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Hepatitis C Virus In Children In Beni –Suef Governorate

Abdel Megeed Aboul Magd Abdel Megeed [a], *Mahmoud Mohamed Hodeeb* [b] *and Fatma El Zahraa Saad Ahmed* [b]

[a] Pediatrics department, Faculty Of Medicine,Beni- Suef University.

[b] Pediatrics department, Faculty Of Medicine,Beni- Suef University.

Abstract:

The aim of this study is to study HCV infection in children in beni-suef governorate and to detect epidemiology and risk factors in studied group. HCV antibodies by4th generation ELISA. , alanine aminotransferase (ALT) levels and aspartate transaminase(AST) were done for children at the age of 6-17years . Every child with positive HCV antibodies was tested for HCV RNA by PCR. We studied 47 children positive for HCVantibody . 41 of them were HCV RNA positive and 6 of them had negative HCV RNA.Blood transfusion,frequent iv injection,hospitalization,previous operation,family history of HCV infection,circumcision and ear piercing are significant risk factors for infection.Pallor,jaundice and abdominal distention are common symptoms among HcvAb positive childrens. 100% of negative cases in HCV.Ab analysis were the same in PCR analysis in contrast from positive cases where 87% of positive cases in PCR agreed with HCV.Ab analysis but 13% of cases were negatively infected with HCV.ALT and AST were significantly higher in positive cases with HCVAb and PCR as compared to negative cases

Keywords: Hepatitis C,Interferon, Children.

1. Introduction

Hepatitis C virus (HCV) infection is a major medical challenge affecting around 200 million people worldwide. The main site of HCV replication is the hepatocytes. The incubation period for HCV infection ranges from as low as two weeks to as high as six months[1].

Hepatitis C virus is a member of the flaviviridae family of RNA-containing viruses. The primary immune response to hepatitis C virus is mounted by cytotoxic T lymphocytes. Unfortunately, this process fails to eradicate infection in most people[2]. Blood transfusion, Direct percutaneous

exposure are the primary means of transmission. Hemodialysis is apossible cause of hepatitis C virus infection.Currently, the use of injected drugs is the most important epidemiologic risk factor,probably accounting for around 50% of both acute and chronic infection[3]. Other parenteral routes may be involved. Vertical transmission may occur. Perinatal transmission is possible and affects an estimated 5% of babies born to mothers with infection[4].

More than three quarters of the affected children are symptomless. Early diagnosis primarily relies on identifying the risk factors of transmission because infected individuals typically have few or no symptoms[5].

In children over 2 years of age HCV is diagnosed by testing similar to that used in adults. If a child or adolescent is suspected of having HCV, intial testing is to screen for antibodies made by the body against HCV[6]. Worldwide the prevalence of hepatitis c virus infection in pregnant women and children has been estimated to be 1-8% and 0.05 -5% respectively. The vertical transmission rate has been estimated to be 3-5% and there is a high rate of spontaneous clearance (25-50%) in the children [7].

The prevalence of HCV was higher among children treated for malignancy, those with renal failure requiring hemodialysis and those who had undergone surgical procedure . Nowadays , vertical transmission from mother to the child is the main route of acquistition of HCV in childhood[8].

IFN-free treatment option is yet available for children younger than 12 years infected with HCV. There is uncertainty about how to manage these children . In the past ,most of the children who received the therapy were treated independently of the stage of HCV – related liver damage in order to cure the infection and prevent the unpredictable progression of the disease[9]. The aim of this study is to study HCV infection in children in beni-suef governorate and to detect epidemiology and risk factors in sudied group.

2. Patient and methods:

We will conduct cross sectional study on children for hepatitis C the study will include 47 children.

2.1 Inclusion criteria:

children aged(6-17) years.-

2.2 Exculsion criteria:

Infant and children below 6 years or above 17 years.- Transfusion dependent children. –

- Children on hemodialysis.

All children will be subjected to:

1- History taking to fulfill the following data:

- Demographic Data, age, sex, residence, socioeconomic standard.
- History of blood transfusion, previous operation, frequent iv injection, hospitalization, dialysis and insulin injection.

- Familay history of HCV.
- History of circumcision and ear piercing.

