PREVALENCE OF HEPATITIS C VIRUS (HCV) AMONG THALASSEMIA PATIENTS IN IBN-ALBALADY HOSPITAL

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Abstract

Background: thalassemia is one of most dangerous disease; it is an inherited impairment of hemoglobin production, in which there is partial or complete failure of the synthesis of globin chain.

Objective*:* the aim of this study is to determine the prevalence of Hepatitis C Virus (HCV) infection among thalassemic patients in Ibn-albalady hospital in Baghdad.

Patients and methods*:* The study was carried out on 111 transfusion dependent beta-thalassemia (74 males and 37 females) with a mean age 12.51 yrs attending to the Ibn – Alba lady Hospital, in Baghdad during the period March 2008 to September 2008. The control group was thirty – one (12 males and 19 females) with mean age of 11.5 yrs and investigated to serve as a control group; they were randomly selected from community. Blood sample was collected in morning for biochemical assays (hepatitis C virus (HCV), Glutamic Oxaloacetic (GOT),Glutamic Pyruvic Transaminase (GPT), Alkaline phosphates (ALP), Total serum bilirubin (TSB), Direct serum bilirubin(Dir.SB), Indirect serum bilirubin (Indir.SB).

Results*:* Out of 111 thalassemic patients there was 51 (46 %) sera was confirmed positive for anti-HCV- antibodies. The remaining 60 (54 %) were seronegative, while among 31 healthy controls only one (3.22%) was seropositive the result was statistically of a high significant difference (P=0.0001).Out of 51 seropositive, 13 (72.3%) patients were positive among those above 20 years, while only one (16.7) was positive among those from (0 – 4) years. It was found no significant correlation in (sex, TSB, Indir.SB, ALP) between patients with HCV+ve compared with HCV –ve. The current study demonstrated that there was a highly significant difference in (GPT, GOT, and Dir.SB) levels between patients with seropositive HCV and patients with seropositive HCV.

Conclusions*:* The main causes of liver injury in thalassemia are hepatitis C virus and the finding suggests that HCV is the main cause of abnormal liver function in patients with thalassemia.

Keywords*:* *Prevalence, Thalassemia, Hepatitis-C virus.*

Introductio

Thalassemias are a heterogeneous group of genetic disorders, which result from a reduced rate of synthesis of α or β-chain (1). In thalassemia, the imbalance of globin chain synthesis leads to red cell damage resulting in destruction of red cells in the marrow (ineffective erythropoiesis) and peripheral circulation (hemolysis) (2). There are two different chains of protein in the hemoglobin a molecule, α and β and either can be affected (3). Thus, thalassemia is divided into α-thalassemia, in which, the production of α-globin is deficient, and β-thalassemia, in which, the β-globin production is defective (4). The most common type is β-thalassemia (5) alpha thalassemia is the reduction or absence of alpha chain synthesis and common in South East Asia. There are two alpha gene loci on chromosome 16 (6), and therefore each individual carries four alpha globin gene, two from the paternal chromosome and two from maternal chromosome. This result in four possible genotypes, each resulting in different clinical syndrome (7). If one is deleted, the silent carriers of α–thalassemia in which there is no clinical effect is produced. If two are deleted the patient exhibit the feature of α- thalassemia trait in which there is a mild hypochromic anemia (8). β thalassemia is an autosomal recessive disorder characterized by reduced or absent β globin chain synthesis, which can be caused by one of 180 mutations in the gene coding for the β chain of hemoglobin tetramer (9). The beta globin gene located on chromosome 11 (10). Hepatitis C

virus (HCV) is a blood borne virus. Most epidemiological studies have focused on group at risk infection such as thalassemic patients through multiple blood transfusions. Moreover, HCV is now considered as the leading cause of post transfusion hepatitis world wide (11). The risk acquiring HCV infection as a result of transfusion was about 10% (12). Tt was found that the HCV is responsible for at least 90% of transfusion associated NANB (Non A Non B) hepatitis (13). Repeated blood transfusion in thalassemic patients is necessary for their survival; however, such transfusions increase the exposure not only to HCV but also other blood borne viruses (Hepatitis B virus (HBV), Hepatitis G virus (HGV), Human Immunodeficiency virus (HIV) (14). It was stated that the second commonest cause of death in thalassemic major patients over 15 years of age is liver disease, due to blood borne viral hepatitis (15). Interestingly, more studies addressed that patients, on long-term transfusion therapy, were at risk of experiencing HCV in a prevalence ranging from (12.2%–16%) (16). Furthermore, the infection with HCV may not induce immunity, in which they documented, that multiple distinct episodes of acute hepatitis were observed in individuals of poly transfused thalassemic patients and re infection with different strain (17).

