The Professional Medical Journal
www.theprofesional.com

ORIGINAL PROF-2689

LIVER CIRRHOSIS;
FREQUENCY AND SEVERITY OF THROMBOCYTOPENIA IN PATIENTS

1. Postgraduate
Department of Medicine
Liaquat University of Medical and Health Sciences
Jamshoro, Sindh, Pakistan (LUMHS)
2. FCPS
Assistant Professor
Department of Otorhinolaryingology
Liaquat University of Medical and Health Sciences
Jamshoro, Sindh, Pakistan (LUMHS)
3. MD, Dip.card
Associate Professor
Department of Medicine
Liaquat University of Medical and Health Sciences
Jamshoro, Sindh, Pakistan (LUMHS)
4. Department of Medicine,
Liaquat University Hospital
Hyderabad
5. Department of Medicine,
Liaquat University Hospital
Hyderabad
6. Postgraduate
Department of Medicine,
Liaquat University Hospital
Hyderabad

Correspondence Address:
Dr. Syed Zulfiquar Ali Shah
House No: 279, Doctor's Colony
Hirabad, Hyderabad, Sindh, Pakistan
zulfikar229@hotmail.com

Article received on :
29/10/2014
Accepted for publication:
05/01/2015
Received after proof reading:
17/04/2015

Dr. Sadia Niaz Siddiqui[1], Dr. Mushtaq Ali Memon[2], Dr. Ghulam Hussain Baloch[3], Dr. Hamid Nawaz Ali Memon[4], Dr. Suneel Arwani[5], Dr. Syed Zulfiquar Ali Shah[6]

ABSTRACT… Objectives: To determine the frequency and severity of thrombocytopenia in patients with liver cirrhosis. **Study Deisgn:** Cross sectional study. **Period:** 01-03-2013 to 31-08-2013. **Setting:** Liaquat University Hospital, Hyderabad. **Methods:** The cirrhotic patients were assessed for thrombocytopenia and its severity. The data was analyzed in SPSS version 11.00 and frequency and percentage was computed. The chi-square test was applied and p -value ≤0.05 was considered as statistically significant. **Results:** Total one hundred patients were evaluated for thrombocytopenia, 70% males and 30% females. The mean ± SD for age in cirrhotic subjects was 41.16±14.24 whereas the mean ±SD for age in male and female cirrhotic patients was 42.81±10.96 and 40.63±9.85. The thrombocytopenia was detected in 68%, of which 43(63.2%) were males and 25(36.8%) were females. Mean±SD for platelet in all subjects was 130.85±8.33 whereas it was 68.82±6.52 in thrombocytopenic cirrhotic patients. Mean±SD platelet count in male and female thrombocytopenic patients was 70.94±7.42 and 64.72±5.84. Out of sixty eight thrombocytopenic cirrhotic subjects 23 had mild thrombocytopenia, 25 had moderate thrombocytopenia and 20 had severe thrombocytopenia while in relation to Child-Pugh class B ($p<0.01$) predominant. Regarding the duration of the liver cirrhosis, the thrombocytopenia was predominant in patients between 6-12 months. The common presenting feature observed in relation to gender were malaise 21%, fatigue 17, nausea / vomiting 14% and combine feature in 21 cirrhotic patients ($p=0.04$). **Conclusions:** The thrombocytopenia was detected in patients with liver cirrhosis, therefore frequent platelet assessment is one of the most important step to monitor platelet count and reduce severe and life threatening episodes of bleeding.

Key words: Cirrhosis, thrombocytopenia, liver, platelet, and chronic liver disease - CLD

Article Citation: Siddiqui SN, Memon MA, Baloch GH, Memon HNA, Arwani S, Shah SZA. Liver cirrhosis; frequency and severity of thrombocytopenia in patients. Professional Med J 2015;22(4):426-431.

