



A study of Some Factors Affecting the Prevalence of Renal Disease in Children

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Keywords: Nephrotic syndrome, Chronic kidney disease, Pediatrics, Blood groups, Socioeconomic status.

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Abstract:

The current study was carried out in the period from 1 to 25 November 2023. It included sixty-two pediatric patients in the age range of (1-12) years and male and female children: twenty-six pediatric patients with chronic renal failure and thirty-six pediatric patients with nephrotic syndrome, who were outpatients and inpatients in the renal diseases unit and dialysis unit of both Al-Mansour Pediatric Teaching Hospital and Child's Central Teaching Hospital in Baghdad, Iraq. The control group consisted of twenty-six children in the same age range as the sick groups of males and females. Blood samples were collected from patients and controls. Then renal function was evaluated by applying the laboratory tests as urea and creatinine levels were measured in serum, besides blood group and Rh factor tests. Factors that may affect renal disease incidence and progress were recorded, such as socioeconomic status, residence (North, Middle, and South), and family history. The results explained the significant increase in both urea and creatinine concentrations ($P < 0.001$) in serum compared with controls. The blood group and Rh factor had no significant differences among children of both sick groups. The entire affected factors had no significant association with renal disease incidence or progress in the current study. The age and gender of each child patient had no significant effect on the type of renal disease (at $P \text{ value} \leq 0.01$).

Keywords: Nephrotic syndrome, Chronic kidney disease, Pediatrics, Blood groups, Socioeconomic status.

دراسة بعض العوامل المؤثرة على انتشار المرض الكلوي في الأطفال

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الخلاصة:

أجريت الدراسة الحالية في الفترة من 1 إلى 25 تشرين الثاني (نوفمبر) 2023. وشملت اثنين وستين مريضاً من الأطفال في الفئة العمرية (1-12) سنة، حيث كان من الأطفال الذكور والإناث: ستة وعشرون مريضاً من الأطفال يعانون من مرض الكلى المزمن. كان هناك ستة وثلاثون مريضاً من الأطفال يعانون من المتلازمة الكلوية، والذين كانوا مرضى خارجيين ومرضى داخليين في وحدة أمراض الكلى ووحدة غسيل الكلى في كل من مستشفى المنصور التعليمي للأطفال ومستشفى الطفل التعليمي المركزي في بغداد، العراق. وتكونت المجموعة الضابطة من ستة وعشرين طفلاً في نفس الفئة العمرية للفئتين المرضيتين من الذكور والإناث. تم جمع عينات الدم من المرضى ومجموعة السيطرة. ثم تم تقييم وظائف الكلى عن طريق إجراء الفحوصات المختبرية حيث تم قياس مستويات اليوريا والكرياتينين في مصل الدم، بالإضافة إلى اختبارات فصيلة الدم وعامل Rh. تم تسجيل العوامل التي قد تؤثر على حدوث مرض الكلى وتقدمه، مثل الحالة الاجتماعية والاقتصادية والإقامة (الشمال والوسط والجنوب) والتاريخ العائلي. أوضحت النتائج وجود زيادة معنوية في تركيز كل من اليوريا والكرياتينين ($P < 0.001$) في مصل الدم مقارنة مع مجموعة السيطرة. لم يكن هناك فروق ذات دلالة إحصائية بين فصيلة الدم وعامل Rh بين الأطفال في كلا المجموعتين المرضيتين. لم يكن للعوامل المصابة بأكملها ارتباط كبير بحدوث مرض الكلى أو التقدم في الدراسة الحالية. لم يكن للعمر والجنس لكل مريض طفل أي تأثير كبير على نوع المرض الكلوي (عند قيمة $p \leq 0.01$).

الكلمات المفتاحية: المتلازمة الكلوية، المرض الكلوي المزمن، طب الأطفال، فصول الدم، الحالة الاجتماعية والاقتصادية.

