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Single Center Analysis of HS Purpura and HS Nephritis in Children in Libya

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ABSTRACT

Aim: To describe the clinical features and the presenting symptoms of HS purpura and HS nephritis in Misrata Medical Center and evaluate prognosis of the disease. **Materials and methods**: A retrospective study of children diagnosed as HS purpura in Misrata Medical Center (single center). All patient's data were collected and reviewed from follow-up records in pediatric nephrology Outpatient Clinic in Misrata Medical Center in the period between November 2016 and May 2021. **Results**: In this study, 55 HSP patients were included, 37 patients were boys and 18 were girls giving a male to female ratio of 2.05: 1. The mean age was 5.8 years (range of 1-12). 20 cases presented in spring season (36%), while 19 cases in winter (34%) and 16 cases in autumn. No cases presented in summer season. The most common manifestation was skin rash (100%). 12 cases (21.82%) had renal involvement (nephritis). The most common HS Nephritis manifestation was microscopic hematuria in 21% of cases then proteinuria (11%) and macroscopic hematuria (7%). Only one case had hypertension (1.82%). All patients had normal renal function tests. No cases progressed to End Stage Renal Disease (ESRD). All cases were self-limiting (complete disappearance of renal manifestations occurred within 3 months) except one case (1.82%) that had persistent proteinuria after 1 year of follow-up, she was a 12-year-old girl, presented with headache, edema, skin rash, high BP, gross hematuria and proteinuria. **Conclusion**: From our review for a single center we conclude that HSP is a self- limiting disease with good prognosis. Most cases occur in spring and winter. HS Nephritis occurred in 22% of cases.

تحليل مركزواحد لمرض فرفرية هينوخ-شونلاين والتهاب الكلية المصاحب له للأطفال في ليبيا

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الكلمات المفتاحية:
القصور الكلوي
فرفرية هينوخ-شونلاين
التهاب الكلية
مركز مصراتة الطبي

الملخص

الهدف: وصف المظاهر السريرية والأعراض الظاهرة لمرض فرفرية هينوخ-شونلاين والتهاب الكلية المصاحب له في مركز مصراتة الطبي وتقييم مصير المرض. **المواد والطرق:** دراسة تراجعية للأطفال الذين تم تشخيص إصابتهم بفرفرية هينوخ-شونلاين في مركز مصراتة الطبي (مركز واحد). تم جمع جميع بيانات المرضى ومراجعتها من سجلات المتابعة في العيادة الخارجية لأمراض كلى الأطفال بمركز مصراتة الطبي في الفترة ما بين نوفمبر 2016 ومايو 2021. **النتائج:** في هذه الدراسة، تم تضمين 55 مريضا بفرفرية هينوخ-شونلاين ، 37 مريضا كانوا من الذكور و 18 من الفتيات، مما أعطى نسبة الذكور إلى الإناث 2.05: 1. وكان متوسط العمر 5.8 سنوات (تتراوح من 1-12). 20 حالة ظهرت في فصل الربيع (36%)، و19 حالة في الشتاء (34%)، و16 حالة في الخريف. لم تظهر حالات في فصل الصيف. وكان المظهر الأكثر شيوعاً هو الطفح الجلدي (100%). 12 حالة (21.82%) كانت مصابة بقصور كلوي (التهاب الكلية). كان المظهر الأكثر شيوعًا لالتهاب الكلية هو بيلة دموية مجهرية في 21٪ من الحالات ثم بيلة بروتينية (11٪) وبيلة دموية منظورة (7٪). حالة واحدة فقط كانت مصابة بارتفاع

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ضغط الدم (1.82%). كان لجميع المرضى اختبارات وظائف الكلى طبيعية. لم تتطور أي حالة إلى المرحلة النهائية من مرض الكلى . كانت جميع الحالات تشفى تلقائياً (حدث الاختفاء التام للمظاهر الكلوية خلال 3 أشهر) باستثناء حالة واحدة (1.82%) كانت تعاني من بيلة بروتينية مستمرة بعد عام واحد من المتابعة، وكانت فتاة تبلغ من العمر 12 عامًا تعاني من صداع ووذمة وطفح جلدي وارتفاع ضغط الدم وبيلة دموية وبيلة بروتينية.
الاستنتاج: من مراجعتنا لمركز واحد نستنتج أن فرفرية هينوخ-شونلاين هو مرض قابل للشفاء تلقائياً مع مصير جيد. وتحدث معظم الحالات في فصلي الربيع والشتاء. حدث التهاب الكلية المنسق في 22٪ من الحالات.

