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CHARACTERISTICS OF LUPUS NEPHRITIS IN NEPHROLOGY UNIT OF TERTIARY CARE HOSPITAL: A RETROSPECTIVE AND PROSPECTIVE OBSERVATIONAL STUDY

Nephrology

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ABSTRACT

Background: Lupus nephritis is a frequent and severe complication of systemic lupus erythematosus. 40% of SLE patients experience LN development, which occurs most frequently five years after diagnosis or may even be present at the time of initial diagnosis. 10% of LN patients progress to end-stage renal disease (ESRD). **Objectives:** To evaluate the clinical and laboratory outcomes in lupus nephritis patients, evaluate the prevalence of different classes of lupus nephritis, and assessing the risk of End Stage Renal Disease in patients with lupus nephritis. **Materials And Methods:** An Ambispective observational study was carried out for a period of 6 months where the patients were screened based on inclusion and exclusion criteria. The data was collected in the data collection forms. A total of 70 subjects were included in the study based on the inclusion criteria. **Results:** Based on ISN/RPS Classification we found that Class IV Diffuse lupus nephritis as the most frequent, representing about 41.42%, 25.71% were of Class III Focal lupus nephritis of the total cases. Some clinical characteristics like allergic to foods (p=.03896), skin rash (p=.01925), joint pains (p=.03512), oral ulcers (p=.03348), alopecia (p=.01462), pedal edema (p=.01009), OTC medications (p=.00732), facial puffiness (p=.01464), family history (p=.02064) showed significant association with ISN/RPS classification system. The Glomerular Filtration Rate (GFR) was calculated both at week 1 and at week 4 using Cockcroft-gault equation and shows a significant association (p <.00001). **Conclusion:** We conclude that racial and geographical variation has a deep impact on clinical characteristics of Lupus Nephritis.

KEYWORDS

Systemic Lupus Erythematosus (SLE), Lupus Nephritis (LN), End Stage Renal Disease (ESRD), Glomerular Filtration Rate (GFR), Skin Rash.

INTRODUCTION:

An autoimmune condition called systemic lupus erythematosus (SLE) causes chronic inflammation and organ damage. The condition can affect a variety of bodily organ systems and shows clinical signs of remission and relapse. Even though the cause of SLE is not fully known, several genetic, epigenetic, and environmental risk factors have been shown to increase the likelihood of developing the disease. SLE is distinguished by the development of autoantibodies against nuclear and cytoplasmic antigens. A common and serious symptom of SLE is kidney involvement, often known as lupus nephritis (LN).[1] Lupus has evolved from a dermatological symptom to a complex multisystemic disorder. It is critical to monitor kidney function in SLE patients because early detection and treatment of renal impairment can greatly improve kidney function findings. Lupus nephritis frequently develops three to five years after the onset of SLE. The majority of SLE patients, including those who do not have clinically evident renal disease, have histological evidence of lupus nephritis. Urinalysis, urine albumin-to-creatine ratio, and serum creatinine levels are all used to detect the development of lupus nephritis. This helps determine whether the serum creatinine level has increased since the beginning of the disease, as well as the presence of proteinuria, which is common in lupus nephritis. Due to the high risk of increased morbidity associated with lupus nephritis, therapy is crucial in halting the development of end-stage renal disease (ESRD). [2]

Patients with lupus nephritis already have varying clinical manifestations of SLE. These clinical symptoms include malar or discoid rash, fatigue, fever, rash, photosensitivity, serositis, oral ulcers, non-erosive arthritis, seizures, psychosis, or hematologic disorders. Some patients with lupus nephritis may develop polyuria, nocturia, foamy urine, hypertension, and edema. Symptoms seen in active lupus nephritis may include peripheral edema because of hypertension or hypoalbuminemia. Significant peripheral edema is more commonly seen in patients with diffuse or membranous lupus nephritis because these renal lesions have a remarkable association with heavy proteinuria. [3]

Hence, here we have discussed regarding clinical manifestations, laboratory outcomes to know the severity of the disease in our geographical area, to analyse how many patients have landed into end stage renal disease after diagnosed with lupus nephritis and also to assess the severity of joint pains.

