PROSPECTIVE COHORT STUDY OF CLINICAL OUTCOMES AND PROGNOSTIC FACTORS IN LUPUS NEPHRITIS IN A TERTIARY CARE CENTRE IN SOUTH INDIA

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Certificate

This is to certify that “Prospective Cohort Study Of Clinical Outcomes and Prognostic Factors in Lupus Nephritis In A Tertiary Care Centre in South India” which is submitted as thesis requirement of the MD GENERAL MEDICINE Branch examination of the Dr. MGR Medical University is the bonafide work of the candidate:

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CONTENTS

INTRODUCTION

Systemic Lupus Erythematosus (SLE), more a syndrome than a disease, is the prototype of immune complex mediated systemic autoimmune diseases. A prevalence study in India showed a crude incidence rate of 4 per 100,000 population per year[1]. It has been diagnosed in 1.5 million people in the United States. Women have a much higher risk of developing SLE, and the woman-to-man ratio is about 10-15:1[2]. Racial differences are present and it is seen that women of black, Hispanic, Asian, and Native American backgrounds are more frequently affected than their white peers[3].

SLE, though a disease known for over half a century, still carries a grim prognosis. More than half of these patients develop irreversible organ damage over time[1]. Lupus nephritis occurs in about half of SLE patients in India as per published series reporting between 35-73% occurrences [4-9]. Renal involvement in SLE occurs early in the disease and is usually within 10 years of the appearance of SLE[10]. Studies have suggested that male lupus nephritis patients have more severe disease than their female counterparts[10]. Lupus nephritis is seen more in Asians, African-Caribbeans and African-Americans[10]. In a retrospective study published in 1988 by McCune et al, male sex, young age (<33years), and non-European ancestry were determinants of earlier renal involvement in SLE patients[11].

With modern treatment, the survival of SLE patients have improved in the west to about 80% at 10 years after diagnosis[12] but, the figures for the Asian Indians are not so good. Murali et al in a study of 98 patients between 1981 and 1993 showed 50%-60% survival of SLE patients at 10 years[13,14]. It is a therapeutic challenge to treat lupus nephritis, since early intervention can dramatically change the disease course.

Unfortunately, thirty or more years ago, patients with severe Class IV nephritis surviving for more than a year or two were few, and at least 50% of those with less severe form of nephritis used to die within 5 years[15]. It is really heartening to see that Cyclophosphamide introduction into the treatment of lupus nephritis 20 years later made a significant impact on prognosis and renal involvement no longer affects the survival rates of these patients[16].

While studies on SLE in India have been previously published, there has been a paucity of data with regards to prognostic factors and clinical outcomes in lupus nephritis patients, which constitutes a major subset of severe SLE patients. A study done by Abraham et al in 1987-1999, looked at the prognostic factors in class IV lupus nephritis over 50 months. In the present decade, with newer drugs in the armamentarium, has there been a change in the general outlook of this disease as compared to the west? Are the prognostic factors different in our population?

We endeavour to fill these lacunae in our present understanding of the clinical presentation and outcome of the disease in our population.

LITERATURE REVIEW

Systemic Lupus Erythematosus (SLE) is a classic model of immune complex mediated disease. Its expression and clinical course varies from the very mild, with arthralgias and skin rashes, to life threatening features, when it affects renal and central nervous system.

Coexistence and evolution into other autoimmune disorders can also occur.

Diagnosis Of SLE

The American College of Rheumatology has a criteria for the classification of patients as having SLE[17]. If a patient has, at any time in his or her medical history, 4 of the 11 criteria documented, the diagnosis of SLE can be made with about 95% specificity and 85% sensitivity. These criteria are actually meant for epidemiological purposes to ensure that SLE patients reported in the literature do in fact have the disease and not for bedside diagnosis of an individual patient. The diagnosis of SLE is based on clinical judgement and supportive laboratory evidence. SLE can be suspected whenever 2 or more organ systems listed in ACR criteria are involved[1].

Epidemiology Of Systemic Lupus Erythematosus

A prevalence study in India (carried out in a rural population near Delhi) by Malaviya et al published in 1993 surveyed a population of 91,888 and found a point prevalence of 3 per 100,000 (95%CI= 0-6.86 per 100,000)[18]. This is a much lower figure than reported from the west. Various studies have shown prevalence to be about 12.5 per

100, 000 adults in England [19] to 39 per 100,000 in Finland [20] and 124 per 100,000 in USA[21]. Any large hospital in India, do encounter a good number of SLE cases[1]. The Copcord Bhigwan, a prospective study from Pune, has found a crude incidence rate of 1 per 25,000 person years i.e. 4 per 100,000 population per year[1].

SLE occurs three times more commonly in females than in males among children. Between puberty and the fourth decade of life, the female to male ratio is 9:1 and the incidence is 60%. The ratio reverts back to 3:1 in the older age groups[22].

The annual incidence of SLE in the African Carribean blacks which is the race that is maximally affected, ranges from six to 35 new cases per 100,000 population in relatively low-risk to high-risk groups[22].

Presenting Signs and Symptoms Of SLE

80% of patients with SLE will present with involvement of the skin or joints. They may also present with fever accompanied by single organ involvement, such as inflammatory serositis, glomerulonephritis, neuropsychiatric disturbance or hematological disorder. On the other hand, patients present with severe, generalized acute lupus crisis with multiorgan involvement [2].

There are regional variations in clinical features reported from different parts of India[4-9]. Raynaud's phenomenon is almost absent in patients from Southern India whereas lymphadenopathy occurs more often[4-9]. Also low frequency of neuropsychiatric manifestations at onset in Northern India has been noted. On follow up, there was lower frequency of photosensitivity and neuropsychiatric manifestations in Western India, lower frequency of nephritis in Central India and the rarity of Raynaud's in Southern

India in comparison to other parts of the country[4-9]. But these studies are hospital based studies and hence could have confounding variables.

Evaluation of disease activity and severity

A number of validated indices are available for quantifying disease activity. The more popular indices include- BILAG [23], SLEDAI [24], SLAM [25] and LAI [26]. These help in formulating the overall treatment plan and assessment of prognosis. The details of SLEDAI activity index is shown in (**Annexure A**). In our study SLEDAI index has been used as a measure of disease activity. A valid measure of damage in patients with lupus is the SLICC/ ACR Damage Index (DI)[27].

Definition Of Lupus Nephritis(LN)

One of the following must be present: 1. a renal biopsy showing mesangial, focal proliferative, or membranous lupus nephritis; 2. a 30% decline in creatinine clearance over a 1 year period; 3. greater than 1G urine protein in a 24-hour urine specimen. If none of these features are present, at least three of the following are required in a 12 month period: 1. s.albumin of <3g/dl; 2. 2 to 4+ proteinuria; 3. oval fat bodies; granular, hyaline, or red cell casts in the urine; 4. persistent haematuria or greater than five red cells per high power field in the urine. Finally, other etiologies of genitourinary disease (e.g., diabetes, hypertension, drug- induced nephropathies, infection) must be excluded [12].

Epidemiology Of Lupus Nephritis

Renal involvement in systemic lupus erythematosus (SLE) is quite common and is a strong predictor of poor outcome. Eight large cohort studies consisting of 2649 SLE patients, showed that the prevalence varied from 31 to 65%[12]. A Study done at the Johns Hopkins Medical Center between 1992-94, analyzed the annual incidence of nephritis in 384 lupus patients. The one year incidence of acute renal disease was 10%[22]. Lupus nephritis occurs in about half of SLE patients (range 35%-73%) in India[1].

A retrospective study published in 1986 evaluated 107 active lupus nephritis patients over a median follow up of seven years and found that male sex, young age (<33years), and non-European ancestry were determinants of earlier renal involvement in SLE patients[16].

Etiology Of Systemic Lupus Erythematosus And Lupus Nephritis

The etiology of SLE is multifactorial. Disordered immune response could be triggered by genetic predisposition, sex hormones, and environmental insults[22].

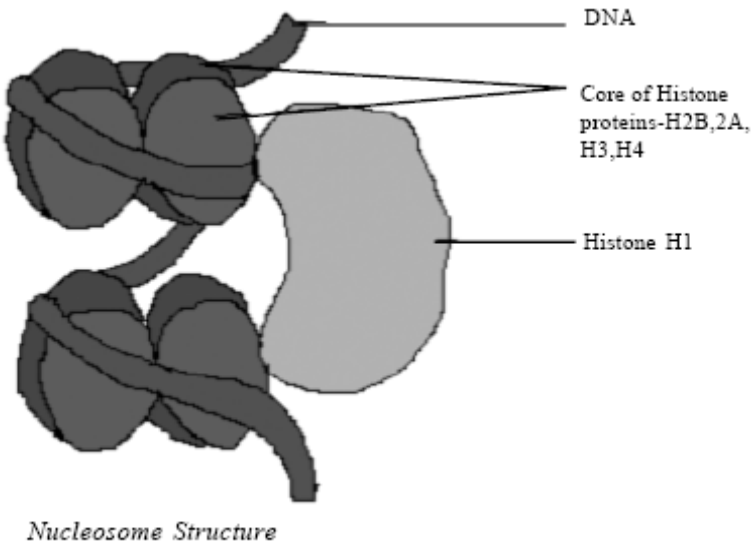
Among the HLA antigens, HLA-DR2 and HLA-B8 are more associated with the development of lupus renal disease[23-25]. Polymorphisms of Fc receptors for IgG (Fc gammaR) have been recently identified as a risk factor, implicating defective handling of circulating immune complexes in the development of renal disease[28]. Heredity does play a role, shown by a concordance rate of 25 and 60% among monozygotic twins. The polygenic nature and the contribution of environmental factors are suggested by the moderate concordance rate[22].

Immunopathogenesis Of Lupus Nephritis

There are at least three immuno-pathogenic mechanisms supported by experimental data[29]. First, circulating immune complexes consisting chiefly of DNA and anti-DNA are deposited in the kidney. Local inflammatory process occur due to resultant complement activation and chemotaxis of neutrophils[29]. Nucleosomes, the fundamental unit of chromatin, are the target and mediators of antibody-related glomerular immune-complex deposition[29]. The nucleosome is released by internucleosomal cleavage by endonucleases activated during cell apoptosis and consists of a core composed of an octamer of two copies each of Histones H2A, H2B, H3 and H4, around which is wrapped a stretch of helical DNA, approximately 150bp in length[29] (**figure 1**). Antibodies reactive to nucleosomes have been detected both in patients with lupus and murine models even prior to the development of anti-dsDNA and anti-histone antibodies. These antibodies are IgG in isotype and usually are of IgG2a and IgG2b in subclass consistent with a T-cell mediated antigen driven response[29] (**figure 2**).

Second mechanism is by in situ formation of antigen and antibody complexes leading to complement activation and leukocyte-mediated injury. Thirdly, antibodies against specific cellular targets produce renal injury. For example, antibodies, such as anti-ribosomal P, bind to cytoplasmic antigens that have been translocated to the cell membrane with subsequent penetration and disruption of cellular function[29].

An additional mechanism is seen in SLE patients with the antiphospholipid antibody syndrome. Glomerular thrombosis can result from the hypercoagulability that



Nucleosome Structure

Figure 1 : Structure of a nucleosome

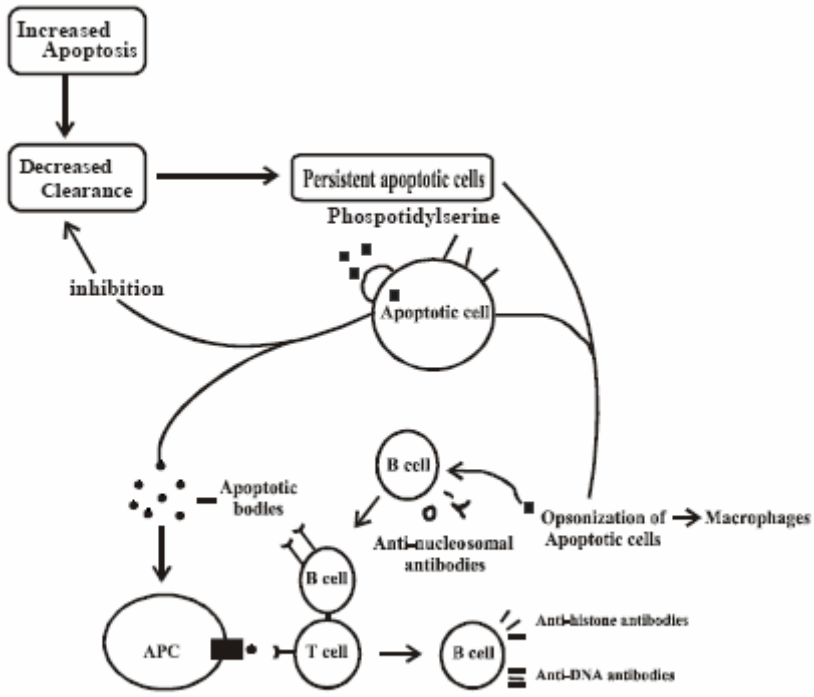


Fig 2:Schematic representation of the role of apoptosis and nucleosomes in the pathogenesis of SLE

accompanies antibodies directed against negatively charged phospholipid-protein complexes (e.g. biologic false positive VDRL, anticardiolipin antibodies, and lupus anticoagulant)[29].

New PathologicalClassification of Lupus Nephritis

The Renal Pathology Society Working Group and the International Society of Nephrology Working Group in 2002 approved a new classification of LN (**Table 1**)[30]. This new classification supercedes the modified World Health Organization (WHO) classification of 1995. Lupus Nephritis involves more than 1 component within the kidney. In fact, it may extend from the glomeruli to the tubuli, the interstitium, and the surrounding blood vessels. The renal involvement presents a pleomorphic morphology and a high variability in glomerular lesions from patient to patient
LN is thus divided into 6 classes according to severity of the lesions observed[30]
Class I, minimal mesangial LN;
Class II, mesangial proliferative LN;
Class III, focal LN;
Class IV, diffuse segmental LN;
Class V, membranous LN; and
Class VI, advanced sclerosing LN.

As illustrated by Dr. Sheshan[31], Class I LN shows normal findings at light microscopy, but abnormal immunofluorescence & ultrastructural changes.
Class II LN is associated with mesangial pathology and may be associated with necrosis of cells in the capillary walls, of fibrinoid nature, with hyaline thrombi due to an excess of immune complexes, with or without proliferative changes.

Class III LN is characterized by segmental or global endo/extracapillary proliferation with active sclerosing lesions with subendothelial deposits.

Class IV is characterized by > 50% glomerular involvement with pathology similar to class III, more diffuse with segmental or global lesions. Subendothelial deposits are very frequent, with infiltration of inflammatory cells and proliferation. Proliferation and necrosis (with antineutrophil cytoplasmic antibodies related disease) can be segmental (class IV-S) or global (class IV-G). Differentiation of IV-S from IV G is important from a prognostic point of view. The majority of class IV cases (65%) are IV G. Class IV-S cases are characterized by higher hematuria, less proteinuria, fewer deposits, but more necrosis. In the presence of monocyte infiltration, outcomes are worse.

Class V is called membranous presenting predominantly with nephritic syndrome without active urinary sediments and it has a higher risk of renal vein thrombosis.

Class VI is associated with > 90% glomerulosclerosis. Characteristic features at immunofluorescence include deposit of IgG, IgM, and IgA; complement factors C3 and C1q; and Ig light chains. Activity and chronicity indices are being provided to the clinician for LN patients, as they represent predictors, although weak, of long-term prognosis. Such a weakness may be related to the still-lingering interobserver and intraobserver variations. A value of 1+ corresponds to an involvement of < 25%, 2+ to 25% to 50%, and 3+ to > 50%. As reported by different investigators, negative prognostic indices include crescents in more than 30% of the glomeruli, a chronicity index > 5, male sex, and a higher lesion activity in the glomeruli[31].

The association of LN with antiphospholipid antibodies also has a significant effect on prognosis because it leads more frequently to irreversible organ damage, with

destruction of most renal findings, hence, the lack of association with a specific LN class[31].

TABLE 1: NIH RENAL PATHOLOGY SYSTEM

ACTIVITY INDEX	CHRONICITY INDEX
Glomerular abnormalities	
1. Cellular proliferation	1. Glomerular sclerosis
2. Fibrinoid necrosis, karyorrhexis	2. Fibrous crescents
3. Cellular crescents	
4. Hyaline thrombi, wire loops	
5. Leukocyte infiltration	
Tubulointerstitial abnormalities	
1. Mononuclear cell infiltrates	1. Interstitial fibrosis
	2. Tubular atrophy

Severity of each index quantitated as 0 = absent, 1 = mild, 2 = moderate, and 3 = severe. Fibrinoid necrosis and cellular crescents are weighted by a factor of 2. Maximum activity index is 24 and that of chronicity index 12.

Renal Biopsy

The strongest argument for a renal biopsy is likelihood that the pathologic findings will influence initiation, selection or discontinuation of therapeutic agents. In determining the role of renal biopsy in lupus renal disease several points are relevant. Although it is possible to infer the WHO class of renal disease by evaluating the urinalysis, 24 hour urine protein excretion, and serologies, this is not inviolate. There is data correlating WHO Classification and National Institute of Health activity and chronicity indices with prognosis and these can be obtained reliably only by a biopsy[32].

Also membranous lupus nephritis has a different prognosis and treatment than proliferative disease[32].

A renal biopsy is indicated when the clinical findings are indeterminate and objective evidence of active lupus nephritis is required prior to initiating treatment. A biopsy may be required to determine whether cytotoxic therapy is warranted. A biopsy may also help distinguish a patient with a high activity but low to moderate chronicity index, from a patient with moderate to high chronicity in whom the likelihood of reversibility is too small to justify aggressive immunosuppressive therapy[32].

