

Henoch-Schonlein purpura in Saudi Arabia: A retrospective study of 27 children in Taif region.

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Abstract

Objective: The aim of this retrospective study was to assess epidemiologic, demographic characteristics and clinical findings of Henoch-Schönlein purpura (HSP) in the Taif region of Saudi Arabia.

Methods: Records of 27 patients who were followed-up with the diagnosis of HSP between January 2012 and December 2015 in the department of pediatrics in Alhada armed forces hospital of Taif region. Demographic characteristics of the patients, season of presentation, clinical findings, triggering factors, laboratory data, and the duration of follow-up periods were evaluated.

Results: Of the 27 patients, 14 were boys (52%) and 13 were girls (48%), with a ratio of 1.1:1. Ages ranged from 2 years to 18 years, with a mean of 8.3 years. About 45% of the patients had a history of preceding upper respiratory infection. All of them had the typical skin rash. The percentages of joint, gastro-intestinal and renal manifestations were 85.2%, 77.8% and 37%, respectively. Testicular involvement was found in two patients, while no involvement was recorded for the central nervous system.

Conclusion: It is obviously that HSP patients could have various clinical symptoms and exceptional complications; however, it can lead to long-term illness particularly in patients with severe kidney involvement. In this study, there were mean age and season distribution differences for the HSP patients in Taif region comparing to other area in KSA.

Keywords: Children, Henoch-Schönlein purpura, Abdominal pain, Joints, Renal involvement, Saudi Arabia.

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Introduction

Henoch-Schönlein Purpura (HSP) is the most commonly vasculitic disease observed during childhood. It is characterized clinically by a generalized palpable purpura, arthritis, arthralgia, nephritis and gastrointestinal symptoms (abdominal pain, GI bleeding). HSP was first recognized in 1801 by the physician Heberden and next in 1808 by the dermatologist Willan. However, the illness was named by two German physicians Henoch and his teacher Schönlein in 1837 [1]. Schönlein defined the correlation between purpura and arthritis, while Henoch discovered its association with abdominal pain in 1874. Also, Henoch discovered the association between purpura and renal involvement [2].

It is a systemic vasculitis disease with unknown etiology and distinguished by skin, joint, Gastrointestinal System

(GIS), and kidney involvements [3]. Even though HSP can happen in all age groups, it is most commonly occurred in childhood. The annual incidence has been reported as 10-20 cases per 100,000 [2]. HSP is more commonly occurred in winter and spring. Usually boys are affected more than girls. 75% of the children patients are under 8 years of age, while 90% are less than 10 years of age. So, in average, the mean age of HSP patients in several studies is 6 years [4-6].

Although the etiology of HSP is not well known, several factors considered as a reason for the disease include infections (bacterial, viral, parasites), medications, vaccines, tumors, insect bite, and some foods [7-9]. From literature, the most important significant factor indicating long-term prognosis is the severity of kidney involvement [10]. Also, the antibody immunoglobulin A (IgA) and some proinflammatory cytokines have a key role in the

pathogenesis of HSP [11]. It is a well-known that the typical clinical characteristics involved in HSP are the triad of palpable purpura, abdominal pain, arthralgia and arthritis. While, progressive renal function injury, bowel perforation, central nerve system involvement are rare. The existence of purpura, which is non-thrombocytopenic, is the main part for the diagnosis of HSP. Regularly, the purpura is located on lower extremities and buttocks parts [12]. Finally, in general HSP is considered benign, self-limited and the treatment is supportive.

The aim of this retrospective study is to assess the demographic and epidemiologic characteristics of HSP in Saudi children reside in Taif governorate. It is believed that the clinical features could help doctors to make the correct diagnosis and deliver the correct medicine and nursing.

Methods

Records of patients who were followed-up with the diagnosis of HSP between January 2012 and December 2015 in the department of pediatrics of Alhada armed forces hospital, Taif region, were retrospectively evaluated. The study was conducted and approved by the research and ethics committee of the participating hospital. The patients were re-assessed according to EULAR/PRINTO/PRES criteria and those having the diagnostic criteria were involved [13]. Data on the following items were analyzed: age, gender, season of presentation, complaints on admission, triggering factors, clinical manifestations (including location of skin and joint lesions, gastrointestinal and renal manifestations), weight, height, blood pressure, complete blood count, C-reactive protein level, erythrocyte sedimentation rate, albumin level, fecal occult blood (FOB), complete urinalysis, type of treatment, and follow-up periods.

