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Auto antibodies in Nigerian lupus patients

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Abstract

Background: Systemic lupus erythematosus (SLE) has hitherto been uncommonly reported among Nigerians and other black Africans. Recently, however, there have been increasing number of reports. The auto antibodies are diagnostic hallmarks in SLE and are also of significance in terms of prognosis and organ involvements. There have been scanty reports on the auto-antibodies profiles in black African SLE patients.

Objective: The objective of this study was to highlight the auto antibodies profile of SLE patients seen in a private practice rheumatology clinic in Lagos, Nigeria as well as to review the literature.

Method: This was a retrospective study of serology profiles of all SLE patients seen in a private practice clinic. Patients were diagnosed using the American College of Rheumatology Criteria for SLE. Sera were sent to Pathcare Laboratory, an internationally certified facility in Lagos.

Results: ANA was present in 95.7% of the patients and were mostly in high titres with speckled staining pattern on immunofluorescence. Other auto antibodies seen include Anti dsDNA(54.4%); Anti Sm (75.2%); Anti RNP (81.8%); ENA screen(79.5%); Ro/SSA (69.7%); Anti chromatin(66.7%).

Conclusion: ANA is sensitive in diagnosis of SLE being present usually in high titres most of the patients. The frequency of some of the other serology profiles are similar to those seen in other SLE populations but differ in others. The value of auto antibodies in the diagnosis and their association with specific organ involvement is also confirmed.

Keywords: *Auto antibodies, Nigerian lupus patients*

Résumé

Contexte: Le lupus érythémateux disséminé (LED) a été jusqu'ici peu fréquemment signalés chez les Nigérians et chez les autres noirs-africains. Cependant, récemment, il ya eu un nombre croissant de rapports. Les auto-anticorps sont les caractéristiques de diagnostic dans le LED et sont également importants en termes de pronostic et d'implications d'organes. Il ya eu peu de rapports sur les profils des auto-anticorps chez les lupiques de l'Afrique-noire.

Objectif: L'objectif de cette étude était de mettre en évidence le profil auto anticorps des patients atteints de vues dans un cabinet privé de rhumatologie à Lagos, au Nigeria, ainsi que d'examiner la documentation.

Méthode: Il s'agissait d'une étude rétrospective des profils sérologiques de tous les patients atteints de LED que l'on a examinés dans une clinique médicale privée. Les patients ont été diagnostiqués à l'aide des critères du Collège américain de Rhumatologie pour le LED. Les sérums sont envoyés au Pathcare Laboratoy, un centre international certifié à Lagos.

Résultats: ANA était présente dans 95,7% des patients et était pour la plupart dans les titres élevés avec ne image mouchetée sur l'immunofluorescence. D'autres auto-anticorps examinés incluent l'ADN (54,4%); l'anti Sm (75,2%); l'anti RNP (81,8%); l'ENA écran (79,5%); le Ro / SSA (69,7%); l'Anti chromatine (66,7%).

Conclusion: ANA est sensible dans le diagnostic de lupus érythémateux disséminé présent habituellement dans la plupart des titres élevés des patients. La fréquence de certains autres profils sérologiques sont semblables à ceux observés dans les populations atteintes de LED, mais diffèrent dans d'autres. La valeur d'auto-anticorps dans le diagnostic et leur association avec l'implication spécifique d'organe est également confirmée.

Introduction

Systemic Lupus Erythematosus (SLE) is an auto immune disease with multisystemic manifestations affecting mostly females of child bearing age. Its pathogenesis is complex, involving immunological, genetic, hormonal and environmental factors.

There have been few reports of SLE among black Africans, prompting Symmons [1] to suggest a prevalent gradient hypothesis which describes an increasing prevalence of the disease as we move from Africa to North America and Europe. However,

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lower frequency of 15.4% among Jamaican blacks[15]. However, a higher frequency of 83.3% is seen among Omani subjects [10].This variability among the black populations needs to be explained.

The presence of Ro/SS-A is useful for the diagnosis of SLE especially in patients positive for ANA and negative for Anti ds DNA [19]. In our study, 69.7% of our patients were positive, comparable to 60.5% in South African blacks, but differing from a low frequency of 9.9% seen among Jamaican blacks. Anti La(SS-B) is disproportionally lower in our patients just as with South African and Jamaican blacks as well as in Malaysians [20]. The varying frequencies may be a reflection of different methodologies used between the immuno diffusion and Western Blot methods.

Anti-RNP is a useful marker for SLE among our patients, with a frequency of 81.8% compared with 65.5% among South African blacks and a very low 7% among Jamaicans. Although anti-RNP may be suggestive of Mixed Connective Tissue Disease, however in such cases, Anti Sm is invariably negative. Moreover none of our patients had features of Mixed Connective Tissue Disease and the anti- RNP can only be attributed to SLE.

