Abstract

Introduction: The frequency of glomerulonephritis (GN) is reported to be changing in the world over the past four decades. Few studies arise from the western region of Saudi Arabia. Aims: The aim of this study was to address the frequency of primary GN (1ry GN) and secondary GN (2ry GN) over a period of 26 years in the western region of Saudi Arabia and compare to previous data from other regions of the country.

Subjects and Methods: The records of adult renal biopsies, 448 1ry GN and 263 2ry GN, are analyzed. Frequencies of GN subtypes are compared for period 1 (1988–19999) and period 2 (2000–2013). Results: Postinfectious GN (PIGN) and minimal change disease (MCD) show significant changes ($P \leq 0.05$). PIGN increased to 6.5% in period 2 from 0% in period 1. MCD decreased to 5.9% in period 2 from 13.5% in period 1. Membranous GN is the most common 1ry GN for both periods with similar percentages (23.8% and 24.2%, respectively). Focal segmental glomerulosclerosis (FSGSC) is the second in period 2 (23%); immunoglobulin A nephropathy at 9.6% became the third, and MCD is the last place instead of the fourth in period 1. Lupus nephritis is the most common 2ry GN. Pooled data from Saudi studies show FSGSC the most common 1ry GN in both periods. Conclusions: The western region of Saudi Arabia presents with a different 1ry GN pattern than the rest of the country that is likely attributed to its unique geographical and environmental characteristics.

Keywords: Postinfectious glomerulonephritis, primary glomerulonephritis, Saudi Arabia, secondary glomerulonephritis, western region
include insufficient tissues for diagnosis, nonglomerular diseases, normal glomeruli by all studies, and advanced global sclerosis. The cases which were analyzed in the study constitute 448 cases of 1ry GN and 263 cases of 2ry GN [Table 1].

All cases included in the study had been investigated by the three modalities: light microscopy, immunofluorescence (IF) labeling, and EM. Tissue handling and preparation was performed following the routine standard techniques in the EM unit and the hospital histopathology laboratory.

The selected cases of 1ry GN and 2ry GN categories were analyzed separately. Each GN category was further arranged into GN subtypes. Furthermore, the 2 GN categories are divided into two period groups based on the date the biopsy was performed. The two periods are as follows: period 1 representing the years 1988–19999 and period 2 representing the years 2000–2013.

Comparison of the frequency of 1ry GN and 2ry GN subtypes in the two periods was performed. Also correlation of GN subtypes frequencies with age groups and gender was performed.

**Ethical Statement**

The research is approved in the Pathology department board meeting - no. 128482/40 /d; Date 28 / 12 / 1440 Hijra (30/8/2019). Approved by the Dean of the College of Medicine; King Abdulaziz University - Approval no.128482/40 /d / 9; Date 11/01/ 1441 Hijra (11/09/2019). Consent forms are signed by patients before the renal biopsy which includes agreement to use tissue biopsies and patient’s data for education and research purposes. The procedures follow the guidelines laid down in Declaration of Helsinki (year 2013).

**Statistics**

The Statistical Package for the Social Sciences (SPSS) version 22 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp.) was used to analyze the data. Descriptive analysis (frequencies and percentages) were used to obtain variable distribution. Chi-square ($X^2$) was used to obtain the relationship between study variables at a significant level of 0.05; in addition, Bonferroni method was used to investigate the differences between each group within the variable.

**Data collection for 1ry glomerulonephritis in Saudi Arabia**

Data regarding the frequencies of some major 1ry GN subtypes such as FSGSC, minimal change disease (MCD), immunoglobulinA nephropathy (IgAN), MGN, immunoglobulin M nephropathy (IgMN), membranoproliferative GN (MPGN), and postinfectious GN (PIGN) were extracted from original articles coming from Saudi Arabia over the past three decades. The purpose was to compare GN frequencies in the current study and GN frequencies from different parts of the country.

A total of 14 studies were retrieved, of which most of them were retrospective ($n = 12$) and two were prospective. Eight studies came from the central region, two from the western region, one from the eastern region, and three were multicenter studies from different regions of Saudi Arabia [Table 2].

