

## Acute glomerulonephritis after upper airway or skin infection: descriptive analysis of 82 cases between 14 and 64 years-old

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We declare no conflict of interest.

### ABSTRACT

**Introduction:** Acute glomerulonephritis (AGN) after infection of the upper airways or skin is a kidney disease usually caused by streptococcal nephritogenic strains and may present with sudden onset of gross hematuria, hypertension, edema and, occasionally, acute renal failure, is common in childhood and little incident in adults and younger individuals. **Objective:** To analyze, in a descriptive way, data from the initial presentation of GNA after infection of the upper airways or skin in patients over 14 years of age, with emphasis on its epidemiological and clinical aspects. **Patients and Methods:** We reviewed the clinical data of 82 patients treated at our department during the period 1972-2001, divided into three groups: group 1, with individuals between 14 and 20 years ( $n = 52$ ), group 2, between 21 and 30 years ( $n = 19$ ) and group 3, aged  $\geq 31$  years ( $n = 11$ ). **Results:** There was a predominance of the table among younger patients (group 1), male and white, mostly preceded by infection of the skin, appearing most commonly on lower extremity edema and/or face. In some cases, even with nephrotic syndrome, and hypertension, especially in adults over 30 years (group 3), being the least frequent finding of gross hematuria, and rarely, acute renal failure. **Conclusion:** Our findings underscore the importance of studying the AGN after infection of the upper airways or skin in younger individuals and adults, seeking to better characterize its clinical, mainly because it is a group of patients where the disease is less incident.

**Keywords:** glomerulonephritis, infection, infectious skin diseases, respiratory tract infections.

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### INTRODUCTION

Acute glomerulonephritis (AGN) occurring 7 to 21 days after upper airway or skin infection is a self-limited kidney disease. It is usually caused by nephritogenic streptococcal strains, being then denominated acute post-streptococcal glomerulonephritis (APSGN). It includes immune response stimulation, immune complex formation, and complement system activation, that culminate with a diffuse inflammatory infiltration of glomeruli.<sup>1,2</sup>

That type of AGN affects mainly children aged 2 to 6 years, and is rarely described in adults and younger individuals.<sup>3</sup> From the epidemiological point of view it can occur in the form of isolated cases or in endemic or epidemic outbreaks, being more prevalent in men, regardless of race and color.<sup>4,5</sup>

The clinical findings are markedly variable, ranging from asymptomatic forms to severe, symptomatic cases. It more commonly begins with sudden macroscopic hematuria, edema of lower limbs and/or face, and arterial hypertension. Occasionally, hypervolemia with acute pulmonary edema can occur, as well as hypertensive crisis with encephalopathy and convulsions, and acute kidney failure (AKF), which can require emergency dialysis.<sup>6</sup>

The present study aimed at assessing and describing the initial presentation of AGN following upper airway or skin infection in 82 patients aged 14 years and above, cared for at our service over 29 years, with an emphasis on epidemiological and clinical aspects of a disease that is uncommon in that age group.

## PATIENTS AND METHOD

The study assessed clinical data at presentation of 82 patients aged 14 to 64 years, diagnosed with AGN following upper airway or skin infection at the Hospital de Clínicas of the Federal University of Triângulo Mineiro (Universidade Federal do Triângulo Mineiro, UFTM), in the city of Uberaba, Minas Gerais state, from 1972 to 2001.

The diagnosis of AGN was based on the history of a previous (7 to 21 days) purulent upper airway or skin infection, and clinical and laboratory parameters, such as complete blood count and blood biochemistry (electrolytes, urea, creatinine, lipid profile, serum protein profile), serum complement levels (C3 and C4), serum anti-streptolysin O, urinalysis, and 24-hour proteinuria.

Kidney biopsy, which is not a routine indication for such cases at our service, was performed in two of the patients studied, and the histological findings confirmed the diagnosis of acute diffuse glomerulonephritis, probably post-streptococcal. In one of the cases, clinically manifested as rapidly progressive glomerulonephritis, crescentic glomerulonephritis was found.

The parameters assessed in the study were as follows: age (years); sex (male or female); color/race (white or non-white); site of the primary purulent infection (upper airway or skin); and occurrence, at presentation, of macroscopic hematuria, edema of the lower limbs and/or face, arterial hypertension (blood pressure > 140 x 90 mm Hg), and AKF (sudden onset of oliguria or anuria, with initial serum creatinine  $\geq$  1.5 mg/dL).

