AFRICAN JOURNAL OF MEDICINE and medical sciences

VOLUME 43 NUMBER 2 JUNE 2014

Editor-in-Chief
O. BAIYEWU

Assistant Editors -in-Chief
O. O. OLORUNSOGO
B. L. SALAKO

ISSN 1116–4077

Nephritis as an initial diagnosis of lupus in Nigerian patients

OO Adelowo[1], T Umeizudike[2], H Olaosebikan[1] and JO Awobusuyi[2]
Rheumatology Unit[1] and Nephrology Unit[2], Department of Medicine,
Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria

Abstract

Background: Systemic Lupus Erythematosus (SLE) is a multi-systemic autoimmune disease. Renal involvement is a common complication, causing considerable mortality and morbidity.SLE is rarely reported among black Africans, though recent reports from Nigeria indicate otherwise. Nephritis, though a common complication of SLE has rarely been reported as the initial diagnosis of lupus among black Africans.
Aims: The aim of our study is to highlight the clinical, laboratory and histological features in Nigerian patients presenting with features of nephritis and subsequent diagnosis of SLE.
Methods: This is a three year prospective study of patients with renal diseases, who were admitted to the rheumatology and nephrology units of the Lagos State University Teaching Hospital (LASUTH) Ikeja. Serology, biochemical, haematologic tests, kidney biopsy were done.
Results: Twelve patients were studied (F11; M1); mean age 30.4 years (SD± 9.8);mean illness 8weeks(SD±6.6) . Six patients had a nephritic condition. Nine of the patients had baseline hypertension while 3 had a rapidly progressive nephritis. Two patients had baseline End Stage Renal Disease (ESRD).All had dipstick proteinuria 2+ / 3+ , mean protein creatinine ratio 2.2 (SD ±0.6) ,mean 24hr protein 2.8gm(SD±2.7);more than 10 red blood cells/hpf haematuria(n-6),hyaline casts(n-5), granular casts(n-2),mean GFR 31.4ml/min(SD±21.3),mean serum creatinine 6.9mg/dl(SD± 5.3); mean urea 138.8mg/dl(SD±56.2). For the serology, Anti Nuclear Antibody (ANA) was positive in all the 12 subjects; positive anti dsDNA -10 patients; ENA - 10. Renal biopsy showed mostly WHO/ISSN classes III, IV and V. Treatment was with Euro Lupus regimen and rituximab/ cyclophosphamide. Four patients had dialysis. In terms of the outcome, there were 3 deaths while 9 patients were discharged.
Conclusion: A high index of suspicion is needed to diagnose Lupus Nephritis in black Africans especially when their presentations do not fulfil the America College of Rheumatology (ACR) diagnostic criteria for SLE.

Keywords; *Renal, diseases, initial, diagnosis, lupus*

Correspondence: Prof. O.O. Adelowo, Department of Medicine, LASUTH, Ikeja, Lagos, Nigeria. E-mail: femiadelowo2003@yahoo.com.

Résumé

Introduction: Le lupus érythémateux disséminé (SLE) est une maladie multi-systémique. Une atteinte rénale est une complication courante, cause de morbidité et mortalité considérable. Le SLE est rarement signalée chez les noirs africains. Le but de notre étude est de mettre en évidence les laboratoires cliniques, et des caractéristiques histologiques chez des patients nigérians présentant des caractéristiques de la néphrite et diagnostic ultérieur d'SLE.
Méthodes: Il s'agit d'une étude prospective de trois ans des patients atteints de maladies rénales, qui ont été admis dans les unités de rhumatologie et de néphrologie au centre universitaire hospitalier d'Ikeja, l'état de Lagos(LASUTH). Les examens sérologiques, des tests biochimiques, hématologiques et biopsie rénale ont été effectuées.
Résultats: Douze patients ont été l'objet d'étude (F11; M1); âge moyen 30,4 années (SD ± 9,8); signifier maladie 8 semaines (SD ± 6,6). Six patients avaient une maladie néphrétique. Neuf des patients présentaient une hypertension de base alors que 3 avaient une néphrite rapidement progressive. Deux patients avaient référence d'insuffisance rénale terminale (IRT). Tout avait évalué: protéinurie 2/3, signifie protéine créatinine 2.2 (SD ± 0,6), 24hr protéines 2.8 gm(SD±2.7) ; plus de 10 globules rouges/hpf hématurie (n-6), hyalines (n-5), moulages granulaires (n-2), équivalent au GFR 31,4 ml/ min(SD±21.3), taux de sérum créatinine moyenne 6,9 mg/dl(SD± 5.3) ; équivalent à la concentrationd'urée de 138.8mg/dl(SD±56.2). Pour la sérologie, ANA a été positif dans l'ensemble des 12 sujets; positif anti ADN bicentenaire -10 patients; ENA - 10. Biopsie rénale a montré surtout qui/ISSN classes III, IV et V. Le traitement était avec Euro Lupus chimio et rituximab/cyclophosphamide. Quatre patients avaient fait la dialyse. En termes de résultat, il y a eu 3 décès et 9 patients ont été déchargés.
Conclusion: Un indice élevé de suspicion est nécessaire pour diagnostiquer la néphropathie lupique chez les Africains noirs en particulier lorsque leurs présentations ne remplissent pas les critères de diagnostic de l'ACR pour SLE.