1. Introduction

Henoch-Schönlein purpura (HSP) is an idiopathic systemic immune complex–mediated vasculitis associated with IgA deposition within small-vessel walls. It is the most common vasculitis in children, and nephritis (IgAVN or HSPN) is the most important and only chronic manifestation of the disease. It occurs worldwide and affects all ethnic groups but is more common in white and Asian populations. The incidence of HSP is estimated at 14-20 per 100,000 children per year and affects males more than females, with a 1.2-1.8: 1 male/female ratio. Approximately 90% of HSP cases occur in children, usually between ages 3 and 10 yr. HSP is more common in the winter and spring and is unusual in summer months. [1,2]

The hallmark of HSP is its rash, However, in at least 25% of cases, the rash appears after other manifestations, making early diagnosis challenging. Musculoskeletal involvement, including arthritis and arthralgias, is common, occurring in up to 75% of children, Gastrointestinal (GI) manifestations occur in up to 80% of children, Renal involvement occurs in up to 30% of children, manifesting as microscopic hematuria, proteinuria, hypertension, frank nephritis, nephritic syndrome, and acute or chronic renal failure. [3]

diagnosis of HSP is clinical and often straightforward when the typical rash is present. There are no specific laboratory findings of HSP. Renal biopsy rarely is needed for diagnosis, but it is used to assess the severity of glomerulonephritis. Biopsy is required in the care of patients with severe initial manifestations (nephritic, nephrotic, or decreased renal function) or with heavy proteinuria >1 g/day/m2 that persists longer than 1 month. The biopsy indication for with slight proteinuria <1 g/day/m2 that persists longer than 3 months may be considered. HSPN presents more like Immunoglobulin A (IgA) nephritis in older than in younger children. The more severe the clinical presentation, the larger is the percentage of glomeruli affected by crescents and segmental lesions. [4, 5, 6]

Treatment for mild and self-limited HSP is supportive, Although corticosteroids enhance the rate of resolution of the arthritis and abdominal pain, their effectiveness in the prevention of nephritis is debated. In an uncontrolled study of severe HSP cases concluded the corticosteroid therapy does not prevent nephritis [7]. A meta-analysis [8] has evaluated the benefits and harms of different agents (used singularly or in combination) compared with placebo or no treatment or another agent for the prevention or treatment of kidney disease in patients with HSP. It has revealed that data from randomized controlled trials for any intervention used to improve kidney outcomes in children with HSP are very sparse except for short-term prednisone and that there was no evidence of benefit of prednisone in preventing serious long-term kidney disease in HSP. According to a retrospective study on Chinese children: Combined steroid and immunosuppressant therapy was significantly associated with HSPN remission during the initial disease phase. This treatment more effectively reduced proteinuria in patients with HSPN compared with steroid treatment alone. [9]

The 2021 KDIGO Clinical Practice Guideline for IgAV-associated nephritis in children reported that there are no data supporting the use of glucocorticoids to prevent nephritis in children with HSP nephritis and suggested that urinary monitoring is necessary for >6 months and optimally 12 months from initial presentations of systemic diseases. In cases of children with persistent proteinuria for >3 months they should be treated with an ACEi or ARB. Oral predinsolon or pulsed Intravenous methylpredinsolone should be used in mild or moderate diseases, while in severe cases use oral prednisone with immunosuppressive drugs was recommended. [10]

The prognosis of HSP nephritis for most patients is excellent, Nephritis is associated with older age at presentation, persistent rash, and recurrence of HSP, while proteinuria 420 mg/m2/h was associated with recurrence and severe abdominal pain. Only 1-3% of patients progress to ESRD. [11]

The aim of this study is to describe the clinical features and the presenting symptoms of HS purpura and HS nephritis in Misrata Medical Center and evaluate prognosis of the disease.

2. Materials and Methods:

A retrospective study of children diagnosed as HS purpura in Misrata Medical Center (single center). All patients data were collected and reviewed from follow-up records in pediatric nephrology Outpatient Clinic in Misrata Medical Center in the period between November 2016 and May 2021.

Diagnosis of HSP was made by applying EULAR/PRINTO/PRES criteria (European League Against Rheumatism, Pediatric Rheumatology International Trials Organization, and Pediatric Rheumatology European Society) [12] which consist of palpable purpura and one of the following: abdominal pain, arthritis/arthralgia, nephropathy or IgA deposits in biopsy finding.

