ORIGINAL ARTICLE

PREVALENCE OF HEPATITIS B AND HEPATITIS C VIRUSES AND ITS CORRELATION WITH BETA THALASSEMIA MAJOR PATIENTS IN PESHAWAR, KHYBER PAKHTUNKHWA

Asad Ullah[1], Adnan Shinwari[2], Shahid Ullah[3], Ashfaq Ahmad[3], Sarzamin Khan[4], Muhammad Zeeshan[5], Najeeb Ullah[6], Muhammad Rabnawaz[7], Wasim Muhammad[8]

ABSTRACT

Introduction: The term "thalassemia" refers to a group of hereditary blood disorders characterised by anaemia. The two primary proteins that make up the oxygen-carrying HB (haemoglobin) component of red blood cells (RBCs) are beta and alpha chains. To create beta globin chains, two globin genes from each parent are required; if one or both of these genes are defective, beta thalassemia will result. The most common complication of beta thalassemia major that is iron over-loading in vital organ of the body like liver, spleen, heart and endocrine system due to regular blood transfusion, the second most common complication is transfusion transmission infection (TTI) hepatitis B, hepatitis C and HIV infection. Globally, the most common infection is hepatitis B and hepatitis C viruses' infection.

Material & Methods: Cross sectional correlational study was conducted at the Fatimid Foundation and Hamza in Peshawar, Pakistan. Research study had started from 1st March 2021 to 1st October 2021. In this study 184 beta thalassemia major patients had been included, 105 from Fatimid foundation and 79 from Hamza foundation.

Results: Total of one hundred and eighty-four participants were included in the study. Among them 6= (3.3%) were positive for hepatitis B virus antigen, while hepatitis C virus was found in 43 (23.8%) patients. Furthermore, 4 (2.2%) were infected with both HBV and HCV virus infection.

Conclusion: Cousin or other blood relation marriage was significant or risk factor for thalassemia disease. There was no significant relation found of hepatitis B or hepatitis C virus infection with thalassemia major patients. In order to minimize the risk of HBV and HCV infection, it is essential to utilize the most sensitive and specific Nucleic acid test for donor screening. Safe blood transfusion centres for thalassemia patients are needed which are well-equipped and all the facilities must be available in it.

Key Words: Hepatitis B Virus, Hepatitis C Virus, Prevalence, Thalassemia

Authors' Declaration: The authors declared no conflict of interest and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors contributed substantially to the planning of research, question designing, data collection, data analysis and write-up of the article.

Authors' Affiliation

[1]Demonstrator, Institute of Allied Health Sciences, Lakki Marwat
[2]Institute of Global Health Care Management, United Kingdom
[3]Baqai Institute of Haematology, Baqai Medical University, Karachi, Pakistan
[4]Nation College of Sciences (NCS), Peshawar, Pakistan
[5]Department of Biochemistry, University of Malakand, Lower Dir, Pakistan
[6]Training Medical Officer, Khyber Teaching Hospital, Peshawar, Pakistan
[7]Lecturer, Department of Allied Health Sciences, Iqra University, Peshawar, Pakistan
[8]Lecturer, Institute of Paramedical Sciences, Khyber Medical University, Peshawar, Pakistan

Corresponding Author

Wasim Muhammad
Lecturer, Institute of Paramedical Sciences, Khyber Medical University
Email: wasimkmu@gmail.com

This article may be cited as: Ullah A, Shinwari A, Ullah S, Ahmad A, Khan S, Zeeshan M, Ullah N, Rabnawaz M, Muhammad W. Prevalence of hepatitis b and hepatitis c viruses and its correlation with beta thalassemia major patients in Peshawar, Khyber Pakhtunkhwa. Rehman J Health Sci. 2023;5(2). 177-183

