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Different techniques to assess microvascular damage in systemic sclerosis

Ruaro B1, Sulli A1, Smith V2, Paolino S1, Pizzorni C1, Cutolo M1

Blood perfusion
Systemic Sclerosis (SSc) is a connective tissue disease with multifactorial aetiology and autoimmune pathogenesis. SSc is characterized by structural and functional alterations of microcirculation, with important clinical implications, such as Raynaud Phenomenon (RP) and digital ulcers1,2. For these reasons, morphological and functional assessment of the peripheral microvasculature is a must for diagnosis, prognosis and therapy in SSc patients2.

Nailfold videocapillaroscopy
Nailfold videocapillaroscopy (NVC) is the best safe and non-invasive method to detect morphological microvascular abnormalities. NVC allows to distinguish secondary RP from both primary RP and healthy subjects, identify morphological patterns that are specific to various SSc stages (‘Early’, ‘Active’ and ‘Late’ patterns of microvascular damage) and calculate the Microangiopathy Evolution Score (MES) to follow disease evolution3,4.

The video-capillaroscope makes use of a magnification system (from 50x up to 500x magnification), and it has an optical/digital probe which can be moved over the surface of the finger nails from the 2nd to the 5th finger of both hands2. The normal NVC image is characterized by normal skin transparency, morphology of the capillary to “U” or “hairpin shape”, morphological/structural homogeneity, 10-12 capillaries / linear millimetre, one capillary inside dermal papilla, diameters of capillary branches <20 μm, and lack of morphological atypia2. Nailfold capillaries are frequently normal in primary RP, but it is possible to observe capillaries with efferent branch enlargement or tortuous capillaries. Therefore in normal conditions, or in the presence of primary RP, the NVC examination is characterized by a regular array of capillary loops along the nailfold bed, without abnormal enlargements nor capillary loss. Conversely, secondary RP is characterized by the morphological signs that represent the microvascular damage: these include giant capillaries, microhaemorrhages, capillary loss, presence of avascular areas and angiogenesis. These sequential capillaroscopic changes are typical of the microvascular involvement observed in more than 95% of SSc patients and are described by the term “SSc pattern”2,3.

NVC technique identifies morphological patterns specific to various stages of SSc (‘Early’, ‘Active’ and ‘Late’ patterns)3,4. The ‘Early’ SSc pattern is characterized by few enlarged/giant capillaries, few capillary microhaemorrhages, no evident capillary loss and a relatively well preserved capillary distribution. The ‘Active’ SSc pattern, a marker of disease progression, is characterized by frequent giant capillaries (more than 66%), frequent capillary microhaemorrhages, moderate (up to 33%) capillary loss, absent or mild ramified capillaries and a mild disorganization of the capillary architecture. In the ‘Late’ SSc pattern there is irregular enlargement of the capillaries, severe (>66%) capillary loss with evident avascular areas, ramified or bushy capillaries and a severe disorganization of the normal capillary array, although giant capillaries and microhaemorrhages are almost absent3,4 (Figure 1). NVC is also used to make a quantitative assessment (i.e. quantify certain characteristics and make semi-quantitative scoring) of the microvascular damage. The usual capillaroscopic parameters (diagnostic parameters, such as irregularly enlarged capillaries, giant capillaries, microhaemorrhages; and progression parameters, such as reduced capillary number, capillary ramifications and capillary architectural disorganization) are evaluated by a semi-quantitative scale. Score 0-3 has been adopted for all these parameters3,4.
Figure 1: Nailfold videocapillaroscopy images (x200) in healthy subject (A), early (B), active (C) and late patterns of scleroderma microangiopathy (D)

A “Microangiopathy Evolution Score” (MES) (the sum of progression parameters; score 0-9) was also selected to assess the vascular damage progression\(^7\). Data provided by NVC are also markers of SSc severity and progression, such as reduced capillary density, which has been associated with a high risk of developing digital skin ulcers and pulmonary arterial hypertension\(^3\). The inclusion of the NVC patterns in diagnosis could increase the sensitivity of classification criteria for SSc\(^6\).

**The analysis of the peripheral blood flow**

Assessment of the peripheral circulation may also be useful for the evaluation of some drug effects, better if performed along with blood perfusion\(^2\). However, capillary blood flow/perfusion cannot be quantitatively measured by NVC in standard conditions, as only a qualitative evaluation may be performed. Blood flow may be assessed by NVC as regular, granulous, or stasis\(^5\). The assessment and quantify of cutaneous blood perfusion in SSc may be performed by different laser techniques and by thermografy\(^9\). Other emerging technologies (e.g. optical Doppler tomography and spectroscopy) are possibly used to evaluate skin flow\(^10\).

**Different methods to analyse the peripheral blood flow Laser techniques**

The different laser techniques most commonly used to assess vascular impairment in SSc are: Laser Doppler Flowmetry (LDF), that assesses and quantifies the blood perfusion at a single skin point (1 mm\(^3\)); Laser Doppler Imaging (LDI), that measures blood flow of an area; Laser Speckle Contrast Imaging (LSCI), that quickly measures blood flow of an area (the contrast is calculated based on one pixel in a time sequence); Laser Speckle Contrast Analysis (LASCA), that quickly quantifies the blood flow of an area (the contrast is calculated based on multiple pixels in one image), allowing analysis of specific areas in a second time \(^{10,11}\).

**Laser Doppler techniques**

LDF is a non-invasive and user-friendly method to assess microvascular flow at a single skin point. It provides an index of skin perfusion by measuring the Doppler shift induced by coherent light scattering caused by moving red blood cells\(^{11,12}\). The blood perfusion evaluated by LDF is recorded as Perfusion Units (PU) and it is represented in a graph. Moreover, LDF technique may evaluate blood perfusion at basal finger temperature (usually at the level of fingertips from 2\(^{nd}\) to the 5\(^{th}\) digit on both hands), and the capillary dilation capacity after having heated the probe to 36°C\(^{11,12}\).

Some studies have demonstrated that SSc patients have a lower blood flow than both healthy subjects and primary RP patients and that patients with the ‘late’ SSc microangiopathy pattern on NVC had a lower blood flow at LDF than patients with ‘active’ and ‘early’ SSc NVC patterns\(^{11-13}\). SSc patients have also an abnormal microvascular regulatory responses to heat stimulation\(^1\).

LDF is also efficacious for the evaluation of the variation in peripheral blood perfusion during treatment with vasodilatation drugs within a few days or even over a long follow-up period of years\(^{11,12}\). Sulli et al\(^{14}\) in a recent study have demonstrated, in SSc patients, the correlation between blood perfusion, evaluated by LDF, and dermal thickness, measured with high frequency ultrasound, at fingers level.

One problem with the LDF technique is the large site-to-site variation, which limits its efficacy in comparing blood flows between sites and in monitoring change over time\(^{10,11}\). Laser Doppler Imaging (LDI), which evaluates blood flow over a skin area might overcome this problem\(^\text{10,11}\). Murray and colleagues\(^9\) showed that NVC, LDI, and thermal imaging (another technique to measure indirect blood flow) each independently provide good discrimination between patients with SSc and those with primary RP and healthy controls. In conclusion, they observed that the combination of all three techniques improves classification of SSc patients and that LDI and thermal imaging give equivalent information on dynamic changes in the cutaneous microcirculation. The study also confirms that NVC is the best method to classify patient groups.

**Laser speckle contrast techniques**

Laser Speckle Contrast Analysis (LASCA) is a relatively new technique to quantify blood perfusion. LASCA is based on the principle that when laser light illuminates a tissue, it forms a speckle pattern. Changes in the speckle pattern are recorded by a Charge-Coupled Device (CCD) camera and analyzed by a software. The static areas result in a stationary speckle pattern, in contrast the moving objects (e.g. red blood cells) cause the speckle pattern to fluctuate and appear blurred. Level of blurring (contrast) is analyzed and interpreted as blood perfusion\(^{10,13,15}\).

LASCA has the advantages to quantify the blood flow
over an area and to be a non-contact technique. It is a fast imaging technique and with a high resolution. It combines perfusion image and real-time graphs (Figure 2). The blood perfusion is reported in perfusion units (PU)\(^1\). With LASCA it is also possible to create different regions of interest (ROI) and time regions of interest (TOI) to evaluate the perfusion. LASCA has been applied in research studies on RP and SSc\(^{13,15,16}\). One such study demonstrated that peripheral blood perfusion evaluated by both LDF and LASCA correlates to the extent of the microangiopathy\(^1\). It also reported that when evaluated by both methods, patients with the ‘Late’ SSc microangiopathy pattern had a lower blood flow than patients with the ‘Active’ or ‘Early’ SSc patterns on NVC\(^1\).

**Figure 2:** Laser speckle contrast analysis images of hand palmar aspect in healthy subject (A) and patient with a “Late” pattern of scleroderma microangiopathy (B). Blue colour = low blood perfusion, yellow colour = intermediate blood perfusion, red colour = higher blood perfusion

In another study we have showed that BP, as assessed by LASCA technique, is significantly lower in SSc patients in comparison with healthy subjects at the level of fingertips, periungual areas, and palm of hands, and a statistically significant negative correlation exists between nailfold microangiopathy extent and BP values at the level of the same skin areas in SSc patients\(^6\). In our last study we have demonstrated that LASCA may safely monitor digital ulcers evolution in SSc patients, by evaluating their blood perfusion and area during standard treatment\(^7\). The instrumentation of Laser Speckle Contrast Imaging (LCSI) is similar to LASCA but the contrast is calculated in single pixel over a number of time frames. Spatial resolution increases five times over LASCA but poor temporal resolution. Processing takes quite longer time than LASCA due to calculation over number of frames.

**Thermal imaging or infrared thermography**

Thermal Imaging (TI) is a method that evaluates indirectly the perfusion, by using a thermal camera to image the temperature of the skin, and it was shown to be representative of underlying blood flow\(^7\). In several studies TI was used for the evaluation of RP, and the response to cold change was reported to be able to differentiate between primary RP and SSc. Distal dorsal difference > 1°C between one or more fingertips and the dorsum of the hand (fingers cooler) at 30°C is predictive of a SSc-spectrum disorder\(^1\). This method has several limitations (e.g. poor sensitivity to detect variations of blood perfusion and low spatial resolution).

**Conclusions**

The growing interest in the microcirculation caused a rapid development of new methods for its assessment, but all techniques require studies to validate their use in clinical practice. The NVC is currently the only validated method to study microvascular morphology for the evaluation of capillary abnormalities to distinguish secondary RP (associated to connective tissue disease) from primary RP. For this reason abnormal capillaroscopy is also one of the new classification criteria for SSc\(^6\).

The evaluation of microvascular structure by NVC, in combination with function by laser techniques or thermal imaging, not only can help to distinguish between primary RP to secondary RP, but also to evaluate the response to therapy, and the disease progression\(^7\)\(^11\)\(^12\). It would therefore be desirable that these techniques should have a wide diffusion in the clinical rheumatological practice.

**Key words:** Systemic sclerosis, Cutaneous microcirculation, Nailfold videocapillaroscopy, Laser techniques

**Competing Interest:** None declared.

**References**


DMARD use in rheumatoid arthritis: can we predict treatment response?

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**Abstract**

**Objective:** To review the current and emerging predictors of treatment response by DMARDS in Rheumatoid Arthritis (RA) patients.

**Data source:** Published original research work and reviews were searched in English related to determinants of treatment response in rheumatoid arthritis on DMARDS

**Study design:** Only articles that emphasis on determinants of rheumatoid arthritis treatment response with DMARDS

**Data extraction:** Online and library searches done.

**Data synthesis:** Data added and summarized

**Conclusions:** Treatment of RA has been based on the use of a group of Disease-Modifying Anti-rheumatic Drugs (DMARDs), of which methotrexate is the most widely used. Although comprehensive clinical experience exists for MTX and synthetic DMARDs, to date it has not been possible to predict correctly whether or not a patient will respond to treatment with these drugs. Predicting response to MTX and other DMARDs would allow the selection of patients based on their likelihood of response, thus enabling individualized therapy and avoiding unnecessary adverse effects and elevated costs. Distinguishing responders from non-responders at treatment start as studies have failed to consistently reproduce similar determinants. Variables possibly influencing drug effectiveness may be related to disease, patient, treatment, clinical or biological (genetic and non-genetic) factors. This study seeks to review the current data regarding biomarkers of treatment response to DMARDS.

**Key words:** Rheumatoid arthritis, DMARDS, Determinants of treatment response

**Introduction**

Current rheumatoid arthritis management emphasises the benefits of early Disease-Modifying Anti-Rheumatic Drugs (DMARDs). These agents are characterised by their ability to reduce or reverse signs and symptoms, disability, impairment of quality of life, inability to work, and progression of joint damage and thus to interfere with the entire disease process. DMARDs form two major classes: synthetic chemical compounds and biological agents. Examples of synthetic DMARDs include methotrexate, hydroxychloroquine, lefunomide, sulphasalazine and azathioprine. Rheumatoid Arthritis (RA) treatment has changed dramatically during the last decade after the introduction of biologic DMARDs that target important mediators of the immunological mechanisms in RA. Examples of biologic DMARDs include Tumour Necrosis Factor (TNF) inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab and infliximab), the T cell co-stimulation inhibitor, abatacept, the anti-B cell agent, rituximab, the interleukin (IL)-6 receptor (IL-6R)-blocking monoclonal antibody, tocilizumab and the oral Janus Kinase inhibitor molecule tofacitinib. The benefits from using DMARDs extensively must be balanced against patients’ wishes to minimise drug use, potential toxicities, and costs of long-term DMARDs. One of the main challenges in RA management for over two decades has been the ability to predict treatment response to DMARDs.

This would be of benefit in several ways. Identifying patients less likely to respond will avoid needless exposure to potentially toxic drugs and the waste of precious time to achieve disease control, a crucial endpoint to prevent development of structural damage<sup>1</sup>. Likely responders would be maintained with the most appropriate DMARD with more certainty, avoiding an early or possibly unnecessary, switch to other potentially less effective DMARDs or to more costly biologicals. This will lead to having a more personalized tailor made therapy for each patient. While predictors of poor RA prognosis are well established<sup>2, 3</sup>, they do not accurately correlate with response to treatment. This is because a heterogeneous response is most likely the result of multi-
factor interactions and cannot be explained by a single cause-effect mechanism. Factors that possibly influence drug effectiveness can be divided into patient-related (age, gender, ethnicity, comorbidities), disease-related (duration, activity, disability, biomarkers), treatment-related (compliance, dose, previous drugs) and genetic factors. We conducted a literature review on current available data on predictors of response to DMARDs (clinical factors, non-genetic biomarkers and genetic biomarkers), discuss and analyse the possible translation into clinical practice.

How to assess for treatment response

The goals in treating patients with rheumatoid arthritis are managing the symptoms of disease, preserving joint structure and achieving disease remission. Studies have shown that treatment decisions driven by quantitative rather than subjective monitoring of disease activity result in significantly improved patient outcomes. Various assessment tools are available that measure both clinical and patient-reported outcomes. Some measurement tools may be more appropriate for use in clinical trials, several have been developed that are simple and practical to use, even in a busy clinic. They are many tools, the most common being the CDAI, DAS28 (ESR or CRP), PAS, PAS-II, RAPID-3, and SDAI. These six produce a single continuous index and have defined ranges for indicating low, moderate, or high disease activity or clinical remission. These clinical assessment tools are indicators that measure different aspects of RA and have their pros and cons. Tools such as the Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI) were designed for use in clinical practice. They are both derived from the DAS28 and have high correlations to DAS28 scores. However, both the SDAI and CDAI are simpler to use and easier to calculate than the DAS28. The SDAI and CDAI include 28-joint counts, patient global assessment of disease activity, and physician global assessment of disease activity. Unlike SDAI, CDAI does not require a blood test for evaluation of an acute phase reactant; therefore, complete results can be obtained and used to drive treatment decisions at the same time as the patient’s visit.

Clinical, radiographic, and biochemical markers of DMARD response

Several clinical, radiological and biochemical factors have been studied. It has been difficult to reach a consensus on which factors can predict the response to treatment with DMARDs. Most studies have evaluated responsiveness to methotrexate.

Gender

A systematic review by Drouin et al found that male gender was associated with a better clinical response to MTX both in early and established RA. Similar conclusions were reached in a large meta-analysis of Randomized Controlled Trials (RCTs) by Anderson et al n 1,435 patients, in terms of achieving American College of Rheumatology (ACR) 20 responses. Saevardsdottir et al, in a population of early RA patients (SWEFOT trial) also reported a worse European League Against Rheumatism (EULAR) response in women (odds ratio (OR) = 0.50, 95% confidence interval (CI) 0.31 to 0.81). Stranzl et al also found female sex to be an independent predictor of poor response to MTX (OR = 3.3, P = 0.009). Vázquez et al reported in early RA patients, male gender was associated with remission after two years of MTX ± gold treatment in the univariate analysis but not in the multivariate analysis. It seems that most of the evidence points in the direction of male gender being a predictor of good response to MTX in both early and established RA. A predictive model for 24-month remission was developed for patients with early RA treated in a RCT with MTX ± corticosteroids ± cyclosporine; it was validated in an early RA cohort (ERAN) of patients treated with MTX or other conventional DMARDs. The authors concluded that one of the three variables that predicted remission at 24 months was male gender (OR = 3.14, P <0.001). As in this latter study, most of the analyses of response to other DMARDs have been done together with MTX, so their individual effect is difficult to predict. A meta-analysis and an observational study from the 1990’s, comprising a significant number of patients, demonstrated that gender did not influence the response to treatment with sulphasalazine, gold and penicillamine. Another open label trial showed no influence of gender on whether patients with early RA started on hydroxychloroquine would have to step up therapy to MTX. Other studies have also failed to detect a significant effect of gender on treatment response to DMARDs, other than MTX. Overall, it seems that under the light of current evidence it is not possible to generalize the better response to MTX treatment seen in men to other conventional DMARDs. Hider et al postulated that gender influence on MTX responsiveness, is due to hormonal factors influencing the pharmacokinetics and pharmacodynamics of each drug thus contributing to a better or worse response. This may explain the apparent discrepancy in the influence of this factor on different DMARDs.

