

# Impaired renal function among children in Alexandria, Egypt

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## ABSTRACT

**Objectives:** Impairment of renal function may occur as a result of a variety of conditions. Progression to chronic renal-disease may be prevented by early detection. This epidemiologic study aimed at revealing the predisposing factors and determinants for the development of impaired renal function among Egyptian children.

**Methods:** This is a case-control study conducted at Alexandria University Children's Hospital, Alexandria, Egypt. All cases below 12 years of age diagnosed with impaired renal function over a total duration of 6 months (October 1999 through to March 2000) were investigated. The primary study tool was a structured questionnaire, which focused on variables suspected to play a role in the impairment of renal function. For each patient, one control matched for age and sex was selected.

**Results:** Primary renal disease tends to account for a relatively small proportion of the etiologies of renal impairment in Egyptian children. Most of the cases

encountered in this study suffered functional renal impairment secondary to severe dehydration or sepsis. Presence of congenital abnormalities of the gastrointestinal tract, heart or urinary tract, increased the possibility of suffering from impaired renal function approximately 9 times. Delays in seeking medical advice increased the risk substantially.

**Conclusion:** Awareness of individuals at an increased risk, along with early diagnosis and adequate management of many predisposing conditions could prevent progression to more severe renal disease which has potentially devastating effects on every aspect of a child's life.

**Keywords:** Impaired renal function, functional renal failure, child, risk factors, prevention.

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**T**he kidney plays the major role of guardian of the internal milieu of the human body through excretory, metabolic as well as endocrine functions. Acute renal failure (ARF) occurs as a result of sudden severe impairment of glomerular or tubular function, or both.<sup>1</sup> Moreover, while the kidneys have a unique capacity to regain function following acute renal injury, renal injury of a more prolonged nature often leads to progressive and irreversible destruction of nephron mass. Eventually, sclerosis of the residual glomerular population may occur, resulting in chronic renal failure.<sup>2</sup> Impaired renal function has

potentially devastating effects on many aspects of a child's life. This includes growth, neurologic, and psychologic development. Consequently, children present a unique challenge in the field of nephrology.<sup>3</sup> In a social and economic environment where satisfactory treatments for permanent and end stage renal disease (ESRD) are simply not available to the vast majority of the patients, a valuable approach would be to adopt suitable preventive measures.<sup>4</sup> Since impairment of renal function may occur in the face of diverse conditions, progression of many diseases to chronic or ESRD requiring

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dialysis and transplantation may be ameliorated by early detection of impaired renal function and close attention to predisposing factors. Within the last 2 decades very little research has been carried out to elucidate the causes of impaired renal function among Egyptian children. The aim of this epidemiologic study was to disclose the determinant and predisposing factors for the development of impaired renal function among this group. Such knowledge is essential for the adoption of suitable preventive as well as curative health care measures.

**Methods.** The study was designed as a case control study. It was conducted in Alexandria University Children's Hospital, Alexandria, Egypt, since it is the main tertiary referral unit in Alexandria, Egypt. All cases below 12 years of age, diagnosed with impaired renal function between October 1999 and March 2000 (a total duration of 6 months) were studied. The sample included 2 categories of patients. The first category included all cases that presented to the dialysis unit, whether they were diagnosed with end stage renal disease and required permanent dialysis or they were incident cases of acute renal failure. The 2nd category included patients arriving to the clinics or inpatients in whom a progressive elevation of blood urea nitrogen (BUN) and creatinine were discovered on routine laboratory investigation. Values were compared with normal ranges specific for each age group since normal values vary with age.<sup>5</sup> For each patient, one control matched for age and sex was selected. Most of the controls were obtained from the outpatient surgery clinic. Only children presenting with minor surgical complaints were taken. Whenever possible, relatives, visitors and accompanying siblings were also included as controls. Controls were then examined to ensure their freedom from any problem relating to the kidney and urinary tract. The primary study tool was a structured questionnaire, which focused on variables suspected to play a role in the impairment of renal function. Personal and demographic data about the child was collected. History of exposure to nephrotoxic agents, drugs, and environmental pollutants; dietary habits; underlying diseases and history of medical care received, were all sought for. Family history included history of maternal exposure during the index pregnancy, presence of similar conditions among siblings or near relatives, consanguinity of the parents, education and working status of each parent and income. A pre-tested socio-economic score<sup>6</sup> was utilized in order to obtain an objective assessment of socio-economic status. In order to confirm the diagnosis, a detailed present history of the current condition was included. All patients were subjected to a complete physical examination. Arithmetic mean and standard deviation (SD) were used in analysis of tabular forms of data. Chi square test and Fisher's

exact test were used as tests of significance. The chosen level of significance was 5%. Crude odds ratio was used to measure the risk of associated conditions and exposures. Multivariate regression analysis was employed to control confounding factors.