Introduction

Systemic Lupus Erythematosus (SLE) is a multisystemic autoimmune disease with protean

clinical manifestations. Though previously said tobe rare among black Africans, recent reports of 66 SLE cases; and auto antibodies in Nigerian lupus patients [1,2] as well as 2 cases of lupus digital gangrene from Nigeria [3] have shown that this condition may not be rare in black Africans after all; and that it is possibly under reported.

Renal involvement in SLE includes diverse presentations such as proteinuria, glomerulonephritis, nephrotic syndrome, interstitial nephritis, tubular disease, thrombotic microangiopathy, vasculitis, atherosclerosis, and lupus vasculopathy. Patients may also present to the hospital as chronic renal failure and end stage renal disease.

Lupus Nephritis(LN) is defined by the clinical and laboratory manifestations that meet the American College of Rheumatology(ACR) criteria of 1) persistent proteinuria at least 0.5 gm per day, dipstick of 2+/3+; 2) microscopic haematuria and 3) presence of urinary cellular casts such as red blood cells [RBCs], haemoglobin, granular, tubular, or mixed [3]. A review of 1997 ACR case definition for LN has recommended the following for diagnostic purposes- a spot protein/creatinine ratio (PCR) of more than 0.5; active urinary sediments of at least 5 red blood cells/high-power field [hpf]; at least 5 white blood cells /hpf in the absence of infection; cellular casts limited to red blood cell or white blood cells. The foregoing are as substitutes for 24-hour urinary protein measurement and cellular casts respectively. A renal biopsy specimen demonstrating immune complex-mediated glomerulonephritis compatible with LN is also regarded as being definitive [4].

One identified shortcoming of the ACR definition criteria for LN, however, is that it requires interpretation in the context of background or established SLE and may therefore exclude patients who might present early with renal disease. To address this limitation and others, the Systemic Lupus International Collaborating Clinics(SLICC) has proposed a new classification criteria for SLE ,such that a biopsy -proven LN in the presence of positive serological findings of ANA or Anti ds DNA is diagnostic of SLE; even in the absence of other common features of SLE(5). This in effect makes for diagnosis of SLE earlier than if the ACR criteria for SLE is strictly used. It also recognises the fact that lupus can present in various ways. Renal involvement is one of the more serious manifestations of SLE, with increased morbidity and mortality especially among black patients.

Although studies from USA revealed that the overall survival in patients with SLE is approximately 95% at 5 years after diagnosis and 92% at 10 years after diagnosis, the presence of lupus nephritis reduces survival to approximately 88% at 10 years, with even lower survival in African Americans [6]. Previous studies have identified adverse prognostic factors of SLE in blacks to include severe renal manifestation, abnormal renal indices such as haematuria, proteinuria and cellular casts; serological profiles; histopathological features of focal and diffuse proliferative nephritis resulting in worse treatment outcomes [7]. Approximately 50% of patients with SLE will develop lupus nephritis, with the associated increased risks for renal failure, cardiovascular disease and death [8]. Most patients with SLE will develop LN within five years following the diagnosis. However, LN as initial presentation of SLE is uncommonly reported.

