IJFANS INTERNATIONAL JOURNAL OF FOOD AND NUTRITIONAL SCIENCES

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **Volume 11, Sp.Iss 6 , 2022**

THE SCENARIO OF ANAEMIA IN THE SPECTRUM OF CHRONIC LIVERDISEASEANOBSERVATIONAL DESCRIPTIVESTUDY

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DOI : 10.48047/IJFANS/11/S6/006

Abstract. Background: As we are aware that chronic liver disease frequently associated with haematological abnormalities whichpresents Anaemia of diverse etiology occurs in about 75% of patients and also this condition may be exacerbated bydeficiency of folic acid and/or vitamin B12 that can occur secondary to inadequate dietary intake or malabsorption. So Inthis study we want to evaluate chronic liver disease patients having anaemia without overt bleeding in the past 3 monthsto know the severity and type of anaemia in these patients so as to enable us better management and decrease associatedmorbidity and mortality.

Key words: ALC (Alcoholic Liver Cirrhosis), HBV (Hepatitis B Virus), HCV (Hepatitis-C Virus), NAFLD (Non-alcoholic,fattyliver disease)

1. Introduction

Asweallknow thatLiverplaysanimportantroleinnormalerythropoiesisespecially informationanddestruction of Red blood cells. Chronic liver diseases frequently are associated with haematological abnormalities. Thecauses of anaemia include acute or chronic gastrointestinal haemorrhage,[1]. Anaemia of diverse etiology occurs in about75% of patients with chronic liver disease.[2]and hypersplenism secondary to portal hypertension. Acute haemorrhage mayinduceseverehypovolemiaandsubsequentlysecondaryirondeficiencyanemia.Thrombocytopeniaisb yfarthecommonesthaematological abnormalityseeninpatientswithcirrhosisfollowedbyleucopeniaand anemia.[3]

And severe hepatocellular disease predisposes to haemorrhage because of impaired blood coagulation caused bydeficiency of blood coagulation factors synthesized by hepatocytes, and/or thrombocytopenia. Aplastic anaemia, which ischaracterizedbypancytopeniaandhypocellularbonemarrow,mayfollowthedevelopmentofhepatitis[4,5]. Andthrombocytopenia is by far the commonest haematological abnormality seen in patients with cirrhosis followed byleukopenia and anemia.[6]Its presentation includes progressive anaemia and haemorrhagic manifestations. There areseveralmechanismsbywhichanaemiamayoccurduringcombinationtherapyforHCVinfection,andriba virinand/orinterferons may contribute toanaemia. In this context,haemoglobin concentrations decrease mainly as a result ofribavirin-inducedhemolysis.[7]Ribavirininducedhaemolysiscanbereversedbyreducingthedoseofthedrugordisconti nuing italtogether.Interferonsmay contributetoanaemiaby inducing bonemarrow suppression.Alcoholingestion is implicated in the pathogenesis of chronic liver disease and may contribute to associated anaemia. In patientswith chronic liver disease, anaemia may be exacerbated by deficiency of folic acid and/or vitamin B12 that can occursecondary toinadequate dietaryintake ormalabsorption.The anaemia is also due toseveral otherfactors, includingblood dilution secondary to

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increased plasma volume and splenic pooling of red cells, which can trap up to 25 per cent ofthe total circulating red cell mass, depending upon the size of the spleen. Red cell survival is also decreased, by up to 50per 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% ofpatients with liver cirrhosis[8]In this study we evaluated chronic liver disease patients having anaemia without overtbleedinginthepast3monthstoknowtheseverityandtypeofanaemia inthosepatients.

2. 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 theprevalence of Chronic liver diseasecases admitting Gastroenterology departmentwas 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 is50% and L=20% allowable error in 'P' that is 10 so N=100. All the cases of clinically diagnosed chronic liver diseasepatients having anaemia whose Hb levels <10 g/dl without overt bleeding in the past 3 months admitted in the wardduring the above period up to reach the required sample size was included in the study after receiving return consent byduly explaining the detail procedure and purpose of the study and also duly following the inclusion and exclusion criteriaas indicated below**. Inclusion criteria:** 1.Age>18 yrs 2.All Patients with chronic liver disease with Hb of less than10g/dl. **Exclusion criteria:**1.Age<18 years.2.Patients with Overt bleeding in the form of Hematemesis , melena in thepast3months.3.PatientswithknownGITmalignancyorknownhepatocellularcarcinoma.4.Patientswith primaryHaematological/coagulationdisorder.5.AcutedecompensationofCLD6.Liverfailureduetoseptic aemiaorendotoxemia other than primary liver causes. . The objectives of the study were 1. To identify the sociodemographicprofiles of the study subjects 2.To study the type, causative factors and severity of anaemia in the spectrum of chronicliver disease. After receiving the Ethical committee clearance from the institution the study was began and the requireddata was collected by using a pretested proforma pertaining to their socio-demographic profiles, type, grading andseverity of anaemia in the spectrum of chronic liver disease andassociated factors with different types of chronic liverdiseasesetc.Allthe cases(studysubjects)ofthestudyweremanagedand followed untildischarge.

