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HEMATOLOGICAL AND COAGULATION ABNORMALITIES IN CIRRHOTICS WITH DECOMPENSATION.

General Medicine

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ABSTRACT

BACKGROUND: Decompensated cirrhosis is cirrhosis characterised by the development of jaundice, ascites, variceal haemorrhage, or hepatic encephalopathy. Liver diseases can manifest with a number of systemic symptoms like circulatory changes, endocrinopathy, renal dysfunction, electrolyte disturbances and haematological abnormalities. Haematological abnormalities add to significant morbidity and mortality in chronic liver disease. Hence, the present study was undertaken to estimate the various haematological abnormalities in decompensated cirrhosis.

METHODOLOGY: The present Cross sectional observational study "Haematological and coagulation abnormalities in decompensated cirrhosis" was carried out in the Department of General Medicine, GSL Medical College and General Hospital, Rajahmundry from OCTOBER 1st-2016 to MARCH 30th-2018. A total of 130 patients were observed after following the inclusion and exclusion criteria.

RESULTS: The mean age was 55.66 years. The study population constituted 10.8% females and 89.2% males. The most common form of decompensation was ascites in 123 cases (94.6%). Commonest etiology was alcohol abuse in 89 (68.4%). Mean hb% of the study population was 8.97 ± 2.21 g/dl. Normocytic normochromic anemia was commonly observed. 22 cases (16.9%) had leukopenia and 24 cases (18.5%) had leucocytosis. 91 cases (70%) had thrombocytopenia. PT was prolonged in 93 cases (71.5%) and aPTT was prolonged in 60 (46.2%) cases.

CONCLUSION: Haematological and haemostatic abnormalities are very common in decompensated cirrhosis. Hence all the cirrhosis patients must be evaluated for haematological and haemostatic abnormalities and should be monitored for the development of complications. Early anticipation, detection and appropriate treatment can prevent significant morbidity and mortality associated with cirrhosis.

KEYWORDS

haematological abnormalities, coagulation abnormalities, decompensated cirrhosis.

INTRODUCTION:

Cirrhosis is defined as a diffuse hepatic process with the development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury, that leads to portal hypertension and end stage liver disease. [1]

Cirrhosis is considered to be compensated in the asymptomatic patient with or without gastroesophageal varices. Decompensated cirrhosis is defined by the development of jaundice, ascites, variceal haemorrhage, or hepatic encephalopathy.

Liver diseases can manifest with systemic symptoms like circulatory changes, endocrinopathy, renal dysfunction, electrolyte disturbances and haematological abnormalities. [2]

Haematological abnormalities commonly include anaemia, thrombocytopenia, leukopenia, clotting and coagulation defects. [2] Cause of these haematological abnormalities is multi factorial.

MATERIALS AND METHODS:

Aims and objectives:

1. To assess the prevalence of anaemia.
2. To assess the type and severity of anaemia.
3. To assess the severity of thrombocytopenia.
4. To assess the extent of coagulopathy in the study subjects.

INCLUSION CRITERIA:

- A compatible Clinical profile (signs of liver cell failure or reduced liver span) along with Biochemical (altered liver function tests, reversal of albumin-globulin ratio) and Sonographic evidence (altered echo texture of liver) or biopsy of liver disease.
- Alcoholic, post infective and metabolic causes of liver diseases will be included the study.

EXCLUSION CRITERIA:

- Patients with GIT malignancy or primary hepatocellular carcinoma.
- Patients with primary hematological disorder.
- Acute liver cell failure.
- Liver cell failure due to septicemia or endotoxemia other than primary liver causes.
- All patients with history of renal and cardiac disease.

Methodology : Cirrhotics with decompensation are identified with thorough history and clinical examination. Patients who full the inclusion and exclusion criteria are observed. The diagnosis is confirmed by USG abdomen. In some cases where diagnosis is not ascertained by USG ,CECT /Biopsy was done . All confirmed cases are evaluated for features of decompensation. Hematological and coagulation abnormalities are detected using Complete Blood Picture ,peripheral smear , Prothrombin Time and Activated Partial Thromboplastin Time.

