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A Retrospective Study of Glomerulonephritis Patterns Among Jordanian Children

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Abstract

Background and Aim: Glomerular diseases affecting pediatric patients differ from conditions encountered in adults. Additionally, the pattern of glomerular disease varies in different regions of the world. In the Mediterranean region, data on glomerular diseases in children patients remain sparse. Therefore, we conducted a study to assess glomerulonephritis disease patterns at our institute and assess for recent incidence trends.

Methods: A retrospective study conducted at a university affiliated tertiary hospital located in the capital city of Amman. We included native kidney biopsy reports of patients who fulfilled our age criterion of < 15 years old.

Results: Our study showed a total of 178 kidney biopsies, of which 71 patient fulfilled our inclusion criteria. the mean age of the study population was 7.6 ± 4.1 years. Our study had more males compared to females, 56% and 44%, respectively. In nephritic syndrome, IgA nephropathy emerged as the leading etiology (13%), which was followed by Post-Infectious glomerulonephritis (8%). In children with nephrotic syndrome, MCD was exceedingly more common in male children when compared to females, 14 versus 8 patients, respectively. While FSGS was more common among females compared to males, 5 versus 2 patients, respectively.

Keywords: Glomerulonephritis, child, Focal segmental glomerulosclerosis, kidney biopsy, nephrotic syndrome.

INTRODUCTION

Inflammation of the glomerular units in the kidneys is known as glomerulonephritis (GN). This condition represents a diverse group of diseases, as each type has unique pathological features and pathophysiology mechanisms. The differentiation between these types is critical to treatment decision making, as each disease condition responds differently to immunosuppressive therapies.

Glomerular diseases affecting pediatric patients differ from conditions encountered

in adults. Nephrotic syndrome in children occurs most commonly due to minimal change disease, while membranous glomerulonephritis is most common among adults. Additionally, the pattern of glomerular disease varies in different regions of the world; e.g. western countries have declined incidence rates of membranoproliferative glomerulonephritis (MPGN) compared to other countries which demonstrated no decline [1, 2, 3]. These comparative studies conducted in different geographical areas have helped elucidate contributing etiologies of glomerulonephritis; such as that improvements in the socioeconomic conditions might be responsible for the decline in MPGN rates in developed countries [4].

In the Mediterranean region, data on glomerular diseases in children remain sparse. Multiple studies demonstrated higher than expected rates for Focal Segmental Glomerulosclerosis (FSGS) [5, 6]. A Jordanian study on FSGS patients reported familial FSGS reaching as high as 20% of total FSGS cases [6]. Although these results are strikingly high, these studies reflect single center experiences and were focused only on FSGS. More studies are required to assess the broader GN spectrum among our population.

Therefore, we conducted a study of GN types among Jordanian children. Our aim was to assess GN disease patterns at our institute and assess for recent trends in GN incidence among our population

METHODS

A retrospective study conducted at Prince Hamzah Hospital in the period between January 1st 2013 till December 31st 2020. This is a tertiary hospital located in the center of Jordan, the capital city of Amman, and is affiliated to the Hashemite University. Our inclusion criteria were composed of the two criterions: (1) Pediatric patients, defined as any patient < 15 years of age. (2) Patients who underwent percutaneous native kidney biopsies. We excluded patients with biopsies from renal graft biopsies and surgical nephrectomies.

Data collection of studied patients was obtained through the electronic medical chart. Gathered information included the following: Demographic data, clinical presentation and assessments, indication for kidney biopsy, laboratory testing results, pathological reports, treatments attempted, and response to treatment. Our pathological assessment depended on routine performance of both light microscopic examination and immunofluorescences techniques. Electron microscopy were requested only for selected patients at the discretion of the treating physician. Patient data were anonymized and securely stored in electronic form. The study was approved by the Hashemite University and the Hospital Institutional review boards.

Continuous variables were reported in mean ± standard deviations. Percentages were used to reflect proportion from overall studies patients and summed counts were used to quantify subgroup proportions. After testing for assumptions of normality, statistical analysis was performed using independent t-test and chi square-test. The statistical significance was set at $p < 0.05$.

