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Original Article

Frequency of renal manifestations in patients of Henoch-Schonlein purpura

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Abstract

Background Henoch-Schonlein Purpura (HSP) is a multisystem disorder that has cutaneous, musculoskeletal, gut and kidney manifestations. It is the most common childhood systemic vasculitis and is less frequent in adults. It carries significant morbidity and mortality especially in context of renal outcomes. The purpose of this survey was to determine the frequency of renal manifestations in patients of HSP presenting to a tertiary care center in Pakistan.

Methods The study was conducted in King Edward Medical University (KEMU)/ Mayo Hospital Lahore. 32 patients with clinical HSP were included and detailed history and examination was done followed by laboratory investigations. Patients were followed up for 6 months. All data was recorded in a predesigned proforma.

Results 18 male and 14 female patients in the ratio of 1.3:1 with mean age 26.9±14 years were enrolled. Palpable purpura, abdominal pain and joint pain occurred in 100%, 50% and 41% cases respectively. Anemia (53%) and thrombocytosis (37%) were the most frequent abnormalities on laboratory workup followed by proteinuria (28%). Blood renal parameters were deranged in only 15% and improved on follow-up. More than 90% cases recovered completely without any residual damage.

Conclusion Urinary and blood renal parameters that were deranged among the small percentage of our patients improved over time. HSP in our cohort had very good clinical and renal prognosis.

Key words
Henoch-Schonlein Purpura, IgA vasculitis, IgA nephropathy.

Introduction

Henoch-Schonlein purpura (HSP) also known as Immunoglobulin A (IgA) vasculitis, is a systemic disorder involving immune-complex mediated small vessel damage.[1] HSP is the most common childhood systemic vasculitis and is less frequent in adults.[2] Its incidence varies from 3.0 to 26.7 per 100,000 children, and 0.8 to 1.8 per 100,000 adults each year.[3] The majority of cases occur in the first decade of life and the prognosis gets worse with increasing age.[4]

The diagnosis of HSP is clinical with the classical triad of purpura, arthritis and abdominal pain, however, several other manifestations can arise from involvement of virtually any internal organ.[5] Cutaneous palpable purpura is a prerequisite for diagnosis.[6] In addition, HSP presents with pain and swelling in large joints of lower limbs, although the arthritis is transient and non-erosive.[7] Abdominal symptoms involve colicky abdominal pain and occasionally vomiting.[7,8]

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The overall prognosis is excellent in the majority of cases with complete recovery in four to six weeks. Occasionally chronic remitting and relapsing cases occur with complications such as renal damage, hepatosplenomegaly, myocardial infarction, pulmonary hemorrhage, pleural effusion, intussusception, gastrointestinal bleeding, bowel infarction and seizures.[9]

The most common risk factor for poor prognosis in HSP is renal damage. Renal involvement occurs in 50% cases but long term kidney damage only occurs in 5% patients.[9] The clinical presentation may vary from mild asymptomatic hematuria, to fully developed nephritic syndrome. Most cases develop renal abnormalities early in the disease course. Risk factors for renal damage include age more than 10 years, male gender, persistent purpura and gastrointestinal symptoms and pre-existing renal disorder.[10-12]

The objective of our study was to assess frequency of renal manifestations in patients of HSP. According to our knowledge no such study has been carried out in Pakistan.

Methods

The study was conducted in Dermatology Department of KEMU/ Mayo Hospital Lahore in collaboration with Nephrology Department after permission from Institutional review board from Jan to June 2019. Patients suffering clinically from HSP of all age groups and gender were included. Those having thrombocytopenia or other systemic vasculitis were excluded. Following Laboratory protocol was followed: Anemia if hemoglobin was less than 12 g/dl, Leucocytosis: White cell count more than $11x10^9$/L, Thrombocytosis: Platelet count more than $450x10^9$/L, Elevated 24 hours proteins: more than 80mg/24 hour urine, Pyuria: More than 4 pus cells per high power field, Raised Serum Creatinine: more than 1.2 mg/dl, Raised Blood Urea: more than 40 mg/dl, Hyponatremia: Sodium less than 135 mmol/L, Hyperkalemia: Potassium more than 5 mmol/L. Total 32 patients were enrolled. After detailed history and examination, laboratory investigations were done. Patients were followed up clinically for six outpatient visits over a total of 6 months (at presentation, 1 week, 2 weeks, 1 month, 3 months and 6 months) and complete clinical examination and relevant investigations were repeated. All data was recorded in a predesigned proforma.

Results

A total of 32 patients with HSP were enrolled in this study. Among these there was a slight male predominance at 56% (N=18) compared to females that comprised 44% (N=14). The mean age was 26.9±14 years and range was 7-60 years **(Table 1)**. Pediatric age group (upto 18 years) represented 11 cases (34%) while the rest were adult patients.

Table 1 Demographic data and etiologic factors in patients with HSP.

