



Retrospective Assessment of Children with Henoch-Schonlein Purpura in and around Kocaeli Province and Comparison with Literature

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ORIGINAL
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ABSTRACT

Objective: The aim of this retrospective study was to evaluate demographic, etiologic and epidemiologic characteristics, and clinical and laboratory findings of Henoch-Schonlein purpura (HSP) and to determine risk factors increasing the kidney involvement in our region.

Materials and Methods: Records of 151 patients who were followed-up with the diagnosis of HSP between May 2002 and December 2010 in the Department of Child Nephrology in Kocaeli University Medical Faculty and fulfilled the inclusion criteria were retrospectively evaluated. Demographic characteristics of the patients, season of presentation, complaints on admission, triggering factors, pathological examination, laboratory data, and the duration of follow-up periods were assessed.

Results: Of 151 patients, 90 (60%) were male and 61 (40%) were female. The mean age was 7.4 ± 3.4 years (range, 1.8-16.5 years). While 33 (22%) patients did not have purpuric rash on admission, they were then observed to have purpuric rash during the follow-ups. Increasing age was found to be a risk factor for kidney involvement ($p=0.011$). Testicular involvement was identified as a negative risk factor for kidney involvement ($p=0.020$). Factors such as gender, GIS and musculoskeletal system involvement, recurrence, and steroid treatment were not found to be associated with kidney involvement.

Conclusion: Etiologic, epidemiologic, and clinical findings of HSP patients in our region were found to be similar to those reported in the national and international studies. In parallel to the literature, the present study showed an increased risk of kidney involvement with increasing age.

Key words: Primary care physicians, sexual disorders, physiologic, sexual dysfunctions, sexuality, sexually transmitted diseases

INTRODUCTION

Henoch-Schonlein purpura (HSP) is a systemic vasculitis with unknown etiology and characterized by skin, joint, gastrointestinal system (GIS), and kidney involvements (1). Although HSP can occur in all age groups, it is most commonly encountered in childhood. The annual incidence has been reported as 10-22/100,000. HSP is more common in males and frequently encountered in winter and spring. Although its etiopathogenesis is not well known, infections (bacterial, viral, parasitary), medications, vaccines, tumors, insect bite, and some foods are considered responsible. HSP is generally a self-limiting disease with benign character. The most important factor indicating long-term prognosis is the severity of kidney involvement (2). The aim of this retrospective study was to evaluate demographic, etiologic and epidemiologic characteristics of HSP and effects of steroid use in preventing kidney involvement and to determine frequency, severity and prognosis of kidney involvement and risk factors in our region.

MATERIALS and METHODS

Records of patients who were followed-up with the diagnosis of HSP between May 2002 and December 2010 in the Department of Child Nephrology in Kocaeli University Medical Faculty were retrospectively evaluated. The patients were re-evaluated based on EULAR/PRINTO/PRES criteria and those having the diagnostic criteria were included (3). In order to evaluate the records, the patients were informed by phone calls and their consents were obtained.

Patients' data regarding age, gender, season of presentation, complaints on admission, triggering factors, weight, height, blood pressure, pathological examination findings, complete blood count, C-reactive protein level, erythrocyte sedimentation rate, albumin level, blood lipid levels, fecal occult blood (FOB), complete urinalysis, type of treatment (corticosteroids, immunosuppressives, antiaggregants, angiotensin-converting enzyme inhibitors), and follow-up periods.

Hypertension was defined as a systolic and/or diastolic blood pressure of ≥ 95 percentile based on 3 separate measurements according to age, height, and gender (4). Joint involvement was defined as joint swelling and/or

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functional limitation of joint and GIS involvement was defined as stomachache and/or FOB positivity and presence of melena, hematemesis, hematochezia, or invagination (5, 6). Recurrence was defined as new skin rashes developed at least 4 weeks after disease recovery or reoccurrence of other signs (7). Kidney involvement was defined as microscopic (presence of ≥ 5 erythrocytes in the centrifuged urine at 40X) or macroscopic hematuria and/or proteinuria (presence of protein >4 mg/m²/h or protein/creatinine >0.2 in 24-h urine) and/or impairment in kidney functions (8).

Testicular sensitivity or scrotal edema was considered as testicular involvement; convulsion and infarction on MRI was considered as central nervous system (CNS) involvement; and presence of ventricular extrasystoles was considered as cardiac involvement.

Statistical analysis

Data were analyzed using SPSS 15.0 (Chicago, IL, USA) program. Descriptive statistics were expressed as mean \pm standard deviation (minimum-maximum). Univariate analysis and chi-square test were used for categorical variables. Logistic regression and multivariate analysis were performed for probable variables. A p value of <0.05 was considered statistically significant.