MATERIALS AND METHODS:

The ethics committee of the Guntur Medical College approved the study, which was carried out at the Department of Nephrology, Government General Hospital, Guntur, Andhra Pradesh, India, with a sample size of 70. The study used a retrospective and prospective observational design and it ran for about six months, from 1st September 2022 to 28th February 28 2023. Those with SLE and biopsy-proven lupus nephritis between the ages of 12 to 60 of both the sexes were included; those under the age of 12, people with decreased kidney size, individuals with a single kidney, immunological compromise (HIV, hepatitis), and bleeding or coagulation disorders were excluded. With the help of Graph Pad Prism 9.3.1 programme, two tailed student t test was used for clinical parameters, ANOVA testing for laboratory

parameters, chi-square tests was used for evaluating End Stage Renal Disease (ESRD), with a significance level of $p<0.05$ and a 95% confidence interval. Descriptive statistics were reported as percentages, means and standard deviation.

RESULTS:

Table 1: Distribution Over Age And Gender

Parameters	No. of patients
Gender	
Female	65
Male	5
Age group (years)	
<15	1
16-20	2
21-25	6
26-30	21
31-35	13
36-40	11
41-45	7
46-50	7
>50	2

It describes that about a total of 70 participants are included in the study, with 5 men and 65 women, representing a remarkable gender distribution. The age group with the highest representation (n=21) is 26-30, followed by (n=13) is 31-35, (n=11) is 36-40 and (n=7) is observed in both the age groups i.e 41-45 and 46-50. There are fewer subjects in the age groups under 15, 16-20, 21-25 and over 50 like 1, 2, 6 and 2 respectively.

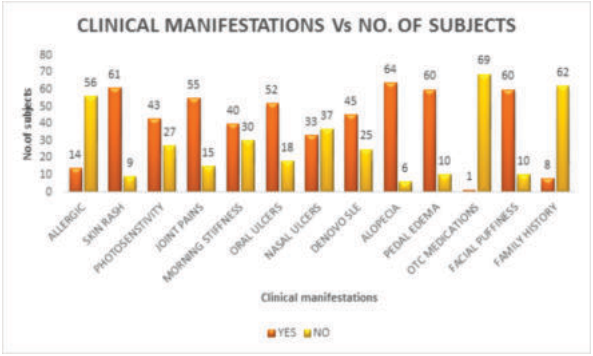

Figure 1: Clinical Manifestations Vs No. Of Subjects

The study's clinical manifestations showed that skin rashes (n=61), alopecia (n=64), pedal edema and facial puffiness (n=60) were the most common clinical manifestations. On the other hand, allergies, family history and usage of OTC medications showed up in lowest number (n=14, 8, 1) respectively.

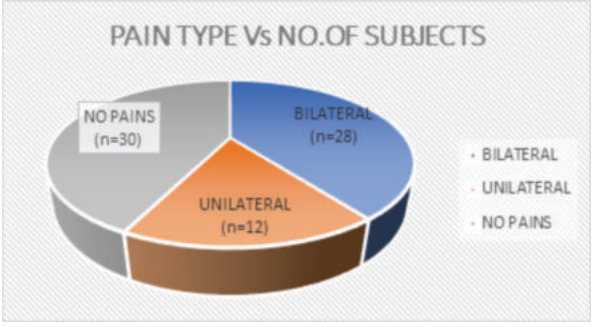

Figure 2: Pain Type Vs No. Of Subjects

It depicts the information regarding the distribution of subjects based on the type of the pain they are experiencing. Majority of the subjects show no pain (n=30), followed by bilateral pain (n=28) and unilateral pain (n=12).

