

Original Research Article

Frequency of hepatic hydrothorax in patients with decompensated cirrhosis in Zagazig university hospitals (single center study).

Background and study aim: Hepatic hydrothorax is the presence of more than 500 ml of pleural effusion in a patient with liver disorder. The work aimed to study the frequency of Hepatic hydrothorax in patients with decompensated cirrhosis admitted to the Tropical Medicine department, Faculty of Medicine, Zagazig University (inpatients, outpatient and intensive care unit) trying to determine the frequency of this disorder.

Patients and methods: This study was performed on 208 decompensated cirrhotic patients (112 males and 96 females), their ages ranged from 27 to 73 years old (53.8 ± 7.09) between April 2014 to April 2015. Which were randomly divided into Group I included 182 decompensated cirrhotic patients without pleural effusion. Group II included 26 cirrhotic patients with pleural effusion. Clinical assessment, laboratory evaluation, plain chest x-ray and diagnostic paracentesis and pleurocentesis for cytological, biochemical analysis and bacteriological.

Results: In this study; the frequency of pleural effusion in decompensated cirrhotic patients was 26/208 cases with a percentage of (12.5%) Also, this work showed (76.9%) of pleural effusion patients had effusion on right side, (15.4%) on left side, and (7.7%) have bilateral pleural effusion. This study showed; (23.1%) of cases with pleural effusion had mild effusion, (46.1%) had moderate effusion and (30.8%) had massive effusion.

Conclusion: Hepatic hydrothorax is an uncommon complication of advanced liver disease. In this study; the frequency of pleural effusion in decompensated cirrhotic patients was (12.5%), the majority of patients with hepatic hydrothorax were in child (C) 61.5%

Key words: pleural effusion- paracentesis- pleurocentesis

26 INTRODUCTION

27 Hepatic hydrothorax is the presence of more than 500 ml of pleural effusion in a patient with
28 liver disorder, who does not show pulmonary or cardiac diseases or malignancies⁽¹⁾. Hepatic
29 hydrothorax is an uncommon complication of chronic liver disease occurring in approximately 0.4 to
30 12.2% of patients⁽²⁾.

31
32 Pleural effusion develops when rate of fluid accumulation exceeds its removal. The
33 overwhelming cause is the increase of the intra-abdominal pressure as a result of ascites, coughing,
34 or straining which might lead to small herniations (pleuroperitoneal blebs) of the peritoneum
35 through these gaps into the pleural cavity which may rupture and allow free communication
36 between the peritoneal and pleural space⁽³⁾.

37 The negative intrapleural pressure compared to that of the peritoneal cavity facilitates the one-
38 way transfer of fluid and its subsequent trapping into the pleural space with predomination of right-
39 side hepatic hydrothorax⁽⁴⁾.

40 The transdiaphragmatic defects probably result from anatomic thinning and separation of the
41 collagenous fibers of the tendinous portion of the diaphragm⁽⁵⁾. Congenital factors, high intra-
42 abdominal pressure and prolonged bed rest may contribute to the diaphragmatic thinning. Another
43 possible explanation for the formation of transdiaphragmatic holes that allow the peritoneum to
44 rupture into pleural space may be an increase of pressure caused by valsalva maneuvers (cough,
45 defecation, parturition) and trauma. These defects are on the left side because the left diaphragm is
46 thicker and more muscular⁽⁶⁾.

47 Other mechanisms involved in the development of hepatic hydrothorax such as azygous vein
48 hypertension causing formation of collateral anastomosis between portal and azygous systems⁽⁷⁾,
49 passage of fluid from peritoneal to the pleural space via transdiaphragmatic lymphatics,
50 hypoalbuminemia resulting in decreased colloid osmotic pressure and lymphatic leakage from the
51 thoracic duct⁽⁸⁾.

52
53 The principles of medical management in hepatic hydrothorax are identical to those of ascites in
54 cirrhotic patients⁽⁹⁾. The aim of the therapy should be to create and subsequently maintain a
55 negative sodium balance. Therefore, a sodium-restricted diet is recommended⁽¹⁰⁾. A combination
56 of a distal acting diuretic agent plus a loop diuretic is indicated⁽¹¹⁾.