INTRODUCTION

Liver diseases affect millions of people, however, in the developing countries long lasting disorders such as liver cirrhosis and its complications are major health issues.[1,2] Cirrhosis represents a late stage of progressive hepatic fibrosis and considered to be irreversible in advance stage.[3,4] Most of cirrhotic patients are immuno-deficient and all host system are compromised; there seems to exist association between infections and the cirrhosis related complications.[5-6]

Liver cirrhosis results from prolonged, widespread but patchy hepato-cellular necrosis due to various reasons.[7]The most important classification of cirrhosis is based on etiology. The most common and important causes are alcoholic hepatic disease and chronic viral hepatitis B & C viruses. The less important causes are hemochromatosis, α1 anti trypsin deficiency, Wilson's disease, cystic fibrosis and glycogen storage disease.[7]The term compensated and decompensated cirrhosis is often used. A patient with compensated cirrhosis has no problem with regard to cirrhosis while a patient with decompensated cirrhosis either has signs of liver cell failure or complication of cirrhosis.[8]

Platelets are the cytoplasmic fragmentation of megakaryocytes. Circulating inert platelets are disc shaped with smooth surfaces. They measure around 2-3 microns in size & 1.5-4 lakhs / cumm in number. They are viable in circulation for 10 days.[9] Megakaryocyte produces platelets, playing an important role in hemostasis.[5] Findings of thrombocytopenia and hypoalbuminemia

reported in chronic hepatic disease.[6] Patients with hepatic cirrhosis have hemostatic impairment and thrombocytopenia is a feature of such disturbance.[10-12] Other factors responsible for thrombocytopenia includes bone marrow suppression by chronic hepatitis and reduction in the level or activity of the thrombopoietin.[13]

Therefore by considering such association the study was determines the frequency and severity of thrombocytopenia in patients with liver cirrhosis at tertiary care teaching hospital of Hyderabad / Jamshoro.

PATIENTS AND METHODS

The present cross sectional descriptive study of six months was conducted at Liaquat University Hospital, Hyderabad. The inclusion criteria of the study were known cases of liver cirrhosis were ≥ 13 years of age and of either gender while the exclusion criteria were known case of idiopathic thrombocytopenic purpura (as platelets are lyzed in this disease), known case of aplastic anemia, myelodysplastic syndrome, osteopetrosis (in which platelet production is impaired), patients who were already on drug therapy (fansidar, septran, thiazides and chemotherapeutic agents that can lead to thrombocytopenia), the patients had history of repeated blood / platelet transfusion and the non cooperative patients who refused to give written consent for participation in the study. All the subjects with liver cirrhosis were evaluated and admitted in the ward, after taking history, performing specific examination; the treatment plan was decided under the supervision of ward consultant physician. Thereafter all the cirrhotic subjects were assessed for platelet count. For that 3 cc venous blood sample was taken and sent to laboratory for analysis. The severity of thrombocytopenia was categorized as mild thrombocytopenia <150,000 to >50,000/l, moderate thrombocytopenia <50,000 to >20,000/l and severe thrombocytopenia <20,000/. The child pugh score was calculated which included the presence of ascites, encephalopathy, albumin, prothrombin time and serum bilirubin. The ascites was detected by clinical examination (shifting dullness and fluid thrill) and was confirmed on ultrasound, the serum albumin, PT/INR and bilirubin were evaluated by blood biochemistry with comparison to normal values and hepatic encephalopathy by history, clinical examination and serum ammonia level while the bleeding time >6 minutes was considered as prolonged. By summing the score, the class was decided i.e. the class A has 5-6 points, class B 7-9 points and class C 10-15 points. An informed consent was taken from every patient before include them in the study while in case of epistaxis the ENT opinion was also taken as far as management strategy was concerned. A proforma was designed for the collection of data. The data was analyzed in SPSS version 11.00. The frequency and percentage was computed. The chi-square test was applied between categorical variables and p-value ≤0.005 was considered as statistically significant.