Most research has found that male patients are more likely to respond or achieve remission with TNFi. This was reported by Kleiner et al who evaluated adalimumab in 2,625 RA patients, the Research in Active RA trial (ReAct), a 12-week study open label on adalimumab that enrolled 6,610 RA patients and the Trial of Etanercept and Methotrexate with Radiographic Patient Outcomes (TEMPO) that had 682 patients receiving ETN. In the 540 RTX-treated patients included in British society of
rheumatology biologics register who had at least one TNFi failure, female sex was significantly associated with lower odds of disease remission\textsuperscript{18}.

Age

Age seems to be a predictive factor of response to biologics unlike MTX or other DMARDs. Most studies showed a lack of effect of baseline age on clinical response to MTX therapy, including two large meta-analyses\textsuperscript{6}. Some studies have contradicting results, such as the SWEFOT trial\textsuperscript{18} which showed that older age was associated with a higher likelihood of both EULAR and the Clinical Disease Activity Index (CDAI) response to MTX treatment at three to four months. Another study by Ma et al\textsuperscript{22} showed older patients (>50 years old), on the contrary, were less likely to be in remission at 24 months after the start of MTX + cyclosporine. Thus, despite these two early RA studies, where age seemed to influence response to MTX treatment, although in opposite directions, most studies, including large meta-analyses, showed that age is not a predictor of response to MTX. There is limited literature on other conventional DMARDs. One study showed that younger patients respond better to SSZ, with no effect of age on the response to penicillamine and gold\textsuperscript{27}. All other publications excluded age as an independent predictive marker of response to conventional DMARDs\textsuperscript{10, 19, 20}.

Data on biologics favours age as a predictive factor. Kleinert et al and the ReAct study found younger patients had better clinical outcomes\textsuperscript{21}. Tocilizumab in the Japanese multi-centre retrospective study (REACTION) revealed that younger age was independently associated with a good EULAR response and remission at 24 weeks\textsuperscript{22}. No association between clinical response and gender or age were found in the South Swedish Arthritis Treatment Group Register, the Orencia and Rheumatoid Arthritis and British Society for Rheumatology Biologics Register (BSRBR) between EULAR responders and non-responders\textsuperscript{23-25}.

Smoking

Smoking has a negative impact on disease outcomes and is associated with higher disease activity\textsuperscript{26}. In early RA, current smokers respond worse to MTX treatment. Wessels et al\textsuperscript{27} showed that early RA patients have a worse response to MTX monotherapy were associated with smoking and positive rheumatoid factor. In an early RA cohort, where 873 patients started MTX monotherapy at inclusion, current smoking was independently associated with significantly worse early and late EULAR, Disease Activity Score (DAS) 28 and joint count responses, when adjusted for other clinical, serologic and genetic factors (OR = 0.60, 95% CI 0.39 to 0.94)\textsuperscript{6}. SWEFOT trial done on a similar population showed that current smoking was the strongest predictor of achieving a poor response\textsuperscript{6}. Studies have shown that smokers tend to consume a higher number of conventional DMARDs over time, suggesting that smoking can reduce therapeutic efficacy and that non-smokers are more likely to achieve an ACR response than smokers\textsuperscript{28}. Saeverrdsdottir et al\textsuperscript{9} proposed that smoking may interfere with the pharmacodynamics and pharmacokinetic properties of the drugs, thus altering responsiveness. Stamp et al\textsuperscript{29} showed that smokers have reduced intracellular levels of some MTX polyglutamates, suggesting that MTX metabolism is altered which leads to a poor response. Whatever the mechanism, active smoking is an important modifiable factor that seems to be associated with a poor response to MTX. Tobacco discontinuation should be encouraged and considered an important part of the therapeutic approach.

BSRBR patients who smoke cigarettes have a lower treatment response to infliximab\textsuperscript{29}. This result was duplicated in other studies such as a retrospective case control study of 395 RA, in a prospective cohort of 617 Portuguese and in a Swedish register that included 1,998 early RA (Epidemiological Investigation of Rheumatoid Arthritis EIRA)\textsuperscript{8, 30-31}. However, smoking cessation has not been associated with increasing the chance of response to therapies. A Swedish study on 1,460 RA patients with early disease and had patients who had quit smoking found no difference in treatment response between the smokers and those who quit (BARFOT (better anti-rheumatic pharmacotherapy)\textsuperscript{32}. No data is currently available on the influence of smoking on response to TCZ, ABA, or RTX.

Disease activity and severity

Data on disease activity at baseline as a potential marker of response have yielded inconsistent results. This can be related to the different clinical instruments and response criteria used in the studies. Disease activity can be assessed using clinical-laboratory variables (CRP), Erythrocyte Sedimentation Rate (ESR), Tender Joint Count (TJC), Swollen Joint Count (SJC), global assessment of disease activity on a Visual Analogue Scale (VAS) or by composite scores (DAS, DAS28, CDAI, Simplified Disease Activity Index (SDAI) and different criteria are used to define response (EULAR, ACR, DAS/ SDAI remission). It is thus important to consider this information when interpreting literature data. A meta-analysis by Drouin et al\textsuperscript{33} identified high disease activity at baseline as measured by DAS or SDAI as a predictor of a weak response to MTX monotherapy. Wessels et al\textsuperscript{27} also found poor response to MTX monotherapy in an early RA population was associated with high DAS and high SJC were associated with a poor response to MTX monotherapy as defined as achieving a DAS ≤2.4 at 6 months. Other factors such as VAS, ESR and CRP had no effect on response. In established RA, higher disease activity defined by DAS has been associated with decreased likelihood of response to MTX\textsuperscript{34}. Studies by Aleisha et al\textsuperscript{34} and Saevardottir et al\textsuperscript{35} showed that early RA patients with higher baseline SDAI (but also CDAI and DAS28) were less likely to achieve remission or low disease activity on MTX monotherapy. Vázquez et al\textsuperscript{36} demonstrated that in early RA, patients with low
to moderate disease activity at baseline were four times more likely to be in remission after two years of MTX ± gold therapy. Two other studies also demonstrated that in patients with recent onset RA treated with MTX, SSZ or both, a lower baseline DAS was predictive of remission at two, three and five years.\textsuperscript{33-36}

The literature seems to show that when disease activity is assessed by composite measures, lower activity at baseline predicts better responses to MTX. When disease activity is determined by isolated laboratory and clinical variables, evidence is inconsistent. Anderson \textit{et al}\textsuperscript{17} found lower patient, but not physician, global assessment at baseline to be predictive of worse response to MTX and other DMARDs. This contradicts with the above and other studies. High SJC has been found to predict poor response to MTX in early RA by Wessels \textit{et al}\textsuperscript{7}. This was not confirmed in established RA\textsuperscript{27, 37}. Ma \textit{et al}\textsuperscript{12} showed that a TJC higher than 5 at baseline decreased the likelihood of achieving DAS remission at 24 months. This was independent of effect for SJC. Verstappen \textit{et al}\textsuperscript{18} determined a lower Thompson joint score at baseline as predictive of remission patients treated with MTX, gold or HCQ. Majority of the data where SJC and TJC as isolated variables have been identified not to be predictors of response to treatment with MTX and other DMARDs\textsuperscript{36, 39-40}. As a whole, these data suggest that low disease activity defined by isolated clinical variables is probably associated with a better response to treatment as part of composite measures. Composite scores such as DAS or SDAI, are better predictive tools.

Similarly, role of inflammatory markers to assess disease activity is also far from being in consensus. Meta-analysis by Drouin \textit{et al}\textsuperscript{9} determined neither CRP nor ESR were predictors of response to MTX monotherapy. Other studies regarding therapy with MTX ± other DMARDs have shown no effect of ESR and/or CRP on treatment response\textsuperscript{9-12, 36, 39}. One study by Combe \textit{et al}\textsuperscript{9} identified ESR and CRP as two of the five independent predictive factors of disability at five years in early RA patients treated mainly with MTX and SSZ. Data on other DMARDs is also inconsistent. A low baseline CRP was the only predictor of a favourable response to HCQ monotherapy in early RA patients which contradicts Matteson \textit{et al}\textsuperscript{40} found that ESR had no influence. Van Roon \textit{et al}\textsuperscript{15} identified that the lower the ESR (<35 mm.h-1) at initial treatment Initiation was able to predict better response to leflunomide. Contrary to these findings, Capell \textit{et al}\textsuperscript{40} observed that a lower ESR was associated with a worse response to gold, penicillamine or SSZ. As a whole, these results are not sufficient to state whether ESR or CRP alone are predictive factors of response to MTX and other DMARDs. While some studies showed a significant association between inflammatory markers and response, usually with higher baseline values associated with weaker treatment responses, others, including large meta-analyses, do not find these variables to be good predictive markers, at least when considered independently. In the light of current evidence, for the purpose of predicting DMARD response, it is probably better to integrate ESR and CRP components as part of disease activity scores and not judge them individually. Disease severity and disability at baseline have been proposed as being predictive of treatment response. Using the Steinbrocker criteria to identify a lower functional status, Anderson \textit{et al}\textsuperscript{7} found it to be associated with a weak response to MTX and other DMARDs. Other RA studies found that patients with low baseline Health Assessment Questionnaire (HAQ) score treated with MTX, SSZ,HCQ or in combination were more likely to be in remission (DAS < 1.6) at two or three years.\textsuperscript{8, 27, 36, 43}

However, several studies showed contradictory results, with baseline HAQ not being an independent predictor of responsiveness to MTX and other DMARDs\textsuperscript{3, 12, 20, 37, 41}. While some studies seem to suggest that a higher HAQ predicts a weaker response to MTX and other DMARDs, several other studies with similar populations did not confirm this association.

Most studies on TNF inhibitors, patients with higher baseline HAQ scores are less likely to respond or to achieve remission\textsuperscript{16-18, 23, 31}. Studies have also shown that higher baseline DAS28 scores are a good predictor of DAS28 decrease\textsuperscript{16, 17, 21, 23, 24}. Similar finding were found for other therapies. In the 97 patients treated with TCZ registered in the nationwide Danish DANBIO registry, lower HAQ score at baseline was associated with EULAR response and higher DAS28 at baseline was significantly associated with achieving a low DAS28. The ORA registry identified higher initial DAS28 in ABA responders (5.4 (4.7–6.5)) than in non-responders (4.9 (4.0–6.0), p < 0.0001)\textsuperscript{27}. Several studies on rituximab have also showed association between EULAR response and low HAQ, high DAS28 and low number of previous biological agents\textsuperscript{18, 43-44}.

**Duration of disease**

It has been widely shown that treatment of early RA yields better results than treatment of established disease\textsuperscript{35-46}. This has led to the concept of ‘window of opportunity’. Longer disease duration was identified by Anderson and colleagues’ in a meta-analysis as the most important factor to predict worse response to MTX. Similar findings have been reported in other studies, regarding both MTX and other conventional DMARDs\textsuperscript{6, 8, 13, 15}. However Hoekstra \textit{et al}\textsuperscript{13} in a RCT on 411 patients treated with MTX did not find an association (although the mean disease duration was lower). Several other studies have found no association with MTX and other DMARDs\textsuperscript{6, 10-12, 27, 47}. Discrepancies in these results may be due to evaluations performed mostly in established RA patients, who probably have a more uniform response to MTX, or in early RA populations that have short-term disease and a narrow disease-duration span making it harder to detect differences in response rates. In conclusion while it is likely that patients with early disease respond better than those with established RA, disease duration seems to lose its negative influence with long-term progression of disease and this might confound the results of studies addressing this factor.
RA drugs history: prior and current

Despite the existence of a few reports suggesting that previous DMARD use does not affect response to further treatments. Most literature findings include references to a negative effect of previous DMARD use on the response to treatment with MTX and other DMARDs. Lie et al. found that patients who had previously taken other DMARDs had significantly lower response rates to MTX monotherapy. Similar findings by Aletaha et al. in patients taking consecutive DMARD courses, with the first DMARDs obtained a greater decrease in C reactive protein (CRP) than subsequent ones. Based on these studies, the absence of any past DMARD therapy was identified as one of the predictive factors of a favourable response to MTX monotherapy. Another study reported that the DMARD response was higher when started after non-steroidal anti-inflammatory drugs (NSAIDs) than following another DMARD. One reason postulated was that patients who do not respond to a certain drug might have a globally more severe and less responsive disease, but other mechanisms might explain these observations. Hider et al. proposed that previous therapies may alter drug kinetics and influence metabolism in such a way that the effectiveness of subsequent drugs can be lowered. This hypothesis has not been adequately tested so far. Concomitant NSAIDs has been associated with an increased efficacy of MTX monotherapy in established RA and a similar but weak association was found in early RA (OR = 1.31, 95% CI 0.84 to 2.06). Further studies on effect of NSAIDs are needed to confirm this association, although a beneficial effect may be expected.

Data on use of concomitant corticosteroid therapy are more difficult to interpret because of different doses and timings for starting steroids (before DMARD therapy, during, or both). Saevarsdottir et al. found that RA patients who responded early were already on stable low-dose prednisolone at the start of MTX (OR = 2.84, 95% CI 1.43 to 5.63). Hider et al. identified that absence of steroid use predicted MTX inefficacy at two years, but not at one year. These results are in agreement with trials that showed that patients treated with combination therapies including steroids have better responses than those on DMARD monotherapy. However, some studies have found no association between corticosteroid use and DMARD response. Despite these latter findings, most literature supports that patients on corticosteroid concomitant treatment are more likely to respond to DMARD therapy. The concomitant use of MTX and biologics is associated with good clinical outcomes in many different studies including Kleinert’s study, GISEA, BSRBR, and ReAct. The concomitant use of MTX is thought to largely improve treatment response through synergic actions of the drugs on RA. It is also thought to probably impact on drug immunogenicity since the occurrence of antidrug antibodies is less frequent with MTX combined with biological therapies.

Ethnicity

Ethnicity may play a role in predicting DMARD response in RA. Genetic differences influence drug-metabolizing enzymes thus causing a different responses between ethnic groups. This can limit the ability to generalize data from clinical trials to different population groups or choosing the best DMARD for a specific patient based on their ethnicity. This can be particularly relevant in some geographical areas for example North America, where patients’ origins can be very heterogeneous. Some authors have found no association between ethnicity and likelihood of response. Majority of the studies have not analysed its predicting role. Despite its favourable theoretical rationale, ethnicity is currently not a definite predictor of response to MTX and other DMARDs. More research with large populations are needed to clarify its influence on responsiveness.

Genetic biomarkers of response

Pharmacogenetics may provide an explanation to the discrepancies in treatment response to DMARDs among RA patients. Research has focused on polymorphisms and genetic patterns associated with increased or decreased drug response. The HLA-DRB1 shared epitope (SE) has been associated with RA severity and disease progression. Studies on its associated with treatment response to DMARDs have yielded conflicting results. A Japanese study found that carriers of SE positive 04 alleles were more likely to be resistant to DMARDs including MTX than non-carriers. A Pakistani study on 91 RA patients found non-responders to have the SE allele HLA-DRB1*03. Another study showed that SE positive patients responded better to MTX, sulfasalazine, and hydroxychloroquine combination therapy compared to MTX alone, while SE-negative patients responded well irrespective of treatment. Patients, who have previously failed one DMARD, O’Dell et al. showed that SE-positive patients are more likely to respond if put on combination treatment (MTX plus SSZ plus HCQ) compared to MTX monotherapy. There was no difference seen in patients who were SE negative. In a study of 457 RA patients, the presence of two HLA-DRB1 alleles encoding the SE were associated with good treatment response to etanercept as compared to MTX. No effect was observed in other alleles, including DRB1*04 and DRB1*01. Overall, SE seems to have an influence on response to DMARD treatment, with an apparent negative effect on MTX response. Further studies looking on this genetic marker are needed in order to clarify its true influence on drug effectiveness.

Another area of interest is the reduced folate carrier1 (RFC1) 80G>A (membrane transporter) which may influence influx of MTX into the cell. Its impact on drug responsiveness is still not established. Several studies have shown that patients with the RFC1 80A/A
genotype have a greater response to MTX than wild-type 80G/G patients. This was based on disease activity measurements. It is thought that gene polymorphisms may affect the response to MTX as several other SNPs in the RFC1 gene have been associated with poor response to MTX. Further research is still needed in this area. Targets for biologics have included SNPs related to TNFα or TNFα receptors (TNFR). A study on 59 patients IFX found that those with TNFA-308G/G responded better than those with A/A or A/G genotypes. Some other studies have confirmed this data. However a meta-analysis of 11 studies did not find a significant association between TNFα-308 and TNF. A response. A multi-variate analysis on 1,283 RA patients that looked into thirty-one SNPs associated with the risk of RA (i.e., TNFAIP3, STAT4, PTPN22, HLA class II, etc.) found that the SNP at the CD45 (also called PTPRC) gene locus (rs10919563) was associated with EULAR good response versus no response (OR = 0.55). Similar results were found in a study on 1,115 English patients.

Overall, studies evaluating the role of individual SNPs on response to DMARDS have been inconsistent and few. Majority of the data is on MTX. Inconsistencies may be related to different study designs, insufficient statistical power and several clinical and pharmacological confounders, such as ethnicity, outcome measures used, folate supplementation, drug dosing, duration and route of administration and concurrent therapies. While large prospective studies are missing, meta-analysis may overcome this problem, but because there are numerous pathways and a considerable number of targets that can be affected by DMARDS, an individual genetic variant within a single gene is unlikely to result in a significantly altered response, enough to be detected and replicated in different studies. It would probably be more advantageous to address gene polymorphism through polygenic analyses, haplotype analyses or gene-gene interactions rather than single genes.

**Radiographic and biochemical correlates**

RF and anti-citrullinated protein antibodies (ACPA) play important roles in diagnostic and prognostic of RA. The role of RF in treatment response has still not been established. Majority of studies have shown that RF factor has no influence on treatment response to DMARDS. Some studies for example Wessels’ et al found RF-positivity was associated with worse response to MTX monotherapy in early RA patients. Similarly, Morgan et al found that RF positive patients were more resistant to three or more DMARDS. RF-negativity has been found by Verstappen et al to be associated with four-year remission in early RA patients started on HCQ, MTX or gold. In a meta-analysis of 23 studies found an association between RF positivity and better treatment response in 14 studies with RTX and 6 studies with TCZ. Other studies with ABA found no association between response and RF. Overall, most of the available evidence seems to show that baseline RF status does not influence the effectiveness of DMARDS.