57 Therapeutic thoracentesis is performed in order to relieve symptoms of dyspnea in patients with
58 large effusions. Moreover, it is indicated in cases with recurrent or refractory hydrothorax⁽¹²⁾.

59 Several surgical interventions have been used in the management of hepatic hydrothorax such as
60 tube thoracostomy with chemical pleurodesis by injection of sclerosing agent, repair of defects in
61 the diaphragm, and peritoneovenous shunts. The performance of transjugular intrahepatic
62 portosystemic shunts (TIPS) is the procedure of choice in patients with hepatic hydrothorax who do
63 not respond to diuretic treatment and/or repetitive therapeutic thoracentesis⁽⁶⁾.

64

65 The work aimed to study the frequency of pleural effusion in decompensated cirrhotic patients in
66 cases admitted to the Tropical Medicine department (inpatients, outpatient and intensive care unit)
67 trying to determine the frequency of this disorder.

68 PATIENT AND METHOD

69

70 This cross sectional study was performed on 208 cirrhotic ascitic patients (112 males and 96
71 females), their ages ranged from 27 to 73 years old (53.8 ± 7.09) who were seen at Tropical
72 medicine Department, Faculty of medicine, Zagazig University Hospitals between April 2013 to April
73 2014

74 Patients were divided into two groups;

- 75 ➤ Group I included 182 cirrhotic ascitic patients without pleural effusion.
- 76 ➤ Group II included 26 cirrhotic ascitic patients with pleural effusion.

77 Inclusion criteria:

78 208 decompensated cirrhotic patients were enrolled. The diagnosis of liver cirrhosis was based on
79 the presence of at least 2 of the following: characteristic imaging features, esophageal or gastric
80 varices, ascites, increased international normalized ratio (INR) that could not be attributed to any
81 other cause⁽¹³⁾. The severity of the liver disease was assessed according to the Child-Pugh Turcotte
82 classification⁽¹⁴⁾.

83

84 Exclusion criteria:

- 85 1. Patient had ascites not attributed to hepatic cirrhosis.
- 86 2. Hepatic patient without ascites.
- 87 3. Hepatic patient had pulmonary or cardiac diseases or malignancies.

88 II- Methods

89 All patients were subjected to the following:

90 1- Full clinical history.

91 Patient medical and nutritional history was taken with special stress on gastrointestinal
92 manifestation (especially abdominal enlargement and abdominal pain), chest symptoms (especially
93 dyspnea, cough and chest pain). History of fever, bleeding tendency, and neuropsychiatric
94 symptoms were also taken.

95

96 2- Thorough clinical examination.

97 Including manifestations of liver cell failure (jaundice, palmar erythema, flapping tremors, spider
98 naevi, lower limb edema and ascites). All patients were classified according to Child Pugh Turcotte
99 (CPT) classification⁽¹⁴⁾. In addition to chest examination (inspection, palpation, percussion and
100 auscultation).

3- Laboratory investigation:

- Complete blood picture (white blood cell, hemoglobin level and platelet count)
- Liver function tests (total protein, albumin, total bilirubin, direct bilirubin, alkaline phosphatase) and liver enzymes (AST, ALT).
- Kidney function tests (blood urea nitrogen and creatinine).
- International normalizing ratio (INR)

4- Pelviabdominal ultrasound to show the condition of liver, spleen and ascites.

5- Plain chest X-ray to detect the fluid. CT was done when needed

6- Diagnostic paracentesis and pleurcentesis for cytological, biochemical analysis and bacteriological.

- Cytological (total and differential leucocytic count), using hemocytometer and microscopic method⁽¹⁵⁾. The fluid obtained in a tube containing an anticoagulant to avoid clotting.
- Biochemical: (total protein, LDH, glucose) using autoanalyzer.
- Bacteriological culture using aerobic and anaerobic standard blood culture bottles, brain-heart infusion broth, which were inoculated with 10ml of ascitic fluid and incubated for 48 hours at 37C⁽¹⁶⁾. Identification of the isolated organism by gram stain, biochemical reaction (API system) and agglutination with specific antisera.

