ORIGINAL ARTICLE

AGE RELATED CHARACTERISTICS OF CHILDREN AND ADOLESCENT WITH HENOCH SCHÖNLEIN PURPURA AND SYSTEMS INVOLVEMENT: AN EXPERIENCE FROM TERTIARY CARE CENTER

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Background: Henoch-Schönlein Purpura (HSP) is the most common vasculitis among children and adolescent characterized by skin, joints, renal and gastrointestinal involvement. There is different presenting feature of Henoch-Schönlein Purpura (HSP) and systemic involvement may vary at a certain age group. **Methods:** This was a ten-year retrospective cohort study done at a tertiary care hospital of Pakistan conducted from 2011–2020. Patients admitted with the diagnosis of Henoch-Schönlein Purpura (HSP) and in accordance with inclusion criteria were divided into groups based on their age, gastrointestinal symptoms and renal symptoms with the objective to compare the clinical features and investigations of Henoch-Schönlein Purpura (HSP) patients. Younger age group had patients age 7 years and less while the other group included patients who were older than 7 years. *p*-value <0.05 was considered as significant and SPSS 23 was used to analyzed the data. **Result:** Total 104 patients diagnosed with Henoch-Schönlein Purpura (HSP) were studied. Henoch-Schönlein Purpura (HSP) was more prevalent in males with an increased frequency during autumn and winter. Purpuric rash was present in more than 90% of the patients involved. Joint swelling was significantly (p=0.029) more common in the younger age group (73.3%) while renal involvement was seen more frequent in the older age group (57.1%) (p=0.002). Renal symptoms were less commonly seen in patients with GI involvement. There was no significant difference in platelet count, WBC count and ESR levels among any of the groups**. Conclusion:** Age related difference in presentation help us to anticipate more renal involvement in older children and adolescent likewise joint involvement is more commonly seen in younger children.

Keywords: Vasculitis; Purpura; Arthritis; Haematuria; Gastrointestinal Bleeding

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INTRODUCTION

Henoch Schönlein purpura (HSP) is the most common vasculitis in children. The annual incidence is of about 10 cases per 100 000 and majority of cases occurring in children between ages of 4 years and 6 years with Asian population being at the highest risk.[1,2] In 1800's Schoenlein first described the syndrome of acute purpura and arthritis in children and later its manifestations of colicky abdominal pain and of nephritis were reported by Henoch.[3]

HSP is a small vessel vasculitis manifested by leukocytoclastic angiitis as a consequence of IgA deposition in vessel wall.[4] It has an abundance of cytokines and inflammatory mediators. The exact cause of HSP is not known, but it is clear that IgA enhanced by TGF-β plays a critical role in immunopathogenesis of HSP. IgA has two subclasses, but HSP is associated exclusively with abnormalities of IgA1.[5,6] Frequently, serum levels of IgA higher than normal are seen in patients with HSP.[3]

Cutaneous purpura, arthritis, abdominal pain, gastrointestinal bleeding, and nephritis are the predominant clinical features of HSP.[5] Skin lesions which is the most common presentation in children with HSP is characterized by rash consisting of palpable purpura, 2–10 mm in diameter, concentrated, but not restricted to the buttocks and lower extremities.[7] Arthritis involving the lower extremities is the most common initial manifestation and may precede the onset of the purpura by up to a week in 15–25% of patients. HSP arthritis is usually oligoarticular and painful resulting in a difficulty to walk.[2,5,8] Gastrointestinal bleeding is usually occult, but rarely patient may present with gross bleeding or melanotic stools.[5] Renal manifestations with proteinuria or haematuria occur in 20–60% of children with HSP, of which 1% develop end-stage renal failure.[9]

HSP is generally considered a self-limiting disease and treatment is primarily supportive. Steroids have been noted to be helpful in severe gut disease and renal complaints. Relapse may occur in one-third of the patients, and are more frequent in those treated with Corticosteroids.[8] No specific treatment has yet been agreed for disease complications, but prognostic studies have determined that 6 months is appropriate to follow-up children and monitor for renal complications.[10] Long term outcome of patients with HSP is usually good, with occasional fatality associated with severe gastrointestinal and renal disease.[11] HSP in children has

been studied in Europe and America, however there still is scarce data from low middle income countries and especially from adolescent age group.[12] It is therefore need of time to describe our local data on different presenting feature of HSP and their relation with age and system involvement.

