INTRODUCTION

IgA nephropathy is the most prevalent primary chronic glomerular disease worldwide. Overall incidence has been estimated to be 2.5 cases per 100,000 persons per year, with a higher incidence in Eastern Asian populations and a very low incidence in African populations. The annual incidence among children in the United States is about 0.5 cases per 100,000; however, in Japan, the incidence is ten times higher.

Older adults usually present with proteinuria, microscopic hematuria, or hypertension, alone or in combination. In the United States, more than 50% of adults older than 30 years of age at diagnosis have chronic kidney disease at stage 3 to 5. In North American cohorts, the male-to-female ratio is about 2:1 for children and adults, whereas the ratio is approximately 1:1 in Asian populations.

The diagnosis of IgAN always requires renal biopsy. Nephrotic syndrome is uncommon, occurring in only 5% of all patients with IgAN, but is more common in children and adolescents. Patients may develop nephrotic-range proteinuria at different stages of the disease, both when there is mild glomerular injury and when there is advanced glomerulosclerosis.

The diagnostic hallmark of IgA nephropathy is the predominance of IgA deposits, either alone or with IgG, IgM or both, in the glomerular mesangium. The frequency of IgA without IgG or IgM varies greatly, from 0 to more than 85% across centers. Complement C3 and properdin are almost always present. C4 or C4d, mannose-binding lectin, and terminal complement complex (C5b-C9) are frequently detected, whereas C1q is usually absent.

This study was conducted to determine the frequency of IgA nephropathy with year-wise break-up in our population.

METHODOLOGY

It was a retrospective descriptive study conducted from November 2008 to November 2014. Renal biopsies done for the cause of nephropathy were included. The cases with inadequate biopsy specimens, either for light or immunofluorescence microscopy, were excluded from the study. Two separate cores of renal tissue were obtained for histological and immunofluorescence studies. Specimens of renal biopsies were received in 10% formalin for light microscopy and in normal saline for immunofluorescence along with clinical history and particulars of the patients. Moreover, 3 - 4 µm thick sections stained with hematoxylin and eosin were prepared from formalin fixed paraffin embedded renal biopsies.
was made by light microscopic examination. For direct immunofluorescence, biopsies were snap frozen and 4-5 um thick sections were cut on cryostat and air dried. These were then stained with fluorescence isothyocyanate (FITC) labelled antibodies against IgG, IgA, IgM, C3, C4 and C1q. Stained specimens were then observed under fluorescent microscope. Fluorescence intensity was graded as mild, moderate or bright. The patterns were classified morphologically being unaware of the immunofluorescent findings.

The study data was analyzed by using SPSS software version 16.0. Descriptive statistics was applied to calculate mean, standard deviation and ranges from continuous variables and frequency as well as percentages from categorical variables.

RESULTS

One thousand five hundred and fifty-eight patients were included, out of which 458 were males and 1100 were females with an age ranging from 23 - 65 years. One hundred and forty-two (8.6%) patients were found to be IgA positive.

The mean age of patients was 33.2 ±6.9 years ranging from 23 to 70 years. More than half (55.7%) cases were between 21 and 40 years and almost three-forth (74.0%) were found below 40 years of age, showing a younger population with IgA nephropathy (Table I). Male gender was predominant having IgA nephropathy with 98 (69.0%) cases. The clinical features noted in IgA positive cases were proteinuria in (95.1%). Figure 1 is depicting the year-wise breakup of the IgA cases with gradual increase in trend from 2% in 2008 and 9.4% in 2014.

Out of the total 142 IgA positive cases, 16 (11.5%) were IgA alone, 59 (42.0%) were IgA + C3, 11 (7.7%) were IgA + IgM/G, 44 (31.0%) IgA + IgM/G + C3, and 12 (8.45%) cases were found to be IgA + IgM/G C1/q on immunofluorescence.