RESULTS

Our initial screen of kidney biopsies showed a total of 178 kidney biopsies, we included a total of 71 patients who fulfilled the inclusion criteria. One hundred and six excluded patients were adults, which were analyzed and published in another report [7]. The number of tissue cores per patient was at least 2 cores for approximately 84% of

patients, with an average of 14 glomeruli per patient.

The average age of the studied population was 7.6 years ± 4.1. Only two infants (< 1 year) had kidney biopsies. In this study, there were more males compared to females 56%, 44%, respectively. Female patients (8.4 ± 3.8 years) were slightly older compared to male patients (7.0 ± 4.2 years), a result that was not statistically significant (p=0.157). Male patients had slightly higher creatinine at presentation and higher degree of proteinuria (p-values: 0.919, 0.984, respectively).

Indications of kidney biopsy were proteinuria 52%, hematuria alone 5.6%, hematuria with proteinuria 36%, and renal impairment 5.6%. Proteinuria was almost evenly divided between nephrotic range proteinuria (30 patients) with sub-nephrotic range proteinuria (31 patients).

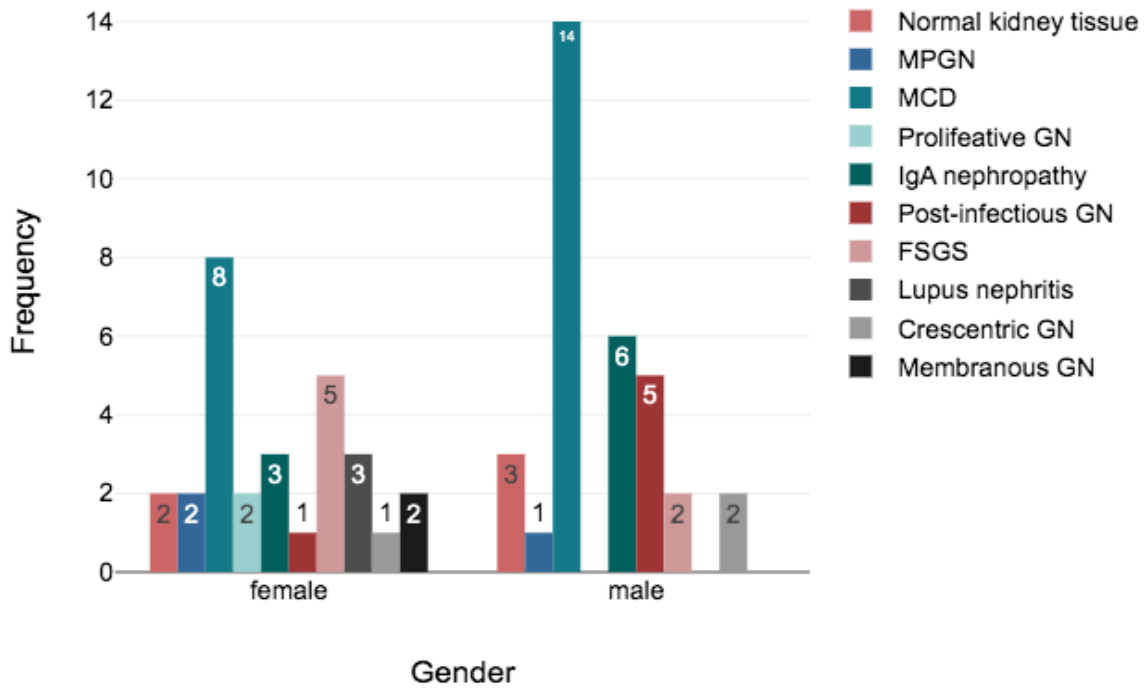
The results of biopsy specimens were classified as nephritic syndrome (55%), nephrotic syndrome (34%), other classification in (8%) and inadequate (4%), as demonstrated in table 1. In nephritic syndrome, IgA nephropathy emerged as the leading etiology (13%), with 4 of them manifesting as Henoch-Schönlein Purpura (HSP). The second leading condition was Post-Infectious glomerulonephritis (8%). The remaining patients were almost equally divided between lupus nephritis (4%), MPGN (4%), crescentic GN (4%) and proliferative GN (3%).

