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Kenya

Prof Femi O Adelowo, MBBS, FWACP, FRCP, FACP
Rheumatology Unit
Lagos State University Teaching Hospital
Ikeja, Lagos
Nigeria

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Prof G Omondi Oyoo, FACP, FRCP (Edin)
Department of Internal Medicine and Therapeutics
College of Health Sciences
University of Nairobi
Nairobi
Kenya

Prof Femi O Adelowo, MBBS, FWACP, FRCP, FACP
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Senior Consultant Rheumatologist
Apollo Indraprastha Hospitals
New Delhi
India

Prof Paul Davis, FRCP(UK), FRCPC
562 HMRC,
University of Alberta
Edmonton
Canada
T6G 2S2

Prof Paul E McGill, MD, FRCP (Ed), FRCPS (GLAS)
Department of Rheumatology
Stobhill Hospital
Balornock Rd
Glasgow G22 3UW
Scotland

Prof Carol Hitchon, MD, FRCP, MSc
University of Manitoba
Arthritis Centre
RR149 800 Sherbrook Street Winnipeg, Manitoba
R3A 1M4 Canada

Prof Helen Foster, MD, MBBS (Hons), Cert Med Ed (Cert Medical Education), DCH (Diploma Child Health), FRCP, FRCPC
Professor Paediatric Rheumatology
Newcastle University
UK

Prof Luis R Espinoza, MD, MACP, MACR
Section of Rheumatology
LSU Health Sciences Center
New Orleans, LA 701122922
Luis R. Espinoza, M.D., 1212 Conery Street
New Orleans, LA 70115

Prof Anwar Samhari b Mat Arshad
Bone Joint and Pain Specialist Center
57@59 Jalan Todak 6, Sunway Perdana
Seberang Jaya
Penang

Prof Zhan-Guo Li
Professor and Chief, Department of Rheumatology and Immunology
Director, Clinical Immunology Center
Beijing University Medical School People’s Hospital
11 Xizhimen South St. 100044
Beijing
China

Prof Abewale Adeboje, MBBS, FMCP, FACP, FRCP
Faculty of Medicine, Dentistry and Health
University of Sheffield
Beech Hill Road
Sheffield
S10 2RX
United Kingdom
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A field guide to rheumatology

Rheumatology is well known for the diagnostic difficulty of rare and heterogeneous disease presentations, unpredictable benefit and high expense of tests, and severe consequences of late or misdirected therapy. Additionally, our profession has reached a point where two critical aspects of medical diagnosis move in apparently opposite directions: the limited access to providers in geographic areas where disease prevalence is expanding, and the superabundance of progress in recognizing and treating rheumatic disease. These elements provide reason to improvise new approaches to teaching rheumatologic diagnosis with methods that are affordable, effective for primary care, and mobile.

Expansion of broadband and popular use of mobile devices enable both patient and provider rapid access to disease diagnosis support. However, the majority of these sites utilize relatively ineffective systems, such as an A-to-Z list of disease possibility for a given search key word (e.g. “joint pain”), binary algorithms that risk premature closure of differential diagnosis, or textbook-like encyclopedic content. In other words, it is not access to diagnostic support for a particular disease that is lacking, but rather an initial organizational method to orient the diagnostic process.

Successful treatment is of course tied directly to diagnostic accuracy. Without accuracy, drug availability and safety become virtually moot. Diagnostic accuracy in rheumatology is a slippery slope: our numerous diseases overlap or vary enough in their presentation that taking too rigid of an approach with diagnostic criteria may impinge more natural clinical judgment. Although criteria are standardized, they flux over time and place, often include tests not widely available or affordable, and require an artificial starting point (thinking of the specific disease in the first place). Furthermore, diseases present in individuals: a patient-centered approach is necessarily a flexible one.

The notion of overdiagnosis and overutilization of specialty care and technology may sound absurd to African physicians accustomed to more pressing matters. But lessons being learned in the U.S. may influence African choices for care delivery models and reward simple good sense. The healthcare share of the U.S. Gross Domestic Product, at 17% far higher than other countries, often impoverishes citizens and small businesses paying the majority of costs. Overutilization of referrals and tests represents an ineffective organization of the diagnostic process. We may blame our behavior on time constraint, malpractice risk, or patient demands, but ultimately it is influenced by the pressure to quickly seek a static answer within a process that is inherently slow and fluid.

One response to these challenges is a pilot project in Eldoret, Kenya funded this year by ILAR. We propose to introduce a novel diagnostic methodology for rheumatic disease, formatted for mobile devices and fashioned as a bedside cognitive tool that orients the user to diagnostic options by reproducing how rheumatologists think when they confront a new patient’s illness. Functioning like a field guide or menu, the basic concept is to provide rapid and flexible access to clinical diagnosis support that emphasizes grouped disease patterns, their epidemiologic likelihood, red flags, and mimics, and key critical thinking skills.

An expanding population of patients with rheumatic disease emphasizes the need for a practical approach to education for students and diagnosis support for providers at the first point of care. Disseminating knowledge is important for all specialties that hope to grow. If scaled up, educational efforts can improve access to specialty care by expediting triage of the most critical situations, minimizing wasteful use of technical resources by primary providers, and keeping specialists in the center of the spokes of care.

Daniel Sager, MD, FACR, Clinical Assistant Professor of Medicine, Oregon Health and Science University, Portland, Oregon, Providence Hood River Arthritis Center, Hood River, Oregon 1715 Prospect Avenue, Hood River, Oregon 97031 USA. Email: dansager@gorge.net rheumatologyCDS.com
References


Antiphospholipid syndrome in Africa: a review

Akintayo RO1, Aworinde OO2, Olawumi HO3, Yusuf IA4

Abstract

Objective: To review the extent of research findings on Antiphospholipid Syndrome (APS) across the African continent.

Data source: Published original researches and reviews were searched in English related to APS in Africa.

Study design: Only studies conducted on Africans living in Africa were reviewed. Related review articles done with main focus on the African experience of APS, its manifestations and laboratory findings were also included. Articles summarizing international consensus and background of APS were also included.

Data extraction: A PubMed search using the keywords “Antiphospholipid Syndrome” was done. This yielded 9167 results. The results were filtered in two arms. First, studies of APS in Africa were extracted. These were 63 out of which 27 relevant studies on Africans living in Africa were selected. Second, studies on international consensus and background of APS were filtered. These were 51 out of which 13 with relevant contents were selected. This brings the total selected articles to 40.

Data Synthesis: Data added and summarized.

Conclusion: The Antiphospholipid Syndrome (Hughes’ syndrome, APS) was first described in 1983 and has since been reported all over Africa. Over the years, several studies have been undertaken in Africa focused on different aspects of APS and new findings keep emerging revealing atypical manifestations and pointing to a likely under-recognition of the magnitude of APS in the causation of thromboembolic diseases and pregnancy morbidities in Africa. Recent findings repeatedly refute the old belief that many systemic autoimmune and rheumatic diseases are rare in Africa. APS, in the “primary” form and in the setting of Systemic Lupus Erythematosus (SLE) and other autoimmune diseases may not be uncommon in Africa. It is recognized that much work still needs to be done in understanding the true burden and the probable peculiarities of APS among Africans.

Key words: Antiphospholipid syndrome, Africa, Abortion, Thrombosis, Rheumatology, Systemic lupus erythematosus

Introduction

Antiphospholipid Syndrome (APS) is a well studied composite of clinical and immunological disorders with protean manifestations and sometimes bizarre complications. Since its first description in 19831, several cases have been reported from all over Africa2-7, and like across the rest of the world, the core features have been repeatedly affirmed. These features include arterial and venous thromboses, recurrent spontaneous miscarriages, thrombocytopenia and the presence of high titres of antiphospholipid antibodies (aPLs) in the blood of the subject.

Not many systemic syndromes have been better researched than APS and despite the apparently incorrect erstwhile belief of the rarity of many systemic autoimmune and rheumatic disorders in Africa, extensive documentation of APS has been done. APS has emerged as the most important treatable cause of recurrent miscarriage accounting for approximately 15% of cases of recurrent miscarriage. It is also an important cause of early onset pre-eclampsia and of Intra-Uterine Growth Restriction (IUGR)8,9. Fourteen percent of patients with recurrent venous thromboembolic disease have aPLs10. The frequencies of antiphospholipid antibodies (aPL) in general-population patients with pregnancy morbidity, deep vein thrombosis, myocardial infarction, and stroke are 6%, 10%, 11%, and 14% respectively11.

The World Forum on Rheumatic and Musculoskeletal Diseases, in its white
paper on the global challenges and opportunities in the practice of rheumatology, states that developing countries in Africa are worst hit with the spate of inadequacy of rheumatologists and limited understanding of the burden of rheumatic and musculoskeletal diseases among public health professionals and policy makers means that these diseases are often not considered a public health priority.

**Methodology**

A PubMed search using the keywords “Antiphospholipid Syndrome” was done. This yielded 9167 results. The results were filtered in two arms. First, studies of APS in Africa were extracted. These were 63, out of which 27 relevant studies on Africans living in Africa were selected. Second, articles on international consensus and background of APS were filtered. These were 51 out of which 13 with relevant contents were selected. This brings the total selected articles to 40.

The antiphospholipid antibodies

The antiphospholipid antibodies include antibodies to cardiolipin (aCL) and beta-2-glycoprotein-1 anti-beta(2) GPI, as well as the Lupus Anticoagulant (LAC). These antibodies, which used to be thought as mere laboratory nuisance, have been linked to APS and the presence of at least one of them is required for the diagnosis of APS. In Dakar, Senegal, a two year retrospective study showed 11 patients of a dermatology clinic fulfilling the diagnosis of APS. These studies and many more to be discussed have shown that, although there is endless room for researching the epidemiology of APS in various regions of Africa, there are ample pointers to the abundance of it around the continent.

It is known that the presence of aPLs in the serum does not translate to invariable manifestation of symptom. Certain infections are associated with a higher likelihood of developing aPLs. In a study of 137 individuals chronically exposed to malaria and living in Africa or Asia, high prevalence of serum co-factor-independent IgG and IgM aCL were detected and IgG aCL levels were found to be related to the clinical/endemic status of the subjects. In another study of 272 South African patients with various infectious diseases, raised levels of aCL, anti-beta(2) GPI, and anti-prothrombin (aPT) antibodies were found in all patient groups studied. aCL was found in 7%, anti-beta (2) GPI in 6%, and aPT in 43% of 100 HIV patients, in 29%, 89%, and 21% of 112 patients with leprosy, in 8%, 8%, and 28% of 25 patients with syphilis, in 12%, 8%, and 28% of 25 patients with malaria, and in 20%, 30%, and 30% of 10 HCV patients studied, respectively. The prevalence of LAC was, however, found to be low in a group of 104 HIV-infected Nigerian patients: 2.9% and 1.9% HIV-infected patients and controls, respectively.

On account of the knowledge that aPLs may be found in a small proportion of normal individuals and in patients with infective conditions without any clinical symptom of APS, the main indications to test for aPLs have been established. These include systemic lupus erythematosus and other selected autoimmune conditions, spontaneous venous and arterial thrombosis, recurrent fetal losses, and autoimmune thrombocytopenia, among others.

**Classification of antiphospholipid syndrome**

Long before the eventual clarification of the existence of APS in patients without SLE, all patients fitting the description of APS were thought to be manifesting further features of SLE. However, it is now known that a sufficiently homogenous group exists with the features of APS without the other clinical or immunological manifestations of SLE or any other autoimmune disorder. It was first recognized by Asherson in 1985 while at the Hammersmith Hospital when he identified 25 patients conforming to this new class of disease. A publication of these cases was not achieved until 1988 when it was better accepted that “primary” APS indeed existed.
was the earliest to be known but has now been overtaken by the cases with isolated APS in number. In 2006, Gould et al. published a cross-sectional study of 100 South African SLE patients in whom the clinical characteristics, including features of APS, disease activity, and damage were observed. Positive aCL, anti-beta (2) GPI, aPT and LA were found in 53, 84, 20 and 2 patients, respectively. This study also showed that IgA anti-beta (2) GPI was associated with both a history of thrombosis alone (p<0.05) and a history of any clinical feature, thrombosis, and/or spontaneous abortion of the APS (p<0.05). IgA aCL was also associated with a history of any clinical APS event (p<0.05). Cooper et al., in another study conducted in Capetown, South Africa, found a good positive predictive value (70%) between aCL and overall SLE disease activity. A strong association was also observed between aCL and renal involvement (80%). Out of the 57 SLE patients studied by Cooper et al., 9 fulfilled both the clinical and serological criteria for APS and a further 18 patients fulfilled the serological criteria.

Pregnancy complications

Pregnancy related morbidities are among the most common presentations of APS in Africa. Various case reports and clinical studies across Africa have shown the high frequency of pregnancy wastage, pre-eclampsia and premature deliveries in patients with APS. In the first ever case series from Nigeria, Adelowo et al. reported pregnancy loss as the most common presentation. From the 11 cases of APS in dermatology in Dakar, 9 patients had obstetric incidents which include repeated spontaneous abortions, intra-uterine foetal deaths and precocious deliveries.