1. Introduction:

Chronic kidney disease (CKD) is a worldwide public health problem that progresses towards end-stage renal disease (ESRD). In childhood, it is generally a non-curable and progressive condition that leads to death. Nephrotic syndrome (NS) is an important CKD in children which is characterized by the presence of proteinuria, hypoalbuminemia, hyperlipidemia, and edema [1]. The other important CKD in childhood is chronic renal failure (CRF) which is a progressive irreversible destruction of the kidney tissues leading to the loss

of renal function [2]. Many studies found a relationship between both blood groups and the Rh factor and the incidence of renal disease. The occurrence of renal disease varies with age and gender. The mortality rate in ESRD, in addition to renal illness, is related to many factors [3]. Some of them are malnutrition, poor hospital care, poor socio-economic status, racial and geographic distribution, and family history. Children with CKD are susceptible to the condition frequently; the estimated annual incidence in children aged 1 to 5 years old is 3% [4]. After receiving appropriate medication, 5–15% of children patients do not get complete remission and are classified as treatment-resistant; however, the scientific recommendations for early detection and appropriate treatment of childhood chronic kidney disease over time based on scientific evidence even though there are differences in the causing aspects of management, despite the general concepts being the same [5]. Accordingly, the current study was carried out to :

1. Examine the kidney functions in children with NS and CRF to assess whether and to what degree the kidney may be affected.
2. Detect the effect of hereditary and other environmental factors on the prevalence of renal disease .
3. Find the distribution of renal disease in children according to age range and gender.

2 .Experimental Procedure

2.1 Materials:

The blood urea kit and serum creatinine kit were equipped from (BioMérieux / France) and the ABO blood group kit was equipped from (Randox/ U.K). They were used for detecting the blood urea, creatinine, and blood groups, respectively.

2.2 Methods:

2.2.1 Study groups:

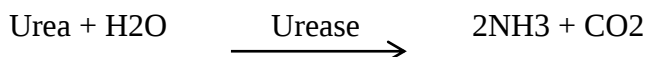
This study was carried out between 1 - 25 November 2023. The pediatric patients were 26 of CRF and 36 of NS at the age of 1 to 12 years of both genders, who were outpatients and inpatients in the dialysis unit in both Al-Mansour Pediatric Teaching Hospital and Child's Central Teaching Hospital. The control group consisted of 26 children of both genders in the same age range as the study groups .

2.2.2 Blood samples:

Three ml of venous blood were obtained from each child in the study and control group and distributed in suitable containers (Plain tubes and capillary tubes) according to the use in different tests.

2.2.3 Renal function tests:

A. Blood urea: (BioMérieux Company) The serum concentration of urea in the current study was determined by enzymic method (Urease –Modified Berthelot Enzymatic-Colorimetric) according to the following reaction:



In an alkaline medium, the ammonium ions react with salicylate and hydrochloride to form a green-colored indophenol .



Assay procedure:

1. The working solution was prepared by mixing one vial of R2 enzyme into one bottle of R3; so gently mixed to dissolve contents.
2. The following solutions were pipetted into the three test tubes .

Solution	Blank	Standard	Sample
Working Solution	1ml	1ml	1ml
Sample	—	—	10 μ L
Standard Solution	—	10 μ L	—

3. All the tubes were mixed separately and then incubated for 5 min at 20–25°C.
4. A volume of 200 μ L of R4 was added to all tubes, then they were shaken and incubated for 10 min at 20-25°C.
5. The absorbance (A) was read against the reagent blank at 580 nm .

Calculation:

$$\text{Urea} = \frac{A(\text{Sample})}{A(\text{Standard})} \times \text{Standard conc.}$$

Normal values of blood urea in children = (20 – 45) mg/dl

B. Serum creatinine: (BioMérieux Company)

This assay was done by using the calorimetric method. Creatinine in an alkaline solution reacts with picrate to form a colored complex.

Assay procedure: A working solution was prepared by mixing 4 parts of sodium hydroxide with 1 part of picric acid. One ml of TCA was added to 1 ml of serum and they were mixed well by using a glass rod until the dispersion of the precipitate. Then the mixture was centrifuged at 2500 rpm for 10 min, and then the supernatant was poured off. Into test tubes, the following solution was pipetted.