2- thoroug physical Examination :

- the presence or absence of jaundice
- Abdominal Examination with assessment of liver and splenic size.

3- Lab investigations:

After explaining the procedure to the patients, five cc of venous blood was collected from each patient using a sterile plastic syringe. The blood samples were allowed to clot at room temperature for 30 minutes and then centrifuged for 10 minutes. Sera were separated, alliquoted and stored at –20° C until used in:

a- Liver enzymes (ALT, AST).

b- Testing for HCV antibodies (IgG) using the 4th generation ELISA.

c- HCV RNA by PCR for ELISA +ve patient.

4- Abdominal Ultrasonography:

5- Data analysis:

Data will be statistically described in term of mean and standard deviation , frequencies and relative frequencies (%) . Also the study will be statistically analysed by using tests as t-test for comparison between each group and parametric data , chi –square test will be used acorrelation is asingle number that describes the degree of relationship between two variabies .The most common type ,called the person correlation .approbability (p-value <0.05) will be considered statistically significant,statistically package for social science(SPSS) software will be used.

Statistical methodology:

All data were expressed as count and percent (%) for qualitative variables and mean ± S.E.M (standard error of mean) for quantitative variables. All statistical procedures were done using Statistical Package for Social Sciences (SPSS) computer software (version 24). Chi square test or ficher exact test (forclls have expected count less than 5)were used to test significance and association between different qualitative variables and HCV.Ab followed by Bonferoni post hoc analysis for multi-levels qualitative variables. Independent t test was used to test significant effect of different 2-levels variables on quantitative variables; AST and ALT while one way anova followed by Tukey'sposthoc analysis for pairwise comparisons was used to test significant effect of different multi-levels variables on quantitative variables; AST and ALT. Wilson-Brown method was used for calculating sensitivity, specificity, positive predictive value and negative predictive value from obtained cross tab tables of chi square test between HCV.Ab and rPCR. Statistical significance is set at $P<0.05$. Power of sample size was estimated from association of AST and ALT with HCV.Ab and PCR using gpower software version 3.1.9.2 where power was more than 80% (99.9-100%).

3. Results:

We studied 47 children positive HCV antibody, 41 of them were HCV RNA positive and 6 of them had negative HCV RNA.Blood transfusion,frequent iv injection,hospitalization,previous operation,family history of HCV infection,circumcision and ear piercing are significant risk factors for infection.Pallor,jaundice and abdominal distention are common symptoms among HcvAb positive childrens. 100% of negative cases in HCV.Ab analysis were the same in PCR analysis in contrast from positive cases where 87% of positive cases in PCR agreed with HCV.Ab analysis but 13% of cases were negatively infected with HCV.ALT and AST were significantly higher in positive cases with HCVAb and PCR as compared to negative cases.

Table (1) :Association between demographic risk factors and HCVAb in our studied cases.

Demographic risk factors			HCV.Ab		X^2	Sig.
			Positive	Total		
Age	=<12 y	Count	29	47	0.005	S
		%	61.7%	100.0%		
	>12 y	Count	18	47		
		%	38.2%	100.0%		
Gender	Male	Count	29	47	4.643	S
		%	61.7%	100.0%		
	Female	Count	18	47		
		%	38.2%	100.0%		
Residence	Rural	Count	31	47	5.023	S
		%	65.9%	100.0%		
	Urban	Count	16	47		
		%	34%	100.0%		
Social class	High	Count	0^s	0	17.00	S
		%	0.0%	100.0%		
	Middle	Count	18^s	47		
		%	38.2%	100.0%		
	Low	Count	29^s	47		
		%	61.7%	100.0%		

Data were expressed as count and % for 47 cases.

Results are illustrated in table (1).

Regarding Age, there was significant association between age and HCVAb. 2 groups of children did differ significantly from each other where 61.7% of children <12 years old showed significant positive HCV Ab as compared to children >12 years old where only 38.2% showed positive HCV Ab.

Regarding gender, there was a significant association between sex and HCVAb, where 61.7% of males showed significant positive HCVAb as compared to females where only 38.2% showed positive HCVAb.