Recurrent miscarriage, the loss of three or more consecutive pregnancies, affects 1% of couples trying to conceive. This is significantly higher than that expected by chance alone and suggests that some couples have a persistent underlying abnormality to account for their pregnancy losses. A study of the prevalence of antiphospholipid antibodies, factor V G1691A (Leiden) and prothrombin G20210A mutations in early and late recurrent pregnancy loss conducted in Tunisia showed aPL frequencies of 45% and 9% among patients and controls, respectively (P < 0.001). Stemming from the study conducted in Abidjan, Cote d’Ivoire, Kouassi et al. argued that systematic aPL screening should be done in African women with obstetrical complications, and could further improve the management of patients at risk. They studied patients with recurrent foetal loss, pre-eclampsia, retroplacental haematoma and chronic foetal suffering and found a frequency of 11.8% of aPL positivity as compared to 0% in controls. Similarly, Thiam et al. found prevalence rates of 14.6 and 21.1% of LAC and aCL, respectively, among Senegalese patients with history of repeated abortion. In another study from Kenya, Mwenda et al. showed that 33.8% of Kenyan women visiting Kenyatta National Hospital, Nairobi, for recurrent pregnancy losses had APS. Although, it seems worthwhile, routine screening of patients with unexplained recurrent abortions for APS may still be unachievable in most regions of Africa because of the cost implication and sometimes inavailability of facilities for the tests.

Thromboembolism

Venous or arterial thrombosis, which forms another key clinical criterion in the diagnosis of APS, has not seen much research attention from the African continent. Thromboembolism is believed to be the basis for several manifestations of APS affecting varying calibers of vessels. In 2004, Maaroufi et al. suggested that APS may play an important role in the pathogenesis of retinal vascular occlusion. They found a diagnosis of APS in 33% of patients with retinal vein and artery occlusions. Anakwue et al., in 2013, reported a case of toe gangrene in a 21 year old Nigerian girl. The prevalence of APS has not been studied in patients with DVT, stroke or Myocardial Infarction (MI) on the African continent. However, Abid et al., in a study of 21 patients with transmural MI with normal coronary vessels seen in the Hedi Chaker Hospital, Tunisia, were able to identify a subset of these patients with various coagulation disorders including APS.

Vascular occlusion is implicated in the pathology of various neuropsychiatric manifestations of APS and SLE, although studies have not been done in Africa to differentiate the population of patients with pure central nervous system thrombosis from those with inflammation. In a group of 69 SLE patients studied by Whitelaw et al. in South Africa, a correlation was found between aPL positivity and neuropsychiatric morbidities in SLE patients.

Also, several pulmonary manifestations of APS are known to be directly associated with thromboembolism. Pulmonary embolism and infarction, pulmonary hypertension, pulmonary arterial thrombosis, pulmonary microthrombosis, acute respiratory distress syndrome and postpartum syndrome have all been identified as part of the spectrum of possible thrombotic complications of APS. Albeit, other non-thromboembolic pulmonary features of APS which include intrafoveal haemorrhage and non thromboembolic pulmonary hypertension are well known.

Catastrophic antiphospholipid syndrome

The earliest and probably the most amount of research works on this very rare subset of APS were led by a组
South African, Dr. Ronald A. Asherson, after whom Catastrophic Antiphospholipid Syndrome (CAPS) has been named. Many of Asherson’s studies were conducted on African patients. CAPS is an accelerated form of APS which was first described in 1992 and has been shown to be dominated by widespread small vessel thrombosis. Although catastrophic APS patients represent less than 1% of all patients with APS, they are usually in a life-threatening medical situation that requires high clinical awareness. While it is fatal in approximately 50% of cases reported, thrombocytopoenia is usually marked, and a Coombs positive microangiopathic-type anaemia may accompany the condition. Features of disseminated intravascular coagulation may be evident in some patients.

In a 2005 review of 250 patients, Asherson showed that triggering factors are identifiable in approximately 50% of patients and consist predominantly of infections, trauma (including minor surgical procedures such as biopsies), obstetric-related multiorgan failure and malignancy-associated CAPS. The patients present mainly with multiorgan failure resulting from predominantly small vessel occlusions affecting mainly intra-abdominal organs such as bowel, liver, pancreas and adrenals.

The international consensus statement on classification criteria and treatment guidelines of 2003 states that the optimal management of catastrophic APS must have three clear aims: to treat any precipitating factors (prompt use of antibiotics if infection is suspected, amputation for any necrotic organ, high awareness in patients with APS who undergo an operation or an invasive procedure), to prevent and to treat the ongoing thrombotic events and to suppress the excessive cytokine ‘storm’.

**Unusual manifestations**

From less-than-typical to extremely strange features are sometimes seen in the setting of APS. Many unusual manifestations of APS can be grounds for diagnostic confusion and a potential for worse outcome. A large variety of clinical manifestations have been less frequently described in patients with the APS, with prevalences lower than 5%. These include, among others, large peripheral or aortic artery occlusions, Sneddon’s syndrome, chorea, transverse myelopathy, intracardiac thrombus, adult respiratory distress syndrome, renal thrombotic microangiopathy, Addison’s syndrome, Budd-Chiari syndrome, nodular regenerative hyperplasia of the liver, atherosclerotic lesions of the bone, cutaneous necrosis or subungual splinter hemorrhages. Although, the largest proportion of APS are primary, secondary cases occurring on primary SLE, Sjogren’s syndrome, rheumatoid arthritis, or systemic sclerosis have been established. Hence, other features of the background connective tissue disease may colour the outlook of the APS. The case of a 57 year old woman was reported from South Africa in 2000 in whom a diagnosis of APS evolved into Waldenstrom’s macroglobulinaemia over a 5 year follow up period. In 2008, the case of a woman with primary APS presenting with partial HELLP syndrome, palmar lesions and recurrent DVTs was reported. Variable combinations of usual and unusual manifestations of APS may appear in the same patient thereby presenting a potential diagnostic challenge. APS may also be a part of an evolving systemic disorder. As such, it may accompany or precede an undifferentiated connective tissue disease.

**Possible peculiarities of APS in Africa**

Since many infectious diseases that have been associated with aPL are more abundant in Africa, it may be an important research focus to compare the true prevalence of clinical APS and the overall prevalence of aPLs in Africa. The scarcity of studies comparing the features of APS in Africans and non-Africans limits the extent of possible distinctions that may be identified between the two groups. It is known that blacks with SLE are more likely to develop lupus nephritis and their renal disease is more likely to run an aggressive course. It is yet to be known if renal vascular thromboembolism, end stage renal disease, glomerular disease or hypertension occurs at higher frequencies in Africans with APS. Also, it is not known if there are uniquenesses to the calibers of affected vessels or preferences of the organ affectations in Africans. APS being a systemic autoimmune disorder of multifactorial cause may show striking differences along racial and continental lines.

**Treatment**

There has not been much work on the treatment and outcome of APS in Africa. For this reason, it is yet to be known if Africans with APS on standard treatments currently available fare different from non Africans. The only study so far in this line is a non-controlled prospective clinical trial conducted at Khartoum, Sudan, to investigate the efficacy of unfractionated heparin and low-dose aspirin as prophylaxis against pregnancy loss in pregnant Sudanese women with recurrent (≥ 3) miscarriages associated with APS. From this study, 81% of the treated women progressed to have live term deliveries and there was no case of thromboembolic event or maternal death. This is comparable to what is known of similarly treated APS-associated recurrent miscarriages outside Africa. In a 2010 study by Adelowo et al., they reported that management in the Nigerian setting is variously with heparin, aspirin and warfarin, although other modalities are being used. They also suggested that management is best coordinated by a rheumatologist and an obstetrician.
Conclusion

APS may be in abundance across Africa and probably at a proportion more important than already realized. However, epidemiological data are lacking to assess the magnitude of the burden. The widespread reports of various presentations of the syndrome across Africa give credence to the notion that it may be far underdiagnosed. Hence, APS deserves better heights of clinical consciousness among physicians. Vascular thromboses are known to be the most common presentation of APS and several cases of recurrent pregnancy wastages may benefit from being routinely checked for aPLs as the detection of this highly treatable condition may mean the turnaround in the clinical outlook for these patients.

References


Echocardiographic abnormalities in systemic lupus erythematosus patients at Kenyatta National Hospital

Conteh S¹,², Ogola EN¹,², Oyoo GO¹,², Gitura BM², Achieng L¹,²

Abstract

Background: The cardiovascular system is frequently affected in patients with Systemic Lupus Erythematosus (SLE). Involvement of the pericardium, endocardium, myocardium, coronary and pulmonary vessels has been found in several clinical and autopsy studies in patients with SLE; most of which can be detected by noninvasive two dimensional and Doppler echocardiography. More than half of SLE patients experience clinical cardiovascular manifestation during the course of the disease and cardiovascular complications are among the leading causes of morbidity and mortality in patients with SLE.

Objective: To determine the prevalence and spectrum of cardiac abnormalities; determined by echocardiography in SLE patients at Kenyatta National Hospital (KNH).

Methods: This was a cross-sectional descriptive study of SLE patients attending clinic at KNH. A targeted history and physical examination and a detailed trans-thoracic echocardiography were performed for all patients. The independent variables included; age, sex, duration of disease and medications. The echocardiogram outcome variables included; pericardial effusion, thickening and calcification, systolic and diastolic dysfunction, mitral valve thickening, stenosis and regurgitation, aortic valve thickening, stenosis and regurgitation, and pulmonary hypertension.

Results: Sixty three SLE patients participated in the study, the mean age was 36.7 years, with a female to male ration of 20:1 and a meadian duration of disease of 36 months. Over 70% of participants were on at least 2 disease modifying medication. The overall prevalence of echocardiographic abnormalities was 88.9%, the major drivers of this high prevalence being pericardial and valvular thickening. The single moast common cardiac lesion was pericardial thickening at 77.8%. The mitral valve was the most commonly affected valve with 69.8% and 30.2% having mitral thickening and regurgitation respectively. Aortic valve thickening and regurgitation was found in 25.4% and 6.3% of participants respectively. Diastolic dysfunction was found in 50.8% of participants and was found to be associated with older age at diagnosis. Pulmonary hypertension was found in 22.2% of participants.

Conclusion: The study demonstrates a high prevalence of cardiac abnormalities among SLE patients despite being on disease modifying medications. Even though the majority of these abnormalities comprised of clinically insignificant pericardial and valvular thickening, the prevalence of valvular insufficiency and pulmonary hypertension are substantially high and relatively higher than the prevalence seen in other studies in the case of pulmonary hypertension.

Introduction

Systemic lupus erythematosus is an autoimmune disorder resulting in multi-systemic inflammatory damage, the epidemiology of which is still largely undetermined in Africa. The general view had prevailed that the incidence of SLE in black Africans is low¹. However recent studies by African researchers have clearly demonstrated that SLE may be common in Black Africans. Tikly et al² described the clinical features and antibody profile of 111 black South Africans with SLE and Adelowo et al³ described a series of 66 SLE cases diagnosed at a Rheumatology clinic in Lagos Nigeria.

Cardiovascular disease is common among patients with SLE and has recently been acknowledged as a major cause of morbidity and mortality. A survey to determine the clinical spectrum and outcome of SLE in hospitalized Black Africans in Durban, South Africa, demonstrated a high mortality rate of 29% and the commonest causes of death...
were renal, infection, neurological and cardiac. The heart specifically is frequently affected in SLE and all its constituents can be involved from the pericardium to the endocardium.

The pericardium is the most commonly affected constituents of the heart, with pericarditis being one of the most characteristic manifestation of SLE and included in the American College of Rheumatology (ACR) classification of SLE. Pericardial effusion occurs at some point in over half of patients with SLE and is the most frequent cause of symptomatic cardiac disease. The course of pericarditis is benign in the large majority of cases however, it is usually associated with active disease in other organs.

Myocarditis is a rare but potentially fatal manifestation of SLE. It is often subclinical in nature, but 5 to 10% of all SLE patients develop symptomatic myocarditis. Myocardial dysfunction may develop as a consequence of myocarditis and several other factors including; premature atherosclerosis, hypertension, renal failure, valvular disease and toxicity from medication.

Both anatomical and functional valvular abnormalities have been described in SLE. Libman–Sack endocarditis is the most characteristic lesion, though valvular thickening and regurgitation are more frequently observed. The clinical recognition of Libman-Sack endocarditis during life is extremely difficult, because valvular distortion is usually minimal even though large vegetation may be present. However verrucae may fragment and produce systemic emboli, leading to stroke and peripheral vascular disease. Furthermore infective endocarditis can develop in already damaged valve and has been reported in 7% of SLE patients with valvular heart disease. Haemodynamically significant valvular lesions have been reported in 3-4% of SLE patients and only half of these require surgical treatment.

Pulmonary hypertension is a serious and potentially life threatening complication of SLE. The reported prevalence of pulmonary hypertension among SLE patients ranges from 0.5 to 14%. Although pulmonary arterial hypertension is the most common cause of pulmonary hypertension in SLE, interstitial lung disease, thromboembolism, primary cardiac involvement and pulmonary veno-occlusive disease may be implicated in a minority of these cases. The onset of pulmonary hypertension in SLE does not correlate with disease duration or degree of extra-pulmonary manifestations and may be the presenting feature before the diagnosis of SLE. It is the most severe form of lupus associated pulmonary involvement, with poor long term outcome despite therapeutic intervention and a mean survival from onset of 2 years.