Table 1. Histopathological disease types of kidney biopsy samples among 71 Jordanian children with reported frequency rates and percentages.

Histopathological Disease	N (%)
Nephrotic Syndrome	
Minimal Change Disease	22 (31%)
Focal Segmental Glomerulosclerosis	7 (10%)
Membranoproliferative Glomerulonephritis	3 (4%)
Membranous Glomerulonephritis	2 (3%)
Nephritic Syndrome	
IgA Nephropathy	9 (13%)
Post-infectious Glomerulonephritis	6 (8%)
Lupus Nephritis	3 (4%)
Crescentic Glomerulonephritis	3 (4%)
Proliferative Glomerulonephritis	2 (3%)
Conditions Classified as Other	6 (8%)
Normal Examination	5 (7%)
Inadequate	3 (4%)

The comparison between patterns of glomerular disease in each gender revealed considerable differences, as demonstrated in figure 1. In children with nephrotic syndrome, MCD was the exceedingly more common in male children when compared to females, 14 versus 8 patients, respectively. While FSGS was more common among females compared to males, 5 versus 2 patients, respectively. Comparing steroid responsiveness in the two conditions, steroid responsive patients were 11 out of 22 in MCD and 3 out of 7 patients with FSGS. Analysis of the received treatments was divided into: conservative without immunosuppression (30%); steroid responsive (27%) and steroid resistant (43%).

Figure 1. Glomerular disease frequency rates among Jordanian children divided according to gender. Notice that Minimal change disease is more common in males (teal green), while FSGS is more frequently seen in females (light pink).



Abbreviations: MPGN = Membranoproliferative glomerulonephritis, MCD = Minimal Change Disease, GN = Glomerulonephritis, FSGS = Focal Segmental Glomerulosclerosis.

The latter group required the addition or substitution of a second immunosuppressive agent. The second immunosuppressant agent were: Calcineurin inhibitor (17 patients), purine antimetabolites (8 patients), alkylating agent (4 patients) and anti-CD 20 antibody (2 patients).

Immunofluorescent staining showed positivity rates for: IgM (32%), IgG (36%), IgA (31%), C3 (38%), and C4 (17%). Contrarily, serum hypocomplementemia was found in 11% of patients. All

hypocomplementemia patients tested negative for anti-nuclear antibody except for two patients, one of whom was diagnosed with lupus nephritis. Low C3 complement was present in two out of three patients with MPGN and four out of six patients with Post-infectious GN patients.

DISCUSSION

Our study of pediatric patients with glomerulonephritis demonstrated MCD to be the most common glomerulopathy overall, followed by IgA nephropathy and PIGN. This pattern is similar to the spectrum reported in the united states but slightly different from studies conducted in the region [8]. A retrospective study conducted in Turkey showed MCD as the most common glomerular disease, followed by MPGN and FSGS [9]. The latter finding probably reflects rising incidence rates of FSGS reported internationally [9, 10, 11]. In recent years, this shift in GN patterns has gained a surge of research attention in both pediatric and adult patients [9, 10, 11, 12]. However, more concentrated research effort is needed to explore reasons behind these trends and appropriate preventive strategies.

In this study, FSGS was the second leading common cause in nephrotic syndrome patients. This finding reflects that this condition remains among the leading causes of nephrotic syndrome in children. In a previous report in Jordan, Al-Salaita et al reported FSGS as the most common GN accounting for 54% of total studied children [13]. Another study Alwahaibi el al reported FSGS at 22% in a systematic review of 22 manuscripts in the multiple countries surrounding Jordan [14]. Our study results show notably lower rates of FSGS at 10%, which is probably an underestimation of the true incidence, as almost half of MCD patients did not respond to steroid therapy alone, these cases might represent patients with undetected FSGS. Moreover, a portion of patients with normal microscopic examination could represent additional unsampled FSGS cases; both findings indicate an anticipated underestimation of FSGS frequency rates.

Our study demonstrated that some glomerular disease showed predilection for particular gender types. IgA nephropathy and post-infectious GN were more common in males. Whilst FSGS, membranous GN and lupus nephritis were more common in female children, the latter two entities almost did not occur in males. Nevertheless, these results should be interpreted carefully, as our sample size could be a limiting factor, as it might over-exaggerate minor differences overserved between subgroups.

