### Hepatitis C virus infection among school students: Pattern and correlates.

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#### Abstract

Background: Hepatitis C Virus (HCV) infection is a serious health issue. To estimate the prevalence of HCV infection among 6 years-18 years of school children in Beni-Suef Governorate, Egypt, and to determine the risk factors for HCV infection.

Methods: This cross sectional study carried out among school children aged 6 years-17 years in Beni-Suef Governorate, using a structured interviewer-administered questionnaire. All subjects were exposed to third-generation enzyme-linked immunosorbent assay, then positive cases were confirmed by polymerase chain reaction method.

Results: Forty-three out of the 934 students tested positive for the HCV giving an overall seroprevalence of 4.6%. The multiple logistic regression model revealed that urban residence, blood transfusion, family history of HCV, surgical intervention, and dental procedures as significant risk factors for HCV infection among the participants after adjusting for all other potential risk factors.

Conclusion: The HCV infection among school children living in Beni-Suef Governorate in Egypt was relatively high. Urban residence, history of blood transfusion, family history of HCV, surgical and dental procedures were significant risk factors for HCV infection in Egypt. We highly recommend avoidance of unnecessary blood transfusion and enforcement of infection control guidelines to control HCV infection.

Keywords: HCV infection, School children, Risk factors, Egypt.

### Introduction

Hepatitis C infection is a significant global health concern. The World Health Organization (WHO) reports that the virus has infected up to 3% of the world's population. The infection rate fluctuates from as low as 0.1% in Canada to a remarkably high rate of 18.1% in Egypt. Nonetheless, HCV disease has become the world's contributing cause of liver transplantation P [1].

### Highlights

- Hepatitis C infection is a significant health concern among both adults and children.
- Most studies have used Enzyme-Linked Immunosorbent Assay (ELISA) rather than using Polymerase Chain Reaction (PCR) methods.
- All participants were subjected to third generation enzymelinked immunosorbent assay, then positive cases were confirmed by polymerase chain reaction method.
- Screening for HCV infection among children has become mandatory to prohibit liver complications.

In Egypt, few studies have evaluated the epidemiology and risk factors of HCV disease in children. In community-based researches, the HCV prevalence in Egyptian children was 9% and 3% in the lower and upper Egypt respectively. While the prevalence of HCV antibody and HCV RNA were 0.4% and 0.2% respectively among children 1 years–14 years old.

Most surveys have revealed the percentage of anti-HCV positivity by Enzyme-Linked Immunosorbent Assay (ELISA) rather than by the adoption of Polymerase Chain Reaction (PCR) techniques for detection of positivity. While ELISA is an economical means to screen a large sample and to rule out HCV infection, HCV-RNA presents a direct measure of viral load. Given the silent progression of HCV disease among children, periodic screening for early diagnosis of the infection has become mandatory to prohibit liver complications and to anticipate evolving a more aggressive form of the disease [2].

The aim of the present study was to estimate the prevalence of HCV infection among 6 years-17 years school children in Beni-Suef Governorate, Egypt and to determine the risk factors for HCV infection.

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### **Materials and Methods**

### Study design and locality

A cross sectional study carried out among school children aged 6 years-17 years in Beni-Suef city between September and December 2019. Based on the 2017 census, the total population of Beni-Suef Governorate was more than 3.15 million people. It is surrounded by Giza and Cairo Governorates from the North, by El-Minya Governorate in the South, in the East by the Red Sea resorts, and in the West by Fayoum Governorate [3].

### Study population and sampling method

School students 6 years–17 years old of both gender whose parents accepting their participation were eligible for this study, while school students on hemodialysis or transfusion-dependent were excluded.

The minimum sample size was determined to be 360 using the Epi-Info version 7 Stat Calc, (CDC) and (WHO). Based on the following criteria: HCV prevalence among school children was estimated to be 5.8%, a confidence level of 95%, and a margin of error of 5%.

With the expected low prevalence of HCV infection, a sample size of 1000 school children (aged between 6 years and 17 years) were targeted.

### Sampling technique

The representative sample of school students was gathered employing a multistage cluster sample. In the first stage: Beni-Suef district was chosen randomly from seven districts in Beni-Suef Governorate. Then, in the second stage: 6 schools were randomly picked among primary, preparatory, and secondary schools in Beni-Suef district. Lastly, in the third stage: From each selected school, one class was selected randomly from each grade. All class students were offered an informed consent form to be signed by their parents, only eligible students whose parents agreed to participate in the study were recruited [4].