Statistical analysis

Data were checked, entered and analyzed using SPSS 14 for Windows. Data were expressed as mean $\pm$ SD for quantitative variable, number and percentage for qualitative one. Chi-squared (X²) or t test and paired t test were used when appropriate. P<0.05 was considered significant.

RESULTS

Demographic data of both groups: Group I shows more males 53.8% than females 46.2% and their ages ranged from 27 to 73 years old. While group II shows more males 53.8% than females 46.2% and their ages ranged from 35 to 70 years old (table 1). 12.5% of decompensated cirrhotic patients have pleural effusion (Table 2 and figure 1). The majority of cases with pleural effusion have right side effusion (76.9%), 15.4% have left side effusion and 7.7% on both sides. Of all; 23.1% have mild effusion amount, 46.1% and 30.8% have moderate and massive effusion amount respectively (Table 3 and figure 2). Cases with pleural effusion are more in patients with Child C (61.5%) and (38.5%) are in child B while, in group I patients most cases are in child C (52.8%) (Table 4). There is no significant difference between the chemical and bacteriological analysis of ascitic and pleural fluids in group II patients (table 5, 6, and 7). There was a significant difference between the degree of pleural effusion and the degree of ascitic fluid (table 8). (69.2%) of cases in group II show improving due to control of ascites (table 9 and figure 3).

Table (1): Demographic data of decompensated cirrhotic patients among the two groups.

			decompensated Cirrhotic Patients	
			<i>Group I</i> (n=182)	<i>Group II</i> (n=26)
Sex	Male	N, %	98 53.8%	14 61.5%
	Female	N, %	84 46.2%	12 42.3%
Age	mean±SD		53.7 ± 7.18	54.5 ± 6.84
	range		27-73 ys	35-70 ys

Table (2): Frequency of cases of pleural effusion in decompensated cirrhotic patients.

		n	%
Cases	<i>Group II</i>	26	12.5
	<i>Group I</i>	182	87.5
	<i>Total</i>	208	100

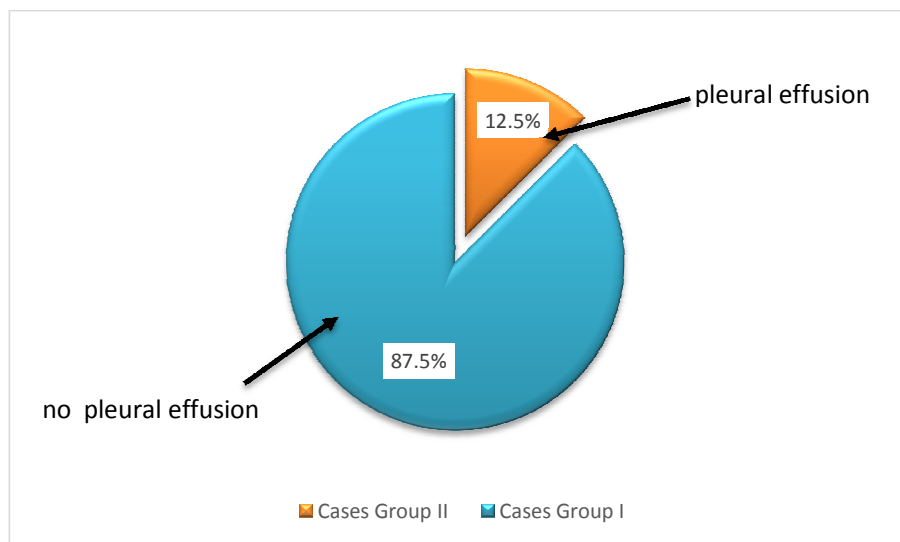
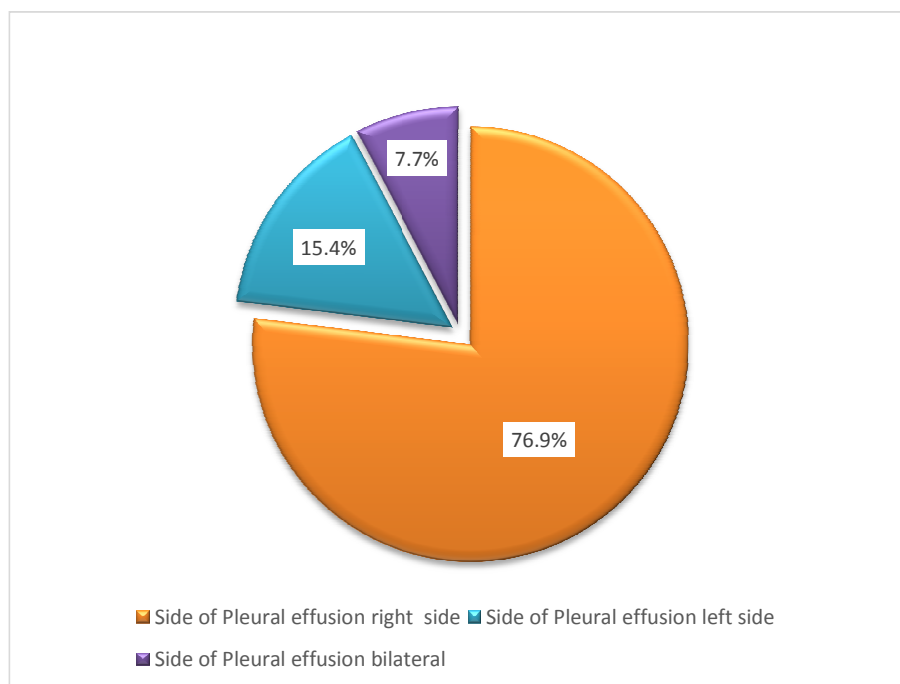


