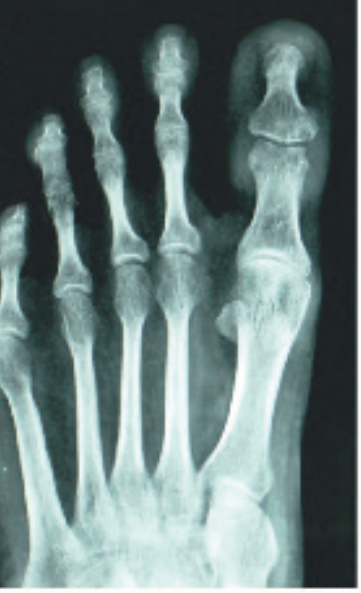

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CONTENTS

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Opportunities for advancement of African rheumatology and rheumatic musculoskeletal diseases on the African continent

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Rheumatology is a young subspeciality on the African continent[1,2]. Rheumatic Musculoskeletal Diseases (RMDs) in children and adults are increasingly presenting themselves at primary care institutions and general hospitals and optimal care by general physicians is scarce. The overwhelming issue is that of late diagnosis of debilitating diseases such as Juvenile Idiopathic Arthritis (JIA), Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE) and osteoporosis, to name a few. The resurgence of activity in the African League Against Rheumatism (AFLAR) provides a unique opportunity to evaluate the prevalence and burden of RMDs across the continent[3]. There is strong evidence that RMDs are on the increase across Africa and the need for specialised care is becoming increasingly important. However, the number of specialist rheumatologists per 100,000 population is in the region of 1:1.5m in some countries, way below the ratios in developed countries. Many regions do not have any rheumatological services whatsoever.

Since AFLAR is an affiliate of the International League of Associations for Rheumatology (ILAR), it seems reasonable to pursue similar aims and objectives as our sister leagues within that organisation, such as the American College of Rheumatology (ACR) and EULAR (the European League). We need to develop collaborative actions involving players from as many countries as possible within Africa, with the aim of standardising and optimising education, service delivery and research in RMDs across the continent. The time has come for us to combine resources, promote centres of excellence in rheumatology and create an environment on the continent which is conducive to promoting health care for patients with RMDs across Africa[4]. We need to canvass governments to understand that the burden of untreated RMDs is equivalent to that of patients with triple-vessel coronary artery disease. Total joint replacements for secondary OA are expensive and require special surgical skills. Effective treatment of RA early will reduce the need for such operations. When the burden of infectious diseases is controlled by improved socio-economic developments, RMDs will become one of the dominant diseases draining the health budget globally and in Africa.

It is incumbent on the executive committee of AFLAR to develop strong sub-committees and other structures to promote our image across the world, not only in Africa. Important strides have been made over the last few years with the participation of AFLAR at the ACR annual meetings. We have established links with the ACR which allow us access to teaching materials and other resources used in the Northern hemisphere, and we should take full advantage of these opportunities. AFLAR has also been interacting with EULAR. In the last year we have had several lectures from prominent members of the EULAR team, and these have been well attended and were highly interactive. We had our AFLAR Congress in Mauritius in 2019 and are looking forward to our next meeting in Kenya, very soon. Our new website can be visited at *www.aflar.org.za.*

The COVID-19 pandemic has clearly had a major impact globally and many of us have had to change the way in which we practice medicine. AFLAR conducted a survey of its members to evaluate the impact of COVID-19 among rheumatologists in Africa and the results of the survey have been published[5]. This could only have been achieved by the collaboration

and broad participation of rheumatologists from the different countries in Africa[6]. As with Chikungunya and Human Immunodeficiency Virus (HIV) infection, there is a possibility of chronic musculoskeletal symptoms and the initiation of Auto-immune Rheumatic Diseases (ARDs) following COVID-19. There is a wealth of research that Africa could contribute to this area and much of this would not require sophisticated diagnostic tools.

Another area where we could make an impact globally is in HIV-associated RMDs. Several reports from across Africa have shown the relationship between HIV and spondyloarthritis (SpA), as well as the reduction in cases with the advent of Anti-Retroviral Therapy (ART) rollout by governments across the continent [7,8]. In addition, the COVID-19 pandemic has been a stimulus for general collaboration between AFLAR member countries[3]. A collaborative research effort in AFLAR has resulted in a publication on consensus evidence-based development of guidelines for management of osteoporosis in Africa[9]. The editor of *Clinical Rheumatology*, the Journal of ILAR, devoted a special issue on rheumatology in Africa in 2021[10]. This could potentially give impetus to the collaborative research and discussions by rheumatologist across our so-called "dark" continent.

The development of disease registries would go a long way towards understanding the impact of debilitating conditions like RA, SLE, Systemic Sclerosis (SSc) and Osteo Arthritis (OA) across the African continent, to name a few[11]. Such registries would enable us to assess the effect of poverty, level of education, socio-economic status, early diagnosis, access to effective medications as well as general lifestyle and other relationships to RMDs on the continent. We may well identify huge differences from other patient groups in other continents. There is also the possibility that genetic factors may differ from other parts of the globe, resulting in more severe disease[12,13].

The education committee could look at developing an undergraduate and post graduate curriculum, evaluating and establishing centres of excellence for rheumatology training and research and disseminating service resources to rural environments. Service delivery could be enhanced by establishing mobile clinics furnished with facilities for extracting and collecting blood samples, basic injections for soft-tissue and joint conditions, and screening for co-morbidities like hypertension, hypercholesterolaemia and diabetes.

The research and scientific committee of AFLAR would have a key role in developing projects and evaluating proposals for research in a manner that will achieve some of the above objectives. The team would need to keep abreast of current developments in rheumatology and identify areas where we might make an impact globally. Randomised Controlled Trials (RCTs) of newer biologic agents are rarely carried out on the African continent due to infra structural limitations. However, this may be the only means whereby needy patients can be offered these expensive therapies, especially in Low- and Middle-Income Communities (LMICs). Such a committee could also liaise with government departments such as health and social services to improve access for our patients to social grants, public places, clinics, expensive medications, and hospital care.

The paediatric committee of AFLAR (PAFLAR) was officially ordained in 2019 and has developed in leaps and bounds. There are regular monthly seminars, which are very well attended and rotate across the different countries. Several successful meetings were hosted last year. The committee successfully conducted a virtual congress of Paediatric Rheumatology in 2021, and the abstracts have been published in *Rheumatology* (Oxford)[14].

While previous editorials have emphasised the challenges that rheumatologist face in Africa[1,2], there is also the potential to exploit several opportunities. These can be discussed and evaluated by a "think-tank" of the AFLAR leadership and presented to the various committees. AFLAR has its own Journal of Rheumatology and publishes predominantly on research from Africa [4]. The journal needs support and is dependent on researchers in Africa and elsewhere to publish their findings in this journal. In this regard, the editorial, education, and scientific committees within AFLAR could combine efforts to improve the standard of the journal and increase the impact factor.

The time has come for us to join forces in the promotion of optimal care for our patients with RMDs in Africa. We need to set aside our language differences, forget our political alliances, shake off our obsession with cultural differences, dissipate our artificial borders, and strive towards the common purpose of enhancing and developing the speciality of rheumatology across Africa, where many patients go undetected and suffer enormous consequent disabilities. North, South, Central, East and West Africa need to become a United Force of Rheumatology (UFR).

Very little can be achieved by an organisation like AFLAR without the necessary financial resources. We need to urgently develop a strategy to raise funds by using advertising space, government support, pharmaceutical support, membership fees, philanthropic donations, web-based meetings,

congresses, and other income-generating activities. Through such activities we could establish a reserve of funds which could be utilised towards making some of our dreams a reality. Our sister leagues such as ACR and EULAR had similar humble beginnings but have grown into giants of rheumatology over the years. There is no reason why AFLAR should not aspire and strive towards similar goals in our development strategy. Unity is Strength.