Prevention of cardiovascular disease associated morbidity and mortality among these patients depends on early detection and close follow up of patients with cardiovascular disease. Data on the prevalence and spectrum of cardiac lesions among these patients would therefore be crucial to inform practice guide lines with regards to initial investigation and subsequent follow up of SLE patients. However prior to this study there were no studies documenting the prevalence and spectrum of cardiac lesions including pulmonary hypertension among SLE patients in our setting.

Materials and Methods

This was a cross sectional descriptive study. SLE patients fulfilling the ACR criteria were recruited from the Rheumatology clinic and medical wards over a period of 3 months. Participants were examined clinically to elicit clinical features attributable to SLE. All participants underwent a detailed transthoracic echocardiographic evaluation by a cardiologist, according to recommendations of the American Society of Echocardiography. All echocardiography studies were independently reviewed by a second cardiologist and discrepancies resolved by a joint review of the studies by the two cardiologists to reach a consensus. The results represent the consensus of the two cardiologists.

Pericardial effusion was defined as echo free space surrounding the heart and persistent throughout the cardiac cycle and pericardial thickening as a thickness greater than 3mm. The cutoff for systolic dysfunction was fractional shortening less than 29% and/or left ventricular ejection fraction less than 50%. Diastolic function was defined using mitral flow velocities, early mitral flow deceleration time and isovolumetric relaxation time. Using these parameters diastolic dysfunction was graded as follows:

- Grade 1: Impaired relaxation; mitral E/A < 1, DT > 200msec, IVRT > 100msec
- Grade 2: Pseudonormal pattern; E/A 0.8 – 1.5, DT 150 – 200msec, IVRT 60 – 100msec
- Grade 3: Restrictive reversible; E/A > 2, DT < 160msec, IVRT < 60msec and reversible on valsava manoeuvre
- Grade 4: Restrictive irreversible; same as Grade 3 but irreversible on valsava manoeuvre

Valvular thickening were defined as thickening greater than 3mm and 2mm for the mitral and aortic valves respectively. Mitral valve regurgitation was graded based on the extent of the regurgitant jet into the Left Atrium (LA) as follows; grade 1- jet extending up to proximal ¼ of the LA, grade 2 – ¼ way up LA, grade 3 – up to ¾ of LA and grade 4 – beyond ¾ of LA. Pulmonary hypertension was classified into possible pulmonary hypertension when systolic pulmonary arterial pressure was between 37 and 50mmHg and likely pulmonary hypertension when systolic pulmonary pressure is greater than 50mmHg.
Data collected was coded, entered and managed in the statistical package for social sciences version 21.0 data sheet. Data cleaning, verification and analysis was done using the same programme. The study population was described using demographic and clinical characteristics. Continuous data (age, duration of disease) was analysed into means and medians while categorical data was analysed using percentages. Prevalence of cardiac abnormality was analyzed as a proportion with corresponding 95% confidence interval. Furthermore, various types of cardiac lesions were analyzed and presented as proportions. Associations between various cardiac lesions and demographic and clinical factors were analysed, using Student’s t test to compare means and chi square test for categorical data associations. Criteria for statistical significance was set as a p value of less than or equal to 0.05.

Results

Between 22nd January and 23rd April 2015, 63 SLE patients were recruited into the study. The female to male ratio was 20:1, mean age of 36.7 years (SD ±9.8) and median duration of disease of 36 months (IQR 14.0 – 65.0). The predominant clinical manifestation was arthritis (55.6%) followed by Raynaud’s phenomenon (28%). Over 70% of participants were on at least two disease modifying medication, the most commonly used medication being hydroxichloroquin (73%). Only 6.3% of participants were not on any disease modifying medication.

The overall prevalence of cardiac abnormalities was 88.9%, mostly driven by pericardial and valvular thickening. The most common echocardiographic abnormality was pericardial thickening detected in 77.8% of participants and none of these had features suggestive of constrictive pericarditis. Pericardial effusion was detected in only 1 (1.6%) participant, who was diagnosed with SLE at age 51, duration of disease was two years and was on prednesone, hydroxychloroquin and methotrexate at the time of evaluation.

There was generally good systolic function among participants with mean ejection fraction for the study population of 64.4 (SD 4.4). Only 11.1% had mild systolic dysfunction. On the other hand diastolic dysfunction was more prevalent, detected in 50.8% (Table 1). Diastolic dysfunction was found to be associated with age at diagnosis, the mean ages at diagnosis for participants with and without diastolic dysfunction were 36.7 (SD±9.1) and 28.7 (SD±8.5) respectively (p value 0.001).

Valvular abnormalities were detected in 88.9% of participants (Table 2). The types of valvular abnormalities detected were valvular thickening and regurgitation, the mitral valve being the most commonly affected. No participant was found to have vegetation or stenosis of any valve. Multiple valve involvement was seen in 16 (25.4%); 15 (23.8%) had mitral and aortic involvement and 1 (1.6%) had mitral in pulmonary involvement. The tricuspid regurgitations encountered among participants were associated with raised pulmonary pressures from which the pulmonary pressures where derived.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valvular abnormalities</td>
<td>56 (88.9)</td>
</tr>
<tr>
<td>Mitral valve thickening</td>
<td>33 (52.4)</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>8 (12.7)</td>
</tr>
<tr>
<td>Mitral thickening and regurgitation</td>
<td>11 (17.5)</td>
</tr>
<tr>
<td>Aortic valve thickening</td>
<td>15 (23.8)</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>3 (4.8)</td>
</tr>
<tr>
<td>Aortic thickening and regurgitation</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Pulmonary regurgitation</td>
<td>1 (1.6)</td>
</tr>
</tbody>
</table>

Discussion

An overall prevalence of echocardiographic abnormalities in this population of SLE patients was found to be 88.9%. This represents a composite of pericardial, myocardial and valvular abnormalities as well as pulmonary hypertension. The whole spectrum of cardiac abnormalities that could be evaluated by echocardiography, to provide base line data that could serve as a frame work for documenting cardiac abnormalities in these patients was included. The high prevalence was mostly driven by clinically insignificant pericardial thickening and valve thickening. The pericardial and valvular thickening are described as clinically insignificant because none of the participants with pericardial thickening had any clinical or echocardiographic finding of constrictive pericarditis.
and participants with valvular thickening had no clinical sequel resulting from valvular thickening. The overall prevalence of cardiac abnormalities in this study is similar to a study by Shazzad et al\textsuperscript{15} that reported a prevalence of echocardiographic abnormalities among SLE patients of 80%, using similar echocardiographic modalities and covering a similar spectrum of cardiac abnormalities.

The pericardium is the most commonly affected cardiac constituent in SLE, with over half of patients having an episode of pericarditis during the course of their illness\textsuperscript{6}. Being a sequel of pericarditis, it is not surprising that we found pericardial thickening in 77.8% of participants in this study. The pericardial thickening found in this cohort of SLE patients was not associated with any clinical or echocardiographic feature of constrictive pericarditis. This is in keeping with the natural history of pericarditis in SLE, which is usually acute, occurs during flairs and rarely progress to constrictive pericarditis\textsuperscript{16}. Significant pericardial effusion was found in only 1.6% of the study participants, which is indicative of active pericarditis. This low prevalence of pericardial effusion could probably be explained by the fact that majority of the participants were on two or more disease modifying agents, with only 6.3% not on any disease modifying medication at the time of the study. In a study done in Egypt, Shahin et al\textsuperscript{17} found pericardial effusion in 19% of SLE patients which is relatively high, however the medication profile of the participants was not reported.

In our study we found a generally good systolic function among SLE patients with only 11.1% with mild systolic dysfunction. Most of the systolic dysfunction was accounted for by subtle reduction in fractional shortening. This is comparable to a similar study in Bangladesh that reported systolic dysfunction in 8% of SLE patients\textsuperscript{15}. Shahin et al\textsuperscript{17} found an even lower prevalence of diastolic dysfunction at 4.8% among of SLE patients at a university clinic in Cairo. With regards to diastolic function, we found a higher prevalence at 50.8%. Diastolic dysfunction was found to be associated with older age at diagnosis of SLE. The high prevalence of diastolic dysfunction was not surprising considering the multiple risks for myocardial dysfunction associated with SLE including direct inflammation, hypertension and premature atherosclerosis. Shiruli et al\textsuperscript{18} in a Master of Medicine thesis looked at cardiovascular risk factors in a cohort of SLE patients attending the same clinic and found a high prevalence of cardiovascular risk factors, namely; hypertension (42.5%), dyslipidemia (74.2%) and carotid plaque (22.9%). The high prevalence of diastolic dysfunction may represent a preclinical consequence of these multiple cardiovascular risk factors in this cohort of SLE patients.

In this study we found valvular lesions in 88.9% which was relatively high. The majority of these valvular lesions were valvular thickening with no associated valvular regurgitation. We used similar cut offs for valvular thickening as was used in a study done in Canada by Bourre-tessier et al\textsuperscript{19} that found valvular abnormalities in only 40.1%. From our study we cannot determine the exact reason for this high prevalence of valvular thickening in this population. However, possible explanations include variation in disease phenotype and antibody profile, and concomitant subclinical rheumatic heart disease in this population. Rheumatic heart disease is prevalent in our setting and also predominantly affects the valves on the left side of the heart. There is no local data documenting the prevalence of subclinical rheumatic heart disease in Kenya. However, worldwide estimates demonstrate the highest prevalence of rheumatic heart disease in sub-Saharan Africa, at a rate of 5 to 7 per a thousand\textsuperscript{20}. Okello et al\textsuperscript{21} in a study done in Uganda to determine the burden, risk factors and outcome of rheumatic heart disease, found a prevalence of 14.6 per thousand which is twice the estimate for sub-Saharan Africa. The most commonly affected valve in our study was the mitral valve with 69.8% having mitral thickening and 30.2% having mitral regurgitation. Bourre-Tessier et al\textsuperscript{19} also found the mitral valve to be the most commonly affected valve with mitral valve thickening found in 25.4% and mitral regurgitation in 25.8%.

Pulmonary hypertension was found in 22.2% of participants in our study, though majority of them are classified as possible pulmonary hypertension, this is a significant finding because of the substantial morbidity and mortality associated with pulmonary hypertension in patients with SLE. Pulmonary hypertension is the most severe form of lupus associated pulmonary involvement, with poor long term outcome despite a number of therapeutic interventions. The mean survival from onset of pulmonary hypertension is two years\textsuperscript{14}.

**Conclusion**

The study demonstrates a high prevalence of cardiac abnormalities among SLE patients despite being on disease modifying medications. Even though the majority of these abnormalities comprised of clinically insignificant pericardial and valvular thickening, the prevalence of valvular insufficiency and pulmonary hypertension are substantially high and relatively higher than the prevalence seen in other studies in the case of pulmonary hypertension.

**Study limitations**

Echocardiography is generally not the preferred imaging modality to assess pericardial or valvular thickness because of its inherent lack of accuracy for measurements less than 5mm, variable image quality and inter and intra observer variability.
References


Chronic kidney disease in rheumatoid arthritis at Kenyatta National Hospital

Said SS, Oyoo GO, Kayima JK, Lule GN

Abstract

Objective: To determine the prevalence of chronic kidney disease among patients with rheumatoid arthritis on follow up at the rheumatology outpatient clinic at Kenyatta National Hospital.

Design: Descriptive, cross-sectional study.

Setting: Rheumatology outpatient clinic at the Kenyatta National Hospital, a public national and referral hospital.

Subjects: Patients diagnosed to have rheumatoid arthritis who met the 2010 ACR-EULAR criteria.

Results: Out of 104 patients recruited, 93 (89.4%) were female with a female to male ratio of 8.5:1. Mean age of patients was 48.7(±15.6) years. Majority of the patients (90%) were on at least one Disease Modifying Anti-Rheumatic Drug (DMARD) with methotrexate being the commonest used. Other DMARDs were leflunomide, sulfasalazine and hydroxychloroquine. None of our patients was on a biologic agent. Use of NSAIDs and/or prednisone was very frequent (88.5%). Median duration of disease since time of diagnosis was 4 years. Majority of patients (60%) had active disease. We found the prevalence of chronic kidney disease to be 28.7% (95% CI 19.1-37.2%) based on estimated glomerular filtration rate using the Cockroft-Gault formula. Majority (50%) of which was stage 3a disease and none with end stage renal disease. We found no patients with proteinuria using urinary dipstick.

Conclusion: Although we did not find any proteinuria in our study population, prevalence of chronic kidney disease based on estimated glomerular filtration rate was high with the majority having early stages of kidney disease. Use of urine strips alone is not an adequate screening tool.

Introduction

Rheumatoid Arthritis (RA) is a worldwide health problem with an estimated global prevalence of 0.24%1. The World Health Organisation (WHO) considers it as one of the diseases with the greatest impact on society2 and it is the 42nd highest contributor to global disability1.