Hypertension was determined as a systolic and/or diastolic blood pressure of ≥ 95 percentile using 3 separate measurements according to age, height, and gender [14]. Joint involvement was defined as joint swelling and/or functional limitation of joint. GIS involvement was classified as stomachache and/or faecal occult blood positivity, presence of melena, hematemesis, hematochezia, or invagination [15,16]. Recurrence was characterized as new skin rashes refined at least 4 weeks after disease recovery or return of other signs [17]. Kidney involvement was described as microscopic (presence of erythrocytes by ≥ 5 in the centrifuged urine at zooming power of 40X) or macroscopic hematuria and/or proteinuria (presence of protein >4 mg/m²/h or protein/creatinine >0.2 mg/mg creatinine in 24 h urine) and/or reduced kidney function or nephrotic syndrome [18].

Statistical Analysis

The results presented as mean \pm Standard Deviation (SD) for continuous variables. The Microsoft Excel 2010 was used in such analysis. Categorical variables were expressed by percentages.

Results

This retrospective study was conducted on children during the period of January 2012 to December 2015 to evaluate the clinical course and outcome of the children with HSP. The study included 27 Saudi children as a primary presentation with HSP. Of these, 14 were boys (52.8%), giving a male to female ratio of 1.1:1 (Table 1).

The age range was from 2 to 18 years (mean age 8.3 years). The age and gender distribution showed that most HSP children (20 cases, 74%) were less than 10 years old, while 7 cases of HSP children (26%) were between 11 and 18 years old (Figure 1). This All 27 cases It was found that 12 cases (44.5%) occurred in autumn, 9 cases (33.3%) in summer, 4 cases (14.8%) in winter and 2 cases (7.4%) in spring (Table 1).

Epidemiologic features of 27 patients are presented in Table 1, while the distribution of clinical findings of the patients is presented in Table 2. In less than half of the patients (n=12; 44.5%), upper respiratory tract infection

Table 1. Epidemiologic factors in 27 patients with Henoch-Schönlein purpura

	n (%)
Age at onset (years)	
Range	2-18
Mean	8.3
Gender	
Male	14 (52)
Female	13 (48)
Male to female ratio	1.1:1
Seasonal distribution	
Fall	12 (44.5)
Summer	9 (33.3)
Winter	4 (14.8)
Spring	2 (7.4)
Triggering factors	
Fever alone	15 (56)
URTI*	12 (44.5)
Gastrointestinal	1 (3.7)

*URTI: Upper Respiratory Tract Infection

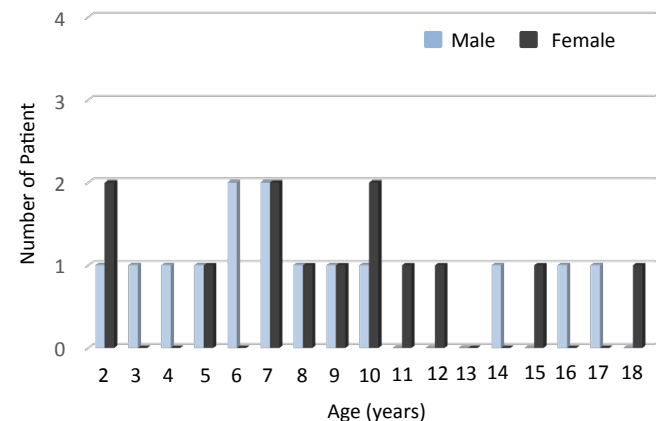


Figure 1. Age and gender distribution of 27 children with Henoch-Schönlein purpura

Table 2. Clinical features of 27 patients with Henoch-Schönlein purpura

	n (%)
Skin purpura	27 (100)
Rash location	
Lower limb	22 (81.5)
Buttocks	7 (26)
Face	2 (7.4)
Arms	2 (7.4)
Abdomen	1 (3.7)
Joint involvement	
Arthralgia	17 (63)
Arthritis	6 (22.2)
GIS involvement	
Abdominal pains	21 (77.8)
Bloody stool	13 (48)
Renal involvement	
Microscopic hematuria	7 (26)
Macroscopic hematuria	2 (7.4)
Proteinuria	7 (26)
Hypertension	2 (7.4)
Nephrotic syndrome	1 (3.7)
Acute kidney injury	1 (3.7)
Testicular involvement	2 (7.4)
CNS	0 (0.0)

CNS: Central Nervous System; GIS: Gastrointestinal System.

