



Demographic, Epidemiologic and Clinical Analyses of Paediatric Patients Hospitalized with Henoch-Schonlein Purpura: A Retrospective Study

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ABSTRACT

Aim: Henoch-Schönlein purpura (HSP) is the most common systemic vasculitis in children. The purpose of this study was to assess the clinical, epidemiological, and laboratory features of 117 children diagnosed with HSP.

Materials and Methods: This study was conducted to evaluate the data of 117 children with HSP, retrospectively. The presence of the cardinal clinical findings such as purpura, abdominal pain, and arthralgia; and the presence of increased erythrocyte sedimentation rate, decreased serum C3 levels, leukocytosis, blood in the stool, haematuria, and proteinuria were assessed in children with HSP.

Results: Of the 117 patients enrolled in the study, 68 were males (58.1%) and 49 were females (41.9%). The median age was 85 (49) months. Purpuric skin lesions were detected in ninety-eight (97.9%) patients, arthritis/arthralgia in 71 (60.6%), gastrointestinal involvement in 52 (44.4%), and renal involvement in 27 (23%) patients. The median duration of hospitalization day was 6 (10) days. Non-palpable purpuric skin lesions mostly located on ankles were the most common involvement in the patients.

Conclusion: Non-palpable purpuric skin lesions were the most common presentations followed by arthritis/arthralgia, and gastrointestinal involvement in our patients. Seasonal distributions, gender, and ages of the patients were concluded to be noncontradictory compared with the literature. Although variable clinical findings in the patients were found, the cardinal features of HSP were determined in almost all subjects in this study.

Keywords: Henoch-Schönlein purpura, children, vasculitis, systemic manifestation

Introduction

Henoch-Schönlein purpura (HSP), also known as immunoglobulin A (IgA) vasculitis which mediates a type III hypersensitivity reaction, is the most common vasculitis that affects the small vessels of the skin, joints, gastrointestinal tract, and kidneys in paediatric patients. HSP was primarily identified by Heberden in 1801 and described as having a

relation with arthritis by Schonlein in 1837. The incidence of HSP is reported to be 10 cases per 100,000 yearly and it is generally seen during childhood between the ages of 5 to 15 years (1,2).

This vasculitis is described by the triad of palpable purpura, abdominal pain, and arthritis. Purpuric skin lesions are the most common clinical findings in HSP followed by joint, gastrointestinal tract, and kidney involvement.

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Palpable cutaneous purpura is the major clinical diagnostic lesion mostly located on the lower extremities and buttocks. The second common involvement is arthritis which occurs in around 75% of patients. This arthritis generally affects the knees and ankles. Gastrointestinal involvement including colicky abdominal pain, vomiting, and gastrointestinal bleeding occurs in 50-75% of patients. Renal manifestation is usually seen as microscopic haematuria and nephritic-nephrotic syndrome. Henoch-Schonlein purpura-associated involvements of neurological systems, cardiac systems, and the lung have also been reported during the disease in some studies (2).

Although the etiology of HSP cannot be clearly identified, the evidence of immunopathological mechanisms and possible trigger factors (upper respiratory system infections, drugs, vaccines, and other environmental exposures, etc.) have been reported in the literature (3). Leukocytoclastic vasculitis, which could be seen in other types of vasculitis, is characteristically demonstrated via skin biopsy. Renal and skin biopsies have displayed several abnormalities in IgA and IgA immune complexes (3,4). HSP is usually a benign and self-limiting disease. Despite the fact that the disease is self-limiting clinically, due to the severity of some systemic involvements, and in rare cases mortality, physicians have sought to investigate it.

Various studies have focused on the function of regional and other environmental impacts in the etiology of HSP for many years. This study aimed to analyse the clinical features of those paediatric patients hospitalized with HSP, and evaluate the epidemiologic characteristics, demographic characteristics, and possible etiologic factors of HSP.

