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THE SCENARIO OF ANAEMIA IN THE SPECTRUM OF CHRONIC LIVER DISEASE AN OBSERVATIONAL DESCRIPTIVE STUDY

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Abstract
Background: As we are aware that chronic liver disease frequently associated with haematological abnormalities which presents Anaemia of diverse etiology occurs in about 75% of patients and also this condition may be exacerbated by deficiency of folic acid and/or vitamin B12 that can occur secondary to inadequate dietary intake or malabsorption. So In this study we want to evaluate chronic liver disease patients having anaemia without overt bleeding in the past 3 months to know the severity and type of anaemia in these patients so as to enable us better management and decrease associated morbidity and mortality. ***Research Question:*** .What is the scenario of anaemia in the spectrum of chronic liver disease in our setup? **The setting** of the study was at department of Gastroenterology, Government General Hospital, Guntur Medical College, Guntur, Andhra Pradesh. A one year observational study was conducted during the period from April 2022 to May 2023 on about 100 chronic liver disease patients having anaemia whose Hb levels <10 g/dl without overt bleeding in the past 3 months admitted during the above period in the department of Gastroenterology by studying their socio-demographic profiles, type of chronic liver disease and anaemia with related laboratory investigations etc**. Results**: It was observed that in ALC the most common anaemia is folic acid deficiency (39.7%) followed by Iron deficiency (37.2%), in HBV most common anaemia was Iron deficiency (54.5%) followed by Folic acid deficiency (36.4%), in HCV both Iron and Folic acid deficiency were equally distributed (42.9%) and in NAFLD Iron and B12 deficiency were equally distributed (25%). Regarding severity, about 14% were severely anaemic flowed by 63% moderately anaemic and 23% were mild anaemic as noticed. In this study among the ALC cases maximum 35.9% were belong to the age group 41-50 years followed by 45.5% belong to 51-60 among HBV,42.9% belong to 41-50 years among HCV and about 50% of cases belong to 41-50 years among NAFLD. Totally it was observed that the majority age group suffering from chronic liver disease was between 41 -60 years. Mean age of study subjects was 46.7 years. And the lowest mean values of serum iron (29.29mcg/dl) and folic acid (4.59ng/ml) was observed among HCV cases and serum vit-B12 (221.3pg/ml) seen in ALC cases in this study.

Key words: ALC (Alcoholic Liver Cirrhosis), HBV (Hepatitis B Virus), HCV (Hepatitis-C Virus), NAFLD (Non-alcoholic, fatty liver disease) ID (Iron Deficiency) and FD (Folic acid deficiency) etc.

INTRODUCTION

As we all know that Liver plays an important role in normal erythropoiesis especially in formation and destruction of Red blood cells. Chronic liver diseases frequently are associated with haematological abnormalities. The causes of anaemia include acute or chronic gastrointestinal haemorrhage,[1]. Anaemia of diverse etiology occurs in about 75% of patients with chronic liver disease.[2]and hypersplenism secondary to portal hypertension. Acute haemorrhage may induce severe hypovolemia and subsequently secondary iron deficiency anemia. Thrombocytopenia is by far the commonest haematological abnormality seen in patients with cirrhosis followed by leucopenia and anemia.[3]

And severe hepatocellular disease predisposes to haemorrhage because of impaired blood coagulation caused by deficiency of blood coagulation factors synthesized by hepatocytes, and/or thrombocytopenia. Aplastic anaemia, which is characterized by pancytopenia and hypo cellular bone marrow, may follow the development of hepatitis[4,5].And thrombocytopenia is by far the commonest haematological abnormality seen in patients with cirrhosis followed by leukopenia and anemia.[6] Its presentation includes progressive anaemia and haemorrhagic manifestations. There are several mechanisms by which anaemia may occur during combination therapy for HCV infection, and ribavirin and/or

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interferons may contribute to anaemia. In this context, haemoglobin concentrations decrease mainly as a result of ribavirin-induced hemolysis.[7] Ribavirin induced haemolysis can be reversed by reducing the dose of the drug or discontinuing it altogether. Interferons may contribute to anaemia by inducing bone marrow suppression. Alcohol ingestion is implicated in the pathogenesis of chronic liver disease and may contribute to associated anaemia. In patients with chronic liver disease, anaemia may be exacerbated by deficiency of folic acid and/or vitamin B12 that can occur secondary to inadequate dietary intake or malabsorption. The anaemia is also due to several other factors, including blood dilution secondary to increased plasma volume and splenic pooling of red cells, which can trap up to 25 per cent of the total circulating red cell mass, depending upon the size of the spleen. Red cell survival is also decreased, by up to 50 per cent, and this is also proportional to spleen size. Depending upon the underlying aetiology of the portal hypertension, there may be an added element of inadequate bone marrow response to anaemia. Anaemia may be seen in 66%-75% of patients with liver cirrhosis[8] In this study we evaluated chronic liver disease patients having anaemia without overt bleeding in the past 3 months to know the severity and type of anaemia in those patients.

