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Henoch-Schonlein Purpura Nephritis in Libyan Children; Single Center Experience

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Abstract

***Background:** Henoch-Schönlein (HSP) is one of the most common vasculitis in children, it is manifested by skin purpura, arthritis, abdominal pain and renal involvement. Typically HSP is considered as self-limiting, benign condition, although renal involvement (HSP nephritis, HSN)is the principle cause of morbidity in this disease.*

***Aim of the study:** To evaluate renal involvement in patient with HSP and to identify factors that are predictive of nephritis based on demographic data, clinical characteristics, and treatment given to those patients and to determine the follow-up time needed for diagnosing HSN patients.*

***Study design:** retrospective descriptive analytic study.*

***Patients and methods:** medical files of 75 children who diagnosed as HSP from January 2005 to June 2017 and were followed up in rheumatology and nephrology clinics at Tripoli Children Hospital were reviewed. For all patients included in the study, we collect the following data: Age, gender, clinical examination at presentation, laboratory data including complete blood count, C reactive protein, ESR, and complete urinalysis at presentation, also we follow the results of urinalysis for up to one year after presentation.*

***Results:** A total of 75 patients with a HSP were enrolled in the study. Of these 40 were boys giving a male to female ratio of 1.14: 1.The mean age of onset was 6.5 ± 1.5 years (range of 2 -12 years), with most cases (93.4%) occurred in those aged less than 10 years old. HSN was the 3rd most common manifestations of HSP in our study preceded by rash in 100% of patients and gastrointestinal manifestations in 65%. HSN occurred in 30\75 of cases (40%).The most common HSN manifestations was microscopic hematuria and proteinuria in 10.7% of patients followed by microscopic hematuria in 8% of patients, isolated hypertension in 5.3% of patients. In other 5.3% of patients hypertension was associated with gross hematuria, table2. We evaluated the relationship between HSN and various factors using a univariate analysis as shown in table3, we noticed that there was no significant statistical difference between patients with and without HSN in terms of sex, gender, presence of severe abdominal pain and arthritis. 93.3% of patients with HSNmanifest within 6 weeks of disease onset and only 2 patients developed their renal involvement months later. Figure3.*

***Conclusion:** HSN occurred in 40% of patients with HSP with 28 out of 30 who developed HSN(93.3%) developing within the initial 6 weeks of the disease. None of the studied factors were associated with higher risk of HSN by univariate statistical analysis.*

Keywords: *henoch-schoolen purpura, children, nephritis*

Introduction

Henoch-Schonlein purpura (HSP) is one of the most common causes of systemic vasculitis. The etiology is unknown,HSP typically affects children between the ages 3and 10 years.It is characterized bynon-thrombocytopenic purpuric rash, non-deforming arthritis, gastrointestinal involvement and nephritis. (1)

The diagnosis is usually based on clinical finding.

The commonly used 2010 EULAR/PRINTO/PReS criteria (European League against Rheumatism, pediatric Rheumatology International trials organization, and Pediatric Rheumatology European Society) (2) include palpable purpura and one of the following: abdominal pain, arthritis/arthralgia, nephropathy or IgA deposits in biopsy finding.Although the short and long-term outcome of HSP is generally favorable, with complete spontaneous resolution of symptoms, outcome depends primarily on the extent of renal involvement which occurs in 40%-60% of pediatric patients with HSP, Patients who develop HSP nephritis generally do so within three months of the onset of rash.(3-6).Majority of patients with HSP nephritis (HSN) have a mild disease, presenting with hematuria and/ or low-grade proteinuria, with a high recovery rate.(1) A small percentage of patients present with nephrotic syndrome or renal function impairment.

Although patients with only hematuria do not develop end-stage renal disease (ESRD), the association of proteinuria and hematuria may be associated with a 15% risk and the combination of nephritic-nephrotic syndrome with a 50% risk of progression to ESRD(7-9) Children with overt renal disease at presentation are therefore managed early by paediatrics nephrologists and may require follow up for at least five years.