Submitted: Nov 12, 2023 Revisions Submitted: Dec 03, 2023 Accepted: Dec 29, 2023

INTRODUCTION

The term "thalassemia" refers to a group of hereditary blood disorders characterised by anaemia. RBCs are tiny, pale, and short lived. The two primary proteins that make up the oxygen-carrying HB (haemoglobin) component of red blood cells (RBCs) are beta and alpha chains. To create beta globin chains, two globin genes from each parent are required; if one or both of these genes are defective, beta thalassemia will result. The degree of alteration depends on multiple genes.[1] A single defective gene is known as minor beta thalassemia. The Two defective genes depending on mild or severe symptoms, these genes might cause Colley's anaemia or thalassemia major, which is also common in people with Mediterranean ancestry.[2]

If the red blood cells malfunction and are unable to carry adequate oxygen, the body does not create enough of either of these two proteins. The underlying anaemia is frequently severe and causes a number of health issues, including an inflamed spleen, malformed bones, frailty and the need for continuous lifelong transfusion, care and medication management.

The HB molecular chain that is impacted determines which type of thalassemia is present. When α-thalassemia occurs, α globin chain production is typically impacted, whereas β globin chain production is typically impacted in β-thalassemia. Two closely related genes on chromosome 16 code for α globin chains, while a single gene on chromosome 11 codes for β globin chains.[2]

β - Thalassemia is more common in the Mediterranean region while its incident rate is higher in South East Asia, Middle East, South Iran, Iraq, china, India and subcontinent.[3] Thalassemia leads to severe anaemia. Thalassemia is divided on the bases of their chain mutation: thalassemia major, intermediated and minor. The main clinical syndrome are observed in thalassemia major patient or blood-transfusion-depended thalassemia.[4] Based on the study, it was shown that children of first cousins, distant blood relatives and intra-caste marriages had a higher incidence of β-thalassemia (96% vs. 4%) due to cultural consanguinity. Although the incidence of thalassemia varies throughout castes, epidemiological studies are necessary to determine the prevalence of heterozygote (carrier) of the β-thalassemia gene, as the true prevalence of the β-thalassemia gene(s) is unknown. When parents of children with βthalassemia visit their children for medical attention, they should be persuaded to test every youngster in their extended family. Heterozygote genetic screening need to be required for all children, not only those from disadvantaged families. Controlling the disease will be aided by the identification of inherited recessive genetic abnormalities in the population through molecular techniques.[5]

β-Thalassemia is the most common single autosomal recessive genetic disease, affecting millions of children worldwide. It accounts for approximately 1.5% of the global population, with 80 to 90 million people being carriers of the β-Thalassemia gene. Additionally, there are 50,000 to 60,000 new cases of β-Thalassemia major reported annually worldwide.[6] In Pakistan, the frequency rate is even higher at 5% to 7%, with 5,000 to 9,000 new cases of β-Thalassemia major being registered each year.[7] On the other hand, α-Thalassemia is less common globally but more prevalent in the Far East. It is characterized by the deletion or mutation of the alpha globin gene in haemoglobin and the severity of α-Thalassemia depend on the number of mutations or inactivation of the alpha globin gene in haemoglobin.[8] Clinical sign and symptom include pale and listless appearance, poor appetite, dark urine (a sign that red blood cells are breaking down), Slowed growth and delayed puberty, jaundice (a yellowish colour of the skin or whites of the eyes).

The most common complication of beta thalassemia major that is iron over-loading in vital organ of the body like liver, spleen, heart and endocrine system due to regular blood transfusion, the second most common complication is transfusion transmission infection (TTI) hepatitis B, hepatitis C and HIV infection.[9]

Globally, the most common infection is hepatitis B and hepatitis C viruses' infection.[10] Recent study showed that 391 million people are infected with hepatitis B virus infection that is 5% of the world population. Asian population is mostly infected that is 75%. One hundred and forty-five million new cause of acute hepatitis

B virus infection was registered this year. According to the WHO report the frequency of HBV virus infection is 0.08 to 6.08 worldwide. Highest prevalence of hepatitis B is in South Africa that is greater than 8%. United States have the lowest frequency of hepatitis B virus infection.[11]

Globally 180 million people are infected with hepatitis C virus. Approximately, 4 million people in United States were infected.[12] Globally chronically hepatitis C virus infection rate is 1% to 2%. Prevalence of hepatitis B virus infection is 0.4 to 5.4% and hepatitis C is 1.7 to 5.5 % in general population in Pakistan.[13,14] Prevalence HCV in beta thalassemia major patient is 28% to 43%, this ratio of hepatitis C is different in different areas of Pakistan.[2,14]

Beta-thalassemia major is a significant genetic disorder with profound implications for affected individuals and their families. Management strategies involve a multidisciplinary approach and ongoing research to improve outcomes and quality of life for those living with this condition.