References

1. McGill PE, Njobvu PD. Rheumatology in sub-Saharan Africa. *Clin Rheumatol.* 2001; **20**: 163-167.
2. Mody G. Rheumatology in Africa: challenges and opportunities. *Arthritis Res Therapy.* March 2017; **19**:49-52.
3. Akintayo R, Kalla A, Adebajo A. COVID-19 and African rheumatology: progress in adversity. *Lancet Rheumatol.* 2020; 30347-357.
4. Genga EK, Oyoo O, Espinoza LR, Adebajo A. Enhancing the visibility of rheumatology in Africa. *Clin Rheumatol.* 2017; **36**: 20167-68.
5. Akintayo RO, Akpabio A, Kalla A, *et al*. COVID-19 and the practice of rheumatology in Africa: big changes to services from the shockwave of a pandemic. *Ann Rheum Dis.* Published online first: 01 July 2020. Doi: 10.1136/annrheumdis-2020-218273.
6. Akintayo RO, Bahiri R, El Miedany Y, *et al*. African League Against Rheumatism (AFLAR) preliminary recommendations on the management of rheumatic diseases during COVID-19 pandemic. *Clin Rheumatol*. 2021; **40**: 3445-54.
7. Njobvu P, McGill P. Human immunodeficiency virus related reactive arthritis in Zambia. *J Rheumatol.* 2005; **32**:7.
8. Mody GM, Parke FA, Revielle D. Articular manifestations of human immunodeficiency virus. *Best Pract Res Clin Rheumatol*. 2003; **17**: 265-287.
9. El Miedany Y, Paruk F, Kalla A, *et al.* Consensus evidence-based clinical practice guidelines for the diagnosis and Treat-to-Target management of osteoporosis in Africa: An initiative by the African Society of Bone Health and Metabolic Bone Diseases. *Archives Osteoporosis*. 2021; **16**: 176.
10. Adebajo A, Kalla A, Tikly M. Editorial – Rheumatology in Africa. *Clin Rheumatol.* 2021; **40**: 3391.
11. Hodkinson B, Mapiye D, Jayne D, *et al.* The African Lupus Genetics Network (ALUGEN) registry: standardised, prospective follow-up studies in African patients with systemic lupus erythematosus. *Lupus.* 2016; **25:** 325-330.
12. Blazer A, Dey ID, Nwaukoni J, *et al.* Apolipoprotein L1 risk genotypes in Ghanaian patients with systemic lupus erythematosus: a prospective cohort study. *Lupus Sci Med.* 2021; 8:e000460. doi:10.1136/ lupus-2020-000460.
13. May A, Hazelhurst S, Li Y. *et al.* Genetic diversity in black South Africans from Soweto. *BMC Genomics.* 2013; **14**: 644. *https://doi.org/10.1186/1471-2164-14-644.*
14. First PAFLAR congress abstracts 2021. *Rheumatology* (Oxford). 2021; **60**: Issue Supplement_5.

Rheumatic disease and malignancy

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Abstract

Background: A number of rheumatic disorders are associated with an increased risk for various malignancies. The reasons for this risk are not well defined. Furthermore, pharmacologic therapy of rheumatic diseases may increase the risk of malignant disease.
Objective: The aim of this literature review is to address the various rheumatic diseases and their pharmacologic therapy that are associated with an increased risk of malignancy.
Data source: The literature review uses medical science based literature published locally and internationally on the risk of malignancy in patients with rheumatological diseases and the use of antirheumatic medications.
Conclusion: Individual rheumatic diseases are associated with increased risk of particular malignancies. A number of the pharmacologic therapies used for the treatment of rheumatic diseases may increase the risk of malignancy. In these patients who are at risk for cancer related to their autoimmune disease, age- and sex-appropriate screening should be performed, and additional screening may be added based upon the risk factors of an individual patient.

Key words: Rheumatic diseases, Cancer, Antirheumatic medication, Malignancy, Screening

Introduction

There are complex bi-directional relationships between rheumatic diseases and cancer. Certain rheumatic diseases like inflammatory myositis, systemic lupus erythematosus and Sjogren's syndrome are associated with an increased risk of malignancy. In addition, treatments for rheumatic diseases may also increase malignancy risk[1]. Specific rheumatic diseases and risk of malignancies; and the contribution of antirheumatic drug therapies to such risk will be reviewed in this article.

Rheumatic diseases with associated malignant disorders

The rheumatic diseases associated with an increased risk for various malignancies include rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis (scleroderma), myositis (polymyositis, dermatomyositis), Sjögren's syndrome, and ANCA-associated vasculitis. The reasons for this increased risk is not well defined, but likely to involve chronic inflammation and autoimmunity[2].

Dermatomyositis and polymyositis

Dermatomyositis is associated with a 6-fold increased risk of malignancy while polymyositis is associated with a 2 fold increased risk of malignancy[3]. Patients with anti–TIF1-γ and anti–nuclear matrix protein–2 have the highest risk. The risk is highest in the first 2 years after diagnosis, gradually decreasing with time[4]. Numerous cancers have been associated with dermatomyositis, particularly breast, ovarian, lung, haematologic and nasopharyngeal cancers especially in Asian population[5]. Clinical features of dermatomyositis that increase the risk of malignancy include male sex, older age, severe skin manifestations, dysphagia, resistance to treatment, history of prior malignancy and absence of interstitial lung disease[6].

Rheumatoid arthritis

The initial link between RA and cancer was established by Isomaki *et al*[7]. He established that patients with RA had a higher incidence of lymphomas, leukemias and myeloma. Numerous other studies and meta-analyses have also shown an increased incidence in lung cancer but a reduced incidence of breast and colon cancer in patients with RA. The standardized incidence ratio of all malignancy risk, lymphoma, lung cancer, breast cancer and colon cancer was 1.09, 2.46, 1.64, 0.86 and 0.78 respectively[8].

The increase in risk for cancers can be attributed to shared risk factors between RA and cancer. For example smoking increases the risk of both RA and lung cancer[9]. RA, in itself can lead to increased risk of lymphoma because of increased chronic immune stimulation in lymphomagenesis[10]. The observation of a reduced risk of colon cancer may be due to the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in RA. It is known that NSAID use is associated with reduced risk of colon cancer[11].

Systemic Lupus Erythematosus (SLE)

There is increasing evidence to suggest that patients with SLE have a slightly higher overall risk of malignancy. A large multisite cohort study by Bernatsky *et al*[12] reported an SIR of 1.14. Patients with SLE are at a moderately increased risk of haematologic malignancies, particularly non-Hodgkin's lymphoma with an SIR of 3.02[12]. Furthermore, these patients presented with advanced stages and extra nodal disease and had poor outcomes despite aggressive treatment. Several individual cohort studies that were reviewed by Choi *et al*[13] have reported increased risk of lung, liver, head and neck, thyroid, vaginal/vulvar, cervical (cancerous and pre-cancerous), dermatologic, bladder or renal, anal, and pancreatic malignancies in patients with SLE.

The factors that potentially mediate or are thought to increase the risk of malignancy in SLE include use of cyclophosphamide[14], autoantibodies such as antiphospholipid antibodies[15] and chronic immune dysregulation[16]. There is a possibility that the increased prevalence of certain cancers in patients with SLE may be due to increased exposure to known environmental risk factors such as smoking and oncogenic viruses[13].

Sjogren's Syndrome (SS)

Monoclonal gammopathies occur in at least 20% of patients with Sjogren's syndrome[17]. It is usually associated with hypergammaglobulinemia, cryoglobulinemia, or haematologic neoplasia. SS patients with monoclonal gammopathies have an increased incidence of lymphoma[18]. In addition, the risk of multiple myeloma and Waldenstrom macroglobulinemia is also increased[19].

Patients with SS have the highest risk of non-Hodgkin's lymphoma amongst all other rheumatologic diseases. In a pooled analysis, the relative overall risk of NHL was 6.6[20], with a life time risk that is 44 times higher than that of the normal population[21]. Persistent salivary gland enlargement is the most important clinical risk factor, while other risk factors includes cutaneous vasculitis, lymphadenopathy, splenomegaly, cryoglobulinemia, and glomerulonephritis. The transition from SS to lymphoma is a process that requires many years[22].

Extra nodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) involving the parotid gland is the most common histologic subtype in SS[20]. Other types of NHL that are common in SS include diffuse large B cell lymphoma and nodal marginal zone lymphoma[23]. The MALT lymphoma is of low grade and indolent with a 15 year survival to 80%[24]. SS patients with persistent salivary gland enlargement should be investigated for lymphoma.

Systemic sclerosis (scleroderma)

Several reports have shown an increased risk of cancer in patients with scleroderma[25,26]. In a nationwide population-based cohort analysis from Denmark, the most frequent cancers were lung, haematologic, esophageal and oropharyngeal carcinoma[27]. The cause of cancer in SSc is not well understood, however it has been observed that patients with autoantibodies to RNA polymerase I/III are at a higher risk of developing cancer[28].

Systemic vasculitis

The malignancies associated with systemic vasculitis include hairy cell leukemia and myelodysplastic syndrome. About 40% of the patients with systemic vasculitis have concurrent malignancy. Antineutrophil Cytoplasmic Antibody (ANCA)-associated vasculitis carries a 1.6 to 2.0 higher risk for developing malignancy[29].

Polymyalgia rheumatica / giant cell arteritis

There is an increased risk of malignancy particularly in the first 6 – 12 months after diagnosis[30]. In some cases, polymyalgia rheumatica may be the initial manifestation of malignancy[31].

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE)

RS3PE usually occurs in adults and presents with edema of the hand and feet along with synovitis. About 15% – 30% of patients with RS3PE have concurrent malignancy ranging from haematologic to solid malignancies[32].

