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Investigation of Lupus Nephritis Cases with Special Reference to Activity and Chronicity Indices

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Abstract

Background & Objectives: The International Society of Nephrology/ Renal Pathology Society (ISN/RPS) classification is based upon criteria which differentiate acute and chronic phases of Lupus Nephritis. Activity/Chronicity Index grants us a higher insight on the level of pathological lesions and treatment outcome by examining the reversibility of lesions. The present investigation was done in order to highlight the importance of activity and chronicity indices in the course of Lupus Nephritis.
Materials & Methods: Seventy-three Kidney biopsy samples of Lupus Nephritis patients were examined. The information was recorded in a check-list and was then statistically analyzed.
Results: Lupus Nephritis is importantly age-related, frequency of Lupus Nephritis increases with age until the age of 40 years; 21–40 years being the most frequent among studied patients. A prominent decline was seen after the age of 40. Regardless of age, the occurrence was more frequent in females. Class IV was most frequent in all ages and in both sexes. Both Activity and Chronicity scores were slightly higher in females. Activity Index was higher in ages of 11 to 30 years, whereas Chronicity Index was highest in 41 to 50 years of age. The highest Activity Index was reported in Class IV while the highest Chronicity Index was reported in Class V. The least Activity Index was shown in Class VI while Classes II and I had the lowest Chronicity Index. Endocapillary hypercellularity was the most frequent active lesion and tubular atrophy was the most frequent chronic lesion. It is noteworthy that fibrotic crescents were significantly less common among chronic lesions.
Conclusion: Histopathological findings, clinical and para-clinical data could furnish more information on disease process, treatment, quality of life and mortality rate.

Keywords: Lupus Nephritis, Activity Index, Chronicity Index, Histopathological features

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Introduction

Systemic Lupus Erythematosus (SLE) is a multi-systemic autoimmune disease. One of the major consequences of this disease is Lupus Nephritis (LN) and prognosis of LN is heavily determined by the WHO, ISN/RPS classification which helps with early management of this disease (1). Patients in whom LN occurs are at an earlier age in comparison with those SLE patients whose Kidneys are not involved. LN generally develops in the first 6 to 36 months during the course of SLE. Patients with LN have a significantly higher mortality rate (2). Factors such as sex, age, and ethnicity influence the incidence and prevalence of SLE in different parts of the world (3, 4). Regardless of age or ethnicity,

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LN has been repeatedly reported to be more common in females in comparison with male patients, specifically before the menopausal age (5-8). Kidney involvement has been reported to be more common in children compared to adults (9).

The incidence of LN has repeatedly been reported to be higher in people of Asian, African and Hispanic backgrounds in comparison with Caucasians (10-12). A more severe involvement of the kidneys has been reported in African, Asian and Hispanic populations (13-18).

The first worldwide classification of LN which was merely based upon Glomerular lesions was arranged by Peyrani and Pollock in 1974 (19). Many LN patients present with glomerular lesions mediated by immune complex structures, usually with Tubulointerstitial changes with the presence or absence of immune deposits. Damage to the vascular system of the kidneys is also common in LN patients; this damage could vary from indolent immune deposits to fibrinoid necrosis as well as thrombotic microangiopathy. Generally, Classes III, IV and V are considered progressive (10).

The ISN/RPS classification included criteria which differentiated the acute and chronic phases of the disease based upon the morphology of the glomerulus. Furthermore, Activity and Chronicity Indices were described to present more information on the level of pathological lesions and therapeutic outcome as determinants of the reversibility of the damage caused by these lesions (20).

The NIH/WHO Activity and Chronicity indices were used to determine the progression of LN to End Stage Renal Disease (ESRD) and although Activity Index is a weaker determinant in the primary biopsy, the Chronicity Index could moderately determine the survival of the Kidney (21). Chronicity Index indicates the loss of Nephrons while Activity Index shows the potential reversible renal damage (22).

The present investigation was done in order to highlight the importance of activity and chronicity indices in the course of Lupus Nephritis.

Material & Methods

This retrospective study was conducted on histopathological reports of patients diagnosed as LN from 2014 to 2019. Different criteria such as gender, age, class of LN, Activity and Chronicity indices were taken into consideration in the present study.

In order to discover the distribution pattern of this disease based on the histopathological findings of the biopsy sections, the obtained data were statistically analyzed using chi-square and SPSS version 17. Values less than 0.05 were considered significant.