DISCUSSION

IgA nephropathy causes progressive chronic renal impairment leading eventually to end-stage renal disease. In the current study patients undergoing renal biopsy between 2008 and 2014 were analyzed to determine the frequency and trend of IgA nephropathy. In this study, overall 8.6% positive cases of IgA were noted. The worldwide frequency of IgA nephropathy ranges from 2 to 52%.1 A comparative frequency of IgA cases has been in United States (2 - 10%).4 Higher rates of disease have been reported in biopsy studies from Japan (47%) and Korea (26.0%).3 There is a regional variation in the prevalence of disease as depicted by different studies, which shows an impression of geographical as well as racial differences having some role.

In our country, the incidence of this disease is documented in only few centres as immunofluorescence studies are not available in many laboratories. The frequency of 8.6% of this disease, observed in a period of 7 years (2008 - 2014), is comparable to a local study in which Khan et al. found 5.9% cases.10 Other recent studies done in various other countries showed a higher frequency (10 - 13%) of IgA nephropathy.11,12 The lower frequency of IgA in the current study may be due to long duration/large number of cases, or may be at start of the service. The authors were receiving only in-house cases while now referrals and outpatients are also managed.

According to yearly distribution of cases in last 2 years (2013 and 2014), a higher frequency of 9.4% was noted. This sudden surge may be due to increased number of biopsies being received from the regional centres of different cities, i.e. in 2008 total number of biopsy was 132, and in 2014 it increased to 264 cases. Another possibility of increase is the trend of renal biopsies done by nephrologists.

In this study, the disease was found more common in males (2.2 : 1); however, it has been documented in other international studies as well. The mean age of patients was 33.2 years, which is comparable with that reported from different countries like India and Saudi Arabia.13,14

Similarly, clinical proteinuria was found in 95% cases. Nephrotic syndrome is associated with IgA nephropathy in adults and children. It is well known that clinical features at presentation mark prognosis. Although these

Table I: Baseline characteristics of IgA positive cases (n = 142).

<table>
<thead>
<tr>
<th>Age categories (years)</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10</td>
<td>3</td>
<td>2.1%</td>
</tr>
<tr>
<td>10 - 20</td>
<td>23</td>
<td>16.2%</td>
</tr>
<tr>
<td>21 - 30</td>
<td>45</td>
<td>31.7%</td>
</tr>
<tr>
<td>31 - 40</td>
<td>34</td>
<td>24.0%</td>
</tr>
<tr>
<td>41 - 50</td>
<td>26</td>
<td>18.3%</td>
</tr>
<tr>
<td>51 - 60</td>
<td>8</td>
<td>5.6%</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>3</td>
<td>2.1%</td>
</tr>
</tbody>
</table>

Figure 1: Trend of IgA positivity of renal biopsies from 2008 - 2014.
prognostic features may be informative for populations of patients, they as yet do not have the specificity to identify an individual prognosis with complete confidence. An approach that incorporates sequential information on blood pressure and proteinuria can refine further the prediction of progression risk. Although this still will only account for 30% of overall risk.[15-17] Many studies show different histopathological patterns of disease in different regions; however, none is specific or diagnostic for IgA nephropathy.[2-4] The immunofluorescence findings in the study reveal IgA + C3 and IgA + IgM/G as most frequent. Regardless of these glomerular changes, assessment on interstitial fibrosis tubular atrophy, interstitial inflammation, vascular hyalinosis or red cell casts or proteinuria casts, as seen in other chronic diseases is an important predictor of disease. Immunofluorescence is diagnostic of this disease, its predominant mesangial deposition is characteristic. This study showed alone IgA mesangial deposition in 11.5% of cases while large number of cases showed IgM or IgG deposition along with C3 (88%).

IgA nephropathy is prognostic of poor outcome and putting patient on alert list of end stage renal disease, thus, these patients should be managed timely through proper diagnostic approach. The findings of current study can be generalized; however, further large scale studies are mandated using rigorous research methods on the diagnostic and therapeutic management of these patients.

CONCLUSION

IgA nephropathy is on rise in the Pakistani population. This study has found a high frequency (8.6%) of positive IgA cases. There are concerns regarding this increasing trend thus special health programmes and strategies are the need of hour in resource constraint communities like Pakistan.

REFERENCES