MATERIAL AND METHODS

This was a ten-year retrospective chart review of inpatient admissions for HSP patients from 1st January 2011 through November 31st 2020 at Aga Khan University Hospital Karachi, Pakistan. Data was collected and documented from individual patient's chart and online Patient care Software.

We included a total of 104 patients according to the criteria defined by the American College of Rheumatology (ACR).[3] It includes children and adolescent's ≤18 years at the disease onset with 2 or more of the following a) palpable purpura; b) bowel angina; c) gastrointestinal bleeding; d) haematuria; and e) no history of medication before the onset. The presence of palpable purpura was defined as a slightly elevated purpuric rash, bowel angina was referred as diffuse abdominal pain which worsened after meals. Gastrointestinal bleeding included occult bleed with a positive faecal occult blood test, gross bleeding that is visible to naked eye and melanotic stools. Microscopic haematuria was diagnosed when 5 or more red blood cells were seen at high power light microscopy while gross haematuria was defined as blood in the urine seen with the naked eye.

Patients with haematuria and/or proteinuria were included in the renal involvement group. Proteinuria was defined urine protein: creatinine (UP/UCr) >0.5 in children under 2 years of age, UP/UCr >0.2 in children over 2 years of age, proteinuria over 40 mg/m^2/hr or nephrotic range proteinuria (UP/UCr >2.0). Gastrointestinal involvement group included patients with abdominal pain, bowel angina, gastrointestinal (GI) bleeding and or intussusception. Mean characteristic of cohort in respect of gender, age at presentation, season, weight, height, signs and symptoms at presentation along with pertinent laboratory investigations for all participants were collected at the time of diagnosis. The patients were divided into two groups based on their age of presentation. Younger age group had patients aged 7 years and less while the older group included patients older than 7 years. Both the groups were then studied for their clinical features and prognostic outcomes. Children and adolescents who left the hospital before improvement and recovery were excluded from the study. Characteristics for the cohort were presented as descriptive statistics. Mean and standard deviation was described for continuous variables. Frequencies and percentages will be reported for categorical variables. Histograms and Shapiro Wilk was used to assess normality of data. Student *t*-test was used to assess significance between continuous data with normal distribution. Chi-square test was used to assess significance between categorical data. *p*-value <0.05 was considered as significant and SPSS 23 was used to analyzed the data.

RESULTS

A total of 104 patients were included in the study and were divided into two groups to manifest demographic data and clinical characteristics.

Younger age group had patients age 7 years and less while the other group included patients who were older than 7 years. Mean age of the younger group was 5.5±1.76 while that of the older group was 13.7±1.92. HSP was more common in the males in both the groups. An increased frequency of HSP was seen during winter and autumn season. (Figure-1)

Purpuric rash was present in more than 90% of the patients involved. Gastrointestinal involvement including symptoms such as abdominal pain, GI bleeding had similar frequency in both the groups. Intussusception was seen in 3 patients in the younger age group while none of the patients in the older age groups developed intussusception. Joint swelling was significantly (*p*=0.029) more common in the younger age group and was seen in 73.3% of the patients in this group. Renal involvement was significantly (*p*=0.002) more common in the older age group (57.1%) and haematuria was significantly more frequent symptom in this age group. (*p*=0.012) (Table-1)

Patients when grouped according to gastrointestinal (GI) symptoms showed that gastrointestinal involvement was more common in patients who did not have renal symptoms. Other symptoms including purpura, joint swelling, and edema had a similar prevalence irrespective of the GI symptom. (Table-2) Similarly when patients were categorized on the basis of renal involvement, GI symptoms were more commonly in the patients with no renal involvement (*p*=0.025). (Table-3) There was no significant difference in platelet count, WBC count and ESR levels among any of the groups.