To assess the clinical variables studied and their predominant characteristics in different age groups from 14 years on, descriptive analysis was performed and the 82 patients were distributed into three groups as follows: group 1 (age range: 14 to 20 years); group 2 (age range: 21 to 30 years); group 3 (age range:  $\geq$  31 years).

The results obtained are shown in the descriptive form of absolute and percentage values for the three age groups proposed in the study.

The study proposal was approved by the Committee on Ethics and Research (CER) of the Federal University of Triângulo Mineiro, state of Minas Gerais (protocol 1537).

## RESULTS

The study assessed 82 patients, whose ages ranged from 14 to 64 years (mean age,  $21.29 \pm 10.03$  years).

Age distribution was as follows: group 1, 52 (63.4%) patients; group 2, 19 (23.2%) patients; group 3, 11 (13.4%) patients. The age distribution in group 3 was as follows: from 31 to 40 years,

seven (8.5%) patients; from 41 to 50 years, two (2.5%) patients; from 51 to 60 years, one (1.2%); and from 61 to 70 years, one (1.2%).

Considering the study sample, the male sex prevailed (62.2% *versus* 37.8%). However, when analyzing the groups individually, the male sex prevailed only in group 1 (75% *versus* 25%), while the female sex prevailed in groups 2 and 3 (57.9% *versus* 42.1% and 63.6% *versus* 36.4%, respectively).

Regarding color/race, the incidence of the disease was higher in white individuals compared with non-white (72% *versus* 28%), which was also evidenced in the distribution of the three groups assessed: group 1, 69.2% *versus* 30.8%; group 2, 73.7% *versus* 26.3%; group 3, 81.8% *versus* 18.2%.

The number of cases of AGN following skin infection in the study was higher than that following upper airway infection (54.9% *versus* 45.1%). That was also evident in group 2 (57.9% *versus* 42.1%) and group 3 (72.7% *versus* 27.3%), while the distribution of upper airway and skin infections was even in group 1 (50% of each).

Macroscopic hematuria was found in 26.8% of the patients, and its distribution in each group was as follows: group 1, 25% of the individuals; group 2, 31.6%; and group 3, 27.3%.

Arterial hypertension was detected in 86.6% of the cases, and its distribution in each group was as follows: group 1, 86.5% of patients; group 2, 84.2%; and group 3, 90.9%.

Edema of the lower limbs and/or face was present in 100% of the patients assessed, and the presence of nephrotic syndrome, confirmed by the finding of hypoalbuminemia and 24-hour proteinuria greater than 3.5 g, was identified in six (7.3%) patients as follows: group 1, three patients; group 2, one patient; and group 3, two patients.

Acute kidney failure was found in 8.5% of the patients as follows: group 1, four patients; group 2, two patients; and group 3, one patient. Dialysis and intravenous pulse therapy with methylprednisolone were required in one patient of group 1, whose clinical presentation was rapidly progressive glomerulonephritis and kidney biopsy showed crescentic glomerulonephritis.

Table 1 shows the variables assessed in the study.

## DISCUSSION

Acute glomerulonephritis following upper airway or skin infection, named acute post-streptococcal glomerulonephritis (APSGN) in the presence of nephritogenic streptococcal strains, is a kidney disease

with well-defined clinical characteristics.<sup>1</sup> It involves intriguing pathogenic and immunological aspects,<sup>2</sup> a tendency towards an incidence reduction in past decades in developed countries, while series of isolated cases and endemic or epidemic outbreaks, mainly in children, continue to be described in developing countries.<sup>3,4</sup>

Reports of large case series of that type of glomerulonephritis in adults and young individuals are scarce, which emphasizes the importance of the present study. We report the initial clinical findings of 82 patients over the age of 14 years presenting with AGN following upper airway or skin infection, possibly post-streptococcal, although streptococcal infection had not been confirmed by serological tests or cultures. It is worth noting that data were collected over a period of 29 years, aiming initially at building a registry of that disease in the population of patients cared for at our service, and not at performing an evolutionary analysis of the cases, which can be of great interest and object of a further study. Some authors have already reported the evolutionary characteristics of post-infectious AGN (streptococcal and non-streptococcal) in adults.<sup>5,6,7,8,9</sup>

Our study identified a greater number of cases of AGN following upper airway or skin infection in young patients, aged 14 to 20 years, and a progressive reduction with age increase in the incidence of

the disease, which was less prevalent in individuals over the age of 31 years. However, it is worth noting the finding of two cases over the age of 51 years, one being 64 years-old, confirming that the disease, although being mainly found in children, can occur at any age.<sup>1,5,7,10</sup>

Regarding sex and color/race, we observed more cases of AGN following upper airway or skin infection in male and white individuals. Those findings are in accordance with previous reports, showing that, due to unknown reasons, the disease affects mainly male individuals,<sup>11</sup> but no reference to color is made.