MATERIAL & METHODOLOGY

The setting of the study was at department of Gastroenterology, Government General Hospital, Guntur Medical College, Guntur, Andhra Pradesh. A one year observational study was conducted during the period from April 2022 to May 2023. According to the hospital censes the prevalence of Chronic liver disease cases admitting Gastroenterology department was found to be 50% and the sample size was calculated by using the formula $N=4PQ/L^2$ where P=50%, Q=100-P that is 50% and L=20% allowable error in 'P' that is 10 so N=100. All the cases of clinically diagnosed chronic liver disease patients having anaemia whose Hb levels <10 g/dl without overt bleeding in the past 3 months admitted in the ward during the above period up to reach the required sample size was included in the study after receiving return consent by duly explaining the detail procedure and purpose of the study and also duly following the inclusion and exclusion criteria as indicated below**. Inclusion criteria:** 1.Age >18 yrs 2.All Patients with chronic liver disease with Hb of less than 10g/dl. **Exclusion criteria:**1.Age <18 years.2.Patients with Overt bleeding in the form of Hematemesis , melena in the past 3 months.3.Patients with known GIT malignancy or known hepatocellular carcinoma.4.Patients with primary Haematological /coagulation disorder.5.Acute decompensation of CLD 6.Liver failure due to septicaemia or endotoxemia other than primary liver causes. . The objectives of the study were 1. To identify the socio-demographic profiles of the study subjects 2.To study the type, causative factors and severity of anaemia in the spectrum of chronic liver disease. After receiving the Ethical committee clearance from the institution the study was began and the required data was collected by using a pretested proforma pertaining to their socio-demographic profiles, type, grading and severity of anaemia in the spectrum of chronic liver disease and associated factors with different types of chronic liver diseases etc. All the cases (study subjects) of the study were managed and followed until discharge.

Finally the collected data was analysed by using appropriate statistical tools like percentages, proportions, measures of central tendency, measures of dispersion, standard error of mean and tests of significance etc. with the help of computer software. The study results were compared and discussed in the light of published material of various similar studies belongs to different authors and there by conclusions and recommendations was framed.

Observations

Table 1: Age and sex wise distribution of study subjects

S.No	AGE	SEX		TOTAL
		Male	Female	
1.	21-30	4	1	5
2.	31-40	19	4	23
3.	41-50	30	7	37
4.	51-60	22	7	29
5.	>60	4	0	6
	Total	81	19	100

Majority of the study subjects were males (81%) when compared to females (19%)

- Mean age of the study subjects was 46.7 years
- Totally it was observed that the majority age group suffering from chronic liver disease was between 41 -60 years

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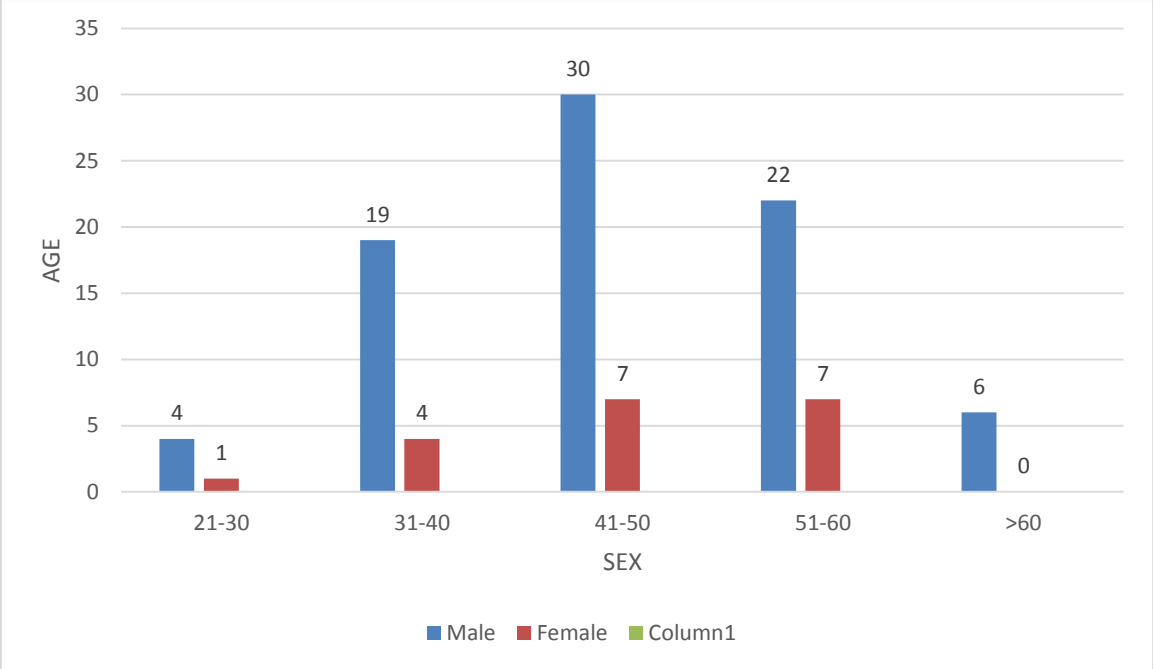