The role ACPA in RA has been associated with worse functional status higher disease activity severe radiographic progression and worse disease course. Studies by Cao et al, Hodkinson et al, Verschueren et al, Vázquez et al, Boire et al, da Mota et al and Gossec et al have found no differences in DMARD response between ACPA-positive and ACPA-negative. However a Japanese study done on patients treated with MTX or SSZ within one year of disease onset found that ACPA positivity was strongly associated with resistance to treatment. Other studies have also found similar results of a lower response to treatment in ACPA-positive patients, in terms of decrease in DAS28, ESR, CRP and other clinical variables. There is limited data on RF and Anti-Citrullinated Protein Antibodies (ACPA) role on predicting treatment response to biologics. Infliximab was investigated in the BeSt study and found that ACPA-positive patients responded as well as those who were ACPA-negative. Treatment response was based on decreases in disease activity, remission rates and functional ability. Interestingly they found that these ACPA-positive patients had good treatment response but had worse radiographic progression and were less likely to maintain drug-free remission. Overall, research is scarce and it does not support the role of ACPA as predictive markers of response to MTX and other DMARDS. We need more studies to confirm its role as a treatment predictor in RA treatment. Cytokines play a key role in RA pathogenesis and has been an area of intense research looking into the ability of cytokines to predict treatment response. Several inflammatory cytokines have been evaluated as treatment response predictors. Some of the cytokines studied include IL-1ra/IL-1beta and TNF-α. Lower levels of IL-1ra/IL-1beta and TNF-α have been associated with good or excellent responses to MTX treatment.

Higher TNF-α production in an individual has been associated with a poorer response. In RISING study, the patients with high baseline TNF were found to have a higher disease activity as measured by DAS28, higher RF and anti-CCP levels. These patients were noted to have better clinical response but it was not statistically significant when compared to patients with low TNF-α levels. IL-7 has also been studied on RA patients on TNFi where it has been found to be significantly higher in non-responders.

Treatment response to TCZ it has been studied using IL-6. The studies showed that higher baseline serum IL-6 levels were significantly associated (p < 0.0001) with higher baseline disease activity using DAS28, erythrocyte sedimentation rate, C-reactive protein, and HAQ. Higher baseline serum IL-6 levels was associated with better clinical response to TCZ versus placebo in DMARD inadequate responders and in MTX-naive populations. However, apart from those defined as TNFi inadequate responders its association with treatment response was found to be weak with threefold difference in baseline IL-6 level corresponded to a DAS28 change of 0.17-unit difference at week 16. This has limited its clinical usefulness of IL-6 in predicting treatment benefit.
Conclusions

One of the main challenges in RA management for over two decades has been the ability to predict response to first-line DMARDs. RA manifestations are complex and variable from patient-to-patient (age, sex, and comorbidities). The prediction of treatment response in individuals to ultimately allow selection of targeted, patient specific therapy will likely be based on novel and integrative biomarker approaches. This would be of benefit in several ways. Identifying patients less likely to respond will avoid needless exposure to potentially toxic drugs and the waste of precious time to achieve disease control, a crucial endpoint to prevent development of structural damage. We have identified clinical and biological factors that predict good response which are male gender, non-smoking, early disease stage, absence of previous DMARD use, lower baseline disease activity, concomitant corticosteroids, inflammatory biomarkers (TNF-α levels, ESR, CRP) and SE-negativity. There is still not enough literature to help determine the influence of factors such as age, genetics, RF, ACPA and inflammatory cytokines like IL-6, IL-7 etc. Another potential area of study is to come up with composite scores of various predictors that will help prognosticate and influence the choice of DMARDs. Further research is needed which will ultimately lead to the goal of a tailor made therapy for each patient.

References


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Pattern of trigger finger among patients attending a musculo-skeletal clinic

Oguntona SA, Edunjobi AS

Abstract

Background: Trigger finger is a common finger problem thought to be due to thickening of tendon sheath with or without localized tendon thickening, resulting in a narrowed tunnel for tendon excursion with ultimate restriction of tendon movement. It can be seen in anyone, it is however seen frequently in diabetic patients and in women, typically in the fifth or sixth decade of life.

Objective: To determine the pattern of trigger finger among patients attending a musculo-skeletal clinic.

Design: A prospective study.

Setting: The study was conducted at the Olabisi Onabanjo University Teaching Hospital, a tertiary hospital located in the South west, Nigeria. The study was conducted over four years between July 2009 and June 2013.

Patients and Methods: All the patients that presented with trigger finger at the outpatient clinic were enlisted for the study. Demographic and clinical information was obtained by direct interview of patients.

Results: Thirty four cases of trigger finger were seen. There were 22 (64.7%) females and 12 (35.3%) males with a female to male ratio of 1.8:1. The age range of patients was 32 to 65 years. The mean duration of symptom was 1 year and 3 months. The ring finger (61.8%) was the commonest finger affected, and the left ring finger was predominantly affected (66.7%). The left hand (76.5%) was commonly affected. There were no cases of multiple finger involvement.

Conclusion: Response to intra-lesional steroid injection was uniformly effective, surgical intervention may be un-necessary in many cases of trigger finger.

Key words: Trigger finger, Pattern, Musculo-skeletal clinic, Nigeria

Introduction

Trigger finger was first described by Notta in 1850. It earns its name from the painful clicking sound elicited by flexion and extension of the affected digit. It is one of the most frequently seen disorders of the upper limb. It is caused by a difference in diameter of a flexor tendon and its retinacular sheath due to thickening and narrowing of the A1 pulley through which the flexor tendon passes at the metacarpal heads, leading to restricted movement of the tendon through the pulley. Inflammation and hypertrophy of the retinacular sheath progressively restrict the motion of the flexor tendon. The retinacular sheath normally forms a pulley system comprised of a series of annular and cruciform pulley in each digit that serves to maximize the flexor tendon’s efficiency of motion.

Trigger finger presents with discomfort in the palm during movement of the involved digit. The flexor tendon causes a painful click as the patient flexes and extends the digit. The patient may present with a digit locked in a peculiar location, usually in flexion which may need gentle passive manipulation into full extension. Management strategies include physiotherapy, splint application, non-steroidal anti-inflammatory drugs, steroid injection, and surgery.

The aim of this research work was to determine the success rate of steroid injection of trigger finger among patients seen in the rheumatology clinic.

Materials and Methods

This was a prospective study of consecutive patients who presented with trigger finger to the rheumatology outpatient clinic of a University Teaching Hospital in the South West, Nigeria. These patients were seen over a period of four years (July 2009- June 2013).

Detailed demographic, occupation and medical history were taken to determine the presence of work related trigger finger and systematic diseases respectively. Physical examination was performed to ascertain the presence of any other local pathology that mimics trigger finger.

Results

Thirty four cases were seen over the study period. Females were 22 (64.7%) with age range of 38 years to 64 years and males 12 (35.3%) with age range of 32 years to 65 years.
years. Female to male ratio was 1.8:1. The mean duration of symptoms was 1 year and 3 months. The ring finger was affected in 21 (61.7%) patients made up of 6 (28.6%) males and 15 (71.4%) females. The right ring finger was involved in 2 (28.6%) males and 5 (71.4%) females while the left ring finger was involved in 10 (71.4%) females. The middle finger was involved in 9 (26.5%) patients with 3 (33.3%) males and 6 (66.7%) females. The right middle finger was involved in one (33.3%) male and 2 (66.7%) females, while the left middle finger involved 2 (33.3%) males and 4 (66.7%) females. The thumb was involved in 4 (11.8%) patients with one (25%) male and 3 (75%) females. Only one female had right thumb involvement while the left thumb was involved in one (33.3%) male and 2 (66.7%) females. Eight patients had diabetes mellitus (23.5%), there were 5 females and 3 males.

Table 1: Demography and analysis of trigger finger cases

<table>
<thead>
<tr>
<th>No. (%)</th>
<th>Female</th>
<th>Male</th>
<th>Ring finger</th>
<th>Middle finger</th>
<th>Thumb</th>
<th>Right hand</th>
<th>Left hand</th>
<th>Multiple finger involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>22 (64.7)</td>
<td>12 (35.3)</td>
<td>21 (61.7)</td>
<td>9 (26.5)</td>
<td>4 (11.8)</td>
<td>8 (23.5)</td>
<td>26 (76.5)</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Table 2: Age range involvement of trigger finger

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Female (%)</th>
<th>Male (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-30</td>
<td>2 (66.7)</td>
<td>1 (33.3)</td>
</tr>
<tr>
<td>31-40</td>
<td>5 (62.5)</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>41-50</td>
<td>12 (66.7)</td>
<td>6 (33.3)</td>
</tr>
<tr>
<td>51-60</td>
<td>3 (75)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>61-70</td>
<td>0 (0)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>12</td>
</tr>
</tbody>
</table>

Table 3: Occupational involvement of trigger finger

<table>
<thead>
<tr>
<th>Occupation</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Student</td>
<td>2 (5.9)</td>
</tr>
<tr>
<td>House wife</td>
<td>2 (5.9)</td>
</tr>
<tr>
<td>Trader</td>
<td>14 (41.2)</td>
</tr>
<tr>
<td>Teacher</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>Medical practitioner</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Farmer</td>
<td>8 (23.5)</td>
</tr>
<tr>
<td>Manual labourer</td>
<td>4 (11.8)</td>
</tr>
</tbody>
</table>

Three females and 2 males had good glycaemic control while the other 3 patients were poorly controlled. Two patients (5.9%) had associated rheumatoid arthritis. The right hand was involved in eight (23.5%) patients with 2 (25%) males and 6 (72%) females, while the left was affected in 26 (76.5%) patients with 10 (38.5%) males and 16 (61.5%) females. Nobody had multiple finger involvement. All the patients had intra-lesional methyl-prednisolone steroid injection. Only three patients had recurrence of the trigger finger to date.

Discussion

Trigger finger is a common finger problem. The diagnosis is usually fairly straightforward, as most patients present with locking of the finger. Primary trigger finger occurs commonly in the middle fifth to sixth decades of life.

The causes of trigger finger are multiple and in each individual often multifactorial. There are reports linking trigger finger to occupations requiring extensive gripping and hand flexion, such as use of shears or hand held tools. Higher incidence of trigger finger has also been found in people with hypothyroidism, rheumatoid arthritis, renal disease, and amyloidosis.

In line with earlier studies, the ring finger was also most affected in this study, followed by the middle finger. Though, this study did not record any patient with multiple trigger fingers, studies in patients with multiple triggers recorded the occurrence in decreasing order as ring finger, the thumb, long, index, and the small fingers.

Twenty-three percent of our patients had diabetes mellitus. The lifetime risk of trigger finger in the general populace is 2-3%, but it is said to be up to 10% in diabetics. The incidence in diabetes is associated with the actual duration of the disease, and not with glycemic control. Higher incidence of trigger finger has also been found in people with hypothyroidism, rheumatoid arthritis, renal disease, and amyloidosis.

Intra-lesional injection of steroid with or without oral non-steroidal anti-inflammatory drugs was the principal treatment modalities in our patients. The three patients with recurrent trigger finger presented above one year of onset of symptoms. Most of them had visited other sources of medical care before visiting the teaching hospital. They all at various times took different analgesics, and this therefore informed the intra-lesional injection of steroid as the available option at the time of presentation to our clinic. The three patients with recurrent trigger finger had a repeat injection. No direct relationship was found between the duration of symptoms and the response to treatment because all the three patients with recurrent trigger finger presented above one year of onset of symptoms just like other patients.
Steroid injection into the flexor sheath was advocated as a method of treatment in 1950 with a success rate between 38 to 93%\(^7\). It was difficult to determine the actual duration of symptoms in most of our patients; however, higher rates of success are likely in patients who present with less than six months symptom duration\(^8\). All our patients had blinded intra-lesional injections of steroid. The shortcoming of this study was the inability to perform ultrasound guided injection because of its non-availability.

In conclusion, although, none of our patients had noticeable complication from the blinded intra-lesional steroid injection, ultrasound guided injection is however, more preferable because of a better clinical outcomes and fewer complications.

References

Clinical characteristics of patients with systemic lupus erythematosus in Nairobi, Kenya

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Abstract

Background: Systemic lupus erythematosus (SLE), a chronic multisystem autoimmune disease with a wide spectrum of manifestations, shows considerable variation across the globe, although there is data from Africa is limited. Quantifying the burden of SLE across Africa can help raise awareness and knowledge about the disease. It will also clarify the role of genetic, environmental and other causative factors in the natural history of the disease, and to understand its clinical and societal consequences in African set up.

Objective: To determine the clinical profile of SLE patients at a tertiary care centre in Nairobi, Kenya.

Methods: Case records of patients who were attending the Nairobi Arthritis Clinic seen between January 2002 and January 2013 were reviewed. This was a cross-sectional study done on 100 patients fulfilling the 2012 Systemic Lupus Collaborating Clinics (SLICC) criteria for SLE attending the Nairobi Arthritis Clinic, Kenya. The patients were evaluated for socio-demographic, clinical and immunological manifestations and drugs used to manage SLE.

Results: Hundred patients diagnosed with SLE were recruited into the study. Ninety seven per cent of the study participants were female with a mean age of 36.6 years. Thirty three years was the mean age of diagnosis. The mean time duration of disease was 3 years with a range of 0-13 years. There was extensive disease as many had multi-organ involvement. Majority (83%) of the study participants met between 4 and 6 manifestations for the diagnosis criteria for SLE. Non erosive arthritis and cutaneous disease were the commonest initial manifestation. The patients had varied cutaneous, haematological, pulmonary, cardiac, renal and neuropsychiatric manifestations. Antinuclear antibody (ANA) assay and anti-dsDNA positivity was 84%, 49% and 43% respectively. None of the patients were on biologic disease modifying anti-rheumatic drugs.

Conclusions: In Nairobi, SLE is a multisystem disorder affecting predominantly young females. Polyarthritis and cutaneous disease were the most common clinical features. This is comparable to other studies done in black African population. We found a higher prevalence of haematological and lower rate of renal disease as compared to other studies done in black Africans. The ANA assay and anti-dsDNA positivity was lower than those in other studies on black Africans. Majority of the patients were on steroids.

Key words: SLE, Nairobi, Kenya

Introduction

Systemic Lupus Erythematosus (SLE) is a chronic inflammatory disease that has varied presentations that follow a relapsing and remitting course. It is characterized by immunologically mediated, clinical and serological phenomena. It may resemble any of a variety of infectious, inflammatory, nutritional, malignant and metabolic disorders. More than 90% of cases of SLE occur in women, frequently starting at childbearing age. Worldwide, the prevalence of SLE appears to vary by race. The highest rates of prevalence have been reported in Italy, Spain, Martinique, and the United Kingdom Afro-Caribbean population. The Centre’s for Disease Control and Prevention (CDC) estimates a range between 1.8 and 7.6 per 100,000 persons per year in the continental United States1. In general, black women have a higher rate of SLE than women of any other race, followed by Asian women and then white women2. The contrast between low reported rates of SLE in black women in Africa and high rates in black women in the United Kingdom suggests that there are environmental influences3. The disease is thought to be less common in tropical Africa because of the high prevalence of tropical infectious diseases, particularly malaria. This phenomenon may be mediated by the presence of immunosuppressive mediators like tumour necrosis factor alpha and nitric oxide in patients with chronic infection4, 5. There is paucity of data on the rates of occurrence of SLE in Africa, although several centres have reported their experience with SLE. Other likely contributors are that of poor
access and infrastructure of health services has led to under diagnosis in Africa.

The pattern of manifestations associated with SLE may differ according to racial and ethnic characteristics. Data from United Kingdom show that the definitive feature in 85% of patients was musculoskeletal and/or cutaneous. A study by Cooper et al. analysed racial differences in the South-eastern USA and found more discoid lupus, more nephritis and a higher prevalence of anti-Sm and anti-RNP antibodies in black patients as well as less photosensitivity or mucosal ulcers in black patients. An Indian study of 100 patients showed that prolonged fever was the commonest presenting symptom. Other presenting symptoms with decreased frequency were arthralgia, haemolytic anaemia, ITP, malar rash. A Zimbabwe study showed that renal involvement was more common and photosensitivity and serositis less common than in the United States. The purpose of this study was to delineate the clinical pattern and laboratory features seen in patients with SLE in Nairobi, Kenya and to compare it with international data on lupus patients. The study also looked at the various therapeutic modalities used on these patients with SLE.

Material and Methods

After prior ethical clearance from the National Ethical Review Board, we reviewed the case records of 9975 patients attending the Nairobi Arthritis Clinic between January 2002 and January 2013. The study site is situated in Nairobi, the capital city of Kenya and serves as a tertiary referral centre. It not only serves the two million inhabitants of Nairobi but also patients from all over Kenya and the greater East and Central African Region. Medical records of patients with SLE were identified and 100 patients satisfying the revised International Systemic Lupus Collaborating Clinics (SLICC) criteria (2012) for SLE were recruited into the study. These patients were on regular follow-up at the Nairobi Arthritis Clinic. Relevant parameters retrieved from patient records included clinical data (age, sex, duration of symptoms, symptoms and clinical signs at diagnosis and during follow-up) and laboratory and radiology data (complete blood count, erythrocyte sedimentation rate, urine analysis, renal function tests, chest X-ray, and X-ray of both hands). Results of immunological investigations like Antinuclear Antibody Assay (ANA), anti-double stranded DNA (anti-dsDNA) were recorded from the file. Statistical methods: Categorical variables were presented as number (%) and continuous variables presented as mean and standard deviation. Data was analysed using SPSS version 21.0.

Results

Nine thousand nine hundred and seventy five patients were evaluated for SLE over a one year period. Ninety seven per cent of the study participants were females with a mean age of 36.6 years. Thirty three years was the mean age of diagnosis. The mean time duration of disease was 3 years with a range of 0-13 years (Table 1). Majority (83%) of the study participants met between 4 and 6 manifestations for the diagnosis criteria for SLE. Non erosive arthritis and cutaneous disease were the commonest initial manifestation. The patients had varied cutaneous, haematological, pulmonary, cardiac, renal and neuropsychiatric manifestations. ANA assay and anti-dsDNA was positive in 82% and 52% (Table 2). Patients on steroids, non-steroidal drugs and synthetic disease modifying anti-rheumatic drugs were 84%, 49% and 43% respectively. None of the patients were on biologic disease modifying anti-rheumatic drugs (Table 3).