(URTI) preceded the onset of the rash by a few days to one week, whereas 15 cases (56%) had fever before the onset of the rash. Clinically, rash was presented in all patients. The purpura lesions of most patients were concentrated on the lower limb and buttocks. Joint involvement occurred in many HSP children (23 cases; 85.2%). Arthralgia and arthritis occurred in 17 (63%) and 6 (22.2%) of the patients, respectively. Ankle joints were most frequently affected, followed by knees, wrist and elbow.

Gastrointestinal tract (GIT) was the second most common system involved and manifested as abdominal pain in 21 cases (77.8%) and bloody stool in 13 cases (48%).

Renal involvement was observed in 10 cases (37%). Of these patients, 7 cases (26%) displayed microscopic hematuria; 2 patients (7.4%) had macroscopic hematuria; 7 cases (26%) had proteinuria, while 2 children (7.4%) were hypertensive. Nephrotic syndrome was documented in one case (3.4%). Two cases (7.4%) reported testicular involvement in the form of scrotal swelling. Central nervous system (CNS) was not detected in any patients. Other laboratory findings of the acute phase were evaluated and presented in Table 3.

Based on this evaluation, an increased ESR (ESR>20 mm/h) was reported in 12 patients (40.7%). Thrombocytosis (platelets > 500 × 10⁹/L) was detected in 4 cases (14.8%), leukocytosis (WBC>12 × 10⁹/L) documented in 3 patients (11.1%) and serum C3 (<900 mg/L) decreased in one patient (3.7%).

Fifteen cases (55.5.7%) received prednisolone with

Findings	Positive cases number (%)
Thrombocytosis (platelets>500 × 10 ⁹ /L)	4 (14.8)
Leukocytosis (WBC>12 × 10 ⁹ /L)	3 (11.1)
Elevated ESR (ESR>20 mm/ h)	12 (40.7)
Low C3 (<900 mg/L)	1 (3.7)

WBC: White Blood Cell; ESR: Erythrocyte Sedimentation Rate; C3: Complement 3

Table 3. Laboratory findings of 27 patients with Henoch-Schönlein purpura

a dosage ranging from 1-2 mg/kg/day for 7 days for abdominal pain and 15-30 days in patients with nephritis. The average duration of prednisolone treatment was about 9.1 days. Regarding outcome; only one child developed acute kidney injury developed to mild chronic kidney disease (CKD), while all the other patients showed full recovery. No recurrence cases were reported through the 4 years follow up.

Discussion

HSP is a systemic vasculitis involving the small blood vessels of skin, joints, intestine, and kidneys. It is the most common element of nonthrombocytopenic purpura in children [12]. It has been documented in all individuals aged from 6 months to 86 years [5,10,19]. But, most cases of HSP occur between the ages of 5 to 15 years, giving mean age approximately 5-6 years [20-22]. In the present study, the epidemiologic and clinical findings were compared with those reported from Saudi Arabia and other countries (Tables 4 and 5).

