Original Article

Prevalence of Nonalcoholic Fatty Liver Disease in Children with Renal Failure Underwent Treatment with Dialysis

Abstract

Background: In this study, we aimed to investigate the prevalence of nonalcoholic fatty liver disease (NAFLD) in children with renal failure under treatment with dialysis and its association with biochemical measurements. **Methods:** In this cross-sectional study, children aged less than 18 years with chronic kidney disease (CKD) who were under treatment with dialysis at least 3 months ago were enrolled. To evaluate fatty liver in those patients who had no recent liver ultrasonography (last 6 months), liver ultrasonography was performed. The characteristics of patients with renal failure with and without NAFLD based on the ultrasonographic evaluation were compared. The association between NAFLD and the studied variables was evaluated. **Results:** In this study, 39 children (31 males and 8 females) with renal failure who underwent treatment with dialysis were included. From the studied population, six (19.4%) had NAFLD based on ultrasonographic evaluation. There were no differences between renal failure patients with and without NAFLD regarding the biochemical and anthropometric characteristics ($P > 0.0$). **Conclusions:** The prevalence of NAFLD in our studied children with renal failure who underwent treatment with dialysis was like the general population and it was not associated with the biochemical and anthropometric characteristics of the patients. Given the importance of NAFLD in renal failure patients as well as its subtle nature, it is recommended to screen patients with CKD for NAFLD.

Keywords: *Adolescent, child, nonalcoholic fatty liver disease, renal insufficiency*

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Introduction

Chronic kidney disease (CKD) in children is an important public health issue due to its related complications and costs. There is no comprehensive epidemiological data regarding the prevalence of CKD in children due to the different classification and diagnostic definitions for CKD in children.[1,2] It is estimated that it ranges between 15 and 74.7 per one million of the age-related population (pmarp).[3]

Cardiovascular complications are the most common complications in children with CKD that are related to a high rate of mortality also.[4]

Evidence indicated that due to the higher rate of cardiometabolic risk for patients with CKD and nonalcoholic fatty liver disease (NAFLD), it is suggested that there is an association between the two mentioned diseases.[5,6] Some evidence reported a potential genetic link between CKD and NAFLD and some recent studies report the link between NAFLD and renal function.[5,6]

Most of the studies regarding the association between NAFLD and CKD both in adults and children are in the direction that patients with NAFLD are at a higher risk for CKD.[7-9] Accordingly, NAFLD could increase the risk of insulin resistance, atherogenic dyslipidemia, and hypertension in CKD mainly through inflammatory mediators. NAFLD is considered an independent risk factor for CKD.[10,11]

The adverse relationship is not studied in many studies, especially in the pediatrics population. Based on the available data, CKD may exacerbate NAFLD due to the changed gut microbiota and barrier function, glucocorticoid metabolism, and the accumulation of toxic uremic metabolites.[12] Considering that one of the early pathogeneses of CKD is insulin resistance, the occurrence of NAFLD in CKD patients, especially with insulin resistance and the presence

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of cardiometabolic risk factors, could support the suggested bidirectional link between NAFLD and CKD in children.[12,13]

Thus, it seems that the investigation of the bidirectional association is an important issue for better management of CKD in children. The association would be evaluated by the investigation of the prevalence and severity of NAFLD in children with CKD. There is no report in this field in the pediatric population and studies in the adult population are rare.[13]

So, considering the lack of study in this field in children as well as the risk of faster progression of CKD-related cardiovascular complications in the children with CKD, in this study, we aimed to investigate the frequency of NAFLD in the children with CKD under treatment with dialysis and its association with biochemical measurements.

Methods

In this cross-sectional study, children aged less than 18 years with renal failure who were under treatment with dialysis were enrolled from March 2019 to 2021.

The protocol of the study was approved by the research ethics committee of the Isfahan University of Medical Sciences with a research project number of 398929 and ethic code of IR.MUI.MED.REC.1399.580.

In this study, children with renal failure were included who were under treatment with dialysis at least 3 months ago.[14] Those with positive hepatitis C and B, autoimmune hepatitis or cholestatic disease, malignancy, history of using any hepatotoxic agents, uncontrolled secondary hyperparathyroidism or hypothyroidism were not included. Those with inappropriate collaboration or death or immigration were excluded.