Materials and Methods

The study was carried out on 111 transfusion dependent beta-thalassemia (74 males and 37 females) with a mean age 12.51 yrs attending to the Ibn – Albalady Hospital, in Baghdad. All patients selected randomly. The control group was thirty – one (12 males and 19 females) with mean age of 11.5 yrs were investigated to serve as a control group; they were randomly selected from community. Blood sample were collected in morning used for biochemical assays (anti HCV Ab, GOT,GPT,ALP,TSB, Dir.SB,Indir.SB). HCV was determined using the (bioelisa, spain). GOT and GPT was determined using the transaminases kit (Bio merieux Sa, France) and ALP was determined using the phosphates alkaline kit (Bio merieux Sa, Farnce). TSB, Dir.SB and Indir. SB was determined using kit (linear, Spain).

Data were analyzed using the computer facility - the available statistical packages of SPSS–11.5 (statistical packages for social sciences–version 11.5).Data was presented in simple measures of number, percentage, mean, SD, range (min-max). The significance of difference between quantitative variables was tested using student t-test for comparing between two means of independent groups. Chi-square test χ^2 was used to test the significance of the qualitative data. P value equal and less than 0.05 was used as the level of significance.

Results

Serum sample from 111 thalassemic patients was screened and confirmed for serum HCV antibodies. Out of 111 thalassemic patients there was 51 (46 %) sera was confirmed positive for anti- HCV- antibodies. The remaining 60 (54 %) were seronegative, while among 31 healthy controls only one (3.22%) was seropositive. The result was statistically a highly significant difference (P = 0.0001) as shown in Table (1).

The distribution of HCV seropositive according to age group shows that there was an increase in rate of infection with age of the patients. Out of 51 seropositive, 13 (72.3%) patients were positive among those above 20 years, while only one (16.7) was positive among those from (0 – 4) years. This result was statistically a highly significant difference (P = 0.01), as shown in Table (2).

Out of 51 affected patient, 37 (50.0%) were males and 14 (37.7%) were females, this result was statistically not significant, as shown in Table (2).

Our study has demonstrated a higher mean value of TSB in patients with HCV seropositive, but the results does not show a significant difference between patients with HCV seropositive and patients with HCV seronegative. A similar result was observed in fraction of indirect serum bilirubin. However, the fraction of direct serum bilirubin was statistically a highly significant difference, as it shown in Table (3).

The current study demonstrated that there was a highly significant difference in GPT

levels between patients with HCV seropositive and patients with HCV seronegative (P=0.002). Also, less significant difference in GOT and ALP level as it shown in Table (4).

Table (1)
Frequency of HCV seropositivity among patients and controls.

	HCV antibodies positive		HCV antibodies negative		Total
	No	%	No	%	
Patients	51	(46%)	60	(54%)	111
Controls	1	(3.22%)	30	(96.77%)	31
P <0.0001					

Table (2)
Distribution of HCV positive and HCV –ve among patient according age and sex.

Variable	Patient with HCV +ve		Patient with HCV -ve		P Value
	No	%	No	%	
Age (years)					
0-4 n=6	1	16.7 %	5	38.3 %	0.01
5-9 n=30	8	26.7 %	22	73.3 %	
10-14 n=46	22	47.8 %	24	52.5 %	
15-19 n=11	7	63.6 %	4	36.4 %	
≥20 n=18	13	72.3 %	5	27.7 %	
Total n=111	51	45.9 %	60	54.1 %	
Sex					
Male n=74	37	72.5 %	37	50.0 %	N.S
Female n=37	14	27.5 %	23	62.2 %	
Total n=111	51	45.9 %	60	54.1 %	

Table (3)
Serum bilirubin levels (µmol/l) between patient with HCV +ve compared with Table HCV –ve.