**Results.** During the 6-month study period, 87 patients were diagnosed with impairment of renal function. More than half (58.6%) of these patients were infants, below one year of age, and 24% were actually neonates. The mean age for all cases was  $2.6 \pm 3.6$  years. The ratio of males to females was 1.3:1 with a slight male preponderance most evident in infants. **Table 1** shows some selected socio-demographic characteristics of the studied sample. **Table 2** shows factors found to play a significant role in impairing renal function. Approximately 30% of patients (number (N) =26) had apparently developed the renal impairment following severe dehydration and 16.1% (N=14) following sepsis. It was found that children suffering from such acute conditions had a risk of suffering from impairment of renal function 13 times as much as children who did not. In 13.8% of cases, renal impairment was diagnosed in patients already suffering from a chronic disease. In order of frequency these were: Insulin-dependent diabetes mellitus (DM), leukemia, and hepatic insufficiency. More than one 3rd of all cases (31 patients) had some form of congenital abnormality or malformation. Surprisingly, the most commonly encountered of these (17 patients) (19.5%) were abnormalities of the gastrointestinal tract rather than the urinary tract which accounted for only 5%. Eleven cases (12.6%) had congenital heart disease. Calculating the risk ratio revealed that children with severe congenital abnormalities had a risk of suffering from an impairment of renal function 9 times as much as children who did not. Another notable finding was that only one quarter of patients presented within the first 2 days of illness. Approximately, 40% presented within the first week of illness, while approximately 10% of cases had presented one month or more, after the development of the first symptoms of the disease. More than three quarters of the patients, with delayed presentation, lived in rural areas. The intake of non-steroidal anti-inflammatory agents and frequent antibiotic use were not found to contribute to the risk of development of renal impairment in children in this sample. Similarly, exposure to environmental pollutants and various dietary habits had no effect. Consanguinity of the parents and maternal exposure (including infection and systemic disease) during the index pregnancy apparently had no effect on a child's risk of developing impaired renal function. Similarly, the family history did not stand out as a predictive factor for such disease.

**Table 1 -** Selected socio-demographic characteristics of patients presenting with impaired renal function in this study.

Characteristics	N	(%)
<b>Age</b>		
Neonates		
28 days > 1 year	21	(24.1)
> 1 year < 6 years	30	(34.5)
> 6 years < 12 years	16	(18.4)
	20	(23)
<b>Sex</b>		
Male	49	(56.3)
Female	38	(43.7)
<b>Residence</b>		
Rural	51	(58.6)
Urban	36	(41.4)
<b>Drinking water</b>		
Treated	76	(87.4)
Untreated (direct from river/well)	11	(12.6)
<b>Consanguinity between parents</b>		
First degree relatives	30	(34.5)
Other degree	25	(28.7)
No consanguinity	31	(36.8)
<b>Socio-economic status</b>		
Low	71	(81.6)
Middle	7	(8)
High	9	(10.4)
N - number		

**Table 2 -** Suspected risk factors for development of impaired renal function and their significance among the studied sample.

Characteristics	N	Test of Significance (OR)	P-value
Low socio-economic status	71	1.607	<0.05* OR
Rural residence	51	1.286	<0.05* OR
Positive family history of kidney disease	3	-	>0.05 F
Maternal disease during index pregnancy	4	-	>0.05 F
Drug intake within last 2 months			
Frequent NSAID	4	2.048	>0.05 OR
Frequent antibiotics	5	1.707	>0.05 OR
Major congenital abnormalities	31	9.079	<0.01* OR
Impaired renal perfusion due to dehydration/sepsis	40	13.814	<0.05* OR
Irregular access to medical care	72	5.640	<0.05* OR
N - number, NSAID - non-steroidal anti-inflammatory, OR - odds ratio, F - Fisher's exact test, *statistically significant following multivariate regression analysis.			

Thirteen cases of chronic renal failure were encountered during the study. Nine of these were diagnosed with ESRD and would require life-long dialysis or transplantation. The mean age of presentation of patients with ESRD was  $6 \pm 2.9$  years. The number of males was almost equal to the number of females. The evident causes of chronic renal failure were membranoproliferative glomerulonephritis (in 4 patients), congenital abnormalities of the urinary tract (in 3 cases) and upper urinary tract infection associated with reflux (in 3 cases). Six cases of hemolytic uremic (HUS) syndrome were diagnosed. Multivariate regression analysis revealed that the significant risk factors for development of renal impairment in children were: severe dehydration, sepsis, presence of congenital abnormalities of the gastrointestinal tract (GIT), heart or urinary tract, and delays in medical presentation. The overall predictive accuracy of this model was 83.9%.

