

Seroprevalence of Hepatitis B and C viruses in children above the age of 3 years: An Observational Cross-Sectional Study

By

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ABSTRACT

Background: Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are the major causes of chronic liver disease (CLD) and its complications in developing countries. The morbidity and mortality of these viruses directly correlate with the duration of infection. So, patients who catch the infection in their childhood period are at great risk for developing life threatening CLD related complications which represent a challenge and an economic burden on their countries, unless early diagnosed and treated.

Aim of the Work: to assess the seroprevalence and risk factors of both HBV and HCV infection in a sample of Upper Egyptian children.

Methods: This is A cross section observational survey study included two hundred, 3-15 years old, eligible children who attended to the outpatient's pediatric clinic of Al-Azhar Assiut University Hospital in the period from 1st October to 31st December 2020 were enrolled in the study. Children with well-known infection and who received blood transfusion were excluded. ELISA based tests (latest generation) for HBV surface antigen (HBsAg) and anti HCV antibodies (HCV Abs) were done in addition to full history taking stressing on risk factors for HBV and HCV infection, thorough clinical examination and complete blood count was done.

Results: Four children (2%) were positive for HCV Abs (3 females and 1 male), 2 children (1%) were positive for HBsAg (both are males), and no co-infections. All positive girls (3 girls) have history of ear piercing by non-medical personnel, all males were circumcised. Three out of sex seropositive children (50%) had history of dental maneuvers, 2 (33.33%) had accidental used-needle stick injury, 2 (33.33%) had accidental used-razor injury and one (16.17%) had one parent with chronic HCV infection.

Conclusions: There is a low prevalence of both HBV (1%) and HCV (2%) infection in the Egyptian children. Ear piercing by non-medical personnel, circumcision, dental maneuvers, and accidental used-sharp objective injury are the most associated risk factors.

Keywords: Hepatitis B in children, Hepatitis C in children, Viral hepatitis, Hepatitis screening.

Introduction:

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are public health problem worldwide and it is estimated that 296 million have chronic hepatitis B infection and 58 million have chronic hepatitis C worldwide (WHO., 2021). The reported global prevalence of HCV in pediatric population under the age of 18 years of age was 0.13%, while global prevalence of chronic HBV in children under age of 5 years of 0.9% (WHO., 2021) & (Schmelzer, et al., 2020).

In Egypt, HBV and HCV are considered the main etiological causes of chronic hepatitis and liver related complications including liver cirrhosis and hepatocellular carcinoma (Elbahrawy, et al., 2021).

Globally, HBV and HCV transmission are associated with direct exposure to contaminated blood products, nosocomial infections (which is related to poor infection control and poor sterilization of medical equipment), intravenous drug use, needle sticks or exposures to sharp instruments, sharing infected needles or syringes as well as sex with an infected partner and household contacts (Doss, et al., 2018), (Prati., 2006) & (Benova, et al., 2014). Vertical transmission of HBV and HCV is the most common mode of transmission among children from an infected HBV and/or HCV mother to her newborn infant (Álvarez, et al., 2021), (Squires and Balistreri., 2017) & (Brown , et al., 2016).

The natural history of children infected with HBV depends on the age of primary HBV infection as more than 90% of infants who are infected perinatally will develop chronic infection and 25–50% of children aged less than 5 years of age will develop chronic HBV

infection while 5% to 10% of adults will develop chronic HBV infection (Fattovich, et al., 2008), (Paganelli, et al., 2012) & (Komatsu, et al., 2017). Regarding to the natural history of children infected with HCV, more than 75% children infected with HCV will progress into chronic infection (Mohan, et al., 2010) & (Pham and Rosenthal ., 2016).

As the majority of children with chronic HBV and HCV infection are usually asymptomatic and not aware of their viral status they will not receive appropriate treatment at the appropriate time (Indolfi, et al., 2010) & (Ogbonna, et al., 2021).

Towards prevention and eradication HBV and HCV, the Egyptian Ministry of Health in accordance with WHO recommendations had adopted universal immunization of HBV for prevention of HBV infection especially in pediatric population since 1992 (WHO., 2021). Also, the Egyptian Ministry of Health had screened 49,6 million Egyptian citizen aged ≥ 18 years old and provide treatment to those with HCV viremia (Waked, et al., 2020).