Indications for a renal biopsy in SLE patients' include[32]:

Hematuria and proteinuria;

Renal dysfunction;

Hypertension;

Low levels of the complement factor C3;

The presence of chronic renal lesions; and modifications in therapy: initiation, changes, or discontinuation.

Renal biopsy can provide 3 mainstays of the final diagnosis: classification, extent of reversibility and chronicity of the renal disease, and outcome prediction. Limitations are represented by the need to obtain renal cortical tissue and to collect adequate specimens, as well as the evaluation of focal lesions with limited sampling of highly heterogeneous glomerular involvement[32].

Management

The management of lupus renal disease should be based on risk stratification and the prognostic information available clinically or by renal biopsy.

WHO CLASS I: Class I nephritis which is defined by normal histologic findings and requires no specific therapy[9,10,15].

WHO CLASS II-MESANGIAL**:** Class II-A, mesangial lupus nephritis with mesangial deposition of immunoglobulin if unaccompanied by proteinuria and active urinary sediment does not require treatment. Class II-B, mesangial lupus nephritis when accompanied by significant proteinuria (e.g.: greater than 1 gram per day) usually requires treatment with steroids, especially if there is evidence of active urinary sediment, elevated anti-double stranded DNA, or low C3[9]. Prednisolone is given in the dose of 0.5 and 1 mg/kg of or equivalent per day for from four to twelve weeks and subsequently, 5tapered by 5-10 mg increments every 1-3 weeks[9].

WHO CLASS III and IV-PROLIFERATIVE**:** Clinicians recommend cyclophosphamide contemporaneously with prednisolone for Class III or Class IV disease, especially in the presence of moderate to high activity and elevated chronicity biopsy scores. Cyclophosphamide is administered at a dose of between 0.5 and 1 gram per m2 of body surface monthly for six months. Cyclophosphamide is typically administered with between four to 24 hours of intravenous hydration to avoid hemorrhagic cystitis. Those centers who use abbreviated intravenous hydration often use two mercaptoethylamine

sulfonate sodium (MESNA) to further minimize the risk of bladder toxicity. Ondansetron or granesetron can be used as an anti-emetic to reduce nausea and vomiting.

Use of prednisolone as first line therapy of even Class III and IV disease is the observation that remissions of proliferative nephritis have been observed with oral steroids, some with no recurrence of nephritis during follow-up periods of 30-40 years[23]. Also, treating with prednisolone alone allows for preservation of reproductive function such that pregnancies can be completed in intervals before relapsed disease requires cyclophosphamide[33]. It is also notable that the efficacy of cyclophosphamide is best established in patients previously treated for their renal disease with steroids. In the study by Austin et al., comparing prednisolone with cyclophosphamide therapy, patient enrollment occurred only after a mean of 22 months of treatment with steroids for nephritis and 3 years for SLE. The benefits of intravenous cyclophosphamide were achieved in groups of patients failing prednisolone, establishing cyclophosphamide as salvage or rescue therapy for patients unresponsive to steroids[16,33,34]. The major argument against using steroids alone for proliferative nephritis, especially Class IV, is concern that any delay in initiating treatment with cyclophosphamide will permit renal scarring, which may be underestimated by serum creatinine and creatinine clearance. Therefore, treatment should be individualized accounting for the prognostic information available from the clinical or biopsy data and the relative risks of treatment in the specific circumstance.

Once initiated the duration of cyclophosphamide therapy is also individualized. For patients with a less prognostically severe biopsy and an early clinical response,

cyclophosphamide can be limited to the six month induction course of treatment. Boumpas et. al. established that patients with a longer course of cyclophosphamide (i.e. 14 treatments over 30 months) had a lower incidence of relapse of nephritis, maintenance therapy consisting of the same dose of cyclophosphamide administered every three months for an additional one to two years is indicated for patients with prognostically severe biopsies[35].

Prednisolone and cyclophosphamide therapy of proliferative lupus nephritis is usually effective in between 60 and 90% of patients. However, there will be patients who will prove refractory, defined as either failing to respond, or relapsing with reappearance of a nephrotic syndrome or nephritic component (i.e. hypertension and active urinary sediment) sometimes even with loss of renal function that require intensification of therapy. These patients may be treated with the resumption of monthly dosing of cyclophosphamide, the addition of higher doses of glucocorticoids which can consist of either 1 mg/kg per day of prednisone or equivalent, or pulses of methylprednisolone such as 1 gram per day for from one to three days. The combination of methylprednisolone and cyclophosphamide on a monthly basis in these patients may prove effective, although is certainly associated with the range of toxicities attributable to each of these aggressive treatments. The addition of plasmapheresis synchronized or otherwise is of uncertain benefit in this setting.

Alternative approaches to patients with proliferative nephritis would include initial therapy with prednisone plus azathioprine, prednisone followed by azathioprine, or

prednisone plus cyclophosphamide during the six month induction followed by maintenance with azathioprine.

In a study by Tak Mao et al, eighty-one percent of the 21 patients treated with mycophenolate mofetil and prednisolone (group 1) had a complete remission, and 14 percent had a partial remission, as compared with 76 percent and 14 percent, respectively, of the 21 patients treated with cyclophosphamide and prednisolone followed by azathioprine and prednisolone (group 2). The improvements in the degree of proteinuria and the serum albumin and creatinine concentrations were similar in the two groups[36].

MMF (2 g/day) was used in combination with steroids in patients with diffuse proliferative glomerulonephritis[43], but not with membranous glomerulonephritis[37]. Indications of use included toxicity (60 %) and lack of efficacy (15 %), while in five patients MMF was used as a first choice agent. Treatment failure was recorded in 20 % of patients, all with class V nephritis, partial remission in another 20 %, while 60 % went into complete remission. Proteinuria and creatinine levels were significantly reduced in patients with proliferative nephritis but not in those with membranous nephritis[37]. Based on the above facts, MMF therapy appears to be safe and probably efficacious for the treatment of lupus nephritis, particularly in proliferative forms in cases of failure or toxicity of conventional therapy.

WHO CLASS V-MEMBRANOUS**:** Class V membranous lupus nephritis is often treated with 1 mg/kg per day of prednisone or equivalent for six to twelve weeks. Regardless of a response, steroids are usually then discontinued. Cyclophosphamide is generally reserved for those patients who have a concurrent proliferative component with their lupus

membranous nephritis and continue to have clinical features of activity which typically requires not only proteinuria but either an active urinary sediment, persistent high anti-DNA, or hypocomplementemia. Therefore, patients with lupus membranous nephropathy and persistent nephrotic syndrome who have a component of proliferative nephritis are considered for cytotoxic therapy. Patients with pure membranous nephritis and incessant nephrotic syndrome are candidates for therapy with cyclosporin[38]. The dose typically is 3.5 mg to 5 mg/kg per day with close monitoring of the blood pressure and for a paradoxical effect on the serum creatinine reflective of the nephrotoxic effects of this agent.

WHO CLASS VI-GLOMERULOSCLEROSIS**:** This improvement has been attributed to a number of different factors including the more judicious use of corticosteroids, refinements in immunosuppressive therapy, more effective treatment of hypertension and cardiovascular disease, and greater availability of dialysis and renal transplantation[39].

In the routine management of lupus renal disease, the addition of plasmapheresis to steroids and cyclophosphamide compared to steroids and cyclophosphamide alone, proved of no benefit[40]. Plasmapheresis is most useful in lupus patients with thrombotic microangiopathic hemolytic anemia or secondary TTP. The renal disease that accompanies this syndrome is clearly responsive to plasmapheresis with plasma exchange. Synchronized plasmapheresis based on the theory of "stimulation depletion" was initially reported to be of benefit[41]. Synergism between pheresis and cytotoxic treatment was predicted on the concept that plasmapheresis is followed by a period of accelerated B cell proliferation such that synchronized doses of cyclophosphamide would

have the greatest cytolytic effect on autoreactive anti-DNA producing clones of lymphocytes. However, a more recent study suggested that synchronization was of no greater benefit than standard cyclophosphamide and low dose prednisolone treatment yet associated with greater toxicity[42,43] .

Intravenous immunoglobulin is a relatively less toxic, although expensive approach to the treatment of lupus and lupus renal disease. However, save for scattered case reports, there is no convincing data to state with any certainty its benefits. Intravenous immunoglobulins can be associated, albeit rarely, with acute renal failure; presumably on the basis of tubular injury related to the infused immunoglobulin.

General Measures

In a study by J. Font et al on the cardiovascular risk factors and the long term outcome in lupus nephritis, compared with controls, LN patients had a higher prevalence of hyperlipidaemia (44% vs. 2%, p=<0.001), hypertension (44% vs. 9%, p=<0.001) and antiphospholipid antibodies (44% vs. 22%, p=0.01) at study onset. Hyperlipidaemia (78% vs. 27%, p<0.001) and hypertension (67% vs. 32%,p=0.01) at study onset were associated with renal failure[44].

Despite the best of efforts some patients will develop ESRD. Seasoned clinicians, familiar with the generally good experience with hemo and peritoneal dialysis as well as renal transplantation in lupus patients[45], recognize the need to abandon immunosuppressive therapy once advanced glomerulosclerosis has developed.

Novel Therapies

Specific agents that are undergoing clinical investigation include LJP397, which is known as a B cell tolerogen. It consist of four oligonucleotides attached to a triethylene glycol platform, which when infused, is bound by the Fab portion of anti-DNA antibodies in the membrane of auto-reactive B cells. Cross linking of anti-DNA antibody in the cell membrane of B cells results in a down regulation of anti-DNA immunoglobulin synthesis and apoptosis of these B cells. In animal models of lupus renal disease, this approach has not only reduced the production of anti-DNA, but mitigated renal disease. Human studies have suggested that this is a non-toxic therapy and beginning in 1997 a multicenter randomized double blind study investigating its efficacy was initiated[46].

Additional agents that may have a role in the treatment of lupus nephritis include a monoclonal antibody to the fifth component of complement. The monoclonal anti-C5 reduces the production of C5a and C5b-9 and the inflammatory reaction which appears consequent to the generation of immune complexes in the kidney.

An additional agent, anti-CD40ligand monoclonal antibody, has the ability to reduce the production of auto-antibodies. Anti-CD40ligand not only inhibits production of pathogenic antibodies but can inhibit inflammatory cytokine production and T cell dependent activation of endothelial cells[46].

Predictors of Outcome In Lupus Nephritis

Because of the high heterogeneity of SLE among patients and the limited

therapeutic resources available at present that may induce substantial toxic effects in the long term[47], it is important to identify those patients who may have a worse prognosis, and thus necessitate more-aggressive treatments to prevent or reduce complications and organ failures.

The predictors of outcome and long-term prognosis in patients with lupus nephritis are[48,49],

1. Disease severity, both in terms of clinical manifestations (serum creatinine and proteinuria) and histopathology;
2. Patients' characteristics: age and sex, race and ethnicity, socioeconomic status and access to healthcare;
3. Response to therapy; and
4. Specific treatment modalities.

Old data published by Estes and Christian[50] in the 1970s pointed to an estimated 5-year survival rate for patients with renal manifestations of about 50% vs. 75% for the whole SLE series analyzed. Such a rate was even lower for patients with severe kidney disease: about 68% for patients with focal proliferation, but only 28% for those with diffuse and membranous lesions. Patients in this series were being treated with 40 mg of prednisolone, the conventional treatment at the time, as immunosuppressive agents were not yet in use [50].

In a 1965-1998 series of 800 patients followed at SUNY/Brooklyn, the average survival rate of SLE patients with kidney disease was, overall, 60% to 65% at 300-350 months[51].

Of note, the effect of the inclusion of socioeconomically disadvantaged patients

had a far less negative effect than reported in other series. It showed a trend, but it did not reach a significant difference. It is unclear whether the socioeconomic factors did not play such a significant role in this cohort or whether better care than average was provided to these patients.

Notwithstanding these successes, and the fact that SLE-related mortality has been significantly reduced with medical intervention in the past 20 years or so, there has been a 3-fold increase in morbidity, thus leading to an increase in the overall burden of disease.

A number of other factors have been shown to be of critical importance in predicting worse outcome for patients with severe LN in a study of 65 patients[32]:

1. Initially high serum creatinine;

2. Lower hemoglobin/hematocrit;

3. Black race; and

4. The presence of interstitial fibrosis and crescents (which are a sign of chronicity and damage).

Effects of Treatment On Outcome Of Lupus Nephritis

Achievement of remission following treatment, as well as the type of treatment given, seem to have a considerable effect on outcome[52], as reported by Korbet and colleagues[53]. Patients receiving conventional treatment had a survival rate of 95% at 5 and 10 years that was reduced to 69% at 5 years and 60% at 10 years in those patients who did not achieve remission. Treatment with high-dose prednisolone plus cyclophosphamide plus/minus plasmapheresis substantially improved the survival rate also in renal patients achieving remission - 94% at 5 and 10 years. Lack of remission was,

however, associated with a far lower survival rate, 45% and 31% at 5 and 10 years, respectively, in patients with refractory renal disease.

Clinical remission in the overall series was achieved in 43% of patients (37/86). Overall time to remission was 16 months (± 14 months) and the median, 10.5 months. The positive predictors of remission included a stable renal function, a lower chronicity index, and white race. Also, the probability of developing end-stage renal disease seemed strongly correlated with choice of treatment. Intravenous or oral cyclophosphamide plus/minus azathioprine was associated with the lowest risk of renal failure (5% to 25%), risk that increased to 40% with azathioprine alone and up to 80% with prednisone only[53].

A recent European study by Houssian and colleagues[54] has reported similar outcome in patients receiving high- vs low-dose cyclophosphamide, being the latter a regimen that is becoming the new standard of care in Europe, to avoid the toxic effects and cancer risk(s) associated with long-term, high-dose immunosuppressive therapies. Long term data on the prognosis of these patients are yet to come.

Influence of Socioeconomic and Genetic Factors on Outcome Of Lupus Nephritis

The influence of race on outcomes of SLE patients shows a different penetrance in different studies, and the underlying mechanisms are still poorly understood. Nonetheless, the survival rates of renal patients evaluated 5 years after renal biopsy were significantly different in 2 cohorts ($P = .007$), with > 90% survival in white vs 60% in black SLE patients[55]. When the effect of race on survival was evaluated with other parameters, it was found to be independent of age, the duration of SLE, hypertension, and

cyclophosphamide treatment. In the SUNY/Brooklyn series mentioned before, there was a trend in favor of white and Asian patients, but such a difference did not reach significant values[51].

In a series of 128 patients evaluated at Columbia University, New York, NY, patients with evidence of poverty had a 3.5% higher relative risk of progression (a shorter time to doubling of serum creatinine) after adjustment for age, hypertension, and cyclophosphamide treatment. In another study performed in New York City, mentioned by Dr. Ginzler[48], the impact of poverty appeared significant with a survival rate at 65 months of 42% in renal patients with evidence of poverty vs. 78% in above-poverty-level patients. It is unclear whether access to healthcare, education, and quality of nutrition are all factors contributing to such differences. It cannot be excluded that different factors may be differentially implicated in the various cohorts studied. Recent investigations of the molecular and genetic mechanisms involved in SLE seem to suggest a genetic predisposition to SLE in black patients[56]. The increased prevalence of the Fcgamma receptor 2A[28], increased titers of immunoglobulin (Ig)G2 specific for C1q[57], and decreased clearance of circulating immune complexes (CICs) reported in these patients may all potentially contribute to a reduce clearance of CICs and, thus, to a higher risk of renal disease.

More insight in the etiopathogenic factors of SLE is expected from the ongoing studies on the basis of gene expression microarrays, genomic analysis, and the refined classification of renal disease in SLE patients. At the same time, glomeruli isolated by laser capture microdissection will allow more detailed analyses of the damage inflicted to the kidney by SLE and correlations with response to medical therapy.

Role of Antiphospholipid syndrome in Lupus Nephritis

APS is characterized by recurrent arterial or venous thrombotic events and/or pregnancy morbidity along with the sustained presence of antiphospholipid antibodies (anticardiolipin antibodies and/or lupus anticoagulant)[58]. Renal disease in antiphospholipid syndrome is characterized by interstitial tubular or glomerural injury due to obstruction of large, medium, or small-sized vessels[59]. In a recent study, Vlachoyiannopoulos et al studied renal involvement in a cohort of 248 patients with SLE and APS syndrome with positive titre of anticardiolpin antibodies, among which 40 % had evidence of renal involvement[60]. A renal biopsy was performed in 79 % of patients for diagnostic purposes. Patients with APS experienced high percentages of hypertension (59 %) compared to those without the syndrome, while increased levels of creatinine, proteinuria, and hematuria with or without the presence of casts were similar in both groups. Renal biopsy analysis revealed that the main histopathologic finding in APS patients compared to controls was hyperplasia of intima (64 % vs. 19 %, $p<0.001$). Thrombi and atrophy of renal tubules were common but not pathognomic, since they were found in both groups. Renal biopsy findings determined further therapeutic approach to these patients. When findings are consistent with lupus nephritis, according to World Health Organization (WHO) classification, standard care with intravenous cyclophosphamide pulses and corticosteroids is recommended[61]. When thrombi and intimal hyperplasia predominate, the patient should be placed on long-term oral anticoagulant therapy.

Lupus Nephritis: Prognosis

With modern treatment, the survival has improved in the west to about

of 80% at 10 years after diagnosis[12] but, the Indian figures are not so good and is about 50%-60% survival at 10 years[13,14]. Possible reasons for poor survival in Indian SLE include delay in diagnosis, referral bias (only the most serious cases are referred by practitioners), suboptimal health care facilities and an inherently more severe disease (genetic factors?) and endemic tuberculosis to which the lupus patients are more susceptible.