It depicts the information regarding the distribution of subjects based on their Pain severity. In Week 1 majority of the subjects were experiencing pain in between the range of 1-3 (n=38), followed by 7-9 (n=20), 4-6 (n=7), 0 (n=5) and 10 (n=0), where as in Week 4 majority of subjects were observed within the range of 0 (n=30), 1-3 (n=20), 4-6 (n=12), 7-9 (n=8) and 10 (n=0).

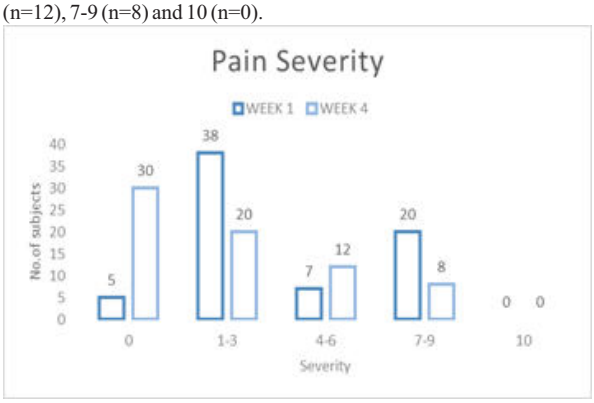

Figure 3: Pain Severity Vs No. Of Subjects

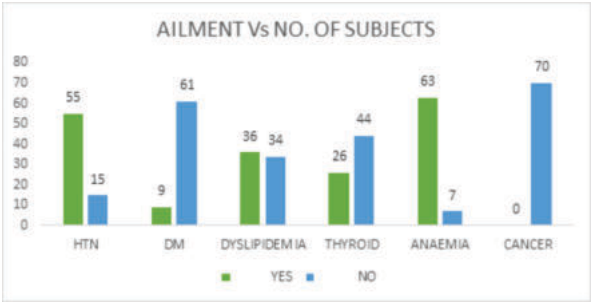

Figure 4: Ailments Vs No. Of Subjects

It depicts the information regarding the distribution of subjects according to certain ailments. Majority of the subjects have shown Anaemia, Hypertension, Dyslipidaemia, Thyroid, Diabetes mellitus and cancer as n= 63, 55, 36, 26, 9, 0 respectively.

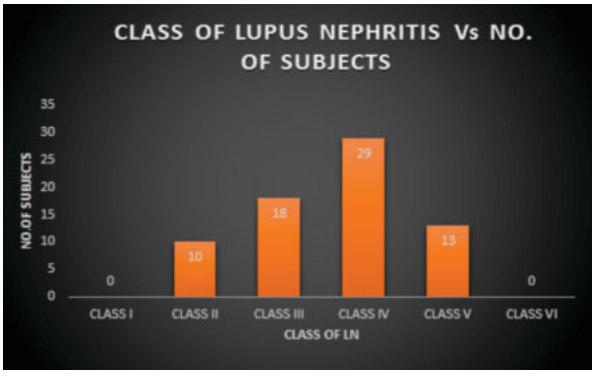

Figure 5: Class Of Lupus Nephritis Vs No. Of Subjects

It depicts the information regarding the distribution of subjects in different classes of lupus nephritis. Majority of subjects were found in the Diffuse lupus nephritis (Class IV) (n=29), followed by Focal lupus nephritis (Class III) (n=18), Membranous lupus nephritis (Class V) (n=13), Mesengial proliferative lupus nephritis (Class II) (n=10).

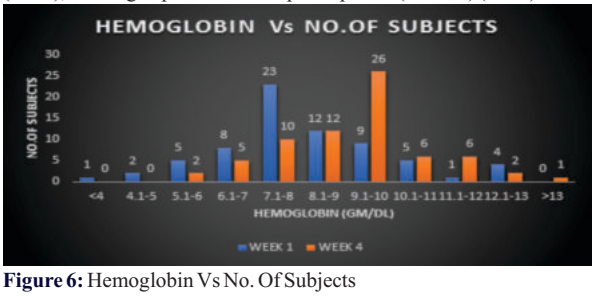

Figure 6: Hemoglobin Vs No. Of Subjects

It shows that hemoglobin levels ranged from 7.1 to 8 gm/dl in most individuals (n = 23) in week 1, with the lowest level being less than 4 gm/dl (n = 1). In week 4 the highest hemoglobin levels ranged from 9.1 to 10 gm/dl (n = 26), with no individual having hemoglobin levels lower than 4 gm/dl.

