count, 6% had leucopenia and 17% had leucocytosis.The minimum leucocyte count observed in this study was 3200/mm^3 and maximum was 22000/mm^3 with a mean value of 7841 and standard deviation was 3552.63/mm^3.

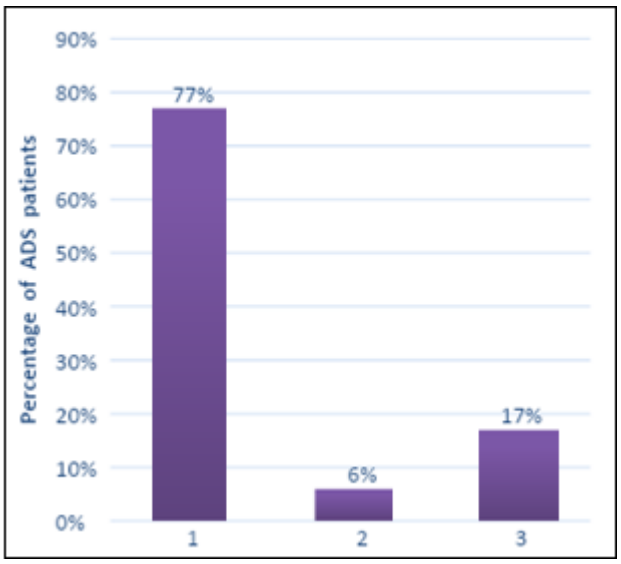

Figure 11: Total Leucocyte Count in Ads Patients

Table 10: Platelet Count in Ads Patients

		No. of ADS Patients (n=100)	Percentage
Platelet count (cells/mm3)	150000 – 400000	81	81%
	< 150000	16	16%
	> 400000	3	3%

In this study majority of patients (81%) had normal platelet count, 16% had thrombocytopenia and 3% had thrombocytosis. It was observed that minimum platelet count was 64000/mm^3, maximum platelet count was 431000/mm^3 with a mean value of 226580/mm^3 and standard deviation was 78591 /mm^3.

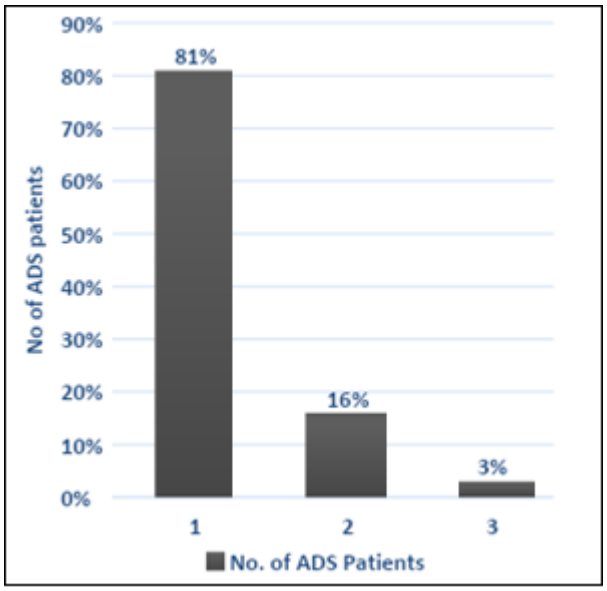

Figure 12: Platelet Count in Ads Patients

Table 11: Descriptive Statistics of the Study

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
Age	100	19.0	80.0	44.730	13.8044
Duration of alcohol(yrs)	100	3.0	60.0	19.450	10.4537
Hb(gm/dl)	100	6.5	18.1	13.136	2.4105
TC(/mm3)	100	3200.0	22000.0	7841.000	3552.6372
Platelets(/mm3)	100	64000.0	431000.0	226580.000	78591.5383
IRON(mcg/dl)	44	12.0	207.0	51.325	37.0370
FERRITIN(ng/ml)	44	2.34	1172.00	373.4798	315.89265

Table 12: Correlation of Haematological Parameters with Duration of Alcohol Intake in Ads Patients

	Mean	Std. Deviation	*Correlation coefficient (r)*	*p value*
Duration of alcohol(yrs)	19.450	10.4537	-0.274	0.006
Hb(gm/dl)	13.136	2.4105		
Duration of alcohol(yrs)	19.450	10.4537	0.126	0.213
TC(/mm3)	7841.000	3552.6372		
Duration of alcohol(yrs)	19.450	10.4537	0.154	0.127
Platelets(/mm3)	226580.000	78591.5383		
Duration of alcohol(yrs)	22.705	10.8662	-0.079	0.612
IRON(mcg/dl)	51.325	37.0370		
Duration of alcohol(yrs)	22.705	10.8662	-0.023	0.884
Ferritin(ng/ml)	373.4798	315.89265		

6. Discussion

The objective of the study undertaken was to study the Haematological profile in patients with Alcohol Dependence Syndrome. The study was conducted on 100 Alcohol dependence syndrome patients.

In this study, majority of the patients were aged between 31 to 45 years (43%). A wide range of age distribution was found with a minimum of 19 years and the maximum being 80 years, with a mean age of 44.73 years. In a study conducted by Chandini et al[61] the commonest age group affected was 31-40 years (40%), their results were similar to this study.

The gender distribution showed 98%of male patients and 2% were of female gender. Studies conducted by Thinnahanumaiah et al[9], Chandini et al[61] and Navin Patel et

al[60] included only male patients. According to a study done by Erhabor et al[64] 68% were male and 32% were female. This is probably due to variations in social lifestyle and ethnic cultures in different countries.