### Data collection

A structured interviewer-administered questionnaire was formed in the English language by authors after an extensive literature review. A panel of professionals insured the content validity of the questionnaire then it was amended based on their suggestions and comments. A bilingual Egyptian researcher translated the questionnaire into Arabic. Then, another translator back-translated it into English, whereas an identical translation was obtained [5].

Lastly, the Arabic version of the questionnaire was pilot tested over 40 students, The determined Cronbach's alpha of the tool was 0.81 which is scientifically accepted. It constituted of three parts as the following:

Part I: Demographic and personal data; such as (gender, age, place of residence, number of family members, number of

rooms, education and occupation of parents, family income, home sanitation, and health care to determine socioeconomic status of students. This scale includes 7 domains with a total score of 84. The socio-economic status was categorized into: Low socioeconomic class for a score of less than 42, Middle socioeconomic class for a score of 43 to 63, and High socioeconomic class for score more than or equal 64.

Part II: It suggests hepatitis C virus-associated risk factors such as (blood transfusion, surgical interventions, family history of HCV, injection, IV catheterization, ear piercing for females, hair cut for males, circumcision, and dental procedures). In the case of the lack of information, students were given Arabic notes for parents about this information to be gathered later.

Part III: HCV antibodies (IgG) test utilizing the 4th generation ELISA, positive cases were investigated for HCV RNA by PCR.

### Laboratory testing

About 5 ml of the venous blood sample was taken from each student using vacationer tubes through vein puncture by a qualified nurse under meticulous aseptic procedure. Each sample was centrifuged within six hours of collection and divided into four serum aliquots for storage at  $-80^{\circ}$ C for further testing [6].

Sera were split and stored conforming to the standard guidelines until analyzed for the serologic evidence of HCV infection by recognizing HCV antibodies in serum, utilizing commercially available Third generation Enzyme-Linked Immunosorbent Assay (ELISA) testing. Sera from positive anti-HCV children was confirmed qualitatively by Polymerase Chain Reaction (PCR), HCV, Ribonucleic Acid (RNA).

### Study design and locality

IBM SPSS (Statistical Package for the Social Sciences) software version 22.0 (SPSS Inc., Chicago, IL, USA) was employed to analyze data. Number and percent were applied to illustrate qualitative data, while quantitative variables were interpreted using mean and standard deviation. All risk factors were investigated for association with anti-HCV positivity in bivariate analysis adopting the Chi-square test, with the calculation of Odds Ratios (OR) and Confidence Intervals (95% CI). Multivariable logistic regression analysis was utilized to determine the association between statistically significant exposures and anti-HCV while controlling other potential risk factors. A P-value <0.05 was considered statistically significant [7].

### Results

A total of 934 children aged 6 years–17 years whose parents signed informed consent were eligible for participation in this study. Nearly two-thirds (62.6%) were of age less than or equal to 12 years with a mean age ( $11.4 \pm 3.3$ ). they are comprising [440 (47.1%)] males, 53.5% of them were from urban. The majority of the students (45.8%) were of middle socioeconomic status (Table 1).

Demographic factors	PCR		Total	P-value	
			(N=934) N %		
	Negative N %	Positive			
		N %			
Age	0.763				
=<12 y	559 (62.7)	26 (62.8)	585 (62.6)		
>12 y	332 (37.3)	17 (37.2)	349 (37.4)		
Gender	0.08				
Male	413 (46.4)	27 (62.8)	440 (47.1)		
Female	478 (53.6)	16 (37.2)	494 (52.9)		
Residence	0.012				
Urban	469 (52.6)	31 (72.1)	500 (53.5)		
Rural	422 (47.4)	12 (27.9)	434 (46.5)		
Socioeconomic status	0.0001				
High	143 (16.0)	0 (0.0)	143 (15.3)		
Middle	414 (46.5)	14 (32.6)	428 (45.8)		
Low	334 (37.5)	29 (67.4)	363 (38.9)		
Total	891 (95.4)	43 (4.6)	934 (100)		

Table 1. HCV prevalence by age, gender, residence and socioeconomic status.

