Prevalence of lupus nephritis and the use of serology in a central South African chronic kidney disease patient cohort

To the Editor: Lupus nephritis (LN) is a frequent kidney manifestation of systemic lupus erythematosus (SLE) and is classified into six histological classes (I - VI), as per the International Society of Nephrology and Renal Pathology Society criteria.[1] Of the six classes, class III, IV and mixed class V are known as the proliferative forms of LN, which have a more aggressive disease course and poorer prognosis.[2] The initial diagnosis of SLE is made based on the Systemic Lupus International Collaborating Clinics criteria and the 2019 European League Against Rheumatism/American College of Rheumatology (ACR) classification criteria.[3-5] Accurate statistics regarding the prevalence of LN in sub-Saharan Africa are limited owing to limited availability of kidney histology registries.[6] However, a substantial amount of research has highlighted worse prognostic factors among individuals of African descent,[2,7-9] attributed to multifactorial factors such as apolipoprotein L1 (*APOL-1*) gene polymorphism, less robust cutaneous manifestations that contribute to delayed diagnosis of SLE and poor access to healthcare.[6-7,10] The delayed identification of LN has become a major underlying cause of chronic kidney disease (CKD) in South Africans.[2] LN research in South Africa (SA) is limited, and although the prevalence is reported as high,[11-12] no representative value has been published for the central SA population. However, the few data that are available indicate that the SA LN population has a consistently poorer prognosis in comparison with other global populations.[11-14] This therefore necessitates further analysis of this population.

It is important to note that our findings form part of the aim of a larger genetic study wherein the human leucocyte antigen (HLA) profiles of patients with biopsy-proven CKD from a single centre in Bloemfontein, Free State Province, were investigated. This was done in order to determine whether specific HLA alleles confer a higher risk for CKD, and therefore, a study population with a well-defined diagnosis was selected. Consequently, as part of the inclusion criteria of the main study, all participants must have undergone a kidney biopsy, and were recruited between January and June 2022. In conducting this research, we were able to determine the distribution of the various chronic kidney diseases in a central SA population, from which we found the prevalence of LN to be noteworthy.

Ethics approval was obtained from the Health Sciences Research Ethics Committee of the University of the Free State (ref. no. UFS-HSD2021/1462/2501), as well as permission from the Free State Department of Health (ref. no. FS_202112_005) and the National Health Laboratory Services, in order to conduct the main study.

In this study of 100 (n=100) patients diagnosed with biopsy-proven CKD from the nephrology clinic at Universitas Academic Hospital, the prevalence of LN in the cohort was found to be 38% (n=38/100). The LN population had a significant female (78.95%, n=30/38) predominance in comparison with the male (21.05%, n=8/38) population. This is attributable to the known fact that SLE commonly affects females of child-bearing age.[7] The ages of the LN cohort ranged between 20 and 61 years, with a mean age of 33.9 years (standard deviation 9.6) and a median age of 32 years (interquartile range 27.3 - 38.8). The ethnic distribution of the LN cohort was almost identical to the distribution of the total CKD population in this study (African descent: 84.21% v. 84%; European descent: 7.89% v. 8%; mixed ancestry: 5.26% v. 6%; Asian/Indian descent: 2.63% v. 2%). Therefore, these results suggest that the prevalence of LN in our CKD cohort is not predisposed by ethnicity. However, the female participants between the ages of 20 and 43 years contributed a substantial proportion (68.42%, n=26/38) of the total LN population.

The majority of participants in this study were diagnosed with class V LN (26.32%, n=10/38), followed by mixed class IV and V LN (23.68%, n=9/38). Class III, mixed class III and V and class IV LN each contributed 15.79% (n=6/38) of the total LN population studied. Only one participant was diagnosed with class II LN (2.63%, n=1/38), and none with class VI LN. This equates to a total of 71.05% of the LN cohort with a proliferative form of the disease, suggestive of a poorer prognosis.[2] The most common clinical features in the LN cohort were hypertension (60.53%, n=23/38) and severely increased proteinuria, including nephrotic-range proteinuria (47.37%, n=18/38).

Anti-nuclear antibodies (ANAs) are considered to be the serological hallmark of SLE.[15] Our results support the prominent role that ANAs have in LN disease aetiology, with 94.74% (n=36/38) of the LN study population being positive for ANA, accounting for 85.71% (n=36/42) of the entire CKD population with positive ANA, but not histologically proven LN. This translates to approximately every 8 in 10 ANA-positive individuals with CKD having LN. Eight participants were not tested for specific ANAs, and were excluded from further serological analysis. Subsequently, specific ANAs, namely anti-double-stranded DNA antibodies (anti-dsDNA) and anti-Smith antibodies (anti-Sm) were equally detected in 57.14% (n=16/28) of the LN population. Anti-dsDNA and anti-Sm antibodies are considered to be highly specific markers for SLE and are predictors of high risk for developing LN in patients with SLE.[15] However, a different type of ANA, namely anti-ribonucleoprotein (anti-RNP) antibody, which is not specific to SLE according to the ACR criteria,[5] was present in more than half (71.43%, n=20/28) of the total LN cohort with positive ANA, indicating that it may potentially be more specific to LN in our population.

We conclude that LN is one of the major causes of CKD in this region, with a relatively high prevalence. We recommend that patients who present with kidney diseases be screened for LN with the appropriate clinical evaluation and highly indicative autoimmune serology, specifically females of child-bearing age.

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