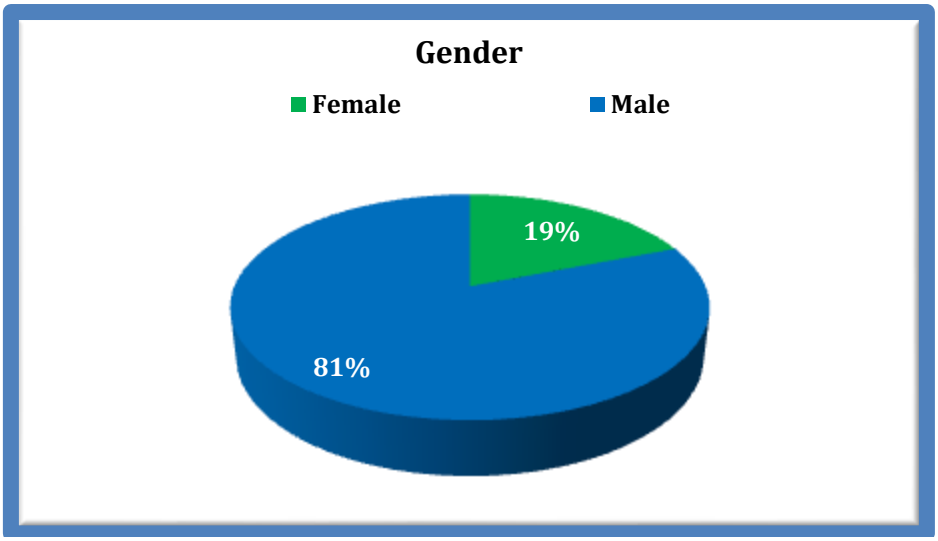

Table 2 : Type and distribution of Anaemia in different Chronic Liver disease cases

TABLE: Etiology ofause of CLD	ETIOLOGY OF ANEMIA											
	BD		FD		FD+BD		IDA		IDA+BD		IDA+FD	
	Count	%	Count	%	Count	%	Count	%	Count	%	Count	%
ALC	6	7.7%	31	39.7%	3	3.8%	29	37.2%	1	1.3%	8	10.3%
HBV	0	0%	4	36.4%	0	0%	6	54.5%	0	0%	1	9.1%
HCV	0	0%	3	42.9%	0	0%	3	42.9%	0	0%	1	14.3%
NAFLD	1	25.0%	1	25.0%	0	0%	1	25.0%	0	0%	1	25.0%

P < 0.05

- It was observed that in ALC the most common anaemia is folic acid deficiency (39.7%) followed by Iron deficiency (37.2%), in HBV most common was Iron deficiency (54.5%) followed by Folic acid deficiency (36.4%), in HCV both Iron & Folic acid deficiency were equally distributed (42.9%) and in NAFLD Iron and B12 deficiency were equally distributed (25%).
- Among all the types of anaemia Iron deficiency anaemia was the commonest one observed.

Table 3: Distribution of Grading and Severity of Anaemia

Hb	SEX		Total
	F	M	

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	Count	%	Count	%	Count	%
<6 (Severe)	3	15.8%	11	13.6%	14	14.0%
6-8.9 (Moderate)	12	63.2%	51	63.0%	63	63.0%
9-12.9 (Mild)	4	21.1%	19	23.5%	23	23.0%
Total	19	100.0%	81	100.0%	100	100.0%

P > 0.05

- Regarding severity about 14% were severely anaemic flowed by 63% moderately anaemic and 23% were mild anaemic as noticed.