Table 1: Socio-demographic characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%)</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>36.6 (10.7)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>19.0-61.0</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>97 (97.0)</td>
</tr>
<tr>
<td>Male</td>
<td>3 (3.0)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>49 (49.0)</td>
</tr>
<tr>
<td>Single</td>
<td>48 (48.0)</td>
</tr>
<tr>
<td>Widowed</td>
<td>1 (1.0)</td>
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<tr>
<td>Missing</td>
<td>2 (2.0)</td>
</tr>
<tr>
<td>Level of education</td>
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</tr>
<tr>
<td>Primary</td>
<td>14 (14.0)</td>
</tr>
<tr>
<td>Secondary</td>
<td>31 (31.0)</td>
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<td>College</td>
<td>49 (49.0)</td>
</tr>
<tr>
<td>None</td>
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<tr>
<td>Missing</td>
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<tr>
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</tr>
<tr>
<td>Unemployed</td>
<td>42 (42.0)</td>
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<tr>
<td>Employed</td>
<td>32 (32.0)</td>
</tr>
<tr>
<td>Self-employed</td>
<td>22 (22.0)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (4.0)</td>
</tr>
<tr>
<td>Age at diagnosis of SLE</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>33.0</td>
</tr>
<tr>
<td>Min-Max</td>
<td>11.0-56.0</td>
</tr>
<tr>
<td>Duration of SLE in years</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>3.6</td>
</tr>
<tr>
<td>Min-Max</td>
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### Table 2: Clinical characteristics

<table>
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<tr>
<td>Number of criteria for diagnosis of SLE</td>
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</tr>
<tr>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
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<td>7</td>
<td>8</td>
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<td>8</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Positive ANA (Antinuclear antibody test)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>82</td>
</tr>
<tr>
<td>Negative</td>
<td>8</td>
</tr>
<tr>
<td>Not done</td>
<td>10</td>
</tr>
<tr>
<td>Positive Anti-ds DNA</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>56</td>
</tr>
<tr>
<td>Negative</td>
<td>10</td>
</tr>
<tr>
<td>Not done</td>
<td>34</td>
</tr>
<tr>
<td>Presence of malar rash</td>
<td>54</td>
</tr>
<tr>
<td>Discoid rash</td>
<td>22</td>
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<tr>
<td>Photosensitivity</td>
<td>44</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>36</td>
</tr>
<tr>
<td>Non-erosive arthritis</td>
<td>90</td>
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<tr>
<td>Pleuritis and/or pericarditis</td>
<td>28</td>
</tr>
<tr>
<td>Renal disorder</td>
<td>24</td>
</tr>
<tr>
<td>History of neurologic disorder</td>
<td>19</td>
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<tr>
<td>Haematologic disorders</td>
<td>67</td>
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### Table 3: Medications

<table>
<thead>
<tr>
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<tr>
<td>Regular use of corticosteroids</td>
<td>84</td>
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<tr>
<td>Dosage</td>
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<tr>
<td>Lower dose; &lt;10mg/day</td>
<td>32</td>
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<tr>
<td>Medium dose; 10-20mg/day</td>
<td>45</td>
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<td>High dose; &gt;20mg/day</td>
<td>7</td>
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<tr>
<td>Hydroxychloroquine</td>
<td>77</td>
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<tr>
<td>Methotrexate</td>
<td>15</td>
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<td>Azathioprine</td>
<td>27</td>
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<td>Mycophenolate Mofetil.</td>
<td>12</td>
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<tr>
<td>Use of NSAIDs</td>
<td>49</td>
</tr>
<tr>
<td>Frequency</td>
<td></td>
</tr>
<tr>
<td>Regular</td>
<td>25</td>
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<td>Intermittent</td>
<td>2</td>
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<tr>
<td>Symptomatic</td>
<td>22</td>
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</table>

### Table 4: Cumulative incidence of clinical and immunological manifestations of SLE in Kenya as compared to other series

<table>
<thead>
<tr>
<th>Year</th>
<th>Jessop (South Africa)</th>
<th>Seedat (South Africa)</th>
<th>Dessein (South Africa)</th>
<th>Binoy (India)</th>
<th>Houman (Tunisia)</th>
<th>Wadee (South Africa)</th>
<th>Adelowo (Nigeria)</th>
<th>Ekwom (Kenya)</th>
<th>Doulla (Cameroon)</th>
<th>Genga (Kenya)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Articular</td>
<td>74%</td>
<td>97%</td>
<td>90%</td>
<td>89.3%</td>
<td>78%</td>
<td>87%</td>
<td>69.2</td>
<td>59%</td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>78%</td>
<td>73%</td>
<td>60%</td>
<td>64%</td>
<td>&gt;63%</td>
<td>81%</td>
<td>73.8</td>
<td>69.2</td>
<td>28.2</td>
<td>78%</td>
</tr>
<tr>
<td>Haematological</td>
<td>64.5%</td>
<td>15%</td>
<td>73%</td>
<td>26.71%</td>
<td>33%</td>
<td>43%</td>
<td>43</td>
<td>17%</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>58%</td>
<td>87%</td>
<td>60%</td>
<td>33%</td>
<td>43%</td>
<td>43</td>
<td>43</td>
<td>17%</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>ANA</td>
<td>90.8%</td>
<td>100%</td>
<td>93.3%</td>
<td>100%</td>
<td>99.1%</td>
<td>99.1%</td>
<td>76.9</td>
<td>86.1%</td>
<td>82%</td>
<td></td>
</tr>
<tr>
<td>Anti-Ds DNA</td>
<td>76%</td>
<td>41%</td>
<td>55.3%</td>
<td>38.5</td>
<td>73.5%</td>
<td>52%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Discussion

In this study about half of the study population were married with 94% of the study participants having received some formal education. There were 3 males and 97 females aged between 11-36 years. All 3 male patients were ANA and anti-dsDNA positive and showed muscular-cutaneous features similar to those seen in females. The female to male ratio was 32:1. This is in keeping with most literature that reports a female predominance ranging from 83–97% (excluding studies that recruited only female or male patients). The female preponderance is also seen in all these reports from Africa e.g Cameroun (F: M – 12:1); Zambia (29:0); Nigeria (10:1); South Africa (18:1); Tunisia (11.5:1); Kenya (13:0) [17, 21-23]. The use of exogenous hormones has been associated with lupus onset and flares, suggesting a role for hormonal factors in the pathogenesis of the disease[10].

The median age at diagnosis of this study population was 33 years. This compares to other studies done in for instance, South Africa (35 years); Kenya (34 years); Nigeria (33 years); Cameroun (38 years) [7,23]. Several comparative studies have, however, shown that the peak age of onset is lower in black women[11,12]. The median age of disease onset in white women ranges between 37 and 50 years[13]. The mean age SLE onset in Africa mirrors studies from Asia range from 25.7–34.5 years, with patients in India (24 years), Malaysia (25.7 years) and Philippines (26.7 years) demonstrating earlier onset compared to patients in the other countries[14]. There was a long disease duration of the study subjects ranging from 0 to 13 years. This may explain the extensive disease seen in this population as many had multi-organ involvement. Majority (83%) of the study participants met between 4 and 6 manifestations for the diagnosis criteria for SLE.

The commonest clinical manifestations reported was articular disease at 90% of the cases. This finding is in keeping with data from elsewhere in African populations[15-17]. Skin manifestations were also common. Malar rash was commonest skin manifestation which is similar to studies from South Africa and India. Malar rash and arthritis were reported in 69.2% of Kenyan patients by Ekwom [2] in a study from Kenya. Adelowo et al[18] reported arthritis in 87% of their patients but had a lower frequency of malar rashes (21.2%); photosensitivity (9%); discoid rashes (43.9%). Doulla et al[19] reported arthritis as the most common feature in 59% and had lower rates of malar rash (15.4%) and discoid (5.1%). Photosensitivity has previously been reported to be less common in black patients as this is often subjectively assessed based on the experience of the patient apart from a study by Ekwom [22] who found 53% of patients in a Kenyan study Photosensitivity was reported lower in this study at 44%. This was however higher than the studies done elsewhere in Africa by Dessein et al[23]. Seedat et al[24], Wadee et al[25] from South Africa and Doulla et al[19] in Cameroon who reported 13%,35% and 7.7% respectively (Table 4). Patients in this study had a low number of oral ulcers (36%). This is similar to a study by Wadee et al[22] and Ekwom et al[25]. Possible reasons for the low numbers are that this clinical feature may be missed as these are usually painless ulcers and may not be reported by the patients. There were low numbers for neurological disease (19%) and renal disease (24%). Doulla et al[19] found low numbers of neurological disease (10.3%) and renal disease (17%). The frequency of renal involvement varies in different populations studied with both ethnic and geographic variation reported (Table 4).

Renal disease in this study was lower than that reported in studies by others 15-18,22 where they found rates >60%. Various studies have demonstrated a higher incidence of LN in black patients15-20,22. In a study done in Tunisia by Houman et al[19], 43% of patients were diagnosed with lupus nephritis. Renal biopsies and 24 hour protein excretion were not done in this patients thus may explain the low numbers. Wadee et al[22] also found low numbers of neurological disease. These numbers however represented only strokes, new onset seizures or psychosis. The prevalence of neurological disease is likely to be higher if commoner lesions like neuropathies were included in the study. Antinuclear antibody (ANA) assay and anti-dsDNA was positive in 82% and 52% respectively which was higher than what Ekwom [22] reported ANA at 76.9%. This is similar to Doulla et al[19] who reported ANA at 86.1%. These are lower than studies from South Africa on 226 patients reported ANA at 99.1% and anti-dsDNA at 55.3% and Nigeria on 95 lupus patients reported ANA at 95.7% and dsDNA-54.4%[17,23]. Majority of the patients were on steroids (84%). Disease modifying drugs used included hydroxychloroquine, azathioprine, methotrexate and mycophenolate mofetil at 77%, 27%, 15% and 12% respectively. Hydroxychloroquine has been reported as the most common drug of choice in SLE patients in Africa as seen by Ekwom [22] (92%) and Doulla et al[19] (69%). Possible reasons for the high usage is that hydroxychloroquine is recommended in international guidelines because of its affordability in our area. It is also known to have a positive effect in preventing end organ involvement[23]. About half of the patients were on regular non-steroidal anti-inflammatory drugs with 25% using them regularly, 22% symptomatic use and 2% intermittently used. There was low use of anti-platelet (4%) and statins (2%). Cyclophosphamide and B lymphocyte cell depletors which have been used in other case series of SLE mainly for lupus nephritis was absent in this study[23,24].

Conclusions

SLE is certainly not as rare in Kenya as previously thought. This study demonstrates that the demographic distribution of patients with SLE in Kenya mirrors that from other areas in the world although with a stronger female predominance, especially in the childbearing period. This was a well-educated population. The commonest manifestation of the disease is articular and muco-cutaneous disease. Majority of the patients had the disease long before diagnosis was made and this...
resulted in multi-organ manifestations. The prevalence of neurological and renal disease is low in this population. ANA assay and anti-dsDNA was positive in 82% and 52% respectively. Majority of this study population were on steroids and hydroxychloroquine.

**Recommendations**

(i) SLE is not rare in Kenya. Diagnosis of SLE should be thought of in female patients of child bearing age presenting with multi-organ disease.

(ii) Studies on the severity of the disease as well as the response to available treatment and mortality are needed so as to assess its exact impact on SLE patients.

**Acknowledgments**

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**Conflict of interest**

The authors declare no conflicts of interest

**References**


Case report

Catastrophic antiphospholipid syndrome: management challenges and lessons learnt in the third world set-up: Case report

Genga EK, Oyoo GO

Abstract

**Background:** Antiphospholipid Syndrome (APS) is a disorder that manifests clinically as recurrent venous or arterial thrombosis and/or foetal loss. Catastrophic Antiphospholipid Syndrome (CAPS) is a very severe variant of the classic APS. It is characterized by clinical evidence of multiple organ involvement developing over a very short period of time, histopathological evidence of multiple small vessel occlusions and laboratory confirmation of the presence of antiphospholipid antibodies, usually in high titre. Although patients with catastrophic APS represent less than 1% of all patients with APS, this is usually a life-threatening condition. The majority of patients with catastrophic APS end up in intensive care units with multi-organ failure. Making the diagnosis is challenging and can be missed. Unless the condition is considered in the differential diagnosis by attending physicians, it may be completely missed, resulting in a disastrous outcome. Catastrophic APS develops rapidly and can result in death of up to 30-50% of cases.

**Case presentation:** A nineteen year old nulliparous lady diagnosed with Systemic Lupus Erythematosus (SLE) four months prior to admission with no prior history of thrombo-embolic events presented at the accident and emergency department with one day history of fevers and convulsions. This was associated with history of progressively worsening memory loss and confusion associated with incoordination of hands. She also reported to have had a productive cough of 3 months which was episodic. The patient was admitted and developed multiple organ failure from lungs, heart and the kidney during treatment in hospital attributed to this disease. She succumbed during treatment.

**Key words:** Antiphospholipid syndrome, Catastrophic antiphospholipid syndrome, Arterial and venous thrombosis, Clinical features, Diagnosis, management

Introduction

Antiphospholipid Syndrome (APS) is a multisystem autoimmune condition characterized by vascular thromboses with or without pregnancy loss associated with persistently positive antiphospholipid antibodies (aPL). The “catastrophic” variant of the antiphospholipid syndrome was first described by Ronald Asherson in 1992. He described it as a condition that develops over a short period characterized by multiple vascular occlusive events usually affecting small vessels. Catastrophic APS (CAPS) is the most severe form of APS with multiple organ involvement developing over a short period of time, usually associated with microthrombosis. Although less than 1% of patients with APS develop this complication, its potentially lethal outcome underlines its importance in clinical medicine today. Most of the patients with catastrophic APS will end up in the intensive care units with multi-organ failure. If this condition is not considered in the differential diagnosis by attending physicians, it may be completely missed, resulting in a disastrous outcome.

‘Definite’ and ‘probable’ CAPS have been defined based on the preliminary classification criteria; however, in a real-world setting, aPL-positive patients with multiple organ thromboses and/or thrombotic microangiopathies exist who do not fulfil these criteria. Previous APS diagnosis and/or persistent clinically significant aPL positivity is of great importance for the CAPS diagnosis; however, almost half of the patients who develop CAPS do not have a history of aPL positivity. The classification criteria for catastrophic antiphospholipid syndrome are summarized in Table 1. In this article we describe a patient with probable catastrophic APS and the challenges in making the diagnosis and managing this disease.
**Case report**

A 19 year old nulliparous lady with SLE with no history of thrombo-embolic events and was taking azathioprine, prednisolone, hydroxychloroquine, meloxicam, pantoprazole. She presented at the accident and emergency department with one day history of fevers and convulsions. The patient had been well until two months prior to admission when she started having bouts of recurrent fevers. She was put on various antibiotics during this period with some improvement. Two weeks prior to admission there was a reported history of progressively worsening memory loss and confusion associated with incoordination of hands. During this period she had complained of headaches which the informant wasn’t able to describe well in detail. On the day of admission she was reported to have had four convulsions. They were described as generalised tonic clonic seizures lasting about one minute. She had a productive cough of 3 months duration which was episodic. The cough was occasionally blood stained and had worsened over the week prior to admission. There was no positive history of contact with a pulmonary tuberculosis patient. There were no night sweats but had some weight loss which the informant wasn’t able to quantify.

Examination on admission revealed mild confusion, intention tremors with a Glasgow coma scale of 13/15 and oral thrush. She was noted to be disoriented in time, place and person. The neck was soft kerning’s negative with no noted focal neurological deficit. Respiratory examination showed mild respiratory distress with bilateral basal crepitations. Her cardiovascular exam showed tachycardia with normal heart sounds. The abdominal exam only revealed suprapubic tenderness. The diagnosis at this time was active lupus with sepsis.

The laboratory investigations are summarized in Table 2. Other tests done included lactate dehydrogenase at 974 IU/L (High), Creatinine Phosphokinase (CPK) at 113mcg/L (Normal), Creatinine Kinase (CKMB) at 33.2ng/ml (Normal), Magnesium at 0.92mg/dl (normal), Calcium at 1.28 mg/dl (low). C-reactive protein was elevated at 14 mg/l, granular cast and Procalcitonin e elevated at 14 mg/l, urinalysis had protein 2++, specific Calcium at 1.28 mg/dl (low). C-reactive protein was 33.2ng/ml (Normal), Magnesium at 0.92mg/dl (normal), at 113mcg/L (Normal), Creatinine Kinase (CKMB) at 974 IU/L (High), Creatinine Phosphokinase (CPK) at 113mcg/L (Normal), Creatinine Kinase (CKMB) at 33.2ng/ml (Normal), Magnesium at 0.92mg/dl (normal), Calcium at 1.28 mg/dl (low). C-reactive protein was elevated at 14 mg/l, granular cast and Procalcitonin eventually succumbed while undergoing treatment.