Forty-seven out of the 934 students tested positive to the anti HCV. While after PCR confirmation, only forty-three were positive giving an overall seroprevalence of 4.6%. Regarding demographic determinant of HCV positivity, no significant age and gender difference were observed but significantly higher rates for urban residents [31 (72.1%)] compared to that of rural inhabitants [12 (27.9%)], (P=0.012). Seropositivity was highest in the low socioeconomic level [29 (67.4%)], (P=0.0001).

All male students had their hair cut at community barbershops;

also, all-female students pierced their ears in gold shops; therefore, the evaluation of the impact of these risk factors cannot be established [8]. Almost half the study participants (52.9% and 48.2%) had injections and circumcised respectively. However, none of the studied children reported sharing toothbrushes, needles or syringes. Only 26 (2.8%) children reported living with an HCV-infected family member. Dental procedures and surgical interventions were reported by (7.2% and 4.8%) respectively (Table 2).

Table 2. Distribution of HCV risk factors among hepatitis C virus positive students.

Clinical risk factors	PCR		Total	P-value	
			(N=934)		
	Negative (N= 891)	Positive	N%		
		(N= 43)			
	N%	N %			
Blood transfusion				<0.0001	
No	876 (98.3)	27 (62.8)	903 (96.7)		
Yes	15 (1.7)	16 (37.2)	31 (3.3)		
Family history of HCV	<0.0001				
No	874 (98.1)	34 (79.1)	908 (97.2)		
Yes	17 (1.9)	9 (20.9)	26 (2.8)		
IV catheterization				<0.0001	
No	873 (98.0)	35 (81.4)	908 (97.2)		
Yes	18 (2.0)	8 (18.6)	26 (2.8)		
Surgical intervention				<0.0001	
No	869 (97.5)	20 (46.5)	889 (95.2)		
Yes	22 (2.5)	23 (53.5)	45 (4.8)		
Dental procedures				<0.0001	
No	857 (96.2)	10 (23.3)	867 (92.8)		

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Yes	34 (3.8)	33 (76.7)	67 (7.2)	
Circumcision				0.03
No	468 (52.5)	16 (37.2)	484 (51.8)	
Yes	423 (47.5)	27 (62.8)	450 (48.2)	
Injection				0.025
No	413 (46.4)	27 (62.8)	440 (47.1)	
Yes	478 (53.6)	16 (37.2)	494 (52.9)	

The relation between risk factors exposure and HCV acquisition, dental procedures, circumcision, and surgical interventions were higher among positive school students than negative ones (76.7% *versus* 3.8%, 62.8% *versus* 47.5% and 53.5% *versus* 2.5%) respectively and these differences were statistically significant (p=0.0001, 0.03, 0.0001 respectively) [9].

Besides, receiving injections, blood transfusion, Family history of HCV, and IV catheterization were significantly higher among HCV positive students (p=0.025, 0.0001, 0.0001, 0.0001 respectively).

In the multiple logistic regression model, urban residence (adjusted OR=1.208, 95% CI=0.801-1.896, P=0.013), blood transfusion (adjusted OR=74.5, 95% CI=15.93- 348.5, P=0.001), family history of HCV (adjusted OR=336.6, 95% CI=64.9-1744.3, P=0.001), surgical intervention (adjusted OR=14.391, 95% CI=3.161-65.597, P=0.001)and dental procedures (adjusted OR=57.142, 95% CI=13.033-250.53, P=0.001)identified as significant determinants for HCV infection among the subjects after adjusting for all other potential risk factors (Table 3).

Table 3. Multiple logistic regression model for HCV risk factors among the enrolled school children.

	В	P value	Significance	Odds ratio	95% C.Ifor Odds Ratio	
					Lower	Upper
Urban residence	-2.398	0.013	Significant	1.208	0.801	1.896
Socioeconomic status	-18.38	0.995	Not Significant	0.35	0.65	1.98
Blood transfusion	4.311	0.001	Significant	74.5	15.93	348.5
Family history of HCV	5.81	0.001	Significant	336.6	64.9	1744.3
IV catheterization	-0.617	.617 0.388	Not Sig	0.54	0.133	2.193
Dialysis						
Surgical intervention	2.66	0.001	Significant	14.391	3.161	65.597
Dental procedures	4.046	0.001	Significant	57.142	13.033	250.53
Circumcision	0.941	0.943	Not	2.5	0.343	4.1
Injection	-0.014	0.999	Not	0.98	0.505	1.586

### Discussion

Hepatitis C Virus (HCV) is a serious global health issue, that appears less frequently in children than in adult patients. An estimated 5 million children worldwide have active HCV infection. HCV infection in children was scarcely explored in Egypt. The study objective was to estimate the prevalence of HCV infection among 6 years-17 years school children in Beni-Suef Governorate, Egypt, and to determine the risk factors for HCV infection [10].

