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Seroprevalence of Hepatitis B and C Virus Infection in Children with Chronic Kidney Diseases; A Historical Cohort Study

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Abstract

Background

The prevalence of hepatitis B and C in Iranian children with chronic kidney disease is limited. Therefore, the present study intends to assess the prevalence of hepatitis B and C in children with chronic kidney disease (CKD).

Materials and Methods: The present study is a historical cohort study which was conducted in a window period of 25 years in Children's Medical Center in Tehran, 1991-2016. Data (age, gender, duration of hemodialysis, kidney transplant, and severity of CKD) were extracted from hospital profiles of admitted patients. Infection with hepatitis B or C viruses was considered as primary outcome. At the end, results were reported as odds ratio (OR) with a confidence interval of 95 per cent (95% CI).

Results: Three hundred and fifty five children (50.1% boys, mean age of 54.5±89.0 months) were assessed. Hepatitis B and hepatitis C were detected in 9 (2.5%) and 5 (1.4%) children, respectively. Ten children had either hepatitis B or C infection with a prevalence of 2.8% (95% confidence interval: 1.4% to 5.1%). Multivariable analyses showed that association between the need for hemodialysis (OR=13.52; p=0.083) and severity of chronic kidney disease (OR=0.28; p=0.072) with incidence of hepatitis infection was borderline. However, risk of hepatitis B or C infection was 5.9-fold greater in girls compared to boys (OR=5.94; p=0.047).

Conclusion: The present study showed that the prevalence of hepatitis B and C were 2.5% and 1.4%, in children with chronic kidney disease, respectively. The prevalence of mentioned infections was significantly higher in girls compared to boys.

Key Words: Child; Hepatitis B; Hepatitis C; Kidney diseases; Prevalence; Risk Factors.

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1- INTRODUCTION

Hepatitis B and C are the most common etiology of liver disease in patients with chronic kidney disease (CKD) (1-3). The prevalence of hepatitis B and C in patients with CKD is diverse among different geographical areas. For example, the prevalence of hepatitis B and C in patients undergoing dialysis is 25 to 36 percent in USA, 2 to 63 percent in Europe and 22 to 55.5 percent in Asia (4-7). Studies show that the type of dialysis (hemodialysis more than peritoneal dialysis), and duration of dialysis affect the prevalence of hepatitis B and C infections. In addition, most hepatitis positive transplant candidates acquire this infection during dialysis period. Both prevalence and incidence of hepatitis C infection is decreasing in patients undergoing hemodialysis due to reduced blood transfusion-acquired hepatitis C and application of preventive measures regarding hospital transmission in dialysis centers (8, 9). However, some studies report a 3 to 85 percent prevalence of mentioned infection among patients undergoing hemodialysis (10-14).

In Iran, 2.6% of population has hepatitis B infection and 4.5% of population has hepatitis C infection. Almost 75 to 80 percent of recently infected patients with mentioned virus progress to chronicity among whom 6 to 70 percent get chronic liver disease at the end. Five to 20 percent of mentioned individuals with chronic liver disease progress to cirrhosis and 1 to 5% of them die because of either cirrhosis or liver cancer (15). Number of blood transfusions is the most important risk factor for hepatitis C infection in patients with CKD. In most studies, it is shown that number of blood transfusions was higher among hepatitis B or C positive patients undergoing hemodialysis compared to non-infected patients (13). Fortunately, risk of acquiring hepatitis C after a blood transfusion has reduced to one unit per 3,000 transfused blood units after introduction of erythropoietin for treatment of anemia and screening of blood products for anti-hepatitis C antibody. However, hepatitis has a high prevalence among patients with CKD. Additionally, treatment of hepatitis is rarely successful in patients undergoing dialysis (16). Multiple efforts have been done to assess the prevalence of hepatitis B and C in patients with CKD during past few years. For example, Szmunes et al. reported that prevalence of hepatitis B in patients undergoing hemodialysis was 16.8% in 1974 (17).

Shah et al. showed that hepatitis B and C have a prevalence of 2.5% and 2.9%, respectively in Pakistani children (18). Other studies report that hepatitis B and C have a prevalence of 5.9% to 15% and 45% to 94.1%, in children with CKD, respectively (19, 20). Overall, there is a huge difference in prevalence of hepatitis among different geographic regions. However, the prevalence of hepatitis B and C infections in Iranian children with CKD and their risk factors is unclear. Therefore, the present study intends to assess the seroprevalence of hepatitis B and C virus infection in children with CKDs.