As shown by Fiehn et al, in the decade from 1990 to 2000 there was significantly less proteinuria (46 v 17g/l, p=0.008), significantly lower rates of renal failure (40% v 17%, p=0.02), and fewer histological signs of chronicity (33% v 10%, p=0.01) at the time of diagnosis of LN than in the decade from 1980 to 1989[62]. The mean (SD) time from the first appearance of proteinuria until kidney biopsy was significantly shorter in the later decade [15.4 (15.6) vs. 3.9 (4.7) months]. Though treatment schedules were not significantly different, the outcome of the disease was significantly better in the patients who were diagnosed with LN between 1990 and 2000 (p=0.045)[62].

A number of factors have prognostic significance from a clinical point of view, as including persistent anemia, severity of the disease[64,65], time to treatment, and duration of remission. In patients treated with intravenous cyclophosphamide, an age at diagnosis of < 29 years was found associated with a higher risk of progression to LN in 5 years. Also, an advanced chronicity index (> 3) at biopsy and a delay to treatment of > 5 months were linked to worse outcomes[66].

Patients who did not have a flare-up of their disease had only a 25% risk of doubling their serum creatinine in 5 years vs. a 75% risk in patients who experienced flare- ups in the observation period. Austin and colleagues[32] reported in 1994 that the

presence of focal necrosis, crescents, proteinuria, lower C3 (< 76 mg/dL) following therapy, female sex, age > 30 years, black race, and hematocrit of < 26% were associated with a worse outlook. The difference reported by the 2 groups in age significance has not been clarified. Treatment can critically improve the survival of SLE patients with renal disease. In a study by Laitman and colleagues[67], patients in group 1a (with relapsing/recurrent grades 2, 3, and 4 LN) had a survival of about 80% at 6 years vs. less than 5% for patients in group 1b who also had grades 2, 3, and 4 LN, but were refractory to medical treatment. Patients in group 2 (with grades 3 and 4 LN) with recurrent disease had an intermediate survival rate.

If patients were treated within 5 months of diagnosis, they had a 25% chance of relapse of their renal disease at 7-10 years. Conversely, if they were treated only after 5 months from biopsy, their chances of relapse increased to 60%[66].

Use of renal biopsies is critical in the management of lupus patients in diagnostic, therapeutic, and prognostic terms[32]. The presence of cellular crescents and interstitial fibrosis was found associated, in addition to endocapillary proliferation, with an increased risk of progression (doubling of serum creatinine) in 40-50 months from 20% to 80% of cases. A global disease activity of < 1.73 was associated with progression (doubling of serum creatinine) at 4000 days in only 15% of cases vs. 80% in patients with a disease activity of > 1.73[68]. Persistent inflammation and positive findings at immunofluorescence are also predictive. Progression was seen in 75% of patients with karyorrhexis vs. 26% in patients who were negative. Similarly, progression was seen in 69% of patients with crescents vs. 33% of control patients. Reinduction therapy with pulse steroids and intravenous cyclophosphamide in 12 refractory LN patients, however,

achieved a reduction of progression risk from 34% to 10.5% in patients with crescents, and from 73% to 6.4% in patients with biopsies positive for endocapillary proliferation. Follow-up biopsies at 6 months were negative for cellular crescents, endocapillary proliferation, and karyorrhexis. Reinduction therapy was effective in salvaging LN patients who were otherwise refractory to treatment[63].

In summary, we find paucity of data regarding short term outcome and its predictors in Indian patients with lupus nephritis. This may go a long way in view of changing scenario of outcome due to early diagnosis and newer drugs. Although majority of the lupus nephritis patients belong to class IV and there is an Indian study on this class of patients[69], the overall picture has not been brought out by any Indian study on lupus nephritis. It is with this background that we have endeavored this study.

AIM

T o describe the presentation of lupus nephritis, its prognostic factors, outcome measures and their correlation in patients with lupus nephritis on treatment for six months.

OBJECTIVES

1. To describe the presentation of lupus nephritis in our population
2. To describe the clinical outcome of lupus nephritis in patients treated with various regimens at six months.
3. To identify predictors of outcome of lupus nephritis in our population.

MATERIALS AND METHODS

Setting

Study was conducted among the patients presenting to the in-patient and out-patient services of the Department of Medicine and Nephrology of the Christian Medical College (CMC), Vellore, South India which is an 1800 bedded tertiary care teaching hospital.

Duration Of Study

August 2004 to July 2006. The recruitment of patients ended in January 2006 and the follow up period in July 2006.

Inclusion Criteria

1. All consecutive adult SLE patients (age >12 years).
2. Diagnosed with lupus nephritis by Renal biopsy in the Department of Medicine and Nephrology.
3. Follow up for 6 months, availing out-patient clinic/ in-patient services between August 2004 and July 2006.

Exclusion Criteria

1. Age < 12 years.
2. Renal disease other than SLE.
3. Less than 6 months of follow up.

Study Design

The study was a **Prospective Cohort** study on *consecutive* Lupus Nephritis patients diagnosed in our centre.

Study Protocol

All *consecutive* adult patients diagnosed to have SLE and admitted for renal biopsy were enrolled into the study. Upon enrolment into the study, complete demographic details, relevant clinical and laboratory parameters were collected. The SLE disease severity was assessed using the *SLEDAI score* (SLE Disease Activity Index) which is a validated index for assessing disease activity[29,30,35] (**Annexure A**).

The following specific data was collected at the time of enrolment into study through a *Proforma* (**Annexure B**):

1. Demography- Age, Sex, Region, Marital status
2. Clinical presentation of SLE
3. Clinical presentation of Lupus Nephritis
4. SLEDAI score
5. Biopsy findings of lupus nephritis
6. Laboratory parameters at enrolment
7. Treatment regimens planned
8. Co-morbidities

The participants underwent treatment as per the policies of the various Departments namely steroids and Cyclophosphamide pulse, steroid and Azathioprine, steroid and MMF, steroid alone, IVIG and others.

The patients who came for follow up at the end of six months were finally enrolled for the analysis. The following specific data was collected at

the end of six months through the same *Proforma* (**Annexure B**).

1. SLEDAI score and other clinical parameters
2. Laboratory parameters at six months
3. Outcome Variables- Complete remission, Partial remission, No Remission, Relapse[70] which are defined below.

A. Complete **Remission**- Defined as <10 dysmorphic erythrocytes per high power field, the absence of cellular casts, and excretion of <1G of protein per day without doubling of s.creatinine level.

B. **Partial Remission-** Defined as the reduction of at least 50% in

- the number of dysmorphic erythrocytes seen in urine sample
- the number of cellular casts
- proteinuria
- without a doubling of the s.creatinine level

C. **No Remission-** >/= 10 erythrocytes per high power field, cellular casts, proteinuria (>1G of protein per day), and doubling of s.creatinine level.

D**. Renal Relapse-** Increase in at least 50% in any two of the following after six or more months of remission: number of dysmorphic RBCs >/=10 per high power field, number of cellular casts, proteinuria >/= 1G per day, or s.creatnine level.

For analysis of data at the end of six months groups “A” and “B” were taken as **RESPONDERS** and groups “C” and “D” were taken as **NON-RESPONDERS.**

4. Various Drug Regimens patients received
5. Drug Toxicities
6. Infections and other complications

Statistical Analysis

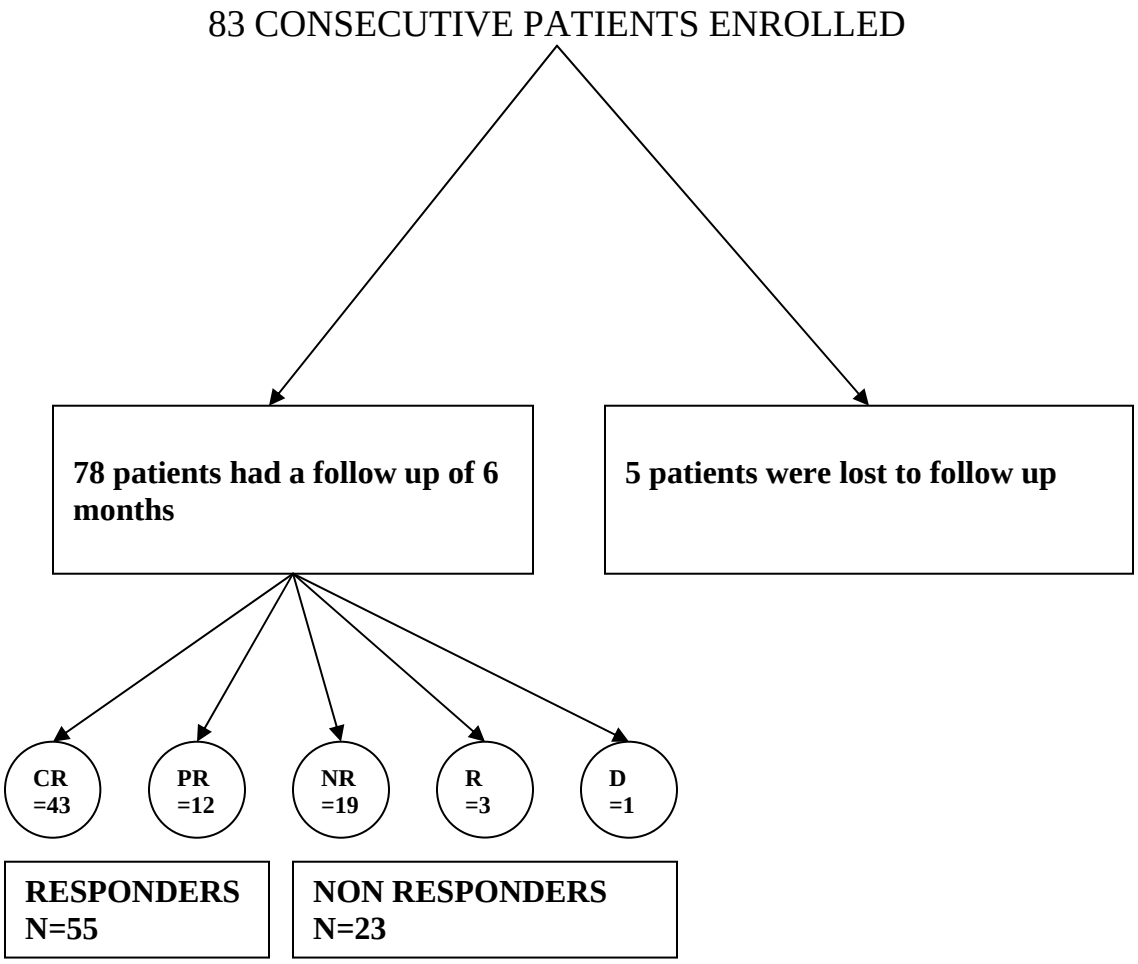
All consecutive patients diagnosed with SLE and who met the inclusion criteria were enrolled into the study between August 2004 and January 2006. Patients zero time corresponded to the time of hospital admission for Renal biopsy after which they were followed up for a total of six months.

Values were expressed in mean +/- SD for continuous variables and No. (%) for categorical ones. Comparisons between responders and non-responders for continuous variables were done using Independent t Test and Mann Whitney score for normal and non-normal (distribution) data respectively.

Paired t Test (normal) and Wilcoxon Signed Rank Test (non normal) were performed to assess the significant improvement over time. Pearson Chi Square test were used for categorical variables. Univariate Analysis was carried out to find significant risk factors associated with poor outcome.

Multivariate analysis were carried out on the various demographic, clinical, lab parameters factors whose univariate analysis had a p value of <0.025. Multivariate analysis was done by Enter Method followed by Forward Step Conditional to find out the significant variable. Values of $p < 0.05$ were considered significant in the multivariate model.. SPSS version 11.5 was used for the statistical analysis.

Consort Diagram



CR= Complete remission
PR= Partial Remission
NR= No Remission
R= Relapse
D= Death

RESULTS

83 consecutive patients were enrolled into the study and 5 were lost to follow up. 78 patients were analyzed at the end of 6 months of follow up. The Responders were 70.5% and Non responders were 29.5%.

1. Majority of patients were between 21 to 40 years of age, in the reproductive age group.

Table 1 (Figure 3): Age Distribution vs. Outcome

Age (years)	**Responders (N=55) (%)**	**Non responders (N=23) (%)**	**Cumulative (N=78) (%)**
0-20	14 (25.5%)	6 (26.1%)	20 (25.6%)
21-40	32 (58.2%)	12 (52.2%)	44 (56.4%)
41-60	9 (16.4%)	5 (21.7%)	14 (17.9%)

p = 0.367 between responders and non responders for all age group

2. Female to male ratio is 8.7:1.2.

Table 2 (Figure 4): Sex Distribution vs. Outcome

Sex	**Responders (N=55) (%)**	**Non responders (N=23) (%)**	**Cumulative (N=78) (%)**
Female	47 (85.5%)	21 (91.3%)	68 (87.2%)
Male	8 (14.5%)	2 (8.7%)	10 (12.8%)

p = 0.481 between responders and non responders between males and females.

Figure 3

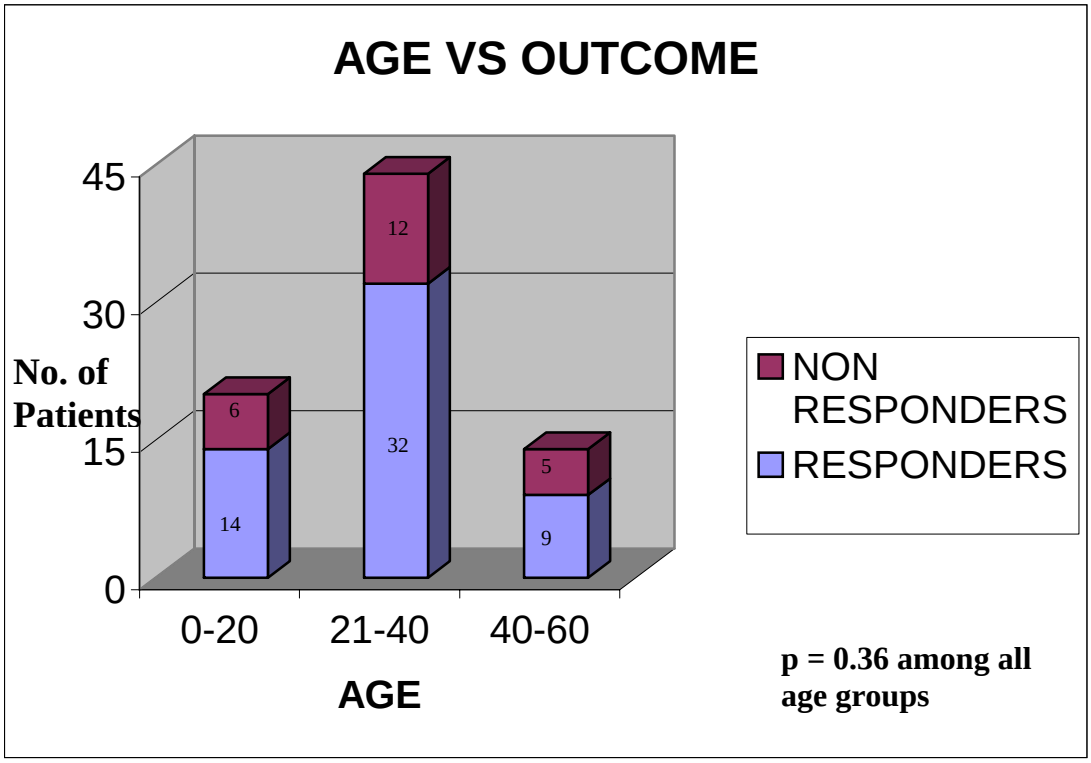
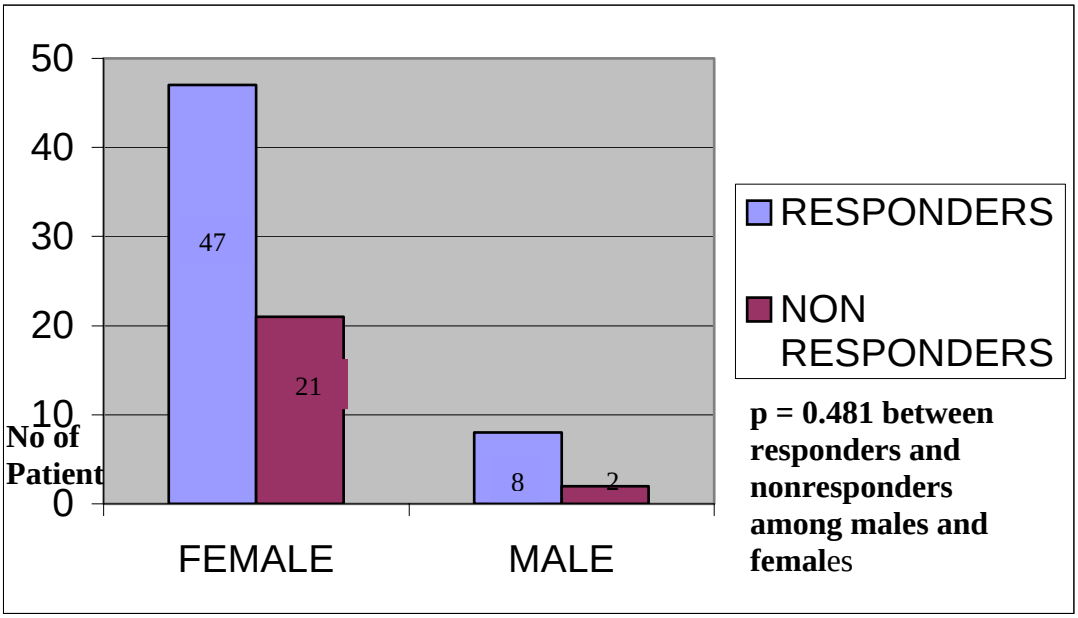