**Table 1: Frequencies of renal diseases in 809 adult renal biopsies**

| Diagnosis                  | n (%)   |
|----------------------------|---------|
| Primary GN                 | 448 (55.4) |
| Secondary GN               | 263 (32.5) |
| Glomeruli no change        | 11 (1.4)   |
| Global glomerulosclerosis  | 41 (5.1)   |
| Others                     | 12 (1.5)   |
| Insufficient tissue        | 34 (4.2)   |
| Total                      | 809 (100.0) |

**Table 2: Gender distribution of 2ry glomerulonephritis subtypes**

| 2ry GN subtypes | Male | Female | Ratio Male:Female |
|-----------------|------|--------|-------------------|
| LN              | 36   | 157    | 0.2:1             |
| DN              | 12   | 15     | 0.8:1             |
| HTN             | 6    | 3      | 2:1               |
| AS              | 0    | 3      | 0.3               |
| CGN-AGBM        | 1    | 0      | 1:0               |
| CGN-V           | 5    | 2      | 2.5:1             |
| AM              | 10   | 4      | 2.5:1             |
| CRYO            | 2    | 1      | 2:1               |
| LCDD            | 2    | 0      | 2:0               |
| MM              | 3    | 0      | 3:0               |
| HSD             | 1    | 0      | 1:0               |
| Total           | 78   | 185    | 0.4:1             |

**Table 3: Pooled frequencies for some 1ry glomerulonephritis subtypes in Saudi Arabia**

| 1ry GN subtype  | Period 1 (1983-2001) | Period 2 (1998-2017) |
|-----------------|----------------------|----------------------|
| FSGSC           | 345 (29.0)           | 322 (35.1)           |
| MCD             | 96 (8.1)             | 90 (9.8)             |
| IgAN            | 108 (9.1)            | 209 (22.8)           |
| MGN             | 127 (10.7)           | 146 (15.9)           |
| IgMN            | 0 (0.0)              | 4 (0.4)              |
| MPGN            | 183 (15.4)           | 77 (8.4)             |
| PIGN            | 7 (0.6)              | 13 (1.4)             |
| Total           | 1188 (100.0)         | 918 (100.0)          |

FSGSC: Focal segmental glomerulosclerosis, IgAN: Immunoglobulin A nephropathy, MPGN: Membranoproliferative GN, IgMN: Immunoglobulin M nephropathy, PIGN: Postinfectious glomerulonephritis, MCD: Minimal change disease, MGN: Membranous glomerulonephritis
The data were then extracted from the publications for the total number of primary GN cases as well as the number of cases in each GN subtype and its percentage. The accumulated data from all studies were divided into two periods: period 1 (1983–2001) and period 2 (1998–2017), to align as much as possible with the present study two periods grouping.

The data are tabulated and pooled and recalculated for some major primary GN subtypes on the pooled data, as shown in Table 3.

Some publications (n = 4) are excluded from the pooled results for the following reasons:

- Incomplete IF and/or EM studies of the biopsy
- Mixed-age groups pediatrics and adults
- Data tabulated in percentages only
- A study including some of the present study cases.

## Results

### Primary glomerular disease frequencies

The total number for cases in period 2 is more than doubled (n = 322) compared with period 1 (n = 126).

### Secondary glomerular disease frequencies

The total number of secondary GN cases in period 2 has almost quadrupled (n = 207) compared with period 1 (n = 56).

### Table 4: The frequencies of primary glomerulonephritis subtypes

| GN categories | GN subtypes | Date category | Period 1 (1988-1999), n (%) | Period 2 (2000-2014), n (%) | Total | P |
|---------------|-------------|---------------|-----------------------------|-----------------------------|-------|---|
| Primary GN    | FSGSC       |               | 27 (21.4)a                  | 74 (23.0)a                  | 101   | 0.016 |
| MCD           |             |               | 17 (13.5)a                  | 19 (5.9)b                   | 36    |   |
| IgAN          |             |               | 28 (22.2)a                  | 63 (19.6)a                  | 91    |   |
| MGN           |             |               | 30 (23.8)a                  | 78 (24.2)a                  | 108   |   |
| IgMN          |             |               | 8 (6.3)a                    | 27 (8.4)a                   | 35    |   |
| MPGN          |             |               | 15 (11.9)a                  | 29 (9.0)a                   | 44    |   |
| MPGN III      | 0 (0.0)a    |               | 1 (0.3)a                    | 1 (0.3)a                    | 1     |   |
| DDD           | 1 (0.8)a    |               | 0 (0.0)a                    | 0 (0.0)a                    | 1     |   |
| PIGN          | 0 (0.0)a    |               | 21 (6.5)b                   | 7 (2.2)a                    | 28    |   |
| C1qN          | 0 (0.0)a    |               | 1 (0.3)a                    | 2 (0.6)a                    | 3     |   |
| IgGN          | 0 (0.0)a    |               | 7 (2.2)a                    | 7 (2.2)a                    | 14    |   |
| FGN           | 0 (0.0)a    |               | 7 (2.2)a                    | 7 (2.2)a                    | 14    |   |