Materials and Methods

The medical records of 117 children with HSP were assessed retrospectively. The children were admitted to Ege University School of Medicine, Department of Paediatrics, General Paediatrics Unit, Izmir, Turkey between January 2013 and December 2019. The diagnosis of HSP was made in accordance with the Paediatric Rheumatology International Trials Organisation (PRINTO) 2005 criteria (5). This study was a continuation of a retrospective clinical study of HSP published in 2014 (DOI number 10.4274/jpr.40085). The Ethics Committee of the Ege University Hospital approved the study (20-1.1T/43).

Detailed demographic characteristics were obtained from the parents with a structured questionnaire. The medical records of these patients were evaluated by physicians and the clinical and laboratory data were extracted from patients' medical files. Studied variables

including previous infections, vaccinations, and insect bites were recorded as precipitating factors.

As for the clinical characteristics, they were as follows: Microscopic haematuria was defined when the urine test result was >5 erythrocytes/mm³; gross haematuria was defined when blood in the urine could be seen with the naked eye; rash location was determined as where purpura particularly accumulated on the parts of the body. Joint involvement was described as the presence of joint swelling and/or limitation of joint movement. Gastrointestinal involvement was identified as one of the following: abdominal pain, vomiting, hematemesis, melena, or positive stool test for occult blood. Recurrence was defined as a case of HSP which had been in remission for at least 1 month presenting with new lesions on the skin or with other systemic manifestations.

The laboratory data were analysed and the sedimentation rate was defined as elevated when it was >20 mm/hour, and the presence of C3 levels <900 mg/L were accepted as low. IgA level, C-reactive protein (CRP) level, anti-nuclear antibodies, albumin, and serum sodium levels were also obtained from all patients.

Statistical Analysis

Statistical analyses were performed using SPSS version 21.0 for personal computers (Chicago, IL, USA). Descriptive statistics were used to summarise the demographics and clinical features of the patients. Chi-square test and Fisher Exact test were used to assess associations between two or more qualitative variables. Continuous values were expressed as frequency (percentage) and mean \pm standard deviation or median and interquartile range (IQR); and when appropriate, categorical variables were determined by percentages.

Results

Epidemiological Characteristics

Table I shows the demographic and epidemiological data of the subjects. The study group included 68 males (58.1%) and 49 females (41.9%). Their ages ranged from 12 months to 16 years (median age 6 years). It was found that 42 (35.8%) cases had been admitted to the ward during autumn (Figure 1). Prior to HSP onset, 50.6% of the patients had been recorded as being infected with an agent in their history, mostly upper respiratory tract infections. In regard to other trigger factors for HSP, 7 patients had enteritis, 3 had urinary tract infection, 1 patient was diagnosed with pneumonia. A predisposition factor was not found in 50.4% of the cases.

Clinical Characteristics

The clinical characteristics of the 117 patients with HSP are shown in Table II. The typical rash with purpuric lesions concentrated mainly on the buttocks and the

Age, month, median (IQR)	85 (49)
Gender	
Boys, n (%)	68 (58.1)
Girls, n (%)	49 (41.9)
Seasonal pattern, n (%)	
Autumn	43 (36.7)
Winter	32 (27.3)
Spring	25 (21.3)
Summer	17 (14.5)
Etiologic factors, n (%)	
URTI	46 (39.3)
Enteritis	7 (6)
Pneumonia	1 (0.9)
Urinary system infection	3 (2.6)
Unknown	59 (50.4)
Duration of hospitalization, day, median (IQR)	6 (10)
City, n (%)	
İzmir	71 (60.6)
Manisa	9 (7.6)
Balıkesir	8 (6.8)
Muğla	5 (4.2)
Uşak	5 (4.2)
Aydın	3 (2.5)
Other cities	16 (13.6)
URTI: Upper respiratory tract infection, SD: Standard deviation, IQR: Interquartile range, HSP: Henoch-Schönlein purpura	