The mean age of the present study was 8.3 years (range, 2-18 years) (Table 1). The present mean age was observed to be consistent with those reported in children who consulted at King Abdulaziz University Hospital, Jeddah, Saudi Arabia and at Asir Central Hospital in the southern province of Saudi Arabia (Table 4) [23-25]. Similarly, Table et al. [25] documented the mean age of children with HSP in Turkey by 8.8 years. By contrast, Lardhi et al. [20] stated that the mean age at onset of the HSP was 6.3 years for children patients who were followed up at King Fahad University Hospital in the eastern province of Saudi Arabia. Also, Özer et al. [26] reported a higher mean age of 9.8 year in Turkish children that had HSP (Table 5). Of the study patients, 52% were males and 48% were females, with a male-to-female ratio of 1.1:1. This ratio was similar to those in the literature inside Saudi Arabia or other countries (Tables 4 and 5). However, there are also some studies representing that HSP is more frequent in females [5,17]. In the present study, HSP was most common in the fall and least frequent in the spring. Several studies in Saudi Arabia documented that the disease symptoms was increased frequently in fall and winter (Tables 4). Additionally, several studies in different countries documented symptom onset during fall and winter (Table 5). By contrast, Al-Harbi stated HSP cases in summer inside Saudi Arabia [24]. Consequently, it can

Table 4. Comparison of the findings of the present study with those of similar studies conducted in Saudi Arabia

	Current study	Lardhi [20]	Bukhari et al. [23]	AI-Harbi [24]	Zimmo and Akbar [27]	AI-Rasheed and Abdurahman [30]
Number of children (n)	27	78	29	55	18	40
Mean age (year)	8.3	6.3	7.5	8.5	5.9	-
Gender ratio (M:F)	1.1:1.0	1.4:1.0	1.07:1.0	1.0:1.1	1:1	-
preceding URTI	12 (44.5%)	41 (52.5%)	12 (41.4%)	-	9 (50%)	-
Most frequent season	Fall	Fall and Winter	-	Summer	-	Winter
Joint involvement	23 (85.2%)	52 (66%)	24 (82%)	42 (76%)	13 (72%)	23 (58%)
GIS involvement	21 (77.8)	37 (47%)	21 (72.4%)	43 (78%)	13 (72%)	23 (58%)
Testicular involvement	2/14 (14.3%)	7/46 (15%)	-	-	-	-
Renal involvement	10 (37%)	19 (24%)	7 (24.1%)	11 (20%)	1 (6%)	15 (38%)
Hematuria	9 (33.3%)	19 (24%)	4 (13.8%)	-	-	-
Proteinuria	7 (26%)	5 (6.4%)	-	-	-	-

URTI: Upper Respiratory Tract Infection; GIS: Gastrointestinal Manifestations

Table 5. Comparison of the findings of the present study with those of the studies conducted from other countries

	Current study	Dawod and Akl [21].	Hamdan and Barqawi [22].	Saulsbury [4].	Jauhola et al. [17, 33]	Chen et al. [12].	Özer et al. [26].
Country	Saudi Arabia	Qatar	Jordan	USA	Finland	China	Turkey
Number of children (n)	27	40	68	77	223	120	53
Mean age (year)	8.3	6.0	5.9	5.9	7.1	6.6	9.8
Gender ratio (M:F)	1.1:1.0	1.6:1.0	1.4:1.0	1.32:1.0	1.2:1.0	1.9:1.0	1.0:1.12
preceding URTI	12 (44.5%)	20 (50%)	-	28 (36%)	161 (72%)	52 (43%)	-
Most frequent season	Fall	-	Fall	Winter	Winter	Winter	-
Joint involvement	23 (85.2%)	32 (80%)	51 (75%)	52 (67%)	200 (90%)	79 (65.8%)	24 (45.3%)
GIS involvement	21 (77.8)	26 (65%)	43 (63%)	46 (60%)	126 (57%)	89 (74.2%)	33 (62.3%)
Testicular involvement	2/14 (14.3%)	1/25 (4%)*	-	2/46 (4%)	17/122 (14%)	-	-
Renal involvement	10 (37%)	7 (17.39%)	20 (29%)	16 (21%)	102 (46%)	65 (54.2%)	25 (47%)
Hematuria	9 (33.3%)	1 (2.5%)	14 (20.6%)	16 (21%)	93 (42%)	32 (26.7%)	9 (17%)
Proteinuria	7 (26%)	1 (2.5%)	6 (8.8%)	7 (9%)	88 (39%)	32 (26.7)	22 (41%)

*Penile swelling; URTI: Upper Respiratory Tract Infection; GIS: Gastrointestinal Manifestations

conclude that symptoms can occur any time throughout the year.