2- MATERIALS AND METHODS

2-1. Study design and setting

The present study is a historical cohort study which was conducted in a window period of 25 years in Children's Medical Center in Tehran between March 1991 and February 2016. Data were extracted form hospital profile of patients by a pediatrician. The present study was approved by Tehran University of Medical Sciences' ethics committee (ID. Number: IR.TUMS.REC.1394.1143).

2-2. Participants

Study population consisted of all children between 3 and 18 years old with CKD. Glomerular filtration rate of less than 75 milliliters per minute per 1.7 square meters

of body surface area (Bedside Schwartz Formula) was another inclusion criterion. Exclusion criteria were age of less than 3 months old and children with duration of less than three months between decline in glomerular filtration rate and diagnosis of CKD. Diagnosis of CKD was made based on Pediatric Risk, Injury, Failure, Loss, End Stage Renal Disease (pRIFLE) criteria (21).

2-3. Variables and data collection

Data collection was done using a checklist containing information regarding demographic data (age, gender); clinical data including duration of hemodialysis, number of hemodialysis sessions, kidney transplant, and age at first hemodialysis and hepatitis B and C infections. Data collection was performed by trained researchers. The mentioned trainings included management of research tools (how to fill the checklist and record the data), and medical data summarization. Data were extracted from hospital profile of admitted patients. Quality of data collection was assessed by the in-charge researcher of the hospital every 24 hours and existing deficiencies were filled if present. In addition, at the end of each week, few checklists were randomly selected and assessed by chief researcher of the study in order to assess the quality of data collection.

2-4. Outcome

Primary outcomes were either hepatitis B or C infection. Infections or deaths during study period were considered endpoints of the present study.

2-5. Statistical analyses

Data were entered and analyzed in STATA version 14.0. Qualitative data were reported as frequency and percentage while quantitative data were reported as average and standard deviation. In order to assess factors affecting hepatitis infection, the association between patients' demographic and clinical factors with their infection status was assessed based on univariate analyses. Hence, meaningful factors in mentioned analysis were entered in a multivariable analysis model to determine independent factors influencing hepatitis infection. As prevalence of hepatitis B and C in children with CKD is not well-known, logistic regression models by penalized maximum likelihood regression were used to decrease error. Data from the mentioned section were reported as odds ratio (OR) with a confidence interval of 95 percent (95% CI). A p-value of less than 0.05 was considered significant in all analyses.

3- RESULTS

At the end, data from 355 children were assessed. The mentioned data consisted of 178 boys (50.1%), and 177 girls (49.9%). Children in the study had a mean age of 89.0±54.5 months between 3 and 201 months of age. They had a mean height and weight of 105.8±32.3 centimeters, and 21.4±11.8 kilograms, respectively. Hepatitis B infection was present in 9 children (2.5%), and hepatitis C infection was present in 5 children (1.4%). In addition, 4 out 5 children with hepatitis C infection had concomitant hepatitis B. In other words, 10 children had either hepatitis B or C infection with a prevalence of 2.8% (95% confidence interval: 1.4% to 5.1%).

Associations between demographic and baseline factors of children with hepatitis (either B or C) is shown in **Table.1**. As shown, girls comprise 90.0% of individuals infected with hepatitis B or C, and boys account for 10.0%% of mentioned population (p=0.011). Additionally, all patients with mentioned infections had undergone hemodialysis (p=0.037). A significant association was not observed between hepatitis and age (p=0.872), CKD severity (p=0.122) and kidney transplant (p=0.954).

It was shown in multivariable analyses that the relation between hemodialysis (OR=13.52; p=0.083), and severity of CKD (OR=0.28; p=0.072) was in a borderline level with incidence of hepatitis. However, risk of hepatitis B or C was 5.9-fold greater in girls compared to boys (OR=5.94; p=0.047) (**Table.2**).

Table-1: Univariate analysis of hepatitis B and hepatitis C virus infection in children with chronic kidney disease.