Variables	Patients with HCV +ve		Patient with HCV -ve		P Value
	Mean	±SD	Mean	±SD	
TSB	35.85	29.90	28.86	25.08	N.S
Dir.SB	9.484	5.233	5.296	5.036	0.0001
Indir.SB	26.11	26.23	23.57	21.14	N.S

Table (4)
Serum COT, GPT and ALP levels between patient with HCV+ve compared with HCV–ve.

Variables	Patients with HCV +ve		Patient with HCV -ve		P Value
	Mean	±SD	Mean	±SD	
GOT	79.92	25.58	67.92	30.90	0.02
GPT	50.65	23.03	36.82	23.21	0.002
ALP	136.0	59.43	133.5	45.5	N.S

Discussion

Surveys on thalassemic patients worldwide have found variable rates of anti- HCV antibody seroprevalence. Our study showed that the prevalence of HCV antibodies was higher among thalassemic patients (46%), and the statistical analysis shows a highly significant difference (P = 0.0001), this was nearly similar to another study done by EL-Nanway et. al, 1995 (18) who found that the prevalence of HCV in Egypt was 44%. However, another study done in Iraq in Najaf city by Majeed, 2002 (19) found that the prevalence of HCV in thalassemic children was 15%, this was probably due to the patients' age. Moreover, Iraqi thalassemic patients have demonstrated a higher rate compared with other countries such as in Jordan 40.7% (14), in Saudi Arabia 40% (11). It would be interesting to find out whether age and geographical differences could account for such variations. Notably, differences in sample size and the introduction of blood donor

screening with restricted policy in other countries may result in a lower prevalence than that reported in the current study. On the other hand, another study done by Chakravarti et.al, 2005 (20) who found that the prevalence of HCV infection was (60% and 63.8%) respectively. As well as another study done in Iraq by Al – Kubaisy et.al, 2003(21), who found that the seroprevalence of HCV antibodies among multi-transfused thalassemic patients was 67.2%. This may be related to large sample size conducted in study.

Our study demonstrated that there is a significant increase in rate of HCV infections with increasing age. This result is compatible with other study performed by Majeed, 2002 (19). The higher anti-HCV prevalence in older age groups may reflect the effect of increase exposures to HCV because increase blood transfusion during their life.

In our study, the anti-HCV antibodies were positive in 51(45.9%) patients; male cases were 37 (72.5%), females were 14 (27.5%). This may lead to high prevalence of HCV antibody in males, but the result was not significant. Probably because of younger age females included in this study exclude an additional need for blood transfusion in pregnancy and other related gynecological problems.

Our study had demonstrated a higher mean value of TSB, but there was no significant difference in TSB between patients with a positive HCV antibody and patients with HCV negative. A similar result was obtained about the indirect serum bilirubin. However, the direct bilirubin fraction showed statistically a high significant difference. These findings agreed with another study done by Chakravarti et.al, 2005 (20) who found that the bilirubin levels were not significantly altered in these patients. This findings were in contrast to other findings reported by Sarkis, (2000 (22) who stated that there was a higher mean value of total serum bilirubin and a highly significant difference between patients with HCV positive and patients with HCV seronegative.This was probably because the increase of direct serum bilirubin among hepatitis C positive patients is expected to be reflected as elevation of TSB as well but this can be masked by equal levels of unconjugated bilirubin in both groups.

Our result had demonstrated that the mean value of GPT, for example was (50.65±23.0 U/L) in HCV positive cases, compared to (36.82±23.21 U/L) in HCV negative cases, and the difference statistically was significant (P = 0.002). This was compatible with other studies Wanachiwanawin et.al, 2003 (23) which all reported that the patients with anti-HCV antibodies had significantly abnormal level of serum GPT compared with patients without anti-HCV antibodies. Shindo et. al, 1995 (24).