Figure (1): Frequency of cases of pleural effusion in cirrhotic ascitic patients

Table (3): Frequency of pleural effusion according to side and amount of effusion.

		n	%
Side of Pleural effusion	<i>right side</i>	20	76.9
	<i>left side</i>	4	15.4
	<i>bilateral</i>	2	7.7
Amount of Pleural effusion	<i>mild</i>	6	23.1
	<i>moderate</i>	12	46.1
	<i>massive</i>	8	30.8
Total		26	100.0

170



171

172

173 **Figure (2):** Frequency of pleural effusion distribution

174

175

176 **Table (4):** Child classification of decompensated cirrhotic patient among the two groups.

177

			Group I (n=182)	Group II (n=26)	P
Child classification	B	Count	86	10	.153
		%	47.2%	38.5%	
	C	Count	96	16	
		%	52.8%	61.5%	
Total		Count	182	26	
		%	100.0%	100.0%	

178

179

180 **Table (5):** Chemical analysis of peritoneal fluid among the two groups.

		Group I	Group II	P
		Mean $\pm$ SD	Mean $\pm$ SD	
Peritoneal fluid	TLC (cells/mm ³)	228.4 $\pm$ 141.2	211.4 $\pm$ 132.3	.958
	Glucose (mg/dl)	130.3 $\pm$ 56.9	115.0 $\pm$ 62.4	.073

	Protein (mg/dl)	1321.6±638.2	1251.9±700.8	.085
--	----------------------------	--------------	--------------	------

	Ascites Degree	P
--	-----------------------	----------

	LDH (U/l)	143.1±123.4	137.7±83.3	.146
--	-----------------------	-------------	------------	------

Table (6): The chemical analysis of pleural fluid.

	Pleural Fluid	
	<i>Mean ± SD</i>	<i>Range</i>
TLC(cells/mm³)	209 ± 121	80-3700
Glucose(mg/dl)	129 ± 40	76-238
Protein(mg/dl)	1389 ± 712	500 -2500
LDH(U/l)	137 ± 67	64-292
Total number = 26		

Table (7 Degree of ascites in cases with pleural effusion

***p<0.05 significant**

Table (8): Comparison between ascitic and pleural fluids in group II.

