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**Original Article** 

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## Prevalence and Risk Factors of Hepatitis C Virus Infection among Highrisk Egyptian Children

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#### ABSTRACT

- **Background:** Hepatitis C virus [HCV] infection is a global health problem. Children with certain risk factors are at high risk of infection.
- **Objective:** The present study aimed to evaluate the prevalence of HCV among high-risk Egyptian children.
- **Methods:** The study included 1357 children aged 3-15 years with risk factors of HCV including receiving blood products, hemodialysis, previous surgical intervention, insulin therapy and positive family history. They were subjected to careful history taking, thorough clinical examination and routine laboratory investigations. All children were tested for HCV antibodies using commercial 4th generation enzyme-linked immunosorbent assay [ELISA] kits. Those with positive results were further assessed using polymerase chain reaction [PCR].
- **Results:** Among the studied patients, there were 89 children [6.6 %] with positive HCV Ab and 73 children [5.4 %] with positive PCR test for HCV. Using multivariate logistic regression, significant predictors of HCV infection in the studied children were blood transfusion [OR: 1.23, CI: 0.019-13.4], Intravenous [IV] injection [OR: 10.962, CI: 1.937-62.026] and previous operation [OR: 3.12, CI: 1.046-31.6].
- **Conclusion:** HCV infection is highly prevalent among high-risk children. Blood transfusion, IV injection and exposure to surgery are independent risk factors for infection in this population.

Keywords: Hepatitis C infection; Perinatal transmission; Hepatitis screening

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Main subject and any subcategories have been classified according to the research topic

#### INTRODUCTION

Hepatitis C virus [HCV] infection is a major medical challenge affecting around 200 million people worldwide including ~11 million children <sup>[1]</sup>. HCV is a member of the Flaviviridae family of RNA-containing viruses. The primary immune response to HCV is mounted by cytotoxic T lymphocytes. Unfortunately, this process fails to eradicate infection in most people <sup>[2]</sup>.

Unfortunately, in contrast to older people, the published estimates of HCV burden among children are misleading due to lack of universal screening <sup>[3]</sup>. Perinatal transmission can also affect an estimated 5% of babies born to mothers with HCV infection <sup>[4]</sup>. Children exposed to blood transfusion or hemodialysis are at high risk of HCV infection. Use of injected drugs is another important epidemiologic risk factor <sup>[5]</sup>. It is noted that the prevalence of HCV is higher among children treated for malignancy and those who had undergone surgical procedures <sup>[6]</sup>.

More than three quarters of the children are symptomless and cirrhosis and hepatocellular carcinoma are rare <sup>[7]</sup>. Spontaneous viral clearance can commonly occur in young children but its rate declines as age advances <sup>[8]</sup>. If a child or adolescent is suspected of having HCV, initial testing is to screen with antibodies made by the body against HCV <sup>[9]</sup>. In all children, use of direct acting antivirals in now recommended. Treatment protocol depends on child age and HCV genotype with the aim of complete viral clearance <sup>[10, 11]</sup>.

#### AIM OF THE WORK

The present study aimed to establish a risk-based selective screening of hepatitis C in children in Beni-Suef Governorate in Egypt.

#### PATIENTS AND METHODS

This cross-sectional study was conducted at Pediatric Departments of the University Faculty of Medicine and the General Hospitals in Beni-Suef during the period from June, 2018 through February, 2020. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki [6<sup>th</sup> revision, 2008] reflected in a priori approval by the institution's human research committee. Informed consent was obtained from the legal guardians of all participants. The sample size was calculated using G Power 3.1 [Kiel University, Germany]. Using  $\alpha$  error probability of 0.05 and study power of 95 %, the minimum required sample size is 806 considering the reported prevalence of HCV among similar population in a previous study [5.8 %].

The study recruited all children aged 3-15 years with risk factors of HCV including receiving blood products, hemodialysis, previous surgical intervention, insulin therapy and positive family history. Children were excluded if they had history of liver disease.