There are few studies that evaluate renal involvement in HSP in children, in some of these reports HSN has been associated with several factors such as age at disease onset, abdominal pain, recurrence of purpura and treatment with steroids(10-13).

There is no consensus for the treatment of HSN (14),and the most effective treatment remains controversial (15).It has been suggested that early corticosteroid therapy may not prevent the development of HSN and should not be routinely recommended. (16, 17)

Data on treatment of severe HSN are controversial and scarce (18).KDIGO guidelines recommended early treatment with angiotensine converting enzyme inhibitor (ACE-I) or angiotensine receptor blockers (ARBs) in patient with persistent proteinuria(14) to improve long term outcome independent on histologic lesions(19).A 6 months course of corticosteroids therapy is recommended in those with persistent proteinuria and glomerular filtration rate more than 50ml\min per1.73$m^{2,}$,early immunosuppressive therapy with high dose corticosteroids have been suggested in patient with significant kidney involvement (proteinuria in nephrotic range\ or progressive kidney impairment(20).

The objective of this retrospective study were to evaluate renal involvement in patient with HSP and to identify factors that are predictive of nephritis based on demographic data, clinical characteristics, laboratory test results and treatment given to those patients and to determine the follow-up time needed for diagnosing renal involvement.

Patients and Methods

This was retrospective study, we reviewed all medical records of children who diagnosed with HSP from January 2005 to June 2017 and were followed up in rheumatology and nephrology clinics at Tripoli Children Hospital. Tripoli Children Hospital is the only referral center in the west region of Libya and the only center that include pediatric rheumatology and nephrology service. Diagnosis of HSP was based on applying EULAR/PRINT0/PReS criteria (European League against Rheumatism, pediatric Rheumatology International trials organization, and Pediatric Rheumatology European Society) (table 1). According to medical literature HSN was defined as presence of gross or microscopic hematuria(>5 cells \high power field from a centrifuged specimen) either with or without proteinuria (21,22). Acute nephritis is defined as nephritis which was evident in the first urinalysis, delayed nephritis is defined as nephritis appearing 3 weeks or more after an initial normal urinalysis (23). Heavy proteinuria is defined as isolated proteinuria exceeding 40mg\$m^2$\hour without edema or full blown picture of nephrotic syndrome, while nephrotic syndrome is defined as proteinuria exceeding 40mg\$m^2$\hour and serum albumin less than 2.5mg\$m^2$\hour with or without edema (24).

For all patients included in the study, we collect the following data: Age, gender, season of presentation, clinical presentation, triggering factors, clinical examination at presentation, laboratory data including complete blood count, C reactive protein, ESR, and complete urinalysis. Type of treatment includes steroid, immunosuppressive drugs, angiotensine-converting enzyme inhibitors, and urine results during follow-up period. Data were analyzed using SPSS 16 program, descriptive statistics expressed as the mean ± standard deviation (minimum-maximum). Univariant analysis and Chi-square test were used for categorical variables.

Table 1. *European League against Rheumatism/Pediatric Rheumatology International Trials Organization/ Pediatric Rheumatology European Society.*

EULAR/PRINTO/PReS 2008
Purpura without thrombocytopenia with predominance in lower extremities with one of four of: [1] Abdominal pain [2] Arthritis or arthralgia [3] Histopathology: leukocytoclastic vasculitis [4] Renal manifestations

Results

A total of 75 patients with a HSP were enrolledin the study. Of these 40 were boys giving a male to female ratio of 1.14: 1.Themean age of onset was 6.5 ± 1.5 years(range of 2 -12 years), with most cases (93.4%) occurred in those aged less than 10 years old.

Renal involvement (HSN)was the 3rd most common manifestations of HSP in our study preceded by rash in 100% of patients and gastrointestinal manifestations in 65%. HSNoccurred in 30\75 of cases (40%). It manifested by isolated microscopic hematuria in 6(8%)patients and by isolated gross hematuria in 3 (4%) patients. While the most common HSN was microscopic hematuria with proteinuria in 8(10.7%) patients.4 (5.3%)patients had isolated hypertension, and 4 patient(5.3%) their hypertension was accompanied with gross hematuria. Testicular swelling observed in 1(1.3%) patient. Table 2.