LN has been described among various populations though the prevalence differs. The highest prevalence of 50.5% is seen in African-Americans in contrast with a prevalence of 43.1% in Hispanics and 14.3% in Caucasians [9] .It has, however, been infrequently reported among black Africans. There are a few retrospective studies of LN from South-Africa [10-12], Jamaica [13] , and Afro-Caribbean [14] but few published reports from sub-Sahara Africa except a report of seven cases from Abidjan [15]. LN is associated with considerable morbidity and mortality, especially among blacks and as such early recognition and prompt initiation of immunosuppressives is desirable.

In view of the foregoing, the objective of this study is to document a case series of nephritis and chronic kidney disease presenting as first manifestation of SLE in Nigerians and to record the demographic, clinical, laboratory, serological and histological features. The management will also be outlined.

Materials and methods

This was a prospective case study of young patients presenting with clinical and laboratory features of renal diseases to the rheumatology and nephrology units during calls and were subsequently admitted to the medical wards. These cases were recorded at Lagos State University Teaching Hospital; Ikeja over a 3 year period (January 2010-March 2013).None of the patients fulfilled the American College of Rheumatology diagnostic criteria for SLE [3] at presentation. Inclusion criteria for the study were i) young patients presenting with renal diseases ii) presence of albuminuria by dipstick iii) presence

ofmicroscopic haematuria iv) elevated creatinine or/ and blood urea v) elevated ESR above 80mm/hr. Exclusion criteria were i) middle aged to elderly patients ii) previously or currently reported hypertension or diabetes iii) diagnosed renal disease iv) patients who have been on chronic dialysis programme v) patients with diagnosed HIV infection or positive serology for HIV vi) positive Tuberculin skin test or Quantiferon gold vii) raised ASO titre. The diagnosis of LN was made using ACR case definition, serological abnormalities with exclusion of common causes of kidney diseases and renal biopsy finding where applicable. The patients were clinically evaluated and blood was taken for haematocrit, full blood counts and differentials, ESR, electrolytes, creatinine, urea, albumin, total protein, plasma cholesterol, serology. Mid-stream urine specimen was collected for dipstick and microscopy, Spot urine for protein creatinine ratio or and 24hour urinary protein estimation were done in some patients. Kidney biopsy was performed in 6 cases and specimens sent to certain centres in United Kingdom and Germany, courtesy of one of the authors (UT)

Patients' management was with an initial three day course of intravenous pulse methylprednisolone 500mg daily, followed by the Euro Lupus Regimen for LN consisting of two weekly intravenous injection of cyclophosphamide 500mg for 3 months as induction treatment. Maintenance phase was with oral azathioprine (2-3mg/kg body weight) daily in divided dosage. Prednisolone was continued after pulse methylprednisolone at a dose of 1mg/kg body weight in divided doses but tapered down to 10mg daily within six months. Rituximab was administered in few patients especially those with a rapidly progressive nephritis while few patients had haemodialysis.

Results

A total of 12 diagnosed LN patients were seen out of a total of the 36 SLE cases seen within the period of study. None of the cases fulfilled 1997 ACR classification criteria for SLE at the point of diagnosis. Retrospectively, 6 cases that had biopsy fulfilled the proposed SLICC criteria for SLE. The demographic characteristics of the patients are as shown in Table 1.

Six cases presented with a nephritic syndrome while 3 had a rapidly progressive nephritis. Two patients presented with End Stage Renal Disease. One patient presented with features of nephrotic syndrome while 9 out of the 12 cases had hypertension at presentation. Most of the patients were anaemic with a mean haematocrit of 21.6%. Leucopaenia and lymphopaenia were also seen in five cases, while the ESR was markedly elevated in most cases as shown in Table 2.Renal scan demonstrated increased echogenicity and loss of cortico-medullary differentiation in all the cases, however 8 cases had normal size kidney while 4 had enlarged kidney. All our patients had dipstick proteinuria of varying degree.