RESULTS

Total one hundred cirrhotic subjects were studied for thrombocytopenia. The mean ± SD for age in cirrhotic subjects was 41.16±14.24 whereas the mean ±SD for age in male and female cirrhotic patients was 42.81±10.96 and 40.63±9.85. The thrombocytopenia was observed in 68% cirrhotic subjects, of which forty three (63.2%) were males and twenty five (36.8%) were females. The mean platelet count in overall population was 130.85±8.33 while it was 68.82±6.52 in thrombocytopenic cirrhotic subjects. The mean platelet count in male and female thrombocytopenic cirrhotic patients was 70.94±7.42 and 64.72±5.84. The age distribution in context to gender and thrombocytopenia is shown in Tab-I and II while the gender distribution in relation to thrombocytopenia is shown in Table-III whereas the severity of thrombocytopenia in context to gender and child-pugh score is shown in Table-IV and V.

		GENDER		Total
		Male	Female	
AGE	13-19	8	4	12
		11.4%	13.3%	12.0%
	20-29	9	6	15
		12.9%	20.0%	15.0%
	30-39	21	4	25

		30.0%	13.3%	25.0%
	40-49	18	6	24
		25.7%	20.0%	24.0%
	50-59	12	2	14
		17.1%	6.7%	14.0%
	60 +	2	8	10
		2.9%	26.7%	10.0%
Total		70	30	100
		100.0%	100.0%	100.0%

Table-. The age distribution in context to gender

		GENDER		**Total**
		Male	**Female**	
AGE	13-19	8	4	12
		11.4%	13.3%	12.0%
	20-29	9	6	15
		12.9%	20.0%	15.0%
	30-39	21	4	25
		30.0%	13.3%	25.0%
	40-49	18	6	24
		25.7%	20.0%	24.0%
	50-59	12	2	14
		17.1%	6.7%	14.0%
	60 +	2	8	10
		2.9%	26.7%	10.0%
Total		70	30	100
		100.0%	100.0%	100.0%

Table-. The age distribution in context to gender

		Thrombo-cytopenia		**Total**	**P-Value**
		Yes	**No**		
GENDER	**Male**	43	27	70	
		63.2%	84.4%	70.0%	
	Female	25	5	30	
		36.8%	15.6%	30.0%	0.03*
TOTAL		68	32	100	
		100.0%	100.0%	100.0%	

Table-III. The gender distribution in context to thrombocytopenia

**Statistically significant* *Chi-square value 4.63; df = 1*

		Thrombocytopenia				
		Severity			**Total**	**P-Value**
		Mild	**Moderate**	**Severe**		
Gender	**Male**	9	18	16	43	
		39.1%	72.0%	80.0%	63.2%	
	Female	14	7	4	25	
		60.9%	28.0%	20.0%	36.8%	
Total		23	25	20	68	0.01*
		100.0%	100.0%	100.0%	100.0%	

Table-IV. The severity of thrombocytopenia in relation to gender

**Statistically significant* *Chi-square value 8.99; df =02*

		Thrombocytopenia				
		Severity			**Total**	**P-value**
		Mild	**Moderate**	**Severe**		
CHILD-PUGH	**A**	4	8	9	21	
		17.4%	32.0%	45.0%	30.9%	
	B	5	12	10	27	
		21.7%	48.0%	50.0%	39.7%	
	C	14	5	1	20	
		60.9%	20.0%	5.0%	29.4%	0.001*
TOTAL		23	25	20	68	
		100.0%	100.0%	100.0%	100.0%	

Table-V. The severity of thrombocytopenia in relation to child pugh score

**Statistically significant* *Chi-square value 18.03; df=04*

DISCUSSION

The present study evaluates the thrombocytopenia in patients with liver cirrhosis and reported 68% prevalence. The study by poordad F stated that the thrombocytopenia is a major disorder in patients with liver cirrhosis whereas a study by Tanaka M. reported 63% prevalence for thrombocytopenia in cirrhotic subjects.[14,15] In present series the majority of individuals were between 30-50 years of age, the finding also observed in the study published in 2011. The thrombocytopenia in liver cirrhosis is due to increased platelet clearance and impaired thrombopoiesis.[16] The high rate of thrombocytopenia in majority old patients as compared to younger indicates that likelihood of liver dysfunction and subsequent fibrosis increases as patients grow older.