The study is in agreement with the ethical guidelines of the declaration of Helsinki and follows the ethical standards of the School of Medicine in which the research took place.

In this study, biopsy sections of 71 LN patients were investigated in detail. Parameters obtained were compared with each other and an in-depth comparison was carried out on the criteria of Activity and Chronicity indices.

In a more detailed analysis of 33 biopsy sections belonging to cases in the age range of 30 to 50 year, Activity and Chronicity indices were studied in accordance with ISN/RPS histopathological criteria of LN.

This project was confirmed by Ethics Committee of the Urmia University of Medical Sciences (#IR.UMSU.REC.1398.358).

Results

The analysis on the age and sex factor was done by comparing the number of cases in each range of 1 to 80 years of age. No cases were recorded between 1-10 years and 71-80 years. The results clearly showed that the incidence of LN was higher between the ages of 11 and 40, and the highest number of cases occurred in the age group of 21 to 40 years. A decline in the number of

cases was seen after the age of 40 (Figure 1A). The results indicated that occurrence of LN in female patients were prominently dominant between ages of 11 to 50 years old. There was a marked increase in the number of female cases from age 11 to 40 compared to male cases. The highest preponderance of the number of female cases compared to the number of male cases was recorded between the ages of 31 and 40. The number of female and male cases in the ages of 51 to 70 was equal (Figure 1B).

Based on the histopathology, the distribution of the different LN classes was recorded in both sexes. Class IV of LN was shown to be most frequent in all age ranges and had the highest occurrence in the age range of 11 – 30 (Figure 1C). Based on the analyzed data, Class IV was the most frequent Class of LN in both genders.

The mean Activity and Chronicity indices scores were each calculated in female and male cases. The results indicated that both Activity and Chronicity scores were slightly higher in female patients, considering that the number of female cases was significantly higher than that of the males (Mean Activity score in female patients: 5.847, Mean Chronicity score in female patients: 2.864, Mean Activity score in male patients: 5.375, Mean Chronicity score in male patients: 2.125).

Cases were also compared based upon the dominance of their Activity or Chronicity scores. It was shown that the Activity score was higher than the Chronicity score in all ages, most significantly in the age range of 11 to 20. However, comparing the Chronicity scores shows that the higher values of the Chronicity scores occur between the ages of 31 and 50, and more specifically, the highest values occur between the ages of 41 and 50 (Figure 1D). Activity and Chronicity indices were compared within different histopathological classes of LN. The highest Activity Index was reported in Class IV while the highest Chronicity Index was reported in Class V. The least Activity Index was shown in Class VI while Classes II and I had the lowest Chronicity Index. There was a significant correlation between the classes of LN and Activity score ($P<0.01$) / Chronicity score ($P<0.01$) in our study (Figure 2).

Among the histopathological lesions included in Activity Index criteria, endocapillary hypercellularity (Figure 5A) was significantly of higher ratio than other lesions, which was followed by interstitial inflammation (Figure 5B), leukocyte infiltration (Figure 5C), hyaline cast, cellular crescent and fibrinoid necrosis showed the least ratio (Figure 1E). With regard to the lesions of Chronicity Index criteria, tubular atrophy (Figure 5D) showed the highest ratio followed by interstitial fibrosis (Figure 5E), glomerular sclerosis and fibrotic crescent (Figure 5F) being significantly of lower ratio than other lesions (Figure 1F).

The result of the comparison of Activity Index with various lesions clearly indicated that there was a significant correlation ($P<0.001$) between all lesions except for cellular crescent lesions (Figure 3) There was a significant correlation ($P<0.05$) between all Chronic histopathological lesions and Chronicity Index (Figure 4).