Paraneoplastic polyarthritis

Symmetric polyarthritis mimicking rheumatoid arthritis can occur as a paraneoplastic phenomenon. Paraneoplastic polyarthritis is more common in male, has an asymmetric onset and associated with high markers of inflammation distinguishing it from RA. It is mostly seen in patients with myelodysplastic syndrome[33].

Palmar fasciitis

This is a rare disorder that is associated with numerous malignancies. The most frequently reported is ovarian cancer but other sites have also been reported. Treatment of the associated malignancy has led to improvement of some cases[34].

Eosinophilic fasciitis

This is an uncommon condition characterized by woody induration of the limbs with peripheral eosinophilia. In 10% of the patient there is usually an underlying haematologic disorders like lymphoma and leukemias[35].

Erythromelalgia

This is a rare syndrome that is associated with myeloproliferative disorders like polycythemia rubra vera in 10% of the patients[36].

Hypertrophic osteoarthropathy

Hypertrophic osteoarthropathy is usually associated with lung cancer[37]. About a third of the patients with lung neoplasm have digital clubbing. It is most frequently associated with peripherally located adenocarcinoma of the lung and more common among men[38]. Treatment of the lung cancer may lead to regression. Bone scintigraphy is a sensitive way to detect skeletal involvement with the disorder. Particular attention to the chest should be paid to a patient presenting with hypertrophic osteoarthropathy as the most common cause of acute hypertrophic osteoarthropathy is a lung neoplasm.

Antirheumatic medication and risk of malignancy

Cyclophosphamide

Cyclophosphamide increases the risk of leukemia, skin cancer and urinary bladder cancer. This is due to direct chromosomal damage and decreased immune surveillance. The most important risk factor is the duration of the treatment, with most cancers occurring in patients treated for more than two years[39]. A long term follow up population-based cohort study found that patients treated with cyclophosphamide had a higher rate of malignancy. The risk was highest for patients who had a cumulative dose of over 36 grams except for squamous cell carcinoma, where the risk increased even at cumulative dose of 10 grams[40]. In patients with Granulomatosis with Polyangiitis (GPA), myelodysplastic syndrome occurred in 8% of patients who had prior exposure to cyclophosphamide and this increased to 13% who had a cumulative dose of more than 100 grams[41].

The risk of bladder cancer is increased with oral cyclophosphamide and likely dose dependent with a standardized incidence ratio of 4.30[40]. The increased risk may be sustained for years even after discontinuation of cyclophosphamide. In a retrospective study of 145 patients with GPA who had been treated with oral cyclophosphamide for at least one year, there was a 5% incidence of bladder cancer at eight years of follow up. This incidence increased to 16% at 15 years of follow up. Two thirds of the patients who developed bladder cancer had had a cumulative dose of more than 50g and had at least one episode of either microscopic or macroscopic haematuria[42]. The tumours tend to be biologically aggressive, mostly grade 3 or 4 transitional cell carcinoma[43].

Azathioprine

There is a possible but small increased risk of malignancy in rheumatoid arthritis patients treated with azathioprine. However, this risk was not significant when adjusted for confounding variables. There is an absolute increase of 1 case per 1000 patients years of exposure for lymphoproliferative malignancy after a 20 year follow up[44].

Methotrexate

A large observational cohort found a non-significant small increase of lymphoproliferative malignancy in patients taking low dose methotrexate. The lymphoproliferative malignancy are usually of B cell origin and are associated with latent Epstein Barr virus infection[45]. Another prospective study from France, described 25 cases of lymphoma in patients with RA who had been treated with methotrexate for three years. Among them, were seven cases of Hodgkin's disease with an SIR of 7.4[46]. Some of these tumours may regress on discontinuation of methotrexate and may not require further chemotherapy. However continued vigilance is necessary as relapse can occur[47].

Mycophenolate

There has been one reported case of CNS lymphoma that occurred in a patient taking mycophenolate monotherapy for myasthenia gravis[48]. In addition, MMF prescribing information has a specific warning label about increased risk of lymphoma as a result of immunosuppression and avoiding MMF in patients with prior history of lymphoma.

Tumour necrosis factor alpha inhibitors

In general, there is a preponderance of evidence that TNF inhibitors do not increase the risk of most solid tumours except skin cancers. However, uncertainty remains. Some meta-analysis of clinical data have found an increased risk but observational data, particularly from registries, have not been able to confirm these findings[49,50]. This discrepancy may be due to more complete recording of malignancies in clinical trials than in routine practice.

The overall risk of lymphoma is not increased. However, a small number of hepatosplenic T cell lymphoma cases, a very rare form of non-Hodgkin's lymphoma, has been associated with use of TNF inhibitors. Most of these cases have occurred in young male with inflammatory bowel disease who had also received concurrent thiopurines[51]. However, there is a slightly increased risk of cervical cancer and non-melanoma cancer in patients using TNF inhibitor[52,53]. The combination of cyclophosphamide and TNF inhibitor heightens the risk of cancer, hence combination of these two drugs is not encouraged[54].

Other biologic DMARDS

The other biologic DMARDS have not been studied. Furthermore, these drugs have been marketed recently and registry data are still immature to allow any firm conclusion. In a meta-analysis involving all biologics, there was no overall increase risk of malignancy with any of the biologic DMARD. However, only four studies were included in the meta-analysis[55].

In a long-term safety report of rituximab, which included 3500 patients with RA who had been followed up for 11 years, did not indicate an increased risk of malignancy when compared with the general US population[56]. Similarly, analysis of eight clinical trials revealed no increased risk of malignancy in patients who were given abatacept[57]. However, long term extension trials and combined analysis of tocilizumab suggest that tocilizumab use may be associated with an increased risk of malignancy. Updated data showed an SIR of 1.36 and 1.81 in comparison with SEER database and GLOBOCAN data respectively[58]. On the contrary, a Japanese study reported an SIR of 0.79. This study also reported an SIR of 3.13 for lymphoma with reference to Japanese population[59].

Screening for malignancy in rheumatic disease

There are controversies on how to appropriately screen patients with rheumatological diseases for an underlying cancer. The most important step is ensuring that age- and sex- appropriate cancer screening has been done regardless of the rheumatological disease the patient is suffering from. For certain patients with rheumatological diseases known to be associated with increased risk of cancer like systemic sclerosis or myositis, their cancer screening should be based according to their risk of developing cancer. For example, in myositis, patients with antibodies to nuclear matrix protein 2 and Transcriptional Intermediary Factor 1 (TIF1) gamma are more likely to have cancer within three years of disease onset (60) accurate identification of patients likely to harbor cancers is important. Using immunoprecipitations from radiolabeled cell lysates, several groups recently showed that anti-transcription intermediary factor 1γ (anti-TIF-1γ. Similarly, in SSc, patients with anti-RNA polymerase III or anti-RNPC3 antibodies and diffuse SSc are more likely to have cancer-associated SSc[61].

Conclusion

Individual rheumatic diseases are associated with increased risk of particular malignancies. A number of the pharmacologic therapies used for the treatment of rheumatic diseases may increase the risk of malignancy. In these patients who are at risk for cancer related to their autoimmune disease, age- and sex-appropriate screening should be performed, and additional screening may be added based upon the risk factors of an individual patient.

Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Carsons S. The association of malignancy with rheumatic and connective tissue diseases - PubMed. *Semin Oncol.* 1997; **24**(3):360–372.
2. Egiziano G, Bernatsky S, Shah AA. Cancer and autoimmunity: Harnessing longitudinal cohorts to probe the link. *Best Pract Res Clin Rheumatol.* 2016; **30**(1):53–62.

