

IgA vasculitis (Henoch-Schonlein purpura) in children: A Kashmir experience

Mohd Ashraf*, Anisa Riyaz, Sayar Ahmed Bhat, Khurshid Ahmed Wani, Naseer Yousuf Mir, Syed Ashiq Nisar Andrabi and Asma Wani

Department of Pediatrics, GB Pant Hospital, Government Medical College Srinagar, Kashmir, India

Received: 23rd November 2020; Accepted: 02nd May 2021; Published: 01st July 2021

Abstract: *Background:* Immunoglobulin A vasculitis (IgAV) also known as Henoch-Schonlein purpura is a common form of primary vasculitis, characterized clinically by palpable skin rash and one or more gastrointestinal, musculoskeletal, and/or renal system(s) involvement. It is more common in less than 10 years, with overall good prognosis. Half of the IgAV patients do have kidney involvement, with very small percentage progress to end stage kidney disease (ESKD). *Objective:* To know the incidence, clinical profile and outcome of IgAV (Henoch-Schonlein purpura) among hospitalized children in Kashmir province. *Methods:* This retrospective study, analysed the case records of all hospitalized patients between 1-18 years, diagnosed with IgAV over the last three years (April, 2017- March 2020). Data on clinical profile, laboratory abnormalities and outcomes were extracted. *Results:* Out of 40681 hospitalised children, 40 had IgAV, where 37 (92.5%) were between 3-10 years, with male female ratio of 1.8:1. Skin rash was observed in 38 (95%) children, gastrointestinal (GI) symptoms in 27 (67.5%), musculoskeletal symptoms in 18(45%) children, while as 11 (27.5%) had renal involvement. Two girls each of 6 and 7 years, and one 7-year boy presented as nephrotic syndrome with hematuria, who underwent renal biopsy, received prolonged immunosuppression, and are doing well with preserved renal functions till last follow up. *Conclusion:* Boys between 3-10 years were the commonest IgAV affected age group, where 95% had skin, 67.5% had GIT, 45% had musculoskeletal and 27.5% children had renal involvement.

Keywords: Children, Hematuria, Henoch-Schonlein purpura, IgA vasculitis.

Introduction

IgAV is an immune-complex mediated small-vessel vasculitis of skin, gut, kidneys and musculoskeletal system, mostly seen in pediatric population [1]. IgAV is diagnosed using clinical criteria like palpable purpura predominantly on the lower extremities, diffuse abdominal pain, hematuria, and arthralgia with or without gastrointestinal bleeding, proteinuria, and/or arthritis. The prevalence of IgAV varies from 3.0 to 26.7 per 100,000 children, more common in preschool boys with increased frequency in autumn and winter [2-3].

The exact cause of IgAV remains elusive; however, it is often preceded by symptoms of upper respiratory tract infection. It has been reported that infectious agents, like hepatitis B and C virus, adenovirus, parvovirus B19, β -

hemolytic streptococcus, mycoplasma, staphylococcus aureus; various drugs, vaccinations, cancers, insect bites and/or exposure to cold weather act as triggering factors for IgAV [2,4].

IgAV term was coined at International Chapel Hill Conference in 2012, replacing the eponym "Henoch-Schonlein purpura (HSP)" based on abnormal deposition of IgA in the vessel walls of the organs involved [5]. Henceforth, the diagnosis of IgAV is based on the EULAR/PRES/PRINTO criteria, that rely on clinical features including the mandatory presence of a vasculitic purpuric rash together with additional symptoms and signs pertaining to GIT, renal, and/or musculoskeletal system yielding an excellent sensitivity (100%) and specificity (87%) [6].

Although conservative management forms the basis of treatment in majority of the cases, but steroids are administered for severe abdominal pain and joint symptoms.

Patients complicated by severe abdominal pain, haematochezia, intussusception, ambulatory impairment, generalized edema, hypertension, or renal insufficiency usually require hospitalization [7-8]. In these situations, oral or parenteral corticosteroids plus mycophenolate mofetil/azathioprine in milder forms of IgAV or intravenous cyclophosphamide and corticosteroids in moderate to severe IgAV disease are administered. Adjunctive therapy like angiotensin system inhibitors are also used in persistent proteinuria and frequently relapsing IgAV. Despite major advances in pediatric medicine, renal outcomes among IgAV affected patients remained same due to lack of reliable markers predicting the prognosis of IgAV, prompting the major research in this field. We aimed this study to acquire the preliminary data and clinical pattern of IgAV among the hospitalized children of Kashmir valley of Jammu and Kashmir, India.

Material and Methods

This retrospective study was based on the data analysis of the records of the discharged patients aged between 1-18 years, hospitalized in the pediatric tertiary care center of Kashmir, from April 2017, to March 2020. Diagnosis of IgAV was based on EULAR/PRINTO/PRES criteria [5].