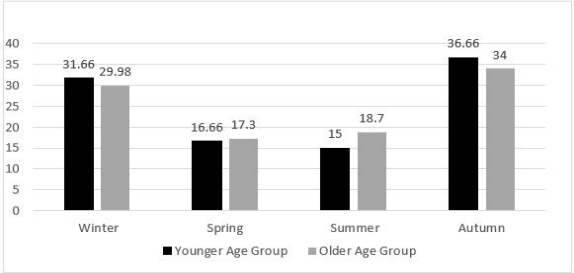

Figure-1: Seasonal Variations in frequency of Henoch Schönlein Purpura (HSP)

Table-1: Clinical findings in different age groups

Variables	Younger Age 60	old Age 42	*p*-value
Mean age (years)	5.5±1.76	13.7±1.92	
Gender (M:F)	1.4: 1	1.6:1	
Weight	15.53±1.39	34.78±1.81	
Height	100.31±1.59	145.87±2.01	
Purpura	58 (96.66%)	38 (90.47%)	0.191
Joint Swelling	44 (73.33%)	22 (52.38%)	0.029
Edema (soft tissue swelling)	3 (5%)	4 (9.52%)	0.374
Gastrointestinal involvement	46 (76.66%)	30 (71.42%)	0.55
Abdominal Pain	45 (75%)	29 (69.04%)	0.57
GI Bleeding	13 (21.66%)	10 (23.80%)	0.79
Intussusception	3 (5%)	0	
Renal Involvement	16 (26.66%)	24 (57.14%)	0.002
Hematuria	13 (21.66%)	19 (45.23%)	0.012
Proteinuria	7 (11.66%)	9(21.42%)	0.182
White blood cell (/µL)	11,360.85±2.23	10,900.34±2.68	0.52
Platelet (×1,000/µL)	320.65±3.21	360.98±2.19	0.67
C-reactive protein (mg/dL)	0.51±0.07	0.64±0.05	0.72

Table-2: GI Involvement and clinical and laboratory characteristics of HSP patients.

Variables	Renal involvement 40	No Renal involvement 62	*p*-value
Mean age (years)	13.2±0.78	8±1.12	
Gender (M:F)	1.4: 1	1.3:1	
Weight	34.40±1.45	20.69±1.73	
Height	146.93±2.25	123.19±2.3=92	
Purpura	39 (97.5%)	57 (91.93%)	0.24
Joint Swelling	26 (65%)	40 (64.51%)	0.96
Edema (soft tissue swelling)	4 (10%)	3 (4.83%)	0.314
Gastrointestinal involvement	25 (62.5%)	51 (88.25%)	0.025
Abdominal Pain	25 (62.5%)	49 (69.03%)	0.068
GI Bleeding	8 (20%)	15 (24.19%)	0.621
Intussusception	3 (7.5%)	0	
White blood cell (/µL)	98410±1.69	89102±1.84	0.71
Platelet (×1,000/µL)	310±1.56	345±1.62	0.39
C-reactive protein (mg/dL)	0.7±0.04	0.5±0.02	0.29

Table-3: Renal involvement and clinical and laboratory characteristics of HSP patients.

Variables	GI involvement 76	No GI involvement 26	*p*-value
Mean age (years)	10.41	9.34	
ender (M:F)	1.5: 1	1.4:1	
Weight	25.87±0.47	21.25±0.84	
Height	134.19±1.95	126.67±2.23	
Purpura	72 (94.73%)	24 (92.30%)	0.65
Joint Swelling	47 (61.84%)	19 (73.03%)	0.301
Edema (soft tissue swelling)	6 (7.89%)	1 (3.84%)	0.481
Renal Involvement	25 (32.89%)	15 (57.69%)	0.025
Haematuria	21 (27.63%)	11 (42.30%)	0.164
Proteinuria	8 (10.52%)	8 (30.76%)	0.014
White blood cell (/µL)	10,780±1.89	11,345±2.47	0.59
Platelet (×1,000/µL)	370±1.51	340±1.93	0.62
C-reactive protein (mg/dL)	0.65±0.06	0.59±0.08	0.86