The study included 1357 children. They were subjected to careful history taking, thorough clinical examination. All children were tested for HCV antibodies using commercial 4<sup>th</sup> generation ELISA kits [OraSure Technologies Inc., Bethlehem, USA]. Those with positive results were further assessed using polymerase chain reaction [PCR]. All children with positive HCV on PCR examination were genotype 4. Children with HCV were treated using oral sofosbuvir 400 mg / ledipasvir 90 mg combination for three months. All treated children achieved sustained virologic response.

#### Statistical analysis

Data obtained from the present study were presented as mean and standard deviation [SD] or number and percent. Comparison between categorical variables was achieved using chi-square test while numerical variables were compared using student t test. Logistic regression was used to identify predictors of binary outcome. Variable were selected to be included in regression models on the basis of previous studies and clinical judgment. Variable that were significant in univariate analysis were advanced to multivariate analysis. P value less than 0.05 was considered statistically significant. All statistical calculations were processed using SPSS, 25 [IBM, Chicago, USA].

#### RESULTS

The present study was conducted on 1357 children with risk factors for HCV. They had and age of  $7.2 \pm 3.6$  years and comprised 785 females [57.8 %] and 572 males [42.2 %]. Among the studied patients, there were 89 children [6.6 %] with positive HCV Ab and 73 children [5.4 %] with positive PCR test for HCV [Table 1].

Comparison between children with HCV and children without according to PCR results is shown in [Table 2]. Factors associated with positive HCV results included blood transfusion, IV injection, previous surgery, previous hospitalization and dialysis.

Using multivariate logistic regression, significant predictors of HCV infection in the studied children were blood transfusion [OR: 1.23, CI: 0.019-13.4], IV injection [OR: 10.962, CI: 1.937-62.026] and previous operation [OR: 3.12, CI: 1.046-31.6] [Table 3].

Table [1]: Clinical data of the studied children [1357]					
	All children	HCV +ve	HCV-ve n=1284	P value	
	N=1357	n=73			
Age [years] mean ± SD	7.2 ± 3.6	6.9 ± 3.5	7.3 ± 2.7	0.2	
Sex n [%]					
Female	785 [57.8]	41 [56.2]	744 [58.0]	0.85	
Male	572 [42.2]	32 [43.8]	540 [42.0]		
Socioeconomic class n [%]					
Low	5 [0.4]	-	5 [0.4]	0.82	
Moderate	1350 [99.5]	73 [100.0]	1277 [99.4]		
High	2 [0.1]	-	2 [0.2]		
Residence					
Rural	1252 [92.3]	68 [93.2]	1184 [92.2]	0.77	
Urban	105 [7.7]	5 [6.8]	100 [7.8]		
Reported risk factors n [%]					
Blood transfusion	385 [28.4]	49 [67.1]	336 [29.9]	<0.001	
Family history	96 [7.1]	6 [8.2]	90 [7.0]	0.7	
Injections	906 [66.8]	73 [100.0]	833 [64.9]	<0.001	
Previous operation	113 [8.3]	15 [20.5]	98 [7.6]	<0.001	
Hospitalization	906 [66.8]	73 [100.0]	833 [64.8]	<0.001	
Circumcision	572 [42.2]	32 [43.8]	540 [42]	0.79	
Ear piercing	767 [56.5]	25 [34.2]	742 [57.8]	0.55	
Dialysis	16 [1.2]	16 [21.9]	-	<0.001	
Insulin injection	30 [2.2]	3 [4.1]	27 [2.1]	0.26	

Table [2]: Comparison between children with HCV and children without regarding the basic data