ANOVA test was done at <0.05 significance
***Statistically significant**
Hemoglobin – f = 12.17845, p = .000649*

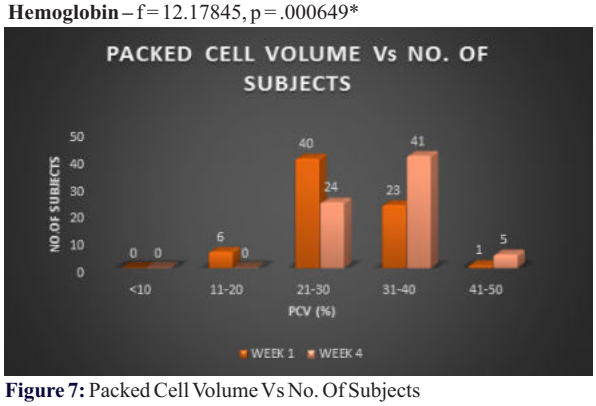

Figure 7: Packed Cell Volume Vs No. Of Subjects

In week 1 the highest Packed Cell Volume (PCV) values ranged from 21–30% (n=40), with <10% (n=0) being the lowest level recorded. During Week 4, the highest PCV range recorded was 31-40% (n=41), and none of the participants had PCV values lower than 10% (n=0).
ANOVA test was done at <0.05 significance
***Statistically significant**
Packed Cell Volume (PCV) – f = 17.12976, p = .00006*

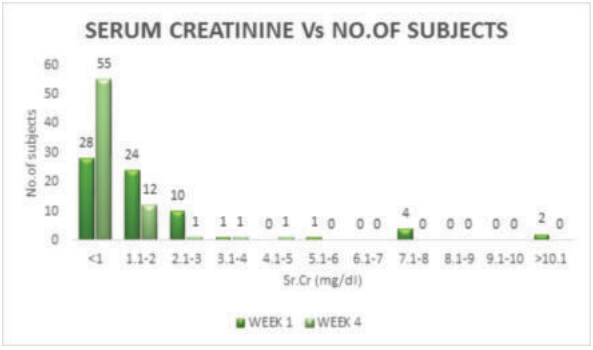

Figure 8: Serum Creatinine Vs No. Of Subjects

It shows that in week 1 the highest recordings of serum creatinine (Sr. Cr) were found to be below 1 mg/dl in most of the subjects (n = 28) and the least were above 10 mg/dl (n=2). During week 4, no subjects had Sr. Cr levels higher than 10 mg/dl, and the highest recorded Sr. Cr value was <1 mg/dl (n=55).
ANOVA test was done at <0.05 significance
***Statistically significant**
Serum Creatinine – f = 14.59655, p = .000201*

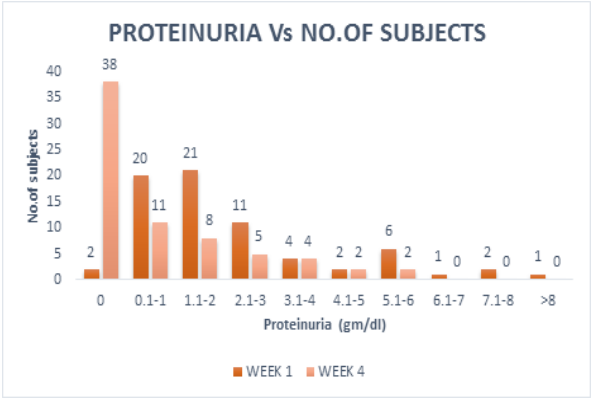

Figure 9: Proteinuria Vs No. Of Subjects

In majority of the subjects the Proteinuria levels in week 1 ranged from 1.1-2 gm/dl (n = 21), with the lowest recorded level being >8 gm/dl (n = 1). No individual had proteinuria levels higher than 8 gm/dl in week 4, and the highest recorded value was 0 gm/dl (n = 38).
ANOVA test was done at <0.05 significance
***Statistically significant**
Proteinuria – f = 25.05544, p <.00001*