Patients with RA are at increased risk of death more than their age and sex matched non-rheumatoid controls. Even with improvement of disease management, there has been no decrease in mortality for patients with RA3. Renal disease is a common cause of mortality in patients with rheumatoid arthritis. This may be as a result of disease itself, drugs used in treatment and other causes of nephropathy4. As most patients with rheumatoid arthritis are above the age of forty years5, age itself and other co-morbid conditions like diabetes and hypertension also have a negative impact on their kidney function.

Cardiovascular complications are the major causes of mortality in these patients. They are at higher risk of silent myocardial infarction and lower risk of angina pectoris. Mortality after these events is also higher than in their non-RA counterparts6.

The effects of kidney dysfunction in RA are adverse. A low estimated Glomerular Filtration Rate (eGFR) increases Cardio-Vascular Disease (CVD) risk and vice versa. Since CVD is the major cause of mortality in these patients, frequent screening and modification of risk factors is of importance in this population7.

Assessment of eGFR is also warranted in RA for drug adjustment. Methotrexate is the commonest Disease Modifying Anti Rheumatic Drug (DMARDs) used in the control of RA. Its use is contraindicated in any person with CKD stage 3 and above8. The use of other drugs, such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) must also be approached with caution in such patients as they can exacerbate kidney injury. CKD is progressive with rapid decline in function if it goes unrecognized and is not addressed early especially in the presence of a high prevalence of chronic kidney disease.
of continued injury. Therefore screening for CKD is of vital importance especially in this group of patients who have several factors that may cause or worsen kidney damage.

**Materials and Methods**

**Study population:** The study was conducted on patients on follow up at the rheumatology outpatient clinic at the Kenyatta National Hospital which is the national referral hospital situated in Nairobi, Kenya. It is the sole clinic catering to patients with rheumatological illnesses in the public sector.

**Patient recruitment:** We screened patients with a file diagnosis of RA at the rheumatology outpatients’ clinic consecutively until a sample size of 104 was reached. All patients aged 18 years and above who met the 2010 American College of Rheumatology—European League Against Rheumatism (ACR-EULAR) criteria for RA and gave written informed consent were recruited. We recorded patients’ age, gender, marital status, highest level of education acquired, disease duration and drug history on a data abstraction tool that had been prepared. Patients underwent an assessment of disease activity using Disease Activity Score 28 (DAS 28) which categorised them into remission, mild, moderate or severe disease. A blood pressure reading was taken using a mercury sphygmanometer. They were also weighed to the nearest kilogram. We requested patients to provide a urine sample for screening on site for a urinary tract infection and proteinuria using dipsticks.

**Laboratory methods:** An automated machine (Mindray BS 400) was used to determine creatinine levels which were subsequently used to calculate eGFR. The Wintrobe method was used to calculate ESR level for calculation of the DAS-28 score. We used the URIT 10V dipsticks to assess for proteinuria and urinary tract infection.

**Ethical considerations:** The study was undertaken after acquiring approval from the KNH Ethical and Research Committee. Only adults who were 18 years and above who gave written, informed consent were recruited.

**Data analysis:** Data was analysed using SPSS version 20 for Microsoft. Continuous variables were summarized into means, medians and standard deviations. Quantitative data was presented using frequency, tables, pie charts and bar graphs. Dependent variables were analysed for correlation with a p value of 0.05 or less considered significant. Chronic kidney disease was correlated with: disease duration using the Kruskal Wallis test, disease activity using the Spearman’s correlation and treatment modality using the Chi-square test.

**Results**

Data was collected over a ten week period. Out of the population of 146 RA patients at the clinic we managed to screen a total of 107. Of these, two did not meet the inclusion criteria; one declined consent and was thus excluded, leaving a total of 104 patients who were enrolled. On screening for proteinuria, 5 patients were found to have a current UTI and were not evaluated for proteinuria. We evaluated 99 of the study participants for proteinuria. Of the total 104 patients screened, results for creatinine level were available for only 102. Figure 1 depicts patient recruitment.

**Figure 1:** Patient recruitment

146 patients with RA attending the clinic

107 patients with RA screened

105 patients eligible

104 patients recruited

Excluded 2: results missing

Excluded 2: did not meet inclusion criteria

Excluded 1: declined consent

Excluded 5: current UTI
In our study population, mean age was 48.7 ±15.6 years and majority of patients were female 93 (89.4%), married 71 (68.3%) and having attained some level of formal education 94 (90.4%). Table 1 shows their demographic and clinical characteristics. Comorbid diseases assessed were diabetes 8 (7.7%) and hypertension 37 (35.6%).

Table 1: Demographic and clinical characteristics of the study population (n=104)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Frequency (n)</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>7</td>
<td>6.7</td>
</tr>
<tr>
<td>25-34</td>
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<td>35-44</td>
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<td>45-54</td>
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<td>19.2</td>
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<td>65 and above</td>
<td>16</td>
<td>15.4</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11</td>
<td>10.6</td>
</tr>
<tr>
<td>Female</td>
<td>93</td>
<td>89.4</td>
</tr>
<tr>
<td>Level of formal education</td>
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<td></td>
</tr>
<tr>
<td>None</td>
<td>10</td>
<td>9.6</td>
</tr>
<tr>
<td>Primary</td>
<td>41</td>
<td>39.4</td>
</tr>
<tr>
<td>Secondary</td>
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<td>25</td>
</tr>
<tr>
<td>Tertiary</td>
<td>27</td>
<td>26</td>
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<tr>
<td>Marital status</td>
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<tr>
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<td>71</td>
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<tr>
<td>Single</td>
<td>17</td>
<td>16.3</td>
</tr>
<tr>
<td>Divorced/separated/widowed</td>
<td>16</td>
<td>15.4</td>
</tr>
<tr>
<td>Disease duration since diagnosis (years)</td>
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<td></td>
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<tr>
<td>Less than 1</td>
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<td>17.3</td>
</tr>
<tr>
<td>1-5</td>
<td>51</td>
<td>49</td>
</tr>
<tr>
<td>More than 5</td>
<td>35</td>
<td>33.7</td>
</tr>
<tr>
<td>Disease activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remission</td>
<td>21</td>
<td>20.4</td>
</tr>
<tr>
<td>Mild</td>
<td>21</td>
<td>20.4</td>
</tr>
<tr>
<td>Moderate</td>
<td>39</td>
<td>37.9</td>
</tr>
<tr>
<td>Severe</td>
<td>22</td>
<td>21.3</td>
</tr>
<tr>
<td>Use of NSAIDs and prednisone</td>
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<tr>
<td>NSAID + prednisone</td>
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<td>41.3</td>
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<td>NSAID</td>
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<td>22.1</td>
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<td>Prednisone</td>
<td>26</td>
<td>25</td>
</tr>
<tr>
<td>Not on NSAIDs or prednisone</td>
<td>12</td>
<td>11.5</td>
</tr>
<tr>
<td>DMARD use</td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>90</td>
<td>86.5</td>
</tr>
</tbody>
</table>

NSAIDs=Non-Steroidal Anti-Inflammatory Drugs, DMARD=Disease Modifying Anti-Rheumatic Agent

Prevalence of CKD: Of 104 patients, creatinine results were available for 102. Using the Cockroft-Gault formula, a total of 28 (27.5%) patients were found to have kidney disease. The staging for kidney disease was as follows; stages 3a (13.7%), 3b (7.8%) and stage 4 at (5.9%). There was no patient with stage 5 kidney disease. Table 3 gives the distribution of patients with CKD according to the KDIGO criteria.

Table 2: Stages of CKD

<table>
<thead>
<tr>
<th>CKD staging</th>
<th>Frequency (n)</th>
<th>(%)</th>
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</thead>
<tbody>
<tr>
<td>Stage 3a</td>
<td>14</td>
<td>50</td>
</tr>
<tr>
<td>Stage 3b</td>
<td>8</td>
<td>28.6</td>
</tr>
<tr>
<td>Stage 4</td>
<td>6</td>
<td>21.4</td>
</tr>
</tbody>
</table>

CKD= Chronic Kidney Disease

Prevalence of proteinuria: The prevalence of proteinuria was found to be 0% among the 99 patients assessed.

Association of eGFR with duration of RA: eGFR was categorized into stages and an association with duration of disease analysed. There was no association found between the two variables (p = 0.502).

Association of eGFR with disease activity: There was no association found between eGFR levels with disease activity. The correlation between eGFR and disease activity was not statistically significant (p = 0.545).

Association of eGFR with drugs used: We assessed whether there was any correlation between use of NSAIDs, prednisolone or both with eGFR level using the Chi square test and found no association between the drug used and eGFR level (p = 0.392).

Discussion

There is paucity of data on chronic kidney disease in rheumatoid arthritis. Majority of the studies have been undertaken in the developed countries and we were unable to access any studies done in Africa.

Whilst assessing eGFR, prevalence of CKD was found to be 27.5% as measured by an eGFR of less than 60ml/min/1.73m². This is a higher prevalence than that of the general African population whose prevalence of CKD is estimated to be 13.9%. It would thus appear that patients with rheumatoid arthritis have an increased risk of CKD as compared to the general population.

When compared to other studies assessing CKD in patients with rheumatoid arthritis, the figures are much higher than 25.3% as noted by Karie et al, 12.75% by Daoussis et al and 18% found by Hill et al which are studies undertaken in Europe. The higher prevalence of CKD in our population may be explained by the fact that CKD is increased in blacks more than in their white counterparts. This has in turn been attributed to genetic predisposition, low socio-economic status and inequities.
in access to healthcare, factors which may apply to our population although this were not assessed by our study.

According to our findings, there were no patients with stage 5 CKD which could indicate that patients may be dying from other causes before their kidney disease worsens to end stage renal failure or their CKD is non-progressive in nature. Proteinuria is a strong indicator of disease progression in CKD. The absence of proteinuria among the study participants may support the postulation of the non-progressive nature of CKD in this population.

Proteinuria has been related to gold or penicillamine use both of which are not used in our setting. Proteinuria may also occur secondary to glomerulonephritis. The high prevalence of CKD in the absence of proteinuria may indicate a non-glomerular cause of CKD in this population. Glomerulonephritis in RA is now considered to be rare. Horak et al\(^7\) notes it to be of little clinical significance and was only noted on either autopsy or biopsy in the past. Interestingly, the MATRIX study\(^12\) also found an absence of patients with stage 5 CKD in their study population which may support the postulation that patients may either have a non-progressive disease or dying from other causes before progression to end-stage renal failure.

Another factor that may explain the lack of proteinuria in our study population is due to the fact that proteinuria is not recommended for CKD screening in a young population due to the low diagnostic yield\(^18\).

Although our study set out to explore associations between CKD and various parameters, we were not powered to make significant conclusions out of these findings. Longitudinal studies may be better designed to assess for an association between disease duration and CKD.

Despite the significant use of NSAIDs and prednisolone (88.5%), either singly or in combination, it is worth noting that there was no association between NSAID or steroid use and CKD. The lack of correlation between the drugs used and kidney disease may be attributed to poor drug compliance by our study population although this was not assessed by this study.

Further studies are needed to ascertain the cause of high CKD prevalence in this population with longitudinal studies for determining disease progression.

**Acknowledgements**

To the KNH-MOPC nursing and records staff for assisting in the recruitment of patients and acquiring of patient records and to the patients for willing to be part of this study.

**References**


Disease activity measurement in rheumatoid arthritis: comparison of 3 disease activity index tools at Kenyatta National Hospital

Ndirangu KM, Oyoo GO, Bhatt KM, Ilovi CS

Abstract

Objectives: To compare the congruence of the Disease Activity Score with 28-joint count (DAS-28) with the Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI) in measuring disease activity in Rheumatoid Arthritis (RA) patients at the Kenyatta National Hospital (KNH).

Design: Cross-sectional descriptive study.

Setting: Rheumatology Out-Patient Clinic (ROPC) at KNH.

Subjects: One hundred and four patients who fulfilled the 2012 American College of Rheumatology Classification Criteria for RA.

Results: DAS28, SDAI and CDAI were significantly correlated with each other on a group level (p < 0.001). Internal consistency was highest for CDAI (alpha = 0.705) and lowest for DAS28 (alpha = 0.67). Kappa statistics revealed substantial degree of agreement with respect to controlled, active, moderate and high disease activity categories according to the three scores.

Conclusion: Both SDAI and CDAI proved to be in congruence with DAS28 in daily clinical routine. SDAI and CDAI were found to be more stringent in defining remission.