Figure 4

2. SEX vs. OUTCOME



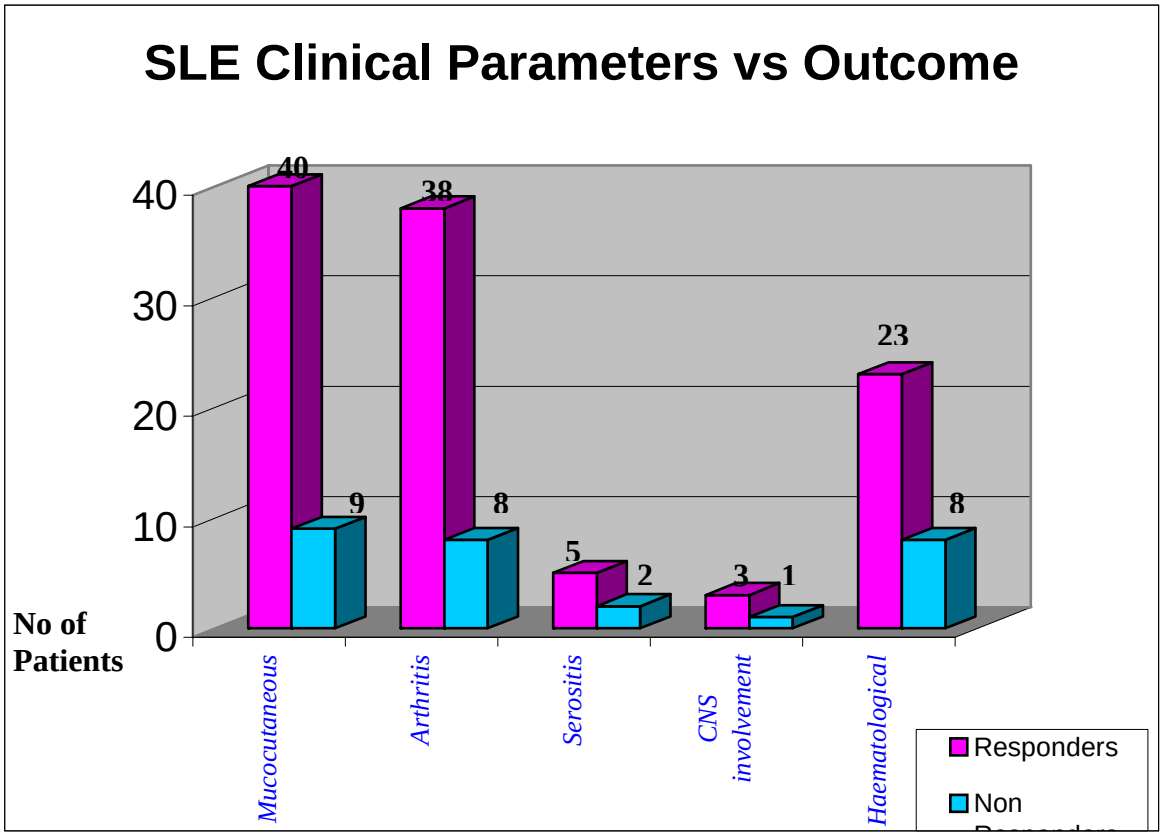
3. The extra renal organ manifestations of Lupus Nephritis were compared between the outcome groups to look for significant predictors of poor outcome. The prevalence of various extra renal manifestations in lupus nephritis patients were 64.5% for mucocutaneous, 60.5% for arthritis, 9.2% for serositis, 5.3% for CNS involvement and 40.8% for hematological involvement. **The responders seemed to have a higher incidence of muco-cutaneous and arthrtic manifestations**. There was no significant correlation of any extra renal organ involvement with poor outcome.

Table 3 (Figure 5): SLE clinical manifestations* vs. Outcome

Clinical Parameters	**Responders (N=53) (%)**	**Non Responders (N=23) (%)**	**Cumulative (N=76) (%)**	**p value**
Mucocutaneous	40 (75.5%)	9 (39.1%)	49 (64.5%)	**0.002**
Arthritis	38 (71.7%)	8 (34.3%)	46 (60.5%)	**0.002**
Serositis	5 (9.4%)	2 (8.7%)	7 (9.2%)	0.919
CNS involvement	3 (5.8%)	1 (4.3%)	4 (5.3%)	0.801
Hematological	23 (43.4%)	8 (34.8%)	31 (40.8%)	0.482

* Overlapping features in a patient will cause the total of each column to be more than the actual number of patients

Figure 5


SLE Clinical Parameters vs Outcome
No of Patients
0
10
20
30
40
40
9
38
8
5
2
3
1
23
8
Mucocutaneous
Arthritis
Serositis
CNS involvement
Haematological
Responders
Non

4. The mean time of biopsy for our patients was 7.98 +/- 1.9 months. There was no significant correlation between responders and non responders (p= 0.191). Among all patients 47% had renal biopsy at diagnosis of SLE, 82% by 1 year and 89.7% by 2 years.

5. We compared the various laboratory parameters of lupus nephritis between the two outcome groups. **It was found that Creatinine clearance <75ml/min, and Proteinuria were significant predictors of poor outcome.** But S.creatinine >1.5 mg/dl, RBCs >10/hpf and elevated dsDNA did not have any correlation with the outcome.

Table 4 (Figure 6): Laboratory Parameters vs. Outcome

Lab Parameters	Responders **(N=55)**	**Non responders (N=23)**	**Cumulative (N=78)**	**p value**
Active sediments (RBCs >10/hpf)	24 (43.6%)	13 (56.5%)	37 (47.4%)	0.299
Proteinuria (>3.5 G)	37 (67.2%)	12 (52.1%)	49 (62.8%)	0.208
S.Creatinine (≥1.5 mg/dl)	7 (12.7%)	6 (26.1%)	13 (16.7%)	0.149
Elevated DsDNA	47 (85.5%)	19 (82.6%)	66 (84.6%)	0.639
Creatinine Clearance (<75ml/min)	20 (36.4%)	14 (60.9%)	34 (43.6%)	**0.047**

However, Proteinuria as a continuous variable using the Mann Whitney test of Significance was found to be significant predictor of non responsiveness to therapy with a p value = 0.032.

6. Among the other lab parameters analyzed, S.albumin showed significant correlation with outcome.

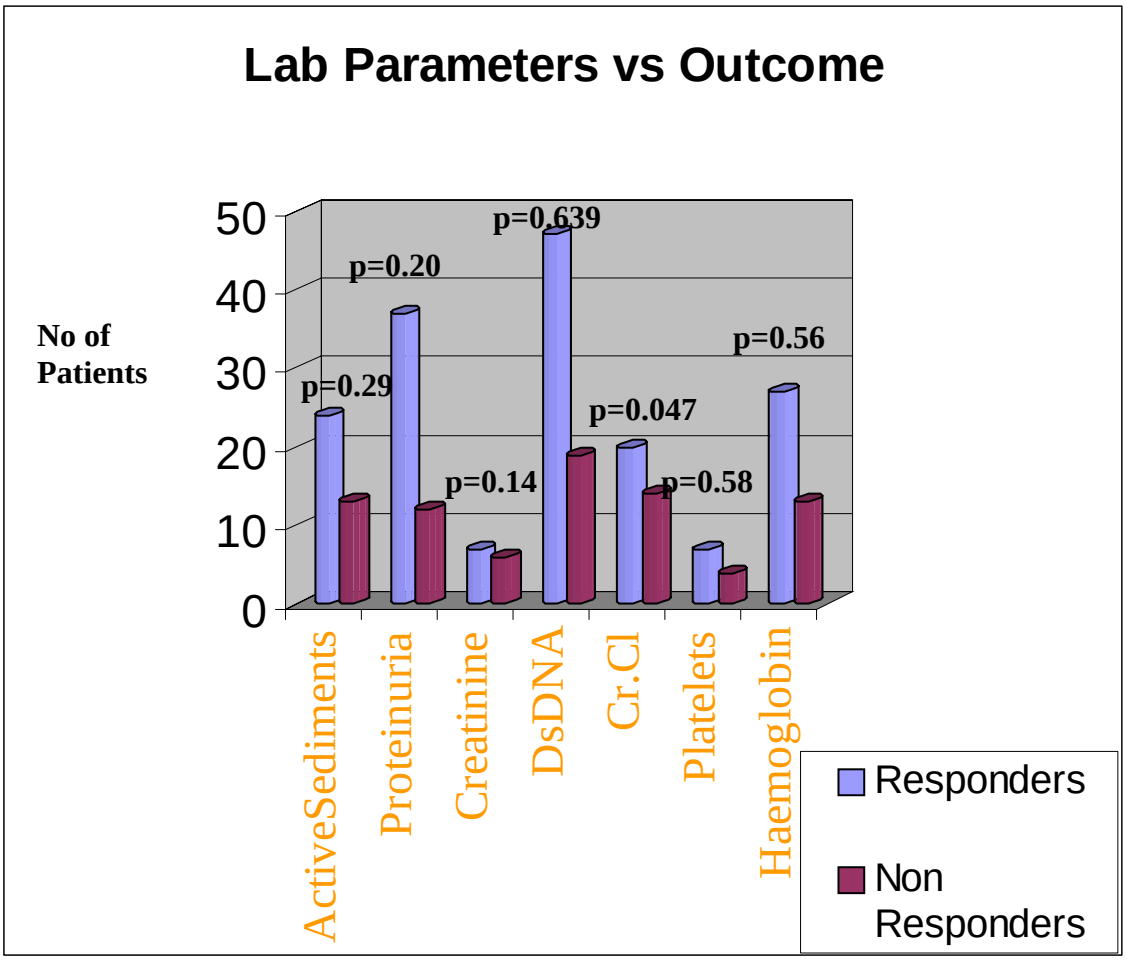
Table 5 (Figure 6): Laboratory Parameters vs. Outcome

Lab Parameters	**Responders (N=55)**	**Non responders (N=23)**	**Cumulative (N=78)**	**p value**
Platelets (<1 lac /cu.mm)	7 (17.4%)	4 (12.7%)	11 (14.1%)	0.589
Hemoglobin (<10 mg/dl)	27 (49.1%)	13 (56.5%)	40 (51.2%)	0.561

S. Albumin was done in 69 out of 78 patients at the time of diagnosis and a value of </=3.0 mg/dl was found to be significant predictor for non responsiveness to therapy (p value of 0.041).

S. Complements (C3/C4) was done on 67 out of 78 patients at the time of diagnosis and low complements was not found to be a significant predictor for non responsiveness to therapy **(**p value of 0.143**).**

Figure 6


Lab Parameters vs Outcome
No of Patients
50
40
30
20
10
0
p=0.29
p=0.20
p=0.14
p=0.639
p=0.047
p=0.58
p=0.56
ActiveSediments
Proteinuria
Creatinine
DsDNA
Cr.Cl
Platelets
Haemoglobin
Responders
Non Responders

7. The SLEDAI score and the various lab parameters were statistically analyzed for any significant change in their values with treatment over six month period in both the outcome groups namely Responders(**R**) and Non responders (**NR**).

Table 6a (Figure 7-9): Change in Parameters over Time

Time	**Hemoglobin Mean(mg/dl) (SD)**		**Platelets mean (Lac/cu.mm) (SD)**		**Proteinuria Mean(G/dl) (SD)**		**S.Albumin (mg/dl) (SD)**	
	R	NR	R	NR	R	NR	R	NR
0 months	10.0 (1.9)	9.2 (2.4)	1.97 (1.01)	1.86 (0.57)	2.8 (3.2)	3.79 (2.26)	2.6 (0.93)	2.2 (0.73)
6 months	11.6 (1.8)	9.8 (2.46)	2.10 (1.00)	1.98 (0.73)	0.61 (0.93)	3.06 (2.36)	3.7 (0.62)	2.7 (1.06)
p value*	0.000	0.372	0.244	0.307	0.000	0.181	0.000	0.155

Table 6b (Figure 10-12): Change in Parameters over Time

Time	**Complement Mean(mg/dl) (SD)**		**DsDNA Mean (Au/ml) (SD)**		**S. creatinine Mean (mg/dl) (SD)**		**SLEDAI Score (SD)**	
	R	NR	R	NR	R	NR	R	NR
0 months	58.2 (19.4)	58.2 (19.4)	51.9 (33.7)	42.5 (13.8)	1.02 (0.56)	1.34 (0.71)	17.9 (6.37)	17.95 (6.7)
6 months	73.7 (15.7)	73.7 (15.7)	25.7 (12.6)	25.07 (9.49)	0.88 (0.59)	1.5 (1.11)	5.6 (4.5)	12.0 (5.9)
p value*	0.000	0.055	0.000	0.004	0.003	0.552	0.000	0.007

*The colours of p value depicted corresponds to the colours in the figure.

Values were also compared between Responders and Non responders at 6 months, and the following parameters were significantly different namely, **SLEDAI score (p value= 0.000), S.Albumin (p value= 0.00), S.Creatinine (p value= 0.00) and Proteinuria (p= 0.00).**

The following graphs from 7-12 show change in different clinical and lab parameters over six months among Responders and Non Responders and their correlation

