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HSP Nephritis in Children, Clinical Behavior, Renal Involvement and Remedy

Chaudhury GN[1*], Chowdhury RA[2], KhondokerT[3], FerdousT[4], Afroz S[5], Hanif M[6]

[1]Dr. Gulshan Nigar Chaudhury, Assistant Professor, Department of Pediatric Nephrology, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh
[2]Dr. Rifat Asma Chowdhury, Medical Officer, Department of Microbiology, Shahid Suhrawardy Medical College & Hospital, Dhaka, Bangladesh
[3]Dr. Tarannum Khandoker, Assistant Professor, Department of Pediatric Nephrology, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh
[4]Dr. Tahmina Ferdous, Registrar, Department of Pediatric Nephrology, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh
[5]Dr. Shireen Afroz, Professor, Critical Care Nephrology Department, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh
[6]Dr. Mohammad Hanif, Professor, Department of Pediatric Nephrology, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh

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***Corresponding author:** Gulshan Nigar Chaudhury

Abstract **Original Research Article**

Introduction: Childhood HSP is a systemic vasculitis of diverse clinical features with a favorable prognosis but renal involvement in HSP can cause chronic kidney disease (CKD) in children which is preventable in most cases if diagnosed and referred early. ***Aim of the study*****:** To determine the occurrence ratio of HSP in children, its clinical behavior, renal involvement, and possible remedies. ***Methods:*** Medical records of 31 HSP patients were evaluated in the Nephrology and Rheumatology department of Dhaka Shishu (Children) Hospital from July 2017 to December 2019. Epidemiological data, clinical and laboratory findings were reviewed. The treatment for each patient was recorded including supportive care antihypertensive, ACE inhibitor, and immunosuppressive drug. ***Result:*** Most children affected during winter and spring (29%). Mean duration of disease 21.19 ±11.54 days. The mean age was 8.63±2.53 yrs. The mean age of renal involvement was 9.5 years. Male-female ratio 5.7:2. Almost all children (96.8%) presented with a rash. Abdominal pain was noted in 74.19% of patients. Joint pain was reported in 51.6% of patients. Renal involvement was presented in 58% of patients commonly in the form of proteinuria (58.6%) and hematuria (48.4%). 9 (29%) patients developed acute kidney injury (AKI). Occasional complications include convulsion, intestinal obstruction, septicemia, and pneumonia. Lab analysis showed thrombocytosis in 54% of patients, leukocytosis in 61% of patients, hypo-albuminemia in 58% of patients. C3 low in 29% patients. A kidney biopsy was done in 10 patients. IgA deposition and mesangial cell proliferation were the most common pathology. Regarding treatment, 12 patients were treated with methylprednisolone and MMF. 8 patients go into remission after taking only oral prednisolone. 6 patients took ACE inhibitor and 2 patients need dialysis. The majority of children (90.3%) achieved remission, though 2 patients died during admission. ***Conclusion:*** Present literature found renal involvement more frequent in the older age group, mean age 9.5 yrs (range 6-14). Recognizing and analyzing the clinical finding for early diagnosis of severe HSP nephritis and creating awareness regarding early referral to nephrology centers for biopsy, immunosuppressive therapy or dialysis is essential for preventing CKD.

Keywords: HSP nephritis, Children, Renal Involvement.

INTRODUCTION

Henoch-Schonlein purpura (HSP) is the commonest small vessels vasculitis, inflammatory and immune-mediated disease affecting mainly children. It is generally characterized clinically by nonthrombocytopenic purpuric rash, non-deforming arthritis, gastrointestinal involvement, and nephritis. Non-thrombocytopenic purpura is the predominant clinical feature followed by arthritis, abdominal pain, and glomerulonephritis. Central nervous system involvement, intussusception, gastrointestinal bleeding, pneumonia, and orchitis are occasional clinical features [1]. HSP is the most common vasculitis in children and can lead to nephritis in about 30% of the cases. It affects all ages, but 9 out of cases are generally found in those less than 10 years of age. About 20 cases per 100,000 have been reported worldwide per year. Renal involvement has been reported to be the prime cause of

mortality in children with HSP [2,3]. Majority of children presented with microscopic or gross hematuria, proteinuria, nephrotic syndrome, acute nephritis, rapidly progressive glomerulonephritis (RPGN), and renal failure [4]. The prognosis for HSP is favorable generally without renal involvement [5, 6]. Recent data suggested that HSP is not a self-limited disease as previously thought and some patients may eventually develop into end-stage renal disease [2, 3]. In children with HSP, kidneys are affected in almost half the cases. This happens when the tiny blood vessels in the kidneys become inflamed, causing a leakage of blood cells and protein into the urine. The main symptom of HSP is small rashes and spots that look like blood spots or bruises. HSP can be reoccurring in 1/3rd of the cases, usually within 4-5 months of initial onset. The recurrence rate is 2.7% - 30% depending on different variables like age, gender, ethnicity, and so on. The objective of our study is to analyze clinical characteristics, identify severe HSP nephritis and start early aggressive immunosuppressive therapy to prevent chronic kidney disease.