The present study confirmed that the overall seroprevalence of HCV among school children was 4.6% which is in accordance with Barakat and El-Bashir who illustrated HCV infection among school children in Alexandria was 5.8%. Also, Egypt found 4.7% of children (6 years–17 years) were positive HCV Antibodies (HCV Ab). Moreover, in Northern Brazil, 6% in

children aged below 19 years old. On the other hand, higher HCV prevalence was revealed in Nile delta (9%) [11].

In the current study, acquiring HCV infection was the dependent variable in the multivariate logistic regression analysis; a family history of HCV, blood transfusions, dental, surgical procedures, and urban residence were significant risk factors of HCV among children. In Alexandria, Barakat and El-Bashir demonstrated blood transfusion and surgical intervention as associated HCV risk factors [12].

This is also analogous to other developing societies like Pakistan where blood transfusion, non-sterile surgical and dental procedures are the dominant risk factors for HCV acquisition. In contrast, dental treatment, blood transfusion, and presence of HCV chronically infected subjects among family members did not feature as contributing risk factors in their study. In Egypt, members of the same family experienced the same unhealthy lifestyle and risky behaviors which may point out the association between HCV acquisition and family history of HCV [13].

In the developed world, with the implementation of successful blood screening, the risk of transmission of HCV by blood transfusion has greatly diminished. Nevertheless, HCV transmission through blood transfusion persists as a dominant risk in developing communities, where screening of blood is restricted by financial and technical factors. Blood transfusion was the exposure with seventy-four times odds ratio among the examined children, suggesting that an anti-HCV scan of the blood donor may not have been reliable. Improved sensitivity of HCV screening tests and changes in blood bank protocols are currently required to prevent further transmission of HCV infection [14,15].

While infection control measures were introduced across the country, they were not consistently applied with the tremendous changes observed in the university hospitals, private sector, army hospitals and Ministry of Health facilities where more resources have been allocated. Meanwhile, urban pediatric government clinics, public school-based clinics, rural healthcare units, and the private sector remain poorly funded and have changed much slower. Considering that surgical interventions and dental procedures are carried out at the poorly equipped hospitals and facilities, with the inappropriate application of infection control standards, HCV exposures caused by surgical and dental interventions were more likely to occur. This may justify the relationship between surgical and dental interventions in our study.

### Conclusion

The frequency of HCV infection among school children residing in Beni-Suef city in Egypt was relatively high as contrasted with developed communities. Urban residence, history of blood transfusion, family history of HCV, dental and surgical procedures were important risk factors for HCV infection in Egypt. Avoidance of unnecessary blood transfusion and enforcement of infection control instructions are extremely recommended to control HCV infection.

**Limitations of the study:** The study was limited by a lack of controls thus could not provide an appropriate judgment. The interpretation of risk factors was based on the subjects' memory thus prone to recall bias.

### **Author Contributions**

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Mahmoud M Hodeib, Fatma S Ewis, Mostafa Sheemy, Shaimaa A Senosy, and Abdelmaged Aboelmged. The first draft of the manuscript was written by [Shaimaa A Senosy] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

### **Compliance with Ethical Codes**

The study protocol was approved by the Research Ethics Committee of the Faculty of Medicine, Beni-Suef University, Egypt. The authorized mangers of selected schools were contacted to facilitate study implementation. The researchers visited the localities and presented themselves to the staff there, explained in detail the aims and procedures of the study. The authorized executives accepted the implementation of the study in favor of school children after assuring the confidentiality of the data gathered by the interview questionnaire, as well as that of the laboratory tests. The investigator received in-depth training specific to interviewing the children.

Written consent was obtained from parents/caregivers in addition to assent from children before enrollment in the study. Data was collected by interviewing each child separately in a private room to ensure the confidentiality of the responses.

### **Consent for Publication**

Consent for publication is not applicable as this study did not include names, images or videos related to individual participants.

### **Conflict of Interests**

The authors declare that they have no competing interests.

### **Financial Support and Sponsorship**

Nil.

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### Availability of Data and Materials

The data used in this study are available from the corresponding author on reasonable request.

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