Variables	Negative cases (n=345)	Positive cases (n=10)	Total (n=355)	P-value
Gender (%)				
Boys	177 (51.3)	1 (10.0)	178 (50.1)	0.011
Girls	168 (48.7)	9 (90.0)	177 (49.9)	
Age (mean ± SD; month)	89.1±54.7	86.3±52.4	89.0±54.5	0.872
CKD severity (%)				
Mild	36 (10.4)	3 (30.0)	39 (9.9)	0.122
Moderate	9 (2.6)	0 (0.0)	9 (2.5)	
Sever	18 (5.2)	1 (10.0)	19 (5.35)	
ESRD	282 (81.7)	6 (60.0)	288 (81.1)	
Kidney transplant (%)				
No	279 (80.9)	8 (80.0)	287 (90.8)	0.945
Yes	66 (19.1)	2 (20.0)	68 (19.2)	
Hemodialysis (%)				
No	67 (19.7)	0 (0.0)	68 (19.4)	0.037
Yes	273 (80.3)	10 (100.0)	282 (80.6)	
Duration of hemodialysis, (mean ± SD; month)	14.5±31.5	4.6±10.8	14.2±31.1	0.209

CKD: Chronic kidney disease; ESRD: End stage renal disease; SD: Standard deviation.

Table-2: Multivariate analysis of hepatitis B and hepatitis C virus infection in children with chronic kidney disease.

Variables	OR	95% CI	P-value
Hemodialysis	13.52	0.71 to 257.27	0.083
Duration of hemodialysis	0.34	0.07 to 1.60	0.174
CKD severity	0.28	0.07 to 1.12	0.072
Female gender	5.94	1.03 to 34.37	0.047

OR: Odds ratio; CI: Confidence interval; CKD: Chronic kidney disease.

4- DISCUSSION

The present study aimed to assess the prevalence of hepatitis B and C in children with chronic kidney disease. The findings showed that prevalence of hepatitis B and C in children with CKD was 2.5% and 1.4%, respectively. Prevalence of mentioned infections was significantly higher in girls compared to boys. Szmunes and colleagues reported that prevalence of hepatitis B in patients undergoing hemodialysis was 16.8% in 1974. They showed that such prevalence does not have any association with history of blood transfusion but, duration of dialysis was the only influential factor on incidence of hepatitis (17). As noted, prevalence of hepatitis in the study of Szmunes et al. is much higher in comparison with the present study. This is probably due to the 40 years gap between two studies as nowadays preventive measures and vaccinations have reduced

risk of hepatitis B and C transmission (22, 23). Moreover, Yakaryilmaz and colleagues reported that prevalence of hepatitis B and C in patients with CKD was 13.3% and 20.2%, respectively in 2009 (24). However, mentioned study was on adults; hence, the observed gap in prevalence could be due to the difference between the age group of population under study in the present study and study of Yakaryilmaz et al. (24).

Shah et al. studied 444 children with CKD and showed that hepatitis B and C have a prevalence of 2.5% and 2.9%, respectively in Pakistani children (18). However, the study by Al-mugeiren et al. in 1992 reports that hepatitis B and C have a prevalence of 15% and 45%, in children with CKD, respectively (19). Additionally, a hepatitis C prevalence of 15% was reported in Italian children with CKD in 1993 (20). As noted, prevalence of hepatitis in children with CKD was very high in 1990 decade but, recent studies show a reduced incidence of hepatitis B infection. As an exception, prevalence of hepatitis C is exceedingly high in Egyptian children with CKD. Overall, there is a huge difference in prevalence of hepatitis among different geographic regions.

The prevalence of hepatitis B and C in Iranian children with CKD was 2.5% and 1.4% respectively, which is far lower than the reported incidence in previous studies. The reason for this diversity is the differences in geographic and demographic characteristics. Other factor may be the difference in the health status of communities, which has led to a significant difference in the prevalence of hepatitis B and C in various studies.

4-1. Limitations of the study

One of the limitations of the present study is its retrospective nature. In retrospective studies data are extracted from patients' hospital profiles which maybe incomplete or lack some data (25-27). However, mentioned issue did not have any effect on major results of the present study as viral hepatitis and HIV infection are routinely screened in Children's Medical Center and their results are present in patient profiles as hard copies. Other limitations include lack of assessment of some probably influential factors on hepatitis such as number of blood transfusions. The mentioned factor was not recorded in most of patient profiles so such data could not be collected in the present study. At the end, exact models were used to assess the association between probable risk factors and incidence of mentioned infections because of low prevalence of hepatitis B and C in the present study. Therefore, results of the present study might differ from finding of future studies.

5- CONCLUSION

Based on a large sample size, the present study aimed to assess the prevalence of hepatitis B and C in children with chronic kidney disease. The findings showed a hepatitis B and C prevalence of 2.5% and 1.4%, respectively in children with CKD. The prevalence of mentioned infections was significantly higher in girls compared to boys.

6- CONFLICT OF INTEREST: None.

7- ACKNOWLEDGMENT

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