Figure7

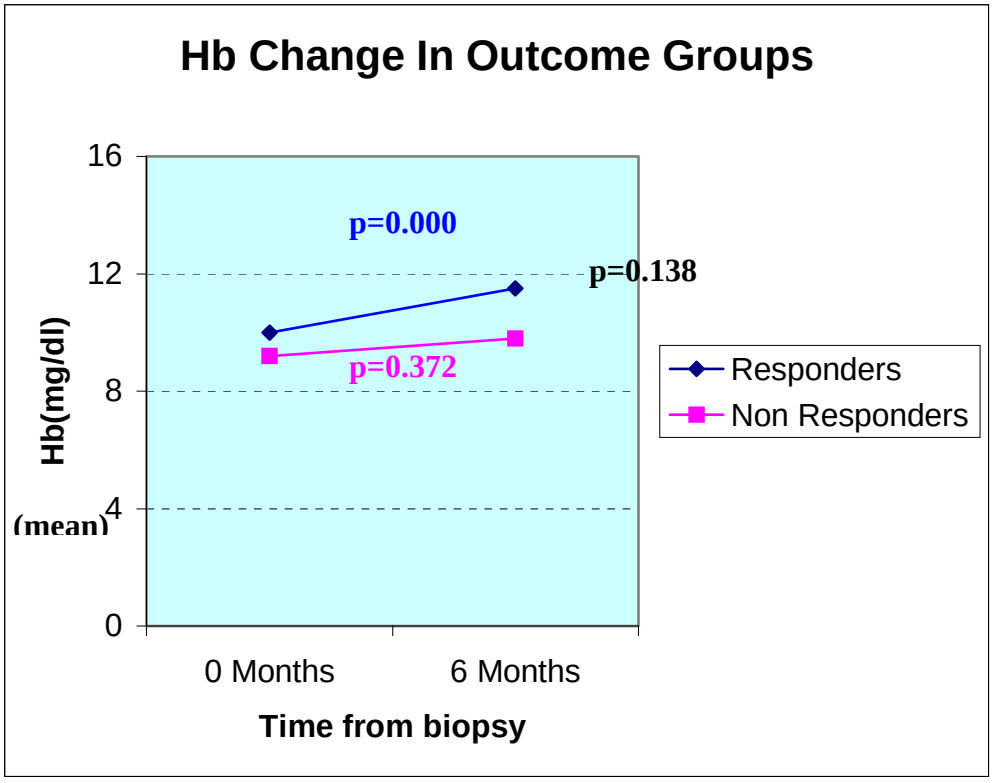


Figure 8

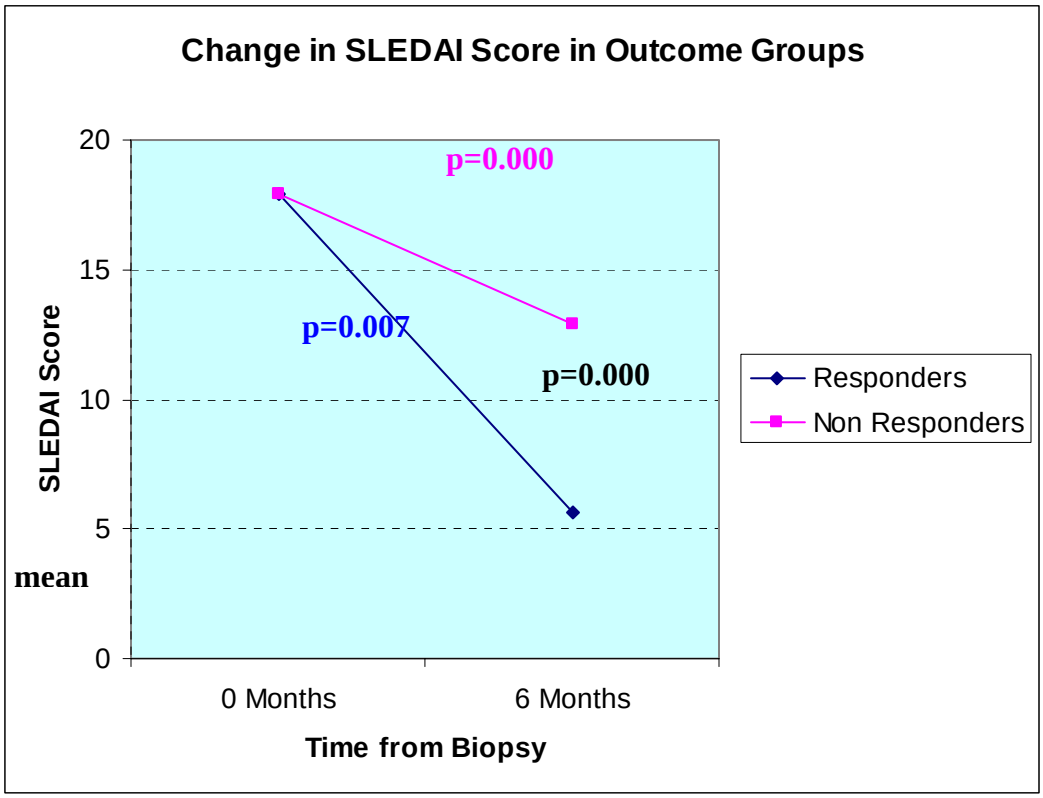


Figure9

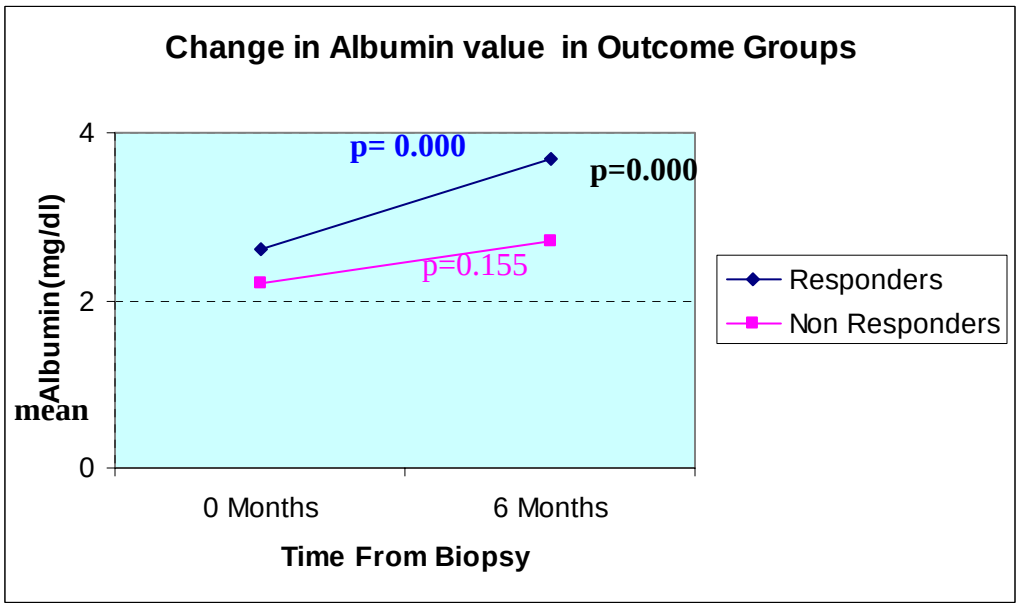
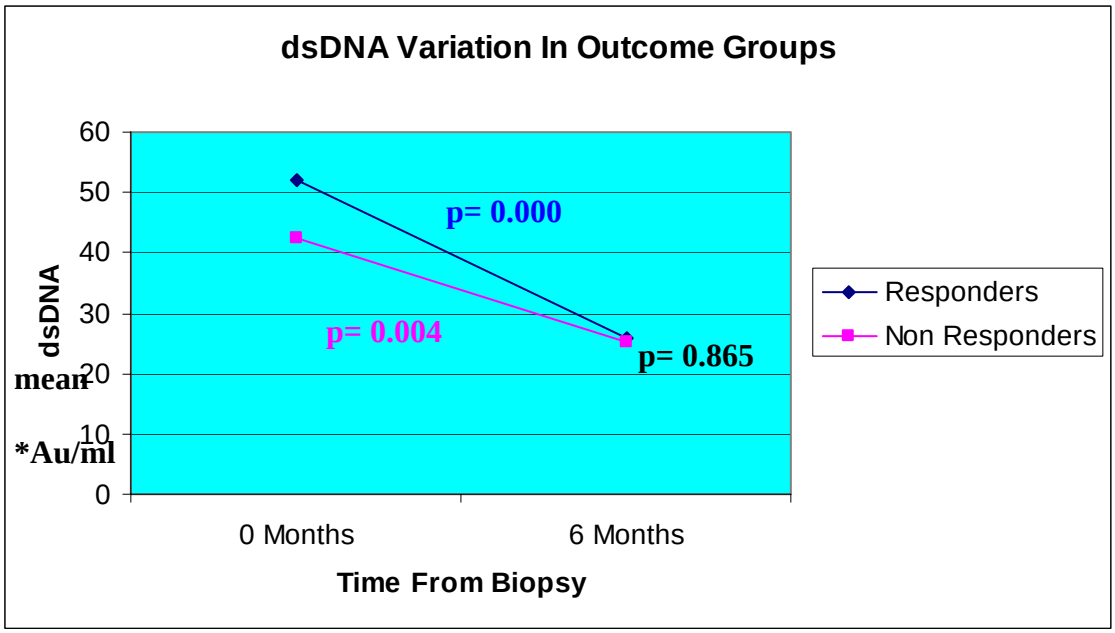


Figure 10



* Au is the arbitrary unit of the commercial kit

Figure11

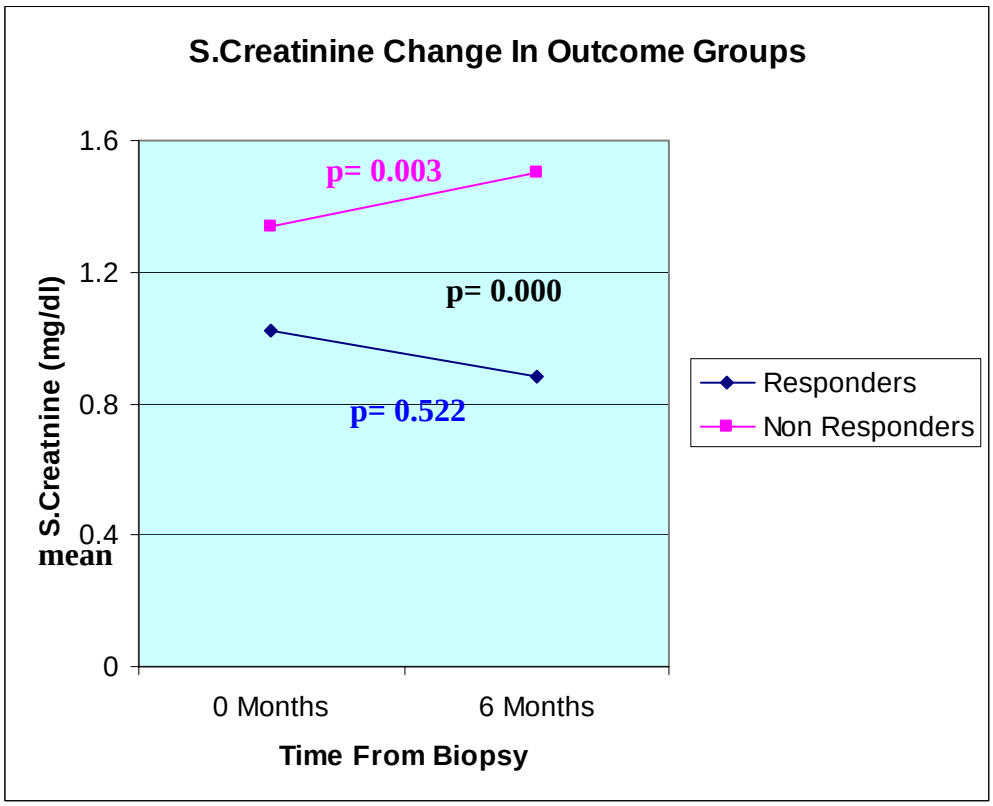
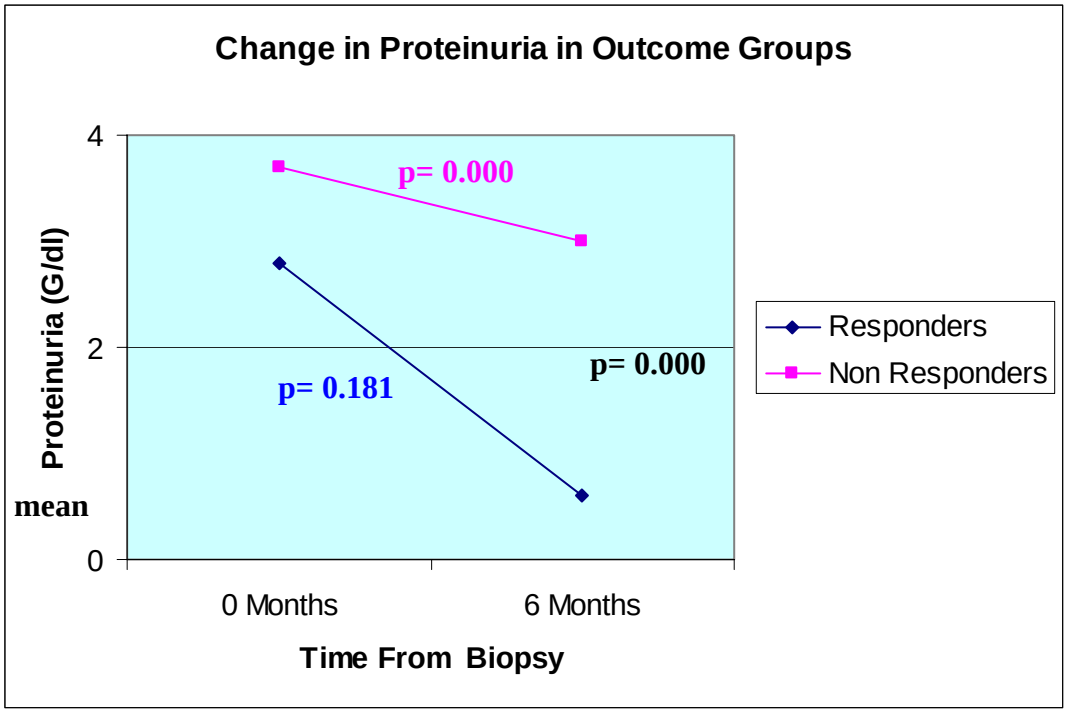


Figure 12


Change in Proteinuria in Outcome Groups
4
2
0
Proteinuria (G/dl)
mean
p= 0.000
p= 0.181
p= 0.000
Responders
Non Responders
0 Months
6 Months
Time From Biopsy

8. Two third (66.7%) of patients had WHO class IV lupus nephritis. The distribution of other classes among the outcome groups have been shown in the table below.

Table 7 (Figures 13a and 13b): WHO Class Histology distribution in the Outcome Groups

WHO Class	**Responders (N=55)**	**Non responders (N=23)**	**Cumulative (N=78)**
I	1 (1.8%)	0	1 (1.3%)
II	15 (27.3%)	2 (8.7%)	17 (21.8%)
III	3 (5.5%)	0	3 (3.8%)
IV	33 (60%)	19 (82.6%)	52 (66.7%)
V	3 (5.5%0	1 (4.3%)	4 (5.1%)
VI	0	1(4.3%)	1(1.3%)

When WHO Class IV was compared with the rest of the classes as a predictor of non responsiveness to therapy, it was significant with a p value= 0.053.

Figure 13a

WHO Class In Responders

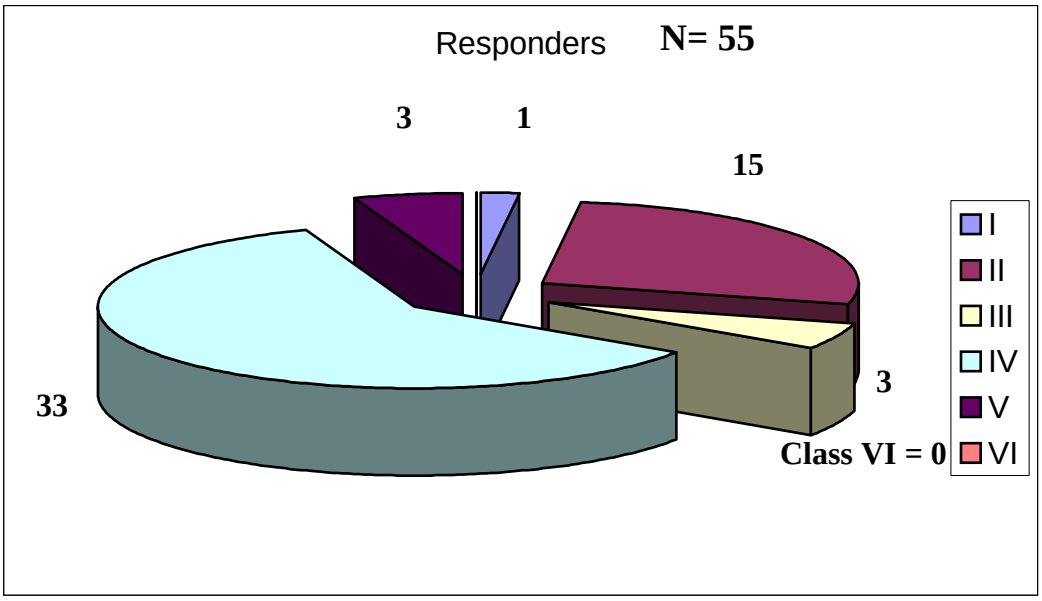
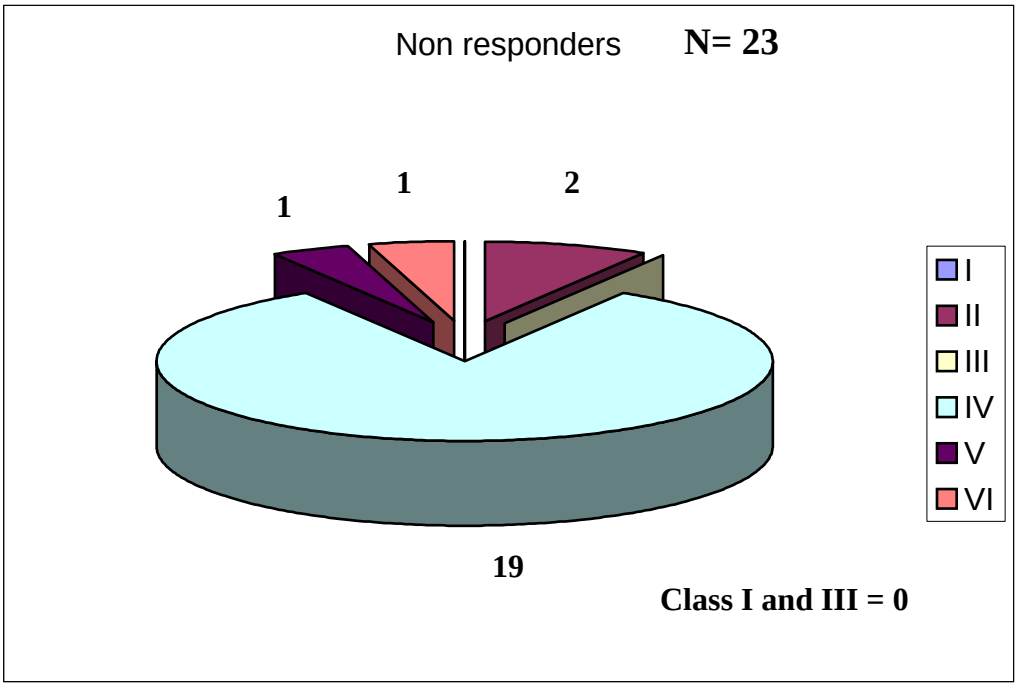


Figure 13b

WHO Class In Non Responders



9. The various co-morbidities studied included hypertension, diabetes, hypothyroidism and associated antiphospholipid syndrome (APLAS).**It was found that hypertension was a significant predictor of poor outcome with a p value = 0.002.**

Table 8 (Figure 14): Correlation between Co Morbidities vs. Outcome

Co morbidities	**Responders (N=55)**	**Non responders (N=23)**	**Cumulative (N=78)**	**P value**
Hypertension	10 (18.2%)	12 (52.2%)	22 (28.2%)	**0.002**
APLA syndrome	12 (21.8%)	3 (13%)	15 (19.2%)	2.223
Diabetes	3 (5.5%)	2 (8.7%)	5 (6.4%)	0.594
Hypothyroidism	14 (25.5%)	2 (8.7%)	16 (20.5%)	0.095