		Mild (n=5)	Moderate (n=16)	Severe (n=5)	
Pleural effusion	Mild (n=6)	1	3	2	.022*
	Moderate (n=12)	1	8	3	
	Severe (n=8)	3	5	0	
Total number = (26)					

	Ascitic fluid	Pleural fluid	P
TLC(cells/mm ³)	211.4 + 132.3	209 + 121	.987
Glucose(mg/dl)	115.0 + 62.4	129 + 40	.081
Protein(mg/dl)	1251.9 + 700.8	1389 + 712	.079
LDH(U/l)	137.7 + 83.3	137 + 67	.993

196

197 Table (9): Frequency of pleural effusion improvement due to control of ascites.

198

		Pleural effusion cases	
		<i>n</i>	%
Treatment	<i>Responder</i>	18	69.2%
	<i>Non responder</i>	8	30.8%
Total		26	100%

199

200

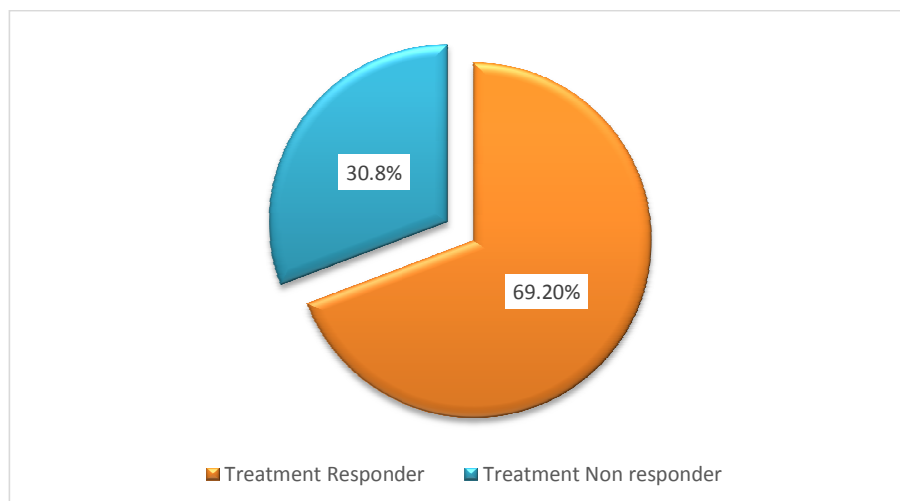


Figure (3): Frequency of pleural effusion improvement due to control of ascites.

Discussion

Hepatic hydrothorax is an uncommon complication of chronic liver disease. It is defined as a significant pleural effusion, usually greater than 500 mL, in a cirrhotic patient, without an underlying pulmonary or cardiac disease or malignancies^(17, 15)

This work aims to study the frequency of pleural effusion in decompensated cirrhotic patients in cases admitted to the Tropical Medicine department (inpatients, outpatient and intensive care unit) at Zagazig University Hospitals between April 2014 to April 2015 trying to determine the frequency and underlying the possible pathogenesis of this disorder. This cross sectional study was performed on 208 patients with cirrhosis and ascites (112 males and 96 females) their ages ranged from 27 to 73 years old (53.8 ± 7.09).

In this study; the frequency of pleural effusion in cirrhotic ascitic patients was 26/208 cases with a percentage of (12.5%). Hepatic hydrothorax is considered an uncommon complication of chronic liver disease. This result coincide with several studies reported that the occurring of pleural effusion ranged from 4 to 12.2% of patients with advanced cirrhosis^(18, 19).

Also, this work showed (76.9%) of pleural effusion patients had effusion on right side, (15.4%) on left side, and (7.7%) have bilateral pleural effusion. So, this study shows that the majority of patients with hepatic hydrothorax have effusion on right side (76.9%). These results coincide with that reported by Strauss and Boyer (1997)⁽¹⁾ who reported incidences of hepatic hydrothoraxes (85.4%) right-sided, (12.5%) left-sided, and (2%) bilateral.