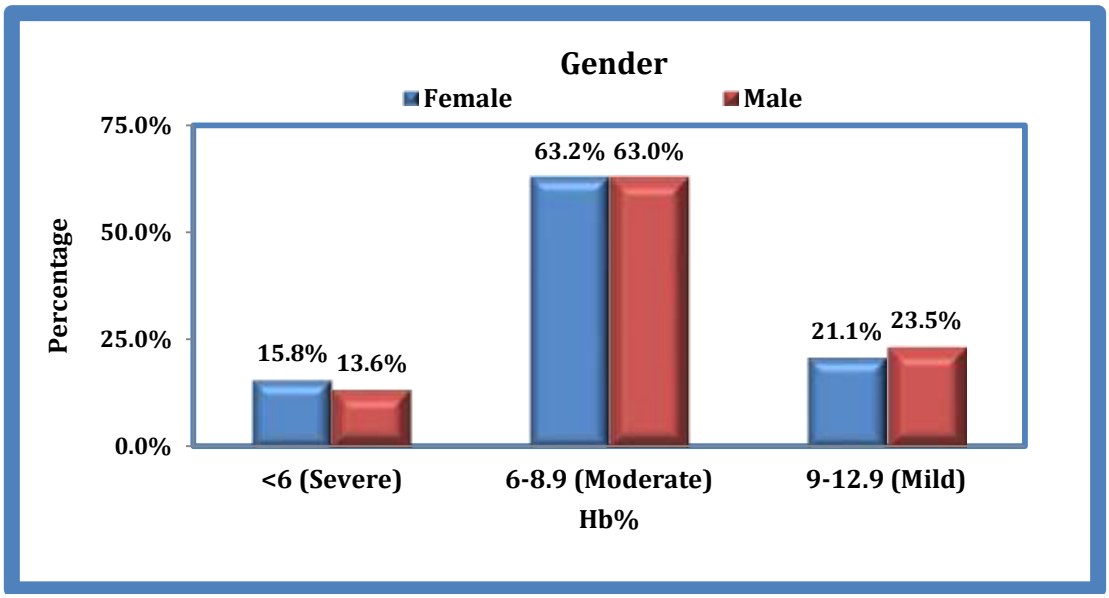

Table 4: Age wise distribution of different types of Chronic Liver diseases

Age	ETIOLOGY							
	ALC		HBV		HCV		NAFLDa	
	Count	%	Count	%	Count	%	Count	%
21-30	3	3.8%	1	9.1%	0	0%	1	25.0%
31-40	20	25.6%	1	9.1%	2	28.6%	0	0%
41-50	28	35.9%	4	36.4%	3	42.9%	2	50.0%
51-60	21	26.9%	5	45.5%	2	28.6%	1	25.0%
>60	6	7.7%	0	0%	0	0%	0	0%

- In this study among the ALC cases maximum 35.9% were belong to the age group 41-50 years followed by 45.5% belong to 51-60 among HBV,42.9% belong to 41-50 years among HCV and about 50% of cases belong to 41-50 years among NAFLD .
- Totally it was observed that the majority age group suffering from chronic liver disease was between 41 -60 years
- Regarding distribution of spectrum of chronic liver disease majority of the study subjects were belong to ALC followed by HBV, HCV and NAFLD.

Table 5: Mean values of different factors associated with Chronic liver disease

Variable	ETIOLOGY							
	ALC		HBV		HCV		NAFLD	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
AGE	47.32	10.05	47.27	8.80	47.43	7.16	45.00	13.34
TB	4.51	6.07	2.32	2.97	2.79	3.18	1.95	1.12
AST	82.83	70.83	44.18	24.20	71.43	59.05	65.50	18.59
ALT	47.76	39.83	31.73	27.40	54.00	39.78	32.50	5.26
ALBUMIN	4.34	12.94	3.03	0.65	2.86	0.46	2.70	0.34
PT INR	1.94	0.53	1.79	0.39	1.86	0.26	1.88	0.39
Hb (gr/dl)	7.92	1.57	6.80	1.60	6.94	1.73	7.23	2.25

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MCH (pg)	26.97	4.70	26.98	4.42	26.29	3.86	23.50	5.45
MCV (fl)	93.28	14.59	86.27	15.35	90.14	10.24	91.25	20.97
SERUM FOLIC ACID(ng/ml)	5.18	2.46	5.13	3.34	4.59	2.61	6.85	3.16
SERUM VitB12 (pg/ml)	431.03	221.30	536.09	232.61	494.86	174.42	400.75	224.31
S.iron	53.74	45.33	50.91	54.53	29.29	24.56	44.75	46.64
Ferritin	178.99	196.64	214.27	267.06	77.00	83.99	147.75	209.06
TIBC	447.18	87.86	412.64	82.91	470.57	82.14	457.50	65.13
CTP SCORE	8.77	2.20	7.55	2.07	8.71	1.98	9.75	2.36
MELD –NA	21.92	8.04	16.36	6.17	22.14	7.06	19.25	10.21

- Mean age of study subjects was 46.7 years
- And the lowest mean values of serum iron (29.29mcg/dl) and folic acid (4.59ng/ml) was observed among HCV cases and serum vit-B12 (221.3 pg/ml) seen in ALC cases in this study.