Figure 14

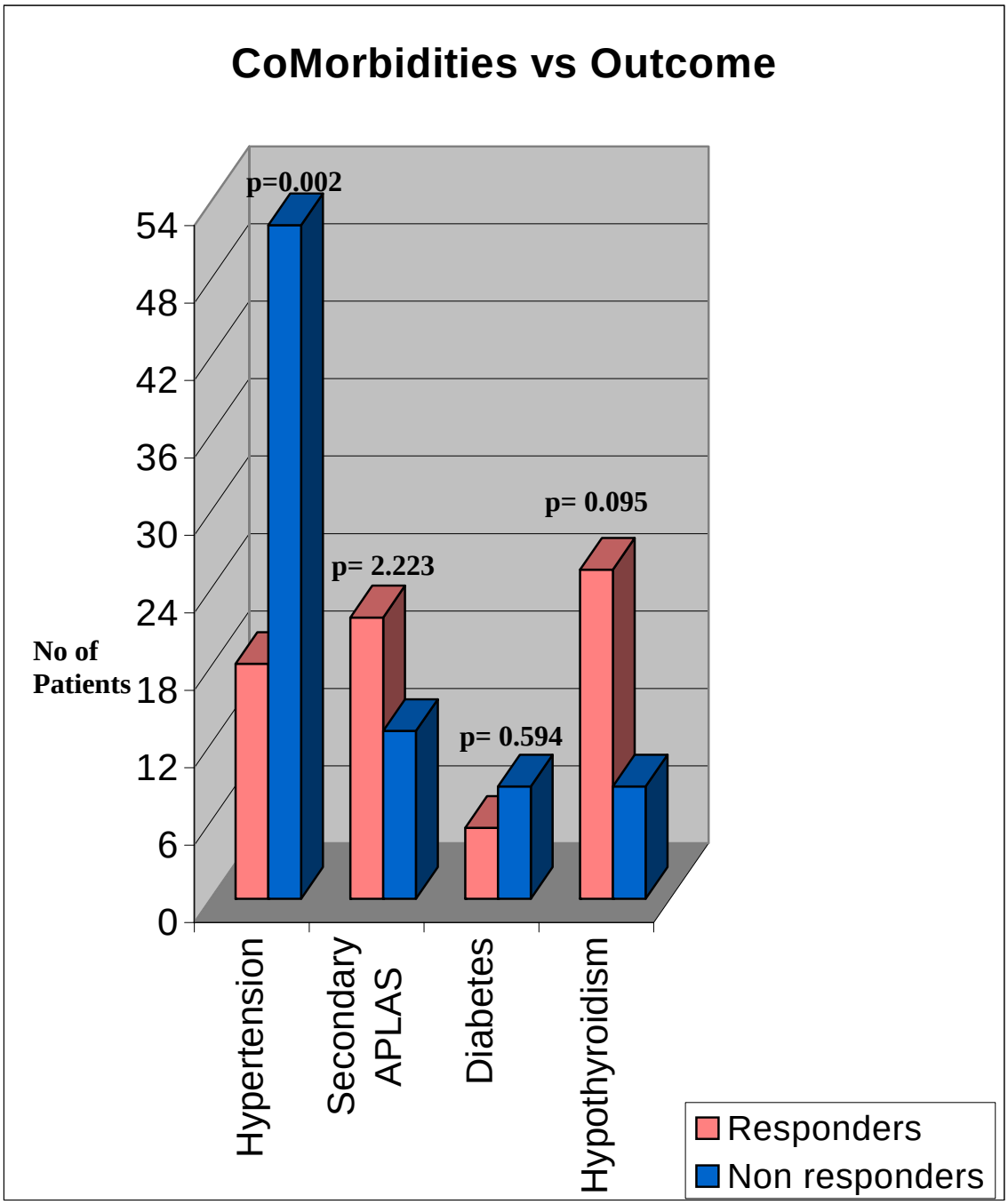

CoMorbidities vs Outcome
No of Patients
0
6
12
18
24
30
36
42
48
54
p=0.002
p= 2.223
p= 0.594
p= 0.095
Hypertension
Secondary APLAS
Diabetes
Hypothyroidism
Responders
Non responders

Table 9: Multivariate analysis for the variables significant in the Univariate analysis using the ENTER method of Logistic Regression.

Variables	**p value**	**Exp (B)**	**95% CI for Exp(B)**	
			Lower	Upper
WHO Class IV	0.295	2.270	0.489	10.52
Creat Cl. (<75ml/min)	0.543	1.563	0.371	6.58
S. Albumin (<3.0mg/dl)	0.184	2.965	0.59	14.7
Hypertension	0.065	3.568	0.92	13.7
Proteinuria	0.797	1.0	1.0	1.0
SLEDAI	0.574	0.973	0.88	1

When the Logistic regression was done using the Forward Stepwise Conditional Method, Hypertension was found to be significant predictor of Non responsiveness to therapy with a p value = 0.007 (C.I.95%=1.556-15.672).

10. Though the treatment regimens were at the discretion of the physicians and nephrologists, most of them followed standard established literature. Only one patient had Class I lupus nephritis and was treated with low dose steroids over 6 weeks and responded to therapy.

Out of the 17 patients in Class II, 12 of them received prednisolone with azathioprine (1 non responders), 4 received prednisolone alone (2 non responders) and one received prednisolone with oral cyclophosphamide.

All 3 patients in Class III and 46 out of 52 patients in Class IV lupus nephritis, received steroids with monthly Cyclophosphamide pulse (0.5-1g/$m^{2)}$ for 6 months followed by three monthly pulse. There were no non responders in Class III and 17 non responders in Class IV. One patient in Class IV developed leucopenia and hence Azathioprine was substituted at two months, as patient could not afford MMF. Total of 3 patients in Class IV received Azathioprine and steroids (2 non responders). Two of these patients did not accept the toxicities of Cyclophophamide and at the same time could not afford MMF for their treatment. One of them was given Azathioprine for cyclophosphamide induced leucopenia and because of the affordability factor. A total of 3 patients in Class IV received MMF.

Out of the 4 patients in Class V, two received Azathioprine with steroids (1 non responder), one received only steroids and one received Cyclosporine. There was only one patient in Class VI who was conservatively managed and was a non responder.

No statistical analysis could be done between the three treatment arms because of very few patients in the Azathioprine and MMF groups.

11. Seventeen patients had only one episode of infection, 5 patients had 2 episodes of infection and 2 patients had 3 episodes of infection. **One patient had Sepsis and died at five months of follow up.** There were no ICU admissions.

Table 10: Infection Sites and Rates in Responders and Non Responders.

	Responders (N=55)	**Non Responders (N=23)**
Infection	16 (29%)	8 (34.7%)
No. of episodes	22 (40%)	11 (47.8%)
Type of infection		
Respiratory Infection	7 (12.7%)	4 (17.3%)
Urinary tract Infection	4 (7.2%)	1 (4.3%)
Tuberculosis	1 (1.8%)	
Muco-cutaneous	7 (12.7%)	4 (17.3%)
Others	3 (5.4%)	2 (8.6%)

Table 11: Complications associated with Steroid during the six months Treatment Period.

Complication	**No. of Patients**
Steroid induced Cushings	4
Steroid induced Diabetes	5
Probable Steroid induced Hypertension	3
Osteoporosis	3
Avascular Necrosis	2
Cataract	3
Gastrointestinal	1

Out 46 patients on Cyclophosphamide for WHO class IV lupus nephritis, 1 had leucopenia. This patient had Azathioprine instead. No patient among the 78 had hemorrhagic cystitis or amenorrhea within the 6 months. Out of a total of 22 patients receiving Azathioprine in the various WHO classes, only one had pancytopenia which recovered and the drug was continued after a period of drug holiday. Only three patients in class IV lupus received Mycophenolate Mofetil and none of them developed any complications.

Discussion

83 consecutive patients who were diagnosed to have SLE and admitted for renal biopsy were recruited into the study. These patients were admitted either in Medicine or in Nephrology wards for biopsy. Follow up was through outpatient visits to either department. Data was collected through Proforma (**Annexure B**). Of the 83, 5 were lost to follow up. All the 5 were from the North Eastern region of the country. Attempts to contact them through post was unsuccessful. The analysis was undertaken in the remaining 78 who had six months of follow up. It compares well with the studies done on outcome in lupus nephritis. Study done in our centre by Abraham et al and published in '99 was done on 29 patients with class IV lupus with a follow up of 5 years [69]. Other studies from the West[36,70,71,72,73] had sample size ranging from 34-82.

The mean age in our study was 29.5 years with a range of 13-55 years. The various studies from India have reported the mean age as 24 years (range 4-55 years)[4], and 25.05 years (range 7-48 years)[5]. This is the reproductive age group in the vast majority of our population. The mean age in our study was in keeping with that in the literature.

The female to male ratio in our study was approximately 9:1 which is the standard ratio in any literature. Malaviya et al in 1997 reported F: M ratio of 11:1 by among 1366 SLE patients from different regions of the country[8]. In the West the female: male ratio rises from 2:1 in prepubertal children up to 4.5:1 in adolescence to the 8 to 12:1 reported in series of adult onset patients, falling back to 2:1 in patients over 60 yr of age[15].

In our cohort of patients with lupus nephritis, 64.5% patients had associated

mucocutaneous manifestations and 60.5% had associated arthritis. It is similar to the findings in the study by Tak et al done among 42 patients with lupus nephritis, where mucocutaneous manifestations were 62% and 43%, arthritis was 71% and 57% respectively, in the two lupus nephritis treatment arms[36].

In the study done by Fiehn et al, published in 2003, the mean time of biopsy from the diagnosis of SLE was 39.3 months in the decade 1990-2000. But the mean time of biopsy was 7.98 +/- 1.9 months for our patients. This could be because of our tertiary care set up and the referral bias associated with it. All patients who had renal biopsy done had evidence of lupus nephritis histologically. This could explain 70% response to therapy we had at the end of 6 months as against other Asian studies showing a poorer outcome[74], as there was less delay in doing a biopsy and instituting immunosuppressive therapy in our cohort. Recent modifications to the classification of lupus nephritis, the emergence of newer scoring indices, and the availability of a variety of therapeutic options predicate a reassessment of the role of the renal biopsy in the management of lupus nephritis, especially for patients with proliferative lupus nephritis[75]. These patients have a poor outcome if not treated optimally and urine analysis by itself fails to accurately predict the histological type[32].

In our study, s.albumin of <3.0mg/dl was found to be significantly associated with poor outcome (p value = 0.041) in the Univariate analysis. Hypoalbuminaemia reflects significant protein loss in urine and the underlying malnourished state and hence decreases the chance for a better outcome .This has been validated in several studies[36,54].

Abraham et al in 1999 in a study of 29 patients from the same centre over a period

of 5 years had shown that hypertension , nephrotic proteinuria, and high Activity Index were predictive of progression to end stage renal failure in patients with diffuse proliferative lupus nephritis[69]. But that study had not looked into low albumin as a significant predictor for poor outcome and s.creatinine also failed to show any significant correlation.

Creatinine clearance of </= 75ml/min was also a significant predictor of non responsiveness (p value =0.047) in the Univariate analysis, though s.creatinine of >/= 1.5mg/dl did not show any significant correlation. This reflects the inadequacy of using s.creatinine as a surrogate marker for GFR[77].

Notably, the parameters reflecting severity and chronicity of kidney disease in SLE like hypertension, hypoalbuminemia, proteinuria, low creatinine clearance and class IV renal histology , rather than the activity parameters like SLEDAI scores, serum anti-dsDNA antibodies, and complement concentrations at the entry time of the study correlated with nonresponsiveness to therapy. In our study therefore, systemic disease activity at the time of kidney biopsy did not show much value for the prediction of renal outcome in lupus nephritis. Several studies using different SLE activity indices at entry like the BILAG score by MacGowan et al[39], ECLAM score by Houssiau et al[54] have failed to show significant correlation with outcome of lupus nephritis.

Majority of our patients (66.7%) had WHO class IV lupus followed by class II in 21.8%. This is in keeping with the various studies like Mok CC et al in 1999 which showed 55%, NUH study in 2001 which showed 82%[74].

Hypertension was the only parameter found to be highly significant in multivariate analysis as an independent predictor of poor outcome in our study with a p

value of 0.002. This has been validated in several studies in India and the West. A study done by Fiehn et al in Germany published in 2003 among 56 patients showed that showed that histological signs of chronicity and either arterial hypertension or renal insufficiency, or both, were predictive for terminal renal failure[62]. We could not comment upon chronicity, as NIH scoring for activity / chronicity in histology was not done in our study.

Font et al studied prospectively 70 patients with lupus nephritis and 70 age and sex matched controls with SLE but no evidence of nephropathy from 1988-1998. Compared to controls, lupus nephritis patients had a higher prevalence of hypertension (44% vs. 9%, $p < 0.001$) at study entry and hypertension at onset was associated significantly (67% vs. 32%, $p=0.01$) with renal failure. This study also showed that hyperlipidaemia (78% vs. 27%, $p<0.001$) had significant association with development of renal failure.

The markedly increased mortality in lupus nephritis from accelerated atherosclerosis mandates a higher state of vigilance in our SLE patients, and they must be monitored closely for symptoms and signs of cardiovascular disease. Primary prevention, by checking and treating hyperlipidaemia, hyperglycaemia and hypertension, counseling patients to stop smoking and exercise, and helping them to loose weight, is of paramount importance[44]. We however did not look into the risk association of hyperlipidaemia with outcomes in lupus nephritis in our cohort. Hypertension being a comorbidity with several cardiovascular risk factors and the changing trend of premature cardiovascular morbidity and mortality in SLE, our finding of hypertension as the only predictor of snonresponsiveness to treatment should raise an alarm bell for ongoing silent

cardiovascular disease in patients with lupus nephritis.

Though our study has failed to show any significant correlation of APLA with poor prognosis in lupus nephritis, Frampton et al. in a study published in 1991 have reported that 44% of lupus nephritis patients had antiphospholipid antibodies compared to 19.2% in our study. The presence of an associated antiphospholipid syndrome in SLE patients may contribute to the development of nephropathy, and represent a new factor related to mortality in lupus nephritis patients[76]. We would probably find such an association if our cohort of patients are followed up for a longer period of time.

The percentage of Responders in our study were 70.5% as against Non-responders who were 29.4% at the end of 6 months of follow up. In a study by Mark F et al. done on 82 patients with a 5 year follow up and published in 1996, only 45% patients had complete renal remission (defined as normal sediment and excretion of <1 G protein per day) at the end of one year[70]. Our study had used the same definitions for outcome measures. It reflects the changing trend in lupus nephritis management over the past decade with better case finding, prompt initiation of immunosuppressive drugs and newer therapy. In the above study by Fiehn et al, in 2003 studied among 15 patients between 1980-89 and 41 patients between 1990-99, the outcome of patients with newly diagnosed LN was significantly better between 1990 and 2000 than between 1980 and 1989. Kidney damage and chronic histological changes at time of diagnosis were significantly less common between 1990 and 2000, which is attributable to earlier diagnosis and treatment in the later decade[62].

The results of our study were similar to a study by Tak et al. done among 42 patients with WHO class IV lupus and published in 2000 in which 81% of the patients

treated with Mycophenolate Mofetil had complete remission as against 76 percent treated with Cyclophosphamide and prednisolone followed by Azathioprine and prednisolone at the end of one year[36]. But they had used a more stringent criteria with complete remission being defined as a value for urinary protein excretion that was less than 0.3g per 24 hours, with normal urinary sediments, a normal serum albumin concentration, and values for serum creatinine and creatinine clearance that were no more than 15 percent above the base-line value and also the outcomes were analyzed at the end of one year as against 6 months in our study[36]. Moreover, we did not have many patients on MMF for economical reasons, so as to compare with those figures.

A study done by Gan et al in National University Hospital in Singapore among fifty patients in 2002 showed much similar rates of response compared to our study. It showed 44% patients were in complete remission, 26% in partial remission (thus responders were 70% similar to our finding) ; 34% had relapsed nephritis, 4% had chronic renal failure and 12% progressed to ESRD and there were five deaths over three years[74]. This further corroborates the fact that Asians have more severe lupus nephritis compared to their western counterparts[10].

In summary, our study shows expected demographic parameters of lupus nephritis in keeping with the literature, namely age, sex, histology type and clinical presentations[4-9]. The variables which were significant in the univariate analysis for a poor outcome of lupus nephritis were those reflecting chronicity and severity like hypoalbuminaemia, WHO class IV histology, hypertension, proteinuria and decreased creatinine clearance, rather than activity parameters. Hypertension, as the highly significant independent predictor of poorer outcome by multivariate analysis is also

keeping with established literature.

Higher prevalence of underlying premature and often silent, ongoing cardiovascular morbidity and mortality in SLE and association of hypertension with chronicity, hyperlipidaemia, antiphospholipid syndrome and cardiovascular complications warrants these aspects to be looked into in future studies along with histological scoring for chronicity and activity.

LIMITATIONS of our study include short duration of follow up, humble sample size, genetic and geographic heterogeneity of our patients from different regions of the country, heterogeneity of treatment regimens, lack of NIH activity and chronicity indices in histology, lack of lipid profiling and APLA in all patients.

CONCLUSIONS

Seventy percent (55/78) patients of lupus nephritis were treatment responders. Significant predictors of poor outcome were Hypertension, WHO Class IV histology , Creatnine clearance <75ml/min, S.albumin <3.5mg/dl, of which Hypertension was an independent predictor of poor outcome at the end of six months of therapy.

Demographic pattern and the clinical presentation of lupus nephritis were in keeping with well established literature from India and elsewhere.

