INTRODUCTION

Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury, which leads to portal hypertension and end-stage liver disease. Patients with cirrhosis can acquire several pulmonary conditions related to portal hypertension, including hepatopulmonary syndrome, portopulmonary hypertension, spontaneous bacterial empyema and hepatic hydrothorax. Hepatic hydrothorax (HH) is defined as the accumulation of significant pleural effusion (> 500 ml) in patients with decompensated liver disease without primary pulmonary or cardiac disease.

A number of different mechanisms have been proposed to explain the development of pleural effusion in patients with cirrhosis. Alteration in splanchnic circulation, elevation of nitric oxide (NO) in splanchnic circulation in cirrhotics, hypoalbuminemia, increased flow and elevated pressure in the thoracic duct, and azygos veins are common in cirrhotic patients with portal hypertension and can contribute in the formation of ascites and pleural effusion.

Pleural effusion causes early symptoms like cough, shortness of breath, and hypoxemia. Spontaneous infection of hepatic hydrothorax is known as spontaneous bacterial empyema (SBEM) and defined as pleural fluid with polymorphonuclear (PMN) cell count > 500 cells/mm³ or positive culture with PMN cell count > 250 cells/mm³ with exclusion of a parapneumonic effusion.

RESULTS: Two hundred and six patients met the inclusion criteria, with mean age of 41.25 ±13.59 years. Among them, 149 (72.3%) were males and 57 (27.7%) females. Twenty-three (11.2%) had hydrothorax; right sided involvement was in 18 (78.3%) subjects, 3 (13%) had left sided while bilateral pleural effusion was found in 2 (8.7%) cases. SBEM was found in 07 (30.43%) cases. Mean serum albumin 3.125 ±0.71 gram/dl. There was association between serum albumin levels and hydrothorax. A significant association of hydrothorax with Child Pugh scoring system (p=0.018), but not with serum albumin (p=0.15).

CONCLUSION: The frequency of hepatic hydrothorax has a significant association with hepatic function as assessed by Child Pugh scoring system, but not with serum albumin.


ABSTRACT

Objective: To determine the frequency of hepatic hydrothorax and its association with Child Pugh Class in patients with liver cirrhosis.

Study Design: Descriptive, analytical study.

Place and Duration of Study: Jinnah Postgraduate Medical Centre, Karachi, Medical Unit-III, (Ward- 7), from June 2012 to May 2013.

Methodology: All patients with established diagnosis of decompensated chronic liver disease were included. Detailed history, thorough physical examination, routine laboratory investigations, chest X-ray and abdominal ultrasound were carried out in all patients to find out the presence of pleural effusion and ascites, respectively. Fifty milliliters of pleural fluid was aspirated in all patients with pleural effusion using the transthoracic approach, taking ultrasound guidance, wherever required. Fluid was sent for microscopic, biochemical, and microbial analysis. SBEM defined if pleural fluid with polymorphonuclear (PMN) cell count > 500 cells/mm³ or positive culture with PMN cell count > 250 cells/mm³ with exclusion of a parapneumonic effusion.

RESULTS: Two hundred and six patients met the inclusion criteria, with mean age of 41.25 ±13.59 years. Among them, 149 (72.3%) were males and 57 (27.7%) females. Twenty-three (11.2%) had hydrothorax; right sided involvement was in 18 (78.3%) subjects, 3 (13%) had left sided while bilateral pleural effusion was found in 2 (8.7%) cases. SBEM was found in 07 (30.43%) cases. Mean serum albumin 3.125 ±0.71 gram/dl. There was association between serum albumin levels and hydrothorax. A significant association of hydrothorax with Child Pugh scoring system (p=0.018), but not with serum albumin (p=0.15).

CONCLUSION: The frequency of hepatic hydrothorax has a significant association with hepatic function as assessed by Child Pugh scoring system, but not with serum albumin.
result, this complication of cirrhosis is not only a threat for patient but a challenge for the clinician too.

The aim of this study was to determine the frequency of hepatic hydrothorax in patients with decompensated chronic liver disease, and an association between presence of hepatic hydrothorax and parameters of Child Pugh scoring system and hepatitis virus type, so that cirrhotic patients at risk of developing hepatic hydrothorax by these simple parameters may be identified.

**METHODOLOGY**

All patients presenting in Medical OPD, emergency department or admitted in medical units of JPMC with established diagnosis of decompensated chronic liver disease were included in the study. Diagnosis of cirrhosis was based on previous liver biopsy or on clinical, biochemical and ultrasonographic findings. A written informed consent was obtained from all the patients after having fully explained the purpose and protocol of the study. Patients were excluded if they had primary pulmonary or cardiac disease, portal vein thrombosis and ascites.