3. Olazagasti JM, Baez PJ, Wetter DA, Ernste FC. Cancer risk in dermatomyositis: a meta-analysis of cohort studies. *Am J Clin Dermatol.* 2015; **16**(2):89–98.
4. Buchbinder R, Forbes A, Hall S, Dennett X, Giles G. Incidence of malignant disease in biopsy-proven inflammatory myopathy. A population-based cohort study. *Ann Intern Med.* 2001; **134**(12): 1087-95.
5. Wang J, Guo G, Chen G, Wu B, Lu L, Bao L. Meta-analysis of the association of dermatomyositis and polymyositis with cancer. *Br J Dermatol*. 2013; **169**(4):838–847.
6. Lu X, Yang H, Shu X, Chen F, Zhang Y, Zhang S*, et al.* Factors predicting malignancy in patients with polymyositis and dermatomyostis: a systematic review and meta-analysis. *PLoS One*. 2014; **9**(4): e94128.
7. Isomäki HA, Hakulinen T, Joutsenlahti U. Excess risk of lymphomas, leukemia and myeloma in patients with rheumatoid arthritis. *J Chronic Dis.* 1978; **31**(11):691–696.
8. Simon TA, Thompson A, Gandhi KK, Hochberg MC, Suissa S. Incidence of malignancy in adult patients with rheumatoid arthritis: a meta-analysis. *Arthritis Res Ther*. 2015; **17**(1): 212.
9. Peacock A, Leung J, Larney S, Colledge S, Hickman M, Rehm J, *et al*. Global statistics on alcohol, tobacco and illicit drug use: 2017 status report. *Addiction*. 2018; **113**(10):1905–26.
10. Baecklund E, Iliadou A, Askling J, Ekbom A, Backlin C, Granath F, *et al.* Association of chronic inflammation, not its treatment, with increased lymphoma risk in rheumatoid arthritis. *Arthritis Rheum.* 2006; **54**(3):692–701.
11. Din FVN, Theodoratou E, Farrington SM, Tenesa A, Barnetson RA, Cetnarskyj R, *et al.* Effect of aspirin and NSAIDs on risk and survival from colorectal cancer. *Gut*. 2010; **59**(12):1670–79.
12. Bernatsky S, Ramsey-Goldman R, Labrecque J, Joseph L, Boivin JF, Petri M, *et al.* Cancer risk in systemic lupus: an updated international multi-centre cohort study. J *Autoimmun.* 2013; **42**:130–135.
13. Choi MY, Flood K, Bernatsky S, Ramsey-Goldman R, Clarke AE. A review on SLE and malignancy. *Best Pract Res Clin Rheumatol.* 2017; **31**(3):373–396.
14. Bernatsky S, Ramsey-Goldman R, Joseph L, Boivin JF, Costenbader KH, Urowitz MB, *et al.* Lymphoma risk in systemic lupus: effects of disease activity versus treatment. *Ann Rheum Dis.* 2014; **73**(1):138–142.
15. Tincani A, Taraborelli M, Cattaneo R. Antiphospholipid antibodies and malignancies. *Autoimmun Rev*. 2010; **9**(4):200–202.
16. Löfström B, Backlin C, Pettersson T, Lundberg IE, Baecklund E. Expression of APRIL in diffuse large B cell lymphomas from patients with systemic lupus erythematosus and rheumatoid arthritis. *J Rheumatol*. 2011; **38**(9):1891–97.
17. Ramos-Casals M, Font J, García-Carrasco M, Brito MP, Rosas J, Calvo-Alen J, *et al*. Primary Sjögren syndrome: hematologic patterns of disease expression. *Medicine* (Baltimore). 2002; **81**(4):281–292.
18. Tzioufas AG, Boumba DS, Skopouli FN, Moutsopoulos HM. Mixed monoclonal cryoglobulinemia and monoclonal rheumatoid factor cross-reactive idiotypes as predictive factors for the development of lymphoma in primary Sjögren's syndrome. *Arthritis Rheum.* 1996; **39**(5):767–772.
19. Kristinsson SY, Koshiol J, Björkholm M, Goldin LR, McMaster ML, Turesson I, *et al.* Immune-related and inflammatory conditions and risk of lymphoplasmacytic lymphoma or Waldenstrom macroglobulinemia. *J Natl Cancer Ins*t. 2010; **102**(8):557–567.
20. Smedby KE, Vajdic CM, Falster M, Engels EA, Martinez-Maza O, Turner J, *et al.* Autoimmune disorders and risk of non-Hodgkin lymphoma subtypes: a pooled analysis within the InterLymph Consortium. *Blood*. 2008; **111**(8):4029–38.
21. Theander E, Henriksson G, Ljungberg O, Mandl T, Manthorpe R, Jacobsson LTH. Lymphoma and other malignancies in primary Sjögren's syndrome: a cohort study on cancer incidence and lymphoma predictors. *Ann Rheum Dis*. 2006; **65**(6):796–803.
22. Voulgarelis M, Dafni UG, Isenberg DA, Moutsopoulos H M. Malignant lymphoma in primary Sjögren's syndrome: a multicenter, retrospective, clinical study by the European Concerted Action on Sjögren's Syndrome - PubMed. *Arthritis Rheum*. 1999; **42**(8):1765–72.
23. Papageorgiou A, Ziogas DC, Mavragani CP, Zintzaras E, Tzioufas AG, Moutsopoulos HM, *et al.* Predicting the outcome of Sjogren's syndrome-associated non-hodgkin's lymphoma patients. *PLoS One*. 2015; **10**(2): e0116189.
24. Vazquez A, Khan MN, Sanghvi S, Patel NR, Caputo JL, Baredes S, *et al.* Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue of the salivary glands: a population-based study from 1994 to 2009. *Head Neck*. 2015; **37**(1):18–22.

25. Rosenthal AK, McLaughlin JK, Gridley G, Nyren O. Incidence of cancer among patients with systemic sclerosis - *PubMed. Cancer.* 1995; **76**(5):910–914.
26. Chatterjee S, Dombi GW, Severson RK, Mayes MD. Risk of malignancy in scleroderma: a population-based cohort study. *Arthritis Rheum*. 2005; **52**(8):2415–24.
27. Olesen AB, Sværke C, Farkas DK, Sørensen HT. Systemic sclerosis and the risk of cancer: a nationwide population-based cohort study. *Br J Dermatol*. 2010; **163**(4):800–806.
28. Moinzadeh P, Fonseca C, Hellmich M, Shah AA, Chighizola C, Denton CP, *et al.* Association of anti-RNA polymerase III autoantibodies and cancer in scleroderma. *Arthritis Res Ther.* 2014; **16**(1): R53.
29. Mahr A, Heijl C, Le Guenno G, Faurschou M. ANCA-associated vasculitis and malignancy: current evidence for cause and consequence relationships. *Best Pract Res Clin Rheumatol*. 2013; **27**(1):45–56.
30. Ungprasert P, Sanguankeo A, Upala S, Knight EL. Risk of malignancy in patients with giant cell arteritis and polymyalgia rheumatica: a systematic review and meta-analysis. *Semin Arthritis Rheum*. 2014; **44**(3):366–370.
31. Sidhom OA, Basaleev M, Sigal LH. Renal cell carcinoma presenting as polymyalgia rheumatica. Resolution after nephrectomy. *PubMed.* 1993; **153**: 2043–45.
32. Li H, Altman RD, Yao Q. RS3PE: Clinical and Research Development. *Curr Rheumatol Rep.* 2015; **17**(8):49.
33. Kisacik B, Onat AM, Kasifoglu T, Pehlivan Y, Pamuk ON, Dalkilic E, *et al*. Diagnostic dilemma of paraneoplastic arthritis: case series. *Int J Rheum Dis.* 2014; **17**(6):640–645.
34. Manger B, Schett G. Palmar fasciitis and polyarthritis syndrome-systematic literature review of 100 cases. *Semin Arthritis Rheum*. 2014; **44**(1):105–111.
35. Lakhanpal S, Ginsburg WW, Michet CJ, Doyle JA, Moore SB. Eosinophilic fasciitis: clinical spectrum and therapeutic response in 52 cases. *Semin Arthritis Rheum.* 1988; **17**(4):221–231.
36. Hou JL, Onajin O, Gangat N, Davis MDP, Wolanskyj AP. Erythromelalgia in patients with essential thrombocythemia and polycythemia vera. *Leuk Lymphoma*. 2017; **58**(3):715–717.
37. Martinez-Lavin M, Pineda C. Hypertrophic osteoarthropathy. In: Rheumatology. In: Hochberg MC, Silman AJ, Smolen JS, editors. Rheumatologyl. London: Mosby; 2003. p. 1763.
38. Sridhar KS, Lobo CF, Altman RD. Digital clubbing and lung cancer. *Chest.* 1998; **114**(6):1535–37.
39. Radis CD, Kahl LE, Baker GL, Wasko MCM, Cash JM, Gallatin A, *et al*. Effects of cyclophosphamide on the development of malignancy and on long-term survival of patients with rheumatoid arthritis. A 20-year followup study. *Arthritis Rheum.* 1995; **38**(8):1120–27.
40. Heijl C, Westman K, Höglund P, Mohamma AJ. Malignancies in patients with antineutrophil cytoplasmic antibody-associated vasculitis: a population-based cohort study. *J Rheumatol.* 2020; **47**(8):1229–37.
41. Reinhold-Keller E, Beuge N, Latza U, De Groot K, Rudert H, Nolle B, *et al*. An interdisciplinary approach to the care of patients with Wegener's granulomatosis: long-term outcome in 155 patients - PubMed. *Arthritis Rheum.* 2000; **43**(5):1021–32.
42. Talar-Williams C, Hijazi YM, Walther MM, Linehan WM, Hallahan CW, Lubensky I, *et al*. Cyclophosphamide-induced cystitis and bladder cancer in patients with Wegener granulomatosis. *Ann Intern Med.* 1996; **124**(5):477–484.
43. Fernandes E T, Manivel J C, Reddy P K, Ercole C J. Cyclophosphamide associated bladder cancer--a highly aggressive disease: analysis of 12 cases - PubMed. *J Urol.* 1996; **156**(6):1931–33.
44. Silman AJ, Petrie J, Hazleman B, Evans SJW. Lymphoproliferative cancer and other malignancy in patients with rheumatoid arthritis treated with azathioprine: a 20 year follow up study. *Ann Rheum Dis.* 1988; **47**(12):988–992.
45. Wolfe F, Michaud K. Lymphoma in rheumatoid arthritis: the effect of methotrexate and anti-tumor necrosis factor therapy in 18,572 patients. *Arthritis Rheum.* 2004; **50**(6):1740–51.
46. Mariette X, Cazals-Hatem D, Warszawki J, Liote F, Balandraud N, Sibilia J. Lymphomas in rheumatoid arthritis patients treated with methotrexate: a 3-year prospective study in France. *Blood.* 2002; **99**(11):3909–15.
47. Yamakawa N, Fujimoto M, Kawabata D, Terao C, Nishikori M, Nakashima R, *et al.* A clinical, pathological, and genetic characterization of methotrexate-associated lymphoproliferative disorders. *J Rheumatol.* 2014; **41**(2):293–299.
48. Vernino S, Salomao DR, Habermann TM, O'Neill BP. Primary CNS lymphoma complicating treatment of myasthenia gravis with mycophenolate mofetil. *Neurology.* 2005; **65**(4):639–641.