Table 2. *Renal manifestations patients with Henoch Schonlein Purpura (HSP)*

Renal manifestations	Frequency	%
Microscopic hematuria	6	8%
Gross hematuria	3	4%
hypertension	4	5.3%
Microscopic hematuria and proteinuria	8	10.7%
Gross hematuria and hypertension	4	5.3%
Gross hematuria and proteinuria	4	5.3%
Testicular swelling	1	1.3%
Total	30	40%

Table 3. *Risk factors for renal involvement in patients with HSP*

Risk factor	Renal involvement NO. Of cases (%)	P value
Boys Girls	17(43.6%) 11(31.4%)	0.164
Age at onset <7yrs Age at onset ≥7yrs	16(30.8%) 10(50.0%)	0.267
Arthritis No	13(28.9%) 53.3(16%)	0.515
Abdominal pain No	19(40.4%) 10(35.7%)	0.438
Within 6 weeks of onset Months later	28(37.3%) 2(2.7%)	0.000
Use of steroid Yes NO	 20(48.4%) 9(26.5%)	0.899

We evaluated the relationship between renal involvement and various factors using a univariate analysis as shown in table3,

we noticed that there was no statistical difference between patients with and without renal involvement in terms of sex as 17 boys and 11 girls had renal involvement (43.6% VS 31.4% with M:F 1.16:1, P value = 0.16).figure1.

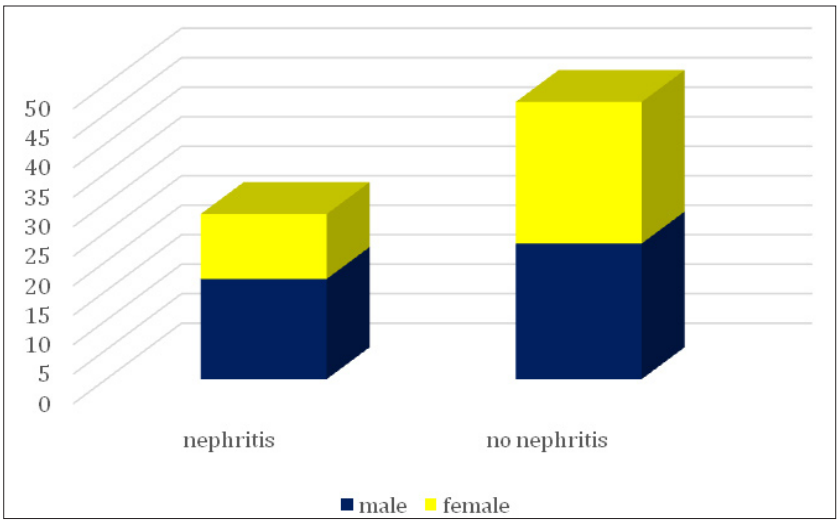

Figure 1. *Relationship of HSP nephritis with gender*

69.3% of our patients with HSP was below 7 years and 26.7% was ≥ 7 years, 30.8% of those below 7 years had nephritis compared with 50% of patients aged 7 and above, p value = 0.18.Figure2: Relationship between age of onset and Nephritis Henoch-Schönlein Purpura.