RESULTS:

A total of 130 cases were observed in the study.

AGE and SEX:

Age of the patients ranged from a minimum of 36 years to a maximum of 75 years. 36.9 % of the study population was between 55 to 65 years. The mean age was 55.66 ± 9.12 years.Out of the 130 patients included in this study, 14 (10.8%) were female and 116 (89.2%) were male.

DURATION OF ILLNESS:

The present study included patients with disease duration more than or equal to six months. Most of the cases included in the present study ranged from 6 to 9 months accounting for 71.6 % of cases and 6 to 12 months duration included 93.7% of cases.

FEATURE OF DECOMPENSATION:

The present study included cases with at least one feature of liver decompensation. Jaundice and ascites were present in majority of the cases. In the present study the frequency of complications of chronic liver disease were ascites 123 cases (94.6%), jaundice 105 cases (80.8%), oesophageal varices 51 cases (39.2%), hepatic encephalopathy 27 cases (20.8%), spontaneous bacterial peritonitis 20 cases (15.4%),and hepatorenal syndrome 11 cases (8.5%).

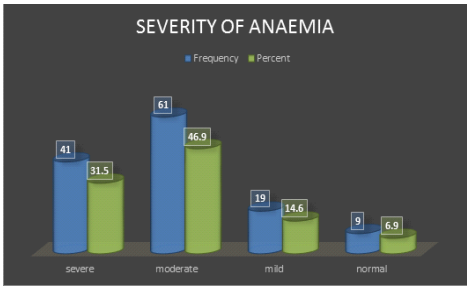
ETIOLOGY: Cause of cirrhosis was alcohol abuse in 89 (68.4%) cases, hepatitis B in 8 (6.15%) cases, hepatitis C in 3 (2.3%) cases, hemochromatosis in 1(0.7%) case and cause could not be ascertained in 29 (22.3%) cases.

HEMATOLOGICAL ABNORMALITIES:

HEMOGLOBIN AND RED CELL INDICES:

Mean hb% of the study population was 8.97 ± 2.21 g/dl. Out of the study population only 9 (6.9%) patients had normal haemoglobin. Majority of the study population had moderate anaemia accounting for 61 cases (46.9%) followed by severe anaemia in 41 cases (31.5%) and mild anaemia in 19 cases (14.6%). The mean MCV, MCH, MCHC were 87.73 ± 12.01 fl, 28.2 ± 5.3 pg and 32.1 ± 2.68 g/dl respectively suggesting normocytic normochromic anemia as the major subtype.

FIGURE1: Severity of anaemia in study subjects.



WBC ABNORMALITIES:

TOTAL AND DIFFERENTIAL LEUCOCYTE COUNTS:

The total WBC counts in the study population ranged from 900-24,900 cells per cumm. The mean WBC count was 7755 ± 4661 cells per cu mm in the study population. Out of the 130 cases, 22 cases (16.9%) had leukopenia and 24 cases (18.5%) had leucocytosis. In the present study 38 cases (29.2%) had neutrophilia, 10 cases (7.6%) had lymphocytosis, 8 cases (6.1%) had eosinophilia and 1 case (0.76%) had basophilia. Neutropenia and lymphopenia are present in 19(14.6%) and 23 (17.6%) cases respectively.

Table 1: Variations in differential counts among study subjects

TYPE OF WBC	INCREASED	DECREASED
POLYMORPHS	38(29.2%)	19(14.6%)
LYMPHOCYTES	10(7.6%)	23(17.6%)
EOSINOPHILS	8(6.1%)	0(0%)
MONOCYTES	0(0%)	0(0%)
BASOPHILS	1(0.76%)	0(0%)

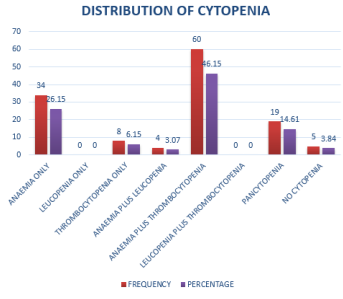
PLATELET COUNTS:

The platelet counts in the study population ranged from 29,000 to 3, 90,000 cells per cu mm. The mean platelet count was 1, 31,015 ± 74220 cells per cu mm. Out of the study population 91 cases (70%) had thrombocytopenia. Of them 56 cases (43.1%), 28 cases (21.5%) and 7 cases (5.4%) belong to grade 1, 2 and 3 thrombocytopenia respectively. There are no cases of grade 4 thrombocytopenia and thrombocytosis in the present study population.