49. Wolfe F, Michaud K. The effect of methotrexate and anti-tumor necrosis factor therapy on the risk of lymphoma in rheumatoid arthritis in 19,562 patients during 89,710 person-years of observation. *Arthritis Rheum.* 2007; **56**(5):1433–39.
50. Bongartz T, Sutton AJ, Sweeting MJ, Buchan I, Matteson EL, Montori V. Anti-TNF antibody therapy in rheumatoid arthritis and the risk of serious infections and malignancies: systematic review and meta-analysis of rare harmful effects in randomized controlled trials. *JAMA.* 2006; **295**(19):2275–85.
51. Parakkal D, Sifuentes H, Semer R, Ehrenpreis ED. Hepatosplenic T-cell lymphoma in patients receiving TNF-α inhibitor therapy: expanding the groups at risk. *Eur J Gastroenterol Hepatol.* 2011; **23**(12):1150–56.
52. Wadström H, Frisell T, Sparén P, Askling J. Do RA or TNF inhibitors increase the risk of cervical neoplasia or of recurrence of previous neoplasia? A nationwide study from Sweden. *Ann Rheum Dis.* 2016; **75**(7):1272–78.
53. Amari W, Zeringue AL, McDonald JR, Caplan L, Eisen SA, Ranganathan P. Risk of non-melanoma skin cancer in a national cohort of veterans with rheumatoid arthritis. *Rheumatology* (Oxford). 2011; **50**(8):1431–39.
54. Etanercept plus standard therapy for Wegener's granulomatosis. *N Engl J Med.* 2005; **352**(4):351–361.
55. Lopez-Olivo MA, Tayar JH, Martinez-Lopez JA, Pollono EN, Cueto JP, Gonzales-Crespo MR, *et al.* Risk of malignancies in patients with rheumatoid arthritis treated with biologic therapy: a meta-analysis. *JAMA*. 2012; **308**(9):898–908.
56. Van Vollenhoven RF, Fleischmann RM, Furst DE, Lacey S, Lehane PB. Longterm Safety of Rituximab: Final Report of the Rheumatoid Arthritis Global Clinical Trial Program over 11 Years. *J Rheumatol*. 2015; **42**(10):1761–66.
57. Weinblatt ME, Moreland LW, Westhovens R, Cohen RB, Kelly SM, Khan N, *et al.* Safety of abatacept administered intravenously in treatment of rheumatoid arthritis: integrated analyses of up to 8 years of treatment from the abatacept clinical trial program. *J Rheumatol.* 2013; **40**(6):787–797.
58. Rubbert-Roth A, Sebba A, Brockwell L, Kelman A, Porter-Brown B, Pulley J, *et al.* Malignancy rates in patients with rheumatoid arthritis treated with tocilizumab. *RMD open.* 2016; **2**(1): e000213.
59. Yamamoto K, Goto H, Hirao K, Nakajima A, Origasa H, Tanaka K, *et al.* Longterm safety of tocilizumab: Results from 3 years of followup postmarketing surveillance of 5573 patients with rheumatoid arthritis in Japan. *J Rheumatol*. 2015; **42**(8):1368–75.
60. Fiorentino DF, Chung LS, Christopher-Stine L, Zaba L, Li S, Mammen AL, *et al.* Most patients with cancer-associated dermatomyositis have antibodies to nuclear matrix protein NXP-2 or transcription intermediary factor 1γ. *Arthritis Rheum.* 2013; **65**(11):2954–62.
61. Igusa T, Hummers LK, Visvanathan K, Richardson C, Wigley FM, Casciola-Rosen L, *et al*. Autoantibodies and scleroderma phenotype define subgroups at high-risk and low-risk for cancer. *Ann Rheum Dis*. 2018; **77**(8):1180–87.

Medication prior to rheumatology consultation in a Togolese Teaching Hospital

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Abstract

Objective: To determine the frequency and nature of the medication prior to specialized consultation in rheumatic patients.

Design: This was a cross-sectional study of patients admitted for the first time for rheumatology consultation at CHU-SO in Lomé, Togo.

Methods: The data relating to the medication prior to the consultation were collected by questioning. The diagnosis of the conditions covered by the consultation was based on clinical and para-clinical examinations.

Results: Two hundred and eleven patients (151 women and 60 men) with a mean age of 49 years were included in the study. Forty-five patients (21%) were covered by health insurance because of their status as state employees, unlike the other 166 (79%) working in the informal sector. Spinal degenerative pathology (76%), knee osteoarthritis (20%) and tendinitis (10%) were the main diseases observed. One hundred and ninety- five patients (92%) were on medication prior to the rheumatology consultation. Non-steroidal anti-inflammatory drugs (118 cases, 75%) and analgesics (93 cases, 59%) were the most common therapeutic classes that were used. Self-medication was observed in 141 patients (67%) at all levels of education combined. Eighty-four of the 141 patients (60%) have used street drugs, and 98 of them (70%) were oriented by word of mouth. General medical practitioners (25%) and medical assistants (19%) were the main prescribers before the rheumatology consultation. Epigastric pain (16 cases) was the main side effect observed. One hundred and forty-four patients (66%) had no idea of the risks of self-medication, added to lack of money by 122 (87%) patients and lack of knowledge of rheumatology by 67 (48%) patients.

Conclusion: Self-medication, the frequency of which is known all over the world, is more notable in Africa and in rheumatic diseases where pain is the main symptom and its relief is one of the criteria for evaluating the effect of any therapy.

Key words: Self-medication, Rheumatology, Togo, Africa

Introduction

Pain is the main symptom of rheumatic diseases for which it is the main reason for consultation. Its relief is the first concern of both the patient and the doctor, hence the importance of symptomatic treatment based on analgesics and non-steroidal anti-inflammatory drugs[1-3]. Analgesics and non-steroidal anti-inflammatory drugs are among the most prescribed drugs in the world, both in private medicine and in hospital medicine. They are among the world's best-selling substandard and falsified drugs according to the World Health Organization[4]. Paracetamol is now legally sold outside the pharmaceutical circuit in some developed countries[4,5]. In sub-Saharan Africa more than elsewhere, the use of these drugs in self-medication is favored by the continent's low medical and paramedical coverage, as well as by poverty and the low rate of social protection coverage[6]. These combined factors explain the recourse to self-medication, which is heavily fueled by street pharmacy in sub-Saharan Africa. This explains the extreme frequency of self-medication observed in rheumatology. The purpose of this study was to determine the frequency and nature of the medication prior to the specialist consultation in Togolese rheumatic patients.

Materials and methods

The study took place in the Rheumatology Department of the CHU-SO in Lomé, Togo. The population of Togo is about 8,000,000 inhabitants. Life expectancy at birth is 66 years. Forty percent of Togolese are aged under 15 years, 56% are aged between 14 and 64 years, and 4% are aged at least 65 years. The gross domestic product per inhabitant is USD 760. Health expenditure represents about 30% of household income. On average, there is one medical doctor for 15,000 inhabitants, one midwife for 12,000 inhabitants, and 1.63 nurses for 10,000 inhabitants. The public sector has 700 healthcare facilities. Seventy percent of Togolese live within a radius of less than 5 km from a healthcare facility[7].