RESULTS

Epidemiologic and etiologic features of 151 patients are presented in Table 1 and distribution of clinical findings of the patients is presented in Table 2.

Rash, mandatory diagnostic criteria, was present in all patients. However, 33 (22%) patients did not have rash on first admission, they were then observed to have rash during the follow-ups.

Of 111 patients having GIS involvement, 50 (33.1%) had only stomachache, 46 (30.4%) had stomachache and FOB positivity, 5 (3.3%) had only FOB positivity, and 1 (0.6%) had invagination.

Joint involvement was present in 87 (57.6%) patients. Ankle (n=49, 32.4%) was involved mostly, followed by knee (n=36, 23.8%) and wrist (n=14, 9.2%) involvements. Joint involvement was commonly in the form of oligoarthritis (41%) and recovered without sequelae.

Steroid treatment was applied to 7 of 13 patients with testicular involvement and 55 of 111 patients with GIS involvement. Steroid treatment was not used for 5 patients as they had BOF positivity on routine tests and for 51 patients as they had mild stomachache that disappeared spontaneously in a few days. Of the patients receiving steroid treatment, 25.8% (n=16) developed kidney involvement and 74.2% (n=46) did not develop. The overall kidney involvement rate was 27.1% (n=41) and previous steroid use had no significant effect on prevention of kidney involvement (χ^2 , p=1.00).

Recurrence was observed in 6 (4%) of 151 patients followed-up with the diagnosis of Henoch-Schonlein purpura. The mean time elapsed from the first attack was 30.6 \pm 18 months (range, 2-108 months). The disease recurred in 4 patients in the form of rash and arthritis, in 1 patient in the form of rash and stomachache, in 1 patient in the form of rash. Steroid use was not found to be associated with recurrence (χ^2 , p=1.00).

Table 1. Epidemiologic and etiologic features of the patients

	n (%)
Number of patients	151 (100)
Age (year)*	7.4 \pm 3.4 (1.8-16.5)
Gender	
Male	90 (59.6)
Female	61 (40.4)
Seasonal distribution	
Winter	50 (33.1)
Fall	41 (27.1)
Spring	34 (22.5)
Summer	26 (17.2)
Triggering Factor	
URTI	33 (21.8)
Gastroenteritis	2 (1.3)
Varicella vaccine	1 (0.6)
Bee stings	1 (0.6)
Fever (alone)	13 (8.7)

*Mean \pm standard deviation (minimum, maximum)
URTI: upper respiratory tract infection

Table 2. Clinical findings of 151 patients diagnosed with Henoch-Schonlein purpura

Skin findings	n (%)
Local edema (hand and foot dorsum)	151 (100)
Purpura	11 (7.2)
GIS involvement	111 (73.5)
Musculoskeletal system involvement	99 (65.5)
Arthritis	87 (57)
Muscle pain	8 (5.2)
Arthralgia	4 (2.6)
Kidney involvement	41 (27.1)
Testicular involvement	13 (8.6)
Testicular sensitivity (n/M*)	8/90 (8.8)
Scrotal edema (n/M*)	5/90 (5.5)
Other Involvement	
CNS	1 (0.6)
Cardiac	1 (0.6)

*Proportions are based upon the number of males.
CNS: Central nervous system; GIS: Gastrointestinal system

Kidney involvement was observed in 41 (27.1%) patients. Thirty-six (23.8%) patients had microscopic hematuria and 2 (1.3%) patients had macroscopic hematuria. While 17 (11.2%) patients had only hematuria and 3 (1.9%) patients had only proteinuria, 21 (13.9%) patients had both hematuria and proteinuria. Sixteen

(44.4%) of 41 patients with kidney involvement were older than 10 years. A significant association was determined between increasing age and kidney involvement in HSP (χ^2 , $p=0.029$).

Variables considered to affect kidney involvement were evaluated using multivariate analysis. The results are presented in Table 3. Based on this evaluation, age was found to be the risk factor affect-

Table 3. Evaluation of factors affecting kidney involvement by multivariate analysis in patients with Henoch-Schonlein purpura

Probable risk factors	%95 CI	OR	p
Age	1.340-1.297	1.158	0.011
Gender (male)	0.490-2.476	1.101	0.816
Testicular involvement	0.058-0.788	0.213	0.020
GIS involvement	0.309-2.183	0.822	0.694
Musculoskeletal system involvement	0.660-3.421	1.503	0.332
Recurrence	0.258-25.104	2.547	0.423

CI: Confidence interval; OR: Odds ratio; GIS: Gastrointestinal system

ing kidney involvement in HSP ($p=0.011$). Testicular involvement was found as a negative risk factor ($p=0.020$).