CYTOPENIAS:

The entire study population was divided on the basis of cytopenia in one or more cell lineages. Study subjects were classified as having anaemia only, leukopenia only, thrombocytopenia only, anaemia plus leukopenia, anaemia plus thrombocytopenia, leukopenia plus thrombocytopenia and pancytopenia and results were 34(26.15%), 0, 8(6.15%), 4(3.07%), 60(46.15%), 0 and 19(14.61%) respectively. There were 5 cases (3.84%) without any cytopenia.

FIGURE 2: DISTRIBUTION OF STUDY POPULATION ON THE BASIS OF CYTOPENIA



COAGULATION ABNORMALITIES:

PROTHROMBIN TIME (PT):

Prothrombin time in the study subjects ranged from 13 sec to 26.9 sec. The mean prothrombin time in this study was 18.7 ± 4 sec. PT was prolonged in 93 cases (71.5%).

ACTIVATED PARTIAL THROMBOPLASTIN TIME (aPTT):

aPTT was prolonged in 60 (46.2%) cases. The aPTT in the study ranged from 29- 58.9 sec. The mean value in the present study was 38.26± 7.51 sec.

FIGURE 3: DISTRIBUTION OF STUDY SUBJECTS BASED ON PT

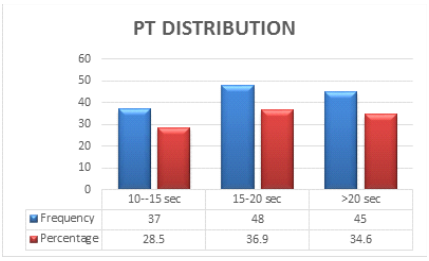
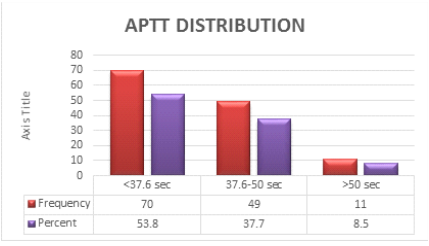


FIGURE 4: DISTRIBUTION OF STUDY SUBJECTS BASED ON APTT



DISCUSSION:

Derangement in haematological indices is frequently seen in patients with cirrhosis and is associated with a poor prognosis. [3] The prevalence of abnormal haematological indices ranges between 6-77%. [4] Haematological abnormalities commonly include anaemia, thrombocytopenia, leukopenia, clotting and coagulation defects. [2]

Cause of these haematological abnormalities is multi factorial. [3] They include portal hypertension causing sequestration, alteration in bone marrow stimulants, bone marrow suppression and consumption or loss. [3]Hypersplenism defined as splenic sequestration and destruction of platelets, WBC and red blood cells. [5] Other factors in pathogenesis of haematological abnormalities include portal hypertensive gastropathy with bleeding with resultant anaemia or thrombocytopenia, alcohol consumption causing hemolysis and low grade DIC contributing to thrombocytopenia. [3]

From the present study, it is evident that the prevalence of anaemia in chronic liver disease is very high. The percentage of anaemics in the present study were comparable with Fahad Khan et al.[6]

Moderate degree of anaemia was more common among study subjects across various study. Results in the present study are comparable with Naimish Patel et al[7] study in terms of severity of anaemia.

