Immunoglobulin a Nephropathy: a Critical Look at the Geographical and Racial Disparity in Reported Prevalence

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ABSTRACT

IgA Nephropathy (IgAN) is undoubtedly the commonest primary glomerulonephritis in the world. The apparent benign nature at presentation in most cases, diagnostic criteria and observed racial disparity in prevalence, make IgAN to occupy a unique position among other primary glomerulonephritides. Surprisingly, IgAN is relatively rare amongst blacks who are known to have a disproportionately high renal disease burden. This review provides an overview of IgAN and discusses the limitations inherent in most of the published studies which have highlighted geographical and racial disparities in its prevalence. An attempt is also made to speculate on possible outcome of prevalence studies after recognised confounding factors have been adequately addressed.

Keywords: *IgA nephropathy; African-American Blacks; Sub-Saharan African Blacks.*

INTRODUCTION

Immunoglobulin A nephropathy, which is commonly referred to as IgA nephropathy, can be said to be a relatively newly recognised form of primary GN, having been first described in 1968 by Berger and Hinglais[1]. It is now widely acclaimed to be the commonest primary GN in the world [2-7]. IgA nephropathy is an immune-complex mediated form of GN which is defined immunohistologically, following renal biopsy, by the presence of predominant mesangial IgA deposits. The mesangial IgA is predominantly of the IgA1 isotype[8]. However, other conditions with similar immunohistological findings, such as Henoch-Schonlein Purpura, Lupus nephritis and chronic liver disease, need to be excluded in the differential diagnosis of IgAN[9]. In an attempt to obviate the need for diagnostic renal biopsy a number of circulating biomarkers for IgAN, such as anti-endothelial cell antibodies(AECA), IgA rheumatoid factor, IgA immune complexes and polymeric IgA1, have been proposed, though none appears to be sufficiently disease specific[10].

The disease has a variable clinical and histological pattern[11-16] . Although initial reports regarded IgAN as a very benign condition[1], it is now known that up to 40% of cases may eventually progress to ESRD[17-19]. Interestingly, IgAN is widely reported to exhibit geographical and racial disparity in prevalence, an observation that is yet to be satisfactorily explained.

Prevalence in Diferent Geographical Regions and Racial Groups

The highest IgA nephropathy prevalence figures of 52% and 47.2% have been reported from Singapore and Japan, respectively [20, 21]. Prevalence figures between 25% and 52% have been reported from other Asian countries[22, 23]. In Europe and North America the figures are not as high as those observed in Asia but the highest prevalence figures of 35.9% and 30.1% have come from Italy and France, respectively[7, 24]. It has also been observed from comparison of studies between different time periods, that there is a general trend towards increasing

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prevalence in IgAN [22]. For example, in a UK study, the prevalence of IgAN was found to increase from 7.1% to 21.1% between two time periods of (1972-78) and (1979-86) and this was partly ascribed to the introduction of more liberal renal biopsy policy over time[25].

Reported prevalence of IgAN varies among racial groups, being most common among Orientals followed by Caucasians and rare among blacks[26]. Most reports on low prevalence of IgAN in blacks have come from studies on African Americans[27-29]. Reports from sub-Saharan African blacks have indicated even much lower prevalence rate[30]. Interestingly, the most populous black country in the world, Nigeria, had her first and only case of IgAN reported in 1992[32]. A subsequent retrospective evaluation of renal biopsies from the same Nigerian centre failed to identify any additional case of IgAN but speculated on possible missed diagnosis on account of a dearth of immunohistological evaluation facilities[33]. Undoubtedly, a multiplicity of factors could be responsible for the difficulty in determining any meaningful prevalence of IgAN in this oil rich nation, which is still nevertheless plagued by low developmental indices.

Any meaningful comparison of IgAN prevalence between different racial groups is better conducted in locations with adequate racial population mix. The United States of America and South Africa can be said to meet such conditions and findings from studies on IgAN in them have been most useful.

Reports from South Africa indicate that IgAN is not uncommon among Whites followed by Indians but very rare among blacks[31]. It is however necessary to bear in mind that these were retrospective studies conducted on renal biopsies done during the Pre-democratic era, with attendant confounding factors that were not controlled for.

Contributory Factors to Disparities in Prevalence

Any factor or group of factors that tend to influence the incidence of IgAN in a geographical area will invariably contribute to any observed disparity in prevalence when comparing studies from different regions. While a few factors may be influencing observed incidence and prevalence of IgAN in the developed countries, additional factors, such as inadequate diagnostic facilities and low level of awareness amongst patients and health care providers are invariably at play in developing countries, particularly those in sub-Saharan Africa.

While the possible contribution of traditional factors, such as level of disease awareness, access to appropriate diagnostic facilities and referral patterns to racial disparity in prevalence may not be too difficult to appreciate, the often assumed genetic basis for such disparity is yet to be confirmed.

Previous studies which have suggested that genetic factors play a role in the pathogenesis or susceptibility of IgAN have focussed on whites and orientals, due to difficulty in identifying black patients[34-35]. Limited efforts at identifying putative protective genes against IgAN in blacks, following a speculation that homozygosity for the A2m(2) allotype of IgA2 would be protective, have however proved abortive[36].

Possible Impact on Racial Disparity in Prevalence From Paediatric Studies

It is well recognised that macroscopic haematuria is far more frequent as a presenting symptom of IgAN in the paediatric age group compared to adults. Paediatric IgAN patients would therefore be more likely to attract and receive early medical attention, which could include an early referral for possible diagnostic renal biopsy. In children therefore, fewer cases of IgAN are likely to be missed, compared to adult cases. In the absence of limitations in available facilities, the privileged position enjoyed by children tends to cut across racial and ethnic barriers. This is so because of the global nature of parental love as well as the compassion that health care providers extend to children, regardless of their race or ethnicity.

In the case of IgAN in children, it follows that any possible racial disparity in prevalence would be less likely due to any racial differences in patterns of referral or biopsy selection practices. The above position is well exemplified by the study of Sehic et al[37] in which the incidence of IgAN among Caucasian children in Tennessee was found to be 3.0 per million population per year, compared with 5.7 per million per year among African-American children. These contrast very much with the very low figures recorded for adult Blacks in comparison with other races.

CONCLUSION

The prevalence of IgAN within a geographical area or racial group will be influenced by a number of factors, some of which are modifiable, such as

prevailing rate of renal biopsy, level of IgAN awareness, availability and access to appropriate diagnostic facilities. While it could be argued that successful implementation of strategies to address the above identified confounding factors in prevalent studies may help to improve true prevalence figures of IgAN in blacks, it is doubtful if such measures would be adequate to bridge the currently widely observed gap in prevalence between blacks and other races. The case for a role of susceptibility genes to IgAN appears to have been made in Oriental and Caucasian subjects [38,39]. However, until efforts at identifying any of the putative genes, believed by some investigators to be protective against IgAN in blacks bear fruit, it is perhaps premature to assume that there is a predominant genetic basis for the apparent rarity of IgAN reported so far in blacks.

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