In current study the bleeding time was also observed which is prolonged in thrombocytopenic cirrhotic patients, the finding is consistent with the studies by Tripodi A and Blake JC et al.[17,18] A prolonged bleeding is because of thrombocytopenia secondary to liver dysfunction. In present study the male population is predominant, this is similar to the study by Nasta P.[19] Thrombocytopenia is a major complication in individuals with cirrhosis. In the study by Jan et al[5], 92% of the cirrhotic patients were thrombocytopenic, while former workers have reported 76%[20] whereas others have also reported thrombocytopeni in cirrhotic subjects.[21,22] Thrombocytopenia in present study was mild in 23% of the cases, moderate in 25% and severe in 20% of the cases. Moderate thrombocytopenia is also reported to be 22% and 27% by two former studies.[23,24]

Liver synthesis thrombopoietin (TPO) need for thrombopoiesis[25] and its levels are observed to rise in thrombocytopenic conditions.[26]Thrombocytopenia in cirrhosis is important, not only as association but because it is a predictive indicator of bleeding. Therefore guidelines for transfusion support in thrombocytopenic patients with cirrhosis during invasive procedures might be useful for the health care providers. Thus by evaluating the platelet count the health care provider can predict the bleeding risk in relation to severity of thrombocytopenia and coagulopathies and can take early effective management steps to save the patient from life threatening bleeding.

CONCLUSIONS

It is concluded that sixty eight percent (68%) of cirrhotic patients had thrombocytopenia with male population predominance. Regarding severity 23 patients had mild and 25 patients had moderate thrombocytopenia ($p=0.01$) with class B predominance (child pugh class) $p=0.001$. Therefore thrombocytopenia is a common biochemical finding in liver cirrhosis, so platelet count should be monitored in every relevant patient to reduce the risk of severe life threatening bleeding.

REFERENCES

1. Schuppan D, Afdhal NH. **Liver cirrhosis.** Lancet. 2008;371(9615):838-51.

2. Liu Y, Meyer C, Xu C, Weng H, Hellerbrand C, ten Dijke P, et al. **Animal models of chronic liver diseases.** Am J Physiol Gastrointest Liver Physiol. 2013;304(5):G449-68.

3. Shafiq M, Khan AA, Alam A, Butt AK, Shafqat F, Malik K, et al. **Frequency of hepatopulmonary syndrome in cirrhotic patients.** J Coll Physician Surg Pak.2008;18(5):278-81.

4. Vilstrup H. **Cirrhosis and bacterial infections.** Rom J Gastrointestinal.2003;12:297-302.

5. Jan A, Hussain J. **Thrombocytopenia and prolonged bleeding time in cirrhosis of liver.** Gomal Journal of Medical Sciences January-June 2009;7(1):55-7

6. Olga OZ, Nikolai DY. **Invasive and non invasive monitoring of hepatitis C virus induced liver cirrhosis: alternates or complements?** Curr Pharm Biotechnol.2003;4(3):195-209.

7. Sheila Sherlock, James Dooley; **Hepatic Cirrhosis; In Diseases of Liver and Biliary System;** Blackwell Science publishers; 11th ed.p.368-80

8. Mendez-Sanchez N, Aguilar-Ramírez JR, Reyes A, Dehesa M, Juorez A, Castneda B, et al. **Etiology of liver cirrhosis in Mexico.** Ann Hepatol.2004;3(1):30-3.

9. Semple JW, Italiano JE Jr, Freedman J. **Platelets and the immune continuum.** Nat Rev

Immunol.2011;11(4):264-74.