Finally the collected data was analysed by using appropriate statistical tools like percentages, proportions, measuresof central tendency, measures of dispersion, standard error of mean and tests of significance etc. with the help ofcomputer software. The study results were compared and discussed in the light of published material of various similarstudiesbelongstodifferentauthorsand there byconclusionsand recommendationswasframed.

3. Analysis

Table1: Ageand sexwisedistributionofstudysubjects

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%)Meanage ofthestudysubjectswas46.7 years. Totallyitwasobserved thatthemajorityagegroupsuffering fromchronicliver diseasewasbetween41-60 years

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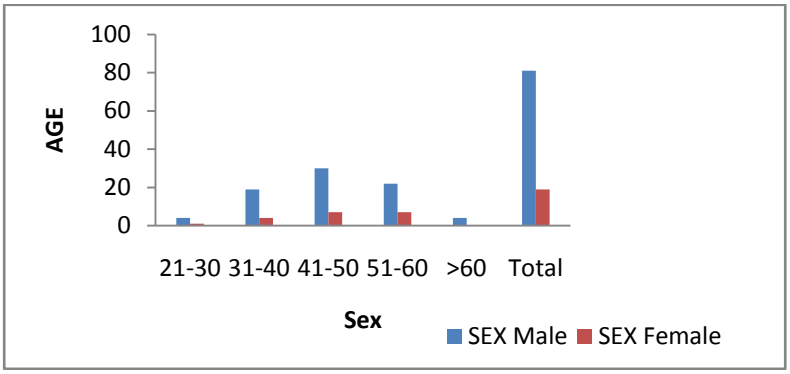

Figure1 Age & Sex Wise Distribution

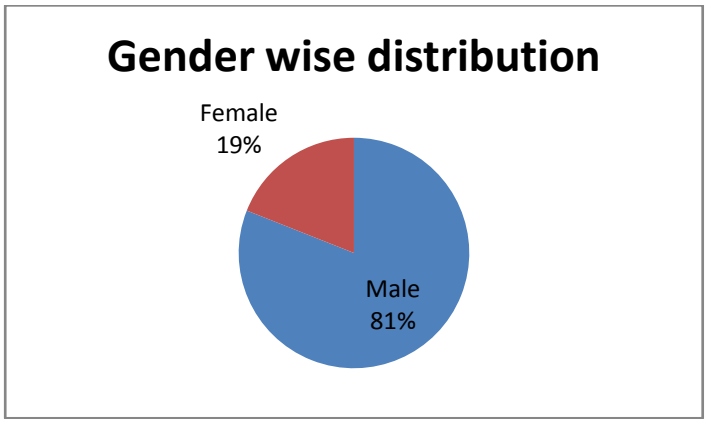

Figure2 Sex Wise Distribution

Table2: TypeanddistributionofAnaemiaindifferentChronicLiverdiseasecases

TABLE: Etiologyofauseof CLD	ETIOLOGYOFANEMIA											
	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& Folicacid deficiency wereequallydistributed (42.9%)and inNAFLDIronand B12 deficiency wereequallydistributed(25%).
- Amongallthetypesofanaemia Irondeficiencyanaemiawasthecommonestoneobserved.

Table3:DistributionofGradingandSeverityofAnaemia

Hb	SEX				Total	
	F		M			
	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

- Regardingseverityabout14%wereseverelyanaemicflowedby63%moderatelyanaemicand23%weremildanaemicasnoticed.

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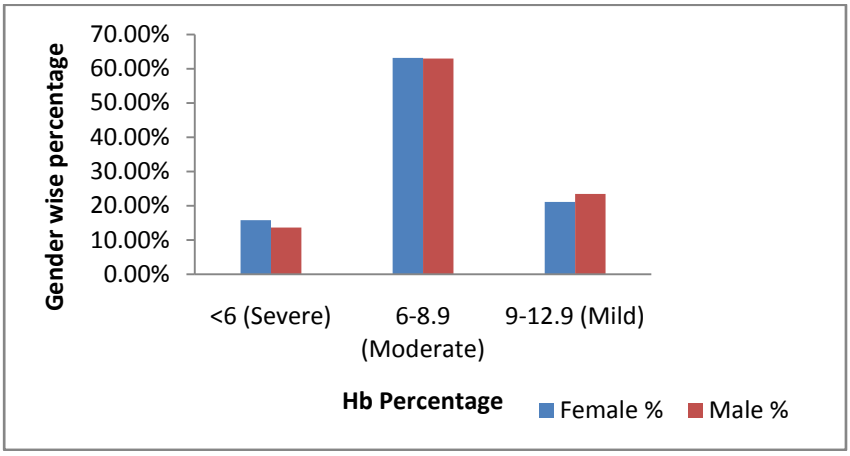

Table4:AgewisedistributionofdifferenttypesofChronicLiverdiseases

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 andabout 50% of cases belong to 41-50yearsamongNAFLD .
- Totally it was observed that the majority age group suffering from chronic liver disease wasbetween 41 -60 years
- Regardingdistributionof spectrum of chronicliverdiseasemajority ofthestudy subjectswerebelongtoALCfollowed byHBV, HCVandNAFLD.