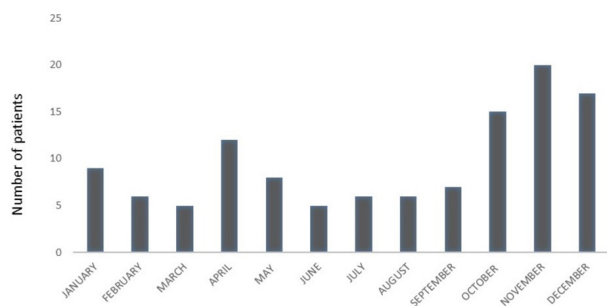


Figure 1. The seasonal pattern of patients

lower extremities was observed in all the patients, except for 2 patients who had presented with gastrointestinal symptoms before the rash appeared. Almost all the patients (97.9%) had the initial symptom, skin purpura, while it was accompanied by joint involvement in 71 (46.6%) patients. The duration of the illness was 6 days as a median value in all the cases.

Symptom	Cases (n)	Percentage (%)
First symptom		
Skin purpura alone	30	25.6
Purpura plus joint pains	46	39.3
Purpura plus sole abdominal pains	25	21.5
Purpura plus, abdominal pains and microscopic hematuria	15	12.9
Without purpura	1	0.8
Rash location		
Only LE	37	31.6
LE plus buttocks	44	37.6
LE plus buttocks plus UE	12	10.3
LE plus UE	8	6.8
LE plus buttocks plus trunk	7	6
LE plus buttocks plus trunk plus face	5	4.2
LE plus buttocks plus trunk plus face plus UE	3	2.5
Without purpura	1	0.8
Joint symptom (n=71)		
Sole ankle involvement	34	47.8
Sole knee involvement	8	11.2
Knee plus ankle involvement	12	16.9
Multiple joint involvements	17	23.6
Digestive tract symptom (n=52)		
Abdominal pains	52	100
Vomiting	30	57.6
Occult blood in the stool	25	21.3
Blood in the stool	3	5.7
Kidney symptom (n=27)		
Microscopic hematuria	15	55.5
Macroscopic hematuria plus proteinuria	10	37.1
Gross hematuria	2	7.4
LE: Lower extremities, UE: Upper extremities, HSP: Henoch-Schönlein purpura		

A skin biopsy was obtained from 75 (64.1%) patients. Thirty-five of the biopsy results showed classical leukocytoclastic vasculitis, and the others had non-specific features. Thirty-seven of 117 patients had localized edema usually appearing on the feet, scalp, hand, and scrotum. Joint involvement was the most common manifestation accompanying skin rashes. The joint regions are summarized in Table II. Twenty-seven (23%) patients had renal involvement, these 27 cases can be further classified as follows: microscopic haematuria in 15 (55.5%), gross haematuria in 2 (7.4%), and haematuria plus proteinuria in 10 children (37%). Renal biopsy was performed on 8 cases, one patient had focal mesangial proliferation with crescent lesions <50%, and the others had mesangial proliferation. Gastrointestinal involvement was detected in 52 (44.4%) patients and the most common symptom was abdominal pain. The number of vomiting presentations of these patients was 30 (57.6%) and 25 of the 52 patients with gastrointestinal involvement had positive occult blood in the stool. Two patients had been hospitalized with bloody stool. As an uncommon feature; orchitis was observed in 2 patients.

Those patients manifesting with arthritis were treated with 45 mg/kg/day ibuprofen and bed rest. Thirty-one of 117 HSP patients (93.3%) were cured. Due to the fact that 32 patients had system involvements (renal or gastrointestinal), they were treated with low dose glucocorticoid medication. A pulse steroid treatment was started for two patients due to being unresponsive to low dose glucocorticoid treatment.