Solution	Blank	Standard	Sample
D.W	0.5ml	—	—
Standard	—	0.5ml	—
TCA	0.5m	0.5ml	—
Supernatant	—	—	1.0 ml

Working Solution 1.0 ml 1.0 ml 1.0 ml

All solutions were incubated at 25°C for 25 minutes after separated mixing .The absorbance (A) was read against the reagent blank at 550 nm.

Calculation:

$$\text{Creatinine} = \frac{A(\text{Sample})}{A(\text{Standard})} \times \text{Standard conc.}$$

Normal values of creatinine in children = (0.7 – 1.4) mg/dl

C. Blood typing and Rh system : Within the ABO system, four major blood groups can be recognized depending on the presence of one or both antigens: A and B. These groups are: A, B, AB, and O. If clumping occurred after a blood sample was exposed to a particular antibody, the person had had that type of blood. People with the particular antigen: Rh factor are Rh+; those without are Rh -. The procedure was done according to (Randox Company/ U.K).

D. Effect of the environmental factors:

The selected factors were recorded and statistically arranged in tables. They included: age range, gender, family history, residence, and socioeconomic status .

3. Statistical analysis:

Statistical analysis was computer-assisted using SPSS (Statistical Package for Social Sciences) 2019, version 17. A P-value less than 0.05 was considered statistically significant.

4. Results:

4.1 The evaluation of renal function:

1. Blood urea values :As recorded in **Table 1**, the blood urea levels were significantly higher ($P < 0.001$) in both NS and CRF groups than in the controls' blood .
2. Serum creatinine values: The levels of creatinine were much higher in both sick groups' sera ($P < 0.001$) than those of the healthy ones. **Table 1**.

Table 1: Biochemical Tests Results of Nephrotic Syndrome, Chronic Renal Failure and Control Group

Test	Group	Mean	S.D ±	Minimum value	Maximum value
Blood urea	NS	59.5	10.3	44.97	74.2
	CRF	96.2	14.4	75.9	115.1
	Control	29.5	6.9	20	44
Serum creatinine	NS	1.85	0.43	1.33	2.73
	CRF	4.93	1.52	2.3	6.9
	Control	0.87	0.14	0.7	1.2

Normal values:

Blood urea: (20-45) mg/dl.

Serum creatinine: (0.7-1.4) mg/dl.

4.2 Distribution of patients according to age range and gender:

Thirty-six patients of NS and twenty-six of CRF were included in the present study as well as twenty-six children of the same age range as controls. All were of both genders. The age groups and gender distribution in the study groups are clarified in Table (2). No significant importance was noticed between the renal disease and age groups (P-value was 0.263). The same matter regarding the effect of gender on the type of renal disease within the age groups was not significant too (P-value was 0.251). Data from **Table 2** indicate that the number and percentage of patients are the lowest in the age range (5-8) years in NS and CRF groups.

Table 2: The Age Groups and Gender Distribution

Group	Gender	Age groups (years)			Total
		1-4	5-8	9-12	
NS	Male	11	3	13	27
	Female	2	3	4	9
	% within the age group	36.11%	16.67%	47.22%	100%
CRF	Male	8	3	8	19
	Female	3	3	1	7
	% within the age group	42.31%	23.08%	34.61%	100%
Control	Male	7	4	3	14
	Female	7	3	2	12
	% within the age group	53.85%	26.92%	19.23%	100%

4.3 Effect of socioeconomic status on disease prevalence :

There was no significant importance between socioeconomic status (Good, Medium, or Low) and the incidence of NS or CRF (P-value was 0.21) as observed in **Table 3**.

Table 3: The Socioeconomic Status of NS and CRF Patients

Socioeconomic status	NS patients	CRF patients	Total
Good	36.11%	50%	26
Medium	55.56%	46.15%	32
Low	8.33%	3.85%	4
Total	100%	100%	62

4.4 Effect of blood group on disease prevalence:

This effect was not significant (P-value was 0.307). **Table 4** expresses the distribution of the four blood groups between the patients of NS and CRF .