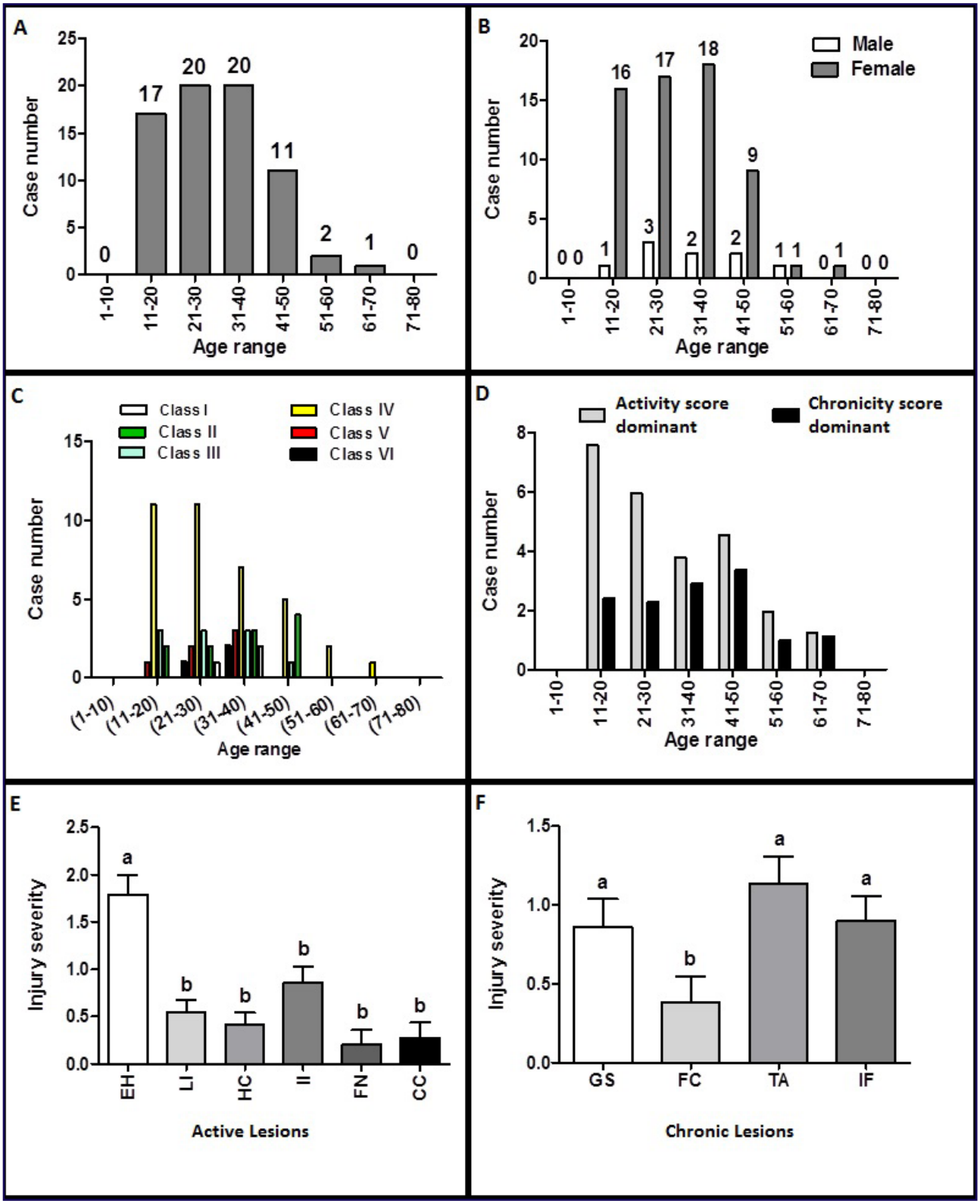


Figure 1. Number of LN cases compared in different age ranges (A), number of LN cases compared based on sex in different age ranges (B), number of LN cases compared based on LN class in different age ranges (C), number of cased compared based on the dominance of Activity or Chronicity Index score in different age ranges (D), severity of each histopathological lesion included in Activity Index criteria (E), severity of each histopathological lesion included in Chronicity Index criteria (F)