A detailed history was taken and thorough physical examination performed in every patient followed by blood sampling for the investigations, i.e. complete blood count, erythrocyte sedimentation rate (ESR), liver function test, liver biochemistry, serum proteins, serum urea, creatinine and urine detailed reports (DR). A chest X-ray and abdominal ultrasound were carried out in all patients to find out the presence of pleural effusion and ascites, respectively. Fifty milliliters of pleural fluid was aspirated in all patients with pleural effusion using the transthoracic approach, taking ultrasound guidance, as required. Fluid was sent for analysis of proteins, glucose, leukocyte count, Gram’s stain, bacterial culture, and sensitivity testing as well as acid fast bacilli (AFB) smear and culture sensitivity testing in selected patients. SBEM was defined as pleural fluid with polymorphonuclear (PMN) cell count > 500 cells/mm³ or positive culture with PMN cell count > 250 cells/mm³ with exclusion of a parapneumonic effusion.

All the data collected from subjects were evaluated on SPSS version 17.0 for statistical analysis. Frequency and percentage were computed for categorical variables like gender, age groups and Child Pugh class. The frequency of hepatic hydrothorax was presented in percentage. Chi-square test was used to assess the association between hepatic hydrothorax and serum albumin. The p-value of 0.05 or less was considered to indicate statistical significance.

**RESULTS**

Two hundred and six patients who met the inclusion criteria were included in the study with mean age of 41.25\pm13.593 years. Among those, 149 (72.3%) were males and 57 (27.7%) females. Over all, 23 (11.2%) cirrhotic patients found to have pleural effusion while on the basis of hemithorax involved, 18 (78.3%) subjects had right sided, 3 (13%) patients have left sided while bilateral pleural effusion was found in 2 (8.7%) cases. SBEM was found in 07/23 (30.43%) cases. The mean serum albumin was 3.125\pm0.718 gram/dl. On the basis of hepatic function, 62 (30.09%) patients were in Child Pugh class A, 61 (29.61%) were in class B, while 83 (40.29%) subjects found to had Child Pugh class C.

Association of hepatic hydrothorax and liver function had found statistically significant (p=0.018). The association between serum albumin levels and presence of hepatic hydrothorax was not statistically significant (p=0.15). Association of hepatic hydrothorax with different variables are given in Table I.

| Table I: Relationship of hepatic hydrothorax with different variables. |
|--------------------------|--------------------------|--------------------------|--------------------------|
| Variable                 | Hepatic hydrothorax      | p-value                  |
| Gender (n)               | Yes                      | No                       |                           |
| Male                     | 149 (72.33%)             | 06 (26.08%)              | 51 (27.87%)              | 0.857                     |
| Female                   | 57 (27.67%)              | 17 (73.91%)              | 132 (72.13%)             |                           |
| Age (years)              | ≤ 40                     | > 40                     |
| Present                  | 91 (44.17%)              | 10 (43.48%)              | 81 (44.26%)              | 0.943                     |
| Absent                   | 115 (58.83%)             | 13 (56.52%)              | 102 (55.74%)             |                           |
| Serum albumin (g/dl)     | >3.5                     | 50 (24.27%)              | 3 (13.0%)                | 47 (25.68%)               | 0.15                     |
|                         | 2.8-3.5                  | 99 (48.06%)              | 10 (43.48%)              | 89 (48.63%)               |                           |
|                         | <2.8                     | 57 (27.67%)              | 10 (43.48%)              | 47 (25.68%)               |                           |
| Ascites                  | Present                  | 152 (73.79%)             | 18 (78.26%)              | 134 (73.22%)              | 0.802                     |
|                         | Absent                   | 54 (26.21%)              | 05 (21.74%)              | 49 (26.78%)               |                           |
| Child Pugh class         | A                        | 62 (30.09%)              | 02 (8.69%)               | 60 (32.79%)               | 0.018                     |
|                         | B                        | 61 (29.61%)              | 06 (26.09%)              | 55 (30.05%)               |                           |
|                         | C                        | 83 (40.29%)              | 15 (65.22%)              | 68 (37.16%)               |                           |
| Virus type               | HBV                      | 45 (21.8%)               | 04 (17.4%)               | 41 (22.4%)                | 0.911                     |
|                         | HCV                      | 133 (64.6%)              | 15 (65.2%)               | 118 (64.5%)               |                           |
|                         | Both HBV+HCV             | 8 (3.9%)                 | 01 (4.3%)                | 07 (3.8%)                 |                           |
|                         | Others                   | 20 (9.7%)                | 03 (13.0%)               | 17 (9.3%)                 |                           |

Association of hepatic hydrothorax and virus type had found statistically significant (p=0.0018). The association between virus type and presence of hepatic hydrothorax was not statistically significant (p=0.15). Association of hepatic hydrothorax with different variables are given in Table I.