Although Immunization program of hepatitis B and direct-acting antivirals (DAAS) for HCV and have changed the game in prevention HBV infection and treatment HCV infection respectively, chronic hepatitis B and chronic hepatitis C still represent great burden in children (Komatsu, et al., 2017), (Indolfi, et al., 2010), (Rogers and Balistreri., 2021) & (Jaffray and Flint., 2003). Thus, knowing the viral status in children and adolescents is very important to adopt proper treatment and to prevent consequent future HCV and HBV related complications in children. In this study, we aimed to assess the seroprevalence of HBV and HCV in children above the age of 3 years.

Ethical consideration:

1. Our study was approved by the ethical committee of Faculty of Medicine, Al-Azhar University, Assiut, and conducted in accordance with Helsinki standards 2013.
2. An informed consent was obtained from all parents and participating children.
3. The results and data of the study are confidential, and the patient has the right to keep it.
4. The authors received no financial support for the research, authorship, and/or publication of this article.
5. No conflict of interest regarding study or publications

Sample size calculations:

The calculated sample size is 139, it was calculated using OpenEpi tool, Version 3, open-

Exclusion criteria:

HBV and/or HCV positive children.
Children less than 3 years.
Children received blood transfusion for any reason.
High risk children, as those with hemophilia and any disease mandate blood or its components transfusion.

source calculator--SSPropor (OpenEpi - Toolkit Shell for Developing New Applications)
Population size (for finite population correction factor or $fpc(N)$): more than 1000,000 ,
Hypothesized % frequency of outcome factor in the population (p): $10\% \pm 5\%$

Confidence limits as % of 100(absolute \pm %)
(d): 5
Design effect (for cluster surveys-DEFF): 1

Sample size $n = [DEFF * Np(1-p)] / [(d^2 / Z^2 1 - \alpha / 2 * (N-1) + p*(1-p))]$.

Inclusion criteria:

Children of both sex, ages from 3 to 15 years, and not known to have liver disease

Study procedure:

This study was conducted in the outpatient's pediatric clinic of Al-Azhar Assiut University Hospital in the period from 1st of October to 31st of December 2020 and included 200 children aged 3 years or more.

All children included in the study were subjected to the following:

I- Complete history taking: was obtained from patients and their parents including Name, Age, Sex, Weight, Height, BMI, Residence (Urban or Rural), Education grade, complaints, history (operations, transfusion, circumcision by nonmedical personnel, ear piercing by nonmedical personnel, dental care, home delivery of the child, accidental exposure to used syringe or razors, parents with viral hepatitis, others), family history of liver diseases.

II – Thorough clinical examination: which includes:

General examination: vital signs and Anthropometric measurements.

Systematic examination: heart, abdomen, chest and neurological examinations.

III- Lab. Evaluation including:

- A. Complete Blood Count (CBC) was done using Horiba ABX cell counter, (Paris, France).
- B. Liver function tests: Alanine Transaminase (ALT) & Aspartate Transferase (AST) were measured using Mindray BS 380 automated chemistry analyzer, China.
- C. C- HBs Ag, and HCV antibodies were done for all participants by ELISA based testing.
- D. 5 mL of peripheral blood was collected from the participant in a sterile plain vacutainer tube. The serum was separated by centrifugation at 4000 rpm for 10 min and stored at -30°C until testing. All participants were tested for detection of Anti-HCV Ab and HBsAg in their serum samples using ELISA kit (DIAPRO, Diagnostic, BioProbes Srl. Milano, Italy) according to the manufacturer's instructions. The enzymatic reaction was read at 450 nm on Stat Fax system (Awareness Technology, USA).
- E. D- Polymerase Chain Reaction (PCR) was done to hepatitis B&C seropositive children.

Statistical analysis:

Data were analyzed using SPSS 26 (IBM SPSS Inc., Chicago, USA)) for windows. Categorical data were expressed as frequency and percent while quantitative data were expressed as minimum, maximum, mean, and standard deviation.