Any form of secondary cutaneous vasculitis due to other connective tissue diseases and those with other recognizable causes of palpable purpura were excluded. Clinical parameters like weight, gender, age, month and year of onset, presence of symptoms like skin rash/purpura, joint pain/swelling, inability to walk, abdominal pain/blood with stools, discoloured urine, recurrence of symptoms, results of endoscopic procedures, abdominal ultrasonography (USG)/computed tomography (CT), and base line investigations like white blood cell (WBC) count, platelet count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), along with renal biopsy reports were analysed. Incomplete records were omitted. Urinary parameters like microscopic hematuria > 5 red blood cells per high-power field (RBC/HPF), gross hematuria >

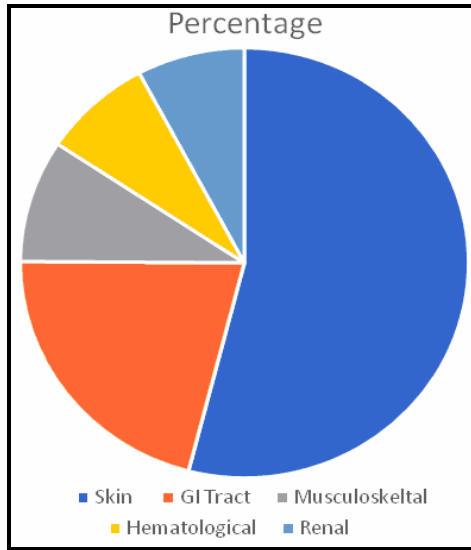
1500 RBC/HPF, sub-nephrotic proteinuria ≥ 4 mg/m²/h but ≤ 40 mg/m²/h, nephrotic range proteinuria ≥ 40 mg/m²/h, with hypoalbuminemia (serum albumin ≤ 2.5 g/dL); were the markers analysed during the evaluation [9]. Outcome at last follow up recorded in the patient's case sheets in the form of past history, treatment, complications, disease progression, recovery, relapse, persistent hematuria with or without proteinuria, was documented and analysed.

Results

Between April, 2017 to March, 2020 a total 40 out of 40681 children hospitalized, had IgAV with a male: female ratio of 1.8: 1 (26 boys:14 girls). Per year patient load was 13, 13, and 14 IgAV patients each for 2017-18, 2018-19, 2019-20 year respectively, providing a hospital admission ratio of ~9/10,000 children. Twenty-five patients (62.5%) were of 3-7 years, where youngest and oldest patient was of 3 and 13 years respectively.

Table-1: Clinical Features of IgAV patients	
System involved	Number (Percent)
Age in years (<8: ≥ 8 years),	25:15
Skin rash	38(95%)
Gastrointestinal manifestations	27(67.5%)
Abdominal pain	27(67.5%)
Gastrointestinal bleeding	4(10%)
Renal manifestations	11(27.5%)
Hematuria	11(27.5%)
Hematuria plus proteinuria	5(12.5%)
Nephrotic syndrome	2(5%)
IgAV Nephritis	2(5%)
Musculoskeletal manifestations	18(45%)
Arthritis	14(35%)
Haematological Manifestations	16(40%)
Anemia (Hb<11g/dL)	12(30%)
Leucocytosis (WBC >11000/ μ L)	16(40%)
Thrombocytosis (Platelets>4lac/ μ L)	5(12.5%)
CRP Positive (>6mg/dL)	5(12.5%)
Fever (>98F)	8(20%)

Fig-1: Pie char depicting various systems involved in IgAV among studied children



During the hospitalization period, cutaneous lesions in the form of palpable purpura were present in 38(95%) children as an initial presentation, while 2 patients presented with abdominal pain as an initial presentation, who were readmitted for same complaint and almost after 2 weeks palpable purple rash appeared on lower limbs. In addition to skin rash, arthralgia/arthritis was the third associated clinical presentation, followed by hematuria and/ proteinuria.

Renal biopsy was conducted in 3 children, one 6 years girl had mesangioproliferative glomerulonephritis, one 7 years boy had nonproliferative glomerulonephritis and one 7 years child had occasional electron dense deposits. Glucocorticoids along with mycophenolate mofetil were prescribed in patients with nephrotic range proteinuria with hypertension. Only glucocorticoids were given for severe abdominal pain, gastrointestinal bleeding, or severe joint involvement. After a mean follow-up of 2 years, one patient with mesangioproliferative nephritis lost to follow up, two patients on mycophenolate mofetil are doing well with preserved renal function, while eight children (14.0%) had persistent proteinuria and/ or hematuria at last follow up.