Age (years)	
Mean±SD	26.9+14
Median	23
Range	7-60
Adult/ pediatric	
Adults	21
Children	11
Adult:Pediatric ratio	1.9:1
Gender	
Males	18
Females	14
Male:Female ratio	1.3:1
Socioeconomic status	
0-10,000 PKR/Month	13 (40.6%)
10,000-25,000 PKR/Month	16 (50.0%)
25,000 and above PKR/Month	3 (9.4%)
Etiology	
Idiopathic	20 (62.5%)
Streptococcal infection	10 (31.2%)
Other causes	2 (6.2%)

SD, standard deviation; PKR, Pakistani Rupee.

Table 2 Salient Clinical Features of patients with HSP (n=32).

Signs and Symptoms	*n (%)*
Cutaneous Features	
Palpable Purpura	32 (100%)
Urticaria	20 (62.5%)
Vesicles	16 (50%)
Bullae	6(18.8%)
Necrotic Ulcers	1(3.1%)
Gastrointestinal Features	
Abdominal Pain	16 (50%)
Abdominal Tenderness	9 (28.1%)
Hepatomegaly	4 (12.5%)
Splenomegaly	1 (3.1%)
Joint Features	
Joint Pain	13 (40.6%)
Joint Swelling	4(12.5%)
Joint Redness	2 (6.2%)
Ocular Features	
Eye Pain	6 (18.8%)
Eye Redness	6 (18.8%)
Cardiopulmonary Features	
Shortness of breath (mild)	14 (43.8%)
Blood stained sputum	1 (3.1%)

Table 3 Laboratory Findings in patients with HSP (n=32).

Findings	*n (%)*
Complete Blood Count	
Anemia	17(53.1%)
Leucocytosis	7 (21.9%)
Thrombocytosis	12(37.5%)
ASO titre	
Elevated	8 (25.8%)
Complement Levels	
Normal C4 level	32 (100%)
Urine Complete Examination	
Proteinuria	
+	2 (6.2%)
++	5 (15.6%)
+++	2(6.2%)
Hematuria	
+	1(3.1%)
+++	1 (3.1%)
Pyuria	4 (12.5%)
24 hours Urinary proteins	
Elevated	4 (12.5%)
Renal Functions Tests	
Elevated Urea/BUN	1 (3.1%)
Elevated Creatinine	1 (3.1%)
Serum Electrolytes	
Hyperkalemia	5 (15.6%)
Hyponatremia	1 (3.1%)

BUN, Blood Urea Nitrogen

Most of the individuals presented with first or second episode of HSP, 20 (63%) and 11 (34%) respectively, and only one person was experiencing his third episode at presentation. The duration of the current episode was up to 1 week in 20 cases (63%) and up to 2 weeks in 6 (19%) while the remaining 6 (19%) gave clinical history of more than 2 weeks. However, none of the cases had had symptoms for more than one month.

The causative agent was identified as streptococcal infection in about one third cases (N=10). But no specific cause could be identified in the majority of cases (N=20) (63%).

All the patients had cutaneous palpable purpura, half had abdominal pain (N=16) and 41% (N=13) had joint symptoms. In addition to purpura almost two third cases (N=20) had other cutaneous lesions including urticarial, vesicular or bullous eruptions or necrotic ulcers. Dyspnea was present in a significant portion of cases (N=14) (44%). About one third (N=10) (31%) had ocular involvement with eye pain and/ or redness. No chest pain or scrotal pain was reported. Hepatomegaly alone was observed in 3 cases (9%) while only one individual had hepatosplenomegaly. Splenomegaly alone was not seen in any patient.

Laboratory investigations at presentation demonstrated mild to moderate anemia (hemoglobin 8-12 g/dl) in about half the cases (N=17) (53%). Leukocytosis and thrombocytosis was present in 7(22%) and 12 (37%) individuals. One fourth (N=8) had raised antistreptolysin O (ASO) titer. Only one patient had significantly raised serum creatinine (2 mg/dl) although urinary abnormalities such as hematuria (N=2) (6%), proteinuria (N=9) (28%) and pus cells of more than 4 per high power field (N=4) (12%) were more frequent. Similarly 4 (12%) had raised 24 hour urinary protein

readings. Isolated proteinuria without hematuria occurred in 7 (22%), while no patient had isolated hematuria. Serum potassium was elevated in 5 (15%). C3 complement levels were raised in 2 cases (6%) while C4 levels remained normal in all patients.

All the patients were prescribed standard treatment according to their clinical condition. More than 90% (N=29) patients recovered completely within 6 weeks of symptom onset with no residual or recurrent abnormalities during follow-up. Two patients relapsed and one patient was lost to follow-up.