**Table 1: Preliminary classification criteria for catastrophic antiphospholipid syndrome**

1. Evidence of involvement of three or more organs, systems and/or tissues
2. Development of manifestations simultaneously or in less than a week
3. Confirmation by histopathology of small-vessel occlusion
4. Laboratory confirmation of the presence of antiphospholipid antibodies

**Definite catastrophic antiphospholipid syndrome**
- All four criteria present

**Probable catastrophic antiphospholipid syndrome**
- All four criteria, except only two organs, systems, and/or tissues involved
- All four criteria, except for the absence of laboratory confirmation of antiphospholipid antibodies

*Vasculitis may coexist, but significant thrombosis must be present as well
“Positive aPL” twice 12 weeks apart*25

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Table 2: Laboratory results

<table>
<thead>
<tr>
<th></th>
<th>Day admission</th>
<th>Day 1 ICU</th>
<th>Day 3 ward</th>
<th>Day 4 ward</th>
<th>Day 1 ICU</th>
<th>Day 2 ICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>133</td>
<td>134</td>
<td>135</td>
<td>134</td>
<td></td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>4.5</td>
<td>4.4</td>
<td>4.3</td>
<td>4.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urea</td>
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<td>11.7</td>
<td>5.1</td>
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<td>Creatine</td>
<td>58</td>
<td>280</td>
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<td>Direct bilirubin</td>
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<td>13.5</td>
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<td>18</td>
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<td>AST</td>
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<td>79</td>
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<td>590</td>
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<td>239</td>
<td>266</td>
<td>246</td>
<td>191</td>
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<td>Total protein</td>
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<td>60</td>
<td>60</td>
<td>63</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>Albumin</td>
<td>31</td>
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<td>22</td>
<td>22</td>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>Day 1 ICU</th>
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<th>Day 3 wards</th>
<th>Day 1 ICU</th>
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<tbody>
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<td>WBC</td>
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<td>8.25</td>
<td>16.7</td>
<td>11.6</td>
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<td>HB</td>
<td>12.3</td>
<td>12.8</td>
<td>12.8</td>
<td>10.6</td>
<td>7.11</td>
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<tr>
<td>MCV</td>
<td>81.7</td>
<td>82.3</td>
<td>80.7</td>
<td>80.9</td>
<td>78.7</td>
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<tr>
<td>PLT</td>
<td>350</td>
<td>293</td>
<td>274</td>
<td>376</td>
<td>204</td>
</tr>
</tbody>
</table>

Na= Sodium; K=Potassium; Alt=Alanine Transaminase; Ast= Aspartate Transaminase; GGT=Gamma Glutamyl Transferase; WBC=White Blood Cells; N=Neutrophils; HB=Haemoglobin; MCV= Mean Corpuscular Volume; Plt= Platelets

Table 3: How to distinguish the various differential diagnosis of catastrophic antiphospholipid syndrome

<table>
<thead>
<tr>
<th></th>
<th>Fibrinogen</th>
<th>Haemolytic anaemia</th>
<th>Schistocytes</th>
<th>Thrombocytopenia</th>
<th>APL</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPS</td>
<td>Normal</td>
<td>Present/Absent</td>
<td>Present</td>
<td>Present/Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Normal/Low</td>
<td>Present</td>
<td>Present/Absent</td>
<td>Present/Absent</td>
<td>Present/Absent</td>
</tr>
<tr>
<td>TTP-HUS</td>
<td>Normal</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>DIC</td>
<td>Low</td>
<td>Present/Absent</td>
<td>Present/Absent</td>
<td>Present</td>
<td>Absent</td>
</tr>
</tbody>
</table>

APL=Antiphospholipid Syndrome; CAPS=Catastrophic Antiphospholipid Syndrome; DIC=Disseminated Intravascular Coagulation; TTP-HUS=Thrombotic Thrombocytopenic Purpura – Haemolytic-Uraemic Syndrome

Discussion

Though APS is one of the most common and fatal thrombocytophilias, it is unfortunately not often looked for and diagnosed. 2–5% of the general population will have detectable anticardiolipin antibodies of which 30–50% of those persons may have symptoms of APS. Patients with recurring thrombosis, especially in an atypical localization or an atypical aetiology and recurrent fetal wastage, APS should be considered. Our patient did not have a history of recurrent thrombosis and fetal wastage. We thought of it only when she decompensated a second time and now the diagnosis of CAPS was made. She had multiple organ dysfunction within a short duration of time in the background of SLE. CAPS is the most severe form of APS with multiple organ involvement developing over a short period of time, usually associated with microthrombosis. The classification criteria for catastrophic antiphospholipid syndrome are summarized in Table 3. Although less than 1% of patients with APS develop this complication, its potentially lethal outcome underlines its importance in clinical medicine today. The diagnosis of CAPS can be challenging because of the acute onset of thrombosis.
at multiple levels with simultaneous dysfunction of different organs. The survival of the patients very much depends on an early diagnosis and treatment. Attempts at documenting the world wide epidemiology has been a challenge due to difficulties in making the diagnosis. In the local set up and Africa as a whole there has been no case report of this rare but fatal disease. This can be attributed to low level of suspicion and limitations from finance and infrastructure support of laboratory and radiological services. In a review by Cervera et al. of 280 patients with CAPS from the website-based international CAPS registry shows that 72% were female, with a mean age of 37 years (range 11–60 years). Approximately 46% had primary APS and 40% SLE. Our patient was female, younger than the mean age at nineteen years and was known to have SLE.

The aetiology and pathogenesis of CAPS is an enigma and remains incompletely understood. Several mechanisms have been proposed such as molecular mimicry, infections and activation of endothelium in the microvasculature and microvascular occlusions. It’s suggested that the vascular occlusions are responsible for the ongoing thrombosis. It’s postulated that clots continue to produce thrombin, an increase in plasminogen activator inhibitor type-1 impairs fibrinolysis. This is compounded by the consumption of the natural anticoagulant proteins such as protein C and antithrombin. These multiple small vessel occlusions cause extensive tissue necrosis which results in a Systemic Inflammatory Response Syndrome (SIRS), with excessive cytokine release from affected and necrotic tissues. Proinflammatory cytokines together with products of the activated complement system (e.g., C3b, iC3b and C5a) and APL antibodies themselves have each been demonstrated to activate endothelial cells thus providing a stimulus and up-regulate adhesion molecules and tissue factor. These molecules are thought to act on leukocytes and platelets to increase their adhesion to vascular endothelium. This promotes microthrombosis and the local release of toxic mediators, including proteases and oxygen-derived free radicals. In the presence of APL antibodies these cells interact leading to the diffuse microvasculopathy that characterizes CAPS and leads to multi-organ failure.

**Clinical manifestations of CAPS**

The clinical manifestations of CAPS depend on the organs that are affected, by the thrombotic events and the extent of the thrombosis, together with manifestations of the SIRS. Unlike classic APS where single venous or arterial medium to large blood vessel occlusions are common it is rare in patients with catastrophic APS. Multiple organ dysfunction and failure, as a consequence of thrombotic microangiopathy, are responsible for the majority of the clinical features. The most common known trigger for CAPS is infection. Other less common causes are anticoagulation withdrawal or low INR, medications (e.g., oral contraceptive), obstetric complications, neoplasia, systemic lupus erythematosus flares, trauma and surgery. In almost half of the cases, no obvious precipitating factors have been identified and CAPS can often occur in patients without any previous thrombotic history. Our patient had no thrombotic history. We suspected a combination of a pulmonary infection and an SLE flare as the triggers of this CAPS episode.

She had presented with respiratory and neurological symptoms on admission. These are the two most common presentations of CAPS. In a review by Cervera et al. of 280 patients with CAPS from the website-based international CAPS registry they reported that the first clinical manifestation at the time of the catastrophic episode was a pulmonary complication in 24% of the cases, a neurologic feature in 18% and a renal feature in 18%. In our case the initial manifestation was a neurological manifestation as seizures and memory loss. Although the initial presentation of CAPS may involve a single organ, in a very short period of time, typically days to weeks, patients develop clinical evidence of multiple organ thrombosis and dysfunction leading to organ failure that requires Intensive Care Unit (ICU) admission. The patient was admitted in ICU with multi-organ failure involving the neurological, respiratory, renal, haematological and hepatic systems. This is in keeping with data by Cervera et al. In the same review on the cohort of CAPS patients during the catastrophic episode, intra-abdominal involvement was identified in the majority of patients, mainly consisting of renal (71%) followed by hepatic (33%), gastrointestinal (25%), splenic (19%), adrenal (13%) and pancreatic (8%) manifestations. Respiratory complications (64%) were common mainly acute respiratory distress syndrome and pulmonary embolism, but occasionally intra-alveolar haemorrhage. Cardiac manifestations (51%), were mainly cardiac failure and myocardial infarction or valve lesions. Cerebrovascular complications were present in 62%, mainly consisting of encephalopathy and cerebrovascular accidents with a smaller number of seizures, headache or silent brain infarcts. Skin manifestations represented 50% with features including leg ulcers, purpura, splinter haemorrhages livedo reticularis, necrotic lesions, digital gangrene, and multiple ecchymosis. Less numbers of deep venous thrombosis (23%) and peripheral arterial occlusive disease (11%) were detected. Rarer manifestations reported included retinal involvement (7%), mononeuritis multiplex (5%) and bone marrow necrosis (4%).

**What are the diagnostic challenges in CAPS?**

Making the diagnosis of CAPS can be an enigma. There are many conditions that mimic CAPS. Examples include sepsis, Disseminated Intravascular Coagulation (DIC), Thrombotic Thrombocytopenic Purpura (TTP) and Haemolytic Uremic Syndrome (HUS). Sepsis was high on our list of differentials because of fever, multiple organ involvement with suggestive laboratory findings in a short duration of time. We suspected the focus of infection to have originated from the lungs. When sepsis is associated with DIC potential complications include bleeding, thrombocytopenia, and microthrombosis; all are also common in CAPS patients. Thus, both the pathophysiology and clinical manifestations of CAPS resemble sepsis with the ultimate development of multiple organ dysfunction syndrome. DIC can also mimic CAPS. The two are similar as they are multi-systemic involving renal, liver, lung and central nervous...
system involvement. CAPS differs from it as it has less widespread haemorrhage. Our patient had multi-organ involvement but no widespread haemorrhage.

TTP, HUS and haemolysis, elevated liver enzymes and Low Platelets (HELLP) syndrome which have to be considered were also considered. These was because of deranged liver function tests but were dropped due to lack of significant haemorrhage, haemolysis and low platelets (Table 3). Some of these conditions at times overlap with CAPS as part of a continuum of thrombotic microangiopathy conditions and can present a diagnostic challenge in differentiating them.

To make the diagnosis of CAPS, there should be clinical evidence of multiple organ involvement developed over a short period of time, histopathologic evidence of multiple small vessel occlusions and laboratory confirmation of the presence of aPL, usually in high titer (Table 1). The presence of aPL, namely anticardiolipin, antiphospholipid antibodies (APL) becomes transiently negative at the time of infection, debridement or amputation of necrotic tissues/organs, careful management of intravascular instrumentation, especially arterial which can lead to new clots, are extremely important and can substantially improve the rate of survival.

The optimal treatment regimen for CAPS is unknown. Current treatment guidelines suggest that early diagnosis and aggressive therapies are necessary to avoid the potentially fatal outcome. The combination of high doses of intravenous (iv) heparin, iv. steroids, iv immunoglobulins and/or repeated plasma exchanges are the basic treatment of choice for all patients with this severe condition (Evidence Level II)\(^{16}\).

In the absence of a clinical randomized control trial, anticoagulation (AC) together with corticosteroids (CS) is the most commonly used regimen (19.8%). We were able to put the patient on anticoagulation and corticosteroids which is readily available in our local health set-up. This is followed by anticoagulation with corticosteroids and/or IV immunoglobulins (IVIG) (17.4%). The highest recovery rate is achieved by the combination of AC with CS with Plasma Exchange (PE) (77.8%), followed by anticoagulation with corticosteroids with plasma exchange and/or IVIG (69%)\(^{16}\). IV immunoglobulins and plasma exchange are not readily available due to financial implications and their availability locally. Maybe this may have produced better results in our patients. Anticoagulation is usually given in the form of heparin, which is the mainstay of treatment in patients with catastrophic APS.\(^{17}\) Corticosteroids act by inhibiting nuclear factor-κB, which is an important mediator in both systemic inflammatory response syndrome and APL-mediated thrombosis\(^{16}\). However analysis of the CAPS Registry shows that corticosteroids alone does not improve outcome. Plasma exchange clearly improves patient survival by removes APL (most likely transiently), as well as cytokines, tumor necrosis factor-alpha, and complement products\(^{18-20}\).

IVIG has multiple therapeutic points of actions and has been shown to improve the outcome according to the CAPS Registry\(^{21}\). There has been promising results on treatment with rituximab, an anti-CD20 monoclonal antibody is effective in catastrophic APS, as evidenced in two patients in a case series that treated with rituximab during the event\(^{22}\). Although more data are necessary to support the use of this drug in the setting of CAPS, current experience seems quite promising, especially in patients with severe thrombocytopenia.

Comparing the data on demographic, clinical and immunologic characteristics of patients who survived to those who died several prognostic factors have been identified. They include older age, pulmonary and renal involvement, the presence of SLE and high titre of antinuclear antibodies (ANA) were associated with a higher mortality rate\(^{23}\). Our patient had three poor prognostic factors which included the presence of SLE, pulmonary and renal involvement.

There have been case reports of CAPS relapse. Precipitating factors in these patients were infection, sub-therapeutic anticoagulation level and anticoagulation withdrawal. The presenting symptoms were very similar to the first CAPS episode (renal failure followed by cerebral, cardiac and pulmonary involvement)\(^{24}\).

Conclusions

APS is a systemic autoimmune disease with both thrombotic and non-thrombotic manifestations. CAPS is the most severe form of APS with multiple organ thromboses, usually accompanied by microthrombosis and haematologic manifestations. Although less than 1% of patients with APS will develop this complication, its potentially lethal outcome underlines its significance in clinical medicine today. The clinical manifestations of CAPS may evolve gradually, commonly overlapping with other thrombotic microangiopathies, requiring a high index of clinical suspicion. The majority of patients with catastrophic APS will end up in intensive care units with multi-organ failure and, unless the condition
is considered in the differential diagnosis by attending physicians. This may be completely missed, resulting in a disastrous outcome.

Third world countries have few case reports due to problems from infrastructure of laboratory to radiology services. This means that diagnosis will have to be on level of suspicion. Patients presenting with multi-organ involvement background of lupus or unexplained atypical or recurrent thromboses should be investigated for CAPS. A prompt diagnosis will enable physicians to take measures to prevent death from this syndrome. An aggressive treatment with steroids, anticoagulation and IVIG in an ICU setting, will help prevent the progression of organ failure or the development of septic shock in the infected patients.

References

Guidelines to authors

The African Journal of Rheumatology is published biannually by the The African League of Associations for Rheumatology (AFLAR). The journal aims to publish papers on basic and clinical research in rheumatism and arthritis and be a vessel of sharing knowledge a close the globe. Original research work, reviews, case reports and other relevant scientific work will be published in the journal on the understanding that the work submitted will not be under consideration in any other journal. This must be stated by the authors when submitting papers. All submitted papers will be acknowledged and are peer reviewed. The journal will strive to communicate to the authors the verdict of the reviewers within three months form date of submission. Papers should be submitted to; The Editor, African Journal of Rheumatology, P. O. Box 29727 – 00202, Nairobi, Kenya. Email: rheumatologyjournal@gmail.com Studies on patients and volunteers require informed consent and this must be clearly stated in the paper. Authors of this kind of papers must as well state the study has been cleared by the relevant ethics committee Submitted papers should follow the guidelines below;

1. Original research papers should follow the IMRAD format and the abstract should be structured and not more than 30 references. The paper should not exceed 3000 words. Reviews should have an abstract, introduction and the rest of the review should have the necessary sub-headings with no more than 50 references. The review should have no more than 4500 words.

2. Case reports should have a background, introduction followed by the discussion with not more than 20 references. The word count should not exceed 2000 words. Perspectives or scientific letters should be in prose form and should not exceed 1500 words.

3. References should be numbered in order of appearance (Vancouver style) and only those cited should appear in the reference list.
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CONGRESS PROGRAMME

MONDAY 21st Sept, 2015 ARRIVAL

TUESDAY 22nd Sept, 2015
6am - 7am Exhibition and poster abstracts stands set up
7.00am - 10.00am Registration opens
10.00am - 11.30am Guest Lecture
11.30am - 12.00noon Tea Break
12.00pm - 1.30pm Guest Lecture
1.30pm - 2.30pm Lunch
2.30pm - 4.00pm Guest Lecture
4.30pm - 6.00pm AFLAR Meeting
6pm Cocktail party

WEDNESDAY 23rd Sept, 2015
8am 5pm - Full Day Scientific Programme
7pm Dinner

THURSDAY 24th Sept, 2015
8am- 2.00pm Scientific Programme
2.00pm - 2.30pm Congress Closure - AFLAR President

FRIDAY 25th Sept, 2015 Departure
Topics to be deliberated include rheumatoid arthritis, SLE, Recurrent pregnancy loss and Antiphospholipid syndrome, osteoarthritis, gout, and back pain.

CME points will be awarded.
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The journey so far - a new rheumatology clinic in Lagos

Edomwonyi Ul, Adetimhin M1, Ayanlowo O2, Akinkugbe A2, Adelowo O2

Background: Few rheumatologists, fewer rheumatology clinics in sub-Saharan Africa, an increasing burden of rheumatic diseases and a poor knowledge of them demonstrate the need to expand rheumatology services in sub-Saharan Africa. As at January 2012 in Lagos, two rheumatology clinics served 17 million people - one a private rheumatology clinic and the other at the State Teaching Hospital. At that point in time a new rheumatology clinic was started in the Federal Teaching Hospital in Lagos. With the recent appointment of a Professor of Rheumatology at the clinic (2015), we assess the patients seen so far.

Methods: This is a retrospective study of patients who presented at the rheumatology clinic of LUTH. Patients who fulfilled classification criteria for a rheumatologic disorder were included. Data was obtained from the clinic register and patients’ clinic records and analysis done with SPSS 21.

Results: The total number of patients seen in the study period was 233 patients, with an age range of 2 to 82 years and a mean age of 43.37 years. The Female: Male ratio was 5.7:1.

Conclusions: The rarity of autoimmune rheumatic diseases in Africa has been disproved. This study highlights the range of rheumatic diseases seen in Africa. Notwithstanding the challenges of commencing a new rheumatology clinic in a resource poor setting, awareness of rheumatic diseases is on the rise evidenced by the range of referring sources. Challenges included cultural perceptions, poor follow-up visits, lack of trained support staff, affordability and availability of appropriate tests and treatments. Advocacy, education and awareness efforts helped encourage referrals and patient follow-up.

Key words: Rheumatologists, New Rheumatology Clinic, Sub-Saharan Africa, Rheumatic diseases.

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Knowledge, Attitude and Practices of health care workers on corticosteroid adverse drug events in rheumatologic, respiratory and dermatologic clinics in a teaching hospital in Nairobi

Ilovi CS¹, Mecha JO¹, Kigamwa P², Mutai K³, Mwachinga M, Genga EK¹, Sheikh A¹, Owino B³, Wanjau W¹, Munyao T¹, Oyoo GO¹

Background: Corticosteroids form the cornerstone of management for a myriad of rheumatological, dermatological and chronic respiratory tract diseases. Whereas these drugs are crucial in reducing morbidity and mortality, they are not without inherent grave risks. Health care workers (HCWs) providing care to patients on long term corticosteroids are required to be well versed with these adverse drug events (ADRs).

