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LIVER FUNCTION VARIABILITY IN COVID-19 PATIENTS ADMITTED IN TERTIARY CARE HOSPITAL IN KISHANGANJ, BIHAR

General Medicine

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ABSTRACT

INTRODUCTION: Covid-19 infects primarily respiratory system, but it also involves almost all the organ involving heart, pancreas, liver and kidney. Many studies are documented involvement of liver as evidenced by abnormal liver function test, but it is not significant. So the aim of this study is to compare the different liver parameters in Covid-19 affected patients according to the severity of the disease. **MATERIAL AND METHODS:** Total 157 Covid-19 affected patients were taken for this study. They were divided into three groups, mild (n=70), moderate (n=55) and severe (n=32) according National guidelines. After admission their blood sample were analyzed for different liver function parameters. **RESULTS:** Amongst 157 Covid-19 patients, males were 94 and females 63. Out of 94 males 59 (62.76%) and 25 out of 63 females (39.68%) demonstrated raised liver enzymes. There was little variation in age difference in different groups but had significant difference in sex groups. High risk groups suffered more from severe infection. In all groups liver enzymes were elevated but AST demonstrated significant difference ($p = 0.02$) amongst the different groups. Though serum proteins and albumin were normal in different groups, but albumin demonstrated significant inter-group difference ($p = 0.01$). **CONCLUSION:** Liver function was deranged in Covi-19 patients, but long term follow-up is required to know proper pathogenesis of the liver injury and at the same time proper monitoring to know whether there will be residual chronicity remain in the liver in future.

KEYWORDS

Covid-19 patients, severity of infection, risk factors, liver function tests

INTRODUCTION:

Covid outbreak started in 2019 December in the Wuhan Province of China and it was found to be caused by coronavirus[1]. Later on virus was renamed as SARS-COV-2[2]. The features of COVID-19 shares some features of SAR-COV-2 reported in 2003 as well as MERS-CoV in the epidemic of 2012. On 11th March 2020, World Health Organization declared CoVid-19 as Global pandemic as it was responsible for more than more than 22 million infective cases and 781,932 deaths throughout the world until 19th August, 2020[3, 4]. SARS-COVID-2 can be detected by real time reverse transcriptase polymerase reaction of nasopharyngeal and oropharyngeal swab and Bronchoalveolar lavage fluid – which is useful definitive diagnosis. But rapid antigen test for measuring the antibody titer is used for surveillance testing which is complemented by different serological and biochemical tests[5].

Though primarily COVID-19 involves respiratory system leading to development of acute respiratory distress syndrome or atypical pneumonia[6], but it is responsible for dysfunction of other organs in the body[6]. Pathological changes occurs in those organs may be the result of direct cytopathic effect due to replication of viruses at the local site of infection or due immune response produced by the viruses. Different autopsies demonstrated multiple infections in different organ by this virus[7]. It involves liver, gastrointestinal tract, spleen and lymph nodes[8, 9, 10]. Expression of ACE 2 receptors are present of the surface of cholangiocytes as well as hepatocytes but expression on the former is much higher and through this potential route virus will enter into the liver tissue leading to hepatic dysfunction[11, 12]. According to recent study affection of ACE 2 receptors present of the surface of cholangiocytes in the liver leading to liver injury resulting in hepatic dysfunction through systemic inflammatory response[13]. Post mortem study of liver in patients died due to COVID-19 infection demonstrated different types of liver damage in the form of the presence of moderate microvascular steatosis, mild portal and lobular activity[14]. Again different hospital studies showed COVID-19 induced liver damage in the form of rise of 14% to 53% rise of liver enzymes like alanine aminotransferase, aspartate aminotransferase[15, 16, 17]. Many studies demonstrated involvement of liver function in most of the COVI-19 infected patients but it is not significant[18]. The cause of this hepatic dysfunction is not known but there may be some direct correlation of hepatic enzyme with disease severity according to some studies but some studies denied it[19]. There is scarcity of data relating to hepatic dysfunction and its correlation with severity of COVID-19 infection. So the aim of this study is to compare the different liver parameters in Covid-19 affected patients according to the severity of the disease.