Regarding residence, there was a significant association between residence and HCVAb, where 65.9% of rural individuals showed significant positive cases with HCVAb as compared to urban individuals where only 34% showed positive HCVAb.

Regarding social class, there was a significant association between social class and HCVAb, where high social individuals significantly did not show any positive cases with HCVAb (0%) as compared to low social individuals who showed significant positive HCVAb (61.7%) and middle social individuals where 38.2% showed positive HCVAb. As described, the higher positive cases were shown in low social individuals while lower positive cases were shown in higher social individuals.

Table (2) :Association between clinical risk factors and HCVAb in our studied cases.

Clinical risk factors			HCV.Ab			X^2	Sig.
				Positive	Total		
Blood transfusion	**No**	Count		31	47	157.192	S
		%		65.9%	100.0%		
	Yes	Count		16	47		
				34%	100.0%		
Family history	**No**	Count		35	47	102.413	S
		%		74.4%	100.0%		
	Yes	Count		12	47		
		%		25.5%	100.0%		
Frequent iv injection	**No**	Count		41	47	22.624	S
		%		87.2%	100.0%		
	Yes	Count		6	47		
		%		12.7%	100.0%		
Previous operation	**No**	Count		24	47	220.910	S
		%		51%	100.0%		
	Yes	Count		23	47		
		%		48.9%	100.0%		

Hospitalization	**No**	Count		13	47	339.931	S
		%		27.6%	100.0%		
	Yes	Count		34	47		
		%		72.3%	100.0%		
Circumcission	**No**	Count		18	47	4.706	S
		%		38.2%	100.0%		
	Yes	Count		29	47		
		%		61.7%	100.0%		
Ear piercing	**No**	Count		29	47	4.643	S
		%		61.7%	100.0%		
	Yes	Count		18	47		
		%		38.2%	100.0%		

Data were expressed as count and % for 47cases.

Results are illustrated in table (2).

Regarding blood transfusion, there was a significant association between blood transfusion and HCVAb, where 34% of cases that received blood transfusion showed significant positive HCV.Ab as compared to cases that did not receive blood transfusionwhere 65.9% of cases showed positive HCVAb.

Regarding family history, there was a significant association between family history and HCVAb, where 25.5% of cases that had family history of HCV showed significant positive HCV.Ab as compared to cases that had not family history of HCV where 74.4% of cases showed positive HCVAb.

Regarding frequent iv injection, there was a significant association between frequent iv injection and HCVAb, where 12.7%% of cases that received frequent i.vinjection showed significant positive HCV.Ab as compared to cases that did not receive frequent i.v. injection where 87.2% of cases showed positive HCVAb.

Regarding previous operation, there was a significant association between previous operation and HCVAb, where 48.9% of cases that received previous operation showed significant positive HCVAb as compared to cases that did not receive previous operation where 51% of cases showed positive HCVAb.

Regarding hospitalization, there was a significant association between hospitalization and HCVAb, where 72.3% of cases that had previous hospitalization showed significant positive HCV.Ab as compared to cases that had not previous

hospitalization where 27.6% of cases showed positive HCV.Ab.

Regarding circumcision, there was a significant association between circumcision and HCVAb, where 61.7% of cases that had previous circumcision showed significant positive HCV.Ab as compared to cases that had not previous circumcision where 38.2% of cases showed positive HCVAb.

Regarding ear piercing, there was a significant association between ear piercing and HCVAb, where 38.2% of cases that had previous ear piercing showed significant positive HCVAb as compared to cases that had not previous ear piercing where 61.7% of cases showed positive HCV.Ab which is an interesting result.

Table (3) : Effect of demographic and clinical risk factors in addition to symptoms on ALT