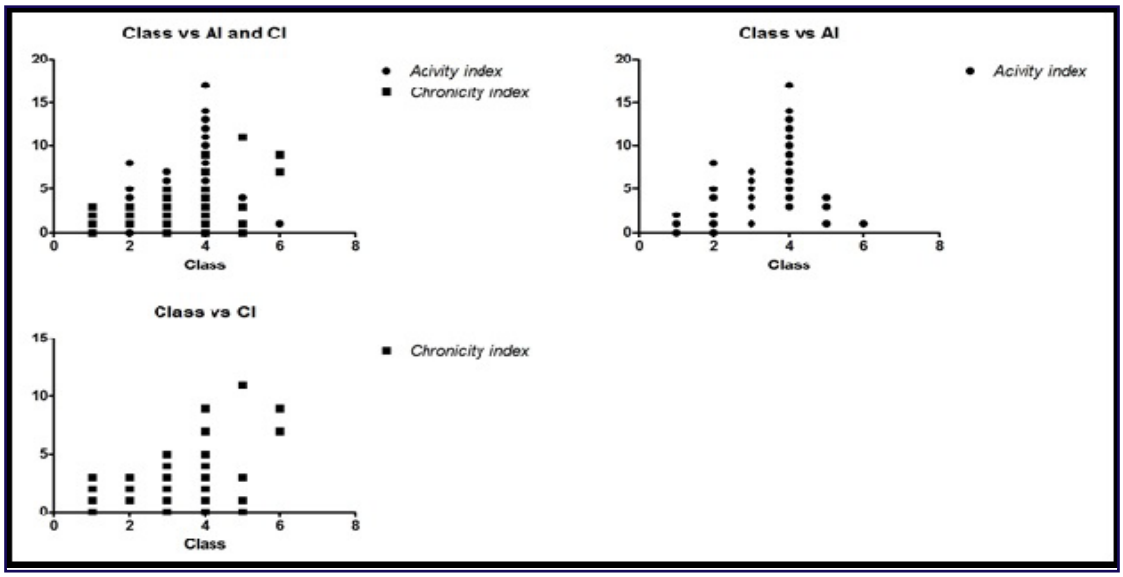


Figure 2. Distribution of Activity Index (AI) and Chronicity Index (CI) scores based on LN classes (P<0.01)