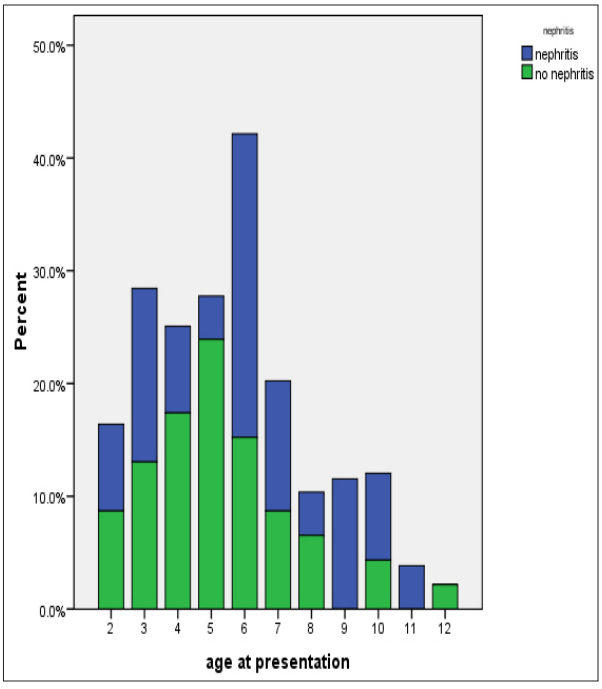

Fig 2. *Relationship between age of onset and Nephritis Henoch-Schönlein Purpura*

We found that neither arthritis (P value=0.51) nor severe abdominal pain(P= value 0.43) were associated with nephritis in our HSP patients. Table 3.

28\30 (93.3%) patients with renal involvement had their manifestations within 6 weeks of disease onset and only 2 patients developed their renal involvement one month later Figure3.

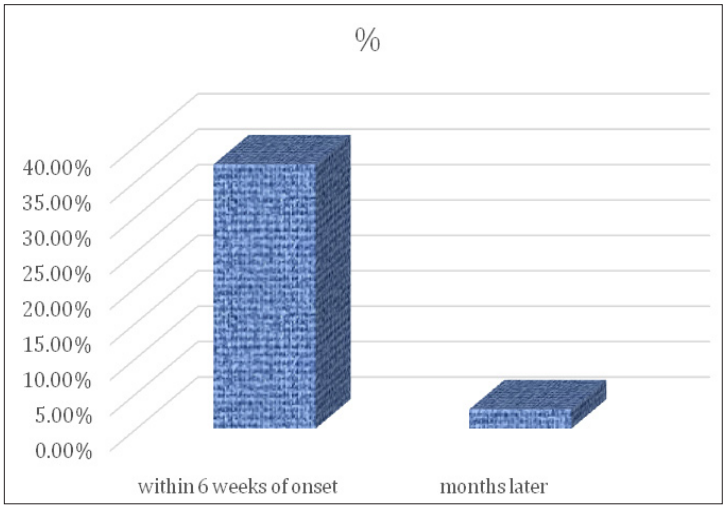

Fig 3. *Relationship between duration after the onset of Henoch-Schönlein Purpura and the percentage of renal involvement.*

Use of corticosteroids in the treatment of HSP patients has no effect on occurrence of nephritis as 48.8% of patients treated with steroids had nephritis compared with 26.5% of those untreated developed nephritis(P value=0.89)

Table 4. *Comparison of the finding of the present study with other studies.*

Variable	Our study	Saudi Arabia	Turkey	China	Indonesia
No. Of patient	75	78	151	71	128
Age (mean)	6.5±1.5ys	6.3yrs	7.3±3.4ys	8.55±2.13 ys	7.9±2.9ys
Gender M: f	1.14:1	1.4:1	1.47:1	1.29:1	1.8:1
URTI as triggers	43(57.3%)	41(52%)	33(22%)	66(93%)	19(14.8%)
Season	Winter, spring	Autumn	Winter	Autumn, winter	Winter, summer
Rash	75(100%)	78(100%)	151(100%)	71(100%)	128(100%)
GIT involvement	49(65%)	37(47%)	111(73%)	40(56.35%)	89(69.5%)
Joint involvement	60(80%)	52(66.7%)	91(60%)	40(65%)	57(44.5%)
Renal involvement Hematouria Protinuria	30(40%) 24(32%) 13(17.3%)	19(24%) 19(24%) 10(12.8%)	41(27%) 38(25%) 24(16%)	37(52.11%) 6(8%) 8(11%)	28(21.9%) 33(25.8%) 28(21.9%)
Testicular	1(1.3%)	7(15%)	--------	5(7%)	----------