Found that anti-HCV positive patients who have elevated serum GPT level are more likely to have a significant liver disease than those who have normal serum GPT level. Serum GPT elevation in anti-HCV positive individuals suggests the presence of liver damage such as viral replication (25) and iron overload (26).Our results have also demonstrated that there was significant difference in GOT between patients with HCV seropositive and patients with HCV seronegative (P = 0.02). Similar results were reported by Al-Sheyyab et. al, 2001 (14) who found that patients with anti-HCV antibodies had significantly abnormal GOT compared to patients without anti-HCV antibodies (P=0.02). In addition, other results performed by Al – Hawsawi,2000 (11) who found that there was a highly significant difference in GOT level between thalassemic patients with HCV seropositive and patients with HCV seronegative. Our results demonstrated that there was not significant difference in ALP activity between patients with HCV seropositive and patients with HCV. This was compatible with other finding reported by Al-Hawsawi, 2000 (11). This was probably because ALP is expected to increase in obstructive jaundice rather than hepatocellular jaundice, which was expected in hepatitis C virus infection.

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الخلاصة

خلفية البحث:يعد مرض الثلاسيميا (مرض فقر الدم البحر المتوسط) واحدا من اكثر الامراض خطورة وهو عبارة عن خلل وراثي في انتاج الهيموغلوبين (خضاب الدم) اي فشل كلي او جزئي في انتاج سلاسل الكلوبين.

هدف البحث: هدف هذة الدراسة هو بيان مدى انتشار مرض التهاب الكبد لفايروسي C بين مرضى الثلاسيميا (مرض فقر الدم البحر الابيض المتوسط) في مستشفى ابن البلدي في بغداد.

المرضى وطريقة العمل: شملت الدراسة 111 مريض من نوع بيتا ثلاسيميا (74 ذكور و37 اناث) بمتوسط عمري 12.51 سنة من المرضى المراجعين لمستشفى ابن البلدي في بغداد للفترة من اذار 2008 الى تشرين الثاني 2008.مجموعة السيطرة كانت 31 شخص(12 ذكور و 19 اناث) الذين يبدون اصحاء حيث تم اختيارهم بصورة عشوائية من المجتمع بمعدل عمري 11.5 سنة.جمعت عينات الدم في الصباح حيث تم استخدامها في قياس المتغيرات الحياتية (التهاب الكبد الفايروسيHCV ،انزيمات الكبد **GOT, GPT, ALP** ووضائف الكبد **(TSB, Dir.SB, Indir.SB)**.

النتائج: اضهرت هذةالدراسة (% 46) 51 من 111 مريض كان لديهم كشف موجب لالتهاب الكبد الفايروسيC.والمصول المتبقية لعينات المصابين (% 54) 60 كان لديهم كشف سالب لالتهاب الكبد الفايروسي C .اما عينات السيطرة فاظهرت نتائج التحاليل عدم اصابتهم بالتهاب الكبد الفايروسي C عدا عينة واحدة (3.22%) التي اضهرت نتيجة موجبة لالتهاب الكبد الفايروسي C .النتائج الاحصائية بين مرضى الثلاسيميا ومجموعة السيطرة اضهرت وجود فرق معنوي جدا على مستوى P = 0.0001 .(72.3%) 13 مصابا من مجموع 51 كانوا من الفئة العمرية الاكثر من عشرين سنة بينما كانت عينة واحدة مصابة(16.7) كانت ضمن الفئة العمرية (4 – 0) سنوات. كما اضهرت الدراسة عدم وجود علاقة معنوية بالنسبة الى (**TSB, Indir.SB, ALP sex**) بين المرضى المصابين والغير مصابين بالتهاب الكبد الفايروسي C.كذلك اضهرت الدراسة وجود علاقة معنوية عالية في (**GPT, GOT, and Dir.SB**) بين المرضى المصابين والغير مصابين بالتهاب الكبد الفايروسيC.

الاستنتاجات: السبب الرئيسي لاضرار الكبد في مرضى الثلاسيميا (فقر الدم البحر المتوسط) هو التهاب الكبد الفايروسيC كذلك اقترحت الدراسة ان التهاب الكبد الفايروسي **C** هو المسبب الرئيسي لوظائف الكبد الغير طبيعية لدى المرضى.