Type of factor	Factor		Mean±S.E.M	T.value or F.value	P.value	Sig.
Demographic risk factors	Age	=<12y	24.57±0.57	1.69	0.092	NS
		>12y	26.80±1.19			
	Gender	Male	25.85±0.91	0.710	0.478	NS
		Female	25.04±0.71			
	Residence	Rural	26.27±0.87	1.505	0.133	NS
		Urban	24.56±0.74			
	Social class	High	22.68±0.51	3.490	0.031	S
		Middle	25.10±0.79			
		Low	27.07±1.17[a]			
Clinical risk factors	Blood transfusion	No	24.45±0.46	3.07	0.004	S
		Yes	55.68±10.15			
	Family history	No	25.13±0.56	3.11	0.002	S
		Yes	36.23±6.27			
	Frequent iv injection	No	24.67±0.46	2.27	0.033	S
		Yes	55.63±13.63			
	Previous operation	No	23.83±0.39	4.25	<0.001	S
		Yes	58.35±8.11			
	Hospitalization	No	23.36±0.32	4.84	<0.001	S
		Yes	54.11±6.35			
	Circumcision	No	25.04±0.71	0.715	0.474	NS
		Yes	25.85±0.92			
	Ear piercing	No	25.85±0.92	0.710	0.478	NS
		Yes	25.04±0.72			

	Dialysis	**No**	25.41±0.57	0.354	0.723	NS
		Yes	19.00±0.00			
	Insulin injection	**No**	25.42±0.57	0.355	0.723	NS
		Yes	19.00±0.00			
Symptoms	**Jaundice**	**No**	23.79±0.32	9.86	<0.001	S
		Yes	148.54±12.65			
	Abdominal distension	**No**	23.59±0.29	7.67	<0.001	S
		Yes	131.18±14.02			
	Haematemsis	**No**	25.34±0.57	4.05	<0.001	S
		Yes	98.00±0.00			
	Dark urine	**No**	25.42±0.57	0.355	0.723	NS
		Yes	19.00±0.00			
	Rash	**No**	25.42±0.57	0.355	0.723	NS
		Yes	19.00±0.00			
	Arthritis	**No**	25.42±0.57	0.355	0.723	NS
		Yes	19.00±0.00			
	Pallor	**No**	23.93±0.37	5.394	<0.001	S
		Yes	110.71±16.08			
	History of DM	**No**	25.42±0.57	0.355	0.723	NS
		Yes	19.00±0.00			
	Haemophilia	**No**	25.42±0.57	0.355	0.723	NS
		Yes	19.00±0.00			
	Renal	**No**	25.16±0.54	1.511	0.270	NS
		Yes	109.33±55.72			
	Hepatomegaly	**No**	23.30±0.25	7.463	<0.001	S
		Yes	115.39±12.34			
	Splenomegaly	**No**	23.92±0.33	7.667	<0.001	`S
		Yes	148.17±16.20			

Data were expressed as Mean±SEM for 47 cases in all parameters. S: means significant.Significance is set at P<0.05.

Results are illustrated in table (3).

Regarding demographic risk factors, all factors had not any significant effect on ALT except for social class that had a significant effect on ALT where lower social class significantly increased ALT as compared to higher level.

Regarding clinical risk factors, blood transfusion, family history, frequent iv

injection, previous operation and hospitalization significantly increased ALT while other factors did not show any significant effect on ALT.

Regarding symptoms, jaundice, abdominal distension, hematemesis, pallor, hepatomegaly and splenomegaly were significantly associated with high ALT levels while other symptoms did not show any significant association with ALT levels.

In addition, ALT was significantly higher in positive cases with HCV.Ab and PCR as compared to negative cases

Table (4) : Effect of demographic and clinical risk factors in addition to symptoms on AST

Type of factor	Factor		Mean±S.E.M	T.value or F.value	P.value	Sig.
Demographic risk factors	Age	=<12y	23.39±0.37	3.401	0.001	S
		>12y	26.26±0.90			
	Gender	Male	25.32±0.66	1.921	0.055	NS
		Female	23.74±0.51			
	Residence	Rural	24.93±0.64	1.115	0.265	NS
		Urban	24.02±0.51			
	Social class	High	22.77±0.52	2.257	0.105	NS
		Middle	24.40±0.56			
		Low	25.35±0.83			
Clinical risk factors	Blood transfusion	No	23.82±0.34	9.103	<0.001	S
		Yes	44.58±7.31			
	Family history	No	24.35±0.40	1.955	0.051	NS
		Yes	29.38±4.66			
	Frequent iv injection	No	24.10±0.37	5.878	<0.001	S
		Yes	39.63±8.05			
	Previous operation	No	23.43±0.28	12.502	<0.001	S
		Yes	46.24±5.94			
	Hospitalization	No	23.20±0.26	12.396	<0.001	S
		Yes	42.18±4.42			
	Circumcision	No	23.70±0.51	2.046	0.998	NS
		Yes	25.38±0.66			
	Ear piercing	No	25.32±0.66	1.921	0.998	NS
		Yes	23.74±0.51			
	Dialysis	No	24.48±0.41	0.498	0.619	NS