Table 1: Demographic characteristice of 12 LN patients

Female	11
Male	1
Female: male ratio	F:11, M:1
Mean age (SD)	30.4 (SD±9.8)
Mean duration of symptoms weeks (SD)	8(SD±6.6)

Table 2: The haematological profiles in 12 cases with UN

Test	Mean (SD)
Haematocrit mean	21.6 (±S.D.)
White blood cell counts mean	$4.8X10^9/L(\pm 2.5)$
(Leucopaenia)	5 patient
Lymphopaenia	5 patient
Platelet	$205.6X10^3(+135.9X10^3/L)$
(Thrombocytopenia)	3
Erythrocyte sedimentation rate	120mm/hr(±24.1)

The renal biochemical, urinary, and biopsy abnormalities are summarized in Table 3. Of the histopathology findings among the six patients investigated, one patient each had lupus nephritis changes of Classes III, IV, V respectively. Two patients had findings of both Classes III and V while the sixth had changes of both Classes IV and V associated with fibrinoid vasculitis. All the twelve patients had positive anti-nuclear antibody (ANA) while 10 cases each were positive for anti dsDNA and extractable nuclear antigen (ENA). The titres of the ANA were high with 1 patient having titre of 1:5120; two patients each with titres of 1:1280 and 1:160 respectively. Four patients had titre of 1:640 while the remaining had a titre of 1:320. The immunofluorescence staining pattern was mainly speckled (8 patients) while the remaining 4 was homogeneous. Anti dsDNA and Extractable antigen (ENA) were positive in 10 patients respectively.

Table 3: Biochemical finding in 12 cases with LN

Test (number of patients)	Mean (SD)
Serum creatinine (12)	6.9mg/dl\9±5.3)
Serum urea (12)	135.8mg/dl(±56.3)
GFR (12)	31.4ml/min/1.73m2(±21.3)
Protein creatinine ratio (5)	2.2(±0.6)
24hr Urinary protein (7)	2.8g/24hr(±2.7)
Dipstick proteinuria (12)	Positive
Microscopic haematuria (12)	Positive
Urinary sediment assessment (10)	
Hyaline cast (2)	
granular cast (5)	
No cast (3)	

Treatment

Seven patients had immunosuppressive induction using the Euro-lupus low dose cyclophosphamide regimen for LN which consists of intravenous pulse methyl prednisolone 0.5g-1g once daily for 3 days followed by two weekly intravenous pulse cyclophosphamide 500mg for a total of three months. Four patients who had rapidly progressive LN had induction with intravenous rituximab 500mg weekly for three doses with intravenous cyclophosphamide 500mg being given after the first and last rituximab dosages. Mycophenolate mofetil was administered for induction in one patient. Azathioprine was used for maintenance therapy in all the patients. Other medications used included oral prednisolone, hydroxychloroquine, low dose aspirin, lisinopril, atorvastatin, Calcium and vitamin D supplements. Haemodialysis was instituted in 5 patients but 3 cases continued haemodialysis despite immunosuppressives.

Discussion

LN as an initial diagnosis of SLE without fulfilling the ACR criteria has uncommonly been reported in literature. Bastian et al reported 39 cases of LN who otherwise did not fulfil the ACR lupus diagnostic criteria among 353 SLE cases seen in a multiethnic cohort study [9]. Our patients did not fulfil the ACR criteria for SLE at presentation, though they had presented to various hospitals with mostly non specific symptoms of recurrent fever, fatigue, headache which had been variously treated as malaria fever and typhoid infection. None of them was however diagnosed as renal disorder. However, this may not be surprising as Bertsias et al, have shown that about 10% of patient with clinical lupus did not fulfil ACR criteria for SLE at onset although 65% of patients did eventually fulfil it [16].

The low frequency of LN as initial diagnosis of SLE may be explained by- (i) most renal abnormalities emerge few years after diagnosis, (ii) LN patients may initially present to nephrologists rather than rheumatologists, and lupus may not be high on the list of aetiological consideration (iii) strict application of ACR criteria often leads to under diagnosis of this condition. Most reports of lupus nephritis at presentation have often been seen in association with other features of SLE, and not as an isolated condition. In a report among Europeans lupus patients, renal involvement was initially present in 16% of the cohort increasing to 50% during subsequent follow-up [17]. In another study, 75% of diagnosed SLE cases eventually developed renal involvement within 1 year of presentation [13]. Among a group of 111 Afro-Caribbean SLE patients, 50% subsequently developed LN [14]. In another study conducted in USA, 35% of adults with SLE had clinical evidence of nephritis, even at the time of diagnosis. An estimated 50–60% of this eventually developed nephritis during the first 10 years of the disease [18].