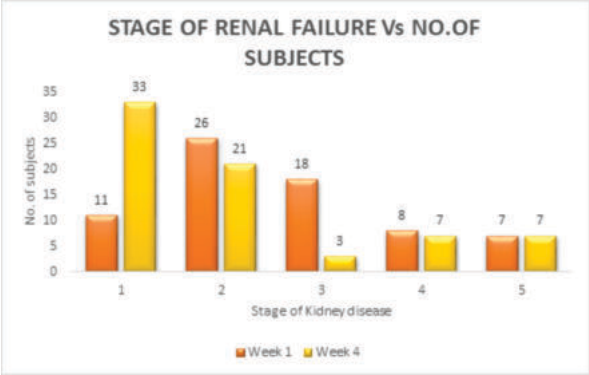

Figure 10: Stage Of Renal Failure Vs No. Of Subjects

It depicts the information regarding the distribution of subjects based on their stage of renal failure. In week 1 majority of the subjects were in Stage 2 (n=26), followed by Stage 3 (n=18), Stage1 (n=11), Stage 4 (n=8) and Stage 5 (n=7), where as in Week 4 majority of subjects were observed in Stage 1 (n=33), Stage 2 (n=21), Stage 4 (n=7), Stage 5 (n=7), Stage 3 (n=3).

Chi square test was done at <0.05 significance
***statistically significant**
End stage renal disease (ESRD) – Chi square statistic = 22.3069, p = .000174*

Table 2: Clinical Manifestations Based On ISN/RPS Classification Vs No. Of Subjects

Clinical manifestations	Class II (N=10)	Class III (N=18)	Class IV (N=29)	Class V (N=13)	Total (N=70)	p value
Allergic	3	6	4	1	14	.03896*
Skin rash	8	17	26	10	61	.01925*
Photosensitivity	5	11	21	6	43	.32282
Joint pains	6	15	23	11	55	.03512*
Morning stiffness	4	8	20	8	40	.52037
Oral ulcers	9	14	20	9	52	.03348*
Nasal ulcers	6	9	13	5	33	.75612
Denovo SLE	10	14	12	9	45	.24363
Alopecia	9	16	28	11	64	.01462*
Pedal edema	9	15	24	12	60	.01009*
OTC medications	0	0	0	1	1	.00732*
Facial puffiness	7	16	24	13	60	.01464*
Family history	1	1	2	4	8	.02064*

Table 2 shows that Class IV LN has the highest frequency of clinical symptoms in the ISN/RPS classification of LN with n = 28 cases of alopecia, n = 26 cases of skin rash, n = 24 cases of pedal edema, and n = 24 cases of facial puffiness followed by Class III LN with n=17 cases of skin rash and n=16 cases of alopecia and facial puffiness. On the other hand, Class V LN has the lowest incidence of manifestations, with the most common symptoms being joint aches (n=11), baldness (n=11), facial puffiness (n=13), and pedal edema (n= 12).

t test was done at <0.05 significance
***Statistically significant**
Allergic – t = 2.63186, p = .03896, **Skin rash** – t = 3.17246, p = .019259, **Joint pains** – t = 2.70914, p = .03512, **Oral ulcers** – t = 2.74575, p = .03348, **Alopecia** – t = 3.39419, p = .01462