		Yes	18.00±0.00			
	Insulin injection	**No**	24.48±0.41	0.498	0.618	NS
		Yes	18.00±0.00			
Symptoms	**Jaundice**	**No**	23.35±0.25	36.537	<0.001	S
		Yes	110.08±8.28			
	Abdominal distension	**No**	23.26±0.24	32.28	<0.001	S
		Yes	95.06±10.04			
	Haematemsis	**No**	24.43±0.41	3.525	<0.001	S
		Yes	70.00±0.00			
	Dark urine	**No**	24.48±0.41	0.498	0.618	NS
		Yes	18.00±0.00			
	Rash	**No**	24.48±0.41	0.498	0.618	NS
		Yes	18.00±0.00			
	Arthritis	**No**	24.48±0.41	0.498	0.618	NS
		Yes	18.00±0.00			
	Pallor	**No**	23.52±0.30	21.466	<0.001	S
		Yes	80.00±10.42			
	History of DM	**No**	24.48±0.41	0.498	0.618	NS
		Yes	18.00±0.00			
	Haemophilia	**No**	24.48±0.41	0.498	0.618	NS
		Yes	18.00±0.00			
	Renal	**No**	24.30±0.39	1.491	0.274	NS
		Yes	83.00±39.37			
	Hepatomegaly	**No**	23.06±0.22	31.936	<0.001	S
		Yes	84.65±8.65			
	Splenomegaly	**No**	23.46±0.26	31.741	<0.001	`S
		Yes	108.00±11.27			

Data were expressed as Mean±SEM for 47 cases in all parameters S: means significant.Significance is set at P<0.05.

Results are illustrated in table (4).

Regarding demographic risk factors, all factors had not any significant effect on ALT except for age that had a significant effect on AST where >12yhad significantly higherAST as compared to lower age.

Regarding clinical risk factors, blood transfusion, frequent iv injection, previous operation and hospitalization significantly increased AST while other factors did not show any significant effect on ALT.

Regarding symptoms, jaundice, abdominal distension, hematemesis, pallor, hepatomegaly and splenomegaly were significantly associated with high AST levels while other symptoms did not show any significant association with AST levels.

In addition, AST was significantly higher in positive cases with HCV.Ab and PCR as compared to negative cases.

4. Discussion:

Hepatitis C virus (HCV) infection remains a major public health burden, with an estimated worldwide prevalence of 2.5% of the population (177.5 million infected adults); this ranges from 1.3% in the Americas to 2.9% in Africa[10].

Hepatitis C Virus (HCV) infection is a major global health challenge; it is estimated that more than 80 million people are chronically infected worldwide, with 3–4 million new infections and 350 000 deaths occurring each year because of HCV-related complications[11]**.**

Although the prevalence of chronic HCV is lower in children than adults, an estimated 5 million children worldwide have active HCV infection [11]**.**

Data from the National Health and Nutrition Examination Survey (NHANES) indicate that 0.2% of 6- to 11-year-olds (31,000 children) and 0.4% of 12- to 19-year-olds (101,000 adolescents) in the US are HCV antibody positive [12].

This study was conducted on 47 children in beni-suef governorate.

In our study, we found that there was a significant association between sex and HCV, where 61.7% of males showed significant positive HCVAb as compared to females where 38.2% showed positive HCVAb.

Similar to our study, the study of[13] found that although a higher proportion of study subjects were female than male, more males than females were positive for HCV. The higher prevalence of infection with the hepatitis viruses among males is thought to be related to the higher clearance rate of this virus by females compared with males and the study of [14]found that male blood donors had a higher prevalence than their female counterparts in anumber of studies which conducted among blood donors.