Discussion

HSP is the most common systemic vasculitis in the pediatric age group.[2] Although less common in adults it carries more morbidity especially in terms of renal prognosis.[10] Patients with HSP frequently present in the dermatological outpatient department due to the typical purpuric rash which is a prerequisite for the diagnosis of HSP.[6]

The mean age of our subjects was 26.9±14 years and age range was 7-60 years. Only one third were less than 18 years of age. However, most large epidemiological studies demonstrate pediatric age group as the mainly affected population.[4] The reason for this adult predominance in our study may be our relatively small sample size. In addition some pediatric HSP cases may have presented to the pediatric medical department and not to our dermatology outpatient and, therefore, would not have been enrolled in the current research. Our study showed a slightly higher male (N=18) to female (N=14) ratio (1.3:1). This is similar to several studies on HSP that demonstrate a male predominance.[2,3] On the other hand, some researchers have observed a slight female majority especially in childhood HSP.[13,14]

One third (N=11) of our patients gave a history of one previous episode of HSP, while almost two thirds (N=20) (63%) presented with the first ever episode. Trapani from Italy and Calvo-Rio from Spain also detected one third recurrence rate in their study on HSP.[2,15] Some studies from Israel and Taiwan, on the other hand, have identified a lower rate of recurrent HSP ranging from 2.7% to 16.4% especially in the pediatric age group.[16,17] This difference in our group may be due to predominance of adults who have a worse HSP prognosis. About two thirds (63%) of the patients presented within first week of symptom onset, while the remaining presented later. Range of duration of symptoms was 1-30 days. This early presentation of HSP cases is likely due to the prominent skin changes which are characteristic of the disease, and present early in the clinical course.[18]

The most common causative factor of HSP was a preceding infection especially streptococcal infection in about one third cases. However, no specific cause could be identified in the majority of our cases (63%). Blanco *et al*. also failed to identify the causative agent in more than two thirds of their subjects.[19] In contrast, many previous studies have identified several causative agents in more than half patients with HSP such as infections, drugs, vaccines.[2,18,20,21] It is possible that some adult patients in our study had previously experienced some subclinical infections and were unable to associate them with the current disease.

All the patients had cutaneous palpable purpura, half had abdominal pain and 41% had joint symptoms. These clinical findings agree with prior data that reveal similar rates (around 40-50%) of joint and gastrointestinal involvement.[22,23] There was no difference between adults and children in regards to abdominal symptoms. However, 11 out of 21 adults had joint involvement as compared to

only 2 out of the 11 children. Our findings support previous studies which demonstrate significantly more articular manifestations in adults.[24]

Laboratory workup revealed anemia, leukocytosis and thrombocytosis in 17 (53%), 7 (22%) and 12 (37%) cases, respectively. Kuret *et al*., in contrast did not observe any significant elevation in total leucocyte or platelet counts.[23] This difference could be attributed to the fact that only 10% of their patients had underlying infection as the triggering agent compared to 31% in our subjects. Renal blood markers were significantly deranged in only one of our subjects with serum creatinine value of 2mg/dl while serum potassium was elevated in 15%. Audemard-Verger and co-workers, in contrast, have observed a very high percentage of renal involvement in adult patients with 30% having renal failure at baseline.[10] This significant difference may be due to the older age range of their subjects (50.16±18 years) who might be more prone to renal injury from vasculitis. Urine analysis revealed isolated proteinuria in 22% and concomitant proteinuria and hematuria in 6% of our subjects. 24 hour urinary proteins were also raised in 12% individuals. Chen and fellow scientists detected similar values of proteinuria (27%) and hematuria plus proteinuria (2.5%) in their research.[18] However, hematuria alone was present in a much higher number of their patients (27%). This could indicate more renal damage in the cohort of patients observed by Chen *et al*. which translated into poorer prognosis compared to our subjects. Furthermore, Trapani *et al*. observed an even greater ratio of proteinuria (42%) in their subjects with 35% of their patients experiencing recurrences.[2] We noticed C3 complement levels elevation in 6% of our cases. However, previous researchers have detected low levels of C3 around 10%.[18] This difference might be due to less complement activation in our patients which led to better outcomes. C4 levels remained normal in all our patients.

More than 90% of our subjects had a complete recovery and no persistent or recurrent abnormality occurred during follow up. Two patients, both adults, relapsed and one patient was lost to follow up. The very good prognosis observed in our cohort agrees with several previous studies by other surveyors.[2,19,24] However, some studies demonstrate poorer prognosis in adult patients with HSP especially in terms of renal outcomes.[4] It is possible that some of our patients had subclinical renal damage not picked by routine urine analysis and renal function tests. This can be remedied by performing renal biopsies of all cases, but keeping in view the benign nature of the illness and lack of poor prognostic indicators this invasive procedure was not done. Furthermore, a longer follow up over several years might demonstrate a slightly higher recurrence rate in our cohort, but it was beyond the scope of the present study.

Conclusion

A small percentage of our patients had abnormal urinary abnormalities at presentation but none progressed to chronic renal insufficiency. Renal parameters improved over time in all our patients. HSP in our cohort had very good clinical prognosis, despite a higher ratio of adults surveyed.

Long-term morbidity of HSP is predominantly attributed to renal involvement. During the study period, no patient had renal insufficiency or end stage renal disease after various combinations of immunosuppressive treatment. It is recommended that patients with HSP nephritis are followed for longer periods of time with a regular measurement of renal function and proteinuria.

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