**Discussion.** While several studies from many parts of the world report that the HUS is the most common cause of ARF in children,<sup>7,8</sup> only 6 cases of HUS were diagnosed during this 6 month study. An increase in this figure may be expected if general physicians are more aware of this diagnosis. A study conducted in the United States of America in 1994, stated that many physicians are not aware of the diagnosis of HUS.<sup>9</sup> This syndrome occurs following a diarrheal prodrome that is usually caused by infection with *Escherichia coli* serotype O157:H7, which can produce specific enterocytotoxins that target endothelial cells producing endothelial cell injury followed by intrarenal aggregation of platelets. This results in both thrombocytopenia and renal failure. Microangiopathic anemia results from mechanical damage to red blood cells (RBCs) as they pass through altered vasculature. Thus, what appears initially as gastroenteritis, ultimately, becomes the final diagnosis of HUS.<sup>10,11</sup> In many developing countries, infections and nephrotoxicity are still incriminated as the most important causes of ARF.<sup>12-14</sup> Further studies directed towards highlighting epidemiological features of this disease in Egypt, may give valuable data. In this study, the most frequent cause of renal impairment was severe dehydration mostly secondary to severe gastroenteritis. In a small percentage of cases the dehydration was post-surgical. Dehydration results in a decreased plasma volume, extracellular dehydration and a resulting impairment of renal perfusion. The 2nd most important cause of renal impairment was sepsis. It is worth noting that this form of renal impairment is commonly asymptomatic and is diagnosed when a recent increase in blood urea nitrogen and serum creatinine is detected, often during routine biochemical screening of hospitalized patients. When symptomatic, the presenting signs

and symptoms may be dominated or modified by the precipitating disease.<sup>15</sup> A variety of congenital abnormalities were found to increase the risk of development of impaired renal function. The most important of these were abnormalities in the gastrointestinal tract. Since, almost two thirds of these patients had also undergone some form of intestinal surgery or had a history of recurrent diarrhea or protracted vomiting, it is proposed that these patients developed a functional renal failure as a result of fluid loss. Most of the cases suffering from congenital heart disease had severe cardiac anomalies associated with cyanosis and a poor cardiac output. In one study conducted among Spanish children, researchers revealed that 62% of cases of acute renal failure occurred secondary to some form of cardiopathy.<sup>16</sup> This may be explained by the fact that dehydration and sepsis are probably less frequently encountered in developed countries. Chronic diseases were encountered in almost one fifth (18.3%) of patients suffering from impairment of renal function. The most frequently encountered were insulin-dependent DM (5.7%) and leukemia (4.6%). While clinical diabetic nephropathy is a well-recognized cause of morbidity and mortality in patients with type-one diabetes, screening for microalbuminuria is recommended only after 5 years of diagnosis.<sup>17,18</sup> However, uncontrolled diabetic states with excessive water loss and fluid electrolyte imbalance may result in functional renal impairment. Since no patients in this study were suffering from diabetes for more than 5 years, it is justifiable to speculate that renal impairment in such young diabetics is probably a result of this excessive water loss and fluid electrolyte imbalance rather than actual diabetic nephropathy. As regards leukemia, patients suffering from malignancy were found to be at risk of developing an impairment of renal function in several studies.<sup>19,20</sup> Proposed explanations include hyperuricemia due to breakdown of cells, renal infiltration by malignant cells, urinary tract obstruction and treatment with various chemotherapeutic agents, which can impair renal function. One patient suffering from endstage renal failure in this study had taken large doses of aminoglycosides before the onset of renal failure. This patient was also suffering from impaired hearing. Nephrotoxicity and ototoxicity are recognized as the 2 most dangerous side effects of aminoglycosides.<sup>21</sup> A delay in presentation of at least one week was noted in at least one third of the children. More than 75% of patients with such a delayed presentation were living in rural areas. The high incidence of renal impairment due to infective gastroenteritis reflects poor socio-economic and hygienic conditions, inadequate facilities in rural areas, delays in seeking medical advice, and lack of knowledge on fluid and electrolyte therapy among staff responsible for initial patient care in rural area.

In conclusion, the findings of this study highlight the important fact that primary renal disease tends to account for a relatively small proportion of the etiologies of renal impairment in Egyptian children. However, several factors seem to predispose to the development of impaired renal function. Awareness of individuals at an increased risk, along with early diagnosis and adequate management of many predisposing conditions could prevent progression to more severe renal disease which has potentially devastating effects on every aspect of a child's life.

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