The patients were selected by the convenience sampling method.

All the patients were selected based on the level of the Glomerular filtration rate (GFR) and CKD staging scoring tool.[15]

Written informed consent forms were obtained from the selected children or their parents.

The baseline characteristics of all selected patients including their demographics (age, sex, address and…), anthropometric (including height, weight, and Body mass index(BMI) measured by a trained nurse), disease history, and medical history were recorded in the checklists developed for the study.

During the follow-up period as per the patients' routine biochemical tests, additional tests including 1,25(OH) vitamin D, liver function test or lipid profile, and serum insulin level were performed.

The body weight and height were measured using a digital scale SECA 76 (Hamburg, Germany*)*. The measurements were performed in the children with light clothing and barefoot.

To evaluate fatty liver in those patients who had no recent liver ultrasonography (last 6 months), liver ultrasonography was performed.

The results of the biochemical tests and ultrasonographic evaluations were recorded in the mentioned checklist.

The characteristics of the patients with renal failure with and without fatty liver based on ultrasonographic evaluation were compared. The association between fatty liver and the studied variables was evaluated.

Ultrasonographic evaluation

An ultrasound multi-frequency curvilinear 3.5–5 MHZ probe by Siemens Company (Sonoline G50 series, model number 7474922) was used for the liver ultrasound to check for sonographic fatty liver (SFL). The presence of SFL was defined as increased echogenicity of the liver parenchyma to the extent that it was reported by ultrasound and disturbed the visibility of the portal vein and liver artery.[14] The severity of the fatty liver disease including mild, moderate, and severe, and steatosis severity including grades of S0, S1, S2, and S3 were determined based on the extent of fat in the liver as follows—S0: steatosis of less than 5%, S1: steatosis of 5%–33%, S2: steatosis of 34–66%, and S3: steatosis of more than 66%.[16]

Statistical analysis

Data were analyzed using SPSS version 24 software. Continuous and categorical variables were presented as mean (SD) and number (%) and were compared in the CKD patients with and without fatty liver using the Chi-square and Student's t-tests. For variables without normal distribution, we used nonparametric tests. A *P* value of less than 0.05 was considered statistically significant.

Results

In this study, 39 children (31 males and 8 females) with renal failure who underwent treatment with dialysis in the Imam Hossein children's hospital were included. The characteristics of the studied population are presented in Table 1. From the studied population, six (19.4%) had fatty liver based on the ultrasonographic evaluation. The characteristics of children with renal failure and with and without fatty liver are presented in Table 2. There was no significant difference between the children with renal failure and with and without fatty liver regarding the studied variables.

The results of the Mann– Whitney test indicated that there was not any association between the fatty liver and biochemical or anthropometric variables ($P > 0.05$).

Table 1: Characteristics of children with chronic kidney diseases who underwent dialysis

Variables	Mean (SD)
Age (years)	11.64 (3.50)
Weight (kg)	32.98 (20.02)
Height (cm)	130.34 (22.61)
AST	37.84 (17.67)
ALT	26.05 (18.50)
Vitamin D	36.92 (23.52)
Fasting blood glucose	81.15 (36.80)
Cholesterol	158.48 (51.30)
Triglyceride	154.46 (99.22)
Insulin	7.90 (5.13)
Type of dialysis (*n* [%])	
Hemodialysis	27 (69.2%)
Peritoneal dialysis	12 (30.8%)

Table 2: Characteristics of children with chronic renal diseases who underwent dialysis with and without fatty liver based on ultrasonographic evaluation

Variables	Renal failure patients with fatty liver *n*=6	Renal failure patients without fatty liver *n*=33	*P**
Age (years)	12.50 (3.20)	11.48 (3.58)	0.52
Weight (kg)	43.33 (29.02)	31.11 (17.90)	0.21
Height (cm)	150.83 (16.72)	130.30 (22.28)	0.39
AST	30.16 (7.54)	39.24 (18.67)	0.24
ALT	21.50 (7.96)	26.88 (19.79)	0.92
Vitamin D	41.00 (30.77)	36.18 (22.47)	0.86
Fasting blood glucose	67.33 (19.93)	83.66 (38.78)	0.56
Cholesterol	135.00 (39.46)	162.75 (52.54)	0.41
Triglyceride	224.00 (177.32)	141.81 (75.53)	0.22
Insulin	10.96 (9.35)	7.35 (3.95)	0.11
Type of dialysis (*n* [%])			
Hemodialysis	6 (100%)	21 (63.6%)	0.85
Peritoneal dialysis	-	12 (36.4%)	