The mean haemoglobin percentage among study groups was around 9 gm/dl. The mean haemoglobin in the study is comparable with Gajanan Balaji Kurundkar et al study. [8]

The most common type of anaemia in the study was normocytic normochromic. The same pattern is observed with almost all the studies. The results are closely comparable to Naimish Patel et al [7]and Selvamani et al studies.[9]

Most of the studies show normal WBC counts in majority of the study subjects. The results of our study also emphasize the same fact. The mean WBC counts in the present study were in concordance with Yusheng Jie et al,[10] Deepak Jain et al[11] and Fadi N Bashour et al[12]. Different studies show varying degrees of leukopenia and leukocytosis in study subjects. The percentage of patients with

leukopenia in our study was similar those observed in Fahad Khan et al[6] and Deepak Jain et al[11]. The percentage of patients with leukocytosis in our study was in concurrence with Selvamani et al[9] and Fahad Khan et al.[6]

The leukopenia in chronic liver disease can be secondary to hypersplenism and decrease in granulocyte and granulocyte monocyte colony stimulating factors. [13] Leukocytosis in chronic liver disease is secondary to repeated paracentesis, spontaneous bacterial peritonitis and sepsis.

In the present study we haven't evaluated the cause for leukopenia but lymphocytosis was seen in only 4 cases with spontaneous bacterial peritonitis suggesting raise in counts to be due to secondary infections and/or paracentesis.

Mild thrombocytopenia is the most common grade in the present study which is concordance with Jun Liongchin et al.[14] 70 % of cases had thrombocytopenia which is similar to the results observed in Fahad Khan et al[6] , Jun Liongchin et al[14] and Duzgun Ozalti et al[15] studies. The mean platelet count of present study was 131015/cu mm which is similar to the observations in Duzgun Ozalti et al[]15, Yusheng Jie et al[10] and Yoshida et al[16]. The most common cause of thrombocytopenia was hypersplenism secondary to portal hypertension.

Amir A Qamir et al study[17] is a study on compensated chronic liver disease. In that study monocytopenia was the most common abnormality, followed by bicytopenia. Pancytopenia was negligible in the study and there were significant number of normal cases. This in contrast to the Abdur Rahman Sahin et al study[18], Yun Fu Lu et al study[19] and the present study which were studies on decompensated chronic liver disease. There is a clear change in trend where normal individuals were almost negligible. The number of cases of bicytopenia and pancytopenia increased significantly.

This indicates that with progression from compensation to decompensation the haematological parameters shift from monocytopenia to pancytopenia.

The frequency of PT prolongation in the present study was similar to the observations in Rajkumar Solomon et al[20] and Sohail Ahmed Siddiqui et al[21] studies. The frequency of APTT prolongation of the present study was similar to Shah Shaila et al[22] and Bikha Ram Devrajani et al[23] studies.

Hemostasis is a complex interplay between procoagulants, anticoagulants, fibrinolytics and platelets. [24] There is increased risk of bleeding in cirrhotics. All the coagulation factors are decreased in cirrhosis except factor 8 and VWF. Hemostasis is still maintained as the anticoagulants like antithrombin and protein C are also reduced. [24]

Thrombocytopenia and platelet dysfunction associated with cirrhosis is partly compensated by increased levels of VWF and factor 8 and decreased levels of ADAMTS 13 [25] that limits the functions of VWF. Thus a stable state is maintained in stable cirrhotics despite alterations in coagulation factors. [24]

Infections, portal hypertension, renal failure and endothelial dysfunction results in activation of coagulation as well as fibrinolysis and impaired platelet aggregation. Endogenous heparanoids are released into circulation resulting in destabilizing the critically balanced system and causing increased bleeding tendency. [24]

CONCLUSION:

- Haematological and haemostatic abnormalities are very common in decompensated cirrhotics.
- Hence all the cirrhosis patients must be evaluated for haematological and haemostatic abnormalities and should be monitored for the development of complications.
- There is a change in trend from monocytopenia with compensated cirrhosis to pancytopenias with decompensation, thereby increasing the morbidity and mortality.
- Early anticipation, detection and appropriate treatment can prevent significant morbidity and mortality associated with chronic liver disease.

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