Total (n) 126 322 448

a, b=Groups with same letter no significant difference. GN: Glomerulonephritis, DDD: Dense deposit disease, C1qN: Complement 1q nephropathy, IgGN: Immunoglobulin G nephropathy, FGN: Fibrillary GN, FSGSC: Focal segmental glomerulosclerosis, IgAN: Immunoglobulin A nephropathy, MPGN: Membranoproliferative GN, IgMN: Immunoglobulin M nephropathy, PIGN: Postinfectious glomerulonephritis, MCD: Minimal change disease, MGN: Membranous glomerulonephritis

### Table 5: Change in frequencies of primary glomerulonephritis subtypes in years 1988-1999 versus 2000-2013

| Period 1 (1988-1999) (%) | Rank (GN subtype) | Rank change | Rank (GN subtype) | Period 2 (2000-2014) (%) |
|--------------------------|-------------------|-------------|-------------------|--------------------------|
| 23.8                     | MGN               |             | MGN               | 24.2                     |
| 22.2                     | IgAN              |             | FSGSC             | 23.0                     |
| 21.4                     | FSGSC             |             | IgAN              | 19.6                     |
| 13.5                     | MCD               |             | MPGN              | 9.0                      |
| 11.9                     | MPGN              |             | IgMN              | 8.4                      |
| 6.3                      | IgMN              |             | PIGN              | 6.5                      |
| 0                        | PIGN              |             | MCD               | 5.9                      |

MGN: Membranous glomerulonephritis, FSGSC: Focal segmental glomerulosclerosis, IgAN: Immunoglobulin A nephropathy, MPGN: Membranoproliferative GN, IgMN: Immunoglobulin M nephropathy, PIGN: Postinfectious glomerulonephritis, MCD: Minimal change disease, GN: Glomerulonephritis
The number of cases and percentages of 2ry is shown in Table 6. There is no significant difference in the percentages of case between the two periods with $P = 0.492$ except for the lupus nephritis (LN) cases. LN remains the most common 2ry GN in the two periods with a noticeable rise in percentage from 66% in period 1 to 75.4% in period 2. Diabetic nephropathy (DN) follows as the second most common 2ry GN, slightly decreasing from 14% in period 1 to 9.2% in period 2. The percent of hypertensive nephropathy (HTN) cases has not changed (3.6% and 3.4%, respectively). Cases of crescentic GN with vasculitis (CGN-V) have slightly risen from 1.9% to 5.4% of cases.

### Relationship between glomerulonephritis subtypes and age

Most of the 1ry GN subtypes occur at a younger age (between 19 and 29 years) except for FSGSC and MGN which occur at an older age (30–39 years). These are shown in Graph 1.

LN is diagnosed mostly in the younger age group of 19–29 years. The remaining 2ry GNs occur at an older age; DN, HTN, and CGN-V are diagnosed mostly at 50–59 years, multiple myeloma at >60 years, and amyloid at 40–49 years. These are shown in Graph 2.

### Gender distribution of glomerulonephritis subtypes

1ry GN is more common in males with total male: female ratio of 1.4:1 with the exception of dense deposit disease and fibrillary GN that appear more common in females [Table 7].

The two most common 2ry GN subtypes (LN and DN) are female predominant, with a male: female ratio of 0.2:1 and 0.8:1, respectively. The remaining 2ry GN subtypes are male predominant, as shown in Table 2.

### Total primary glomerular disease cases pooled from the previous Saudi Arabia studies

The details of the Saudi Arabia published data for 1ry GN subtypes are shown in Table 8, and Table 3 presents the pooled data of 1ry GN subtypes in Saudi Arabia for two time periods: period 1 (1983–2001) and period 2 (1998–2017).

FSGSC is the most common 1ry GN in Saudi Arabia for both periods 1 and 2. It accounts for 29% and 35% of the cases,

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**Graph 1:** Relationship between 1ry GN subtypes and age