Also, this is in agreement with that reported by Lazaridis et al., (1999)⁽²⁰⁾ which explain that the main cause in development of hepatic hydrothorax is transferring of peritoneal fluid into the pleural space via diaphragmatic defects. These diaphragmatic defects tend to occur more commonly in the right hemidiaphragm due to embryonic development, but less in the left hemidiaphragm which is more thicker and muscular and this explain why the right pleural effusion occur more common than the left pleural effusion in hepatic hydrothorax.

This study showed; (23.1%) of cases with pleural effusion had mild effusion, (46.1%) had moderate effusion and (30.8%) had massive effusion. These results were in agreement with that reported by Dhanasekaran et al., 2010 and Krok and Cárdenas, (2012)^(21, 22).

In this work (23.1%) only of cases had mild effusion who had less symptoms and don't need to admission and most of the cases were diagnosed accidentally when they were examined for other symptoms not related to chest symptoms. Most of cases had moderate effusion about (46.1%) who had more symptoms and need to admission to hospital, (30.8%) had massive effusion that had severe chest symptoms. They needed aggressive treatment by salt restriction, full dose of diuretics, albumin transfusion or even thoracentesis so converted to moderate effusion. The patients cannot sustain massive pleural effusion for long time⁽²³⁾.

This study showed that the cases with pleural effusion were more in Child (C) 61.5% than child (B) 38.5%. Because the hepatic hydrothorax is one of complication of decompensated liver disease. This agrees with study of Roussos et al., (2007)⁽¹³⁾ who reported that a majority of patients with hepatic hydrothorax have advanced liver disease and may be potential candidates for orthotopic liver transplantation.

In this work hepatic hydrothorax is represented by signs and symptoms of end stage liver diseases (cirrhosis) in additional to chest manifestation. This study showed a highly significant increase in incidence of dyspnea in pleural effusion cases, about (78.8%) of cases in group II suffer from dyspnea in spite of about (27.5%) only of cases in group I suffer from dyspnea which mainly occur in tense ascites. This agrees with several studies which reported that dyspnea is the most common symptom of pleural effusion. As the effusion grows larger with more fluid, the harder it is for the lung to expand and the more difficult for the patient to breathe^(21, 24).

Additional to presence of dyspnea, there is other chest symptoms related to hydrothorax such as dry cough which was reported in (84.6%) Of cases and chest pain (15.4%) both occur due to irritation of pleural lining by fluid. The chest pain is usually described as pleuritic. These results are in concordance with these reported by Rossle and Grebes' (2010)⁽²³⁾, who reported dyspnea in (75%) of cases, dry cough in (82.5%) and chest pain in (14.3%).

This study showed that, there was a highly significant difference in size of abdominal enlargement between the two groups; (28.8%) only of cases in group II have mild ascites. Cases with mild ascites were asymptomatic, and don't need to be admitted or even have no chest symptoms to be admitted to chest department.

The study showed that (61.5%) had moderate ascites and (9.6%) only had massive ascites. these were in concomitant with that reported by Abd-El-Sattar (2006)⁽²⁵⁾. There is significant difference of LL edema between two groups. Group I has (88.7%) LL edema and group II had (75.0%) LL edema. The patients with pleural effusion were more interested to take diuretics and do salt restriction to avoid chest manifestation especially dyspnea which increase by increasing amount of effusion and this control LL edema.

This study showed that there was no significance relation between development of abdominal hernia and development of pleural effusion; (49.0%) of cases in group I have abdominal hernia and (50.0%) of cases in group II have abdominal hernia. This indicates that the development of pleural

effusion does not depend on pressure or amount of ascites. These results are similar to that reported by Assouad et al.,) 2003)⁽¹⁹⁾.

A diagnostic thoracentesis was performed in all patients with suspected hepatic hydrothorax to confirm diagnosis and exclude the infection. In this study the chemical analysis of pleural fluid shows TLC (209 ± 121) cells/mm³, glucose (129 ± 40) mg/dl, total protein (1389 ± 712) mg/dL, and LDH (137 ± 67) U/l. So, all cases showed transudate pleural effusion, this is agreed with studies of⁽²¹⁾ which reported that pleural effusions of cirrhotic patients are always transudative. Polymorph nuclear cells count is less than 250 cells/mm³, total protein less than 2.5 g/dL, pleural fluid total protein/serum total protein ratio less than 0.5, pleural fluid lactate dehydrogenase/serum lactate dehydrogenase less than 0.6.