Table 3: Ailment Based On ISN/RPS Classification Vs No. Of Subjects

Ailment	Class II (N=10)	Class III (N=18)	Class IV (N=29)	Class V (N=13)	Total (N=70)	p value
Hypertension	7	15	23	10	55	.03132*
Diabetes	1	3	3	2	9	.01450*
Dyslipidemia	4	11	13	8	36	.88101
Thyroid	1	8	11	6	26	.20946
Anaemia	10	17	27	9	63	.01633*

Table 3 shows that Class IV LN, according to the ISN/RPS classification, has the greatest frequency of related conditions, such as

anemia (n = 27), hypertension (n = 23), dyslipidemia (n = 13), thyroid (n = 11), and diabetes mellitus (n = 3) followed by Class III LN has the highest incidence of Anemia and Hypertension with (n=17 and 15) respectively. On the other hand, Class II LN has the lowest incidence of related illnesses, with thyroid (n=1) and diabetes mellitus (n=1) being the least common and Class V LN has diabetes (n=2) and thyroid (n=6) as the least common illnesses.

t test was done at <0.05 significance
***Statistically significant**
Hypertension – t = 2.7966, p = .03132, **Diabetes mellitus** – t = 3.39935, p = .01450, **Anemia** – t = 3.30366, p = .01633

DISCUSSION:

Lupus nephritis is a severe complication of Systemic lupus erythematosus (SLE). There are several factors which trigger this condition and we observe changes in various clinical and biochemical characteristics. As there are many characteristics, our study mainly focuses on the clinical characteristics of lupus nephritis. This is a non-experimental prospective and retrospective observational study which was carried out on "Characteristics of Lupus Nephritis patients in the Nephrology Unit of Tertiary Care Teaching Hospital, Guntur." 70 subjects met with inclusion criteria and were included in the study. The data obtained was tabulated, calculated, and analysed.

According to our study, subjects of age group 26-30 years of age were more prone to the disease (n=21) as shown in (Table 1). Mean age of the patients was 34 ± 8.77 years. Another study from Bangabandhu Sheikh Mujib Medical University, Bangladesh, in 2006 showed mean age of the LN patients of 25.5 ± 8.8 years. Similar studies were carried out in Singapore and China showing the mean age of the patient as 35.4 years and 33 ± 14 years, respectively. A study in Iran and Bangladesh showed mean age of 25.6 ± 10.3 years and 26 ± 11.97 years, respectively. In some other studies the mean age varied from 33.5 ± 14 years to 36.8 ± 13.8 years. However, the mean age of the patients of our country is concordant with the mean age of the patients of China and Singapore but differs with the mean age of the patient of LN in Bangladesh and Iran. Present study includes majority of females (n=65, 92.85%) and it has shown male: female ratio of 1:13 (Table 1) which is similar with a previous study from Iran with a male: female ratio of 1:13 and is quite similar to the study carried out in the Bangladesh with a male: female ratio of 1:10. But our study differs with the study carried out in Singapore showing a male: female ratio of 1:4. This difference could be due to racial and geographical variation of LN. This establishes the fact that clinical manifestations vary according to geographic location of the patients with LN.

In the present study, it is found that ISN/RPS Class IV Diffuse lupus nephritis as the most frequent, representing about 41.42% (n=29), 25.71% (n=18) were of Class III Focal lupus nephritis, 18.57% (n=13) were of Class V Membranous lupus nephritis, and 14.28% (n=10) were of Class II Mesengial proliferative lupus nephritis of the total cases (Figure 5). In a Bangladesh study it is found that ISN/RPS class 4-G as the most frequent, representing about 64.7% of the total cases and 11.8% cases were class 4-S patients. In a cohort study carried out in China with 172 patients belonging to ISN/RPS class IV patients, they found 152 cases in class 4-G and only 20 cases in class 4-S. The present study was also concordant with these studies as the majority of the cases were of Class IV.