Introduction

It has been recognized for decades that survival among persons with RA is significantly worse compared to survival in the general population. Premature death has been long recognized as a manifestation of RA. The cause of these premature deaths include a higher risk of several serious co morbid conditions with worse outcomes after the occurrence of these illnesses, sub-optimal primary or secondary preventive care and the systemic inflammation and immune dysfunction associated with RA appears to promote and accelerate co morbidity and mortality. It is also established that duration of active disease is associated with joint damage and disability. Therefore, early initiation of treatment and continuous monitoring of disease activity is needed to reduce structural damage in RA. The current treatment approach for patients with RA involves early initiation of aggressive therapy with Disease Modifying Anti-Rheumatic Drugs (DMARDs) and biologic agents. The goal of treatment is remission and therefore regular assessment of disease activity is necessary in the clinic for guiding treatment. In this respect, the patients should understand the term ‘disease activity’ as they understand glucose values or blood pressure in diabetes and hypertension, respectively. This can be the key to success of and compliance to therapy. Numerous RA disease activity measurement tools are currently available for use. Since the 1950’s when the first composite disease activity measurement tool for use in RA was developed, many attempts have been made to improve RA disease activity monitoring. The psychometric data related to these tools have been published over the course of decades and across numerous journals. The last two decades have witnessed a dramatic improvement in the treatment of RA, with disease remission now considered a realistic goal for most patients. Surrogate measures of outcome such as disease activity index measures can facilitate clinical decision making to achieve these goals and studies in RA show that treating to target improves outcome. Though there are 63 currently available RA disease activity measurement tools, three are commonly used: CDAI, DAS28 (Erythrocyte Sedimentation Rate or C-Reactive Protein) and SDAI. All three produce a single continuous index and have defined ranges for indicating mild, moderate or high disease activity or clinical remission. By applying these tools systematically in clinical practice, physicians are able to “treat to target” and effectively implement the ACR and EULAR recommendations for the treatment of RA. Given the heterogeneity of settings in which healthcare is delivered to patients with RA, these measures offer a full range of data collection options. This study intends to compare the performance of the three disease activity measurement tools i.e. DAS-28, SDAI and the CDAI in a clinical routine setting with the aim of recommending routine use of SDAI and CDAI during every visit to the rheumatology outpatient clinic.
**Materials and Methods**

This was a hospital based study done between January 29th and March 9th 2015, at the rheumatology out-patient clinic of KNH. A minimum sample of 101 patients was required. The subjects were patients aged 18 years and older fulfilling the 2012 ACR classification criteria for RA.

Targeted clinical history was taken followed by joint assessment out of a 28-joint count. The patient global assessment of general health (on a scale of 0-100mm for DAS-28 and 0-10cm for SDAI and CDAI) and the provider general assessment of general health for SDAI and CDAI only (on a scale of 0-10cm) were carried out. Approximately 4ml of venous blood was drawn aseptically, following standard guidelines from each patient for measurement of quantitative C-Reactive Protein (CRP).

Calculation of disease activity scores was then calculated as per the specific guide for each tool. Patients were then categorized as having controlled disease (remission + low disease activity) or active disease (moderate and high disease activity) and as being in remission, having low, moderate or high disease activity using the following cut-off points: DAS-28 (≤ 2.6 for remission, ≤ 3.2 for low, ≤ 5.1 for moderate and 5.1 for high ), SDAI (≤ 3.3 for remission, ≤ 11 for low, ≤ 26 for moderate and > 26 for high) and CDAI (≤ 2.8 for remission, ≤ 10 for low, ≤ 22 for moderate and > 22 for high).

Spearman’s rank correlation coefficient was used to test the congruency and agreement of the tools at the group level while kappa statistics was used to test for that between the disease categories.

**Results**

In this ten week-time based study (January 29th to March 9th 2015) targeting RA patients attending the KNH ROPC, 106 patients confirmed to have RA (2012 ACR classification criteria and confirmed by a rheumatologist) were consecutively screened for recruitment. Two patients were not eligible for the study after declining to give consent (Figure 1).

**Figure 1:** Demographic characteristics of the study population

<table>
<thead>
<tr>
<th>KNH ROPC-107 RA patients screened</th>
<th>2 Excluded-Did not fulfill criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>105 Eligible</td>
<td></td>
</tr>
<tr>
<td>104 Recruited</td>
<td>1 Declined consent</td>
</tr>
<tr>
<td>104 Assessed</td>
<td></td>
</tr>
</tbody>
</table>

The mean age of the patients was 48.7 years (SD = 15.6). Most of the study participants were female 93 (89.4%) giving a female to male ratio of 9:1 (Table 1).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in years (SD)</td>
<td>48.7 (15.6)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>93 (89.4)</td>
</tr>
<tr>
<td>Male</td>
<td>11 (10.6)</td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>9 (8.7)</td>
</tr>
<tr>
<td>Primary</td>
<td>41 (39.5)</td>
</tr>
<tr>
<td>Secondary</td>
<td>26 (25.0)</td>
</tr>
<tr>
<td>Tertiary</td>
<td>28 (26.9)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>17 (16.3)</td>
</tr>
<tr>
<td>Married</td>
<td>71 (68.3)</td>
</tr>
<tr>
<td>Separated</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Divorced</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Widowed</td>
<td>13 (12.5)</td>
</tr>
</tbody>
</table>

Ninety six point two per cent of the patients had had RA disease symptoms for more than 1 year while 82.7% had had a diagnosis of RA for the same period. Eighty six point five per cent of the patients were on DMARDS and 62.5% were on steroids. A good proportion of the patients on steroids had controlled disease (Table 2).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration since diagnosis (years)</td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>18 (17.3)</td>
</tr>
<tr>
<td>1-5</td>
<td>51 (49.0)</td>
</tr>
<tr>
<td>&gt;5</td>
<td>35 (33.7)</td>
</tr>
<tr>
<td>Duration of symptoms (years)</td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>4 (3.8)</td>
</tr>
<tr>
<td>1-5</td>
<td>45 (43.3)</td>
</tr>
<tr>
<td>&gt;5</td>
<td>55 (52.9)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>60 (57.7)</td>
</tr>
<tr>
<td>No</td>
<td>44 (42.3)</td>
</tr>
<tr>
<td>Steroids</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>65 (62.5)</td>
</tr>
<tr>
<td>No</td>
<td>39 (37.5)</td>
</tr>
<tr>
<td>DMARDs</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>90 (86.5)</td>
</tr>
<tr>
<td>No</td>
<td>14 (13.5)</td>
</tr>
</tbody>
</table>

The median disease activity score of the study population was 3.5 (IQR: 2.5-4.7) i.e. moderate disease activity. That of SDAI and CDAI was 14.1(IQR: 7.7-25.9) and 11.0(IQR: 6.0-20.7) respectively, both signifying moderate disease activity (Table 3).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28</td>
<td>3.5 (2.5-4.7)</td>
</tr>
<tr>
<td>SDAI</td>
<td>14.1 (7.7-25.9)</td>
</tr>
<tr>
<td>CDAI</td>
<td>11.0 (6.0-20.7)</td>
</tr>
</tbody>
</table>
There is significant congruence of SDAI and CDAI with DAS28 for moderate and high disease activity categories. DAS28 over-classifies patients as being in remission by redistributing them from the low disease activity category. SDAI and CDAI are in almost perfect agreement for all disease activity categories. When disease activity is categorized as either controlled or active disease, the three tools show significant agreement to one another (Table 4).

**Table 4: Correlation amongst the disease activity score tools**

<table>
<thead>
<tr>
<th>Disease activity</th>
<th>DAS28</th>
<th>95% CI</th>
<th>SDAI</th>
<th>95% CI</th>
<th>CDAI</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission</td>
<td>32 (30.8)</td>
<td>21.2, 40.4</td>
<td>7 (6.7)</td>
<td>2.9, 11.5</td>
<td>10 (9.6)</td>
<td>3.8, 16.3</td>
</tr>
<tr>
<td>Low</td>
<td>12 (11.5)</td>
<td>5.8, 17.3</td>
<td>32 (30.8)</td>
<td>22.1, 39.4</td>
<td>38 (36.5)</td>
<td>26.9, 45.2</td>
</tr>
<tr>
<td>Moderate</td>
<td>41 (39.4)</td>
<td>30.8, 49.0</td>
<td>39 (37.5)</td>
<td>27.9, 47.1</td>
<td>31 (29.8)</td>
<td>21.2, 38.5</td>
</tr>
<tr>
<td>High</td>
<td>19 (18.3)</td>
<td>10.6, 26.0</td>
<td>26 (25.0)</td>
<td>17.3, 33.7</td>
<td>25 (24.0)</td>
<td>16.3, 31.7</td>
</tr>
<tr>
<td>Controlled</td>
<td>44 (42.3)</td>
<td>32.7, 51.9</td>
<td>39 (37.5)</td>
<td>27.9, 46.2</td>
<td>48 (46.2)</td>
<td>36.5, 55.8</td>
</tr>
<tr>
<td>Active</td>
<td>60 (57.7)</td>
<td>48.1, 67.3</td>
<td>65 (62.5)</td>
<td>53.8, 72.1</td>
<td>56 (53.8)</td>
<td>44.2, 63.5</td>
</tr>
</tbody>
</table>

The correlation coefficient between DAS28 and SDAI was 0.960 while that between DAS28 and CDAI was 0.892 which were both statistically significant with a $p<0.001$ (Table 5).

**Table 5: Correlation at the group level**

<table>
<thead>
<tr>
<th>Spearman’s rank coefficient (rho)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDAI</td>
<td>0.960</td>
</tr>
<tr>
<td>CDAI</td>
<td>0.892</td>
</tr>
</tbody>
</table>

The agreement of DAS28 and SDAI in disease activity categorization revealed a kappa value of 0.78 while that of DAS28 and CDAI was 0.69 both of which were statistically significant with $p<0.001$ (Tables 6 and 7).

**Table 6: Agreement of disease activity categorization between DAS28 and SDAI**

<table>
<thead>
<tr>
<th>Disease activity</th>
<th>DAS28</th>
<th>SDAI</th>
<th>Spearman’s rank (rho)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled</td>
<td>2.28 (1.79-2.52)</td>
<td>5.80 (3.99-8.04)</td>
<td>0.850</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Active</td>
<td>4.51 (3.77-5.44)</td>
<td>24.71 (17.00-34.86)</td>
<td>0.912</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Table 7: Agreement of disease activity categorization between DAS28 and CDAI**

<table>
<thead>
<tr>
<th>Disease activity</th>
<th>DAS28</th>
<th>Total</th>
<th>McNemar’s p value</th>
<th>Measure of agreement Kappa, p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDAI</td>
<td>36</td>
<td>3</td>
<td>39</td>
<td>0.227</td>
</tr>
<tr>
<td>Active</td>
<td>8</td>
<td>57</td>
<td>65</td>
<td></td>
</tr>
</tbody>
</table>

| Total            | 44    | 60    | 104              | 0.78, <0.001                      |
Table 8: Multivariate analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controlled</th>
<th>Active</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>48.0 (15.7)</td>
<td>49.2 (15.7)</td>
<td>-</td>
<td>0.695</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>41 (44.6%)</td>
<td>51 (55.4%)</td>
<td>2.1 (0.5-8.6)</td>
<td>0.345</td>
</tr>
<tr>
<td>Male</td>
<td>3 (27.3%)</td>
<td>8 (72.7%)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>25 (41.7%)</td>
<td>35 (58.3%)</td>
<td>0.9 (0.4-2.1)</td>
<td>0.877</td>
</tr>
<tr>
<td>No</td>
<td>19 (43.2%)</td>
<td>25 (56.8%)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Steroids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>25 (38.5%)</td>
<td>40 (61.5%)</td>
<td>0.7 (0.3-1.5)</td>
<td>0.305</td>
</tr>
<tr>
<td>No</td>
<td>19 (48.7%)</td>
<td>20 (51.3%)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>DMARDs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>38 (42.2%)</td>
<td>52 (57.8%)</td>
<td>1.0 (0.3-3.0)</td>
<td>0.964</td>
</tr>
<tr>
<td>No</td>
<td>6 (42.9%)</td>
<td>8 (57.1%)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>DOS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>1 (25.0%)</td>
<td>3 (75.0%)</td>
<td></td>
<td>0.641</td>
</tr>
<tr>
<td>1-5</td>
<td>21 (46.7%)</td>
<td>24 (53.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥5</td>
<td>22 (40.9%)</td>
<td>33 (60.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>5 (27.8%)</td>
<td>13 (72.2%)</td>
<td></td>
<td>0.362</td>
</tr>
<tr>
<td>1-5</td>
<td>24 (47.1%)</td>
<td>27 (52.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥5</td>
<td>15 (42.9%)</td>
<td>20 (57.1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was no significant association between disease activity as scored using the three tools with gender, treatment modality, duration of symptoms (DOS) or duration of disease (DOD) as shown in Table 8.

Discussion

The main aim of this study was to evaluate the correlation and agreement between the DAS-28 with SDAI and the CDAI tools in routine assessment of disease activity in RA patients attending KNH ROPC in daily clinical routine.

The study also set out to establish the utility of CDAI and possibly SDAI in the routine assessment of disease activity in these RA patients and to document correlation of disease activity as measured with the above tools with the age, gender, modality of treatment, duration of symptoms and duration of disease.

Routine measurement of disease activity in clinical practice correlates with improved patient outcomes (independent of aggressive disease control). The commonly used disease activity measurement tool in RA is DAS-28. DAS-28 although currently considered the gold standard in RA disease activity assessment, is complex, expensive and time consuming. Although computation of the SDAI is simply a summation of its variables it still requires a laboratory parameter. CDAI on the other hand involves simple summation of its parameter and requires no laboratory parameter. In our set up many patients lack access to ESR or CRP due to many reasons and CDAI would be the best tool to use in daily clinical routine.

DAS-28 has proved to be in line with patients’ thoughts about their disease and therefore the DAS-28 Categories (DAS-28C) can be regarded as presenting the patients position\textsuperscript{12}, hence we felt justified in taking DAS-28C as the reference for comparison.