Results:

Our results will be demonstrated in the following tables:

Table (1) Demographic data of the screened children

		Number (n)	Percent (%)
Age group	≤ 6 ys	107	53.5
	6-12 ys	89	44.5
	>12 ys	4	2.0
Sex	Female	95	47.5
	Male	105	52.5
Residence	Rural	154	77.0
	Urban	46	23.0
Education	Preschool	83	41.5
	Primary school	114	57
	Preparatory school	5	2.5

Table (1) Shows the demographic data of the studied cases.

Table 2: Risk factors for viral hepatitis in screened children

Risk factors for viral hepatitis	Number (n)	Percent (%)
Surgery	23	11.5 %
Circumcision	102	51 %
• Circumcision by medical personnel	89	44.5 %
• Circumcision by non-medical personnel	13	6.5 %
• Not Circumcised	98	49 %
Ear piercing	91	45.5 %
• Ear piercing by medical personnel	31	15.5 %
• Ear piercing by non-medical personnel	60	30 %
Dental maneuvers	33	16.5 %
Home delivery	20	10 %
Parent/s with hepatitis	6	3 %

Table (2) Showed that Circumcision was the most common risk factor 51%, followed by ear piercing by non-medical personnel 30%.

Table 3: Anthropometric measurements of screened children

	Minimum	Maximum	Mean	Std. Deviation
Age (years)	3.0	15.0	6.930	2.931
Weight (Kg)	11	63	23.96	9.298
Height (cm)	85	160	117.01	18.020
BMI (Body Mass Index)	15.89	22.91	19.136	2.513

Table (3) Showed that Wight, Height and Body Mass Index of screened children are within normal range according to the age, sex and nutritional status.

Table 4: Laboratory data of screened children

		Minimum	Maximum	Mean
Haemoglobin (gm/dl)		9.0	14.5	11.337
Platelets (x 10 ⁹ /L)		189	512	290.77
WBCs (x 10 ⁹ /L)		4.2	16.2	8.089
Neutrophils %		48 %	74 %	56.618
ANC (x 10 ⁹ /L)		46.56	8280	4532.279
Lymphocytes % (x 10 ⁹ /L)		26 %	61 %	36.350
ALC %		22.62 %	6608 %	2928.193
NLR		0.54	3.70	1.734
Monocytes% (x 10 ⁹ /L)		1 %	12 %	4.05
AMC		49	1284	332.426
Liver Function tests	ALT (IU/L)	6	66	32.125
	AST (IU/L)	10	57	29.625

Table (4) Showed that minimum level of Hemoglobin 9 and maximum 14.5 with no abnormalities in platelets and white blood cell counts, **WBCs**: White Blood Cells, **ANC**: Absolute Neutrophil Count, **ALC**: Absolute Lymphocyte Count, **NLR**: Neutrophil-Lymphocyte Ratio, **AMC**: Absolute Monocyte Count.

Table 5: Sero-prevalence of viral hepatitis in the screened children

Sero-prevalence of viral hepatitis in the screened children			
HBs Ag (IU/mL)	Positive	2	1%
	Negative	198	99%
HCV Abs (IU/mL)	Positive	4	2%
	Negative	196	98%

Table (5) Showed that 2 children (1%) out of 200 were hepatitis HBs Ag positive while 4 children (2%) were HCV Abs positive.

Table 6: Correlations between demographic data and risk factors for viral hepatitis in seropositive children

		All seropositive children N=6		HCV Abs positive N=4		HBsAg positive N=2	
		Frequency	Percent	Frequency	Percent	Frequency	Percent
Sex	Female	3	50.0	3	75	0	0
	Male	3	50.0	1	25	2	100
Residency	Rural	2	33.33	2	50	0	0
	Urban	4	66.66	2	50	2	100
Surgery		2	33.33	1	25	1	50
Circumcision		3	50	1	25	2	100
circumcision by non-medicals		0	0	0	0	2	100
Ear piercing		3	50	3	75	0	0
Dental manoeuvres		3	50	2	50	1	50
Used-needle stick injury		2	33.33	1	25	1	50
Used-razor injury		2	33.33	1	25	1	50
Family member/s with HBV or HCV		1	33.33	1	25	0	0
Age group	≤ 6 years	3	50.0	2	1	1	50
	6-12 years	3	50.0	2	1	1	50
	>12 years	0	0	0	0	0	0