Health coverage began in stages, through the National Health Insurance Institute, set up in 2011 for the benefit of State employees and equivalent, corresponding to a coverage rate of 7% of the population. For three years, a social assistance has been set up for the benefit of 1,500,000 primary and secondary students in the public sector. In addition, initiatives to enlist the informal sector are underway. These different provisions are called upon to converge towards a national system of universal health coverage governed by a regulation[7].

This was a cross-sectional study carried out over three months in the Rheumatology Department of CHU-SO. All patients admitted to consultation for the first time were included. A survey sheet made it possible to collect the socio-demographic characteristics of the patients, the presence or absence of medical coverage by insurance, the reason for consultation, the treatment taken before the consultation and its effects, the reasons for resorting to such treatment. These data were added to those for diagnostic purposes resulting from the clinical and the para-clinical examinations.

Results

Two hundred and eleven patients (151 women and 60 men) were included in the study. The mean age of these patients was 49 years (range from 12 to 85 years). Forty-five of these patients (21%) were state employees and consequently had health insurance. The other 166 patients (79%) belonging to the informal sector, did not have a health insurance scheme. The level of education was primary school for 40 patients, secondary school for 82 patients and university level for 40 patients. The mode of installation of the pain was progressive in 186 (88%) patients. The pain was chronic in 195 (92%) patients, acute in 191 (91%). Degenerative spine disease (76%), knee osteoarthritis (20%) and tendinitis (10%) were the major diseases observed. Activities of daily living were impaired in 95 (66%) patients.

Ninety-five patients (92%) were under medication prior to rheumatology consultation, and non-steroidal anti- inflammatory drugs (118 cases, 75%) and analgesics (92 cases, 59%) were the most common therapeutic classes that were used.

Self- medication was observed in 141 (67%) patients, all levels of education combined: eighty-four of the 141 (59.57%) patients used street drugs, and 98 (70%) of them were referred by word of mouth. General medical practitioners (25; 46%) and medical assistants (19; 42%) were the main prescribers before the rheumatology consultation. Epigastric pain (16 cases) were the main side effect observed. One hundred and forty-four patients (66%) did not have any idea of the risks of self-medication, which 122 (87%) patients joined due to lack of funds, and 67 (48%) due to ignorance of the rheumatology.

Discussion

This was a cross-sectional study aimed at determining the profile of the medication prior to the specialist consultation in 211 rheumatic patients. As a result, 195 (92%) patients had treatment prior to the specialist consultation. This treatment was self-medication in 41 (67%) patients. The treatment prior to the specialist consultation finds its origin in the important place occupied by pain in rheumatic diseases, in the heavy consumption of analgesics and non-steroidal anti-inflammatory drugs in daily medical practice, in the over-the-counter sale of these drugs as well in the classical pharmacy as in that of the street, and in the important place of these drugs among those of inferior quality and falsified.

Another aspect of the medication prior to the consultation is that relating to medicinal plants. The use of these plants is very frequent in Africa, all pathologies combined. In our study, we did not conduct a systematic research on the use of these plants but this could be the subject of another work. The drugs used by our patients before the consultation were both generics and specialty drugs. The two types of drugs are sold in pharmacies as well as in streets. Medication through friends and family members is based on word of mouth as mentioned above. Although our sample only included 211 patients, the results of our study are probably superimposable on all rheumatism diseases and beyond, to all medical specialties

Several studies have shown that self-medication is a real public health problem in

emerging countries[9]. The prevalence of self-medication in these countries is difficult to quantify because it varies according to the populations, pathologies and drugs used [9,10]. The limits of our study are represented by the mode of data collection on a declarative basis of patients, which can be a source of bias.

Self-medication and the recourse to non-specialist are favored by low rheumatology and medical coverage (Togo has only about ten rheumatologists) and low health insurance coverage (about 40% of Togolese are covered). Only a fifth of our patients, because of their status as State agents, benefit from health insurance[7].

In addition to the low health and insurance coverage, other factors favoring self-medication are added: financial constraints, low level of education, actual or *de facto* over-the-counter sale of drugs (even for those to be sold on medical prescription), substandard or falsified drugs trafficking, important proportion of analgesics and anti-inflammatory drugs among the trafficked drugs. This is the case with level 1 analgesics, paracetamol in particular, and even those of level 2, like tramadol, the subject of significant seizures in recent years in West Africa[8-11].

The results of the study are consistent with the observations both in the Third World and the West 12-16. Globally, analgesics are the most commonly used drugs in self-medication14. The frequency of the medication before the consultation in our study was 92% and that of self-medication was 67%. This frequency is close to that of studies conducted both in Europe in the field of rheumatology12 and in Africa in other specialties[13,16]. The place of pain in rheumatic pathology explains the important role of analgesics and non-steroidal anti-inflammatory drugs in self-medication and during the period preceding the specialist consultation.

Conclusion

This study shows that the fight against self-medication involves the eradication or reduction of its contributing factors which are poverty, insufficient medical coverage, extension of health insurance, the fight against substandard and falsified drugs trafficking. In daily rheumatology practice, the correct management of the patient requires taking into account self-medication and medications taken upstream of the specialist consultation, with a dual diagnostic and therapeutic purposes.

References

1. Rôle du pharmacien d'officine dans la prise en charge pharmacologique de la douleur non cancéreuse par des antalgiques de prescription médicale facultative disponible sur : *http// thesesante.ups-tise.fr.* -
2. Evaluation de la prescription des anti-inflammatoires non stéroïdiens chez le sujet âgé disponible sur : *http/www.bichat.lapi*
3. Naïm RO, Escher M. Antalgiques en automédication : quels sont les risques ? *Rev Med Suisse*. 2010 ; **255**: 1338 - 41.
4. Organisation Mondiale de la Santé. *Lignes directrices pour l'évaluation réglementaire des médicaments destinés à l'automédication.* Genève (CH): OMS; 2000. p. 31. Rapport n° WHO/EDM/QSM/001. [Google Scholar]
5. Lechat P. L'ordonnance et les règles de prescription des médicaments, Pharmacologie. *Université Marie Curie*. 2006; **56**: 349.
6. Etame Loe G, Ngoule CC, Ngene JP, Kidik Pouka MC. Evaluation de l'automédication par les antalgiques chez l'adulte : cas des clients d'officine de Douala, Cameroun. *Int. J Biol. Chem. Sci.* 2017; **11**: 1461-70.
7. Ministère de la santé. Direction Générale des Etudes, de la Planification, de l'Information et des Statistiques. *Statistiques Sanitaires. Lomé,* Togo, 2019.
8. Ebi OA, Babatunde OA, Fadare JO, Ojo OJ, Durowade KA**,** *et al.* Self-medication among health workers in a tertiary institution in South-West Nigeria. *Pan Afr Med J*. 2016; **24**:31.
9. Ouédraogo DD, Zabsoure/Tiendrebeogo JW, Zongo E, Kakpovi, Kaboré F, Drabo JY, Guissou IP, *et al.* Prevalence and factors associated with self-medication in rheumatology in sub-Saharan Africa. *Eur J Rheumatol*. 2015; **2**:52-56.
10. Gbeasor-Komlanvi FA, Zida-Compaore WIC, Tairou S, Ekouevi DK. Evaluation de l'automédication dans les officines de Lomé, Togo. *J Rech. Sci Univ Lomé.* 2017; **19**:411-421.
11. Fianyo E, Kakpovi K, Houzou P, Amouzou Y, Koffi-Tessio VES, Tagbor KC, Oniankitan O, Mijiyawa M Automédication en milieu rhumatologique à Lomé (Togo). *J Rech Sci Univ Lomé*. 2019; **21**: 115-119.
12. Hesbert A, Louis V, Curis E, Briot K, Gossec L, Poireaudeau S, *et al*. Automédication en rhumatologie. *Le pharmacien hospitalier et clinicien.* 2012; **47**: 48. *http://dx.doi.org/10.1016/j.phclin.2011.12.116. [Google Scholar.*

13. Suleman S, Ketsela A, Mekonnen Z**.** Assessment of self-medication practices in Assendabo town, Jimma zone, southwestern Ethiopia*. Res Social Adm Pharm*. 2009; **5**: 76-81.
14. Garofalo L, Di Giuseppe G, Angelillo IF. Self-medication practices among parents in Italy. *Biomed Res Int.* 2015; 2015: 580650. Published online 2015 Jan 20. doi: 10.1155 / 2015 / 580650.
15. Kombate K, Técléssou JN, Saka B, Akakpo AS, Tchangaï KO, Mouhari-Toure *et al*; Prevalence and factors associated with self – medication in dermatology in Togo. *Dermatol Res Pract.* 2017; **5**:1.
16. Beyene, KG, Beza, SW. Self-medication practice and associated factors among pregnant women in Addis Ababa, Ethiopia. *Trop Med Health.* 2018; **46***:* 10. https://doi.org / 10.1186/ s41182 - 018 - 0091 - z.