The total number of patients identified with RA over a period of 10 weeks was 107 which was slightly more than the numbers seen in previous studies\textsuperscript{13-15}. This is a clear indication that there is an increase in number of patients with RA being seen in KNH. This increase is probably due to improvement in health awareness among the population, a better referral system and increasing urbanization.

The mean age of the study population was 48.7 years. Other studies done on this population had a similar mean age\textsuperscript{14-16}. This can be attributed to the fact that RA has an onset between the 3\textsuperscript{rd} and 5\textsuperscript{th} decades of life. Female subjects represented 90% of the 104 subjects. This is also similar to what was found in previous studies on this population of patients\textsuperscript{14-16}. We can attribute this to the fact that RA, like a majority of other connective tissue diseases affects females to a greater degree than males\textsuperscript{17}. This was considerably higher than what has been the commonly reported ratio of 1:3. This could be due to the fact that we are seeing more RA patients and the health care seeking behavior is different in the two sexes.

In the treatment of RA most patients (86.5%) were on DMARDS. In 2007 only 46.7% of patients were on DMARDS\textsuperscript{15} and by 2012, this had risen to 75%\textsuperscript{14}. Though encouraging since the current approach to treatment for patients with RA involves early initiation of aggressive therapy with DMARDS and biologic agents\textsuperscript{18}, more than 13% of patients are not receiving the right treatment. Most of these were new patients i.e. diagnosed within 1 year and were yet to get or fill their DMARDS prescription. However, none of the patients in this study...
were on a biologic agent. This is due to the prohibitive cost of these agents. The referral hospital is a public health care facility where patients pay out of pocket for all the services they receive in the clinic. Few have private health care insurance and even these are unable to cater for biologics. Over 60% of study participants were on a steroid. This high figure could be due to the fact that 13.5% of the study subjects were not on a DMARDS and majority of the study subjects had active disease.

Alpha, a measure of internal consistency was 0.67 for DAS-28, 0.69 for SDAI and 0.705 for CDAI showing the highest reliability for the test omitting acute phase reactants. Testing for agreement at the group level revealed, as expected, almost complete congruence between SDAI and CDAI ( Spearman’s Rank Correlation [rho] = 0.989, p<0.001). DAS-28 and SDAI as well as CDAI were also highly significantly correlated in this patient group (rho = 0.960 for DAS-28/SDAI and rho = 0.892 for DAS-28/CDAI; both p<0.001). Kappa, a particularly individual measure used to estimate the relationship between disease activity categories as classified with the three tools was 0.78, p<0.001 for the relationship between DAS-28 and SDAI when they classified disease as either controlled (remission and mild disease activity) or active (moderate and high disease activity). For the relationship between DAS-28 and CDAI for the same classification was 0.69, p<0.001. This depicts substantial agreement of the tools in assigning disease activity scores of this patient group to the two categories.

For the assessment of the relationship where the four categories i.e. mild, moderate and high disease activity, plus the remission category, there was substantial agreement between DAS-28 and SDAI and between DAS-28 and CDAI in the moderate and high disease activity categories. However there was less than substantial agreement in the remission and mild disease activity categories in that DAS-28 classified more patients as being in remission as compared to SDAI and CDAI. This is because DAS-28 redistributes patient from the mild disease activity category to the remission category. The reason for this is that remission in RA has not been strictly defined. Although the DAS-28 level maybe indicating remission, mathematically 12 swollen joints can be present. However when applying SDAI and CDAI, the maximum joint count possible within remission range is 2 for both tender joint count and swollen joint count.

Our observations are in line with a large international study looking at disease activity and remission rates in 5848 RA patients in clinical practice from 24 countries with the highest remission rates when assessed according to DAS-28 (19.6%) and only 13.8% when assessed according to CDAI.

A clinical trial involving more than 6600 RA patients receiving adalimumab open label for 12 weeks found 30% of the patients in remission according to the DAS-28, but only 24% and 27% according to SDAI and CDAI respectively.

There is an ongoing discussion to define remission more restrictively. A study done in Brazil in 2014 using different cut-off points for both DAS-28ESR and DAS-28CRP and comparing these to SDAI and CDAI categories showed improved agreement with lower cut-off points for DAS-28ESR and CRP. The more stringent remission criteria by SDAI and CDAI may be of advantage in clinical practice for monitoring sustained remission. Not only is treatment as early as possible mandatory, but monitoring as close-matched as possible and also monitoring tools as accurate as possible very important. This seems to favor SDAI and CDAI for patient assessment. The highest internal consistency was with the CDAI, despite the fact that alpha increases with the increasing number of composite scale parameters. Thus CRP values add little to and contribute to the heterogeneity of a disease activity scale.

Full congruence between the three tools to assess RA patients cannot be expected because these instruments do not use exactly the same parameters. Also, different calculation methods are applied. This is also the reason why the weighting of the single items within the three composite scores is different.

Existence of threshold values is necessary for categorizing patients. It facilitates documentation of disease status which helps in justifying expensive disease regimens in clinical routine. It is important to always use the same scoring system in an individual patient in routine clinical care. Current evidence does not recommend any tool as a gold standard for disease activity monitoring in RA.

The CDAI offers some advantages: first, remission is more stringently defined than with DAS-28 although no studies exist to show any long term differences between the patients classified as being in remission with CDAI and DAS-28. Second, lack of a laboratory test makes CDAI cheaper with potential to be used widely in resource poor settings. The primary requirement for efficient routine clinical work calls for easy and rapid organization of patient monitoring without losing reliability. Disease activity assessment tools should enable physicians to obtain reliable information about the disease course and should be sensitive enough to sound the alarm if deterioration occurs. The more easily applicable the assessment tool indexes are, the more they will be used by physicians. A simpler, affordable and uniform way of documenting a patient’s disease will definitely result in improved RA patient care.

This study shows that assessment of disease activity with CDAI is comparable with DAS-28 in RA patients on follow-up in the KNH ROPC. CDAI was also more stringent in defining the lowest disease activity achievable i.e. remission.
References


5. Anderson JK, Zimmerman L, Caplan L, et al. Measures of rheumatoid arthritis disease activity: Patient (PtGA) and Provider (PrGA) Global Assessment of Disease Activity, Disease Activity Score (DAS) and Disease Activity Score With 28-Joint Counts (DAS28), Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Patient Activity Score (PAS) and Patient Activity Score-II (PASII), Routine Assessment of Patient Index Data (RAPID), Rheumatoid Arthritis Disease Activity Index (RADAI) and Rheumatoid Arthritis Disease Activity Index-5 (RADAI-5), Chronic Arthritis Systemic Index (CASl), Patient-Based Disease Activity Score With ESR (PDAS1) and Patient-Based Disease Activity Score Without ESR (PDAS2), and Mean Overall Index for Rheumatoid Arthritis (MOIRA). *Arthritis Care Res.* 2011; 63(S11):S14-S36.


Epidemiologic and clinical aspects of osteomyelitis in the rheumatology ward at Point G’s University Hospital Center

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

Abstract

Background: Osteomyelitis is a bone infection that results from haematogenous spread, and that affects both genders. It is found in children and adolescents and is mainly found in Africans with sickle-cell disease. Management of osteomyelitis in Mali faces difficulties because of the possible passage to chronicity.

Objective: To specify the epidemiologic and clinical characteristics of osteomyelitis and to evaluate the disease prognosis with treatment.

Patients and methods: This was a retrospective study covering a 7 year period (1st January 2006 to 31st December 2012), which included hospitalization files of patients diagnosed with osteomyelitis, whether referred or not.

Results: Thirty seven patient files were studied. All patients admitted in the ward were later followed either as outpatient or transferred to the orthopaedic surgery ward according to the evolution. Osteomyelitis is frequent, representing 5.8% of hospitalizations, with a mean age of 23.5 years. Trauma and sickle-cell disease were the main predisposing factors, each with a frequency of 18.9%. Consultation at advanced stages led to complications: neighbouring arthritis, skin fistula, multiple localizations. Probabilistic antibiotherapy, although sometimes excessive, was used. Staphylococcus aureus was mostly incriminated (45.9%). One case of tuberculosis was retained. Of the 12 patients voluntarily tested for HIV 1 and 2, one patient was positive for HIV 1. Long bones were preferably infected but damage to the iliac bone was not rare. Medical treatment as well as local care were not sufficient to prevent pathologic fractures in 18.9% of patients.

Conclusion: Acute osteomyelitis appears at all ages but is more predominant in young teenagers. Sickle cell disease is the most frequent co-morbidity. HIV immunodepression can be associated. Tuberculosis although endemic is not really incriminated.

Key words: Osteomyelitis, Sickle cell disease, Rheumatology, Mali

Introduction

Osteomyelitis is a bone infection that results from haematogenous spread, and that affects both genders. It is mainly observed in children and teenagers, especially in Africans with sickle cell disease. The portal of entry is often unknown, otherwise it may be a cutaneous, pulmonary or digestive infection. Frequently ear, nose and throat and/or urogenital areas are incriminated. The germ isolation inside the bone biopsy fragments is necessary to confirm diagnosis. Clinical presumptive elements such as standard radiography, ultrasonography of soft tissue, and positive haemocultures also permit to anticipate the therapeutic decision. The disease prognosis depends on early management. Septicemias, septic arthritis, the passage to chronicity and pathological fractures are the main complications. Management of osteomyelitis in Mali is difficult because of the possible passage to chronicity. The aim of the study was to specify epidemiologic and clinical aspects of osteomyelitis and to evaluate the disease prognosis before the treatment.

Materials and Methods

The study was retrospective covering a 7 year period from January 1st 2006 to December 31st 2012. Files of patients diagnosed with osteomyelitis who had been admitted were included (referred or not), regardless of age and sex. Data was collected on standardized anonymous investigation for measuring patient confidentiality. Data was analyzed using SPSS software version 18.0

Results

Thirty seven files were included. All the patients were hospitalized at least two weeks in the ward and then followed...
as outpatients or transferred to an orthopaedic surgical ward depending on the evolution. Osteomyelitis represented 5.8% of all hospitalizations, with a mean age of 23.5 years; mostly represented by the 15-25 year age group. The first cause for consultation was a painful swollen limb (83.8%). Trauma (18.9%) and sickle-cell disease (18.9%) were the principal predisposing factors. Consultation at an advanced stage led to complications: neighbouring arthritis (75.7%), skin fistula (48.6%), multiple localizations (59.4%). Hyperleucocytosis was noticed in 73% of patients, the sedimentation rate was increased in 94.6% of patients, and CRP positive in 83.8% of patients. An inflammatory anaemia was found in 78.4% of patients. X-rays showed sequestrum and thickening of periostea in all the patients, Brodie’s abscess and bone cysts in respectively 21.6% and 64.9% of cases. Eighty three point eight percent of patients who benefitted from ultrasonography had soft tissue anomaly. Probabilistic antibiotherapy, was prescribed based on clinical analysis, biological and imaging studies. Staphylococcus species were found in 45.9% of cases (Table 1).

Table 1: Patients distribution according to isolated germs

<table>
<thead>
<tr>
<th>Isolated germs</th>
<th>Effective (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>17</td>
</tr>
<tr>
<td><em>Salmonella typhi</em></td>
<td>2</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>4</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Chryseemonas lutéala</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Acinetobacter</em></td>
<td>1</td>
</tr>
<tr>
<td><em>Mycobacterias</em></td>
<td>1</td>
</tr>
<tr>
<td>Sterile</td>
<td>8</td>
</tr>
<tr>
<td>Culture not done</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>37</strong></td>
</tr>
</tbody>
</table>

Staphylococcus was causal in 45.9% of cases

Although rare, there was one case of mycobacterium tuberculosis. One out of the 12 patients voluntarily tested for HIV1 and 2 was positive for HIV1. Long bones were affected (femur in 30.9% of cases, tibia in 23.6% of cases, humerus in 16.8% of cases) and iliac involvement was found in 12.7% of patients. Antibiotherapy was adjusted and maintained in all patients for at least three months. Pathologic fracture complication was observed on 18.9% of cases.

Discussion

Osteomyelitis is frequent with 5.8% of hospitalizations, Moyikoua et al[^1] had reported 1.4% on 1800 hospitalizations during 4 years in the orthopaedic and surgical ward of Brazzaville’s. The age group of 15-25 years was the most represented with a mean of age of 23 years and 6 months. Kouame et al[^6] in their study had found 7 years and 5 months. Moyikoua et al[^8] affirmed that this affection is rare in adults, that it comes from an infectious awakening and rarely from the evolution of a childhood osteomyelitis. This assertion is not antithetic to the results of our study. A painful febrile swelling was the main reason for consultation (83.8%), superior to Guindo’s study results[^4] which reported 53.2%. Traumatism was frequently reported before the episode, (18.9%); it was the frequent predisposing factor in male children, probably because of their vivacity[^5]. Imaging was a determinant factor in the orientation for diagnosis of osteomyelitis. In a prospective study in the Middle-East by William[^6] including 31 children, a sensitivity of 74% and a specificity of 63% was found with the use of ultrasonography in the diagnosis of osteomyelitis using the presence of an under periostea collection of 4 mm or more. The co-morbidity of osteomyelitis/sickle-cell disease, has been reported by other authors[^2,4,7]. It was 18.9% in this series. One case of immunodepression to HIV1 was noticed, this co-morbidity is rarely reported. Three positive HIV serologies reported by Moyikoua et al[^2] and the only one case identified by Traore et al[^8] makes it difficult to come to a conclusion. Staphylococcus was a predominant factor in confirming anterior data[^1,9]. Antibiotherapy combined with local care (abscess drainage) did not always prevent pathological fractures (18.9%), thus making complementary orthopaedic surgery necessary. According to Chevrel and Richarme[^2], fractures occur willingly on fistulized callous osteomyelitic lesions. Eighty one point one percent patients were considered in remission (clinical and biological improvement) because of the possible risk of relapse.