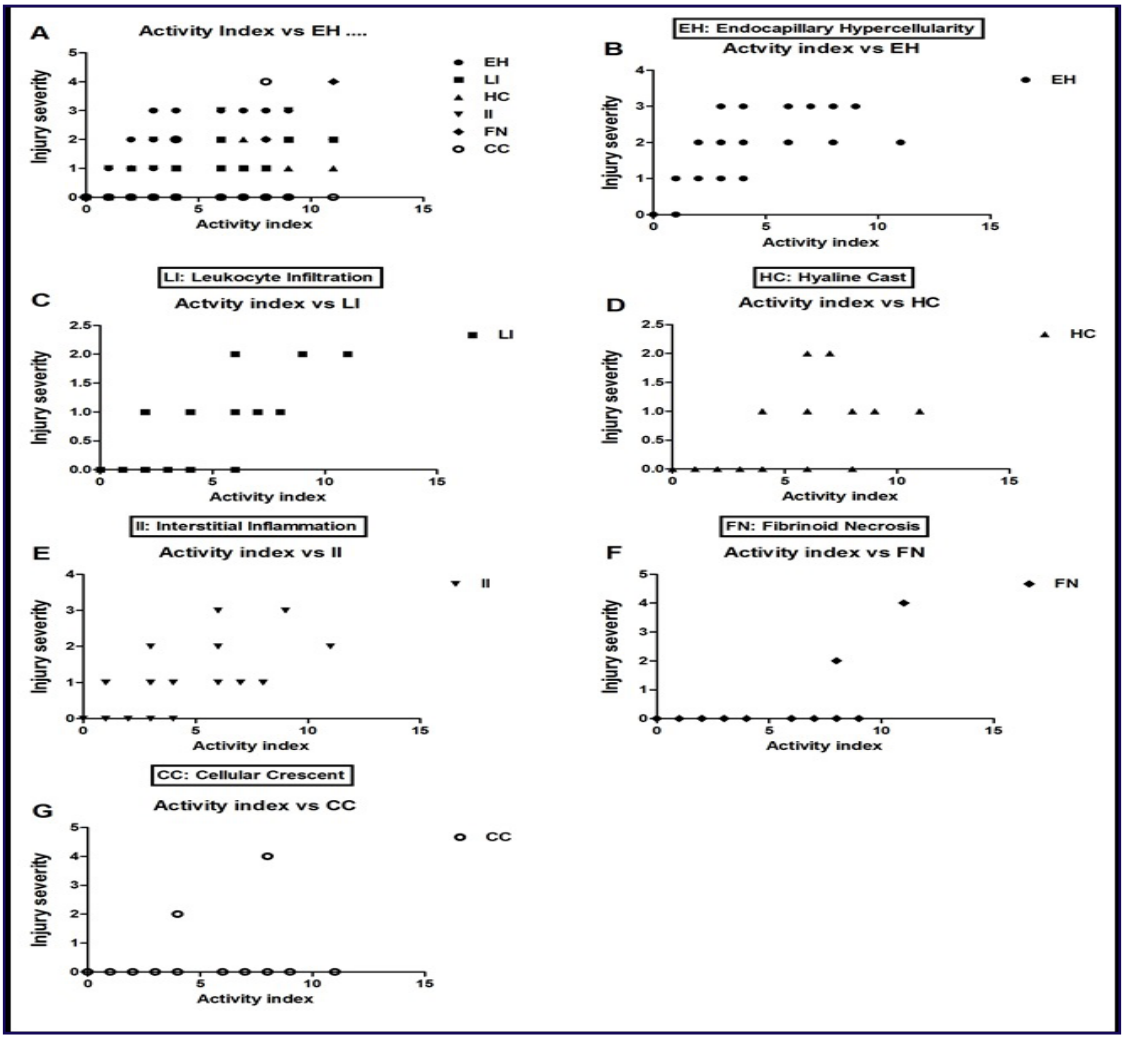


Figure 3. Comparison of severity of histopathological lesions [Endocapillary Hypercellularity (EH), Leukocyte Infiltration (LI), Hyaline Cast (HC), Interstitial Inflammation (II), Fibrinoid Necrosis (FN), and Cellular Crescent (CC)] included in the Activity Index criteria with Activity Index scores (P<0.001)