Table5:MeanvaluesofdifferentfactorsassociatedwithChronicliverdisease

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
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
SERUMFOLIC 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
CTPSCORE	8.77	2.20	7.55	2.07	8.71	1.98	9.75	2.36

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MELD –NA	21.92	8.04	16.36	6.17	22.14	7.06	19.25	10.21

- Meanageof studysubjectswas46.7years
- And the lowest mean values of serum iron (29.29mcg/dl) and folic acid (4.59ng/ml) was observed among HCV casesand serumvit-B12(221.3pg/ml) seeninALCcasesinthisstudy.

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

It was also observed that in ALC the most common anaemia wasfolic acid deficiency (39.7%) followed by Irondeficiency (37.2%), in HBV most common was Iron deficiency (54.5%) followed by Folic acid deficiency (36.4%), inHCV both Iron & Folic acid deficiency were equally distributed (42.9%) and in NAFLD Iron and B12 deficiency wereequally distributed (25%). And among all the types of anaemias Iron deficiency anaemia was the commonest oneobserved in this study and similar findings were reported by Özatli Det al[11] and ManraiM et al[12] and Gkamprela E etal[13] studies. Iron deficiency (ID), with or without anaemia, is associated with many symptoms and complications thathave a significant and negative impact on patients. It can increase cardiovascularmorbidity andmortality, impaircognition, and decrease quality of life[14]In Alcoholic liver cirrhosis besides, nutritional deficiencies including those ofiron, Vitamin (Vit) B12, B6, and folate are common in patients suffering from cirrhosis and also besides increasing therisk of mortality, anaemia is associated with a higher incidence of acute on chronic liver failure (ACLF) and increasedrisk of hospitalization as reported by Scheiner B et al [8]. With reference to severity about 14% were severely anaemicflowed by 63% moderately anaemic and 23% were mild anaemic in our study which were on par with the findingsreported by E. H. Kumar et al(2014),Kurundkar et aland Naimesh patel et al [9] studies. In our study the Meanhemoglobin concentration was 7.7 gr/dl which correlates with the figures of G.Anbazhagan et.al[15] And the lowest meanvalues 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 andalso very lowmeanserumferritinlevel(77ng/ml)observedinHCVchroniclivercaseswhichcorrelateswiththereportsofIntagumtornchai T et al [16],Lipschitz da et al[17] Nelson R et al [18] and Gyuatt GH et al [19] in their studies. Andamong HCV&NAFLDcaseslowalbuminlevelswereobservedwhichcorrelateswiththereportsofScheinerB etalstudy.

LimitationsOfTheStudy

- It wasahospitalbased study
- Duetolackoffollowupofthestudysubjectsafterdischarge,wedidnotgetthechronologyoftheirdiseaseprocess.
- Wewere notableto do bonemarrowbiopsyinallcases
- Onlyserum folicacidwasdone.Thestudycouldbebetter ifweincludeRBCfolatelevelsalso.
- Wedidonlystoolexaminationfor3consecutivedaystoruleoutactiveparasiticinfection.Wehaslessspecificitywith highsensitivity

4. ConclusionsandRecommendations

- Asthemajorityofthepatientsbelong tomiddleagegroup(40-60years)which producesbig damagetothefamilyintermsofsocial,economicalandpsychologicalaspects,itisimportanttofocuspreventiveaspectsofthediseaseasearly as possible so as to minimise the loss because these causative factors for thechronic liver disease is largelypreventable. And it is necessary to motivate people to receive vaccination against HBV & HCV and also createawareness and wide publicity by means of health education by health personnel and the print & electronic and socialmediatowardsthe harmfuleffectsof thehabituationofalcoholintake.
- And also in order to control and prevent anaemia, it is advisable to prescribe Iron & Folic acid tablets and B-ComplexorMultivitaminsupplementstothepatientshavingh/oregularalcoholconsumptionandHBV&HCVviralinfectionsasearlyaspossible.
- The individuals who are having family h/o NAFLD, habituation of alcohol consumption and HBV, HCV positiveshould undergo regular periodical Liver check-up so as to

ISSN PRINT 2319 1775 Online 2320 7876

Research paper Volume 11, Sp.Iss 6 , 2022

prevent or limit the progress of chronic liver disease therebywecouldreducemorbidityandmortalityassociatedwithchronicliverdisease.

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