Table (6) Showed that 6 children were positive for viral hepatitis either B or C with no coinfection, 4 (2%) children were positive for HCV antibodies (3 girls and one boy) and 2 (1%) were positive for HBsAg (both were boys), 3 were in the preschool age, and 3 in the primary school (6-12 years) with no positive children above the age of 12. All positive boys (3 boys) have history of circumcision, 2 of them circumcised by non-medical personnel, all girls (3 girls) have history of ear piercing, 3 children with dental maneuvers history, 2 with used needle-stick injury and 2 with used razor injury .

Discussion:

Viral hepatitis has a great burden on children's health worldwide and eradication and preventions of HCV and HBV infection is still an ongoing challenge worldwide especially in pediatric population even after the new era of DAAS for HCV and immunization programs of hepatitis B because the most of children with chronic HCV or HBV infection are usually asymptomatic (**Indolfi, et al., 2010**) & (**Ogbonna, et al., 2021**).

The actual prevalence of HBV and HCV among children in Egypt is also unknown due to a lack of uniform screening strategies in children so in the present study we aimed to assess the seroprevalence and risk factors of HBV and HCV infection among Upper Egyptian children attending the pediatric outpatient clinic of Al-Azhar University Hospital. Assiut, Egypt.

Our study showed that the prevalence of HBsAg among the children is 1% (2 boys) which match with global prevalence of children chronically infected with HBV (**WHO., 2021**). The decrease in childhood HBV prevalence is attributed to improvements in vaccination coverage (**Wong, et al., 2019**).

As regarding to children infected with HBV, one child (50%) aged ≤ 6 years and one child (50%) aged between 6-12 years. All of infected HBV children (2 children) had history of circumcision by non-medical personnel, dental maneuver and one child had history of used needle-stick injury and one had history of used razor injury. All of them were living in urban area.

Our results showed circumcision by non-medical personnel increase the risk

transmission of HBV probably due to poor sterilization practices of the instruments and this result agree with **Eke et al.** study and **Ogbonna et al** study (**Eke, et al., 2015**). Also, our results agree with **Rukunuzzaman** et al., who found that exposure to dental procedures is associated with increase the risk HBV infection (**Rukunuzzaman and Afroza., 2011**).

Regarding HCV, the prevalence of HCV antibodies among the children was 2%. In HCV infected children (3 girls and 1 boy) and, 2 were in the preschool aged ≤ 6 years, and 2 in the primary school aged 6-12 years with no positive children above the age of 12. The positive boy had history of circumcision and the positive girls (3 girls) had history of ear piercing, also 2 children had history of dental maneuvers, 1 child had history of used needle-stick injury and 1 had history of used razor injury and one child have history of parent infection with HCV and two were living in urban area and two were living in rural area.

Our results agree with **El-Raziky, et al., (2007)** who showed that prevalence of HCV infection was 2.02% among children and was higher than in **Kandeel et al., (2017)** study that showed the prevalence of HCV antibody and HCV RNA among children aged 1–14 years old were 0.4% and 0.2% respectively

Concerning risk factors for transmission of HCV, our results agree with **Esmat et al., (2012)** study who showed that family history of HCV is risk factor for HCV in Egypt. Also, our results showed that exposures to used needle-stick injury, used razors or dental procedures are risk factors for HCV infection in children this agree with **Hyder et al., (2001)** and **Esmat et al., (2012)** Study.

Conclusions:

There is a low prevalence of both HBV (1%) and HCV (2%) infection in the Egyptian children. Ear piercing by non-medical personnel, circumcision, dental maneuvers, and accidental used-sharp objective injury are the most associated risk factors.

Recommendation:

- Assurance that all babies must receive one dose of hepatitis B immunoglobulin in the first 24 hours of life.
- Close follow up of children at high risk of hepatitis B and C infections.
- More studies must be done including large numbers of children.

Limitations:

- The limitations of our study were the small sample size; the children were chose from a single center and further investigation could not be done because the facility was not available in our hospital. A limited sample size included was some of the limitations of our study.
- Funding: None

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