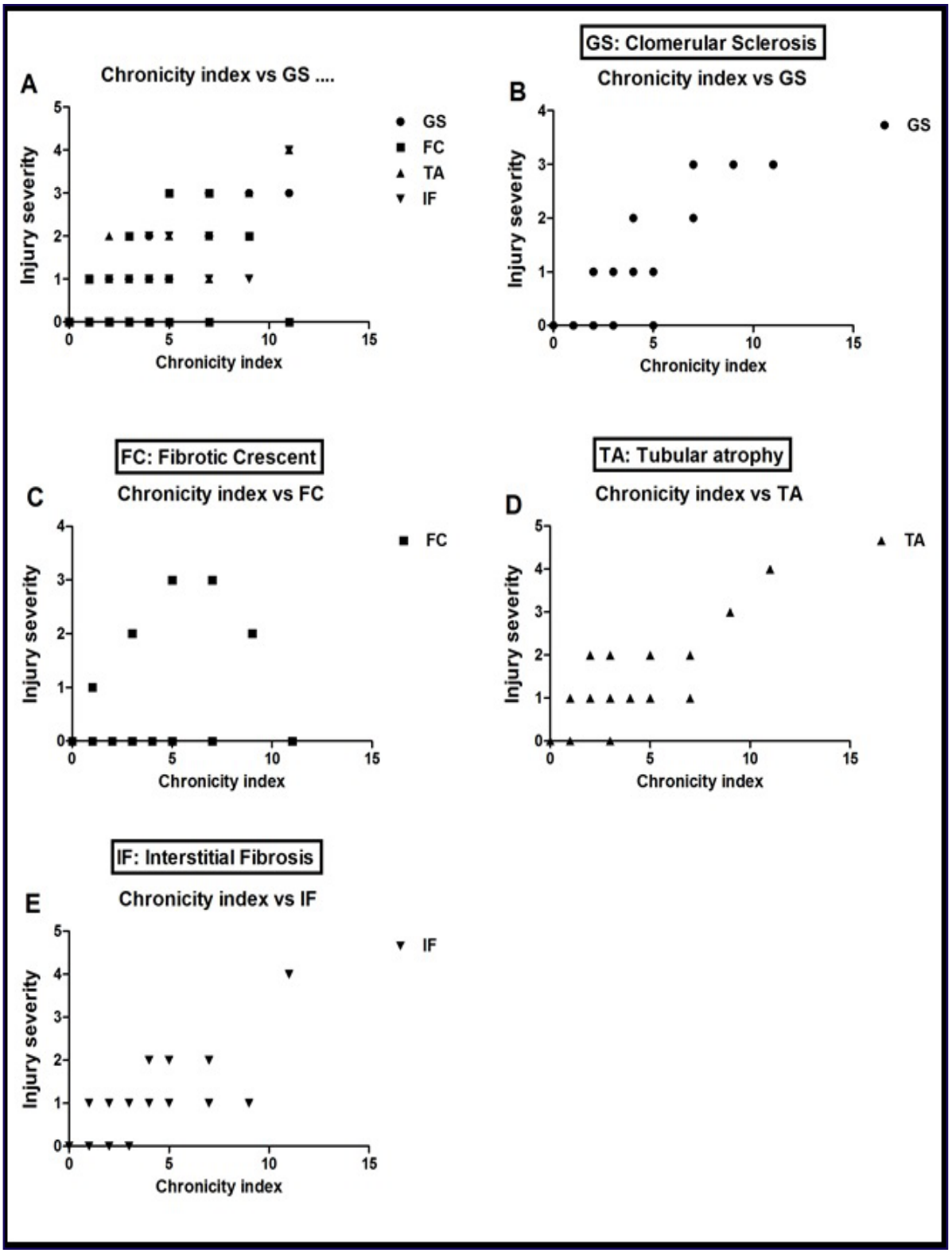


Figure 4. Comparison of severity of histopathological lesions [Glomerular Sclerosis (GS), Fibrotic Crescent (FC), Tubular Atrophy (TA), and Interstitial Fibrosis (IF)] included in the Chronicity Index criteria with Chronicity Index scores ($P<0.05$)