METHODOLOGY AND MATERIALS

The medical record of 31 HSP patients was evaluated in the Nephrology and Rheumatology Department of Dhaka Shishu (Children) Hospital from July 2017 to December 2019. The HSP patients were diagnosed with typically distributed palpable purpura or petechiae and at least one of the following findings arthralgia or arthritis, abdominal pain, or nephritis. The diagnosis of HSP fulfills the 1990 criteria of the American College of Rhematology [7]. HSP nephritis was defined as the presence of gross or microscopic hematuria (more than 5 RBC/HPF in centrifuged urine) RBC cast with or without proteinuria [8]. The criteria for inclusion were age <16 years and exclusion include thrombocytopenia, other systemic diseases (eg SLE), drug hypersensitivity, and incomplete data. Epidemiological data, clinical and laboratory findings were reviewed. Age, sex, seasonal variation, clinical data including skin lesion, renal involvement hypertension, joint pain, and gastrointestinal symptoms were reported. The lab test performed were Hb, WBC, platelet, blood urea, serum creatinine, serum albumin, cholesterol, CRP, C_3, C_4, anti-d_s DNA, urinalysis for microscopy, culture, and spot/24 hours urine protein creatinine ratio. Renal biopsy was done in patients with nephrotic range proteinuria, acute nephritis, and acute worsening of renal function to exclude crescentic glomerulonephritis or acute tubular necrosis. Renal pathology data included deposition of IgA, IgG, IgM, C_3, C_4, C1q, and fibrinogen in the kidney. The treatment for each patient was recorded including supportive care antihypertensive, ACE inhibitor, and immunosuppressive drug. The statistical analyses were conducted using SPSS version 20. P value<0.05 was considered statistically significant.

Inclusion Criteria

- Children under 16 years of age
- Presence of microscopic hematuria
- Proper authorization is taken from legal guardians

Exclusion Criteria

- Mentally ill.
- Unable to answer the criteria question.
- Exclude those affected with other chronic diseases etc.

RESULTS

Among 31 patients 23 (74.2%) male and 8 (25.8%) female. The mean age was 8.63±2.53 years (range 4-14 years). The mean age of renal involvement was 9.5 years. Mean duration of disease 21.19 ±11.54 days. Most children are affected during winter and spring (29%). Almost all children (96.8%) presented with a rash. 48.4% of patients had a fever, abdominal pain was noted in 23 (74.19%) patients. Joint pain was reported in 16 (51.6%) patients. Renal involvement was present in 18(58%) patients commonly in the form of proteinuria in 18 (58.6%) patients and hematuria in 15 (48.4%) patients. Both hematuria and proteinuria were evident in 14 (45.16%) patients while one patient had hematuria only. 6 patients had hypertension. 9 (29%) patients developed acute kidney injury. Occasional complications include convulsion (6.4%), intestinal obstruction (5.2%), septicemia (5.2%) and pneumonia (2.6%). Lab analysis showed thrombocytosis in 17 (54%) patients, leucocytosis was present in 19 (61%) patients, hypoalbuminemia was present in 18 (58%) patients. C3 was low in 9 (29%) patients, C4 low in 5 (16%) patients. A kidney biopsy was done in 10 patients. IgA deposition and mesangial cell proliferation were the most common pathology. 4 patients had less than 50% crescent. Regarding treatment 12 patients treated with methylprednisolone and MMF. 8 patients goes into remission after taking oral prednisolone. 1 patient took cyclophosphamide, 1 patient took tacrolimus as there was no response after taking MMF. 6 patients took ACE inhibitor, 2 patients need dialysis. Most of the children (90.3%) achieved remission though 2 patient died during admission and 1 patient left the hospital before improvement and recovery.

Table-1: Patient's demographic and clinical characteristics at presentation(n=31)

Characteristics	Number	Percentage
Age(years)		
Mean±SD	8.63±2.53	
Minimum-Maximum	4-14	
Gender		
Female	8	25.8
Male	23	74.2
Etiology		
Unknown	23	74.2
Upper Respiratory Tract Infection(URTI)	8	25.8
Seasonal Pattern		
Summer	4	9.9
Spring	9	29.0
Winter	18	58.1
Place of residence		
Urban	8	25.8
Rural	23	74.2
Onset pattern of Disease		
First	29	93.5
Recurrent	2	6.5
Duration of Disease(days)		
Mean±SD	22.19±11.54	
Minimum-Maximum	7-60	
Fever	15	48.4
Oligouria	10	32.3
Hypertension	6	19.4
Convulsion	3	9.7
Rash	30	96.8
Site of Rash		
Upper & lower limb	4	12.9
Lower limb	21	67.7
Lower limb & buttock	5	16.1
Joint Symptom	16	51.6
Abdominal Pain	20	64.5
Vomiting	12	38.7
Melaena	5	16.1
Hematemesis	4	12.9
Haematuria	15	48.4
Proteinuria	16	51.6
Miscellaneous		
pneumonia	1	3.2
Respiratory distress	1	3.2
Septicaemia	2	6.5
Urinary tract infection	1	3.2