Laboratory Findings (Table III)

The mean serum IgA concentration was 217.8±93.7 mg/dL and C-reactive protein levels ranged between 0-2 mg/dL

Table III. Laboratory findings of study group	
Parameters	Results
IgA (mean ± SD) mg/dL	217.8±93.7
CRP [median (IQR)] mg/dL	0.9 (2.3)
ESR mm/1 hour, n (%) (>20)	20 (26.5)
Albumin (mean ± SD) mg/dL	3.7±0.5
C3 [median (IQR)] mg/dL	134.5 (36.5)
C4 [median (IQR)] mg/dL	25.5 (14)
Positive ANA, n (%)	15 (12.8)
Histopathology (n=75)	
Leukocytoclastic vasculitis, n (%)	35 (45.4)
IgA: Immunoglobulin A, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, ANA: Anti-nuclear antibody, SD: Standard deviation, IQR: Interquartile range	

in 70 (70.7%) patients. The erythrocyte sedimentation rate was found to be high in 20 children (26.5%). Anti-nuclear antibody positivity was present in only 15 (12.8%) patients without any other autoimmune disease features.

Discussion

HSP described as a triad: palpable purpura, abdominal pain, and arthritis, is the most common vasculitis in childhood. Although several pathogeneses of HSP have been reported, the exact etiopathogenesis is still a mystery. One of the most widely accepted pathogeneses is its association with the accumulation of "immune complexes containing IgA" and "complement components" in the walls of small vessels (1,6). In this multisystemic disease, clinical features are usually self-limiting. However, the renal manifestations could result in chronic kidney disease in HSP patients (1).

In this study, we analysed the demographics, epidemiologic and clinical features of 117 children who were hospitalized with their first attack of HSP in Ege University Children's Hospital, General Paediatrics Unit. Similar to other epidemiologic studies for HSP, our study showed that the most common admission season was autumn. Several case series and longitudinal population-based surveys have reported that HSP in childhood is generally seen during both the autumn and winter seasons consistent with the literature (7,8). Our reports showed that 50.6% of patients experienced infectious diseases, of which, the most common one was upper respiratory tract infection. Gastroenteritis and urinary system infections have also been proposed as a trigger factor for HSP. Several studies have reported other trigger events such as vaccinations, drugs, insect bites etc. (1,9). Chen et al. (1) stated that 60.8% of their patients had an infection history before the onset of the clinical features of HSP as a possible predisposition factor. They also stated that food allergy or parasite infection may be a potential trigger factor for HSP (1). In our study, there were no relevant factors for HSP onset in 59 patients. Although there are a lot of suspected factors, the etiology of HSP has not been clearly determined yet.

HSP generally presents in children aged 5 to 15 years, predominantly in boys (10). In accordance with other studies, the demographic features of our study group showed that the median age was 85 months and more than half of the patients were male (58.1%). Almost all of the patients with HSP were between the ages of 5-10 years. Anil et al. (11) reported a retrospective analysis of 430 HSP children in which they found that the mean age was 7.9 years. The disease has generally been associated with a male dominance, however; some studies defined this feature as a reverse condition (12).

Skin purpura alone was found as the first manifestation for HSP in 25.6 % of the patients. All our patients showed the characteristic rashes on the lower extremities but some also on other trunk regions such as the arms or face. Four out of 117 patients had skin manifestations associated with bullous lesion concentrated on the lower extremities. The dominant initial symptom in this present study was skin rash and ankle involvement that required hospitalization for bed rest. Due to the fact that all our patients had not only skin manifestation but also joint involvement, our most frequent initial symptom was the coexistence of skin and joint involvement. The average time of the skin eruption was 14 days, ranging from 7 to 40 days in our patients. Chen et al. (1) determined that a majority of their HSP patients (69.1%) displayed skin purpura alone as the first symptom, purpura with abdominal pain was described in 11.7% and purpura with joint pain in 9.2% of their patients. Dolezalova et al. (13) also determined palpable purpura as the main symptom at onset of HSP in their study population.

Gastrointestinal system (GIS) involvement may occur in 50%-80% of patients with mild-moderate symptoms such as vomiting, nausea, abdominal pain, and transient paralytic ileus (14). Gastrointestinal haemorrhage, bowel ischemia/necrosis, intussusception, bowel perforation have also been reported in HSP. Detection of severe gastrointestinal bleeding is an important evaluation as it might engender a life-threatening event in 15 to 35% of patients, especially precedence of the typical rash (15,16). Before any skin manifestation is seen, bloody stool with abdominal pain may be initially treated as acute gastroenteritis (17). Intussusception is extremely rare, but it is the most common surgical indication for gastrointestinal involvement of HSP (18). Two cases in our study group had gastrointestinal bleeding which was not massive before skin manifestation. Cull et al. (19) investigated the clinical findings of 183 patients with HSP of whom 95 presented with GIS bleeding, and about 40% of their patients had bleeding before the typical lesions. Except for the bloody stool before purpura in two patients, our subjects did not show any rare presentations during the disease.