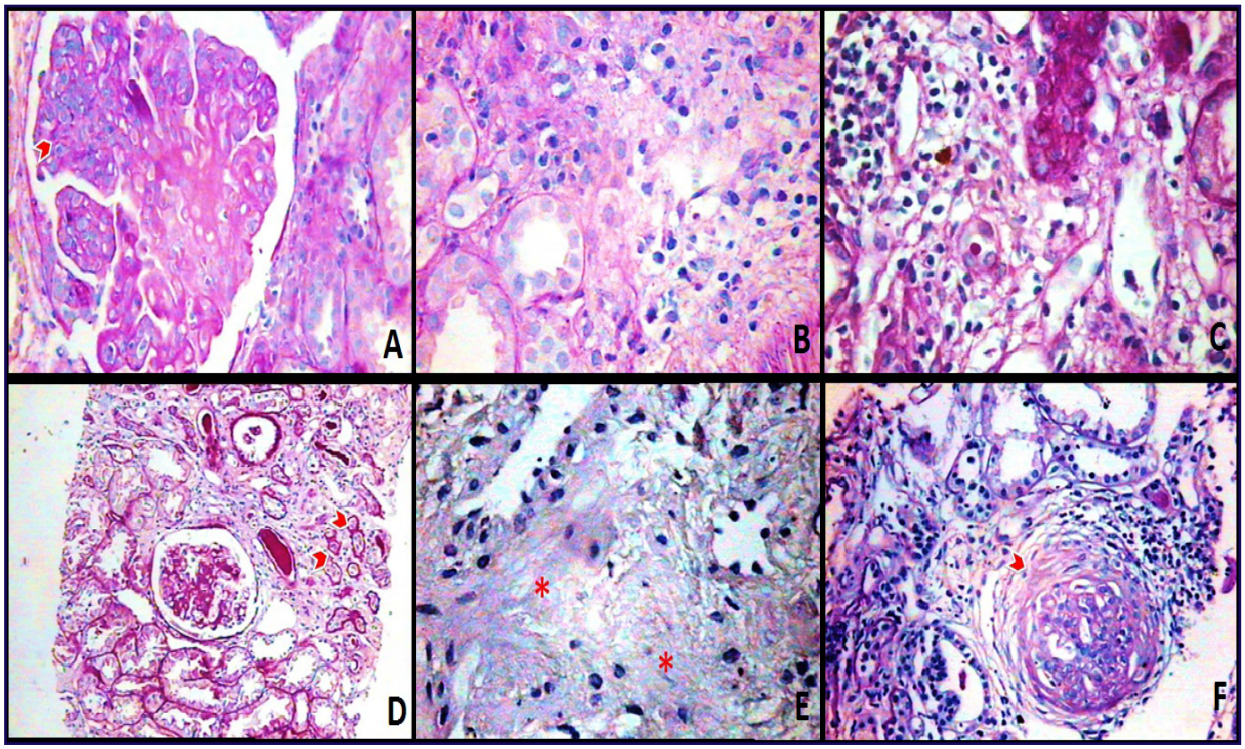


Figure 5. Kidney section of a 24 y/o Female with Class IV Lupus Nephritis, AI: 13/24 , CI: 1/12, Endocapillary Hypercellularity (Arrow-head), PAS X200 (A), Kidney section of a 24 y/o Female with Class IV Lupus Nephritis, AI: 13/24, CI: 1/12, Interstitial inflammation is evident, PAS X400 (B), Kidney section of a 42 y/o Female with Class IV Lupus Nephritis, AI: 7/24, CI: 3/12, Diffuse leukocyte infiltration (Interstitial inflammation) is evident, PAS X200 (C), Kidney section of a 16 y/o Female with Class III Lupus Nephritis, AI: 5/24, CI: 2/12, Tubular atrophy (Arrow-heads), PAS X100 (D), Kidney section of a 20 y/o Female with Class III Lupus Nephritis, AI: 7/24, CI: 5/12, Interstitial Fibrosis (Stars), H & E X200 (E), Kidney section of a 20 y/o Female with Class III Lupus Nephritis, AI: 7/24, CI: 5/12, Formation of a "Fibrotic Crescent" (Arrow-head), H & E X200 (F)

Discussion

The present study clearly showed that the occurrence of LN has a special relation with age, in which the incidence of this disease increases accordingly. The highest prevalence of LN was seen in 21 to 40 years of age. On the other hand, after the age of 60, the frequency of LN declines significantly. In this context, different studies were carried out on patients from various geographical locations which showed different results (5, 23, 24), whereas similar results to the present research were reported from Saudi Arabia with the mean age of 24. In Tunisia the disease was reported to occur mainly in the third decade of life (25). Similar results were also obtained from a study in India, in which the highest occurrence of LN at the age of 27.53 ± 12.26 was indicated (26). Esdaile and Austin reported LN prevalence with a very fast progression of the disease under 20 years of age (27, 28). Similar research in Iran reported mean age of disease prevalence to be 21.5 with the range of 12 to 45 years of age (29). More specifically, in southern Iran, the onset of disease and gender factor of LN was similar to other ethnic groups (30).

In the present study, differences reported in the age factor of LN patients could be related to ethnic distribution (5, 8, 28). Also, environmental

factors such as nutrition and socio-economic status could be considered as predisposing factors for LN (17, 31, 32). Rastin et al. studied the clinical and immunological characteristics of SLE and reported that genetics and environmental factors affect the clinical and paraclinical findings (30).

Our findings clearly brought to light that the disease occurrence has a higher incidence in female patients than male patients regardless of age. It also showed a significant decline of LN incidence in female patients over the age of 50. This finding with regard to the sex was in agreement with the work of many other researchers (5, 6, 25, 27, 33). The higher incidence of LN in female patients could be related to genetic and metabolic status and gonadal sex hormones or the release of Gonadotropin modulating immune responses regarding the double X chromosomes and differences in Estrogen levels (3). The decline of frequency in female LN patients after the occurrence of menopause could justify the effect of sex hormones on LN.

In the present study, Class IV was ranked the most frequent class regardless of age or sex. Similar reports have been documented, indicating Class IV to be the most frequent among cases (5, 7, 23, 34, 35, 36). On the contrary, some reports from specific Arab countries showed Class III to be the most frequent among patients (37, 38).

Our study showed that both Activity and Chronicity scores were slightly higher in female patients. A study done by Lu et al., showed that both sexes have similar Activity and Chronicity indices scores during the course of the disease (39), whereas other studies report that LN in male patients are more severe (36, 40).

In the present study, Activity Index score was higher in the ages of 11 to 30 and Chronicity Index score in 41 to 50 years of age, meaning older patients develop more chronic lesions over time while younger patients mostly develop acute lesions.

Our study showed that the highest Activity Index score was reported in Class IV patients and the highest Chronicity Index score was reported subsequently in Classes V and VI. The least Activity Index score was shown in Class VI and Classes II and I showed the least Chronicity Index scores. Similar work of Azoicăi et al., on these indices indicated the highest Activity/Chronicity Index scores belonged to Class IV LN patients while Class II LN patients had significantly lower scores (20).

With regard to the pathological lesions observed, the Activity and Chronicity indices in the present work were in agreement with the findings of other reports on these lesions and their relations to these two scores. Hashmi et al. also reported that the active lesion of endocapillary hypercellularity is the most frequent one but conversely, glomerular sclerosis was reported to be the most common chronic lesion (7).

Conclusion

The present study clearly showed, histopathological findings, clinical and para-clinical data could furnish more information on disease process, treatment, quality of life and mortality rate.

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Conflicts of Interest

The authors declare no competing interest.

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