In this work, physical, chemical and bacteriological analysis of ascitic and pleural fluid is similar, all cases were transudates, and these results are in concordance with that reported by Lazaridis et al., (1999)⁽²¹⁾ this may be due to movement of peritoneal fluid into the pleural space via diaphragmatic defects.

There was a significant difference between the degree of pleural effusion and the degree of ascetic fluid. This study showed that the amount of pleural effusion does not depend on amount of ascites. Some cases with mild ascites have massive pleural effusion and vice versa. This is consistent with studies of^(26, 27) which reported that hepatic hydrothorax may occur with absence of ascites. It might be caused by a rapid transdiaphragmatic movement of fluid from the peritoneal cavity to the pleural cavity prior to the formation of ascites.

This study showed that (69.2%) of cases with pleural effusion were improved due to control of ascites by salt restriction, diuretics, and albumin transfusion and paracentesis. Because hepatic hydrothorax and ascites share the same pathophysiological mechanisms, hepatic hydrothorax is ascitic fluid that has entered the pleural cavity. So, the principles of medical management of hepatic hydrothorax are identical to those of ascites in cirrhotic patients⁽⁹⁾.

This study showed that (30.8%) of cases with pleural effusion did not show any improvement in spite of control of ascites. When patients with persistent hydrothorax despite fluid and sodium restriction and use of maximal tolerable doses of diuretics are considered to have refractory hydrothorax so, more invasive therapeutic modalities should be considered⁽¹⁷⁾.

Funding: None.

Ethical approval: The protocol of the study was approved by the ethical committee of Faculty of Medicine, Zagazig University. Informed consents were obtained from all patients.

REFERENCES

1. Strauss, RM. and Boyer, TD. (1997): Hepatic hydrothorax. *Liver Dis*; 17: 227-32.
2. Goto, T.; Oyamada, Y.; Hamaguchi, R. et al. (2011): Remission of Hepatic Hydrothorax after OK-432 Pleurodesis. *Ann Thorac Cardiovasc Surg*; 17: 208–211.
3. Pop, CM; Gherasim, RM. and Dumitrascu, DL. (2003): Hydrothorax without ascites in liver cirrhosis. *Rom J of Gastroenterol*; 12: 315-17.