Majority of the patients 25 (25%), had a history of alcohol consumption for a duration of 16 to 20 years with a mean duration of 19.45 years. Similarly, in a study conducted by Chandini et al[61] on 100 patients, the maximum duration of alcohol consumption was 15-20 years noted in 33 (33%) alcohol dependence patients. The result of their study was similar to the present study. This is probably because a majority of the patients are brought in for medical care after a longer duration of alcohol consumption.

A total of 100 ADS patients were investigated for Hb, Total Leucocyte count, Platelet count.

Out of 100 patients 44 patients (44%) had anaemia in this study. According to the study done by Chandini et al[61] 36% individuals had anaemia. A study conducted by Pathak om k et al[63] observed 42.1% of anaemic patients in their study. This is because prolonged and excessive consumption of alcohol suppresses haematopoesis leading to decrease in red cell production. These 44 anaemic patients were further classified into mild, moderate and severe anaemia. 27 patients (61%) had mild anaemia, 14 patients (32%) had moderate anaemia and 3 patients(7%) had severe anaemia.

Patients with anaemia were evaluated with peripheral smear, serum iron and ferritin. Among anaemic patients 32(72.72%) of them had a low serum iron and 20 (45.45%) patients had high serum ferritin values. A study conducted by Whitfield JB et al[65] concluded that low level of alcohol intake increases serum ferritin and body iron stores.

Ioannou GN et al[66] published a study on "The effect of alcohol consumption on the prevalence of iron overload, iron deficiency, and iron deficiency anaemia" in 2004. They observed that on comparing patients with history of alcohol consumption against those without similar history, markers of iron overload were significantly higher in alcoholics who consumed >2 drinks/day.

Alcohol causes hepatic inflammation which leads to release of iron and ferritin from the hepatocytes. However in this study alcohol consumption was associated with low serum iron and high serum ferritin.

Majority of patients in this study (50%) had normocytic normochromic anaemia,12 patients(27%)had dimorphic anaemia, 8 patients (18%) had microcytic hypochromic anaemia and 2 patients (5%)had macrocytic anaemia.

Veda P[62] conducted a study to identify the underlying causes of macrocytosis. This study was conducted in the department of pathology, ESI PGIMSR, Bangalore, India from July 2009 to December 2010.Of the total 178 patients with macrocytosis, history of alcoholism was present in 65 patients(36.5%). Thinnahanumaiah M, et al[9] and Navin Patel,et al[60] observed significantly high MCV in alcoholics. This is probably due to ethanol having a direct toxic effect on the marrow erythroid precursors. However this pattern could not be demonstrated in this study . The probable explanation being size of MCV returns to normal following abstinence from alcohol for a period of 3-4 months and the precise duration of abstinence was not available in this study.

In this study 77 patients (77%) had normal leucocyte count, 6 patients (6%) had leucopenia and 17 patients (17%) had leucocytosis. A study conducted by Chandini et al[61]on alcoholic dependence syndrome observed that 82%ADS patients had normal leucocyte count,11% had leucocytosis and 7% had leucopenia. Their results were similar to this study.

In this study, 81 patients (81%) had normal platelet count, 16 patients (16%) had thrombocytopenia and 3 patients had thrombocytosis. Adias TC et al[5], Navin patel, et al[60] and Chandini, et al[61] observed thrombocytopenia in alcoholic patients. On contrary we observed normal platelet count in majority of the patients. The possible explanation was most of this study patients were selected from deaddiction department, abstinence from alcohol for a duration of 7 days has reversible effects on platelet count.

Pearson correlation coefficient was analysed between duration of alcohol and Hb, Total leucocyte count, Platelets. There was significant correlation observed between duration of alcohol and Hb with a p value of 0.006.

Limitations of the study

1) Small study population.
2) Duration of period is short.
3) As study was done in tertiary care hospital, sample is not representative of general population needs multicentre approach for further conclusion.

7. Summary

- 100 ADS patients were included in the study and the haematological profile was studied
- The age group most commonly involved was 31-45 years with a mean age of 44.73 years.
- Majority of the patients were males. 98 % patients were males and 2 % were females.
- Majority of patients (25%) consumed alcohol for a duration of 16 to 20 years with a mean duration of 19.45 years.
- All 100 ADS patients were investigated for hb, total leucocyte count, platelet count.
- Among 100 ADS patients, 44 patients (44%) had anaemia. They were further classified as mild, moderate and severe anaemia. Majority of the patients (61%) had mild anaemia.
- All 44 anaemic patients were evaluated with peripheral smear, serum iron and ferritin.A low serum iron was seen in majority (73%) of these patients with a mean value of 51.32 microgm/dl. High serum ferritin was seen in majority (46%) of patients with a mean value of 373.47nanogm/ml. Most of the patients (50%) had normocytic normochromic anaemia.

- Among 100 ADS patients a majority (77%) of the patients had normal leucocyte count and 81% had normal platelet count.
- Pearson correlaton coefficient was analysed between duration of alcohol consumption and Hb, Total leucocyte count, Platelets. There was significant correlation observed between duration of alcohol and Hb with a P value of 0.006, which was statistically significant.

8. Conclusion

- Alcohol consumption is a major risk factor for many health problems. Alcohol consumption has been associated with numerous haematological complications by affecting various cell lines.
- This study found a negative correlation between the duration of alcohol intake and haemoglobin in ADS patients with a p-value of 0.006 which was statistically significant.
- Most common haematological complication observed was anaemia. Normocytic normochromic anaemia was the most common type of anaemia noted in this study.

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