	HCV +ve	HCV –ve	P value
	n=73	n=1284	
Age [years] mean ± SD	$6.9 \pm 3.5$	$7.3 \pm 2.7$	0.2
Sex n [%]			
Female	41[56.2]	744 [58.0]	0.85
Male	32 [43.8]	540 [42.0]	
Socioeconomic class n [%]			
Low	-	5 [0.4]	0.82
Moderate	73 [100.0]	1277 [99.4]	
High	-	2 [0.2]	
Residence n [%]			
Rural	68 [93.2]	1184 [92.2]	0.77
Urban	5 [6.8]	100 [7.8]	
Reported risk factors n [%]			
Blood transfusion	49 [67.1]	385 [29.9]	<0.001
Family history	6 [8.2]	90 [7.0]	0.7
Injection	73 [100.0]	833 [64.9]	<0.001
Previous operation	15 [20.5]	98 [7.6]	<0.001
Hospitalization	73 [100.0]	833 [64.8]	<0.001
Circumcision	32 [43.8]	540 [42]	0.79
Ear piercing	25 [34.2]	742 [57.8]	0.55
Dialysis	16 [21.9]	-	<0.001
Insulin injection	3 [4.1]	27 [2.1]	0.26

IJMA 2021; 3 [4] October-December: 1792-1796 Hodeib M, et al. Table [3]: Logistic regression analysis for predictors of HCV 95% CI P-value OR Upper Lower 1.23 **Blood transfusion** < 0.001 0.019 13.4 Positive Family History 0.914 1.084 0.252 4.650 0.007 10.962 1.937 62.026 Injection **Previous operation** < 0.001 3.121 1.046 31.60 Hospitalization 0.992 0.000 0.000 Circumcision 0.446 0.529 0.103 2.715 Ear piercing 0.326 0.426 0.078 2.337 0.000 Dialysis 0.998 0.000 -Insulin injection 2.825 0.299 0.310 0.034

#### DISCUSSION

Hepatitis C is an important health challenge worldwide. Egypt is the most affected country with hepatitis C. The estimated sero-prevalence of hepatitis C in Egypt was 14.7% in 2009 and 10% in 2015. Egypt has recently developed a national strategy for prevention, diagnosis, and treatment of hepatitis C with the goal of achieving a national chronic infection prevalence of less than 2% by 2025 <sup>[12]</sup>. The prevalence of hepatitis C among Egyptian children is in general lower than that of the general population. As of 2015 estimates, the seroprevalence of hepatitis C in Egyptian children 1-14 years old was 0.4%, and that confirmed by PCR was 0.2% <sup>[13]</sup>.

There are several risk factors associated with higher prevalence of hepatitis C. In this cross-sectional study, we screened 1357 children aged 3-15 years with certain risk factors for the presence of hepatitis C. Among the studied patients, there were 89 children [6.6 %] with positive HCV Ab and 73 children [5.4 %] with positive PCR test for HCV. These figures are comparable to that reported by another Egyptian study conducted on healthy children including high and normal risk subjects in the pre-DAA era where 5.8 % of the studied 500 children were anti-HCV positive and 4.4 % were positive for HCV PCR test [14]. In other countries, however, the seroprevalence of HCV among children was notably lower. In Mexico, it was 2.0 % [15], 0.24 % in Brazil <sup>[16]</sup>. The prevalence of HCV reported by the present study is also higher than the global estimate of 0.13 % reported by a recent modeling study [17].

In the present study, factors associated with positive HCV results included blood transfusion, IV injection, previous surgery, previous hospitalization, and dialysis in univariate analysis. However, using multivariate logistic regression, significant predictors of HCV infection in the studied children were blood transfusion, IV injection and previous operation.

Previous studies consistently showed that blood transfusion and IV injection are significant risk factor of hepatitis C in children [14, 18]. Also, the study of Abd El-Wahab, Abdel Maksoud [19] noted a significant association between history of previous surgery and HCV infection in children.

Nonetheless, other studies identified a significant association between other risk factors and HCV infection in children. These factors included family history of HVC infection <sup>[14, 18]</sup>, circumcision <sup>[14, 19]</sup>, ear piercing <sup>[18]</sup> and hemodialysis <sup>[20]</sup>.

#### CONCLUSION

In conclusion, HCV infection in children still constitutes a significant challenge particularly in the high-risk groups even in the DAA era. Efforts should continue to accomplish the national target of clearing Egypt from HCV by 2030.

## Financial and Non-financial Relationships and Activities of Interest

None

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