Table 4: The Distribution of Patients within Blood Groups

Blood group	NS patients	CRF patients	Total
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A	36.11%	19.23%	18
B	30.56%	30.77%	19
O	19.44%	38.46%	17
AB	13.89%	11.54%	8
Total	100%	100%	62

4.5 Effect of blood Rh on disease prevalence:

There was no statistical significance of the Rh factor in the patients' blood of each study group (P-value was 0.847). **Table 5** indicates this result .

Table 5: The patients' distribution according to Rh factor

Rh factor	NS patients	CRF patients	Total
Positive	91.67%	96.15%	58
Negative	8.33%	3.85%	4
Total	100%	100%	62

4.6 Effect of residence on CKD incidence:

The relationship between the residents of Iraq (North, Middle, and South) and the prevalence of both CRF and NS was not significant (the P-value was 0.678) as in **Table 6**.

Table 6: The patients' distribution according to residence

Residence	NS patients	CRF patients	Total
North	2.78%	0%	1
Middle	77.78%	80.77%	49
South	19.44%	19.23%	12
Total	100%	100%	62

4.7 Effect of family history on CKD incidence:

The effect of family history (positive/ negative) was not significant (the P-value was 0.957) as shown in **Table 7**.

Table 7: The family history presence in both sick groups.

Family history	NS patients	CRF patients	Total
Positive	19.44%	19.23%	12
Negative	80.56%	80.77%	50
Total	100%	100%	62

5 .Discussion:

The measured renal function tests: The current results agree with the findings of [6] regarding CRF patients and agree with [7] regarding NS patients regarding urea concentrations in the serum of patients. The current findings show that the patients may reach end-stage renal disease with impaired renal function and damaged tissues of the kidney resulting in high blood urea levels [8]. The current results regarding creatinine levels in serum agreed with many results [6] about CRF. It also agreed with [7] about NS patients. Any rise in blood creatinine is a sensitive indicator of kidney malfunction because it is normally and rapidly removed from the blood and excreted [8]. The increase in urea and creatinine levels in serum (called renal impairment) could be due to the decrease in the number of functioning nephrons in addition to their subsequent hypertrophy [2].

The relationship of age and gender within CKD groups: The results concerning the non-significant effect of age and gender on CKD in the current study agreed with those of [9] about NS. In CRF children, the majority was in the age group below 2 years in the study of [10]. The mean age was not significant in the CRF group compared to the control group. It was suggested that children, especially infants, are less resistant to diseases and are much affected by environmental conditions compared with people in other age categories and the explanation of these results may be attributed to an immature immune system, which will enhance the probability of infection; and thereby the development of renal disease; concerning differences among countries [4]. The number of male patients in the current study was larger than that of females in both sick groups, as the ratio was 3:1 for males to females in the NS group. This finding differs from the results published in NS was frequent in male children, with a male-to-female ratio of 2:1. Nevertheless, [7] recorded that the male-to-female ratio was 4:1. The previous study suggested that non-diabetic renal diseases progress more rapidly in males [9].

Socioeconomic status effect on CKD incidence: The current result is similar to those obtained by [10] about the effect of residence. In the study of [11], it is mentioned that there is a strong relationship between infant and child mortality and the mode of living and parental education, and the improvement of socioeconomic status can be indicated by the reduction of mortality rate in infants and children. The previous study [12] evaluated the relationship between socioeconomic status and susceptibility to renal diseases due to the effect on the development of the fetal kidney, or due to malnutrition, and this may represent a higher risk of progression of renal disease. The low activating nephrons number might promote the

development of renal disease in children [5]. Children of educated parents have higher chances of survival than those of non-educated parents because they seem to have more understanding of the importance of health care, standard of living, the quality of curative services available, and utilization [12]. Besides socioeconomic and cultural factors, other factors can affect the prevalence and progression of renal disease in childhood which might not be limited to age, recurrent illness, where malnutrition is also due to gastrointestinal problems or depression, inflammation, and medications [1].