DISCUSSION

Our retrospective study on HSP patients aimed to evaluate the clinical features of HSP patients with respect to their age and different system involvement. HSP is the most common cause of vasculitis in children most frequently from age 5-7 years with a slightly higher prevalence in males as compared to females. Previous studies have shown that male patients have more propensity toward the disease.[13–15] Our study yielded similar results with M: F being 1.4:1 in younger age group while 1.6: 1 in the older age group. The peak incidence of HSP was during winter and autumn, while the lowest number of cases were reported during summer which is consistent with literature, however the exact cause of increased incidence at a certain time of the year is not exactly known.[13,16] There was no difference in stature, weight, or laboratory findings between the two age groups.

HSP has a widespread clinical manifestation with palpable clinical purpura on lower extremities, arthritis, gastrointestinal involvement and renal involvement being the major clinical symptoms. The incidence of purpura was 96%, in the younger age group while 90%, in older age group which is consistent with Rostoker *et al* and Calvo-Rio *et al*.[17,18] GI involvement was slightly high in our cohort with 76.6% in younger patients and 71.4% in older group. Similar incidence of GI involvement was seen in a study done in Korea.[15] Joint involvement was seen to be significantly higher in the younger age group (73.3%) as opposed to the older age group (52.38%). These findings were consistent with the result of prior studies conducted to compare the symptoms of HSP in younger and older children.[13,15,16]

Rokoster in his study defined that the likelihood of renal involvement in HSP children increases with age.[17] Study done in China showed that older age group had significantly higher chances of developing renal symptoms and proposed that one major risk factor for development of renal symptoms could age greater than 7 years.[19] Ozen *et al* reported renal involvement in 45–85% of adult paediatric population while in only 20–60% of paediatric HSP.[20] In our study rate of renal involvement seen was 57% in the older age group which was significantly higher than the 26% incidence found in the younger age group which is a commonly observed finding in many previous studies.[15,21,22] In most of the adult children renal symptoms presented with symptoms of haematuria rather than proteinuria. Previously, nephrotic syndrome has been frequently seen in children of older age group, however nothing as such was demonstrated in our study and the incidence of proteinuria was almost similar in both the groups.[14,23]

An important and unique finding of our study also was that GI involvement was significantly higher in HSP patients with no renal involvement. These results were opposing to the study done in Korea which showed that risk of GI involvement had a direct correlation with renal involvement.[15] Similarly, when the HSP patients were group with respect to GI symptoms, the rate of renal involvement was significantly more in the group with no GI involvement. (Table 2)

A prognostic scoring system consisting of peripheral blood leukocyte, albumin, D-dimer, coagulation factor XII and potassium levels to assess the disease prognosis and gastrointestinal involvement has been previously proposed. (24) We studied the blood levels on White blood cell (WBC), Platelets and C-reactive protein (CPR) in both the group and noted no significant difference among the results. WBC count was within the upper normal limit in both the groups (11 x1000/ μL and 10 x1000/μL, respectively), while Platelet and CRP were within normal ranges. These results were similar with the findings of study by Lee *et al*. (15) However, more studies are needed to investigate the use of laboratory values as markers of HSP severity and for prognostic purposes.

The main limitation of our study was its retrospective nature. We suggest future prospective studies to further discuss the features of HSP in children and adolescent to anticipate early system involvement and making prompt steps for managing these patients.

CONCLUSION

Our study revealed significant difference in the clinical presentation of HSP patients when evaluated on basis of their age and system involvement. Joint symptoms were more common in the younger age group, while renal symptoms were seen widely in the older age group. One striking finding was the higher involvement of GI system in patients with no renal involvement. Haematuria was the major presentation in patients with renal involvement.

Conflict of Interest: None
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AUTHORS' CONTRIBUTION

DA and FS contributed to the conception and design of the study. MT contributed to data collection. DA and MT contributed to the analysis and interpretation of the data, DA and FS did the drafting and critical revision of the manuscript. All the authors have read and approved the final version of the manuscript

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