Kidney biopsy was performed on 15 (35.6%) of 41 patients with kidney involvement. Of the patients undergoing biopsy, 14 had nephrotic proteinuria and 1 had CNS involvement accompanied by nephritic syndrome. According to the classification of kidney involvement by the International Study Kidney Disease in Children, 3 patients had grade 1, 6 patients had grade 2a, 3 patients had grade 2b, 1 patient had grade 3a, 1 patient had grade 3b, and 1 patient had grade 6.

Treatment was applied to 17 patients due to nephrotic proteinuria in 14 patients, CNS involvement in 1 patient, and previous commencement of medication in an external center in 2 patients. Steroid treatment alone was applied to 9 (21.9%) patients; steroid, immunosuppressive and antiaggregant were applied to 6 (14.6%) patients; and steroid, immunosuppressive, antiaggregant, and angiotensin-converting enzyme inhibitor were applied to 2 (4.8%) patients. As an immunosuppressive treatment, 1 patient received azathioprine, 5 patients received cyclophosphamide, and 2 patients received cyclophosphamide followed by cyclosporine A. Two patients were diagnosed with familial Mediterranean fever during the follow-ups.

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

	Muslu et al. (9)	Peru et al. (10)	Anil et al. (11)	İnal et al. (12)	Current Study Turkey
Number of patients (n)	135	254	430	77	151
Age, mean±SD* (year)	-	8.65±3.59	7.9±2.9	7.1±3.3	7.4±3.4
Gender (M/F)	1.45	1.37	1.09	1.48	1.47
URTI as a triggering factor	55 (41)	-	139 (32)	28 (36)	33 (22)
Season (most frequent)	Winter	-	Fall	Spring	Winter
Those without rash on first admission	-	-	64 (15)	10 (13)	33 (22)
Palpable purpura	135 (100)	254 (100)	430 (100)	77 (100)	151 (100)
GIS involvement	84 (62)	144 (56)	148 (34)	46 (60)	111 (73)
Invagination	-	8 (3)	4 (0.9)	2 (3)	1 (0.6)
Joint involvement	51 (38)	168 (66)	195 (45)	52 (67)	91 (60)
Testicular involvement	11 (14)	-	6/199 (3)	2/46 (4)	13/90 (14)
Other					
CNS	-	-	3 (0.7)	-	1 (0.6)
Cardiac	-	-	-	-	1 (0.6)
Recurrence	-	-	24 (5)	12 (15)	6 (4)
FOB+	-	61 (42)	80 (18)	31 (40)	51 (34)
Kidney involvement	75 (55)	76 (30)	192 (45)	16 (21)	41 (27)
Hematuria	75 (55)	76 (30)	192/430# (44)	16 (21)	38 (25)
Proteinuria	25 (18)	60 (24)	‡	7 (9)	24 (16)

*Data are presented as n (%) except for that indicated by.

#patients with kidney involvement were assumed to have hematuria.

‡Unspecified

URTI: Upper respiratory tract infection; GIS: Gastrointestinal system; CNS: Central nervous system; FOB: Fecal occult blood

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

	Saulsbury et al. (13) Virginia USA	Calvino et al. (14) Luga Spain	Trapani et al. (6) Florence Italy	Jauhola et al. (15) Oulu Finland	Current study Turkey
Number of patients (n)	77	78	150	223	151
Age, mean±SD* (year)	5.9±2.9	6.2±3.1	6.1±2.7	7.1±3.5	7.4±3.4
Gender (M/F)	1.32	0.85	1.8	1.20	1.47
URTI as a triggering factor	28 (36)	28 (36)	63 (42)	161 (72)	33 (22)
Season (most frequent)	Winter	Fall	Winter	-	Winter
Those without rash on first admission	20 (26)	30 (38)	40 (27)	59 (27)	33 (22)
Palpable purpura	77 (100)	78 (100)	150 (100)	223	151 (100)
GIS involvement	46 (60)	57 (73)	77 (51)	126/221 (57)	111 (73)
Invagination	2 (3)	1 (1)	1 (0.7)	-	1 (0.6)
Joint involvement	52 (67)	61 (78)	111 (74)	200/221 (90)	91 (60)
Testicular involvement	2/46 (4)	3/36 (8)	20/95 (21)	17/122 (14)	13 (14)
Other					
CNS	2 (2)	-	4 (3)	-	1 (0.6)
Cardiac	-	-	-	-	1 (0.6)
Recurrence	12 (15)	10/69 (15)	41/118 (35)	55/221 (25)	6 (4)
FOB+	23/77 (30)	12/78 (15)	23/114 (20)	26/117 (22)	51 (34)
Kidney involvement	16 (21)	42 (54)	81 (54)	102/223 (46)	41 (27)
Hematuria	16 (21)	41 (53)	39 (26)	93 (42)	38 (25)
Proteinuria	7 (9)	19 (24)	63 (42)	88 (39)	24 (16)