Table-II: Laboratory parameters at presentation (n=31)

Laboratory Parameters	Number	Percentage
Biochemical parameters		
Hb%		
Mean±SD	10.34±2.2	
Minimum-Maximum	4.80-15.20	
WBC(Mean±SD)	29637.58±4568.17	
Platelet(Mean±SD)	426714.28±125019.65	
Haematuria(RBC present)	15	48.4
Blood Urea		
Mean±SD	5.95	
Min-Max	2.80-46.00	

Laboratory Parameters	Number	Percentage
S. Creatinine		
Median	45.2	
Min-Max	2.07-651.00	
Urine Albumin(Median)	23.60	
Urine Albumin(3+)	5	16.1
Immunological Parameters		
C3(Decreased)	9	29.0
C4(Decreased)	5	16.1

DISCUSSION

According to our study mean age of HSP was 8.63± 2.53 yrs (range 4-14 years). Previous studies described HSP children are mainly between the ages of 5 and 15 yrs and the mean age is 5 to 6 yrs [6, 8, 9, 10, 11, 12]. Several studies reported that renal involvement in HSP is more common in older children [13,14]. In Sano and Colleagues' study [8] children older than 4 years had a higher risk of renal involvement. Our study also found older age had an increased risk of renal involvement. The mean age of renal involvement was 9.5 years (range 6-14 years) in the present study. In another report, renal involvement and gastrointestinal complications were less frequent in children less than 2 years [8]. In the present study among 31 patients 23 (74.2%) male and 8 (25.8%) female. The male-female ratio 2.8:1. Gender discrepancy about the HSP incidence like boys is more affected than girls was also reported in other studies [9, 15, 16] The incidence of upper respiratory tract infection (URTI) before HSP onset is 36-63% in the literature [17-20] and lower 25.8% in our study. In the present literature highest incidence in winter (58.1%). This finding was similar to some previous reports [6, 8, 9, 12, 21, 22]. Increased frequency in cold months suggests a correlation with HSP with upper respiratory tract infection and this was similar to other studies [9, 12, 13]. Allergy, vaccination, insect bite, and drugs may also act as a possible trigger for HSP onset which is alike to various other literature [24, 25]. Many HSP patients presented with purpuric rash at disease onset. We found almost all our children (96.8%) presented with petechia/purpura in the lower limbs and buttocks. In view of purpura distribution, a study by Kang [26] revealed higher involvement of the upper limb. Among gastrointestinal involvement in our research abdominal pain (64.5%) was most frequent followed by vomiting (38.7%), Malena (16.1%), and hematemesis (12.9%). Malena is assumed to occur in HSP patients with severe abdominal pain [9, 17, 27]. Joint symptom-was noted in 51.6% patients. Knee and ankle joints were affected usually which is correspond to Sandra and co-workers [9]. Renal involvement was present in 18 (58%) patients in the form of hematuria, proteinuria, hypertension, and acute kidney injury in the present study. Sixty-five (33.5%) of 194 patients developed renal involvement in a Japanese study [28]. Hypoalbuminemia was present in 18 (58%) patients in our study. All those patients had proteinuria. Outi Jauhola *et al*. [29] reported 49 patients of them had subnormal serum albumin level without renal loss which arouses suspicion of intestinal protein loss. Studies on complements in children showed C3 low in 9 (29%) patients and C 4 low in 5 (16%) patients. Previous research reported that some patients showed a transient decrease in C3, but low levels are neither risk factor of renal involvement nor a prognostic outcome [30, 31]. However other reports revealed that it is important whether complement activation is required for the pathogenesis of HSP [32]. In our study 12 (38%) HSP nephritis patients were treated with methylprednisolone and MMF. 8(25%) patients go into remission after taking the only steroid. 7 (22%) patients achieved spontaneous remission without steroids. Mollica *et al*. [33] suggested that treatment with prednisolone (1mg/kg per day) for all patients with HSP should be started at the onset of the disease. However, in view of the favorable course of purpura nephritis, the study of Glassock, Cohen, and Adler [34] found that aggressive management is not generally indicated. We also found in our study that not all patients required prednisolone routinely.

Limitations of The Study

The study was conducted in a single hospital with small sample size. So, the results may not represent the whole community.

CONCLUSION

HSP patients displayed diverse clinical features and the outcome of HSP is generally favorable without renal involvement. The present study found renal involvement more frequent in the older age group. The mean age of renal involvement was 9.5 years in our study. Though glucocorticoids effectively treated all the symptoms of HSP, not all HSP patients required glucocorticoids routinely. Immunosuppressive drugs like MMF/ cyclophosphamide need to start as early as possible to prevent only severe renal damage and chronic kidney disease. So early diagnosis of severe HSP nephritis after analyzing the clinical data and early referral to nephrology center for biopsy, immunosuppressive therapy, or dialysis is crucial for renal survival.

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