Anti-Chromatin was only recently introduced into the serology profile by our corresponding laboratory. It is specific for SLE and may be associated with lupus nephritis. Of the total of 15 patients tested, 10 (66.7%) showed positivity. Other reports have shown frequencies of between 50%-100% with report from Egypt at 80% [21, 22]. This test may become more relevant in our patients especially for those with negative Anti- dsDNA.

Although SLE has been infrequently reported among African blacks, a recent report from Nigeria shows this may not be the case. Serology profiles among Nigerian are similar to those reported in other black populations for certain auto antibodies but differ widely in others. However, all the profiles differ from other reported non black populations. Such variations may be real but could also be due to the varying methods of assay. The number of subjects is however rather small to reach any definite conclusion. However, for a disease hitherto said to be rare among African blacks, the result will provide a point of reference for future studies.

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Antinuclear antibodies

This was possible in all the 95 patients. 91 (95.7%) were positive while the remaining 4 were negative[Table 2]. With a normal positivity of titres not exceeding 1:40, most subjects had significantly positive ANA result with a large number (74.7%) having positive results at titre of 1:160 and above. Two patients were however reported as being positive for ANA without the titre stated. Both however were positive for ds DNA. The patients who were negative had positive ENA screen. One also had positive dsDNA in addition.

The staining pattern was mostly speckled (77.5%); homogeneous- 16.2%; speckled + homogeneous - 3.8%; ribosomal. 2.5%.

Rheumatoid factor

As shown in Table 3, 24 sera (42.1%) were positive for rheumatoid factor out of the 57 sera tested.

Extractable nuclear antigen (ENA)

A total of 44 patients had ENA screen, out of which 35 (79.5%) tested positive. Various components of the extractable nuclear antigen were also assayed as shown in Table 3 with a large percentage of the sera tested being positive for anti-Sm (75.7%). The others were anti-RNP- (81.8%), Ro/SS-A (69.7%), anti chromatin (66.7%). However a smaller number of patients, 5 out of 33 tested (15.2%) had positive result for La/SS-B.

Anti-ds DNA

As shown in Table 3, out of the 68 sera tested, 37 (54.4%) were positive for Anti dsDNA.

Anti-cardiolipin antibody

Thirty eight sera were tested for Anti cardiolipin antibody. Of this, 11 were positive for IgG ACA while only 3 were positive for IgM ACA, both, however at low to moderate titres.

Discussion

Auto antibodies are normally produced in response to tissue breakdown induced by trauma and infections. Such antibodies are however short-lived. It has been suggested that auto antibodies production in auto immune diseases are initiated as response to dying cells but that such immune response is not regulated appropriately. A direct pathogenetic role of auto antibodies has also been suggested though this is controversial [5].

ANA is invariably positive in lupus patients although the frequency of positivity varies with the methodology of assay. The highest is found when human epithelial cells (Hep 2) are used as substrate. The sensitivity of ANA is almost 100% when this substrate is used [8]. However the frequency differs in different populations, though they are invariably found in over 90% of SLE sera . Approximately 5% of SLE patients do not demonstrate the classic antibody systems such as ANA. Such patients tend to have more skin rash, photosensitivity, serositis and Raynaud's phenomenon. Such patients invariably demonstrate positive Ro (SS-A) [9]. Four patients (4.2%) in our study did not demonstrate positive ANA though their ENA screen was positive.

The titre positivity of ANA in our study is rather high, with 57.8% of our subjects having titres of 1:320 and above (Table 2). Reports among Omani SLE patients however show a much higher frequency of 93.3% at such titre [10]. Many studies have put a titre of 1:160 or higher as being supportive of diagnosis of SLE.

However other studies have suggested such titres of 1:80 [11] and 1:40 [12]. 92.7% of our subjects in this study had positive titres at 1:80 and above. The dominant staining pattern in many reports is usually homogeneous. However, 77.5% of our patients had speckled staining pattern with 16.5% having homogeneous pattern. 3.8% had combination of homogeneous and speckled staining patterns while 2.5% had ribosomal staining pattern. Our findings are comparable with reports from Saudi Arabia with 74.5% of SLE patients having predominantly speckled pattern, with homogeneous 9.4%; anti mitochondrial 7.5%; ribosomal 4.7% and nucleolar 3.8% [13]. Reports from India on the contrary showed predominant homogeneous pattern (45.5%); speckled (35.6%) amongst others [14]. It has been reported that black patients have a lower prevalence of photosensitivity [2, 15]. This has been attributed to presence of protective ANA [15].