The main purpose of this study was to find out the prevalence of Hepatitis B and Hepatitis C infection in Beta thalassemia major patient and the association of these infections with these thalassemia major patients.

MATERIAL AND METHODS

Cross-sectional correlational study was conducted in Hamza and Fatimid foundation, blood transfusion centre at Peshawar Pakistan. The duration of this study was six months from 1st March 2021 to 1st October 2021. Moreover, data was collected after received informed consent forms from patient's parents or gardener and also took permission from blood transfusion centre. The study was done totally on questionnaire. Total of 184 thalassemia major patients were included in this study: 105 from Fatimid and 79 from Hamza foundation.

Study design and sampling:

Cross-sectional correlational study was conducted. Non-probability random sampling technique was used. This method was selected because cross-sectional correlational designs are well-suited for exploratory research, where the goal is to identify potential associations between variables. This type of design could generate hypotheses that could be further investigated in more controlled experimental designs.

Statistical Analysis:

Frequencies and Percentages were used to determine the exit value and the correlation with different variable. Statistical Package for Social Sciences (SPSS) version 20 was used and p test was done for the analysis of the data.

Inclusion criteria & Exclusion criteria:

The patients that had β - thalassemia major were included in the study while other patients such as **α-** thalassemia patient and β-Thalassemia minor patients were excluded from this study.

Ethical Approval

All investigations were performed as a part of routine medical care with no need for separate informed consent.

RESULTS

This study had included 114 (63%) male and 67 (37%) female. Out of the total 184 beta thalassemia major patients 6 (3.3%) were infected with hepatitis B virus infection. Hepatitis B infected male ratio was 83% (5) and female ratio was 17% (1). Beta Thalassemia major patients hepatitis C virus infected ratio was 23.8% (43). Male hepatitis C virus infected ratio was 63% (27) and female 37% (16). Both hepatitis B and hepatitis C virus infected ratio was (2.2%). Hepatitis C virus ratio was 75% (3) male and 25% (1) female. **Figure 1**

On the basis of age and the correlation of hepatitis B and hepatitis C virus infection in thalassemia major patients: mean age 8.5 years, minimum age was 0.5 years and maximum age 25 years. The highest ratio of thalassemia patients were found in the age group 0.5-3 years. The least ratio of thalassemia patient was found in the age group more than 15 years of age. As the age of beta thalassemia major patients increased the ratio of thalassemia patients decreased. While the hepatic viruses infection rate was directly proportion to the age of thalassemia patients as the age of thalassemia major patients increased, the frequency of hepatic viruses infection was also increased.

Hepatitis B virus infected 1(16%) thalassemia patients in his/her age 3-5 years and 5 (84%) thalassemia patients had hepatitis B virus infection in the of age 5-10 years, no other age group patients was infected with hepatitis B virus infection. Hepatitis C virus infected 3 (7.9%) thalassemia patients in the age of 0.5-3 years. At the age of age 3-5 years hepatitis C virus infected thalassemia patients was 5 (12.2%). The beta thalassemia patients with the age of 5-10 years have hepatitis C virus

infection there ratio was 9 (20.9%). The highest ratio was 13 (31%) in thalassemia patients who have hepatitis C virus were found in the age between 15-19 years. Moreover, as the age of thalassemia patients increased the ratio of hepatic virus infections increased. By performing p-test on a specific age group, the value was significant. As age increased, more blood transfusion is required for haemoglobin level and the risk of transfusion transmissible infection increased. **Figure 2**

The other significant variable was Hb F level in thalassemia patients, because patient's body didn't synthesis normal haemoglobin level and needed more blood transfusion.