Profile of cervicobrachial neuralgia among rheumatology patients in Lomé, Togo

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Abstract

Objectives: To determine the frequency and the different clinical forms of cervicobrachial neuralgia in a rheumatological setting in Lomé, Togo.
Design: This was a cross-sectional multicenter study conducted from January 2012 to December 2018 on the records of patients seen in the three rheumatology units in Lomé, Togo.
Methods: Patients who reported for consultation purposely because of cervicobrachial neuralgia were included. Diagnosis of the various clinical forms of degenerative cervical spine disease was essentially clinical, whereas radiological imaging findings contributed to the diagnosis of spondylodiscitis and neoplastic disease.
Results: Cervicobrachial neuralgia was the reason for the clinic visit in 143 (0.69%) out of the 14,346 patients examined over the eight year study period. These 143 patients comprising 84 women (58.74%) and 59 men (41.26%) had a mean age of 53.36±13.33 years. The average time to consultation was two years. Degenerative disease (138 cases, 96.5%) was the most commonly observed pathology. It included the following clinical forms: cervical osteoarthritis (n=120; 83.91%), cervical myelopathy (n=13; 9.10%) and herniated disc (n=5; 3.49%). Disc degeneration in isolation (60.83%) was the main radiographic finding in patients with degenerative disease. Spondylodiscitis was probably due to tuberculosis in the four patients who had it and two of them were HIV-positive. Bone metastasis from prostate cancer was found in one case.
Conclusion: Cervicobrachial neuralgia appears to be significant among rheumatology patients in Lomé. It predominantly affects adult women in professional activity. Although mainly dominated by degenerative pathology, its aetiologies can also be infectious as well as neoplastic, hence the relevance of modern imaging modalities.

Key words: Cervicobrachial neuralgia, Osteoarthritis, Spondylodiscitis, Tumours, Sub-Saharan Africa

Introduction

Studies on spinal diseases in Africa, although mostly conducted in hospital setting, have established the presence of such diseases on this continent[1-4]. However, they are more often dealt with as low back pain[5], low back pain with radiculopathy[6] and neck pain[7,8] than with Cervicobrachial Neuralgia (CBN)[9,10]. CBN is a frequent symptom in cervical spinal disease, with an annual incidence, adjusted and estimated at 83 per 100,000 people[11]. It is caused by injury to the nerve roots following a degenerative, infectious, neoplasmic or inflammatory disease of the spine[12,13]. Its aetiological diagnosis has been clearly improved by the advent of neuroradiological means of investigation, in particular Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). The aim of our study was to determine the clinical signs and symptoms as well as the distribution of the different clinical forms of cervicobrachial neuralgia in a rheumatological setting in Lomé, Togo (West Africa).

Materials and methods

This was a multicenter, cross-sectional study carried out from January 1, 2012 to December 31, 2018 on the records of patients aged 18 years and above, received in consultation or

hospitalized for cervicobrachial neuralgia in the three rheumatology units in Lomé: CHU Sylvanus Olympio (Sylvanus Olympio Teaching Hospital), CHR Lomé-Commune (Lomé-Commune Regional Hospital) and Hôpital de Bè (Bè Hospital). The study was approved by the ethics committee. Data was collected using a survey sheet including data such as demographics (age, sex), clinical data (pain timeline, onset, clinical course, reason for hospitalization, and details from physical examination), paraclinical data (standard radiography (X-ray), Computed Tomography (CT), Magnetic Resonance Imaging (MRI)) and Etiological data on CBN. Diagnosis of the different clinical forms of degenerative cervical spine disease was essentially clinical, while radiological imaging findings contributed to the diagnosis of spondylodiscitis and neoplastic disease. Patients with no imaging were excluded. Data analysis was performed using SPSS software for Windows (Version 17.0).

Results

Cervicobrachial neuralgia was the reason for the clinic visit in 143 (0.69%) out of the 14,346 patients seen over the eight year study period. These 143 patients comprising 84 women (58.74%) and 59 men (41.26%) had a mean age of 53.36±13.33 years (age range 23-85 years). Retailers were the most affected (28.673%) (Table 1).

Table 1: Distribution of patients by profession

	No.	(%)
Retailer	41	28.67
Housekeeper	18	12.59
Craftsperson	14	9.79
Office personnel	13	9.09
Labourer	13	9.09
Farmer	11	7.69
Health personnel	11	7.69
Teacher	07	4.90
Military	06	4.20
Engineer	03	1.40
Religious	03	2.10
Pensioner	03	2.10
Student	01	0.69
Total	143	100.00

The average consultation time was 2 ± 4.87 years with extremes of 7 days and 40 years. All of our patients consulted for neck pain radiating into one or both upper limbs. Neck pain preceded radiculalgia (115 cases; 80.41%), immediately radiated (17 cases; 11.9%) and occurred after radiculalgia (11 cases; 7.69%). A triggering factor was found in 39 cases (30.47%). Data from the patient medical history and physical examination are summarized in Tables 2 and 3. Degenerative disease (138 cases, 96.5%) was the most commonly observed pathology (Table 4).

Table 2: Distribution of key data from patient medical history according to aetiology

	Cervical osteoarthritis (120 cases) No. (%)	Cervical myelopathy (13 cases) No. (%)	Herniated disc (5 cases) No. (%)	Spondylodiscitis (4 cases) No. (%)	Tumours (1 case) No. (%)
Onset					
Gradual	78(65.00)	8(61.53)	3(60)	1(25)	1(100)
Sudden	35(29.16)	2(15.38)	2(40)	3(75)	0(0)
Clinical course					
Flare-ups	26(21.66)	1(7.69)	1(20)	0(0)	0(0)
Intermittent	24(20)	2(15.38)	0(0)	1(25)	0(0)
Constant	11(09.16)	2(15.38)	0(0)	3(75)	1(100)
Pain timeline					
Mechanical	86(71.66)	8(61.53)	5(100)	0(0)	0(0)
Inflammatory	23(19.16)	3(23.07)	0(0)	4(100)	1(100)
Mixed	9(7.50)	1(7.69)	0(0)	0(0)	0(0)
Paresthesia					
T-N*	44(36.66)	4(30.76)	3(60)	0(0)	0(0)
Tingling	30(25.00)	5(38.46)	0(0)	1(25)	0(0)
Numbness	5(4.16)	2(15.38)	1(20)	1(25)	0(0)
Radiation					
C5	24(20.00)	1(7.69)	0(0)	0(0)	1(100)
C6	11(09.16)	3(23.07)	0(0)	0(0)	0(0)
C5-C6	30(25.00)	0(0)	1(20)	0(0)	0(0)
C7	11(09.16)	1(7.69)	0(0)	0(0)	0(0)
C6-C7	8(06.66)	1(7.69)	1(20)	0(0)	0(0)
C8	5(4.16)	1(7.69)	0(0)	0(0)	0(0)
Poorly localized	14(11.66)	2(15.38)	3(60)	2(50)	0(0)

*: Tingling-Numbness

Table 3: Distribution of key data from physical examination according to aetiology

	Cervical osteoarthritis (120 cases) No. (%)	Cervical myelopathy (13 cases) No. (%)	Herniated disc (5 cases) No. (%)	Spondylodiscitis (4 cases) No. (%)	Tumours (1 case) No. (%)
BMI (kg/m^2) $\bar{x} \pm$ SD	27.16 ± 5.32	23.13 ± 2.31	20.78 ± 4.58	20.29 ± 5.70	-
Torticollis	9(7.50)	0(0)	0(0)	0(0)	0(0)
Painful mobilization	75(62.50)	3(60)	8(61.53)	3(75)	1(100)
Elective	75(100.00)	3(100)	8(100)		0(0)
Global	0(0)	0(0)		0(0)	
			0(0)		1(100)
				3(100)	
Stiffness	42(35.00)	3(60)	6(46.15)	4(100)	0(0)
Elective	34(80.95)	3(100)	6(100)		
Globale	08(19.05)	0(0)		0(0)	0(0)
			0(0)		
				4(100)	0(0)
Tinnitus	38(31.66)	0(0)	6(4615)	2(50)	1(100)
Sensory disorders					
Hypoesthesia	04(3.33)	0(0))	3(23.07)	1(25)	0(0)
Hyperesthesia	01(0.83)	0(0)	0(0)	0(0)	0(0)
Motor disorders					
Hemiparesis Mono-	02(1.66)	0(0)	0(0)	0(0)	0(0)
paresis Paraparesis	05(4.16)	1(20)	3(23.07)	0(0)	0(0)
Tetraparesis Tetraplegia	03(2.50)	2(40)	3(23.07)	2(50)	0(0)
	0(0)	0(0)	4(30.76)	0(0)	0(0)
	0(0)	0(0)	0(0)	1(25)	0(0)
Reflex disorders					
Bicipital					
Exaggeration	4(3.33)	2(40)	4(30.76)	1(25)	0(0)
Abolition	6(5)	0(0)	1(7.69)	0(0)	0(0)
Diminution	3(2.50)	0(0)	0(0.00)	1(25)	1(100)
Tricipital					
Exaggeration	4(3.33) 5(4.16)	2(40)	4(30.76)	1(25)	0(0)
Abolition	2(1.66)	0(0)	1(07.69)	0(0)	0(0)
Diminution		0(0)	0(0)	1(25)	1(100)
Brachioradialis					
Exaggeration	4(3.33)	2(40)	4(30.76)	1(25)	0(0)
Abolition	5(4.16)	0(0)	1(7.69)	0(0)	0(0)
Decrease	3(2.50)	0(0)	0(0)	1(25)	1(100)
Ulnar					
Exaggeration	4(3.33)	2(40)	04(30,76)	1(25)	0(0)
Abolition	5(4.16)	0(0)	01(07,69)	0(0)	0(0)
Decrease	2(1.66)	0(0)	0(0)	1(25)	1(100)