Out of the 206 subjects, 152 (73.79%) had clinical or radiological evidence of ascites. In relation to ascites, 18/23 patients had hydrothorax in the presence of ascites while five did not have ascites.

**DISCUSSION**

Hepatic hydrothorax is a manifestation of decompensated chronic liver disease, similar to the presence of ascites, hepatic encephalopathy, or variceal haemorrhage.

Although several mechanisms are proposed for the development of hepatic hydrothorax in liver cirrhosis patients; but its absence in most chronic liver disease
patients, which is relatively uncommon nature, is not appropriately answered by those mechanisms. Furthermore, the rectification is still to be made regarding its right-sided predominance. Overall frequency of hepatic hydrothorax in this study was 11.2%, which is slightly higher than the observed in previous studies.\textsuperscript{10,13} Reasons of that bit higher frequency might be advanced Child Pugh class of subjects enrolled in current study (Class C: 83 (40.29%) versus Class A: 62 (30.09%) and Class B 61 (29.61%). In regard to hemithorax involvement, our results were almost identical to previous studies; right side being the highest followed by left hemithorax, and lowest number of subjects had bilateral involvement.

Although there are no studies specifically addressing the exact relationship of serum albumin and presence of hydrothorax, but this study results found the lack of that association. This lack of association might be answered by the facts and purposed mechanisms of hydrothorax development; it indicates that the most likely cause is passage of a large amount of ascites from the peritoneal to the pleural cavity through diaphragmatic defects,\textsuperscript{14-17} which represent small holes, usually < 1 cm, in tendinous portion of the diaphragm. Microscopic examination of these defects revealed discontinuities in the collagen bundles that make up the tendinous portion of the diaphragm.\textsuperscript{14} As a result of raised intra-abdominal pressure (e.g., ascites, coughing, or straining), it might lead to small hernations (so-called pleuroperitoneal blebs) of the peritoneum into the pleural cavity, which on rupture may allow free communication between the peritoneal and pleural space.\textsuperscript{5,10,11} Furthermore, the negative intrathoracic pressure favours the transfer of fluid across these defects; and hence, patients usually have mild ascites. This might be the explainable ground for development of hepatic hydrothorax irrespective of serum albumin levels. Paradoxically, several case reports have disclosed the unilateral pleural effusions in cirrhotic patients without clinical or even ultrasonic evidence of ascites.\textsuperscript{18-21} These contradictory statements regarding the mechanism culpable for the development of hydrothorax in cirrhotic patients might be answerable that no single offender is responsible.

Another finding of this study was a significant association of hydrothorax and hepatic function besides disclosing that as the hepatic function deteriorated (assessed by Child Pugh scoring system), the frequency of hydrothorax increased. Therefore, it can be considered as an additional parameter for Child Pugh scoring system.

Regarding SBEM, current study results were in accordance with Xiol \textit{et al.}, who studied the clinical course of 120 cirrhotics with hydrothorax and reported the presence of SBEM in as many as 13%.\textsuperscript{22} Although the term SBEM may be confusing because in most cases there is no evidence of pus or abscess in the thoracic cavity. Moreover, some authors have proposed it to be called spontaneous bacterial pleuritis.\textsuperscript{23} There were few limitations of present study; firstly, limited sample size with single centre-based study did not reflect overall population estimation. Secondly, microbial culture and treatment response assessment could not be carried out. Further studies are required to establish the exact mechanism of hepatic hydrothorax development, treatment outcome, and prognosis.

**CONCLUSION**

This study highlighted a high frequency of hepatic hydrothorax besides a significant association with hepatic function as assessed by Child Pugh scoring system, but no significant association with serum albumin.

**REFERENCES**

15. Emerson PA, Davies JH. Hydrothorax complicating ascites. 

   Management of pleural effusion of cirrhotic origin. 

17. Zenda T, Miyamoto S, Murata S, Mabuchi H. 
   Detection of diaphragmatic defect as the cause of severe hepatic 
   hydrothorax with magnetic resonance imaging. 

18. Singer JA, Kaplan MM, Katz RL. Cirrhotic pleural effusion 
   in the absence of ascites. *Gastroenterology* 1977; 73: 
   575-7.

19. Rubinstein D, McLnnes IE, Dudley FJ. Hepatic hydrothorax in 
   the absence of clinical ascites: Diagnosis and management. 

20. Llaneza PP, Salt WB II. Unilateral pleural effusion without 

21. Kirsch CM, Chui DW, Yenokida GG, Jensen WA, Bascom PB. 
   Case report: Hepatic hydrothorax without ascites. 

22. Xiol X, Castellvi JM, Guardiola J. Spontaneous bacterial 
   empyema in cirrhotic patients: A prospective study. 

23. Streifler J, Pittik S, Dux S, Garty M, Rosenfeld JB. Spontaneous 
   bacterial pleuritis in a patient with cirrhosis. 