In agreement to several studies conducted in Saudi Arabia (Table 4) and other countries (Table 5), upper respiratory tract infections (URTI) have been described to precede HSP [12,17,20,21,23]. In the current study, 44.5% of the patients had symptom of URTI. This result is similar to some reports performed in Saudi Arabia and in Qatar [20,21,23]. In the present study, joint involvement occurred in about 85.2% of the cases; arthralgia in 17 cases and arthritis in 6 cases. Different studies reported that joint involvement can be found in 45-90% of the patients [17,23]. In our children patients, ankles and knees were the most commonly involved joints, followed by wrists and elbows, whereas hip and shoulder involvement was not reported in any case. Similarly, Lardhi et al. [20] found that hip and shoulder involvement was very rare and was found only in one case each.

In many studies, GIT involvement has been reported in approximately two thirds of patients with HSP in Saudi Arabia which is consistent with our study [23,24,26,27]. Abdominal pain and bloody stool were the most frequent symptoms seen in 77.8% and 48% of our patients, respectively. Kawasaki et al. [28] who designated

infrequent complications, such as intussusception, bowel ischemia, acute appendicitis, pancreatitis, bowel infarction, and intestinal perforation with this disease. However, these rare complications were not seen in our cases.

Renal involvement is a matter of concern between patients with HSP, because it may increase the frequently of hypertension, nephrotic or nephritic syndromes or renal insufficiency. The rate of children patients who had renal involvement varied between 20%-60% with HSP in different studies [28,29]. In the current study, renal involvement was found in 37% of the children patients and the typical symptoms were hematuria and proteinuria (Table 2). This result was in agreement with the data that reported by AI-Rasheed and Abdurahman in Saudi Arabia and with the study conducted in Jordan [22,30]. By contrast, renal involvement was reported in 54.2%, 47% and 46% of the HSP patients in China, Turkey and Finland, respectively (Table 5) [12,17,26].

During the follow-up period in the present study, only one case was documented to have acute kidney injury that progressed to mild CKD. Two patients were reported with hypertensive; one has nephrotic syndrome and the other had mild CKD. Testicular involvement has been

documented two boys that had scrotal swelling (Table 2). Similar results were reported in Saudi Arabia, USA, and Finland [4,16,20].

Based on literature, there is no specific examination for the diagnostic of HSP. Even though, there is evidence that laboratory patients with HSP have elevated erythrocyte sedimentation rates, C-reactive protein levels, white blood cell counts, platelet counts and immunoglobulin A levels, none of these tests is specific or diagnostic. In the present study, 14.8% of the patients had thrombocytosis platelets over than $500 \times 10^9/L$ and 40.7% patients had an increased ESR. Also, Leukocytosis over $12 \times 10^9/L$ was found in 11.1% of the patients and a low C3 serum level was found in one patient (3.7%). Similar findings have been reported previously in Saudi Arabia and China [12,20].

Many traditional treatments like hydration, bed rest, analgesics and non-steroidal anti-inflammatory drugs were found to be an effective in the majority of the HSP cases. Thus, 44.5% of the patients of the current study managed initially conservatively. Sometime, it is not enough to control the disease symptoms by these traditional treatments, therefore more potent anti-inflammatory drugs like corticosteroids are included especially in the following situations: Severe abdominal pain or GI bleeding, severe soft tissue edema, severe scrotal edema, persistent nephrotic syndrome [31]. In agreement with other studies, almost all our cases showed full recovery, while only one patient (3.7%) developed acute kidney injury [28,29]. Although corticosteroids are used in HSP with severe gastrointestinal symptoms and/or kidney involvement, there are few data from randomized controlled trials to support their use for gastrointestinal symptoms but there is no from randomized controlled trials to support their use for kidney involvement [32,33].

Conclusion

HSP is a vasculitis that can involve mostly with skin and joints and other organs and systems. In the current study, the mean age and occurrence season were diverse than other Saudi studies. The cases with HSP should be closely followed for complications especially with kidney and/or gastrointestinal system involvement that can develop during early or late period. More investigation is necessary to study HSP in Taif region especially for the prevalence, clinical manifestations, preceding factors and complications.

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