We compared other variable with hepatitis B and hepatitis C virus infection in beta thalassemia major patients like resident, hepatic virus infection family history, any surgical procedure history, sibling infected, cousin married etc. but all this value was not significant for p-value testing, except the age group and haemoglobin F level was significant with our study. **Table 1**

We compared both centres' data of hepatitis B & C virus infection in thalassemia major patients, we found that Fatimid foundation patients were more infected from hepatic virus infection as compared to Hamza foundation. All variable and their value were same in these two foundations except the age. Fatimid foundation patient mean age was 9.5 years as compared to Hamza foundation mean age which was 5.6 years.

DISCUSSION

Hepatitis B and hepatitis C virus infection with beta thalassemia major patient and correlation with different risk factor causes these infections. For Thalassemia patients a regular transfusion is necessary after two or three weeks for haemoglobin level. It maintains the normal body function. After multiple transfusions, it is one of the risk factors for Hepatitis B and C. There are other treatments like bone marrow transplantation but that is too expensive.[15]

One of the research studies showed that Hepatitis B virus infected ratio was 5% and hepatitis C virus infected thalassemia participant was 61.2%. Thalassemia patients had been vaccinated for hepatitis B virus infection that is 85% and the remaining were unvaccinated thalassemia patients. All the hepatitis B infected thalassemia patients had unvaccinated for hepatitis B virus.[16] In this research study we had observed that patient who had more blood transfusion had more hepatitis C infected as compared to those who had less blood transfusion.

The key risk factor for hepatitis C virus infection in thalassemia patients is transfusion. Other risk factor includes dialysis, major surgery, injection and drug abuses.[17]

Another study found that consanguineous family is the most common factor that is 34.7% in thalassemia disease. 57% are thalassemia infected with first cousin marriage and 10% second cousin married.[18.19] In our research study, 76.9% were Consanguineous or family relation with thalassemia patients and 23.1 % thalassemia patient had no family relation.

In another study, 300 thalassemia patient had interviewed of different parameter through pre testing questionnaire, their family history indicated that their sibling was infected with hepatitis C virus infection.[20,21,22] In this study (97%) thalassemia major patient and (3%) thalassemia intermediate had been infected. Male were more infected than female. The highest ratio of thalassemia was (34%) infected whose age was about 3 to 5 years.

Immunization, screening, infection control procedures and integrated medical care are all important components of the management and prevention of hepatitis B and C in thalassemia patients. For those with thalassemia, regular monitoring and prompt management can greatly enhance outcomes and quality of life.

This research will help further researcher to investigate the potential of gene therapy and genome editing techniques, such as CRISPR/Cas9, to correct the genetic mutations causing beta-thalassemia major.

Additionally, researchers can plan and carry out carefully monitored clinical trials to assess the efficacy and safety of newly developed treatments. Extensive multicenter trials are necessary to determine the risks and long-term advantages of new medicines.

CONCLUSION

Cousin or other blood relation marriage was significant or risk factor for thalassemia disease. There was no significant relation found of hepatitis B or hepatitis C virus infection with thalassemia major patients.

In this study we had used the most sensitive and specific (Nucleic Acid Test) method for blood donor screening and attempted to reduce the

risk of hepatitis B and hepatitis C virus infection in general population. Hence, it is concluded that the Thalassemia patients must be vaccinated for hepatitis B virus. Along with this, it is important to establish safe blood transfusion centre for thalassemia patient with well-equipped and exiting most sensitive and specific method used for donor screening.

REFERENCES

1. Behzadifar M, Gorji HA, Bragazzi NL. The prevalence of hepatitis C virus infection in thalassemia patients in Iran from 2000 to 2017: a systematic review and meta-analysis. Archives of virology. 2018;163(5):1131-40.

2. Yasmeen H, Hasnain S. Epidemiology and risk factors of transfusion transmitted infections in thalassemia major: a multicenter study in Pakistan. Hematology, transfusion and cell therapy. 2019;41:316-23.