Discussion

While analysing the data of 40 children, IgAV has been observed more in boys, a finding which

is consistent with the earlier studies [10-13]. IgAV is most frequently seen at 5-7 years of age [12-14], which is in conformity with findings of present study where 25/40 patients were of 3-7 years of age. It is worth mentioning that all our IgAV patients were between 3-13 years, which could be explained by low level of awareness about this illness and alternative consultations at dermatology and orthopaedic departments. In the present study 24 (60%) patients presented during October to February while 16 (40%) presented between March to September months of the year, which is in congruent with the observations made in earlier studies [13-17].

Data of this study revealed that 95% of the patients did have skin rash as an initial presentation which to start with used to be red and blanchable but later-on turned purplish, usually involving the lower extremities, a remarkable finding, very well in line with the findings of published studies [12-13, 18].

In most cases, gastrointestinal (GI) involvement is mild where treatment is not required [1]. Nevertheless, severe abdominal pain, GI haemorrhage, and/or intussusception needs an urgent attention and necessary intervention. We observed abdominal involvement as the second commonest association of IgAV. In present study 27 patients (67.5%) had GI involvement and 4 among them had undergone endoscopy, and one patient had intussusception that was managed conservatively. This observation is identical with the findings of earlier studies [12, 19].

During hospital stay, patients with severe abdominal pain responded to IV/oral steroids, without use of methyl prednisolone, cyclophosphamide or immunoglobulin. However, two patients with severe renal and GI involvement received intravenous methylprednisolone and oral mycophenolate mofetil.

Renal disease in children with IgAV is of prognostic significance, which although is usually mild, but a risk of future kidney impairment is a bothering fact [20]. Consistent with the previous studies, patients of present

study had good renal outcomes with complete recovery in the majority of patients. The frequency of kidney involvement in IgAV varies from 20 to 80 % , that may be in the form of isolated haematuria (14 %), isolated proteinuria (9 %), both hematuria and proteinuria (56 %), nephrotic-range proteinuria (20 %) and nephrotic-nephritic syndrome (1 %) [21-22], Usually in IgAV, first urinary abnormalities are detected within 4 weeks of disease onset in 80 % of children, and within the next 2 months in 20% of the patients. It is noteworthy to mention that little number of patients present with urinary abnormalities several months later or as the initial clinical feature [23].

In present study 11 (27.5%) patients had isolated hematuria, where 5 patients had both hematuria and proteinuria. Out of these 5 patients, 3 underwent renal biopsy, among whom 2 patients had IgAV nephritis and are doing well while on mycophenolate mofetil till last follow up.

Financial Support and sponsorship: Nil

In IgAV most children developed joint symptoms simultaneously with rashes that include arthritis and/or arthralgia. In present study a total of 18 (45%) patients had musculoskeletal involvement, among whom 14 (78%) had joint swelling, 4 patients (22%) had isolated arthralgia, an occurrence that is lower than the reported incidence of joint involvement in IgAV [24]. This could possibly be explained by self-medication and interdepartmental referrals.

Conclusion

IgAV seems no longer a rare entity among the hospitalized children, as depicted from present data (1/1000 hospital admissions), where boys between 3-10 years are commonly affected. Skin rash was observed in 95% patients, followed by GIT (67.5%), musculoskeletal (45%) and renal (27.5%) involvement. Early detection and treatment of IgAV nephritis may prove a game changer of the affected patients.

Conflicts of interest: There are no conflicts of interest.