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Annexures

A. SLEDAI Score

B. Proforma

C. Microsoft Excel Master Sheet

ANNEXURE A

SLE Disease Activity Index (SLEDAI)

Descriptor	Definition	Score
Seizure	Recent onset, exclude metabolic, infectious or drug causes	8
Psychosis	Altered ability to function in normal activity due to severe disturbance in the perception of reality. Include hallucinations, incoherence, markedly loose associations, impoverished thought content, markedly illogical thinking, bizarre, disorganised or catatonic behaviour. Exclude uraemia and drug causes	
'Organic brain syndrome' or Acute confusional state	Altered mental function with impaired orientation, memory or other intellectual function, with rapid onset and fluctuating clinical features, inability to sustain attention to environment, plus at least 2 of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, or increased or decreased psychomotor activity. Exclude metabolic, drug or infectious causes	8
Visual disturbance	Retinal changes of SLE. Include cytoid bodies, retinal haemorrhages, serous exudates/ haemorrhages in choroid or optic neuritis. Exclude hypertension, infection or drug causes	8
Cranial nerve disorder	New onset of sensory or motor neuropathy involving cranial nerves	8
Lupus headache	Severe persistent headache: may be migrainous, but must be non-responsive to narcotic analgesia.	8
CVA	New onset of CVA. Exclude atherosclerosis.	8
Vasculitis	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter haemorrhages, or biopsy or angiogram evidence of vasculitis	8
Arthritis	$\geq$ 2 joints with pain and signs of inflammation (tenderness, swelling or effusion)	4
Myositis	Proximal muscle aching/weakness, associated with elevated CPK/aldolase or EMG changes or biopsy evidence of myositis	4
Urinary casts	Haemoglobin, granular or RBC casts	4
Haematuria	> 5 RBC/HPF. Exclude stone, infection or other causes	4
Proteinuria	> 0.5 grams/24 hrs	4
Pyuria	> 5 WBCs/HPF. Exclude infection	4
Rash	Inflammatory type rash	2
Alopecia	Abnormal, patchy or diffuse loss of hair	2
Mucosal ulcers	Oral or nasal ulcerations	2
Pleurisy	Pleuritic chest pain with pleural rub/effusion/pleural thickening	2
Pericarditis	Pericardial pain with at least 1 of the following: rub, effusion or ECG or Echo confirmation	2
Low complement	Decrease in CH50, C3 or C4 below the normal limit of Lab	2
Increased DNA binding	Increased DNA binding using Farr assay	2
Fever	> 38 Deg C. Exclude infection	1
Thrombocytopaenia	< 100,000/cu mm, exclude drug causes	1
Leukopaenia	< 3000/cu mm, exclude drug causes	1

ANNEXURE B

PROFORMA

Name Hosp No. Sex Age
M/S Place Religion
SLE: Time of diagnosis Criteria for Diagnosis: 1/2/3/4/5/6/7/8/9/11/12
Lupus Nephritis: Time of Dx Criteria: 1/2/3/4/5/6/7 Class:

	At Dx	At 6 mts
Hb		
TC		
Plts		
DCT		
ESR		
Urine RBCs		
Urine WBCs		
Casts		
24 hr UP		
Creat		
Urea		
Ds DNA		
Complement		
RF		
ANA		
Total Protein		
Albumin		

Rx: Steroids/ Cyclo/ Aza/ MMF

Outcome: CR/PR/NR/R/D
APLA: present/absent

Co-morbidities: HTN/ DM/ Hypothyroidism

Infections: No. of Episodes
Sites:

Side effects:

Creat clearance:

SLEDAI score:
1. At Dx-
2. At 6mts-

Comments

MASTER CHART

Sl.No	NAME	AGE	Pack years	Cough	Chest pain	wheeze	Dys pnoea	Cre pitation	rhonchai	ECG	X-RAY	SPUTUM AFB	FEV1%	FVC%	$\frac{FEV_1}{FVC}$	$\frac{FEV_1}{FVC\ \%}$	FEF_{50}	FEF_{25-75}	TYPE
1	Ramasamy	35	13	No	-	-	-	-	-	Normal	Normal	Negative	83.5	99	0.84	84.34	83	83	Normal
2	Velayutham	47	18	No	-	-	-	-	-	Normal	Normal	Negative	85.6	110.5	0.77	77.47	81	90	Normal
3	Karuppathevar	53	44	Yes	-	-	-	-	-	Normal	Normal	Negative	86.8	113.7	0.76	76.34	87	89	Normal
4	Muthiah	51	60	No	-	-	-	-	-	Normal	Normal	Negative	80.9	120	0.67	67.42	70	71	Stage I
5	Venkatraman	52	18	No	-	-	-	-	-	Normal	Normal	Negative	89.1	109.9	0.81	81.07	87	86	Normal
6	Suresh	34	15	No	-	-	-	-	-	Normal	Normal	Negative	83.4	109	0.77	76.51	85	82	Normal
7	Chellam	44	40	Yes	-	-	-	-	-	Normal	Normal	Negative	84.1	109.6	0.77	76.73	85	84	Normal
8	Naguppillai	62	24	No	-	-	-	-	-	Normal	Normal	Negative	86.7	111	0.78	78.11	83	84	Normal
9	Raju	53	40	Yes	-	-	-	-	-	Normal	Normal	Negative	81.5	119.2	0.68	68.37	73	72	Stage I
10	Kundan	72	64	No	-	-	-	-	-	Normal	Normal	Negative	77	74.3	1.04	103.6	84	82	Restrictive
11	Rangasamy	51	28	No	-	-	-	-	-	Normal	Normal	Negative	89	106.4	0.84	83.65	80	84	Normal
12	Jeyaram	63	48	No	-	-	-	-	-	Normal	Normal	Negative	80.9	118.3	0.68	68.39	75	74	Stage I
13	Ramu	60	45	Yes	-	-	-	-	-	Normal	Normal	Negative	78.4	72.6	1.08	108	82	81	Restrictive
14	Muthukrishnan	42	16	No	-	-	-	-	-	Normal	Normal	Negative	83.7	99.9	0.84	83.78	88	85	Normal
15	Veeranan	47	40	Yes	-	-	-	-	-	Normal	Normal	Negative	80.5	118.6	0.68	67.88	71	70	Stage I
16	Govindan	51	48	No	-	-	-	-	-	Normal	Normal	Negative	84.8	105.5	0.8	80.38	87	85	Normal
17	Vailumuthu	39	18	No	-	-	-	-	-	Normal	Normal	Negative	85.6	108	0.79	79.26	86	81	Normal
18	Sudarsanam	45	28	Yes	-	-	-	-	-	Normal	Normal	Negative	81.7	118.8	0.69	68.77	73	73	Stage I
19	Ponniah	52	25	No	-	-	-	-	-	Normal	Normal	Negative	84.9	105.3	0.81	80.63	86	87	Normal
20	Periyagoundar	60	36	Yes	-	-	-	-	-	Normal	Normal	Negative	52.4	92.4	0.57	56.71	71	73	Stage II
21	Lakshmanan	58	28	No	-	-	-	-	-	Normal	Normal	Negative	84.8	106.6	0.8	79.55	83	80	Normal
22	Dharmar	45	40	Yes	-	-	-	-	-	Normal	Normal	Negative	84.9	109.4	0.78	77.61	83	87	Normal
23	Ramalingam	32	18	No	-	-	-	-	-	Normal	Normal	Negative	83	98	0.85	84.69	81	87	Normal
24	Subramani	49	30	No	-	-	-	-	-	Normal	Normal	Negative	80.2	119.2	0.67	67.28	73	74	Stage I
25	Vellaiyan	68	40	Yes	-	-	-	-	-	Normal	Normal	Negative	82.1	120	0.68	68.42	73	72	Stage I
26	Mani	68	32	No	-	-	-	-	-	Normal	Normal	Negative	85.2	107.8	0.79	79.04	82	84	Normal
27	Marisamy	56	36	No	-	-	-	-	-	Normal	Normal	Negative	81.9	119.4	0.69	68.59	75	74	Stage I
28	Nalluthevar	53	24	Yes	-	-	-	-	-	Normal	Normal	Negative	83.9	99.9	0.84	83.98	85	81	Normal

Sl.No	NAME	AGE	Pack years	Cough	Chest pain	wheeze	Dys pnoea	Cre pitation	rhonchai	ECG	X-RAY	SPUTUM AFB	FEV1%	FVC%	$\frac{FEV_1}{FVC}$	$\frac{FEV_1}{FVC\ \%}$	FEF_{50}	FEF_{25-75}	TYPE
29	Chinnian	45	18	No	-	-	-	-	-	Normal	Normal	Negative	85.4	111.3	0.77	76.73	81	81	Normal
30	Ranganathan	33	22	Yes	-	-	-	-	-	Normal	Normal	Negative	88.4	108	0.82	81.85	86	83	Normal
31	Krishnamoorthi	58	44	No	-	-	-	-	-	Normal	Normal	Negative	85.1	111.6	0.76	76.25	90	84	Normal
32	Varadhan	57	36	No	-	-	-	-	-	Normal	Normal	Negative	83.4	100.5	0.83	82.99	82	87	Normal
33	Abraham	59	64	No	-	-	-	-	-	Normal	Normal	Negative	76.3	70.5	1.08	108.2	84	88	Restrictive
34	Balusamy	62	44	Yes	-	-	-	-	-	Normal	Normal	Negative	85.9	109.6	0.78	78.38	83	80	Normal
35	Arockiasamy	52	40	Yes	-	-	-	-	-	Normal	Normal	Negative	85.3	110.5	0.77	77.19	90	85	Normal
36	Mujibur	58	21	No	-	-	-	-	-	Normal	Normal	Negative	84.8	106.6	0.8	79.55	83	80	Normal
37	Thomas	59	33	Yes	-	-	-	-	-	Normal	Normal	Negative	81.5	116.9	0.7	69.72	75	72	Stage I
38	Seeni	35	36	Yes	-	-	-	-	-	Normal	Normal	Negative	64.3	109.5	0.59	58.72	71	72	Stage II
39	Kuttiyappan	41	30	No	-	-	-	-	-	Normal	Normal	Negative	84.7	107.4	0.79	78.86	88	82	Normal
40	Abdullah	49	32	Yes	-	-	-	-	-	Normal	Normal	Negative	77.3	72.9	1.06	106	84	87	Restrictive
41	Micheal	52	30	No	-	-	-	-	-	Normal	Normal	Negative	83.6	101.5	0.82	82.36	88	83	Normal
42	Loganathan	57	50	No	-	-	-	-	-	Normal	Normal	Negative	75.9	73.4	1.03	103.4	88	87	Mixed
43	Kannuchamy	61	44	Yes	-	-	-	-	-	Normal	Normal	Negative	83.2	99.9	0.83	83.28	88	89	Normal
44	Joseph	55	45	No	-	-	-	-	-	Normal	Normal	Negative	80.7	116.2	0.69	69.45	74	75	Stage I
45	Kannuthevar	31	26	No	-	-	-	-	-	Normal	Normal	Negative	88.1	114.4	0.77	77.01	88	80	Normal
46	Subbunadar	36	30	No	-	-	-	-	-	Normal	Normal	Negative	86.5	115.3	0.75	75.02	82	85	Normal
47	Arulraj	43	16	No	-	-	-	-	-	Normal	Normal	Negative	86.3	112.7	0.77	76.57	84	87	Normal
48	Veeran	54	28	Yes	-	-	-	-	-	Normal	Normal	Negative	84.3	105.2	0.8	80.13	87	85	Normal
49	Lakshmanan	56	40	Yes	-	-	-	-	-	Normal	Normal	Negative	87.1	118.2	0.74	73.69	84	90	Normal
50	Usman	65	36	Yes	-	-	-	-	-	Normal	Normal	Negative	81.4	119.3	0.68	68.23	75	75	Stage I
51	Kasi Viswanathan	36	30	Yes	-	-	-	-	-	Normal	Normal	Negative	83.7	104.5	0.8	80.1	82	88	Normal
52	Logu	46	28	No	-	-	-	-	-	Normal	Normal	Negative	86.5	115.3	0.75	75.02	82	85	Normal
53	Kannan	41	36	No	-	-	-	-	-	Normal	Normal	Negative	89.4	113.4	0.79	78.84	86	87	Normal
54	Seenithevar	59	20	Yes	-	-	-	-	-	Normal	Normal	Negative	84.9	104.4	0.81	81.32	83	82	Normal
55	Palani	52	36	No	-	-	-	-	-	Normal	Normal	Negative	83.6	102.1	0.82	81.88	85	90	Normal
56	Singaram	62	48	No	-	-	-	-	-	Normal	Normal	Negative	84.7	109.4	0.77	77.42	88	87	Normal
57	Dennis	64	30	No	-	-	-	-	-	Normal	Normal	Negative	83.8	103.3	0.81	81.12	85	86	Normal
58	Arunachalam	54	15	Yes	-	-	-	-	-	Normal	Normal	Negative	83.7	101.1	0.83	82.79	90	84	Normal

Sl.No	NAME	AGE	Pack years	Cough	Chest pain	wheeze	Dys pnoea	Cre pitation	rhonchai	ECG	X-RAY	SPUTUM AFB	FEV1%	FVC%	$\frac{FEV_1}{FVC}$	$\frac{FEV_1}{FVC\ \%}$	FEF_{50}	FEF_{25-75}	TYPE
59	Vellaisamy	59	28	No	-	-	-	-	-	Normal	Normal	Negative	84.2	111	0.76	75.86	87	81	Normal
60	Peer Muhamed	65	32	No	-	-	-	-	-	Normal	Normal	Negative	89.9	113.2	0.79	79.42	83	81	Normal
61	Subburaj	62	18	No	-	-	-	-	-	Normal	Normal	Negative	88	105.5	0.83	83.41	87	90	Normal
62	Narayanan	41	32	No	-	-	-	-	-	Normal	Normal	Negative	85	111.8	0.76	76.03	87	86	Normal
63	Thiruppathi	47	20	Yes	-	-	-	-	-	Normal	Normal	Negative	83.7	100.6	0.83	83.2	86	90	Normal
64	Williams	34	22	No	-	-	-	-	-	Normal	Normal	Negative	86.7	109.9	0.79	78.89	88	81	Normal
65	Palavesam	47	20	No	-	-	-	-	-	Normal	Normal	Negative	83.7	100.6	0.83	83.2	86	90	Normal
66	Yousuf	55	32	No	-	-	-	-	-	Normal	Normal	Negative	85.5	109.3	0.78	78.23	88	83	Normal
67	Panneer	65	15	Yes	-	-	-	-	-	Normal	Normal	Negative	84.4	107.2	0.79	78.73	81	84	Normal
68	Nataraj	64	55	No	-	-	-	-	-	Normal	Normal	Negative	59	104	0.57	56.73	70	71	Stage II
69	Martin	32	16	No	-	-	-	-	-	Normal	Normal	Negative	84.1	105	0.8	80.1	87	86	Normal
70	Maruthu	44	12	Yes	-	-	-	-	-	Normal	Normal	Negative	89.2	112.8	0.79	79.08	83	90	Normal
71	Abbas	60	44	Yes	-	-	-	-	-	Normal	Normal	Negative	80.7	116.2	0.69	69.45	74	75	Stage I
72	Chinnamani	41	18	No	-	-	-	-	-	Normal	Normal	Negative	84.8	106.6	0.8	79.55	83	80	Normal
73	David	51	32	Yes	-	-	-	-	-	Normal	Normal	Negative	84.6	106	0.8	79.81	88	86	Normal
74	Anbarasan	35	12	No	-	-	-	-	-	Normal	Normal	Negative	87.6	115	0.76	76.17	80	82	Normal
75	Periyasamy	46	36	Yes	-	-	-	-	-	Normal	Normal	Negative	85.9	109.9	0.78	78.16	84	89	Normal
76	Natharshah	32	19	No	-	-	-	-	-	Normal	Normal	Negative	83.9	106	0.79	79.15	89	85	Normal
77	Maruthanayagam	42	15	No	-	-	-	-	-	Normal	Normal	Negative	85.6	110.3	0.78	77.61	82	82	Normal
78	Innasi	55	50	Yes	-	-	-	-	-	Normal	Normal	Negative	80.1	116.2	0.69	68.93	75	74	Stage I
79	Pasupathy	43	32	No	-	-	-	-	-	Normal	Normal	Negative	83.1	98.4	0.84	84.45	82	83	Normal
80	Rajkumar	58	36	No	-	-	-	-	-	Normal	Normal	Negative	87.7	116.4	0.75	75.34	89	80	Normal
81	Marthandam	54	32	Yes	-	-	-	-	-	Normal	Normal	Negative	85.9	105.3	0.82	81.58	85	82	Normal
82	Dharmalingam	45	22	No	-	-	-	-	-	Normal	Normal	Negative	84.3	106.7	0.79	79.01	86	84	Normal
83	Prakash	54	27	No	-	-	-	-	-	Normal	Normal	Negative	86	104.3	0.82	82.45	80	84	Normal
84	Nesamani	31	14	No	-	-	-	-	-	Normal	Normal	Negative	85.4	105	0.81	81.33	82	90	Normal
85	Chandran	55	26	No	-	-	-	-	-	Normal	Normal	Negative	85.2	110.6	0.77	77.03	81	83	Normal
86	Palavendran	58	60	Yes	-	-	-	-	-	Normal	Normal	Negative	78.9	74.2	1.06	106.3	85	86	Mixed
87	Sekaran	58	48	No	-	-	-	-	-	Normal	Normal	Negative	81.2	118.9	0.68	68.29	72	71	Stage I
88	Natarajan	62	20	No	-	-	-	-	-	Normal	Normal	Negative	83.9	102.5	0.82	81.85	85	86	Normal