In our study, we found that there was a significant association between residence and HCV, where 65.9% of rural individuals showed significant positive cases with HCV.Ab as compared to urban individuals where 34% showed positive HCV.Ab,

Similar to our study ,the study of[15] found in a number of studies conducted among blood donors. Blood donors from rural areas had a higher prevalence than those from urban areas and the study of[16] found that unhygienic practices, common in rural communities in the northern part of the state, are thought to be responsible for the high HCV prevalence in that region.

In our study, we found that there was a significant association between blood transfusion and HCV, where 34% of cases that received blood transfusion showed significant positive HCV.Ab as compared to cases that did not receive blood transfusion where 65.9% of cases showed positive HCVAb. The study of[17] found that blood transfusion is not reported in more than 20% individuals, but about 70% have infection without identified risk factor in subjects under 19 years of age . In our study ,there was significant association between, circumcision and HCV where 38.2% of cases that had previous circumcision showed significant positive HCV.Ab as compared to cases that had not previous circumcision where 61.7% of cases showed positive HCVAb. Similar to our study, The study of [18] found that circumcision is associated with HCV infection. The study of [17] found that male circumcision is not reported in more than 20% individuals, but about 70% have HCV infection without identified risk factor in subjects under 19 years of age. In contrast to our study, The study of [19] reported that no statistically significant difference in risk factors could be found among HCV antibody positive and negative children and The study of [20] have previously reported that risk factors for HCV infection were mostly obscure among Nigerian patients.

In our study, there was a significant association between family history and HCV, where 25.5% of cases that had family history of HCV showed significant positive HCV.Ab as compared to cases that had not family history of HCV where 74.4% of cases showed positive HCVAb.

Similar to our study, The study of [21] suggested intrafamilial transmission though the exact exposures responsible are not clear. In contrast to our study, The study of[17] found that living in a house with infected family member is not reported in more than 20% individuals, but about 70% have infection without identified risk factor in subjects under 19 years of age. The study of [22]found that the prevalence was 5.7% in a study of family contacts of index patients. In our study, there was a significant association between frequent i.v. injection and HCV, where 12.7% of cases that received frequent i.v. injection showed significant positive HCV.Ab as compared to cases that did not receive frequent i.v. injection where 87.2% of cases showed positive HCV.Ab. Similar to our study, The study of [18]found that injections were associated with HCV infection.

The study of [23]found that the prevalence of injecting drug use in Egypt is estimated to be 0.21%.

The study of[24] found that injecting drug use may explain at most only about 1% of the national HCV prevalence in Egypt Considering that HCV prevalence in the population is 14.7%. In our study, there was a significant association between hospitalization and HCVAb, where 72.3% of cases that had previous hospitalization showed significant positive HCVAb as compared to cases that had not previous hospitalization where 27.6% of cases showed positive HCV.Ab. Similar to our study, The study of[25]found that among children, incident infection was associated with hospitalization.

In our study,There was a significant association between HCV.Ab and PCR, where 100% of negative cases in HCV.Ab analysis were the same in PCR analysis in contrast from positive cases where 87% of positive cases in PCR agreed with HCV.Ab analysis but 13% of cases were negatively infected with HCV although they were considered positively infected using HCV.Ab analysis.To clarify this result, Wilson-Brown method was used to calculate sensitivity (89.3%), specificity (100%), positive predictive value (100%) and negative predictive value (87%) between HCV.Ab and PCR technique. The study of[24]found that RNA prevalence was high across studies in the different population groups. Higher RNA prevalence was observed among studies conducted among high risk groups and special clinical populations compared to the general population and indirect or intermediate risk groups. Overall, the average RNA prevalence among those HCV-antibody positive was approximately 60%.

5. Conclusion and recommendations:

- HCV infection more common in males than females,rural than urban and in low social class individuals than high.
- Blood transfusion, hospitalization, frequent iv injection,family history of HCV infection,circumcision and ear piercing are risk factors for infection.
- HCV positive cases had jaundice, abdominal distention, pallor, hepatomegaly andsplenomegaly.
- ALT and AST were significantly higher in positive cases with HCVAb and PCR as compared to negative.
- Blood donor screening protocol and effective screening techniques are likely to be needed to prevent speared of HCV infection among children.

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