When assessing the diagnostic yield of complement testing, biopsy immunofluorescent for complement was positive in approximately one third of cases, it was conclusive in probably even a lesser portion of patients. This data should not prevent clinicians from routine performance of immunofluorescent staining, rather understand its limitations in pathological assessments. Contrastingly, serum complement levels were diagnostically useful to predict underlying GN types, particularly for MPGN and PIGN. More than two thirds of these patients showed C3 hypocomplementemia in serum samples. This highlights the usefulness of this test, especially among patients with negative anti-nuclear antibodies, a highly sensitive test which almost excludes the possibility of Systemic Lupus Erythematosus and related GN.

To our knowledge, this the first Jordanian study which delineates the broad spectrum of GN among children. We believe that our single center experience is a good

representation of the Jordanian population, as our data were obtained from a tertiary center located in the capital city of Jordan. Additionally, our study showed FSGS as one of the commonest glomerular conditions in Jordanian children, particularly in females. The reasons behind this finding are unknown, but genetic factors likely contribute to this increased incidence rates. We believe that our data will guide future genetic studies, to identify genetic mutations unique to populations in the Mediterranean region.

CONCLUSIONS

Minimal change disease is dominantly the most common GN in Jordanian children. FSGS incidence remains among the leading causes of nephrotic syndrome, particularly in females. Different glomerular diseases have predilection for different gender types.

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دراسة استعادية لنمط التهاب كبيبات الكلى لدى الأطفال الأردنيين

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الملخص

الخلفية والاهداف تختلف أمراض الكبيبات التي تصيب الأطفال عن الحالات التي تماثلها عند البالغين. بالإضافة إلى ذلك، يختلف نمط مرض الكبيبات في مناطق العالم المختلفة. في منطقة البحر الأبيض المتوسط، لا تزال البيانات المتعلقة بأمراض الكبيبات لدى الأطفال قليلة. لذلك ، قمنا بإجراء دراسة لتقييم أنماط مرض التهاب كبيبات الكلى في مستشفانا ولتقييم طبيعة هذه الإصابة.

منهجية الدراسة : هذه الدراسة استعادية أجريت في مستشفى جامعي – مستشفى الأمير حمزة – يقع في العاصمة عمان. وقد تضمنت هذه الدراسة تقارير خزعات الكلى الأصيلة للمرضى الذين استوفوا معيار العمر لدينا وهو أقل من 15 عاماً.

النتائج: أظهرت دراستنا ما مجموعه 178 خزعة من الكلى ، استوفى 71 مريضاً معايير الإدراج الخاصة بنا. كان متوسط عمر المرضى الذين تمت دراستهم 7.6 ± 4.1 سنة. كان لدى دراستنا عدد أكبر من الذكور مقارنة بالإناث ، 56٪ و 44٪ على التوالي. في ما يتعلق بإلتهاب الكبيبات الكلوية ، كان اعتلال الغلوبين المناعي A هو السبب الأكثر شيوعا (13٪) ، تبعه في ذلك التهاب كبيبات الكلى بعد العدوى (8٪). في الأطفال الذين يعانون من المتلازمة الكلوية ، كان مرض التبدل الطفيف الأكثر شيوعا عند الأطفال الذكور مقارنة بالإناث 14 مقابل 8 مرضى، على التوالي. بينما كان تصلب الكبيبات البؤري الأكثر شيوعا بين الإناث مقارنة بالذكور ، 5 مقابل 2 مريض ، على التوالي.

الاستنتاجات : مرض التبدل الطفيف هو الأكثر أنواع التهاب كبيبات الكلى شيوعاً في الأطفال الأردنيين. لا يزال تصلب الكبيبات البؤري من بين الأسباب الرئيسية للمتلازمة الكلوية ، وخاصة لدى الإناث. الأمراض الكبيبية المختلفة لها ميل لأنواع مختلفة من الجنسين.

الكلمات الدالة: التهاب كبيبات الكلى، الأطفال، تصلب الكبيبات البؤري، خزعة الكلى، المتلازمة الكلوية.