3. Rauf A, Nadeem MS, Ali A, Iqbal M, Mustafa M, Muzammal Latif M, et al. Prevalence of hepatitis B and C in internally displaced persons of war against terrorism in Swat, Pakistan. The European Journal of Public Health. 2011;21(5):638-42.

4. Iqbal A, Farrukh H, Aslam S, Iqbal T. Frequency of Hepatitis C in Â-Thalassemia major patients. Rawal Medical Journal. 2013;38(4).

5. Shah T, Hussain W, Ali N, Sardar S, Ishaq M, Rahman MU, et al. Frequency distribution and risk factors of hepatitis B virus and hepatitis C virus infections among thalassemia patients: a regional study. European journal of gastroenterology & hepatology. 2019;31(2):248-52.

6. Ghafoor MB, Memon FA, Saleem M, Shabbir R. Transfusion Transmitted Infections in Multiple Transfused Thalassemia Patients in Rahim Yar Khan. Journal of Liaquat University of Medical & Health Sciences. 2021;20(1):31-6.

7. Bhattacharya D, Bhattacharjee S, De M, Lahiri P. Prevalence of hepatitis C in transfusion dependent thalassaemics & haemophilics. The Indian journal of medical research. 1991;94:430-2.

8. Tanveer T, Masud H, Butt ZA. Are people getting quality thalassemia care in twin cities of Pakistan? A comparison with international standards. International Journal for Quality in Health Care. 2018;30(3):200-7.

9. Jafroodi M, Davoudi-Kiakalayeh A, Mohtasham-Amiri Z, Pourfathollah AA, Haghbin A. Trend in prevalence of hepatitis C virus infection among β-thalassemia major patients: 10 years of experience in Iran. International journal of preventive medicine. 2015;6.

10. Riaz H, Riaz T, Ullah F, Aziz S, Khan MU, Pervaiz R, et al. Assessment of the seroprevalence of viral hepatitis B, viral hepatitis C and HIV in multitransfused thalassaemia major patients in Karachi, Pakistan. Tropical doctor. 2011;41(1):23-5.

11. Seeff L, Hoofnagle J. Epidemiology of hepatocellular carcinoma in areas of low hepatitis B and hepatitis C endemicity. Oncogene. 2006;25(27):3771-7.

12. Abu-Shaheen A, Heena H, Nofal A, Abdelmoety DA, Almatary A, Alsheef M, et al. Epidemiology of Thalassemia in Gulf Cooperation Council Countries: A Systematic Review. BioMed research international. 2020;2020.

13. Din G, Malik S, Ali I, Ahmed S, Dasti JI. Prevalence of hepatitis C virus infection among thalassemia patients: a perspective from a multi-ethnic population of Pakistan. Asian Pacific journal of tropical medicine. 2014;7:S127-S33.

14. Waheed U, Saba N, Wazeer A, Ahmed S. A Systematic Review and Meta-Analysis on the Epidemiology of Hepatitis B and Hepatitis C Virus among Beta-Thalassemia Major Patients in Pakistan. Journal of Laboratory Physicians. 2021.

15. Jallab HR, Eesa ZM. Prevalence of Hepatitis B and Hepatitis C Viruses in β-thalassemia Major Patient in AD-Diwanya Province, Iraq. Indian Journal of Forensic Medicine & Toxicology. 2020;14(2):743.