Sl.No	NAME	AGE	Pack years	Cough	Chest pain	wheeze	Dys pnoea	Cre pitation	rhonchai	ECG	X-RAY	SPUTUM AFB	FEV1%	FVC%	$\frac{FEV_1}{FVC}$	$\frac{FEV_1}{FVC\ \%}$	FEF_{50}	FEF_{25-75}	TYPE
89	Issac	43	12	No	-	-	-	-	-	Normal	Normal	Negative	83.9	99.3	0.84	84.49	88	81	Normal
90	Thanasekaran	52	30	Yes	-	-	-	-	-	Normal	Normal	Negative	84.5	106.9	0.79	79.05	80	88	Normal
91	Annamalai	59	52	No	-	-	-	-	-	Normal	Normal	Negative	87.7	116.6	0.75	75.21	89	82	Normal
92	Saravanan	39	14	No	-	-	-	-	-	Normal	Normal	Negative	87.6	111	0.79	78.92	85	81	Normal
93	Rajagopalan	42	32	Yes	-	-	-	-	-	Normal	Normal	Negative	81.6	118.4	0.69	68.92	75	74	Stage I
94	Namasivayam	57	39	No	-	-	-	-	-	Normal	Normal	Negative	82.4	118.2	0.7	69.71	71	73	Stage I
95	Ibrahim	34	22	Yes	-	-	-	-	-	Normal	Normal	Negative	82.9	117.3	0.71	70.67	73	74	Stage I
96	Kamarajan	64	21	Yes	-	-	-	-	-	Normal	Normal	Negative	80.5	117.4	0.69	68.57	72	74	Stage I
97	Thandapani	41	24	No	-	-	-	-	-	Normal	Normal	Negative	86.2	114.2	0.75	75.48	85	84	Normal
98	Pakker Mohamed	57	48	No	-	-	-	-	-	Normal	Normal	Negative	81.3	120	0.68	67.75	73	74	Stage I
99	Dhanapal	35	15	No	-	-	-	-	-	Normal	Normal	Negative	84.7	112	0.76	75.63	90	82	Normal
100	Amalraj	59	44	Yes	-	-	-	-	-	Normal	Normal	Negative	82.4	118.2	0.7	69.71	71	73	Stage I
101	Mahalingam	41	32	No	-	-	-	-	-	Normal	Normal	Negative	85	111.8	0.76	76.03	87	86	Normal
102	Sundarraj	59	44	No	-	-	-	-	-	Normal	Normal	Negative	66.6	110.1	0.6	60.49	72	71	Stage II
103	Fulgunan	47	28	No	-	-	-	-	-	Normal	Normal	Negative	87.5	107.5	0.81	81.4	84	83	Normal
104	Rajendraprasad	38	22	No	-	-	-	-	-	Normal	Normal	Negative	86.2	103	0.84	83.69	83	85	Normal
105	Senthilkumar	53	48	No	-	-	-	-	-	Normal	Normal	Negative	88	114.3	0.77	76.99	82	90	Normal
106	Rahamadulla	50	40	No	-	-	-	-	-	Normal	Normal	Negative	81.5	116.9	0.7	69.72	75	72	Stage I
107	Chakravarthi	59	60	No	-	-	-	-	-	Normal	Normal	Negative	80.6	118.4	0.68	68.07	74	75	Stage I
108	Nazirudin	46	12	No	-	-	-	-	-	Normal	Normal	Negative	84.7	102.4	0.83	82.71	83	81	Normal
109	Govindaraj	33	25	Yes	-	-	-	-	-	Normal	Normal	Negative	82.2	113.9	0.72	72.17	75	73	Stage I
110	Sarathy	64	55	No	-	-	-	-	-	Normal	Normal	Negative	80.2	116.2	0.69	69.02	74	73	Stage I
111	Nizam Ali	60	20	No	-	-	-	-	-	Normal	Normal	Negative	83.1	98.4	0.84	84.45	88	80	Normal
112	Seeni Rowthar	37	11	No	-	-	-	-	-	Normal	Normal	Negative	83.9	99	0.85	84.75	90	86	Normal
113	Arockiaraj	48	11	No	-	-	-	-	-	Normal	Normal	Negative	83.2	100.1	0.83	83.12	87	88	Normal
114	Jeyapaul	62	36	No	-	-	-	-	-	Normal	Normal	Negative	81.7	119.4	0.68	68.43	74	75	Stage I
115	Sethuraman	42	28	No	-	-	-	-	-	Normal	Normal	Negative	88.3	104.7	0.84	84.34	85	89	Normal
116	Bhaskaran	65	36	No	-	-	-	-	-	Normal	Normal	Negative	83.4	100.5	0.83	82.99	82	87	Normal
117	Karuppanan	32	16	Yes	-	-	-	-	-	Normal	Normal	Negative	84.1	106	0.79	79.34	80	87	Normal
118	Santhakumar	63	24	No	-	-	-	-	-	Normal	Normal	Negative	84.2	108.6	0.78	77.53	81	80	Normal

Sl.No	NAME	AGE	Pack years	Cough	Chest pain	wheeze	Dys pnoea	Cre pitation	rhonchai	ECG	X-RAY	SPUTUM AFB	FEV1%	FVC%	$\frac{FEV_1}{FVC}$	$\frac{FEV_1}{FVC\ \%}$	FEF_{50}	FEF_{25-75}	TYPE
119	Loganathan	65	25	No	-	-	-	-	-	Normal	Normal	Negative	84.6	104	0.81	81.35	84	83	Normal
120	Rahimbai	42	24	No	-	-	-	-	-	Normal	Normal	Negative	80.3	119	0.67	67.48	74	75	Stage I
121	Muniandi	39	24	No	-	-	-	-	-	Normal	Normal	Negative	85.7	101	0.85	84.85	84	86	Normal
122	Jhonson	64	29	No	-	-	-	-	-	Normal	Normal	Negative	84.1	107.5	0.78	78.23	82	80	Normal
123	Parthasarathy	62	40	Yes	-	-	-	-	-	Normal	Normal	Negative	87.6	112.8	0.78	77.66	86	88	Normal
124	Gurusamy	51	64	No	-	-	-	-	-	Normal	Normal	Negative	86.3	112.7	0.77	76.57	84	87	Normal
125	Chinnamani	61	60	No	-	-	-	-	-	Normal	Normal	Negative	67	108.3	0.62	61.87	71	73	Stage II
126	Soundararajan	31	16	No	-	-	-	-	-	Normal	Normal	Negative	84.6	108	0.78	78.33	80	86	Normal
127	Balaji	33	12	No	-	-	-	-	-	Normal	Normal	Negative	85.2	103	0.83	82.72	81	83	Normal
128	Muraldharan	48	36	Yes	-	-	-	-	-	Normal	Normal	Negative	55.7	96.4	0.58	57.78	71	72	Stage II
129	Panneerselvam	54	28	No	-	-	-	-	-	Normal	Normal	Negative	86.4	115.2	0.75	75	81	87	Normal
130	Nagaraja	31	16	No	-	-	-	-	-	Normal	Normal	Negative	89.6	118.2	0.76	75.8	85	87	Normal
131	Jegadeesan	58	30	No	-	-	-	-	-	Normal	Normal	Negative	87.6	116.6	0.75	75.13	80	80	Normal
132	Pandiaraj	53	24	Yes	-	-	-	-	-	Normal	Normal	Negative	85.6	114	0.75	75.09	81	86	Normal
133	Rajappan	64	28	No	-	-	-	-	-	Normal	Normal	Negative	80.7	118	0.68	68.39	75	74	Stage I
134	Kunjappan	51	24	No	-	-	-	-	-	Normal	Normal	Negative	85.4	100.8	0.85	84.72	85	88	Normal
135	Vadivel	57	30	No	-	-	-	-	-	Normal	Normal	Negative	88.1	114.4	0.77	77.01	88	80	Normal
136	Jacob	65	50	No	-	-	-	-	-	Normal	Normal	Negative	79	72.4	1.09	109.1	89	91	Mixed
137	Balu	55	24	No	-	-	-	-	-	Normal	Normal	Negative	88.2	114.3	0.77	77.17	83	89	Normal
138	Ravindran	61	21	No	-	-	-	-	-	Normal	Normal	Negative	83.4	104.9	0.8	79.5	86	85	Normal
139	Sangu Goundar	37	12	Yes	-	-	-	-	-	Normal	Normal	Negative	84.9	111	0.76	76.49	85	81	Stage I
140	Thanikachalam	63	28	No	-	-	-	-	-	Normal	Normal	Negative	86.7	114	0.76	76.05	86	89	Normal
141	Cherian	59	33	No	-	-	-	-	-	Normal	Normal	Negative	53.5	94.8	0.56	56.43	73	72	Stage II
142	Anandan	31	24	No	-	-	-	-	-	Normal	Normal	Negative	85.4	117	0.73	72.99	84	90	Normal
143	Veerabahu	64	42	No	-	-	-	-	-	Normal	Normal	Negative	87.4	112	0.78	78.04	87	88	Normal
144	Duraisamy	52	30	No	-	-	-	-	-	Normal	Normal	Negative	84.7	109.4	0.77	77.42	80	82	Normal
145	Rajangam	40	18	Yes	-	-	-	-	-	Normal	Normal	Negative	83	109	0.76	76.15	84	85	Normal
146	Sudalaiandi	65	48	Yes	-	-	-	-	-	Normal	Normal	Negative	81.1	119.5	0.68	67.87	73	72	Stage I
147	Thiagarajan	48	30	No	-	-	-	-	-	Normal	Normal	Negative	80.1	119.7	0.67	66.92	74	73	Stage I
148	Vincent	65	33	No	-	-	-	-	-	Normal	Normal	Negative	85.6	110.3	0.78	77.61	82	82	Normal

Sl.No	NAME	AGE	Pack years	Cough	Chest pain	wheeze	Dys pnoea	Cre pitation	rhonchai	ECG	X-RAY	SPUTUM AFB	FEV1%	FVC%	$\frac{FEV_1}{FVC}$	$\frac{FEV_1}{FVC\ \%}$	FEF_{50}	FEF_{25-75}	TYPE
149	Kumaraguru	58	20	Yes	-	-	-	-	-	Normal	Normal	Negative	86.4	110	0.79	78.55	81	87	Normal
150	Bangaru	32	20	No	-	-	-	-	-	Normal	Normal	Negative	85.1	106	0.8	80.28	86	83	Normal
151	Rajendran	45	Nil	No	-	-	-	-	-	Normal	Normal	Negative	84.2	115.2	0.84	84.34	83	83	Normal
152	Vellaisamy	38	Nil	No	-	-	-	-	-	Normal	Normal	Negative	85.6	110.5	0.77	77.47	81	90	Normal
153	Subburajan	72	Nil	No	-	-	-	-	-	Normal	Normal	Negative	86.8	113.7	0.76	76.34	87	89	Normal
154	Mookkandi	57	Nil	No	-	-	-	-	-	Normal	Normal	Negative	80.9	120	0.67	67.42	70	71	Normal
155	Nallusamy	64	Nil	Yes	-	-	-	-	-	Normal	Normal	Negative	89.1	109.9	0.81	81.07	87	86	Normal
156	James	70	Nil	No	-	-	-	-	-	Normal	Normal	Negative	83.4	109	0.77	76.51	85	82	Normal
157	Fakrudheen	43	Nil	No	-	-	-	-	-	Normal	Normal	Negative	84.1	109.6	0.77	76.73	85	84	Normal
158	Palavesakonar	39	Nil	No	-	-	-	-	-	Normal	Normal	Negative	86.7	111	0.78	78.11	83	84	Normal
159	Babulal	54	Nil	No	-	-	-	-	-	Normal	Normal	Negative	81.5	119.2	0.68	68.37	73	72	Normal
160	Rangegoundar	67	Nil	No	-	-	-	-	-	Normal	Normal	Negative	77	74.3	1.04	103.63	84	82	Normal
161	Arockiam	59	Nil	No	-	-	-	-	-	Normal	Normal	Negative	89	106.4	0.84	83.65	80	84	Normal
162	Thangadurai	48	Nil	No	-	-	-	-	-	Normal	Normal	Negative	80.9	118.3	0.68	68.39	75	74	Normal
163	Sridharan	64	Nil	No	-	-	-	-	-	Normal	Normal	Negative	78.4	72.6	1.08	107.99	82	81	Normal
164	Rangannan	71	Nil	No	-	-	-	-	-	Normal	Normal	Negative	83.7	99.9	0.84	83.78	88	85	Normal
165	Krishnan	52	Nil	No	-	-	-	-	-	Normal	Normal	Negative	80.5	118.6	0.68	67.88	71	70	Normal
166	Rajarathinam	61	Nil	No	-	-	-	-	-	Normal	Normal	Negative	84.8	105.5	0.80	80.38	87	85	Normal
167	Chokkanathan	48	Nil	Yes	-	-	-	-	-	Normal	Normal	Negative	85.6	108	0.79	79.2	86	81	Normal

Sl.No	NAME	AGE	Pack years	Cough	Chest pain	wheeze	Dys pnoea	Cre pitation	rhonchai	ECG	X-RAY	SPUTUM AFB	FEV1%	FVC%	$\frac{FEV_1}{FVC}$	$\frac{FEV_1}{FVC\ \%}$	FEF_{50}	FEF_{25-75}	TYPE
																6			
168	Williams	57	Nil	No	-	-	-	-	-	Normal	Normal	Negative	81.7	118.8	0.69	68.77	73	73	Normal
169	Dhandapani	60	Nil	No	-	-	-	-	-	Normal	Normal	Negative	84.9	105.3	0.81	80.63	86	87	Normal
170	Karuppan	45	Nil	No	-	-	-	-	-	Normal	Normal	Negative	52.4	92.4	0.57	56.71	71	73	Normal
171	Robert	74	Nil	No	-	-	-	-	-	Normal	Normal	Negative	84.8	106.6	0.80	79.55	83	80	Normal
172	Ismail	47	Nil	No	-	-	-	-	-	Normal	Normal	Negative	84.9	109.4	0.78	77.61	83	87	Stage I
173	Raju	72	Nil	Yes	-	-	-	-	-	Normal	Normal	Negative	83	98	0.85	84.69	81	87	Normal
174	Malleswaran	53	Nil	No	-	-	-	-	-	Normal	Normal	Negative	80.2	119.2	0.67	67.28	73	74	Normal
175	Surianarayanan	68	Nil	No	-	-	-	-	-	Normal	Normal	Negative	82.1	120	0.68	68.42	73	72	Normal
176	Venkatraj	52	Nil	Yes	-	-	-	-	-	Normal	Normal	Negative	85.2	107.8	0.79	79.04	82	84	Normal
177	Manickam	48	Nil	No	-	-	-	-	-	Normal	Normal	Negative	81.9	119.4	0.69	68.59	75	74	Normal
178	Prakasam	56	Nil	No	-	-	-	-	-	Normal	Normal	Negative	83.9	99.9	0.84	83.98	85	81	Normal
179	Thirumal	60	Nil	No	-	-	-	-	-	Normal	Normal	Negative	85.4	111.3	0.77	76.73	81	81	Normal
180	Subbanna	55	Nil	No	-	-	-	-	-	Normal	Normal	Negative	88.4	108	0.82	81.85	86	83	Normal
181	Babuji	42	Nil	No	-	-	-	-	-	Normal	Normal	Negative	85.1	111.6	0.76	76.25	90	84	Normal
182	Velu	37	Nil	No	-	-	-	-	-	Normal	Normal	Negative	83.4	100.5	0.83	82.99	82	87	Normal
183	Duraiappan	42	Nil	No	-	-	-	-	-	Normal	Normal	Negative	76.3	70.5	1.08	108.23	84	88	Normal
184	Jeevanandham	35	Nil	No	-	-	-	-	-	Normal	Normal	Negative	85.9	109.6	0.78	78.38	83	80	Normal

Sl.No	NAME	AGE	Pack years	Cough	Chest pain	wheeze	Dys pnoea	Cre pitation	rhonchai	ECG	X-RAY	SPUTUM AFB	FEV1%	FVC%	$\frac{FEV_1}{FVC}$	$\frac{FEV_1}{FVC}$ %	FEF_{50}	FEF_{25-75}	TYPE
185	Madhavan	59	Nil	No	-	-	-	-	-	Normal	Normal	Negative	85.3	110.5	0.77	77.19	90	85	Normal
186	Chandrasekaran	69	Nil	No	-	-	-	-	-	Normal	Normal	Negative	84.8	106.6	0.80	79.55	83	80	Normal
187	Varadarajan	67	Nil	No	-	-	-	-	-	Normal	Normal	Negative	81.5	116.9	0.70	69.72	75	72	Normal
188	Joel	42	Nil	No	-	-	-	-	-	Normal	Normal	Negative	64.3	109.5	0.59	58.72	71	72	Normal
189	Mohemmad	38	Nil	No	-	-	-	-	-	Normal	Normal	Negative	84.7	107.4	0.79	78.86	88	82	Normal
190	Punniakodi	51	Nil	No	-	-	-	-	-	Normal	Normal	Negative	77.3	72.9	1.06	106.04	84	87	Normal
191	Sitaraman	46	Nil	No	-	-	-	-	-	Normal	Normal	Negative	83.6	101.5	0.82	82.36	88	83	Normal
192	Ilango	62	Nil	No	-	-	-	-	-	Normal	Normal	Negative	75.9	73.4	1.03	103.41	88	87	Normal
193	Dharmarajan	39	Nil	No	-	-	-	-	-	Normal	Normal	Negative	83.2	99.9	0.83	83.28	88	89	Normal
194	Packianathan	44	Nil	No	-	-	-	-	-	Normal	Normal	Negative	80.7	116.2	0.69	69.45	74	75	Normal
195	Arunagiri	57	Nil	No	-	-	-	-	-	Normal	Normal	Negative	88.1	114.4	0.77	77.01	88	80	Normal
196	Paranjothy	53	Nil	No	-	-	-	-	-	Normal	Normal	Negative	86.5	115.3	0.75	75.02	82	85	Normal
197	Innasi Goundar	48	Nil	Yes	-	-	-	-	-	Normal	Normal	Negative	86.3	112.7	0.77	76.57	84	87	Normal
198	Deenadayalan	37	Nil	No	-	-	-	-	-	Normal	Normal	Negative	84.3	105.2	0.80	80.13	87	85	Normal
199	Venkoban	54	Nil	No	-	-	-	-	-	Normal	Normal	Negative	87.1	118.2	0.74	73.69	84	90	Normal
200	Francis	61	Nil	No	-	-	-	-	-	Normal	Normal	Negative	81.4	119.3	0.68	68.23	75	75	Normal