Conclusion

Acute osteomyelitis occurs at all ages but mostly affects the young teenager. Sickle-cell disease is the most frequent co-morbidity. HIV immunodepression is rarely associated. Tuberculosis, even if endemic, is rarely incriminated. Antibiotherapy combined to local care (abscess drainage) does not always prevent pathological fractures.

References


Adult onset still’s disease; a rare disease in Nigeria?

Ohagwu KA¹, Aigbokhan EE², Olaosebikhan BH³, Adelowo OO³

Abstract

Adult Onset Still’s Disease (AOSD) is an inflammatory disease of unknown aetiology. 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.

Case 1

A 19 year old undergraduate had presented to the Lagos State University Teaching Hospital, Ikeja, Lagos State with complaints of fever of 2 months duration described as a high grade fever, intermittent and is worse during the evenings. Fever was associated with a history of weight loss and fatigue. He also complained of polyarthritis involving the wrist, knees, ankles and small joints of the hand for the same duration. There was a 2 weeks history of sore throat. He however did not have a history of skin rash. Examination had revealed a febrile patient at presentation with normal respiratory rate, pulse rate and a blood pressure of 120/80 mmHg. There were no lymphadenopathy or splenomegaly on examination.

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 elevated acute phase reactants. 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. The first patient was treated with steroid, hydroxychloroquine and azathioprine. The second patient was treated with steroid and methotrexate. Both made good clinical recovery.

Introduction

Adult Onset Still’s Disease (AOSD) first described by Bywaters in 1971¹ ² is an inflammatory disease of unknown aetiology³. Its global prevalence is estimated at 1 case per 100,000⁴. 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 2015⁵. 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.
Based on the Yamaguchi criteria, a diagnosis of AOSD was made. He was commenced on azathioprine (AZA) 50mg twice daily, prednisolone 10mg twice daily and hydroxychloroquine (HCQ) 200mg twice daily.

**Case 2**

A 62 year old man presented with one year history of recurrent high grade intermittent fever, weight loss and inflammatory polyarthritis involving the shoulders, elbows, hips, wrists, ankles and small joints of the hands and feet. Fever was associated with chills and rigors and he had lost 12kg body weight at presentation. There was no rash and he did not have sore throat. He had visited several hospitals for treatment to no avail. At presentation he was emaciated, febrile with temperature of 39.2°C, pale but with no peripheral lymphadenopathy. Systemic examination was unremarkable.

He had leukocytosis (24,000 cells/mm³) with neutrophilia (90.2%), microcytic hypochromic anaemia (haematocrit of 14%), thrombocytosis (878,000 cells/mm³), elevated ES (>150mm/Hour), high serum ferritin (4000 ng/ml) and elevated liver enzymes. RF, anti-CCP and connective tissue disease screening were negative. Serum uric acid was normal. Hepatitis B and C and HIV were negative. Chest X-ray, abdominal ultrasound scan and mantoux were normal. Septic work yielded no bacterial growth. Bone marrow aspiration cytology was in keeping with chronic inflammatory reaction. Based on the Yamaguchi criteria, a diagnosis of AOSD was made. Treatment was with intravenous pulse methylprednisolone 500mg daily for three days, oral prednisolone and weekly methotrexate. He was transfused with two units of sedimented red cells. His improvement was remarkable and both platelet and white cell counts normalized after two months.

**Discussion**

AOSD is a chronic inflammatory disorder of unknown aetiology. Its pathogenesis remains poorly understood and due to its rarity, there is no approved treatment guideline for clinical use.

Various infectious agents have been postulated to be involved in the aetiology of AOSD. These include Epstein-Barr virus, erythrovirus B19, parvovirus, cytomegalovirus, human immunodeficiency virus, rubella, hepatitis A, B and C and chlamydia pneumonia. It has been reported to occur as a paraneoplastic syndrome and also as an association with Miller-Fisher syndrome.

In the past decade, it has come to be classified as a polygenic autoimmune disease because of the recognition that its pathogenesis involves mainly the innate immune system. The hallmark of the disease is neutrophil and macrophage activation mediated by cytokines, mainly tumour necrosis factor alpha (TNF-α), interleukin (IL) 1, IL-6, IL-8 and IL-18. Helper T cells may also be involved in the pathogenesis. No familial trend has been described.

Most patients present with fever, polyarthritis involving synovial joints, sore throat, rash and weight loss are other symptoms. Lymphadenopathy, hepatomegaly, splenomegaly and pyrexia >38.8°C are frequently seen.

Anaemia of chronic disease is often present. Leukocytosis with marked neutrophilia, thrombocytosis, elevated serum ferritin but normal glycosylated ferritin levels are seen. Liver enzymes may be elevated. ESR is usually raised. Pro-inflammatory cytokines are elevated. Cytokine level and serum ferritin fluctuate with disease. X-ray of affected joints may show erosions and joint space narrowing but carpal ankylosis is highly specific to AOSD. Diagnosis of AOSD is by way of diagnostic criteria of which the Yamaguchi criteria is the most validated and widely accepted. It has a sensitivity and specificity of 0.96 and 0.92. Exclusion of malignancy, infections and other inflammatory diseases are required.

Patients with AOSD have been treated successfully with non-steroidal anti-inflammatory drugs, corticosteroids and combination of disease modifying anti-rheumatic drugs. Resistant and complicated cases have been treated with biologics like anti-IL 1 (anakinra), anti IL-6 (tocilizumab), anti TNF α (eternacept) and abatacept. Ciclosporin A, intravenous immunoglobulin have also been used.

Complications of AOSD include reactive hemophagocytic lymphohistiocytosis, disseminated intravascular coagulopathy, alveolar haemorrhage, liver failure, myocarditis and thrombotic thrombocytopenic purpura.

**Conclusion**

AOSD is a rare inflammatory disorder of unknown aetiology. The diagnosis requires high index of suspicion. This case report highlights AOSD as an important differential diagnosis of inflammatory polyarthritis.

**References**


Diffuse idiopathic skeletal hyperostosis: case report and literature review

Genga EK¹, Nalawade A², Oyoo GO¹

Abstract

Background: Diffuse Idiopathic Skeletal Hyperostosis (DISH) is a common disorder of unknown aetiology that is characterized by back pain and spinal stiffness. Diffuse idiopathic skeletal hyperostosis is a common disease, which is most prevalent in persons over 50 years of age. Several metabolic derangements and concomitant diseases associated with DISH include obesity, increased waist circumference, hypertension, dyslipidaemia, diabetes mellitus, hyperuricemia, metabolic syndrome and an increased risk for cardiovascular diseases. There is paucity of literature on case reports and prevalence studies in Africa especially with the increase of metabolic diseases. The condition is identified radiographically by the presence of “flowing” ossification along the anterolateral margins of at least four contiguous vertebrae and the absence of changes of spondyloarthropathy or degenerative spondylosis. However, DISH is not limited to the spine it may affect multiple peripheral sites independently. Extra-spinal entheseal ossifications are common and observing their isolated presence may lead to the diagnosis of DISH. Treatment should be aimed at symptomatic relief of pain and stiffness, and measures such as analgesics, NSAIDs, local applications and physiotherapy, might also prove to be useful in patients with DISH. Large-scale controlled studies are needed in order to delineate the entire spectrum of this condition. The role played by the metabolic and constitutional derangements as well as its impact on the diagnosis and treatment of DISH awaits further studies. In order to raise awareness of DISH this article tackles various aspects of DISH from symptomatology, pathophysiology to its management

Case presentation: A 55 year old obese man presented with a 12 month history of lower back pain. The pain was worse in the morning and associated with progressively worsening early morning stiffness. He had noted neck stiffness with forward stooping and some mild odynophagia to solid foods. He had no history of peripheral joint involvement, fevers, cough, bowel dysfunction or psoriasis. On examination he was noted to be obese with restricted movement both active and passive throughout the spine more marked in the neck and lower back. X-rays of the spine showed flowing mantles of ossification in the anterior longitudinal ligament extending from C2 to C6 and L1 to L4 vertebrae consistent with diagnosis of DISH.

Key words: DISH, Enthesopathy, Calcification, Metabolic syndrome

Introduction

Diffuse Idiopathic Skeletal Hyperostosis (DISH) is a skeletal disease characterized by the ligamentous ossification of the anterolateral spine. Forestier and Rotes-Querol¹ first described it more than 50 years ago as a disorder characterized by spinal stiffness, osteophytosis, and “flowing” new-bone formation about the thoracic spine. They termed it “senile ankylosing hyperostosis” and distinguished it from ankylosing spondylitis. Resnick et al² later termed this condition Diffuse Idiopathic Skeletal Hyperostosis (DISH). For diagnosis he used three strict radiographic features of the spine:

(i) Flowing calcification and ossification within the anterior longitudinal ligament involving at least four contiguous vertebral bodies, most commonly the thoracic spine

(ii) A minimal degree of degenerative disc disease

(iii) Absence of apophyseal joint ankylosis and sacroiliac erosions, sclerosis, or intra-articular osseous fusion.

Pathological entities that can be confused with DISH are osteophytes accompanying degenerative disease of the cervical spine, and ankylosing spondylitis.
Case presentation

A 55 year old obese man presented with a 12 month history of lower back pain. The pain was worse in the morning and associated with progressively worsening early morning stiffness. It radiated to the hips and upper back up to the neck and relieved by activity. He had noted neck stiffness with forward stooping and some mild odynophagia to solid foods. He had intermittent paraesthesias of the lower limbs with normal muscle power and normal sphincter function. He had no history of peripheral joint involvement, fevers, cough, bowel dysfunction or psoriasis. On examination he was noted to be obese with kyphosis and forward stooping of the neck. He had restricted movement both active and passive throughout the spine more marked in the neck and lower back. Laboratory work up revealed normal haemogram, ESR, CRP, urea, electrolytes, uric acid levels and calcium levels. X-rays of the spine showed flowing mantles of ossification in the anterior longitudinal ligament extending from C2 to C6 and L1 to L4 vertebrae consistent with diagnosis of DISH.

Figure 1: Lumbar radiograph of the case

Discussion

Diffuse idiopathic skeletal hyperostosis is most prevalent in persons over 50 years of age. The prevalence has been reported to be as high as 15% in women and 25% in men over the age 50 years and 26% in women and 28% in men over 80 years. Boachie-Adjei et al. reported that 28% of the spines of subjects with an average age of 65 years had evidence of DISH. Mata et al. reported a frequency of 2.5% to 10% in persons over age 70 years, with a slight male predominance. There is paucity of literature on case reports and prevalence studies in Africa. One study done in South Africa on black Africans prevalence of DISH was 3.9% (males 3.8% and females 4.2%). There was a rise in the prevalence of DISH with increasing age from 1% in the 40–49 year age group to 13.6% in those over 70 years. Diabetes was the most commonly associated risk factor at 52.4% in the 21 patients with DISH. Our patient was male and was 55 years which is in keeping with literature.

The aetiology of the condition remains unknown. It’s postulated that genetic, metabolic, endocrinology, anatomic, environmental, and toxic factors play a possible pathogenetic role in the new bone growth characterizing it. Metabolic disorders such as obesity, hyperlipidaemia, diabetes mellitus, and hypertension are frequent in patients with DISH. Our patient was obese. We have planned to do the above tests to rule out the above comorbidities to complete the evaluation of the patient.

DISH typically presents as a middle-aged or older patient with chronic mild pain in the middle to lower back associated with spinal stiffness that is worse in the morning or evening and the typical radiographic changes in the spine. The axial manifestations of DISH are the most frequent characteristic. Thoracic vertebrae are involved in almost 100% of affected individuals, lumbar vertebrae in 68-90% of these persons, and cervical vertebrae in 65-78% of affected individuals. Dysphagia secondary to large cervical osteophytes is an occasional complication of DISH. Interestingly, majority of the patients are asymptomatic, and DISH is an incidentally finding. The clinical findings are milder in comparison to the dramatic radiographic findings. Possible reasons for the minimal pain experienced by some patients is as a consequence of the relative stabilization of spinal segments through ankylosis. Our patient had a long history of the back pain and actually only reported to us when the back pain worsened and had developed the odynophagia.