Retrospective studies among black Africans from South Africa [10-12] and Abidjan [15] have demonstrated some cases of LN. These either presented with LN at onset of SLE or subsequently during follow-up. About half of the total number of lupus patients reported from Nigeria [1] had some level of proteinuria at presentation in the clinic, suggestive of renal involvement. The black race appears to be a risk factor for development of LN. This is often associated with adverse prognostic factors including aggressive renal diseases, severe histological features, resistance to treatment and worse outcome [6,7]

The female preponderance in our study (F:M 11:1) is similar to reports in among Jamaicans, with a F:M ratio of 13:1 [13]. Our study showed marked female preponderance (F-11,M-1) ,which is in consonance with a F:M ratio 13:1. This is a reflection of the well recognised female preponderance in lupus. The mean age at onset of LN in our study was 30.4 years, which is not too different from a mean age of 27 years seen in a Pakistani study [19]. This age at onset is however lower than the mean age of 35.0 ± 12.8 years described among South-African patients [10]. Hypertension, seen in 75% of our cases and nephritic syndrome seen in 50% were the commonest clinical manifestations among our patients. Contreras *et al* [20] had reported hypentensionin 70% of LN casesin a case-control study. However, among the Afro-Caribean, hypentension was less often seen, being present in

13% of the group with 11% eventually developing ESRD [14]. Hypertension, chronic glomerulonephritis, diabetes are the leading causes of chronic kidney disease (CKD) worldwide, including Africa [21]. Findings of hypertension and CKD in a young person may therefore prompt search for other causative factors including possibly lupus. All the cases had anaemia while some had leucopaenia, or thrombocytopenia. It has been postulated that the presence of thrombocytopenia, leucopaenia, anaemia and hypertension are predictors for development of LN and are associated with increased probability of renal insufficiency [22].

The mean ESR in our study was 120mm/hr. This test is often used as a screening test for connective tissue diseases including LN, as well as in the monitoring of patient's response to therapy. This test was utilized among our patients as a screening test as it is affordable in contrast to the expensive serology tests which are not even readily available. Elevated ESR above a hypothetical level of 80mm/hr in absence of other conditions that cause this elevation, is often used as screening test in our patients. Proteinuria and haematuria of varying degree as well as elevated creatinine (mean: 6.93mg/dl), reduced GFR(mean:31.4ml/min/1.73m²) and active urinary sediment were observed in most of our patients. A report by Boumpas *et al* showed that about half of SLE patients present with asymptomatic urine abnormalities such as proteinuria and haematuria [23].

Proteinuria, haematuria, hypercreatinemia and active urinary sediments are predictors of proliferative LN and have been identified as adverse prognostic factors [24].Thus, regular screening for urinary abnormalities in SLE patients can facilitate early detection of LN and prompt early commencement of immunosuppressive. Renal biopsy done in our study showed mixed class histopathology finding in three patients while other 3 had changes of only one class. However most of our cases were the severe classes of IV or V. The other six patients were unable to afford the cost of biopsy and the processing of the specimens. The cost of the procedure and histopathology is about 156 dollars which may be prohibitive among our patients. Focal and diffuse proliferative GN(III/IV LN) have often been associated with rapidly progressive glomerulonephritis and 25 to 30 percent of patients with diffuse proliferative lupus nephritis in some studies developed ESRD in spite of optimal treatment regimens [25]. This was observed in our study as 3 patients with Rapidly Progressive Glomerulonephrits (RPGN) had WHO/ISSN stage IV LN.Anti-nuclear antibody. Anti dsDNA has been found to play a pathogenic role in the development of LN as glomerular immune deposits in some lupus nephritis patients are enriched in anti-dsDNA antibodies, and they cross react with endogenous glomerular antigens [26]. In addition, anti dsDNA level has diagnostic and prognostic value including monitoring disease activity. Unfortunately, the quantitative determination of ds DNA titre is not available in Nigeria and therefore could not be used in the monitoring of our patients.