16. Khalil S, Khan HS, Akhtar P. Status of hepatitis B and C in beta thalassemia major

patients. Journal of Islamabad Medical & Dental College (JIMDC). 2016;5(2):71-3.
17. Farooq A, Waheed U, Zaheer HA, Rauf A, Arshad A, Arshad M. Incidence of hepatitis B and C viruses in thalassaemia major patients. Pakistan Journal of Zoology. 2018;50(3).
18. Abid M, Ali S, Hassnain S, Altaf Z, Khalid M, Tariq S. Seroconversion of hepatitis B and C in paediatric patients with thalassemia major and its awareness among parents. Biomedica. 2019;35(03):170-3.
19. KHATTAK IUD, SHAH M, AHMED I, REHMAN A, SAJID M. frequency of hepatitis B and hepatitis C in multitransfused beta thalassaemia major patients in district Swat. Journal of Saidu Medical College, Swat. 2013;3(2):299-302.
20. Qurat-ul-Ain LA, Hassan M, Rana SM, Jabeen F. Prevalence of β-thalassemic patients associated with consanguinity and anti-HCV-antibody positivity–a cross sectional study. Pak J Zool. 2011;43(1):29-36.
21. Bhatti FA, Amin M, Saleem M. Prevalence of antibody to hepatitis C virus in Pakistani thalassaemics by particle agglutination test utilizing C-200 and C22-3 vital antigen coated particles. JOURNAL-PAKISTAN MEDICAL ASSOCIATION. 1995;45:269-70.
22. Ahmed S, Ayub M, Naeem M, Nazir FH, Hussain A, Ghilzai D, et al. Thalassemia Patients from Baluchistan in Pakistan Are Infected with Multiple Hepatitis B or C Virus Strains. The American journal of tropical medicine and hygiene. 2021;104(4):1569.

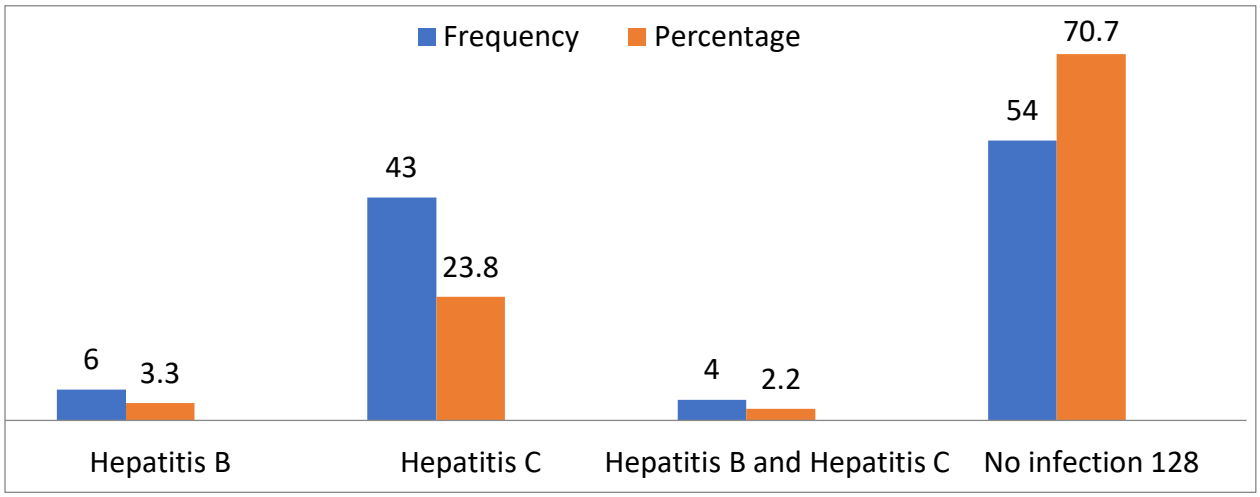
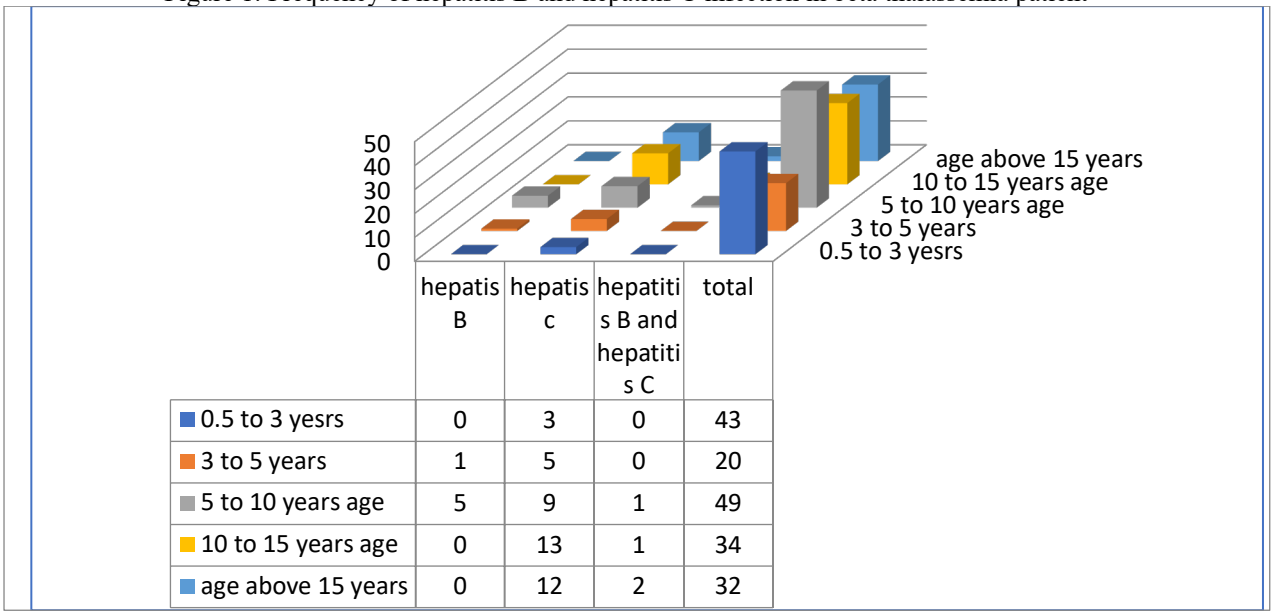