MATERIALS AND METHODOLOGY

It was observed that in this study majority of study subjects were males (81%) when compared to females (19%) which correlates with the figures of Rauf et al (2014) study and E. H. Kumar et al(2014) study and most of the patients belongs to age group between 41-60yrs.with the mean age was 46.7 years which comparable to Naimesh Patel et al[9] and A Frijo jose et al[10] studies. Because of addiction to alcohol and extra marital sexual relations, males are more prone to develop chronic liver disease after 40 years of age usually in our setup. Regarding distribution of spectrum of chronic liver disease majority of study subjects were belong to ALC followed by HBV,HCV and NAFLD respectively which was comparable to Kurundkar et al and Naimesh patel et al[9] studies.

It was also observed that in ALC the most common anaemia was folic acid deficiency (39.7%) followed by Iron deficiency (37.2%), in HBV most common was Iron deficiency (54.5%) followed by Folic acid deficiency (36.4%), in HCV both Iron & Folic acid deficiency were equally distributed (42.9%) and in NAFLD Iron and B12 deficiency were equally distributed (25%). And among all the types of anaemias Iron deficiency anaemia was the commonest one observed in this study and similar findings were reported by Özatli D et al[11] and Manrai M et al[12] and Gkamprela E et al[13] studies. Iron deficiency (ID), with or without anaemia, is associated with many symptoms and complications that have a significant and negative impact on patients. It can increase cardiovascular morbidity and mortality, impair cognition, and decrease quality of life[14] In Alcoholic liver cirrhosis besides, nutritional deficiencies including those of iron, Vitamin (Vit) B12, B6, and folate are common in patients suffering from cirrhosis and also besides increasing the risk of mortality, anaemia is associated with a higher incidence of acute on chronic liver failure (ACLF) and increased risk of hospitalization as reported by Scheiner B et al [8]. With reference to severity about 14% were severely anaemic flowed by 63% moderately anaemic and 23% were mild anaemic in our study which were on par with the findings reported by E. H. Kumar et al(2014), Kurundkar et al and Naimesh patel et al [9] studies. In our study the Mean hemoglobin concentration was 7.7 gr/dl which correlates with the figures of G.Anbazhagan et.al[15] And the lowest mean values of serum iron (29.29mcg/dl) and folic acid (4.59ng/ml) was observed among HCV cases and serum vit-B12 (221.3pg/ml) seen in ALC cases in this study because B12 deficiency is common among alcoholics and also very low mean serum ferritin level (77 ng/ml) observed in HCV chronic liver cases which correlates with the reports of Intagumtornchai T et al [16],Lipschitz da et al[17] Nelson R et al [18] and Gyuatt GH et al [19] in their studies. And among HCV & NAFLD cases low albumin levels were observed which correlates with the reports of Scheiner B et al study.

LIMITATIONS OF THE STUDY

- It was a hospital based study
- Due to lack of follow up of the study subjects after discharge, we did not get the chronology of their disease process.
- We were not able to do bone marrow biopsy in all cases
- Only serum folic acid was done. The study could be better if we include RBC folate levels also.
- We did only stool examination for 3 consecutive days to rule out active parasitic infection. We has less specificity with high sensitivity

Conclusions and Recommendations

- As the majority of the patients belong to middle age group (40-60years) which produces big damage to the family in terms of social, economical and psychological aspects, it is important to focus preventive aspects of the disease as

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early as possible so as to minimise the loss because these causative factors for the chronic liver disease is largely preventable. And it is necessary to motivate people to receive vaccination against HBV & HCV and also create awareness and wide publicity by means of health education by health personnel and the print & electronic and social media towards the harmful effects of the habituation of alcohol intake.

- And also in order to control and prevent anaemia, it is advisable to prescribe Iron & Folic acid tablets and B-Complex or Multivitamin supplements to the patients having h/o regular alcohol consumption and HBV & HCV viral infections as early as possible.
- The individuals who are having family h/o NAFLD, habituation of alcohol consumption and HBV, HCV positive should undergo regular periodical Liver check-up so as to prevent or limit the progress of chronic liver disease there by we could reduce morbidity and mortality associated with chronic liver disease.

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