From the clinical viewpoint, classically, that type of AGN manifests suddenly, being usually preceded by a latency period of 7 to 21 days following an upper airway or skin infection.<sup>1,11,12</sup> In our study, skin infection predominated over upper airway infection, and that was much clearer among the patients over the age of 21 years. Below that age, the incidence of AGN due to both sites of infection was similar.

According to previous reports, macroscopic hematuria, arterial hypertension, and edema are common initial clinical manifestations of AGN following upper airway or skin infection,<sup>1,11,13</sup> and vary from patient to patient. In our study, we observed edema of lower limbs and/or face, at different intensities, in all patients, and nephrotic syndrome, a rare finding in this type of AGN,<sup>11</sup> was detected in six patients. Arterial

**Table 1**

DISTRIBUTION OF THE VARIABLES ANALYZED ACCORDING TO THE THREE AGE GROUPS (ABSOLUTE NUMBERS AND PERCENTAGES)

|                       | Group 1<br>(14 to 20 years) | Group 2<br>(21 to 30 years) | Group 3<br>(≥ 31 years) | Total      |
|-----------------------|-----------------------------|-----------------------------|-------------------------|------------|
| patients (n)          | 52 (63.4%)                  | 19 (23.2%)                  | 11 (13.4%)              | 82 (100%)  |
| sex                   |                             |                             |                         |            |
| male                  | 39 (75%)                    | 8 (42.1%)                   | 4 (36.4%)               | 51 (62.2%) |
| female                | 13 (25%)                    | 11 (57.9%)                  | 7 (63.6%)               | 31 (37.8%) |
| color / race          |                             |                             |                         |            |
| brancos               | 36 (69.2%)                  | 14 (73.7%)                  | 9 (81.8%)               | 59 (72%)   |
| não brancos           | 16 (30.8%)                  | 5 (26.3%)                   | 2 (18.2%)               | 23 (28%)   |
| infection site        |                             |                             |                         |            |
| upper-way infection   | 26 (50%)                    | 8 (42.1%)                   | 3 (27.3%)               | 37 (45.1%) |
| skin infection        | 26 (50%)                    | 11 (57.9%)                  | 8 (72.7%)               | 45 (54.9%) |
| macroscopic hematuria | 13 (25%)                    | 6 (31.6%)                   | 3 (27.3%)               | 22 (26.8%) |
| hypertension          | 45 (86.5%)                  | 16 (84.2%)                  | 10 (90.9%)              | 71 (86.6%) |
| edema                 | 52 (100%)                   | 19 (100%)                   | 11 (100%)               | 82 (100%)  |
| nephrotic syndrome    | 3 (5.8%)                    | 1 (5.3%)                    | 2 (18.2%)               | 6 (7.3%)   |
| acute kidney failure  | 4 (7.7%)                    | 2 (10.5%)                   | 1 (9.1%)                | 7 (8.5%)   |

hypertension was observed in a significant number of cases, prevailing among those over the age of 31 years. Macroscopic hematuria was observed less frequently, and predominated in the age group of 14 to 20 years. Its occurrence decreased as age increased.

Acute kidney failure is a less frequent finding of AGN following upper airway and skin infection, although, when present for more than a few days and mainly when dialysis is required, it can indicate the development of a more aggressive form of disease.<sup>11,14</sup> In our study, AKF occurred in seven cases, and hemodialysis was indicated in one patient with rapidly progressive glomerulonephritis, whose kidney biopsy showed crescentic glomerulonephritis, which is a rare presentation form of that disease.<sup>15</sup>

## CONCLUSION

Our study, assessing 82 patients over the age of 14 years with AGN following upper airway or skin infection, showed the predominant occurrence of the disease in younger individuals, of the male sex, and white color. Glomerular disease following skin infection was more common. From the clinical viewpoint, the major manifestation was edema of the lower limbs and/or face, and occasional manifestations included nephrotic syndrome and arterial hypertension. Less commonly, macroscopic hematuria was found, and, more rarely, acute kidney failure.

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