The primary objective of our study was to evaluate the Clinical outcomes in lupus nephritis patients. In our study, some clinical characteristics like allergic to foods (p=.03896), skin rash (p=.01925), joint pains (p=.03512), oral ulcers (p=.03348), alopecia (p=.01462), pedal edema (p=.01009), OTC medications (p=.00732), facial puffiness (p=.01464), family history (p=.02064) showed significant association with ISN/RPS classification system (Table 2), likely some of the complications such as hypertension (p=.03132), diabetes mellitus (p=.01450) and anaemia (p=.01633) have shown significant association with ISN/RPS classification system (Table 3). Similar clinicopathological study was done by Nezhad et al. in their study, they found that edema (p=.004) and hypertension (p=.001) had significant association with ISN/RPS classification system, another clinicopathological study done by Muhammad Nazmul Baqui et al. found that only arthralgia (p=.011) showed significant association with ISN/RPS classification system, another study reviewed by Budman and Steinberg showed that anaemia occurred in 57-78% of patients with SLE. In this study we also checked the severity of pain using Allina health pain assessment scale both on week 1 and week 4. In week 1 majority of the subjects were experiencing pain in between the score 1-3, followed by score 7-9, score 4-6, score 0 and score 10, where as in week 4 majority of subjects were observed within score 0, followed by score 1-3, score 4-6, score 7-9 and score 10 (Figure 3).

Another objective of the study was to evaluate the laboratory outcomes in lupus nephritis patients. In our study laboratory parameters were assessed at week 1 and at week 4 like Hb (p=.000649), PCV (p=.00006), serum creatinine (p=.000201) and proteinuria (p <.00001) which showed significant association, it agrees with the study by Nehzad and Sepaskhah who also found significant proteinuria and our study contradicts the results of Mok et al., where no significant association was found with proteinuria. In our study we have also assessed the risk of End Stage Renal Disease (ESRD) in patients with lupus nephritis. The Glomerular Filtration Rate (GFR) was calculated both at week 1 and at week 4 using Cockcroft-gault equation. In Week 1 majority of the subjects were in Stage 2, followed by Stage 3, Stage1, Stage 4 and Stage 5, where as in Week 4 majority of subjects were observed in Stage 1, Stage 2, Stage 4, Stage 5, Stage 3 (Figure- 10) and shows a significant association (p <.00001).

CONCLUSION:

Based on the results obtained, our study concludes that females were more predominant than males, it is because Systemic Lupus Erythematosus is an autoimmune disease and auto immune diseases most commonly affect females, and we can see that Lupus Nephritis is predominantly seen in women of child bearing age due to the hormonal imbalances which occur at that age. Most of the patients included in the study were experiencing alopecia, skin rash, pedal edema, facial puffiness, and joint pain as the clinical findings of the disease. Majority of the patients included in the study have shown comorbidities like anaemia and hypertension. As the clinical presentations vary from study to study, we conclude that racial and geographical variation have a deep impact on clinical characteristics of Lupus Nephritis. Observations from our study suggest that we cannot always predict the clinical findings; though some of the clinical parameters of other studies correlated with clinical findings in the present study. Based on the assessment of the pain severity both on week 1 and week 4 where we have estimated that medications and counselling played an important role in reducing the pain and majority of the subjects were in the category of no pain in week 4. Another observation of our study was to evaluate the laboratory parameters like hemoglobin, packed cell volume, serum creatinine, and proteinuria which have shown significant association. Subjects with lupus nephritis are more likely to develop ESRD, so we have calculated the GFR based on Cockcroft-Gault equation to assess the stage of kidney failure. GFR calculation was also done both on week 1 and week 4 to check whether there is any improvement in kidney function after the subjects have started taking the medication regularly. In week 1, most of the subjects were under Stage 2 and 3 kidney failure and after taking the medications regularly majority of the subjects have showed an improvement in the GFR in week 4 i.e., most of them were under Stage 1. We conclude that our study suggests some meaningful correlation between laboratory and clinical findings. It also suggests that biopsies are beneficial for determination of lupus nephritis. By providing leaflets regarding the diet and counselling the patient to follow some therapies to reduce pain we can improve the nutritional status, minimize the pain, and also reduce the risk of developing Lupus Nephritis.

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