MATERIALS AND METHODS:

It is descriptive observational study performed in a Tertiary care Center, Kisangani during 2nd wave of COVID-19 infection from April 2021 to May 2021. This study was approved by the Ethical committee of our institution. All COVID-19 cases were RTPCR positive in nasopharyngeal and oropharyngeal samples admi9tted in COVID word, HUD and ICU according to the severity of the patient during the time of admission. Total number of patients were 157. The severity of patients' condition was assessed according to National guidelines and clinical management protocol for COVID-19 provided by Govt. of India Ministry of Health and family Welfare Directorate General of Health Services[20]. Patients were classified based on clinical history given by the patients or their parties, clinical examination and radiography as mild group (n=70), moderate group (n=55) and severe group (n=32). Patients with fever, upper respiratory tract infection in absence of respiratory distress with normal SpO2 were classified as mild cases; fever, respiratory distress, and cough, respiratory rate of 24 or more per minute with SpO2 level below 94% but more than 90% in room air as moderate cases and patients with severe pneumonia or acute respiratory distress syndrome, respiratory rate of more than 30 per minute, SpO2 less than 90% in room air, radiological demonstration of lung infiltrate along with respiratory or organ failure as severe cases.

Exclusion Criteria: Patients with chronic liver disease due to hepatitis B, C, alcoholic liver disease and nonalcoholic fatty liver diseases; fever due malaria, dengueH1N1 infection.

Inclusion Criteria: Comorbid factors like diabetes mellitus, hypertension, chronic obstructive lung disease, and smoking are included along with patients having no comorbid factors.

Prior to taking the blood samples informed consent was taken from each admitted patient. Venous blood was taken from each patient after 12 hours fasting. In the biochemistry department serum was separated and analyzed in biochemistry analyzer in double blind fashion so that principal and co-investigator were unaware of patient clinical status. Serum bilirubin was measured by Diazo method, liver enzymes by IFCC method, alkaline phosphatase by using AMP buffer, total protein by Biuret and Bromocresol Green reagents[21,22,23,24].

Statistical Analysis:

Statistical analysis was performed by using IBM SPSS version 20 for windows. All the values were expressed in the form of mean ± standard deviation. Then continuous variables are analyzed by ANNOVA software and categorical variable compared by Pearson's chi-square

test. Here p value of < 0.05 was taken as statistically significant. With confidence limit of 95%.

RESULTS:

There are little variation in age in different groups (p=0.42), but there are significant differences in respect of sex (p=0.02). High risk groups (65.62%) suffered from severe Covid infections as compared to moderate infection (45.45%) and mild infection (24.28%). [Table 1].

Serum bilirubin was normal in all the groups with no statistical difference (p=0.78). ALT, AST were raised in all the groups and in case of ALT the difference between all three study groups were not significant (p= > 0.05), but in case of AST difference between the groups were significant (p=0.02). On the other hand, ALP were within the normal limit in all the groups. Serum protein and albumin were within normal limit in all groups but inter-group differences were significant in case of albumin (p=0.01). [Table 2].

Amongst 94 males, 59 patients demonstrated raised AST and ALT (62.76%) as compared to female where 25 out of 63 (39.68%)had raised AST and ALT, so total 84 patients had raised liver enzymes(53.50%) .

Table 1: Demographic characteristic of the COVID-19 patients:

Parameters	-	Group 1 (n=70)	Group 2 (n=55)	Group 32 (n=32)	P value
Age (years)	-	45 ± 12	50 ± 21	52 ± 17	0.42
Sex distribution	Males	40	34	20	0.02
	Females	30	21	12	
Risk factors	-	17 (24.28%)	25 (45.45%)	21 (65.62%)	-

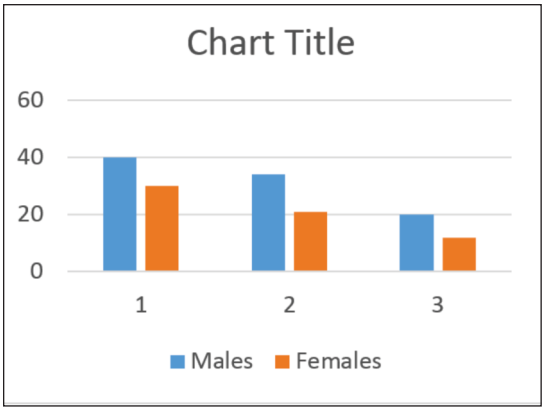
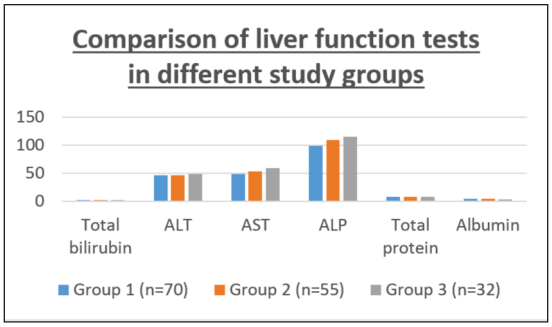