**Graph 2:** Relationship between 2ry GN subtypes and age

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**Table 6: The frequencies of the 2ry glomerulonephritis subtypes**

| GN categories | GN subtypes | Date category | Period 1 (1988-1999), $n$ (%) | Period 2 (2000-2014), $n$ (%) | Total | $P$ |
|---------------|-------------|---------------|-------------------------------|-------------------------------|-------|-----|
| Secondary GN  | LN          |               | 37 (66.1)a                    | 156 (75.4)b                   | 193   | 0.492 |
|               | DN          |               | 8 (14.3)a                     | 19 (9.2)a                     | 27    |     |
|               | HTN         |               | 2 (3.6)a                      | 7 (3.4)a                      | 9     |     |
|               | AS          |               | 1 (1.8)a                      | 2 (1.0)a                      | 3     |     |
|               | CGN-AGBM    |               | 0 (0.0)a                      | 1 (0.5)a                      | 1     |     |
|               | CGN-V       |               | 3 (5.4)a                      | 4 (1.9)a                      | 7     |     |
|               | AM          |               | 3 (5.4)a                      | 11 (5.3)a                     | 14    |     |
|               | CRYO        |               | 2 (3.6)a                      | 1 (0.5)a                      | 3     |     |
|               | LCDD        |               | 0 (0.0)a                      | 2 (1.0)a                      | 2     |     |
|               | MM          |               | 0 (0.0)a                      | 3 (1.4)a                      | 3     |     |
|               | H.SDROSIS   |               | 0 (0.0)a                      | 1 (0.5)a                      | 1     |     |
|               | Total (n)   |               | 56                            | 207                           | 263   |     |

*a, b=Groups with same letter no significant difference. AS: Alport syndrome, GN: Glomerulonephritis, CGN-AGBM: Crescentic GN-antiglomerular basement membrane, CRYO: Cryoglobulinemia, LCDD: Light-chain deposit disease, H.SDROSIS: Hemosiderosis, MM: Multiple myeloma, AM: Amyloid, LN: Lupus nephritis, HTN: Hypertension nephropathy, DN: Diabetic nephropathy, CGN-V: Crescentic GN with vasculitis*
The most prominent change is a marked increase in the frequency of PIGN from 0% of the 1ry GN cases in period 1 (1988–1999) to 6.5% in period 2 (2000–2013). No such marked elevation in PIGN frequency is identified in studies from Saudi Arabia. The most prominent change in 1ry GN cases is the marked increase in PIGN from 0% in period 1 (1988–1999) to 6.5% in period 2 (2000–2013). No such marked elevation was identified respectively. IgAN cases have notably increased from 9.1% to 22.8% in period 2. MCD, MGN, IgMN, and PIGN showed a slight increase in the percentage of cases in period 2. On the contrary, MPGN cases have declined from 15.4% to 8.4%.

**DISCUSSION**

The current study reports results of adult renal biopsy-confirmed glomerular disease cases from our center database over the past three decades. Our institution is the largest tertiary care center for patients who are residing in the western region of Saudi Arabia. This study identified a significant shift in the frequencies of some GN subtypes over the past three decades (1988–2013).

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### Table 7: Gender distribution of 1ry glomerulonephritis subtypes

| 1ry GN subtypes | Number | Ratio |
|-----------------|--------|-------|
|                 | Male   | Female | Male:Female |
| FSGSC           | 61     | 40     | 1.5:1       |
| MCD             | 23     | 13     | 1.8:1       |
| IgAN            | 51     | 40     | 1.3:1       |
| MGN             | 65     | 43     | 1.5:1       |
| IgMN            | 18     | 17     | 1.1:1       |
| MPGN            | 24     | 20     | 1.2:1       |
| MPGN III        | 1      | 0      | 1:0         |
| DDD             | 0      | 1      | 0.1         |
| PIGN            | 11     | 10     | 1.1:1       |
| C1qN            | 1      | 0      | 1:0         |
| IgGN            | 2      | 0      | 2:0         |
| FGN             | 1      | 6      | 0.2:1       |
| Total           | 258    | 190    | 1.4:1       |

**Remarks**

- *Removed from further analysis. Retros: Retrospective, Prosp: Prospective, Multic: Multicenter, Single C: Single center, W: Western region, E: Eastern region, C: Central region, Ped: Pediatrics, GN: Glomerulonephritis*