Discussion

Kidney damage is the principle determinant of prognosis in HSP and occurs in 24-52% of cases in comparable studies. Table 3. It occurs predominantly in preschool and school children with mean age of 6 years and this was comparable to our study, where the peak age of renal involvement was 7-11 years.In this study 30\75(40%) of patients had HSN, with 28\30(93.3%) of theme during 6 weeks from disease onset, which is in accordance with previous observations that 75–100% of patients developing HSN do so within the first 4 weeks after the onset of HSP, and virtually all within 3 months(6-8). Microscopic and macroscopic hematuria was the commonest as it was documented in32% of patients.

40% of our patients hadHSNwhich was relatively high comparable with other studies except the Chinese study(Table 4) none of our patient progressed to acute renal failure, nephrotic syndrome or chronic hypertension. Previous studies reported that renal involvement in HSP occurred more frequently in older children (3-8).

In our study HSP is more frequent in children under the age of 7 years (69.3%) compared with 26.7% in children ≥ 7 years, but HSN occurred in 30.8% of patients below 7 compared to 50% in patient's ≥ 7 years without statistical significance, P value = 0.26. Regarding gender, HSN was slightly higher in boys, 43.6% compared with 32.4% with P value =0.164. So in our study a univariant analysis was not able to show that age and gender had any effect in renal involvement in HSP.

Few studies have assessed initial risk factors for renal involvement in HSP using univariate and multivariate. Kaku et al(3)found evidence that abdominal pain, persistent purpura, and age over 7 years were initial factors associated with HSN.

Sano et al (4) assessed 134 patients with HSP and used a univariate analysis to determine that a significant abdominal pain, persistent purpura and treatment with corticosteroids were most associated with HSN.

Rigante et al (5) demonstrated that the presence of persistent purpura more than one month and severe abdominal pain at the start of the HSP clinical picture were also associated with increased risk of renal involvement in univariant analysis. In our paper it has been demonstrated that the only statistically significant risk factor for the development of renal involvement in HSP is the time as most patients,93.3% who developed renal involvement do so within the first 6 weeks after disease onset. Neither presence of arthritis nor severe abdominal pain was associated with occurrence of HSN with P value of 0.515 and 0.438 respectivly.table3.

Regarding treatment with corticosteroids the previous results described that the use of corticosteroid gave the patients with HSP an earlier resolution of their abdominal pain and joint symptoms(16)in contrast only few reports regarding the effect of steroid in preventing HSN have been published(11,12). Mollica et al (12) described that none of 84 patients with HSP treated with corticosteroids had HSN where's 12(14.3%) of 84 who did not receive corticosteroids developed HSN from 2 to 72 weeks after acute disease. In our study there was no statistical difference between those who treated with steroids and who did not, in fact more patient treated with corticosteroids had HSN and this can be explained as the corticosteroid was used to treat HSN and because of the retrospective nature of the study it is quite difficult to say why more patients treated with corticosteroids had nephritis, table3. Further prospective and \or controlled studies with larger group of patient's are thus necessary in order to justify the need of corticosteroids treatment for preventing HSN.

Frequent urine analysis and follow-up is important, as even patients with mild renal findings at the onset of HSP may run a risk of severe long-term complications and a renal manifestation may be missed because of the short duration of the symptoms and the lack of frequent testing. Even patients with transient renal manifestation in the course of HSP should be followed up for more than 6 months(18).

Conclusions

HSP is one of the most common vasculitis and is considered to be self-limiting disease with excellent prognosis. Renal involvement, HSN occurred in 40% of our patients with 93.3% within 6 weeks of disease onset. Our univariate analysis was not able to show any statistical significance with HSN and presence of arthritis, severe abdominal pain or use of steroids in HSP patients. Further prospective and \controlled studies with multivariate analysis are needed to evaluate the risk factors in development of renal involvement in HSP patients.

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