*Data are presented as n (%) except for that indicated by.
URTI: Upper respiratory tract infection; GIS: Gastrointestinal system; CNS: Central nervous system; FOB: Fecal occult blood

DISCUSSION

Henoch-Schonlein purpura is the most common vasculitis both in Turkey and in the world. In the present study, 151 patients with HSP were evaluated in terms of their etiologic, epidemiologic, and clinic characteristics and the findings were compared with those reported from Turkey and other countries (Tables 4 and 5) (9-15). The mean age was 7.4±3.4 years (range, 1.8-16.5 years) (Table 1). In terms of the mean age, the present study was observed to be consistent with those reported from Turkey and other countries. Of the study patients, 59.6% were males and 40.4% were females. Male-to-female ratio was 1.47 and this ratio was similar to those in the literature (Tables 4 and 5). However, there are also reports indicating that HSP is more frequent in females (14-16). In the present study, HSP was most frequent in the winter and least frequent in the summer. In the series from other countries, the disease was reported to be most frequent in winter (Tables 4 and 5). Similar to the findings that were reported in the studies from Turkey and other countries, upper respiratory tract infection (URTI) ranked first as the triggering factor. In a prospective study conducted in Finland, streptococcus infection was reported in 36% of the patients (15).

The lack of rash on admission makes difficult to diagnose HSP and leads to misdiagnosis. In the present study, there were 33 (22%)

patients without rash on first admission. While lower rates were determined in the studies in Turkey, the rates of lack of rash on admission were reported at higher rates in the studies from other countries (Tables 4 and 5).

In the present study, 73.5% of the patients had GIS involvement. One (0.6%) of our patients had invagination. GIS involvement was reported at a rate between 34% and 62% and between 51% and 73% in the studies from Turkey and other countries, respectively (Tables 4 and 5).

Joint involvement was reported at a rate between 38% and 67% and between 67% and 90% in the studies from Turkey and other countries, respectively. In the present study, ankle involvement was the most common, as was reported in the other series.

Coexistence of HSP and FMF has been reported as approximately at a rate of 5% in the literature (17). This rate was reported as 7.2% and 1.2% in different studies from Turkey (10, 18). In the present study, while 2 (1.3%) patients were followed-up with the diagnosis of HSP, they were also diagnosed with FMF due to repeated stomachache.

Kidney involvement is the predicting and affecting factor of long-term prognosis of HSP. The rate of kidney involvement in HSP varies between 20% and 60% in different studies (19, 20). In the

present study, kidney involvement was observed in 27% of the patients. In a prospective study conducted in Finland, kidney involvement was reported in 46% of the patients (7).

Although kidney involvement has generally good prognosis in HSP, end-stage renal failure can rarely occur. During the follow-up period (mean, 15.6±6.6 months) in the present study, none of the patients had hypertension or renal failure.

In the present study, evaluation of the probable risk factors affecting kidney involvement revealed that age was the only variable increasing risk for kidney involvement. Testicular involvement was detected as the negative risk factor (Table 4). This negative association could be attributed to the fact that testicular involvement is encountered in younger ages contrary to kidney involvement. In the previous studies, risk factors for kidney involvement have been reported as severe purpura, severe stomachache, older age, steroid treatment, moderate kidney involvement at disease onset, and high Factor XIII level in serum (21-25). In their study, Anil et al. (11) reported female gender, atypical onset (without rash), and early steroid treatment as the risk factors for kidney involvement. In the large-scale Finland series, the most reliable study due to its prospective nature, HSP onset above the age of 8 years, stomachache, and recurrence were reported to be the risk factors for kidney involvement (15). In the present study, no significant relationship of kidney involvement with gender, steroid treatment, musculoskeletal involvement, GIS involvement, and recurrence was found.

Study limitations

Retrospective nature of the present study caused a limitation in the evaluation of data, as is in many studies on this issue.

The present study was similar to other HSP series from Turkey and other countries in terms of number, distribution, and clinical feature of the patients. However, the present study is of importance with respect to consistency of outcomes with those of the published series, proving the disease progression with similar clinical and prognostic features almost anywhere in the world, and providing comparative discussion and review with similar published series.

CONCLUSION

As is seen in similar studies, older age was also found to be a risk factor for kidney involvement in the present study and thereby the importance of kidney involvement should be considered during follow-ups.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Kocaeli University School of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Authors' Contributions: Conceived and designed the experiments or case: ZE. Performed the experiments or case: AY. Analyzed the data: AY. Wrote the paper: AY, MBA, ZE. All authors have read and approved the final manuscript.

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