Proteinuria was determined using a urine dipstick test, with a reading of ≥3+ indicating its presence [10]. Hematuria was defined when microscopic examination showed more than 5 red blood cells (RBC)/ul in a fresh uncentrifuged urine sample or when it is positive on dipstick. [13]

We collected patients data in terms of: age, sex, clinical symptoms and signs, laboratory investigation which included CBC, Renal Function Test, urinalysis , ASO titer and treatment received. Renal Function Test and urinalysis were done frequently during follow-up. Management of data was done by Microsoft Excel 2010 software.

2. Results:

In this study, 55 HSP patients were included, 37 patients were boys and 18 were girls giving a male to female ratio of 2.05 : 1 (Figure 1). The mean age was 5.8 years (range of 1-12). 38 patients (69%) was below the age of 7 years and 17 patients (31%) was ⩾ 7 years.

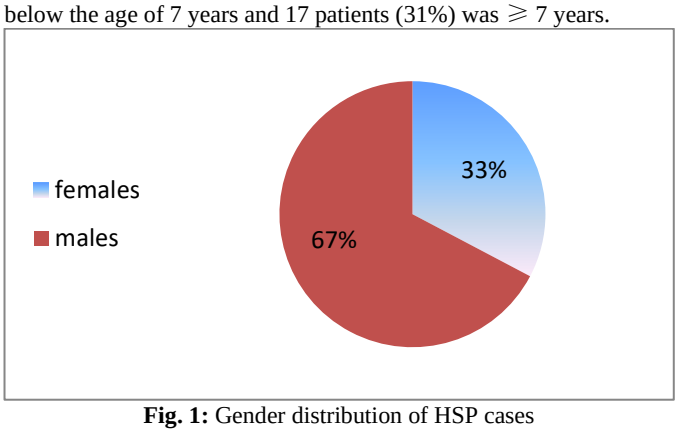

Fig. 1: Gender distribution of HSP cases

20 cases presented in spring season (36%), while 19 cases in winter (34%) and 16 cases in autumn. May was the month with highest number of cases with 13 patients (24%). No cases presented in summer season (Figure 2) .

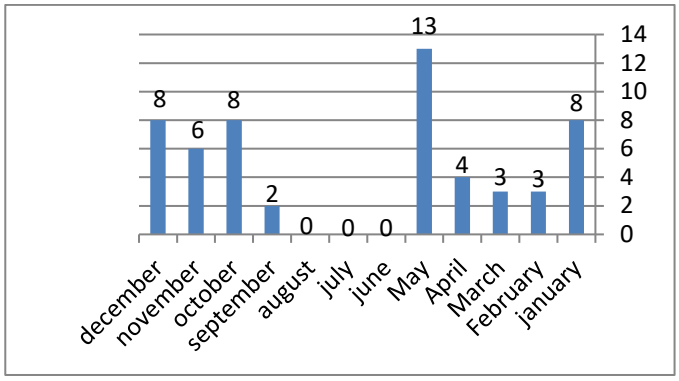

Fig. 2: number of cases in each month (at presentation)

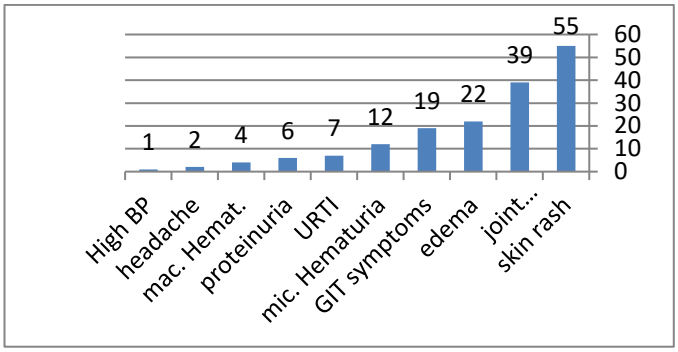

Fig. 3: frequency of clinical manifestations

The most common manifestation was skin rash (100%). 12 cases (21.82%) had renal involvement (nephritis), the mean age for patients with renal involvement was 6.25 years with range of (2-12). The most common HS Nephritis manifestation was microscopic hematuria in 12 patients (21%) then proteinuria in 6 patients (11%) and macroscopic hematuria in 4 patients (7%). Only one case had hypertension (1.82%). Upper or lower limb edema occurred in 22 patients (40%). Upper Respiratory Tract Infection preceded the presentation in 7 patients (12.73%). Gastrointestinal involvement was present in 19 patients (34%). Joint involvement (arthritis/arthralgia) occurred in 39 patients (71%) (Figure 3).