Renal involvement occurs in 40-50% of patients generally as microscopic haematuria and/or proteinuria. The manifestation of nephrotic syndrome or renal failure associated with renal involvement in HSP may manifest in a small percentage of patients. There is a risk of long-term renal sequelae in these patients and this risk increases with age. Renal histology generally shows a glomerular IgA deposition, endocapillary proliferation, epithelial crescents, subendothelial/subepithelial IgA deposits, and

fibrin deposits. Trapani et al. (10) presented a study that evaluated 150 patients with HSP and 81 (54%) children had had urinary abnormalities such as a mild nephropathy detected in 71 (47%) cases: 42 patients with isolated mild proteinuria, 6 with microscopic isolated haematuria, and 23 patients with both abnormalities and normal renal function. Tabel et al. (6) reported that renal involvement was observed in 26.1% of their 107 HSP children. The authors have found that renal involvement was significantly more frequent in patients older than 10 years and that for the group with renal involvement, the frequency of scrotal involvement was significantly higher than for those in the group without renal involvement. Another study from western Turkey reported the renal involvement of HSP to be 44.7% in their cohort (11). During clinical follow-up in our study, our patients were examined for renal involvement by daily urinalysis and 15 (12.8%) of 117 patients presented with microscopic haematuria and 2 (1.7%) had macroscopic haematuria.

Although the dominant involvements of HSP are skin, joint, gastrointestinal, and kidney; infrequent and unusual system manifestations including cerebral vasculitis, scrotal or testicular haemorrhage, and interstitial pulmonary haemorrhage have been described. Neurological involvement of HSP might be present with obtundation, seizures, paresis, and posterior reversible encephalopathy syndrome, etc. There have also been reports of other interesting admission features of HSP in the literature such as orchitis, myositis, carditis, pulmonary haemorrhage, and anterior uveitis. Di Pietro et al. (20) reported a review of 23 paediatric cases with lung involvement associated with HSP. Those cases presenting with the pulmonary symptoms included cough, haemoptysis, epistaxis, dyspnea, tachypnea, chest pain, and shortness of breath through to acute respiratory failure. Therefore, atypical presentations affecting multiple systems should be considered in the outcome of HSP and the possibilities of different responses (20-22).

Study Limitations

There are some limitations to this study. The major limitation factor was the small number of patients. The first reason is that we did not include those patients treated and followed up in the outpatient polyclinics and emergency services of our centre. The second limitation is that as a general rule in our outpatient polyclinics, patients with HSP associated with skin manifestation alone are not hospitalized. Also, we did not focus on the identification of infectious agents that could have been associated with the triggering of HSP. It could have given clinicians an idea of

which agent might be the trigger factor. Finally, we could not obtain skin biopsy from all study groups which could have ruled out other vasculitic disorders.

Conclusion

HSP is the most common vasculitis and it may be associated with risks of various complications in childhood. The underlying mechanisms of HSP's characteristic findings have not been exactly defined yet. This index study presents a descriptive analyse of paediatric patients in Ege University Children's hospital during a 6-year-period. Further studies are needed to investigate the influence of its pathogenesis in these cases and to find new mechanism that may play a role in following up children with HSP.

Ethics

Ethics Committee Approval: The Ethics Committee of the Ege University Hospital approved the study (20-1.1T/43).

Informed Consent: Informed consents were not required because the study was conducted retrospectively.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Data Collection or Processing: Ş.G., B.E.D., A.A., Analysis or Interpretation: Ş.G., B.E.D., A.A., Writing: Ş.G., B.E.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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