Materials and Methods: Kenyatta National Hospital, the teaching hospital of the University of Nairobi, has established rheumatology, respiratory and dermatology clinics. As biologic agents are not yet available in these clinics, corticosteroids, as well as other immunosuppressant drugs remain vital in control of immunological diseases. HCWs in these clinics were requested to complete a self-administered open ended questionnaire assessing their knowledge of corticosteroid ADRs.

Results: Sixty-two HCWs were recruited, comprising of nurses (21%), pharmacy staff (12.9%) and senior house officers (66.1%). Majority (74%) had been stationed for over 1 year at the clinic. ADRs of corticosteroids: Median (IQR) number of correct responses was 6.0 (3.0-9.5). Only 61% identified >5 ADRs. Proportion of respondents who documented the various ADRs; Metabolic disorders- 89%, Cutaneous- 61%, Mineral bone disease- 37%, GIT- 36%, Neuropsychiatric- 32%, Adrenal suppression-24%, Ophthalmic- 21%, Myopathy- 18%.

Drugs that potentiate the ADRs of corticosteroids: Median (IQR) number of correct responses was 1.0 (1.0-2.0). Proportion of respondents who identified the drugs; Cytotoxics- 34%, NSAIDs-35%, Anticoagulants- 15%, Others- 10%.

Advice that should be given to patients on corticosteroids: Median (IQR) number of correct responses was 2.0 (2.0-3.0). Surveillance for ADRs- 53%, adherence to duration and dosage-48%, tapering of corticosteroids- 32%, drug interactions- 16%, drugs to counter corticosteroid ADRs- 13%, steroid cards- 7%.

Conclusion: Although HCWs routinely administer corticosteroids, the awareness of ADRs and potential drug interactions is low. This needs to be addressed in order to ensure adequate surveillance of ADRs.

Key words: Corticosteroid, ADRs, Healthcare workers
**Cutaneous findings in SLE patients at a rheumatology clinic in a tertiary hospital in Nigeria**

Ayanlowo O, Edomwonyi UI, Adelowo F, Akinkugbe A

**Background:** Systemic lupus erythematosus (SLE) is a systemic autoimmune connective tissue disorder. The clinical presentation is protean and affects the skin, joints and other internal organs of the body. It can present with cutaneous lesions only and the skin findings may predate other systemic features. The American College of Rheumatology criteria for diagnosis of SLE has 4 cutaneous signs out of the 11. It could be diagnosed in patients who present with only skin features, in the presence of a serological marker according to the Systemic Lupus International Collaborating Clinics (SLICC). This study aimed to document the cutaneous findings in SLE patients who presented at the Lagos University Teaching Hospital (LUTH) between January 2012 and July 2015.

**Methods:** This was a retrospective study of SLE patients who presented at the rheumatology clinic of LUTH. Data was obtained from the clinic register and patients’ clinic records and analyzed using SPSS 21.

**Results:** Out of the 233 patients with rheumatologic condition seen during the study period, 63 (27.2%) had SLE. Twenty six (45.61%) out of the 57 patients with SLE had cutaneous lesions. Twenty out of the 26 patients (76.9%) had chronic cutaneous (discoid) lupus erythematosus (CCLE); while 3 (11.54%) had subacute cutaneous LE; and another 3 (11.54%) had acute cutaneous LE. Lupus erythematosus affects predominantly females: SLE (28.5:1) and cutaneous LE (9:1). Mean age of presentation for SLE was 33.17 and age range 8 to 68 years; the mean age of those with cutaneous lesion was 31.7 years, age range of 16 to 68 years. We also treated 11 patients without systemic symptoms and negative serological markers: purely cutaneous LE.

**Conclusion:** Studies revealed that cutaneous lesions are common presentations of SLE in Nigerians; CCLE being the most common type. It is advised that all patients with cutaneous lupus should be screened for SLE.

**Key words:** Systemic lupus erythematosus, Chronic cutaneous lupus erythematosus, Skin, Nigerians.
Oral abstract

Functional genomics of apolipoprotein L1 in vascular manifestations of systemic lupus erythematosus


Background: African systemic lupus erythematosus (SLE) patients experience excessive renal morbidity/ mortality, and cardiovascular (CVD). Apolipoprotein L1 (APOL1) risk variants (RV) which confer an evolutionary advantage in resisting African Trypanosomiasis increase the risk of renal and CVD. Moreover immune factors may regulate APOL1 expression. This study focused RV dependent clinical correlates in SLE, type 1 Interferon (IFN) induced APOL1 expression, and the association of IFN and APOL1 mediated endotheliopathy.

Methods: One hundred and two African American SLE subjects and six healthy subjects (cord tissue) were genotyped for APOL1 by PCR sequencing. For the former, SLE activity was evaluated by chart review and sera were evaluated for sE-selectin (ELISA), a marker of CVD risk. For the latter, endothelial cells (ECs) were isolated from umbilical cords of 6 healthy subjects of African ancestry (ancestral (WT/WT) = 2, RV/WT= 2, RV/RV= 2). Assessments of ECs given IFNα (100 units/mL) included qPCR of APOL1, genotyping of transcript to evaluate genetic concordance, and genotype-phenotype relationships of IFN-dependent apoptosis.

Results: For patients the WT/WT, RV/WT, and RV/RV groups comprised 37.6%, 49.4%, and 13% of the cohort respectively. There were no associations between genotype and demographics, SLE activity, or nephritis history. RV/WT and RV/RV groups (compared to WT/WT) showed significantly increased serum sE-selectin with SLEDAI ≥8, increased dsDNA, and decreased C4 (p= 0.009, 0.003, 0.03). Inclusive of all genotypes, exposure of EC to IFN increased APOL1 expression vs untreated (9.21 fold (+/- 1.8; p: 0.001, 4 hrs). RV/WT ECs showed biallelic transcript expression. There was increased apoptosis in the IFN treated vs untreated endothelial cells involving RV/WT (delta= 9.25% +/-1.8; p=0.013) and RV/RV (delta=3.7% +/- 3.22; p=0.18) but not WT/WT ECs (delta= -4.4% +/- 16.4 p=0.69).

Conclusions: Increased IFN and SLE-relevant inflammation may increase APOL1 expression leading to adverse effects on the endothelium. Control of chronic inflammation may be a step forward in preventing APOL1-related organ damage in African SLE patients.

Key words: SLE, APOL1, Cardiovascular disease, Renal disease
Clinical characteristics of patients with systemic lupus erythematosus in Nairobi, Kenya

Oyoo GO1,2, Genga EK1,2, Otieno FO2, Shiruli BC1, Odhiambo J1, Omondi EA2

Background: Systemic lupus erythematosus (SLE), a chronic multisystem autoimmune disease with a wide spectrum of manifestations, shows considerable variation across the globe, although data from Africa is limited. Quantifying the burden and description of symptoms of SLE across Africa can clarify the role of genetic, environmental and other causative factors in the natural history of the disease, and to understand its clinical and societal consequences.

Aim: To determine the clinical profile of systemic lupus erythematosus (SLE) patients at a tertiary care centre in Nairobi, Kenya.

Methods: Patients fulfilling the 2012 SLICC criteria for SLE seen between January 2012 and January 2013 were included in the study.

Results: A hundred patients were evaluated for SLE over a one year period. Ninety seven per cent of the study participants were females with a mean age of 36.6 years. Thirty three years was the mean age of diagnosis. The mean time duration of disease was 3 years with a range of 0-13 years. Non erosive arthritis and cutaneous disease were the commonest initial manifestation. Antinuclear antibody (ANA) assay and anti-dsDNA was positive in 82% and 52%. Patients on steroids, non-steroidal drugs and synthetic disease modifying anti-rheumatic drugs were 84%, 49% and 43% respectively. None of the patients were on biologic disease modifying anti-rheumatic drugs.

Conclusions: SLE is a multisystem disorder affecting predominantly young females. Polyarthritis and cutaneous disease were the most common clinical feature. This is comparable to other studies done in black African population. We found a higher prevalence of haematological and lower rate of renal disease as compared to other studies done in black Africans. The antinuclear antibody (ANA) assay and anti-dsDNA positivity was lower than those in other studies on black Africans. Majority of the patients were on steroids.

Key words: SLE, Nairobi, Kenya.
Juvenile systemic lupus erythematosus

OO Adelowo¹, Olaosebikan H¹, Animashaun AB², Akintayo R¹

Background: Juvenile systemic lupus erythematosus (JSLE) is a severe, relapsing, chronic multisystem disease, characterized by widespread inflammation and damage to any organ. SLE has previously been said to be rare in Africa, recent data show increasing reportage in Nigeria and other African countries.

Aims: The aim of our study is to highlight the demographic, clinical, laboratory and treatment outcomes of Nigerian children with SLE.

Methods: This was a three year retrospective cross-sectional study of children, who were admitted to paediatric and adult emergency unit of LASUTH, Ikeja, Nigeria.

Results: Twelve patients were studied (F:7; M:5); mean age was 14.3 years (SD±2.9); age range was 10 years (minimum-8, maximum-18), mean illness duration was 1.95 years (SD±1.03, Range-3, minimum-1, maximum-4). Clinical presentations included constitutional symptoms (n=12), clinical lupus nephritis (n=8), hypertension (n=5), cardiopulmonary manifestations (n=7), muco-cutaneous manifestations (n=5), arthritis (n=5), central nervous system manifestations (n=4) and infections (n=3). The laboratory features identified were anaemia (n=10), leucopenia (n=4), thrombocytopenia (n=3), dipstick proteinuria (n=8), haematuria (n=6), urinary casts (n=4), positive antinuclear antibody (n=12), positive auto-antibody to extractable nuclear antigens (n=12) and anti-dsDNA (n=10).

The mean erythrocytes sedimentation rates, haematocrit, platelet and leucocytes was 100.8 mm/hr (SD±20.8, range-65, minimum-65, maximum-130), 21.7% (SD±4.6, range-14, minimum-15, maximum-29), 201,000/mm³(SD±88,000) and 3,358/mm³ (SD±1540, range-5200, minimum-1500, maximum-6700) respectively. Treatment was with intravenous pulse methyl prednisolone for three days (n=10), oral prednisolone and hydroxychloroquine (n=12), oral prednisolone, hydroxychloroquine and azathioprine (n=8) and IV rituximab (n=4). In terms of the outcome, there were 4 mortalities while 8 patients had low disease activity and were discharged while 3 were lost to follow up among the discharged patients. End-stage renal diseases from lupus nephritis was the cause of death.

Conclusion: Constitutional symptoms, clinical lupus nephritis and cardiopulmonary diseases are common initial manifestations of JSLE that may be unrecognized as they share similar presentations with common paediatric conditions in our environment. We advocate for investment in training of paediatric rheumatologists in Nigeria as there are no such specialists in West Africa to manage this life threatening condition with high morbidity and mortality.

Key words: Juvenile, Lupus, Lagos Teaching Hospital
**Oral abstract**

**Osteoarticular infections in patients with diabetes in Bamako, Mali**

Kodio B, Pamanta IS, Touré S, Touré M, Ah Cissé I

**Background:** Infectious complications of diabetes are particularly important. Diabetes infection can affect the skin, muscle, bone or joint. Their frequency increases with more serious prognosis and often leading to costly and debilitating surgical amputation.

**Objective:** To describe epidemiological, clinical, bacteriological, radiological, and therapeutic of osteoarticular infections in diabetic patients.

**Methods:** This was a prospective, descriptive study of the diabetic patients with osteoarticluar infections at the rheumatology ward of Point G University Teaching Hospital between January 2005 and June 2006.

**Results:** Prevalence of diabetes was 137/2140 (6.4%). Among the 137 diabetic patients hospitalised, 17 patients (12.4%) fulfilled our inclusion criteria. The baseline profile was as follows: Female (52.94%) Male (47.6%); Mean age of 55.11 years (range 40-69) and normal weight (52.94%). Diabetes type 2 was common (94.25%) with mean duration of 5.33 ± 5 years (range 6-10). Osteoarticluar infections were localized at the foot (64.7%), hand (29.41%), and knee (5.88%). Investigation features were as follows: hyperglycemia (87%), anemia (75.73%) elevated ESR (58.82%), positive CRP (70.58%), leukocytosis (47.2%). Bacteriological proofs: *Staphylococcus aureus* (41.7%), other organisms are *Escherichia coli, Proteus mirabilis, Acinetobacter, Morganella morganii*. Radiological changes were dominated by osteitis (66.7%) predominated in patients with diabetes type 2 and localized at the foot (58.82%) and hand (41.18%). Insulin and appropriate antibiotic therapy (≥ 3 months) improved patients’ clinical conditions. However surgical amputation was indicated in 6 patients.

**Conclusion:** Osteoarticular infections are prevalent in patients with diabetes. Although dominated by foot location, hand was also reached. *Staphylococcus* remains the most offending organism.

**Key words:** Osteoarticular, Infection, Diabetes, Mali
Pattern of medication use in an inception cohort of SLE patients in Ghana, West Africa

Ida Dzifa Dey

**Background:** Systemic lupus erythematosus (SLE) is a multiorgan autoimmune disease of unknown cause. A wide range of medications are used for treatment, subject to organ involvement and severity. We look at the different drugs currently used to treat SLE in a cohort in Ghana, West Africa.

**Materials and Methods:** A retrospective analysis was done of the patients records at the Department of Rheumatology at the Korle Bu Teaching Hospital, 126 patients with SLE fulfilling the criteria of the American College of Rheumatology (updated 1997) had been followed up over the past four years.

**Results:** One hundred and twenty six cases of SLE were seen over the period though some (four) have been lost to follow up and had missing data. Males 7 (5.6%), females 119 (94.4%). Mean age was 33.1 years SD (12.2) range 13-66. Twenty two (17.3%) had their diagnosis at inception being lupus nephritis. Sixty three (52.5%) were on small doses of prednisolone (0-10mg), 25.8% were on moderate doses (10-30mg), 22 (18.3%) were on large doses (30-60mg) and 4(3.3%) had none. 85(86.4%) were on hydroxychloroquine. Azathioprine was used in 38(30.4%) out of 125 patients, with methotrexate being used in 20 (18.7%). Five (4%) patients were on mycophenolate mofetil, four for lupus nephritis and one for resistant myositis. Ten (8%) patients had used cyclophosphamide mainly for lupus nephritis and one patient had a course of rituximab for resistant skin disease.

**Conclusion:** Most patients were on hydroxychloroquine as recommended, and preferred over methotrexate for musculoskeletal manifestations, Eurolupus regime was used mainly to treat lupus nephritis and very few could afford mycophenolate mofetil. Biologics were hardly used. Understanding choices behind the medication use pattern would be useful for efficient management of patients for the future.

**Key words:** Systemic manifestations, Systemic lupus erythematosus, Medication use, Ghana
**Background:** Skin manifestations of chronic inflammatory rheumatism (CIR) are commonly encountered in current rheumatologic practice. Although not pathognomonic, they are very helpful to establish a positive diagnosis. They allow identifying subsets of patients within established nosology by virtue of their prognostic meaning.

**Objective:** To describe skin manifestations of some commonly occurring CIR.

**Methods:** A retrospective chart review of patients with CIR hospitalised to the rheumatology ward of Cocody University Teaching Hospital of Abidjan, Cote d’Ivoire between January 2008 and December 2013.

**Results:** Among the 233 patients hospitalized for CIR, 98% had polyarthritis and extra-articular manifestations which represented: skin signs (33.0%), anaemia (31.3%), gastrointestinal involvement (30.9%), lungs involvement (20.6%). The baseline profile of 77 patients with skin signs was as follows: Female (81.8%) Male (18.2%); mean age of 36.51 years (range 4-74), mean duration of symptoms (25.4 months, range 1-204). The main diagnostics were: SLE (36.4%), RA (15.6 %), systemic scleroderma (9.1%), Still disease (6.5%), dermatomyositis (5.2%) and psoriatic arthritis (5.2%). Rheumatic manifestations of leprosy (n=1), suspected Behçet’s disease (n=1) and systemic sarcoidosis (n=1) were identified. The major skin manifestations are shown in Table 1. Skin biopsy was performed in 8 cases. Investigation results were as follows: elevated ESR (30%), positive CRP (66.23%), positive RF (28.6) positive Anti CCP (12.5%), positive AntiDNA (40%), positive HIV (n=3). Radiological changes in joint X-ray were dominated by erosive arthritis (66.23%).

**Conclusions:** Skin signs were very frequent, occupying the forefront of extra-articular manifestations of CIR. Although our study was limited, it provided for the first time data. There is a suggestion for further investigation in a larger population and collaboration with dermatologists.

**Key words:** Skin, manifestations, Chronic rheumatism
Rheumatology workforce in Africa: The challenges of providing care with limited resources including workforce

Omondi G. Oyoo

Life threatening communicable diseases, inadequate and over-burdened public health systems, and struggling economies place a tremendous strain on health systems with very limited resources in sub-Saharan Africa. Poverty, political instability and unemployment compound these challenges and further contribute to the main disparity between the developed and developing world. The health workforce is alarmingly scarce both in numbers and training.

Musculoskeletal conditions though prevalent in Africa remain largely orphan diseases because of fierce competition for scarce resources.

Health professionals, administrators and government officials need to work together and identify the burden of rheumatic diseases as an important health focus. Partnership between the international community and Africa could be instrumental in achieving this success. Collaboration and funding from international musculoskeletal institutions and the wider community towards the growth and development of rheumatology care in Africa is vital to develop and improve services.

How can you help?
Health care worker training programmes: Sharing the Kenyan experience

Omondi G. Oyoo

Despite what seems to be a significant burden of rheumatic diseases in East Africa, huge deficiencies in education and training of health professionals exist. World health organization recommends that there should be at least one rheumatologist per 100,000 people. However in sub-Saharan Africa (excluding south Africa), there are less than 20 rheumatologists for over 8000 million people and only four for a population of over 100 million in East Africa.

Appropriate training of suitably qualified staff could help rectify this. Unfortunately, a lack of well-developed curricula for teaching rheumatology in East Africa has resulted in inadequate teaching in medical schools.