- 306 4. Huang, PM.; Chang, YL; Yang, CY. et al. (2005): The morphology of diaphragmatic defects in
307 hepatic hydrothorax: thoracoscopic finding. *J Thorac Cardiovasc Surg*; 130: 141-45.
- 308 5. Ayguna, C.; Demirb H. and Senturka, O. (2009): Differential Diagnosis of Hepatic Hydrothorax
309 by 99mTc Sulfur Colloid Peritoneal Scintigraphy: Two Cases. *Gastroenterology Research*;
310 2(4): 248-252.
- 311 6. Roussos, A.; Philippou, N.; Mantzaris, GJ. et al. (2007): Hepatic hydrothorax: Pathophysiology
312 diagnosis and management. *J Gastroenterol Hepatol*; 22: 1388–1393.
- 313 7. Xiol, X. and Castellote, J. (2006): Hepatic hydrothorax and spontaneous bacterial empyema.
314 Chapter XI. In: *Portal hypertension: pathogenesis and management*. Ed. Ahmed Helmy. Nova
315 Science publishers, Inc. P: 195- 209.
- 316 8. Al-sharif, H. and Sharma, S. (2005): Hepatic hydrothorax—how would you manage it? *Can.*
317 *Respir J.*; 12:440–2.
- 318 9. Runyon, BA. (2004): Practice Guidelines Committee, American Association for the Study of
319 Liver Diseases (AASLD). Management of adult patients with ascites due to cirrhosis.
320 *Hepatology*; 39: 841–56.
- 321 10. Moore, KP; Wong, F.; Gines, P. et al. (2003): The management of ascites in cirrhosis: report
322 on the consensus conference of the International Ascites Club. *Hepatology*; 38: 258–66.
- 323 11. Kinasewitz, GT. and Keddissi, JI. (2003): Hepatic hydrothorax. *Curr. Opin. PulmMed*; 9: 261–
324 5.
- 325 12. Kamath, PS; Wiesmen, RH; Malinchoc, M et al. (2001): A model to predict survival in patients
326 with end-stage liver disease. *Hepatology*; 33: 464-470.
- 327 13. Pugh, RNH; Murray-Lyon, I.; Dawson, JL. et al. (1973): Transection of the esophagus for
328 bleeding esophageal varices.
329 *Brit. J. Surg.* 60: 646-654.
- 330 14. Castellote, J.; Xiol, X.; Cortés-Beut, R. et al. (2001): Complications of thoracentesis in cirrhotic
331 patients with pleural effusion. *Rev Esp Enferm Dig.*; 93:566–75.
- 332 15. Runyon, BA; Montano, AA; Akriviadis, EA. et al. (1992): The serum-ascites albumin gradient
333 is superior to the exudate-transudate concept in the differential diagnosis of ascites. *Ann*
334 *Intern Med*; 117: 215-220.
- 335 16. Gordon, FD; Anastopoulos, HT; Crenshaw, W. et al. (1997): The successful treatment of
336 symptomatic, refractory hepatic hydrothorax with transjugular intrahepatic portosystemic
337 shunt. *Hepatology*; 25: 1366–9.
- 338 17. Dumont, AE. and Mulholland, JH. (1960): Flow rate and composition of thoracic duct lymph
339 in patients with cirrhosis. *N Eng J Med*; 263: 471-74.
- 340 18. Assouad, J.; Barthes, Fle P.; Shaker, W. et al. (2003): Recurrent pleural effusion complicating
341 liver cirrhosis. *Ann Thorac Surg.*; 75(3): 986-9.
- 342 19. Garcia, N. Jr. and Mihas, AA. (2004): Hepatic hydrothorax: pathophysiology, diagnosis, and
343 management. *Clin. Gastroenterol*; 38: 52–8.
- 344 20. Lazaridis, KN.; Frank, JW; Krowka, MJ. et al. (1999): Hepatic Hydrothorax: Pathogenesis,
345 Diagnosis and Management. *Am J Med*; 107: 262-67.
- 346 21. Dhanasekaran, R.; west, JK; Gonzales, PC. et al. (2010): Transjugular intrahepatic
347 porotosystemic shunt for Symptomatic refractory hepatic hydrothorax in patients with
348 cirrhosis. *Am J Gastroenterol*; 105(3):635-641
- 349 22. Krok, KL. and Cárdenas, A. (2012): Hepatic hydrothorax. *Semin Respir Crit Care Med.*;
350 33(1):3-10.
- 351 23. Rössle, M. and Gerbes, AL. (2010): hydrothorax: a critical update hepatorenal syndrome and
352 hepatic TIPS for the treatment of refractory ascites. *Gut*; 59: 988-1000.

24. Garcia, N. Jr. and Mihas, AA. (2004): Hepatic hydrothorax: pathophysiology, diagnosis, and management. Clin. Gastroenterol; 38: 52–8.
25. Abd-El-Sattar, N.E. (2006): Role of tumor necrosis factor alpha (α) and nitric oxide in development of renal impairment in SBP patients. MD thesis, Tropical Medicine, Zagazig University 2006.
26. Singer, JA; Kaplan, MM. and Katz, RL. (1977): Cirrhotic pleural effusion in the absence of ascites. Gastroenterology; 73: 575–7.
27. Umino, J.; Tanaka, E.; Ichijoh, T. et al. (2004): Hepatic hydrothorax in the absence of ascites diagnosed by intraperitoneal spraying of indocyanine green. Intern Med.; 43: 283–8.