10. Mehta S, Levey JM. Bonkovsky HL. **Extrahepatiic manifestations of infection with hepatitis C virus.** Clin Liver Dis.2001;5:979-1008

11. Aster RH. Pooling of platelets in the spleen: **Role in pathogenesis of hypersplenic thrombocytopenia J Clin Invest.**1966;45:654-58

12. Pockros PJ, Duchini A, McMillan R, Nyberg LM, McHutchison J, Viernes E. **Immune thrombocytopenic purpura in patients with chronic hepatitis C virus infection.** AM J Gastroenterol.2002;97:2040-45

13. Behnava B, Alavian SM, Asl MA. **The Prevalence of Thrombocytopenia in Patients with Chronic Hepatitis B and C.** Hepatitis Monthly.2006;6(2):67-69

14. Poordad F. Review article: **thrombocytopenia in chronic liver disease.** Aliment Pharmacol Ther.2007;26 Suppl 1:5-11.

15. Tanaka M. **Thrombocytopenia in liver cirrhosis.** Nihon Ketsueki Gakkai Zasshi.1989;52(4):785-91.

16. Tripodi A. **Hemostasis abnormalities in liver cirrhosis: myth or reality?.** Polskie archiwum medycyny wewnętrznej.2008;118 (7-8).
17. Blake JC, Sprengers D, Grech P, McCormick PA, McIntyre N, Burroughs AK. **Bleeding time in patients with hepatic cirrhosis.** BMJ.1990;301(6742): 12-15.

18. Pradella P, Bonetto S, Turchetto S, Uxa L, Comar C, Zorat F, et al. **Platelet production and destruction in liver cirrhosis.** J Hepatol. 2011;54(5):894-900.

19. Nasta P. **Immune activation, aging and gender and progression of liver disease.** Acta Biomed.2011;82(2): 115-23.

20. Iman N, Khan H. **Thrombocytopenia in chronic liver disease due to hepatitis c virus.** RMJ.2009;34(1):72-74.

21. Shattil SJ, Bennet JS. **Platelets & their membranes in hemeostasis.** Physiology & pathophysiology.Ann. intern Med.1981;94:108-18.

22. Durand JM, Lefevre P, Telle H, Kaplanski G, Quiles N, Soubeyrand J. **Thrombocytopenic purpura and hepatitis C virus infection.** Haematologica.1993;78:135.

23. Esannol !, Galiego A ,Enriquez J, Rubella N, LermaE. Hernadez A, Pujol-max N. **Thrombocytopenia associated with liver cirrhosis and hepatitis C viral infection: role of thrombocytopenia.** Hepatogastroenterolgy.2000;47: 1404-6.

24. Kajihara M, Kato S, Okazaki Y, Kawakami Y, Ishii H, Ikeda Y, et al. **Role of autoantibody-mediated platelet destruction in thrombocytopenia in patients with cirrhosis.** Hepatology.2003;37:1267-76.

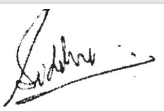
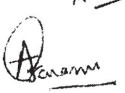
25. Panasiuk A, Prokopowicz D, Zak J, Panasiuk B. **Reticulated platelets as a marker of megakaryopoiesis in liver cirrhosis; relation to thrombopoietin and hepatocyte growth factor serum concentration.** Hepatogastroenterology.2004;51:1124-28.

26. Freni MA, Spadaro A, Ajello A, Barbaro E, Seaffidi M, Alessi N,et al. **Serum thrombopoietin in chronic liver disease: relation to severity of the disease and spleen size.** Hepatogastroenterology.2002;49:1382-5.

"Art is man's expression of his joy in labor."

Henry A. Kissinger

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Sadia Niaz Siddiqui	Contriubtion to conception and deisng, acquision of data, analysis and interpretation of data	
2	Dr. Mushtaq Ali Memon	Drafting the article and shares its expert research opinion and experience in finalizing the manuscript	
3	Dr. Ghulam Hussain Baloch	Contributed in conection and interpretation fo data and give his expert view for manuscript designing	
4	Dr. Hamid Nawaz Ali Memon	Analysis and interpretation of data, contributed in conception and shares its expert research opinion	
5	Dr. Suneel Arwani	Drafting, interpreting and analyzing data	
6	Dr. Syed Zulfiquar Ali Shah	Data collection and manuscript of data