Primary care physicians, internists and middle-level care medical carers such as nurses and clinical officers in Kenya currently play a major role in managing these patients. Despite inadequate training, they have to recognize, diagnose and treat patients with MSK conditions. With few functioning rheumatology clinics, patient management is haphazard and without guidelines or adequate intervention strategies.

Bridging the gap between patients and rheumatologists can be achieved by giving basic training to the nurses, clinical officers and primary care physicians who are often the first point of contact for patients. This method is already being used for managing diabetic patients in Kenya and has been successful.
Youngest juvenile idiopathic arthritis patient ever

Dedeke IA1, Akintayo R2, Olaosebikan BH3, Adelowo OO3

Background: Juvenile idiopathic arthritis (JIA) is the commonest diagnosed Rheumatic disease in children but rarely reported in blacks. This case of JIA in a Nigerian child is particularly interesting, considering the age at onset. To the best of our knowledge, JIA onset as early as 3 months old has never been reported among blacks in literature.

Methodology: Patient was reviewed in an outpatient Rheumatology clinic where a detailed medical history was taken. This revealed a 16 months old male child with history of recurrent polyarticular joint pain and swelling involving the knees, right ankle, feet and wrists, with onset at 3 months of age. There was initial affectionation of the ankles and feet before involving the other joints. There was associated recurrent fever but no rash or other constitutional symptoms. No other systemic symptoms. No prior history of trauma or family history of similar complaints. Patient’s haemoglobin electrophoresis done on several occasions was AS. Patient’s birth weight was 2kg with no delay in reaching developmental mile stones, apart from the delay in walking due to the knees and ankle pain and swelling.

Results: General examination revealed a pale, afebrile, young child with significant peripheral lymphadenopathy in the axillary and epitrochlear nodes bilaterally, and the right submandibular regions. Musculoskeletal examination revealed swollen, warm and tender knees, ankles, hands and feet with no deformity. Examinations of other systems were unremarkable. A working diagnosis of JIA was made, to keep in view juvenile onset connective tissue disease. Investigation revealed anaemia (27%), thrombocytosis (561x10⁹/L), leukocytosis (19.85x10⁹/L), elevated erythrocyte sedimentation rate (100mm/hr). Serum ferritin was also elevated (692ng/dl). Also, his blood film examination revealed no blast cells. Serology revealed a positive Antinuclear Antibody titre (1:80); Rheumatoid factor was <10.0I.U/ml; Extractable nuclear Antibody and viral screening (HIV, HBV, HCV) were negative. Liver and kidney function tests were normal. Electrocardiography, echocardiography, and chest X-rays were unremarkable. A diagnosis of systemic JIA was made, and promptly commenced on DMARDs- subcutaneous Methotrexate 7.5mg weekly and syrup Ibuprofen 5mls twice daily. Patient responded well to treatment as evidenced by complete resolution fever, tenderness and swelling of the joints.

Conclusion: JIA may present as early as 3 months and thus a high index of suspicion is required in infants with joint pains. To the best of our knowledge, this is the youngest ever JIA patient reported.

Key words: Infant, Juvenile idiopathic arthritis, Nigerian, Child
Background: Systemic autoimmune rheumatic diseases (SARD) are chronic autoimmune disorders which affect more than one organ system in the body. They are increasingly being reported among Africans, but there has been no documented report of familial clustering among black Africans. We present 3 Nigerian families with systemic autoimmune rheumatic disease.

Methodology: The patient was a 44-year old female who presented to the Dermatology Clinic with a 3-month history of alopecia, skin rash, recurrent fever and fatigue. Physical examination showed multiple discrete lesions of scarring alopecia on the scalp, and atrophic lesions on both cheeks. She also had bilateral pitting pedal oedema up to the lower half of both legs. Her daughter was a 27-year old female who presented with a two-year history of pain in all the joints of both hands. There was an associated history of early morning stiffness, swelling of the joints and deformities. On physical examination, there was swelling of all the proximal interphalangeal (PIP) joints of both hands, and ulnar deviation at the PIP joints. The squeeze test was positive in both hands.

Results: The mother’s investigations revealed: Full blood count (FBC) with a Haematocrit (Hct) of 35%; white blood cell count (WBC) of 4.4 x 10^9/L; Platelet count- 243 x 10^9/L; ESR was 63mm/hr. Urinalysis showed proteinuria 3+. Serologies done showed that the antinuclear antibody (ANA) was positive, at a titre of 1:2,560, speckled pattern. Anti double stranded DNA antibodies (Anti-dsDNA) was positive. A diagnosis of SLE, with lupus nephritis was made, using the 1997 American College of Rheumatology criteria for SLE. She was treated with tablets azathioprine 50mg bd, tablets hydroxychloroquine 400mg daily, tablets prednisolone 40mg daily (which was tapered to a dose of 10mg daily) and tablets omeprazole 20mg daily.

Her daughter’s investigations were: Full blood count with Hct 26.9%, WBC 8.1 x 10^9/L, Platelets 402 x 10^9/L; ESR was 132mm/hr. She also had a positive rheumatoid factor (RF) 160 IU/ml (reference range: 0-20 IU/ml); anti-CCP was however, normal. Radiographs of both hands showed carpal and periarticular osteopenia; ulnar subluxation at the proximal and distal interphalangeal joints of 1st-4th phalanges of both hands; Swan neck and Boutonniere’s deformities in the proximal and distal interphalangeal joints respectively of the same hands. There was narrowing of the cartilage spaces and erosion of the heads of the phalanges with fusion of the carpometacarpal joints bilaterally. A diagnosis of rheumatoid arthritis (RA) was made. She was managed on an outpatient basis with prednisolone tabs 15mg dly (which was tapered down and subsequently discontinued); tabs hydroxychloroquine 200mg dly; tabs methotrexate 7.5mg weekly (which was increased to 15mg weekly); tabs folic acid 10 mg weekly, tabs sulphasalazine 500mg bd, and tabs omeprazole 20mg daily. They are still being followed up, and are clinically stable.

Conclusion: SARD, as it occurs in the Caucasians is also found in the Black race, if only we take time to look for it. Physicians dealing with auto-immune diseases should therefore take time to search for such diseases in the affected families.

Key words: Systemic autoimmune diseases, Familial clustering, Nigerians
Adult Onset Still’s Disease; a rare disease in Nigeria?

Ohagwu KA¹, Aigbokhan EE², Olaosebikan H³, Adelowo OO³

Introduction: Adult Onset Still’s Disease (AOSD) first described by Bywaters in 1971 is an inflammatory disease of unknown etiology. Its global prevalence is estimated at 1 case per 100,000. Because of its pattern of presentation which mimics many inflammatory and malignant conditions, the diagnosis requires high index of suspicion. Few cases have been reported from Africa. The first case in Nigeria was reported in July 2015. We hereby report two more cases diagnosed in the same rheumatology clinic of Lagos State University Teaching Hospital within six months of the first reported case. This is to highlight the fact that the disease while rare, requires a high index of suspicion for diagnosis.

Methodology: This is a descriptive case series of two patients seen at the Rheumatology Clinic of Lagos State University Teaching Hospital, Lagos State, Nigeria. The first patient was treated with oral prednisolone, azathioprine and hydroxychloroquine. The second patient received intravenous pulse methylprednisolone for three days followed by oral prednisolone and methotrexate.

Results: Both patients were males. The ages of the patients were 19 and 62 years. Both patients had high grade fever, symmetrical inflammatory polyarthritis and weight loss. The first patient had sore throat. On examination, both were found to be febrile. The second was emaciated and pale. Both patients had marked leukocytosis with neutrophil predominance, thrombocytosis, elevated liver enzymes and raised erythrocyte sedimentation rate and C-reactive protein. Rheumatoid factor, anti-CCP, anti-nuclear antibody and extractable nuclear antigen were negative in both patients. Serum ferritin was markedly elevated in both. Retroviral screening, anti-HCV and HBsAg were negative in both. Septic work up and direct Coomb’s test were negative in them. Peripheral blood film was normal and bone marrow aspirate was suggestive of chronic inflammatory condition in the second patient. Both made good clinical recovery.

Conclusion: AOSD is a rare inflammatory condition that requires high index of suspicion for diagnosis. This report highlights AOSD as an important differential diagnosis of inflammatory arthritis.
Is this idiopathic pulmonary fibrosis or systemic sclerosis associated interstitial lung disease? Cutaneous stigmata of disease as the umpire: a case report

Molokwu OA, Onyedum CC, Ojinma UR, Nwabueze AC

Background: Lung fibrosis though the hallmark of idiopathic pulmonary fibrosis (IPF) is a recognized complication of systemic sclerosis (SSc). The existence of some overlap in the clinicoradiological presentations and pathogenesis of the two conditions have created some challenges in correctly diagnosing either of the two disorders. This report highlights the difficulties that may arise in navigating through the diagnostic conundrum and emphasizes the role of recognizing the cutaneous stigmata of systemic sclerosis in answering the question; is this IPF or SSc associated interstitial lung disease (SSc-ILD).

Method: We report a case of 36 year old young man referred to the respiratory unit for evaluation for chronic cough associated with dyspnea and weight loss all of about 2 years duration. He had undergone trial of antikochs therapy with unremarkable response. His chest X-ray had showed reticulonodular shadows suggestive of pulmonary fibrosis complicating pulmonary tuberculosis. Mantoux test and sputum for acid fast bacilli were negative.

Results: Chest CT scan done made a diagnosis of IPF. Spirometry showed a restrictive pattern of lung disease. Steroid therapy was suggested to him and while being worked up for steroid therapy, he was noted to have some skin lesions on the face alongside a puckered mouth. The skin lesions were identified as “salt and pepper” lesions characteristic of systemic sclerosis by the dermatologist. Serological test for auto antibodies showed the presence of ANA and Scl-70. Taking everything together, a clinical diagnosis of SSc-ILD was made. He was counselled on the clinical course, therapeutic options and prognosis of the illness. He reported marginal improvement while on steroid therapy. Unfortunately he was lost to follow-up.

Conclusion: Close examination of the skin can aid in resolving the diagnostic dilemma often seen in diagnosing some rheumatologic disorders.

Key words: Systemic sclerosis, Pulmonary fibrosis, Salt and pepper appearance, Scl 70 antibody
**Arthritis mutilans due to chronic tophaceous gout**

Oluyinka AR, Muyiwa OC, Musbau OG, Sunday OD

**Background:** Arthritis mutilans is a form of destructive arthritis which is often characterized with severe osteolysis. It is more commonly described in association with the most severe forms of psoriatic and rheumatoid arthritis.

**Methods:** This was a retrospective case report of chronic tophaceous gout presenting with arthritis mutilans. Diagnosis was established by polarized light microscopy and bone deformities were demonstrated by radiographs.

**Results:** Examination revealed severe deformities of the hands and feet with several tophi on the elbows, forearms, most joints of the hands and feet as well as on the palms and soles of the feet. Radiographs of the hands and feet showed several punched out erosions with overhanging edges, osteolysis, subluxations and severe disorganization of the joints. A diagnosis of gout was established with the finding of numerous urate crystals on polarized microscopy of aspirated tophi.

**Conclusion:** This case demonstrates that gout can cause arthritis mutilans. This is however rare and is more likely in a patient with long-standing untreated tophaceous gout.
Clinical profiles of patients with osteoporosis in Nairobi

Oyoo GO,2 Genga EK,2 Ilovi CS1, Otieno FO2, Otieno CF1

Background: Osteoporosis, a chronic, progressive disease of multifactorial aetiology and one of the most common metabolic bone diseases worldwide. Despite ample sunshine, the Middle East and Africa register the highest rates of rickets worldwide. Low levels of vitamin D are prevalent throughout the region. There is a paucity of data on osteoporosis in Africa as it’s generally thought not to affect the non Caucasian population. We sought to describe the population with osteoporosis in a Nairobi rheumatology clinic.

Objective: This study sets out to describe the clinical characteristics of patients with osteoporosis seen at a rheumatology clinic in Nairobi.

Methods: This was a cross-sectional study done on patients with the World Health Organization (WHO) definition of osteoporosis of a T-score of –2.5 on bone mineral density scan. The study site was a rheumatology clinic in Nairobi. The study variables were age, sex, clinical presentation and selected comorbidities.

Results: Fifty six patients with a WHO definition of osteoporosis were recruited. The age distribution was 31- 95 years with a mean age of 63.95 years with the most affected being above the age of 60 years at 71.5%. Majority were female (89.3%), with the main presenting complaints as polyarthralgia (30.4%) followed by lower back pain (19.6%) and pathological fractures (12.5%). The most common comorbidity being rheumatoid arthritis (39.3%) followed by steroids therapy (25%). Others included osteoarthritis, fibromyalgia, systemic lupus erythromatosus and diabetes. Seven study participants had history of fracture with lumbar leading at 42.8%. None of the study participants were smokers. The number of patients on calcium supplements was at 71.4% and bisphosphonates was low at 21.4%.

Conclusion: The findings of this study from age to comorbidities on osteoporosis are in keeping with literature. The presence of fibromyalgia as a comorbidity was an interesting finding. The number of patients on bisphosphonates was low which differed from Western literature. Stratification of patients at risk should be done so that active screening and prompt early management for osteoporosis can be instituted. Attempts should be to offer cheaper bisphosphonates so that the affected can benefit from the drugs.

Key words: Osteoporosis, Clinical profile, Nairobi
Anti-ccp positive polyarticular juvenile idiopathic arthritis
Ibrahim DA1, K/Na’isa MB2, Ahmed H2

Background: The ILAR Classification of juvenile idiopathic arthritis (JIA) divides polyarticular JIA into either rheumatoid factor (RF) positive or RF Negative JIA. This was at a time when ACPA were not routinely screened in patients with polyarthritis. We report 2 cases of Anti-CCP positive JIA.

Methodology: This was a descriptive case series of two patients seen at the Rheumatology Outpatient Clinic of Aminu Kano Teaching Hospital, Kano, and Northwestern Nigeria.

Results: The ages of the patients at presentation were 14 and 17 years and disease duration at presentation were 8 months and 48 months respectively. The former was a girl and the latter a young man. They both had a symmetrical polyarthritis of the small and large peripheral joints. The young man had persistent bilateral knee effusive synovitis, with some flexion deformity of the knees.

Anti-CCP was positive in both patients, while rheumatoid factor and ANA were all negative. ESR and C-reactive protein were both elevated. The 2 patients responded well to initial steroids treatment and are currently on methotrexate, hydroxychloroquine and low dose prednisolone, with good response.

Conclusion: We report 2 cases of polyarticular RF negative, Anti-CCP positive JIA in Nigerian children. Further studies are needed to identify the full characteristics of this entity, which may call for a review of the current ILAR criteria for JIA.
Infant-onset juvenile idiopathic arthritis in a Nigerian child

Adelowo OO, Dedeke IA, Olaosebikan BH, Akintayo R

**Background:** This case of juvenile idiopathic arthritis (JIA) is particularly interesting, considering the age at onset. JIA onset as early as 3 months old has never been reported among blacks in literature.

**Case report:** A 16 month old male child presented with history of recurrent episodes of polyarticular joint pain and swelling involving the knees, right ankle, feet and wrists, with onset at 3 months of age. There was initial affection of the ankles and feet before involving the other joints. There was associated recurrent fever but no rash or other constitutional symptoms. No other systemic symptoms. No prior history of trauma or family history of similar complaints. Patient’s haemoglobin electrophoresis done on several occasions was AS. Patient’s birth weight was 2kg with no delay in reaching developmental mile stones, apart from the delay in walking due to the knees and ankle pain and swelling. General examination revealed a pale, afebrile, young child with significant peripheral lymphadenopathy in the axillary and epitrochlea nodes bilaterally, and the right submandibular regions. Musculoskeletal examination revealed swollen, warm and tender knees, ankles, hands and feet with no deformity. Examinations of other systems were unremarkable. A working diagnosis of JIA was made, to keep in view juvenile onset connective tissue disease.

Investigations revealed anaemia (27%), thrombocytosis (561x10⁹/L), leukocytosis (19.85x10⁹/L), elevated erythrocyte sedimentation rate (100mm/hr). Serum ferritin was also elevated (692ng/dl). Also, his blood film examination revealed no blast cells. Serology revealed a positive Antinuclear Antibody titre (1:80); Rheumatoid factor was <10.0LU/ml; Extractable nuclear antibody and viral screening (HIV, HBV, HCV) were negative. Liver and kidney function tests were normal. Electrocardiography, echocardiography, and chest X-rays were unremarkable.

A diagnosis of systemic JIA was made, and promptly commenced on DMARDs- subcutaneous methotrexate 7.5mg weekly and syrup Ibuprofen 5mls twice daily. The patient responded well to treatment as evidenced by complete resolution fever, tenderness and swelling of the joints.

**Conclusion:** JIA may present as early as 3 months and thus a high index of suspicion is required in an infant with joint pains.

**Key words:** Infant, Juvenile idiopathic arthritis, Nigerian, Child
Audit of cases of low back pain and radiculopathy at arthrimed specialist clinic between 2008 and 2012

Edunjobi AS¹, Adelowo OO²

Background: Low back pain has been reported at various times as a non-specific health problem and a general complaint among people of all ages with severe effect and complaints among the middle aged and the old. The complaint is more rampant in the developed nations than in the developing nations of the world and has been reported as a major economic disease burden and a cause of hospital visit, work absenteeism and disability. Few cases have been reported amongst Africans and Nigeria in particular. The cause has generally been accepted by most researchers around the world to be mechanical than infectious.

Methods: This retrospective study was conducted over a 5-year period (2008-2012). Diagnoses were made following detailed history, physical examination as the patients presented. Imaging studies were done as required. Treatment was initiated taking into account the acute or chronic nature of each patient’s complaints at presentation.

Results: Three hundred and sixteen patients presented with low back pain and/or features of radiculopathy with duration of symptoms prior to presentation between 3-24 months. Lumbosacral spondylosis was the major aetiology and accounted for 70% of total cases. Back pain from spinal canal stenosis was the least accounting for 2.9% of total presentation. The patients were aged between 21 and 82 years with a mean of 56.4 years and female preponderance. Female to male ratio of 1.7: 1. Back pain and paraesthesia/neuropathic pain were expectedly the main complaints at presentation. Physical examination revealed most patients had positive femoral nerve stretch test accounting for 44% of total and indicating an upper nerve root involvement. Blood tests were not contributory. One hundred and twenty six patients had plain radiography of the lumbosacral spine done which generally revealed osteophyte formation. Fifty six patients had MRI of the lumbosacral spine done further revealing disc herniation and desiccation, nerve compression and spinal canal stenosis. Treatment modalities were with analgesics-narcotics and NSAIDs, neuromodulators, muscle relaxants and physiotherapy in different combinations. Eight patients (2.5% of total) were referred for surgery.