Effect of blood group and Rh factor on CKD incidence: The obtained results disagreed with the study of [13] in which the distribution of renal patients among the blood groups was significantly different (mainly in the B and O). However, a lack of correlation between blood group phenotypes and renal scarring (most instances are caused by infection in young children) was referred to by [14]. Many investigations tried to demonstrate a relationship between blood groups and renal diseases as a statistical importance between the blood groups AB and O and the occurrence of urolithiasis and detected blood group specificities of some groups in the ABO and Lewis systems in human tumors of the urinary bladder and some renal cell carcinomas; considered males with blood group O and females with blood group A at risk. Also, it was recorded that pyelonephritis is associated with a specific type of pilus, P pilus, which binds to the P blood group substances in the P system [4]. Various important diseases, including renal diseases, show an important connection with blood groups. Some of these are early reports of statistical associations; some are more recent based on scientific findings. For the last 20 years, there has been increasing evidence that blood groups have a function and play a biological role. This often does not relate to the red cells but to the presence of chemical substances on other cells that were initially identified as red cell antigens [14]. Blood groups are genetically determined and each is characterized by the presence of a specific complex of carbohydrates, which are known to be important as receptors or ligands. So, blood groups are classified according to immunological (antigenic) properties, which are determined by specific substances on the surface of red blood cells [15]. Current results may be due to the small number of patients in both groups. No references to the negative or positive relation of Rh factor with CKD were obtained; except that of [3] which dealt with renal cell carcinoma and considered males with blood group O+ and females with blood group A of any Rh factor to have a significant risk of disease [15]. Our result seems to be related to the small number of samples.

Effect of residence on CKD incidence: There was no comparison with this result as there were no specialized studies dealing with the rate of NS or CRF incidence in Iraq, as well as the absence of qualified centers, that consider the racial, socioeconomic, and geographical criteria that may affect Iraqi patients to compare them with those in different parts of the world [16]. There is strong evidence that the regional differentials are converging as a result of the continuous expansion of health facilities in all regions of the country [17]. Some studies suggest that racial and geographic factors may increase renal disease incidence rates. The environmental exposure and/or specific genes may explain the connection between residents and renal disease [18]. In [19], it was concluded that many factors play a role in causing renal disease, concerning differences between countries or even within the same country.

Effect of family history on CKD incidence: In the NS group in the current study, the positivity was 19.44%. In Iraq, Al-Bewyaney [20] found that 15.8% of children were positive for a family history of the NS. In European nephrotic children, the percentages calculated by Agraharker et al. [21] and [22] were 28% and 29.04%, respectively. In the CRF group, our percentage of positive family history was 19.23%. It is asymptotic to that of Mong et al. [23] which was 20% in pediatric CRF patients in Vietnam. In Syrian children, the percentage was 5% as reported by [24]. The positivity was 24% in the study of Fan et al. [25] in the USA. There may be a familial incidence of NS and CRF, which can be divided into 2 categories: patients with an infantile onset and a poor prognosis, and patients with a juvenile onset and a generally good response to conventional therapy [26]. This high frequency of positivity for the familial patients may be attributed to the gene activation and/or may be due to environmental conditions that enhance its expression; as it was clear that the genetic parameters play an important role in disease development. They are thought to speed the rate of renal disease progression or predispose patients with various etiologies of kidney disorders enhancing renal damage [18]. The markers included human antigen-associating genetic susceptibility to renal diseases in addition to mutations [27]. Genetic backgrounds and converging with socio-environmental factors have been proposed to account for the tendency toward excessive renal disease progression [28].

6 .Conclusions:

- The age group spanning from 5 to 8 years old exhibited the lowest frequency of renal illness.
- Both sick groups were predominantly composed of males.

- Within an age range, there was no discernible relationship between gender and renal illness.
- The factors under investigation had no discernible impact on the prevalence of CRD.

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Conflict of Interest

There is no conflict of interest.

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