Anti-DNA is specific for SLE [16] and the reported frequencies among SLE patients vary widely. Our frequency of 54.4% is comparable with those among South African blacks at 66.2 % [6] and among Tunisians at 56 % [17]. It however contrasts with the frequency of 27.5% among Jamaican blacks [15] .

In view of the cost of serology tests to, most of our patients had only screening test for ENA and only those who could afford it had the constituents carried out. Of the 44 that had the screen, 79.5% were positive (Table 3). Tikly [18] has reported high frequencies of antibodies to ENA, especially Anti-Sm and RNP, in many developing countries. As shown in Table 3, anti Sm is seen in 75.7% of our patients while a lower frequency of 44.2% was reported among South African black patients and a significantly

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Introduction

Eighty five per cent of cervical cancer deaths occur in developing countries [1]. Unfortunately, the majority of women in these countries never undergo cervical cancer screening and many die without knowing that the cause of their disease was preventable. Because of organized cervical screening services in developed countries, mortality from invasive cervical cancer is rare indeed. The opportunistic screening offered in most developing countries hardly cover for the at risk women thereby leaving cervical cancer as the leading cause of cancer related deaths [1,2].

Facilities for Papanicolaou smear are hardly found in rural areas in developing countries where the majority of the population at risk resides. No wonder, therefore that the characteristics of patients with cervical cancer in our environment are poverty, illiteracy and rural abode [1]. In some urban areas where screening services are available, most of those who are opportunistically screened are the young, more enlightened women who are at low risk [1-4].

Although the knowledge of cervical cancer was extremely poor in the past [5], it has improved over the years [6]. The same is true regarding awareness of preventive methods. However, the utilization of cervical cancer screening services is still very low [7,8]. This is in spite of the fact that cervical cancer is the leading cancer in women in sub-Saharan Africa [9]. This study is therefore aimed at finding out the profile of women who avail themselves of screening services. Information so obtained will be useful in formulating strategies for cervical cancer prevention.

Materials and methods

This cross sectional, questionnaire based study was conducted among women attending the outpatient clinic in the department of Obstetrics and Gynaecology of the University of Maiduguri Teaching Hospital (UMTH), Maiduguri, and the Federal Medical Centre Yola (FMCY) between June and August 2010. A validated structured questionnaire was used for this study. The questionnaire included both close-ended questions and multiple response open-ended questions. It consisted of 25 questions in three sections. Section 1 included questions on socio-demographic information, section 2 was on knowledge of cervical cancer and section 3 was on attitude and practice of screening. Potential participants were identified as adult women of reproductive age group (15years and above) who attended the two tertiary institutions' Gynaecological clinics during the study period. Sampling was done by convenience sampling through approaching all eligible women who presented to the Gynaecological outpatient department. Initially, the women, as well as the clinic staff who assisted in data collection were informed regarding the purpose of the study. All participants were given full explanation of the methodology and purpose of the study and assurance of confidentiality. Participants were also assured that their participation in the study was voluntary and that they could refuse to participate at any time during the interview. No personal identifying information was collected in the anonymous questionnaire. The questionnaires were then handed out to the women who gave verbal consent and were interested in participating. Help was given to some of the women in the interpretation of the questionnaires. This included both conceptual and written help especially to those who could not write well. A minimum sample size was calculated using a standard formula for known population size for a cross sectional study (Yamane Formula) [10], and was found to be 240. However, to overcome risks of non-responses or poorly answered questionnaires and since convenience sampling was used to interview the participants, 10 extra questionnaires were distributed, and this brought the sample size to 250 participants. After collection, data was verified, coded and transferred into an IBM compatible PC and analyzed using SPSS (SPSS Version 16 Inc., Chicago, USA 2006). Simple descriptive univariate analysis was performed to determine the frequency of the various factors. Means and standard deviations for continuous variables were computed. Bivariate and stepwise multivariate logistic analyses were used to evaluate the effects of the socio-demographic and reproductive characteristics of women on their knowledge and utilization of Papanicolaou smears by estimating odds ratios and their 95% confidence intervals. The model used an entry criterion of P= 0.05 and removal criterion of P = 0.051. Variables that did not fulfill these criteria were removed from the model. The study protocol was approved prior to the implementation of the study by the ethical committees of UMTH and the management of FMCY

Results

A total of 250 women of reproductive age were interviewed during the study period. Fifteen (15) questionnaires were excluded from analysis because of incomplete responses, giving a response rate of 94%. Table1 summarizes socio-demographic and reproductive characteristics of the study participants. Highest numbers (67) of the respondents were in the 25-29year age group (27.2%). Majority (71.1%) of the women were married and sexually active, 47.2% were multiparas, 54.1% were unemployed housewives and 61.3% had tertiary education.