References

1. Piram M, Mahr A. Epidemiology of immunoglobulin A vasculitis (Henoch-Schönlein): current state of knowledge. *Curr Opin Rheumatol*. 2013; 25:171-178.
2. Nielsen HE. Epidemiology of Schönlein-Henoch purpura. *Acta Paediatr Scand*, 1988; 77:125-131.
3. Shin JI, Lee JS. Familial clustering of Henoch-Schönlein purpura or IgA nephropathy: genetic background or environmental triggers? *Pediatr Dermatol*, 2008; 25:651.
4. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised international chapel hill consensus conference nomenclature of vasculitides. *Arthritis Rheum*, 2013; 65:1-11.
5. Ozen S, Pistorio A, Iusan SM, Bakkaloglu A, Herlin T, Brik R, et al. EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: final classification criteria. *Ann Rheum Dis*. 2010; 69:798-806.
6. Ronkainen J, Koskimies O, Ala-Houhala M, Antikainen M, Merenmies J, Rajantie J, et al. Early prednisone therapy in henoch-schönlein purpura: a randomized, double-blind, placebo-controlled trial. *J Pediatr*. 2006; 149:241-247.
7. Weiss PF, Feinstein JA, Luan X, Burnham JM, Feudtner C. Effects of corticosteroid on Henoch-Schönlein purpura: a systematic review. *Pediatrics*. 2007; 120:1079-1087.
8. Nishi S, Ubara Y, Utsunomiya Y, Utsunomiya Y, Okada K, Obata Y, Kai H, et al. Evidence based clinical practice guidelines for nephrotic syndrome 2014. *Clin Exp Nephrol*, 2016; 20: 342-370.
9. Kang Y, Park J-S, Ha Y-J, Kang M, Park HJ, Lee SW et al. Differences in clinical manifestations and outcomes between adult and child patients with Henoch-Schönlein purpura. *J Korean Med Sci*, 2014; 29:198-203.
10. Ardoin SP, Robinson AB, Torok KS, Van Meter H, Reed AM. Pediatric Systemic Lupus Erythematosus, Juvenile Dermatomyositis, Scleroderma, and Vasculitis. In: Firestein GS, Budd RC, Gabriel SE, McInnes IB, O'Dell JR (eds) Kelley and Firestein's Textbook of Rheumatology, Elsevier, 2017; Philadelphia pp 1844-1875.
11. Saulsbury FT. Henoch-Schönlein purpura in children. Report of 100 patients and the review of literature. *Medicine*, 1999; 78:395-409.
12. Jauhola O, Ronkainen J, Koskimies O, Ala-Houhala M, Arikoski P, Hölttä T et al. Clinical course of extrarenal symptoms in Henoch-Schönlein purpura: a 6-month prospective study. *Arch Dis Child*, 2010; 95: 871-876.
13. Masarweh K, Horovitz Y, Avital A, Spiegel R. Establishing hospital admission criteria of pediatric Henoch-Schönlein purpura. *Rheumatol Int*. 2014; 34:1497-1403.

14. Weiss PF, Klink AJ, Localio R, Hall M, Hexem K, Burnham JM, et al. Corticosteroids may improve clinical outcomes during hospitalization for Henoch-Schönlein purpura. *Pediatrics*. 2010; 126: 674-681.
15. Choi SM, Lee KY. Clinico-epidemiologic study of Henoch-Schonlein purpura in children, 1987 through 2003. *Korean J Pediatr*, 2005; 48:174-177.
16. Zhao YL, Liu ZJ, Bai XM, Wang YC, Li GH, Yan XY. Obesity increases the risk of renal involvement in children with Henoch-Schönlein purpura. *Eur J Pediatr*, 2015; 174: 1357-1363.
17. Pillebout E. Henoch-schonlein purpura in adults: outcome and prognostic factors. *J Am Soc Nephrol*, 2002; 13:1271-1278.
18. Chang WL, Yang YH, Lin YT, Chiang BL. Gastrointestinal manifestations in Henoch- Schönlein purpura: a review of 261 patients. *Acta Paediatr*. 2004; 93:1427-1431.
19. Davin JC, Ten Berge IJ, Weening JJ. What is the difference between IgA nephropathy and Henoch-Schönlein purpura nephritis? *Kidney Int*. 2001; 59:823-834.
20. Shin JI, Park JM, Shin YH, Hwang DH, Kim JH, Lee JS. Predictive factors for nephritis, relapse, and significant proteinuria in childhood Henoch-Schönlein purpura. *Scand J Rheumatol*, 2006; 35:56-60.
21. Jauhola O, Ronkainen J, Koskimies O, Ala-Houhala M, Arikoski P, Hölttä T et al. Renal manifestations of Henoch-Schonlein purpura in a 6-month prospective study of 223 children. *Arch Dis Child*. 2010; 95:877-882.
22. Narchi H. Risk of long term renal impairment and duration of follow up recommended for Henoch-Schonlein purpura with normal or minimal urinary findings: a systematic review. *Arch Dis Child*. 2005; 90: 916-920.
23. Trapani S, Micheli A, Grisolia F, Resti M, Chiappini E, Falcini F et al. Henoch Schonlein purpura in childhood: epidemiological and clinical analysis of 150 cases over a 5-year period and review of literature. *Semin Arthritis Rheum*, 2005; 35:143-153.
24. Wang X, ZhuY, Gao L, Wei S, Zhen Y, Ma Q. Henoch-Schonlein purpura with joint involvement: Analysis of 71 cases. *Pediatr Rheumatol Online J*. 2016; 14:20.

Cite this article as: Ashraf M, Riyaz A, Bhat SA, Wani KA, Yousuf N, Andrabi SAN & Wani A. IgA vasculitis (Henoch-Schonlein purpura) in children: A Kashmir experience. *Al Ameen J Med Sci* 2021; 14(3):248-252.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial (CC BY-NC 4.0) License, which allows others to remix, adapt and build upon this work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

*All correspondences to: Dr. Mohd Ashraf, Assistant Professor of Pediatric Nephrology, Government Medical College Srinagar, Kashmir, India. E-mail: aashraf05@gmail.com.