Two cases had nephrotic syndrome (3.64%). All patients had normal renal function tests. No cases progressed to End Stage Renal Disease (ESRD). All cases were self-limiting (complete disappearance of renal manifestations occurred within 3 months of presentation) except one case (1.82%) that had persistent proteinuria after 1 year of follow-up, she was a 12-yaer-old female, presented with headache, edema skin rash, high BP, gross hematuria and proteinuria. Renal function test was within normal, she received antihypertensive treatment, corticosteroid and immunosuppressive drugs. Renal biopsy taken and the result was focal proliferative glomerulonephritis.

For relief of pain, NSAIDs were prescribed for 14 patients (25%) and corticosteroids were prescribed for 3 patients (5%). Immunosuppressive drugs were prescribed for only 2 patients who had renal involvement.

3. Discussion:

We reviewed the results of similar studies in Libya and other countries[14,15] and we made a comparison summarized in Table (1).

Table 1: comparison of results of our study with other similar studies.

Variable	Our study Misrata-Libya	Tripoli- Libya	Egypt	Turkey	China	Indonesia
No. of patients	55	75	60	151	71	128
Age (mean)	5.8	6.5	8,1	7.3	8.55	7.9
Sex M:F	2.05:1	1.14:1	0.94:1	1.47:1	1.29:1	1.8:1
URTI as trigger	7(12.7%)	43(57.3%)	-	33(22%)	66(93%)	19(14.8%)
Season	Spring , winter	Winter, spring	-	Winter	Autumn, winter	Winter, summer
Rash	55 (100%)	75 (100%)	60 (100%)	151 (100%)	71 (100%)	128 (100%)
GIT involvement	19(34%)	49(65%)	48(80%)	111(73%)	40(56%)	89(69%)
Joint involvement	39(71%)	60(80%)	44(73 %)	91(60%)	40(56%)	57(44%)
Renal Involvement	12(21.82%)	30(40%)	11(18%)	41(27%)	37(52%)	28(21.9%)
Hematuria	12(21.82%)	24(32%)	15(25%)	38(25%)	6(8%)	33(25.8%)
Proteinuria	6(10.91%)	13(17.3%)		24(16%)	8(11%)	28(21.9%)

The mean age of presentation in our study was 5.8 years which is in comparison to other studies results slightly higher. Most cases were below the age of 7 years (69%).

From literature, Males are more affected by HSP than females.[1] Male to female ratio was 2.05:1 in the present study, which indicates a higher incidence among males in comparison to above mentioned studies.

Upper Respiratory Tract Infection (URTI) as a trigger is less common in Misrata compared to the other studies. Most cases occurred during spring and winter, then autumn, while no cases occurred in summer season. The seasonal occurrence in Misrata is similar to some studies but varies widely across different regions.

Skin rash was present in all patients -as in other studies- .

GIT involvement occurred in 34%, while joint involvement (arthritis/ arthralgia) was in 39% of patients and both were lower than other studies.

22% of patients had renal involvement, which is similar to the Indonesian study, while other studies had a higher percentage. Microscopic hematuria is the most common manifestation of renal involvement, then proteinuria and gross hematuria respectively. Only in Chinese study proteinuria was more common than hematuria.

We found that all our patients with renal involvement had complete recovery within 3 months of follow-up except one patient (1.82%) who had persistent proteinuria even after one year from onset of symptoms and required a renal biopsy for diagnosis. Frequent urine analysis was done for all patients in follow-up. Tudorache et al reported that even patients with transient renal manifestation in the course of Henoch-Schonlein Purpura should be followed up for more than 6 months. The lack of frequent testing may be the cause of missing renal manifestation and running a risk of severe long-term complications. [16] None of our patients progressed to acute renal failure, which is, from literature, an uncommon complication and accounts for 1-3%. [12]

4. Conclusion:

From our review for a single center we conclude that HSP is a self-limiting disease with good prognosis. Males are affected more than females. Most cases occur in spring and winter. HS Nephritis occurred in 22% of cases.

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