Figure 1: Frequency of hepatitis B and hepatitis C infection in beta thalassemia patient



	hepatis B	hepatis c	hepatitis B and hepatitis C	total
0.5 to 3 yesrs	0	3	0	43
3 to 5 years	1	5	0	20
5 to 10 years age	5	9	1	49
10 to 15 years age	0	13	1	34
age above 15 years	0	12	2	32

Figure 2: HBV and HCV infection in thalassemia patient by age wise

Table 1: Association of other variable with hepatitis B and hepatitis C virus infection in beta thalassemia major patients

Category		Total no of patients	Hepatitis B infection		Hepatitis C infection		Both HBV, HCV	P- value in different correlation	
		T%	frequency	Percentage	frequency	Percentage	Frequency	Percentage	p-value
Genders	Male	63%	5	83.3%	27	62.7%	3	75%	.705
	Female	37%	1	16.7%	16	37.3%	1	25%	
Ages	0.5- 3years	24.2%			3	7.9%			.001
	3- 5years	11.2%	1	16.7%	5	12.2%			
	5-10years	27.5%	5	83.3%	9	20.9%	1	25%	
	10-15years	19.1%			13	31%	1	25%	
	> 15 years	18.0%			12	28%	2	50%	
Resident in area	Urban	60.9%	5	83.3%	28	65.1%	2	50%	.346
	Rural	29.3%			13	30.3%	2	50%	
	FATA	8.2%	1	16.7%	2	4.6%			
	Illiterate	48.1%	3	75%	6	31.57%	1	100	.705
	Matriculated	39.2%	1	25%	10	52.63%			
Parents education	Intermediate	1.3%							
	Bachelor	11.4%			3	15.77%			
	Worker	52.3%	4	100%	10	52.6%	1	100%	.514
Occupation	Government job	37.5%			7	37.8%			
	Private job	10.2%			2	10.5%			
Vaccination for HBV	yes	67.9%	1	25%	15	78.9%			.189
	No	28.2%	2	50%	4	21.1%	1	100%	
	Didn't know	3.8%	1	25%					
	Hepatitis B	15.4%	2	50%	3	15.78%			.364
	Hepatitis C	7.7%			1	5.2%			

(FATA: Federally Administrative Tribal Area, HBV: Hepatitis B Virus, HCV: Hepatitis C Virus)