Using nonparametric Mann–Whitney test

Discussion

In this study, we evaluated the frequency of NAFLD in children with renal failure who underwent treatment with dialysis. In this study from the studied population, 19.4% had NAFLD based on the ultrasonographic evaluation. The comparison of the biochemical and anthropometric characteristics of the studied children with renal failure and with and without NAFLD indicated that there were no significant differences between the groups regarding the studied variables.

The rate of NAFLD in the pediatric population has been reported to be 5–10% worldwide. The rate is higher in some populations such as Asians and boys.[17] The results of a recent systematic review study in Iran reported an estimated rate of 27.88% among Iranian children and adolescents.[18]

In the current study, 19.4% of the studied patients with renal failure had NAFLD. It seems that the rate is similar to the general Iranian pediatric population.

In a literature review, the rate of NAFLD in patients with renal failure has not been reported in the pediatric population. Behairy *et al*.[13] have reported a prevalence of 56.6% in the adult population with CKD. They used elastography for the NAFLD diagnosis. Choe and colleagues recently in Korea indicated that from 819 patients with CKD, 15.7% had NAFLD.[19]

The prevalence of NAFLD in our population was lower than that reported in the study by Behairy *et al*.[13] It may be due to the diagnostic tool and study population. Our finding was similar to that reported by Choe *et al*.[19]

Some studies reported an estimated prevalence rate of 35–85% for NAFLD in CKD patients.[20] It should be noted that the rate is related to the CKD patients who were obese or had diabetes.

The suggested risk factors for the occurrence of NAFLD in this group of patients are insulin resistance, chronic inflammation, increased oxidative stress, and dyslipidemia. These factors are also considered as the identified risk factors for NAFLD. Thus, it is important to determine the pathogenesis of the disease occurrence in patients with end-stage renal disease.

Behairy *et al*.[13] showed a significant association between alanine transaminase (ALT), aspartate transaminase (AST), lipid levels and C-reactive protein (CRP).

In our research, though the mean level of triglyceride was higher in the patients with NAFLD, there was not such a significant association. It may be due to the low sample size of our studied population.

Another explanation is that, in patients with renal failure, the level of ALT is lower and may be due to reduced synthesis and release of ALT and AST from the hepatocytes in the end-stage renal disease. Some evidence demonstrated that in the uremic patients, the normal level of ALT and AST could not exclude the diagnosis of NAFLD.[21,22] It is suggested that NAFLD may develop in this group of patients without any significant biochemical changes, especially AST and ALT, so using noninvasive diagnostic methods, such as ultrasonography and screening of NAFLD in CKD patients, would be helpful for early detection of the disease.

There is also evidence regarding the association between the severity of CKD and NAFLD.[23] Considering the conditions of the studied patients, almost all studied patients in this study had severe renal failure. However, some studies, especially in the pediatric population, have speculated that the association between NAFLD and CKD would be more prominent in milder cases of CKD.[24]

Given the importance of NAFLD in CKD patients as well as its subtle nature which mainly results in the misdiagnosis of the comorbidity during routine follow-up and to prevent or provide proper intervention for NAFLD in this group of patients, it is recommended to screen patients with CKD for NAFLD, especially those in the early stage of CKD.

It is also recommended to plan prospective studies to determine the causal relationship between NAFLD and CKD in the pediatric population.

The limitations of the current study were the cross-sectional design of the study, low sample size, no evaluation of the patients' CRP level, and no investigation of the role of CKD severity or the role of other CKD-related factors such as the patients' hemoglobin in the association of NAFLD with CKD.

Conclusions

The prevalence of NAFLD in our studied children with renal failure who underwent treatment with dialysis was similar to the general population and it was not associated with the biochemical and anthropometric characteristics of the patients. It is suggested that though the patients with CKD are susceptible to NAFLD, it may develop in long term.

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Conflicts of interest

There are no conflicts of interest.

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