The new ACR guideline for management of LN recommends oral Mycophenolate mofetil (MMF) as the preferred induction agent in African-Americans and Hispanics especially as some studies have shown that African Americans and Hispanics with LN may respond less to intravenous cyclophosphamide than do patients of Caucasian or Asian races [27,28]. The use of low dose cyclophosphamide in our patients is supported by, the new European League Against Rheumatism EULAR/ERA-EDTA guideline which recommended either agent (low dose Euro-lupus cyclophosphamide or MMF) for induction. Both agents have comparable efficacy although the latter has the advantage of ease of administration as well as the more favourable gonadal toxicity [8].The Euro Lupus regimen also recommends azathioprine for maintenance which is the agent we use in our centre, bearing in mind its affordability. However, while the ALMS study showed superiority of MMF over azathioprine, the MAINTAIN study concludes that Azathioprine is as effective if not better than MMF in preventing renal flares [29,30]. This conflicting result may be due to different outcome measures adopted in both studies and different sample size (ALMS-105 patients, MAINTAIN-227 patients). The efficacy of rituximab, used in a few of our patients, has been demonstrated by Ng *et al* in an open label study of 30 SLE. Of these, 21 had LN out of which 12 patients had sustained response (no relapse 12-60 months) while the remaining patients relapsed, but however responded to re-treatment [31].

A high index of suspicion is therefore needed in order to diagnose and manage lupus nephritis among Nigerians. Our suggestion is that young patients presenting with renal diseases and high ESR, excluding other causes of elevation, should be further investigated for lupus. Though this is a case series report, a more extensive study as well as community based study may further highlight this condition. It is hoped that the report will heighten the index of suspicion of LN among young females presenting with renal diseases and appropriate immunosuppressives introduced early to avoid ESRD.

Acknowledgements

Dr V Bradley, Addenbrooke's Hospital, Cambridge, United Kingdom for histopathology of patient PA in Table 5. Dr Elisabeth Grone, Heidelberg, Germany for patient's histopathology of patient 2-6 in Table 5, Pathcare Laboratories and Clina-Lancet Laboratories for serology

References

1. Adelowo OO and Oguntona SA. Pattern of systemic lupus erythematosus among Nigerians Clin Rheumatol. 2009 Jun; 28(6):699-703.
2. Adelowo OO, Oguntona AS and Ojo O. Neuropsychiatric systemic lupus erythematosus among Nigerians. Afr J Med med sci. 2009 Mar; 38(1):33-38.
3. Tan EM, Cohen AS, Fries JF, Masi AT, *et al.* The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271–1277.
4. Dooley MA, Aranow C and Ginzler EM. Review of ACR renal criteria in systemic lupus erythematosus. Lupus 2004; 13: 857–860.
5. Petri M Orbai AM, Alarcón GS, Gordon C, *et al.* Derivation and validation of SLE Collaborating Clinic Classification(SLICC) criteria for SLE. Arthritis Rheum,2012 Aug 64(8): 2677-2686.
6. Bernatsky S, Boivin JF, Joseph L, *et al.* Mortality in systemic lupus erythematosus. Arthritis Rheum 2006; 54:2550–2557.
7. Korbet SM, Schwartz MM, Evans J and Lewis EJ. Severe lupus nephritis: racial differences in presentation and outcome. J Am Soc Nephrol. 2007 Jan; 18(1):244-254.
8. Bertsias GK, Tektonidou M, Amoura Z, *et al.* Joint European League Against Rheumatism and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis. Ann Rheum Dis 2012 Nov;71(11):1771-1782.
9. Bastian HM, Roseman JM, Mcgwin G Jr *et al.* Systemic lupus erythematosus in three ethnic groups. XII. Risk factors for lupus nephritis after diagnosis. Lupus (2002) 11: 152-160.
10. Okpechi IG, . Ayodele OE, Jones ES, *et al.*. Outcome of patients with membranous lupus nephritis in Cape Town South Africa. Nephrol. Dial. Transplant. . 2012 Sep;27(9):3509-3515.
11. Okpechi IG, Swanepoel CR, Tiffin N, *et al.* Clinicopathological insights into lupus nephritis in South Africans: A study of 251 patients. Lupus. . 2012 Aug;21(9):1017-1024.
12. Olugbenga EA , Okpechi IG and Swanepoel CR. Predictors of poor renal outcome in patients with biopsy-proven lupus nephritis. Nephrology. June 2010:15(4): 482-490.
13. Winston Williams, DM; Dipak Shah, DM; Lincoln A and Sargeant, DM. The Clinical and Epidemiologic Features in 140 Patients with Lupus Nephritis in a Predominantly Black Population from One Centre in Kingston, Jamaica. Am J Med Sci 2004;327(6): 324–329.
14. C Flower, A Hennis, IR Hambleton and G Nicholson. Lupus nephritis in an Afro-Caribbean population: renal indices and clinical outcomes. Lupus (2006) 15, 689–694.
15. Diallo AD, Nochy D, Niamkey E and Yao Beda B. Etiologic aspects of nephrotic syndrome in Black African adults in a hospital in Abidjan. Bull Soc Pathol Exot. 1997; 90(5): 342-345.
16. Bertsias G, Cervera R and Boumpas DT. Systemic lupus erythematosus: pathogenesis, clinical manifestations and diagnosis. Eular Online Course on Rheumatic Diseases,2011, module 17: page 6
17. Cervera R, Khamashta MA, Font J, Sebastiani GD *et al.* Systemic lupus erythematosus: clinical and immunologic patterns of disease expression in a cohort of 1,000 patients. The European Working Party on Systemic Lupus Erythematosus. Medicine (Baltimore) 1993; 72:113-124.
18. Kasitanon N, Magder LS and Petri M. Predictors of survival in systemic lupus erythematosus. Medicine (Baltimore) 2006;85:147–156.
19 Rabanni MA,Tahir MH, Siddiqui BK, Ahmad B *et al.* Renal involvement in Systemic lupus erythematosus in Pakistan. J.Pak MedAssoc.2005 Aug: 55(8):328-332.
20. Contreras G, Lenz O, Pardo V, Borja E *et al:* Outcomes in African Americans and Hispanics with lupus nephritis. Kidney Int 2006; 69 : 1846 –1851.
21. Alebiosu CO and Ayodele OE . Global burden of Chronic Kidney Disease and the way forward.Ethn Dis 2005 Summer,15(3) 418-423.
22. Thumboo J, Fong KY, Chia HP, Chung HH *et al.* Clinical predictors of nephritis in systemic lupus erythematosus. Ann Acad Med Singapore 1998; 27:16 – 20.
23. Boumpas DT, Austin HA, Fessler BJ, *et al.* Systemic lupus erythematosus: emerging concepts. Part 1: renal, neuropsychiatric, cardiovascular, pulmonary, and hematologic disease. Ann Intern Med 1995; 122:940-950.