### Table 8: Frequencies of some 1ry glomerulonephritis subtypes in Saudi Arabia

| Periods   | Study; author     | FSGSC | MCD | IgAN | MGN | IgMN | MPGN | PIGN |
|-----------|-------------------|-------|-----|------|-----|------|------|------|
| 1998-2017 | AliFaadhel et al., 2019[9] | 213 (39.8) | 37 (6.9) | 156 (29.2) | 91 (17) | 38 (7.1) | 535 |
| 2010-2012 | Al-Homrany et al., 2019[10] | 48 (14.2) | 19 (5.6) | 35 (10.3) | 39 (11.5) | 4 (1.2) | 30 (8.8) | 9 (2.7) | 209 |
| 2005-2009 | Nawaz et al., 2013[11] | ×(27.6) | ×(17.7) | ×(11.5) | ×(9.9) | 192 |
| 2005-2010 | Saleemi et al., 2012[12] | 30 (23.8) | 17 (13.5) | 7 (5.6) | 14 (11.1) | 15 (11.9) | 4 (3.2) | 123 |
| 1988-2005 | Jalalah, 2009[13] | 63 (21.3) | 16 (5.4) | 52 (17.6) | 76 (25.7) | 23 (7.8) | 34 (11.5) | 6 (2) | 296 |
| 1998-2005 | Alkhuwaizi[14] | 25 (35) | 7 (10) | 10 (14) | 3 (4) | 3 (4) | 72 |
| 1990-1999 | Bernih et al., 2000[15] | 13 (15.3) | 25 (29.4) | 13 (15.3) | 3 (3.5) | 7 (8.2) | 5 (5.9) | 70 |
| 1999     | Mousa et al., 2000[16] | 15 (31) | 7 (14.3) | 4 (8.1) | 1 (2) | 34 |
| 1994-1999 | Mitwalli et al., 2000[17] | 44 (22) | 11 (5.5) | 13 (16.5) | 5 (2.5) | 20 (10) | 127 |
| ? Before 2000 | Huraib et al., 2000[18] | 125 (21.3) | 68 (11.6) | 38 (6.5) | 62 (10.6) | 122 (20.7) | 612 |
| 1990-2001 | Al Wakeel et al., 2004[19] | 56 (47.6) | 13 (10.8) | 21 (17.5) | 20 (16.7) | 4 (3.3) | 4 (3.3) | 120 |
| 1989-1994 | Mitwalli et al., 1996[20] | 60 (32.3) | 2 (1.1) | 20 (10.8) | 20 (10.8) | 14 (7.5) | 147 |
| 1983-1988 | Akhtar et al., 1990[21] | 45 (30.4) | 2 (1.3) | 9 (6) | 16 (10.8) | 22 (14.8) | 3 (2) | 148 |

*Removed from further analysis. Retros: Retrospective, Prosp: Prospective, Multic: Multicenter, Single C: Single center, W: Western region, E: Eastern region, C: Central region, Ped: Pediatrics, GN: Glomerulonephritis*
The number of renal biopsies is increasing in the current study, MGN is the most common 1ry GN in both periods. In contrast to other studies from Saudi Arabia, they reported FSGSC as the most common 1ry GN [Graph 3].\cite{6-17} Studies from other parts of the world reported variable results. The United States and Brazil reported similar results to Saudi Arabia, with FSGSC being the most common 1ry GN.\cite{5,13} In the current study the frequency of FSGSC has slightly increased in period 2 to be 23% where it was 21.4% in period 2, and this is not a significant rise as noticed in other studies where FSGSC is particularly reported to increase.

The variations in 1ry GN worldwide can be associated with several factors: geographic location, socioeconomic status, ethnicity, and environmental factors such as infections and pollution. With the improvement in the socioeconomic status, we observe a decrease in IgAN, MGN, and PIGN which might be related to decreasing infectious antigens,\cite{2} MGN may increase due to the rising environmental pollution from industrialization such as heavy metals and organic solvents.\cite{39}

For 2ry GN subtypes, there is no difference between period 1 and period 2 case percentages. However, the total number of biopsies has increased in period 2. LN remains the most common 2ry GN in the two periods. On the contrary, DN frequency decreased in period 2 to become 9.2% from a frequency of 14.3% in period 1. Similarly, LN is reported as the most common 2ry GN in other studies from Saudi Arabia.\cite{6-17} Nowadays, we witness a dramatic increase in the number of renal biopsies for 1ry GN and 2ry GN. One can explain this with increasing population size and improving health care in the country. The primary care facilities have grown in number, and the referrals to tertiary care centers have become more efficient. This reflects on the increased life expectancy of the population to 75 years.\cite{24}

**Conclusions**

The western region of Saudi Arabia presents with a different 1ry GN pattern than the rest of the country; somewhat that is likely attributed to its unique geographical and environmental characteristics. Fewer reports are published from this area which necessitates the development of a Saudi Renal Biopsy Registry as suggested by many other studies.\cite{7,14} Al-Homrany published a plan for establishing a national registry which would unify policies and protocols for renal biopsy to ensure a better understanding of GN pathogenesis and proper patient management.\cite{10} The number of renal biopsies is increasing in
all centers across the country and the number of nephrologists and renal pathologists is increasing as well, and an important achievement would be the establishment of the Saudi Renal Biopsy Registry.

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Conflicts of interest
There are no conflicts of interest.

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