Conclusion: Back pain could be severely debilitating if intervention is delayed. High index of suspicion is required especially in the supposed acute self-limiting cases where imaging studies are usually not advised in order to prevent a progression to a non-reversible disability or death.
Paediatric rheumatic diseases in Lagos Teaching Hospital

Olaosebikan H¹, Animashaun AB², Emorinken A¹, Agbebaku FO¹, Adelowo OO¹

Background: Paediatric rheumatology service in sub-Saharan Africa is virtually non-existent as there are only five paediatric rheumatologists in the continent. This is further compounded by lack of diagnostic and therapeutic resources. Other challenges include notions that arthritis does not occur in children and diagnostic difficulty poses common paediatric conditions in Africa such as haemoglobinopathy, acute leukaemia, acute rheumatic fever and haemophilia mimicking CTD and JIA. This has hampered epidemiological report from Africa with little or no national prevalence study while many cases of chronic arthritis and CTD in children still went undiagnosed and untreated. There were no reports of spectrums of childhood rheumatic diseases from West-Africa, hence the need for this report.

Aim: The aim of our study was to highlight the frequency and clinical spectrums of paediatric rheumatic diseases in Nigeria.

Methods: This was a 5 year retrospective cross-sectional study of children (May 2010-May 2015), who were referred from paediatric and general out-patient units on account of clinical suspicion of paediatric rheumatic conditions to adult rheumatology unit of LASUTH.

Results: Forty patients were studied (F:25; M:15); mean age at presentation was 13.6 years (SD±3.56, range-16.5 years, minimum-1.5 years, maximum-18 years). Frequency of Clinical spectrum included JIA (n=19, 47.5%) and JSLE (n=12, 30%). Conditions such as joint hyper mobility syndrome (n=1), juvenile dermatomyositis (n=1), juvenile SLE/PM overlap (n=1), juvenile systemic sclerosis (n=1), secondary bilateral knee osteoarthritis from Blount disease (n=1), plantar fasciitis (n=1), juvenile ankylosis spondylitis (n=1) and secondary symptomatic osteoporosis from childhood leukaemia (n=1) were also observed.

Conclusions: JIA and JSLE are the more frequent paediatric rheumatic conditions observed in our study. We advocate for investment in training of paediatric rheumatologists in Nigeria as there are no such specialists in West Africa.

Key words: Paediatric, Rheumatic disease, Lagos, Hospital.
More than a butterfly rash, a challenging case of mucocutaneous SLE

Jallow BJ¹, Dey ID²,³, Amissah-Arthur MB²,³,

Background: Systemic lupus erythematosus (SLE) is not an uncommon disease in black Africans. Bad predictors affecting morbidity and mortality include major organ involvement including central nervous system and renal disease, African descent or Hispanic ethnicity and poor socio-economic background.

Methods: An 18-year-old lady presented with malar and maculopapular rash, photosensitivity rash, mouth ulcers and arthritis. Serology was strongly positive for antinuclear and anti-double-stranded DNA antibodies. She was diagnosed with SLE having fulfilled more than 4 of the 11 classification criteria. She was started on prednisolone 30mg daily and hydroxychloroquine 400mg daily. Additional immunosuppression with azathioprine and mycophenolate mofetil was used. She was admitted on several occasions due to worsening mucocutaneous manifestations- acute erythematous rash, vasculitic lesions on hands and feet and superficial ulceration complicated by bacterial infections affecting over 80% of body surface area (face, limbs, trunk and buttock). She received a donation of rituximab at a reduced dose of 500mg two weeks apart with cyclophosphamide.

Results: Azathioprine was not tolerated due to gastrointestinal side effects and mycophenolate mofetil resulted in a Steven Johnsons reaction. Her response to biologic therapy was incomplete. The limited choice and availability of drugs posed a therapeutic challenge leaving her disease active and uncontrolled. On her last admission she presented with BILAG A skin eruption with secondary sepsis and new seizures/psychotic features, which was diagnosed as neuropsychiatric SLE. This was refractory to treatment with anti-epileptic, anti-psychotic medication and three pulses of 1g intravenous methylprednisolone. She succumbed to the active SLE disease.

Conclusions: Cutaneous manifestations, though commonly classified as mild or moderate disease, can involve large areas and be very aggressive or refractory to treatment, increasing the risk of other organ involvement and mortality. Belimumab, a newly approved drug for skin and joint disease, can be used. Survival rates in SLE have improved significantly, however the challenge encountered in the developing world is access to timely investigations and treatment.

Key words: SLE, Mucocutaneous, Disease activity, Immunosuppression
Prevalence of fibromyalgia in ambulatory HIV positive adults with chronic musculoskeletal pain at Kenyatta National Hospital

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Background: Fibromyalgia is a rheumatic condition characterized by chronic widespread musculoskeletal pain with painful pressure points. Other associated symptoms include fatigue, sleep disturbance and depression. The cause of this condition is unknown however chronic viral infections eg Human Immunodeficiency Virus (HIV) have been associated with fibromyalgia. This study aimed to determine the prevalence of fibromyalgia in HIV positive patients.

Methods: This was a cross-sectional descriptive study carried out at the Kenyatta National Hospital, Comprehensive Care Clinic (CCC). The patients attending the clinic between the months of February 2013 and April 2013 were assessed for chronic musculoskeletal pain and subsequently fibromyalgia using the American College of Rheumatology criteria. Those found to have fibromyalgia were given the the revised Fibromyalgia Impact Questionnaire (FIQR) and those without were given the the revised Symptom Impact Questionnaire (SIQR) for comparison purposes. Clinical details eg WHO clinical stage, CD4 counts and Highly Active Anti Retroviral Therapy (HAART) regimen for those on HAART were also documented.

Results: A total of 380 patients with chronic musculoskeletal pain were enrolled in the study. The prevalence of fibromyalgia in these patients was 17.9% (n=68). Their mean age was 42.2 years with a median of 42.5 years. There was a female preponderance of 88.2% (n=60). Fibromyalgia was associated with female gender, OR=3.0, unemployment status, OR=5.4 and retired status, OR=3.4. A majority of the patients were in WHO clinical stage 3 and the mean CD4 count was 276.2cells/ml. There was however no association between fibromyalgia and WHO clinical stage, CD4 count and use of HAART or the specific HAART regimens. The mean FIQR was 50.1 which was significantly higher than the mean SIQR score of 12.4 in those without fibromyalgia.

Conclusion: Fibromyalgia is a prevalent rheumatologic condition among HIV positive patients with chronic musculoskeletal pain. It is also associated with a high FIQR score.
Not all that coughs is Kochs - a case series of pulmonary manifestations of rheumatic disease in Nigerian patients

Ima-Edomwonyi U¹, Adelowo O², Adeyemoye A³, Dania M⁴

Background: Pulmonary manifestations of systemic autoimmune rheumatic diseases (SARDs) like rheumatoid arthritis (RA), systemic sclerosis (SSc), systemic lupus erythematosus (SLE) are not uncommon. Features include cough, dyspnea, pneumonitis, lung fibrosis, consolidation, and cavities. Chronic cough persisting after a course of regular antibiotics, with fever, weight loss and abnormal chest X-ray findings usually suggests pulmonary tuberculosis (TB) in Nigeria, a high-burden TB country (ranked 10th out of 22 globally). We present 10 cases of rheumatic conditions with pulmonary manifestations initially misdiagnosed.

Methods: Case records of 11 patients seen between January 2012 and July 2015 in Rheumatology clinics and unit in Lagos were reviewed. Patients who fulfilled classification criteria for a rheumatic disease, indicative pulmonary tests were included. They were reviewed by a respiratory physician. Chest X-rays and CT scans were reviewed by an experienced radiologist.

Results: Eight patients presented with interstitial lung disease; four had RA, two SLE, one DcSS, one with LcSS. One patient had cavitated rheumatoid nodules with secondary suppurative lung disease on background overlap syndrome. One patient had pulmonary calcinosis in diffuse cutaneous systemic sclerosis and one with spontaneous subcutaneous emphysema in RA. Five patients had initial radiological diagnosis of pulmonary tuberculosis, 2 others initially assessed as pneumonia and one as old tuberculosis lesions on chest X-ray. Two patients subsequently demised- one following discharge and the other as an in-patient.

Conclusion: Pulmonary manifestations of SARDs are varied and often misdiagnosed as infection in Nigeria. They may present in previously undiagnosed patients. Reports suggest a higher number of undiagnosed cases at post-mortem. Mortality in two cases highlights how critical it is to educate physicians and radiologists in early detection of SARDs and their pulmonary manifestations especially in the presence of smear negative sputum for tuberculosis.

Key words: Pulmonary, Systemic autoimmune rheumatic diseases, Radiology
Clinical spectrums of juvenile idiopathic arthritis (JIA) in Lagos Teaching Hospital

Olaosebikan H¹, Animashaun AB ², Agbebak FO ¹ Emorinenk A¹, Adelowo OO¹

Background: Juvenile idiopathic arthritis (JIA) shares similar manifestations with common paediatric conditions in Africa and consequently the diagnosis may be missed. There were no previous reports of JIA series from a public teaching hospital in West-Africa.

Aims: The aim of our study is to highlight the demographic, clinical spectrum, laboratory and treatment outcomes of Nigerian children with JIA.

Methods: This was a 5 year retrospective cross-sectional study of 19 children with JIA over a 5 year period (May 2010-May 2015).

Results: Nineteen patients were studied (F:14 ; M:5); mean age of presentation was 11 years (SD± 5.7); mean illness duration was 22 months (SD±20.7). Frequency of clinical spectrum included polyarticular JIA (n=13, 68.4%), RF-positive polyarticular JIA (n=3), Oligoarticular JIA (n=3, 15.8%), systemic JIA (n=3, 15.8%) and 3 patients had extraarticular manifestations . The laboratory features identified were elevated CRP (n=18, 94.7%), elevated ESR (n=16, 84.2%), elevated serum ferritin (n=17, 89.5%), positive ANA (n=3, 15.8%), positive RF (n=3, 15.8%) and anaemia of chronic disease (n=15, 78.9%).

The mean erythocytes sedimentation rates, haematocrit, CRP, serum ferritin, and leucocytes was 79.5 mm/hr (SD±28.3), 26.4% (SD±5.96), 107 mg/dl (SD±60.3), 677.8ng/ml (SD±472.6) and 16486mm³ (SD±7174) respectively. Treatment was with intermittent dose of non-steroidal anti-inflammatory drugs in all patients, weekly sc methotrexate at a dose of 10mg/ m² (n=13), oral weekly methotrexate 10mg (n=6) and local intra-articular steroid injection (n=2) including oral folic acid, calcium and vitamin D supplementation and rehabilitation therapy. In terms of the outcome, there was complete resolution of tender and swollen joints as well as normalisation of acute phase reactants in 10 patients while 5 patients were lost to follow up and 4 had disabilities from joint deformities.

Conclusion: Polyarticular JIA was the commonest clinical subtype of JIA found in this study. We advocate for investment in training of paediatric rheumatologists in Nigeria as there are no such specialists in West Africa to manage this highly disabling condition.

Key words: Clinical spectrums, JIA, Lagos Teaching Hospital.
Review of the inclusion criteria of clinical trials in psoriatic arthritis with a comparison to routine care cohort

Agbobu AO1, Galloway J2

Introduction: In psoriatic arthritis, the first line agent for many clinicians remains methotrexate, despite an RCT (MIPA) showing no evidence of superiority over placebo. This has led to questions over why MIPA failed – given that many clinicians anecdotally report success in use, as well as inferred data of response rates with methotrexate noted in comparator arms in clinical trials of anti-TNF. We hypothesized that an important reason underpinning the differences in response rates in different trials is the baseline disease severity, acknowledging that PsA is a more heterogeneous disease than other inflammatory arthritides.

Method: Pubmed search for RCTs including MTX as either an intervention or as part of a comparator arm in PsA were identified through using predefined search criteria. Baseline data from the studies were collated and compared using parametric and non-parametric statistical tests as appropriate. Comparisons were then made between these characteristics and the characteristics of a cohort of routine care patients with PsA attending a single teaching hospital in London. Baseline characteristics, for analysis, were obtained prior to starting a DMARD treatment (intended to correspond to their baseline characteristics if they had been recruited to a trial).

Results: These results are displayed in a tabulated form below (Table 1). There was a statistically significant difference in disease duration between MIPA; 4.9 years (±7.5) and the hospital cohort 8.3 years (±8.0) (p =<0.001). Patients recruited to the RESPOND study had a similar disease duration to MIPA, 3.25(±2.65) vs 4.9 years (±7.5) but those in the Toronto observational cohort had the longest disease duration 12 years (±9.25). There was a statistically significant difference between the mean tender and swollen joint counts (T/SJC) between the hospital cohort and MIPA, with patients recruited to MIPA having more tender, 12.8 (±11.2) vs 6.9 (±7.3) (p=<0.001), and swollen joints, 8.3 (±7.9) vs 3.5 (±3.7) (p =<0.001). In comparison, those recruited to the TORONTO observational study had a similar T/SJC to the hospital cohort 6.6(±6.9)/4.3(±4.2). Those recruited to the RESPOND study had a much higher T/SJC than MIPA 20.6(±12.3)/14.7(±9.8). Patients recruited to MIPA had generally shorter disease duration, compared to routine hospital cohort. The disease duration in MIPA was similar to that of patients recruited to the RESPOND study, however, RESPOND study patients were generally more active with respect to T/SJC, which might explain the positive ACR response in both arms of the study, despite the same dose of MTX as used in MIPA.

Conclusions: The results of this study suggest that patients recruited to trials of both non-biological and biological DMARDs are generally not representative of those seen in the selected cohort of patients seen in routine care, especially with regard to T/SJC’s, thus the inferences from these studies may not be generalizable. Patients recruited to MIPA had generally shorter disease duration, compared to routine hospital cohort. The disease duration in MIPA was similar to that of patients recruited to the RESPOND study, however, RESPOND study patients were generally more active with respect to T/SJC, which might explain the positive ACR response in both arms of the study, despite the same dose of MTX as used in MIPA.
Table 1: Baseline disease characteristics of trials/observational and routine cohort patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>MIPA N=221</th>
<th>Routine care Cohort N=266</th>
<th>Mean difference (95% CI)</th>
<th>p value</th>
<th>Baranauskaite et al – MTX arm data N=110</th>
<th>Toronto observational cohort N = 135</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years (SD)</td>
<td>48.6 (±11.5)</td>
<td>50.1 (±14.4)</td>
<td>2.2 (-0.1, 4.6)</td>
<td>0.0574</td>
<td>41.2(±11.4)</td>
<td>46.85(±12.5)</td>
</tr>
<tr>
<td>Gender, n female (%)</td>
<td>97 (44)</td>
<td>135 (51)</td>
<td>-</td>
<td>0.131</td>
<td>50(45)</td>
<td>51(37)</td>
</tr>
<tr>
<td>Disease duration, years (SD)</td>
<td>4.9 (±7.5)</td>
<td>8.3 (±8.0)</td>
<td>3.4 (1.9, 4.8)</td>
<td>&lt;0.001</td>
<td>3.25(±2.65)</td>
<td>12(±9.25)</td>
</tr>
<tr>
<td>CRP, mean mg/L (SD)</td>
<td>13.3 (±14.7)</td>
<td>10.8 (±15.7)</td>
<td>2.4 (-0.4, 5.3)</td>
<td>0.0947</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>TJC, mean (SD)</td>
<td>12.8 (±11.2)</td>
<td>6.9 (±7.3)</td>
<td>5.8 (3.9, 7.7)</td>
<td>&lt;0.001</td>
<td>20.6(±12.3)</td>
<td>6.6(±6.9)</td>
</tr>
<tr>
<td>SJC, mean (SD)</td>
<td>8.3 (±7.9)</td>
<td>3.5 (±3.7)</td>
<td>4.8 (3.6, 6.0)</td>
<td>&lt;0.001</td>
<td>14.7(±9.8)</td>
<td>4.3(±4.2)</td>
</tr>
</tbody>
</table>

Key words: Psoriatic arthritis, Clinical trials, Inclusion criteria, Routine clinical care
The use of CASPAR criteria in Nigerians with psoriasis

Gold-Olufadi SA, Akinkugbe AO, Ayanlowo O, Ima-Edomwonyi U

Background: Psoriasis is a chronic, multifactorial inflammatory disease in which environmental, genetic and immunologic factors play a role. The disease commonly manifests on the skin, scalp and nails. In 5-30% of patients, the joints may be involved. Skin manifestations precede joint affection in 60-80% of patients. However, psoriatic arthritis (PsA) often presents as inflammatory spinal pain, tendinitis, dactylitis or enthesitis rather than a ‘true arthritis’ and is thus often missed. PsA can cause extensive joint damage if not managed early. Several criteria have been used in the diagnosis of psoriatic arthropathy, however the classification criteria for psoriatic arthritis (CASPAR) has a high sensitivity and specificity and is simple and easy to use.

Methods: Case records of patients with psoriasis seen at the dermatology outpatient clinic (LUTH) between January 2010 and June 2015 were analyzed. Patients who fulfilled the CASPAR criteria (greater than or equals to 3 points from the five criteria) were included.

Results: Seven patients met the criteria with M:F ratio of 5:2. Of these, three had a score of four and erythrodermic psoriasis. The remaining four had a score of three and chronic plaque psoriasis. Only one patient had joint involvement before skin manifestations with weakly positive rheumatoid factor and asymmetric polyarthritis. Nail involvement occurred only in the three patients with erythrodermic psoriasis. All patients had commenced DMARDs and made significant improvement.

Conclusion: PsA is a common presentation of psoriasis and the CASPAR criteria offers a simple, easy to use method for screening and early diagnosis. This will translate to prompt treatment with DMARDs and subsequent improvement in quality of life of affected patients.

Key words: Psoriasis, Psoriatic arthritis, CASPAR criteria, DMARDS
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