24. Balow JE, Boumpas DT and Austin HA. Systemic lupus erythematosus and the kidney. In Lahita RG, ed. Systemic lupus erythematosus. San Diego: Academic Press, 1999: 657-685.
25. Chen YE, Korbet SM, Katz RS, *et al.* Value of a complete or partial remission in severe lupus nephritis. Clin J Am Soc Nephrol 2008;3:46-53.
26. Reeves WH, Satoh M and Richards HB. Origins of antinuclear antibodies pg 1271-1277. In: Lahita RG, ed. Systemic lupus erythematosus, Elsevier, 1999, San Diego.
27. Isenberg D, Appel GB, Contreras G, *et al.* Influence of race/ethnicity on response to lupus nephritis treatment: the ALMS study. Rheumatology (Oxford) 2010; 49:128–140.
28. Hahn BH, McMahon MA, Alan Wilkinson, *et al.* American College of Rheumatology Guidelines for Screening, Treatment, and Management of Lupus Nephritis. Arthritis Care and Research .Vol. 64, No. 6, June 2012, pp 797–808.
29. Dooley MA, Jayne D, Ginzler EM, *et al* (ALMS Group).Mycophenolate versus azathioprine as maintenance therapy for lupus nephritis. N Engl J Med. 2011 Nov 17;365(20):1886-1895.
30. Houssiau FA, D'Cruz D, Sangle S, Remy P *et al.* Azathioprine versus Mycophenolate mofetil for long-term immunosuppression in lupus nephritis: results from the MAINTAIN Nephritis Trial. Ann Rheum Dis. 2010 Dec; 69(12):2083-2089.
32. Ng KP, Cambridge G, Leandro M, *et al.* B cell depletion therapy in systemic lupus erythematosus: long-term follow- up and predictors of response. Ann Rheum Dis.2007 Sept; 66(9):1259-1262.