Table 2: Comparison of liver function tests in different study groups:

Parameters	Reference range	Group 1 (n=70)	Group 2 (n=55)	Group 3 (n=32)	P value
Total bilirubin	0.2 – 1 mg%	1.1 ± 1.82	1.3 ± 1.78	1.5 ± 1.86	0.78
ALT	10-40 U/L	45.72 ± 31.65	46.21 ± 24.86	48.76 ± 32.45	0.25
AST	10-35 U/L	48.56 ± 23.67	53 ± 28.69	59.45 ± 46.34	0.02
ALP	80 – 128 U/L	98.34 ± 65.12	109.78 ± 45.79	114.97 ± 24.73	0.12
Total protein	6.4 – 8.5 gm/L	7.5 ± 0.54	7.4 ± 0.65	7.2 ± 0.54	0.25
Albumin	3.5 – 5 gm/L	4.2 ± 0.45	4.4 ± 0.54	3.24 ± 0.78	0.01



DISCUSSION:

Liver dysfunction is fairly common in COVID-19 patients and is more visible in case of severe cases. But severe liver damage leading to hepatic failure and death are very uncommon.

In this study amongst total 157 patients admitted in COVD ward, total 84 patients (53.50%) had raised liver enzymes as compared to 73 patients with normal liver enzymes (64.50%). This is nearly similar to the study done by Saini RK et al, where it was demonstrated that out of 152 COVID patients 89 patients (58.50%) had raised liver enzymes and rest 63 (41.50%) had normal liver enzymes[25]. Other studies also demonstrated 16% to 53% patients with raised liver enzymes in different studies[26, 27]. It suggests that there is some role of corona virus in derangement of liver enzymes. Few earlier studies also demonstrated some amount of liver damage in corona virus affected patient[28]. According various studies ACE2 is the key receptors present on the cholangiocytes through which COVID-19 virus enters into the cells leading to liver damage[22,30,31].

In this study there was noticeably raised liver enzymes in males (62.76%) as compared to females (39.68%) which was comparable to the study done by Sani RK et al[25]. This may be attributed to increased expression of ACE2 present on the cholangiocytes in males as reported in a study in Whan[32,33]. In this study along with abnormally raised liver enzymes, there was evidence of significantly decreased vale of albumin (p=0.01) as compared to total proteins (p=0.25) and liver enzymes. It may be attributed to firstly, poor nutritional intake, secondly, cytokine storm releasing acute phase cytokines leading to downregulation of synthesis of albumin in the hepatocytes after disease onset[34].

This study demonstrated mild elevation of bilirubin in three group of patients which was contrary to study done by Saini RK et al and Paliogiannis P et al[25,35].

Elevation of lever enzymes like AST, ALT were first reported in 43% of cases from the Wuhan Province by Chen et al[36]. But the present study demonstrated much higher incidence of elevated liver enzymes (53.50%). Again, one study from Northern Italy demonstrated raised hepatic enzymes in 62.4% which was much higher as compared to this present study[37].

In this study there was strong correlation between elevation of liver enzymes and the severity of the patients' condition which is similar to the study done by Mukherjee K et al where in group 1, 2 and 3 were 47.02 ± 29.98, 46.92 ± 27.52 and 52.51 ± 32.76 for ALT, 48.7 ± 30.58, 41.31 ± 20.63 and 60.05 ± 39.63 for AST and 99.95 ± 46.95, 115.74 ± 48.34 and 113.21 ± 76.48 for ALP respectively[38]. It may be due to multiple factors that lead to damage of hepatocytes, these may be microthrobotic endolithiasis, dysregulation of immune system, infections of cholangiocytes, and drug induced liver injury. But this hepatic injury seems to be self-limiting as most all the liver injury were recovered without any specific treatment[19,26].

Limitation of this study:

As it is a descriptive observational study, hence long follow up was not performed to ascertain any evidence of chronicity of this virus infected liver disease in future.

CONCLUSION:

SARS-COVID-2 may produce liver injury more commonly in males as evidenced by elevated liver enzymes and lowers the albumin indicating decreased synthetic power of liver. There is correlation of increase in liver enzymes with the severity of the condition of the patients. But till now data are not sufficient to explain the different pattern of liver injuries. So more and more data and at the same time long term follow up is required to explain the proper pathogenesis and pathophysiology implicated in the liver injury in coronavirus infection.

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