Patients with DISH are at high risk for fracture and instability from even minor trauma. The increased incidence of fracture instability in DISH patients is due to ankylosis of the vertebral segments proximal and distal to the fracture, which creates increased lever arms that can cause displacement of the spine even in low-energy injuries. This may explain the delay in diagnosis and a high rate of immediate and delayed neurologic consequences. Hyperextension injuries are frequent, involving either disk disruption or fracture through the middle of a vertebral body. Patients with DISH, neck pain, and a history of trauma must be evaluated for occult fracture with Computed Tomography (CT) or Magnetic Resonance Imaging (MRI). The management plan of this patient should include education, fracture prevention and danger signs to look out when suspecting fracture. Treatment of fractures is similar to that of patients with other ankylosing conditions. The physician must consider the additional instability caused by poor ligament integrity and increased lever arms. It is important to note that the degree of instability is likely to be underrepresented on radiographs. Cervical traction may result in excessive
distraction due to the lack of ligamentous structures and should be used cautiously. The use of open reduction and internal fixation is recommended to prevent progression and delayed neurologic compromise.

Common extra-spinal manifestations include tendinitis and enthesophytes (osseous outgrowths at the sites of attachment of tendon, ligament, or capsule to bone). Many joints can be affected, and some patients have diffuse, vague aching similar to that of polymyalgia rheumatica². Subtle periostitis at the site of ligament or tendon insertion is often seen.

Diagnosis

A careful history delineating the nature and location of back pain is necessary. Back pain that is severe or acute in onset is unlikely to be related solely to DISH. The presence of extra-spinal musculoskeletal symptoms should be sought. There are no diagnostic laboratory findings, but evaluation may exclude other potential diagnoses (Table 1)². The erythrocyte sedimentation rate and C-reactive protein, rheumatoid factor, and antinuclear antibody levels are typically normal. If DISH is suspected in an adult, the thoracic spine should be evaluated radiographically to establish the diagnosis (Table 2). Chest radiographs are adequate as screening tests for DISH¹³. The lumbar spine is usually evaluated radiographically, as also the sacroiliac joints on these films can be helpful in ruling out other entities, such as seronegative spondyloarthopathies. Other sites of pain should be imaged with plain radiography, especially the heel, elbow, sacroiliac joints, and cervical spine. In non-traumatic situations, bone scans are not often helpful and can falsely give the appearance of multiple periarticular metastases.

<table>
<thead>
<tr>
<th>Table 1: Differential diagnosis of back pain and spondylophytosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISH</td>
</tr>
<tr>
<td>Spondylosis deformans</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
</tr>
<tr>
<td>Acromegaly</td>
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<tr>
<td>Hypoparathyroidism</td>
</tr>
<tr>
<td>Fluorosis</td>
</tr>
<tr>
<td>Ochronosis</td>
</tr>
<tr>
<td>Charcot spine</td>
</tr>
<tr>
<td>Sternocostoclavicular hyperostosis</td>
</tr>
<tr>
<td>Intervertebral osteochondrosis</td>
</tr>
<tr>
<td>Spondylitic variants (e.g., psoriasis, Reiter’s syndrome, inflammatory bowel disease, Whipple’s disease)</td>
</tr>
<tr>
<td>Pachydermoperiostosis</td>
</tr>
<tr>
<td>Pseudogout</td>
</tr>
<tr>
<td>X-linked hypophosphatemic</td>
</tr>
<tr>
<td>Osteomalacia</td>
</tr>
</tbody>
</table>

Table 2: Diagnostic criteria for DISH

1. Flowing ossification along the anterolateral aspect of at least four contiguous vertebrae
2. Preservation of disk height in the involved vertebral segment; the relative absence of significant degenerative changes, such as marginal sclerosis in vertebral bodies or vacuum phenomenon
3. Absence of facet-joint ankylosis; absence of sacroiliac erosion, sclerosis, or intra-articular osseous fusion

Therapeutic considerations

The pathogenesis of the disease is not clear, and therefore the current therapeutic interventions are empirical. Aim of treatment is symptomatic relief of pain and stiffness. For patients with isolated back pain or enthesopathies treatment options include activity modification, physical therapy, corset or brace wear, nonsteroidal anti-inflammatory medications, and bisphosphonate therapy are the mainstays of treatment. The literature on efficacy of these modalities has not been well established. Control of associated metabolic disorders, including obesity, hypertension, hyperinsulinaemia (with or without hyperglycaemia), dyslipidaemia, hypertriglyceridaemia and hyperuricemia, may reduce the morbidities associated with these disorders¹⁴, ¹⁵. These may retard future cardiovascular disease and possibly slow down the progression of soft tissue ossification. Therapeutic interventions are aimed at a reduction of insulin secretion and insulin resistance. In patients with non-insulin-dependent diabetes, the use of biguanides, which induce a better usage of insulin, may offer an advantage over the use of sulphonylureas that increase insulin secretion¹⁴-¹⁶. Coexisting hypertension the choice of drugs that might improve insulin resistance such as angiotensin-converting enzyme inhibitors, calcium channel blockers and beta-blockers should be preferred over drugs that might worsen insulin resistance, such as thiazide diuretics¹⁴, ¹⁵. Generally, surgery is not indicated for DISH in the absence of some other diagnosis, such as fracture, stenosis, tumour, infection, or painful deformity. Fortunately, debilitating pain is rare in the absence of neurologic or visceral impingement, probably because bony ankylosis prevents painful motion.

Conclusions

Diffuse idiopathic skeletal hyperostosis is a very common, often occult bone-forming diathesis with many musculoskeletal manifestations. Data from Africa is rare. There has been an increase in metabolic disorders associated with DISH. We hope this article will raise the awareness of this disease. A diagnosis of DISH should be suspected in adult patients who present with back
pain and spinal stiffness especially in the background of metabolic disease. The diagnosis is based on the presence of flowing ossification along the anterolateral aspects of at least four vertebrae, typically in the thoracic spine. Radiographic evaluation of the thoracic spine must be performed, even if pain is localized to the lumbar or cervical areas. All other areas of musculoskeletal pain should be evaluated radiographically, looking for hyperostosis or enthesopathy. Awareness of the disorder and a high index of suspicion can add a great deal to the clinical acumen of practitioners in rheumatology and orthopaedic subspecialty. Treatment should be aimed at symptomatic relief of pain and stiffness, and measures such as analgesics, NSAIDs, local applications and physiotherapy, might also prove to be useful in patients with DISH. Large-scale controlled studies are needed in order to delineate the entire spectrum of this condition.

The highlights of the study are as follows:
(i) DISH is a common disease, but is under reported in our local set up. Doctors need to have a high index of suspicion
(ii) Musculoskeletal manifestations of DISH are not limited to the spine and often affect peripheral sites
(iii) DISH is often associated with metabolic and constitutional derangements, leading to an increased cardiovascular risk
(iv) Prevention of sequelae in DISH is paramount
(v) Management is multi-disciplinary comprising of rheumatologists, surgeons and physiotherapists.

References

Arthritis mutilans due to chronic tophaceous gout

Akintayo RO¹, Opeyemi MC²

Abstract

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.

Case presentation: A 69-year old man presented with a fifteen-year history of recurrent inflammatory joint pains. Over the years, there has been progressive involvement of more joints until most joints of the upper and lower limbs are symmetrically involved. Examination revealed severe deformities of the hands and feet with gross mutilation of most digits. Several tophi are 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 may cause arthritis mutilans. This is however rare and is more likely in a patient with long-standing untreated tophaceous gout.

Keywords: Arthritis mutilans, Gout, tophi, Crystals

Introduction

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 but not gout¹⁻². Gout is a crystal arthropathy which tends to affect the first metatarsophalangeal joint very often and, if untreated, may proceed to involve multiple joints, sometimes bilaterally symmetrically and lead to destructive arthropathy¹. A definitive diagnosis of gout is made by demonstrating urate crystals in joint fluid or tophi by polarized light microscopy. We report the case of a 69-year old man with chronic tophaceous gout presenting with arthritis mutilans of the hands and feet.

Case presentation

A 69-year old man presented with a fifteen-year history of recurrent inflammatory joint pains. Symptoms started in the first metatarsophalangeal joint of the right foot and progressively involved more joints with recurrent attacks over the years until most joints of both hands and feet have been involved. A typical attack starts at night preventing him from sleeping and often associated with early morning joint stiffness lasting more than an hour. He has not identified any aggravating factors but usually gets relieved by using various non-steroidal anti-inflammatory drugs. He has no history of skin rashes and there is no family history of psoriasis. There is no history of back pain, diarrhea or urinary symptoms. There is no history of painful redness of the eyes. He also started noticing multiple subcutaneous swellings around the joints about two years prior to presentation. He was diagnosed hypertensive two years earlier and had been on lisinopril, moduretic and low dose aspirin. He drank various alcoholic beverages at an average of 120g weekly for twenty years but stopped about four years prior to presentation. 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 (Figures 1 and 2). Radiographs showed several punched out erosions with overhanging edges, osteolysis, subluxations and severe disorganization of the joints (Figures 3 and 4). There is also profound osteopenia of the phalanges, metacarpals and metatarsals (Figure 5).
A diagnosis of gout was established with the finding of numerous crystals of urate on polarized microscopy of aspirated tophi. Rheumatoid factor and anti-cyclic citrullinated antibody were negative. C-reactive protein was 122.0 mg/L (reference: up to 7.5mg/L), serum uric acid was 510µmol/L (reference: up to 420µmol/L). Electrolytes, urea and creatinine as well as urinalysis were normal. Fasting lipid profile was also normal. Chest radiograph showed cardiomegaly with a cardio-thoracic ratio of 0.62. There was also a prominent aortic knuckle. Electrocardiogram showed left ventricular hypertrophy while echo revealed moderate diastolic dysfunction in addition to concentric hypertrophy of the left ventricle.

Discussion

Gout is known to be more common among people of African descent than Caucasians living in developed countries\(^4,5\). There is no data on the community prevalence of gout in sub-Saharan Africa. However hospital clinic based studies from throughout the subcontinent have increasingly identified gout as a leading cause of inflammatory arthritis\(^6-8\). While it is possible that the overall incidence of gout in Africa is lower than in the western hemisphere, many true cases of gout in Africa may be undiagnosed. This may, in part, explain why gout has not been identified as a major health challenge in Africa. Our patient had been suffering from gout for more than 10 years before the diagnosis was made. He had seen different primary care physicians over the years but the low clinical consciousness for gout in Africa prevented the suspicion in this case.

A widely agreed definition of arthritis mutilans has not been established\(^9\). However, going by the modified Steinbrocker method of grading radiographic damage, our case can be classified as arthritis mutilans on account of the presence of more than 5 joints with grade 4 radiographic damage\(^10\). Also, by the broad consensus of the Group for Research and Assessment of Psoriasis
and Psoriatic Arthritis (GRAPPA), our case qualifies as arthritis mutilans. Among the features agreed upon are erosion involving entire articular surfaces on both sides of the joint and the involvement of interphalangeal, metacarpophalangeal and metatarsophalangeal joints. A 2015 review of the clinical and radiological criteria for psoriatic arthritis mutilans conducted at the University of Toronto Psoriatic Arthritis Clinic listed the important radiologic findings as bone resorption, pencil-in-cup change, total joint erosions, ankylosis, and subluxation. Of these, only the pencil-in-cup deformity which is classically associated with psoriatic arthritis was not present in our patient. The retraction of unsupported soft tissue unto the proximal bones following osteolysis of the distal phalanges is commonly described as digital telescoping or doigt en lorgnette deformity. This often complicates arthritis mutilans. In our patient, the soft tissues of the toes did not collapse proximally despite the complete osteolysis of most digital phalanges. This is because of extensive deposition of tophi on the toes providing some rigidity for the distal soft tissues.

Since arthritis mutilans is more often associated with psoriatic arthritis or rheumatoid arthritis, features of these two conditions were specifically sought for in our patient. He had no previous or current rashes suspicious of psoriasis and he had no family history of psoriasis. There were no features of dactilitis and serology for rheumatoid factor and anti-cyclic citrullinated peptide antibody were negative. Radiographs of the knees showed advanced secondary osteoarthritis. Due to the scarcity of rheumatologists in sub-Saharan Africa, many burnt-out inflammatory arthritides may be confused for primary degenerative osteoarthritis. Consequently, other smoldering comobidities of the primary arthropathy may be under-recognised. Our patient also had dyslipidaemia and hypertensive heart disease. Other known comobidities of gout include chronic kidney disease, obesity, insulin resistance and cardiovascular disease.

Among the various types of alcoholic beverages, beer is associated with a particularly important risk of gout. In addition to the significant history of beer ingestion, our patient was a male of black African descent who had been on a thiazide diuretic and low dose aspirin for his hypertension. All these constitute risks for gout and in the absence of appropriate treatment over a long time, a severe destructive arthropathy resulted.

Aggressive urate lowering treatment is important in a patient with arthritis mutilans due to chronic tophaceous gout. For this reason, a recombinant uric oxidase like pegloticase may be important. Pegloticase can cause a more rapid reduction in serum urate and tophi mass than older urate lowering agents. Other emerging urate-lowering therapies include lesinurad, arhalofenate, ulodesine, and levotofisopam. However, an established arthritis mutilans may be amenable only to surgery. Unfortunately, the tendency for severe and widespread joint involvement in arthritis mutilans due to gout may limit the acceptability of surgery to the patients.

Conclusion
Arthritis mutilans is a highly disabling type of arthritis which may be caused rarely by gout. This is more likely in poorly managed chronic tophaceous gout in which multiple other comobidities may be present.

References
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