Table 4: Demographics of the 143 patients according to diagnosis

	Sex-ratio (M/F*)	Age (years) at consultation $\bar{x} \pm SD$**	Time to progression (months) $\bar{x} \pm SD$**
Degenerative cervicobrachial neuralgia			
Cervical osteoarthritis	46/74	52.12 ± 12.47	25.15 ± 61.97
Cervical myelopathy	6/7	60.46 ± 14.75	23.20 ± 35.94
Herniated disc	4/1	55.20 ± 23.31	10.25 ± 11.29
Secondary cervicobrachial neuralgia			
Spondylodiscitis	2/2	57.25 ± 03.30	01.82 ± 1.27
Tumours	1/0	85	24

* : Male/Female ;** : mean ± standard deviation

Degenerative disease included the following clinical forms: cervical osteoarthritis (n=120; 83.91%), cervical myelopathy (n=13; 9.10%) and herniated disk (n=5; 3.49%). Disc degeneration in isolation (60.83%) was the main radiographic finding in patients with degenerative disease. Spondylodiscitis was probably due to tuberculosis, with a mean clinical course of 1.82 months in the four affected patients and two of them were HIV-positive. No patient had a gibbosity. Bone metastasis from prostate cancer was identified in one case. The mean duration of treatment was 1.88 ± 1.92 months, ranging from 7 days to 12 months. Treatment was medical (96.50%), functional (13.28%) or surgical (1.39%).

Discussion

Cervicobrachial Neuralgia (CBN) is rare (0.99%) in rheumatology practice in Lomé and it mainly has a degenerative aetiology. Rigorous interpretation of these results requires taking into consideration the shortcomings related to selection bias and limited technical platform. This was a hospital-based study which only took into account consultants from the rheumatology units of Lomé, thus constituting a bias which makes it impossible to generalize our results. Shortage in early diagnostic means (MRI, bone scan) made it impossible to discover certain tumours and infections at the pre-radiological stage. Moreover, not all rheumatic patients report to health centers; many of them consult traditional healers. Nevertheless, these shortcomings of our study do not affect its epidemiological importance.

The low prevalence of CBN in our study is relatively lesser than what was found in other African studies[3,10]. This is due to the fact that its management is multidisciplinary, so patients suffering from it may end up in other departments as well (neurology, neurosurgery).

CBN frequently occurs in young and older adults, regardless of gender according to literature[3,4,7,10,14]. The long timeframe before consultation (2 years) can be explained by the geographical inaccessibility of specialized care structures and the insufficient number of specialists (neurologists, rheumatologists and neurosurgeons). The data from patients' medical history and the physical examination are consistent with literature and are explained by the high mobility of the lower cervical spine and the frequency of osteoarthritis of the C5-C6 and C6-C7 discs[9-10,14]. Predominance of degenerative aetiology, with cervical osteoarthritis dominating our sample, is consistent with other African[8,15,16] and Western[17,18] studies in which psychological factors play an important role in the chronicity and persistence of the pain.

The poor treatment suffered by the cervical spine during our daily activities (especially carrying loads on the head which is a common practice in our country) largely explains this predominance. These practices often lead to disc worn out and thus, genesis of cervical osteoarthritis. Cervical myelopathy occurs between the ages of 50 and 60 years, regardless of gender; it is characterized by a long clinical course and severe neurological dysfunction with a predominance of gait disturbances according to literature[19-21]. The low rate (1.39%) of surgical care can be explained on the one hand by the small number of neurosurgeons together with the limited technical platform and on the other hand by the unfavorable socio-economic conditions limiting the performance of imaging investigations, in particular the CT scan and the magnetic resonance imaging. CBNs secondary to infections are rare[22-24] despite the importance of infectious pathologies which is fairly well known in literature[25-27]. In our sample, the absence of gibbosity can be explained by the short clinical course. CBNs secondary to tumours are very rare in literature[8,5,28].

Conclusion

Cervicobrachial neuralgia appears not to be negligible among rheumatology inpatients in Lomé. It mainly affects adult working women. Although essentially dominated by degenerative pathologies, its aetiologies are infectious and tumoural as well, hence the relevance of modern imaging modalities.

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References

1. Daboiko JC, Ouattara B, Ouali B, Dollo YFI, Eti E, Kouakou NM. Bone and joint disorders in Ivory Coast from about 509 cases in rheumatology department of the University Hospital at Cocody. *Afrique Biomédicale.* 2003; **6**: 4-10.
2. Houzou P, Oniankitan O, Kakpovi K, Koffi-Tessio VES, Tagbor K C, Fianyo E, *et al*. Rheumatic diseases profile of 13517 West African patients. *Tunis Med*. 2013; **91**:16-20.
3. Kakpovi K, Koffi-Tessio V, Houzou P, Fianyo E, Tagbor C, Oniankitan O, *et al.* Rheumatological disorders observed in hospital in Lome (Togo). *J Rech Sci Univ Lomé* (Togo). 2016; **18**:361-370.
4. Kamissoko A B, Diallo M L, Traoré M, Diallo A, Yombouno, Barry A, *et al*. Overview of rheumatic diseases in Conakry. *Eur Sci J*. 2018; **14**: 422-431.
5. Mijiyawa M, Oniankitan O, Kolani B, *et al.* Low back pain in hospital outpatients in Lomé (Togo). *Joint Bone Spine.* 2000; **67**:533-538.
6. Oniankitan O, Magnan A, Fianyo E, Mijiyawa M. Low back pain with radiculopathy in hospital outpatients in Lomé (Togo). *J Bone Spine*. 2008; **75**:235 –241.
7. Oniankitan O, Fianyo E, Mijiyawa M. Cervicalgia observed in rheumatologic practice in Lomé, Togo. *Med Trop*. 2008; **68**:104.
8. Zomalhèto Z, Gounongbé G, Dossou-Yovo H, Onzo R, Avimadjè M. Hospital frequency of neck pain at national hospital university of Hubert Koutoukou Maga at Cotonou. *Rev Int Sci Méd*. 2013; **15**(suppl 3): 244-247.
9. Abdelmoula LC, Daoud L, Yahia CBH, Tekaya R, Chaabouni L, Zouari R. Uncommon cervicobrachial neuralgia: about 17 cases. *Tunis Med*. 2011; **89**: 598 – 603.
10. Maiga Y, Fara A, Sogoba Y, Diango D, Diakite S, Diallo M, *et al*. Longitudinal study of cervico-brachial neuralgia in the neurology department of the Gabriel Touré University Hospital, Bamako (Mali). *Pan Afr Med J.* 2013; **16**:46.
11. Caridi JM, Pumberger M, Hughes AP. Cervical radiculopathy: a review. *HSS J*. 2011; **7**: 265-272.
12. Carette S, Fehlings MG. Clinical practice - Cervical radiculopathy. *N Engl J Med*. 2005; **353**:392–399.
13. Ellenberg MR, Honet JC, Treanor WJ. Cervical radiculopathy. *Arch Phys Med Rehabil.* 1994; **75**:342–352.
14. Bouvier M. Clinica semiology of common cervicobrachial neuralgia. *J Neuroradiol*. 1992; **19**:146–148.
15. Djaha KJM, Dabolko JC, Diomandé M, Gbané-Koné M, KouakouEhaulier CL, Yao JC, *et al*. Etiological aspects of cervical pain in rheumatology at the Cocody University Hospital in Abidjan (Côte d'Ivoire). *Biomed*. 2011; **16**:49-52.
16. El-Sayed AM, Hadley C, Tessema F, *et al.* Neck pain and psychopathology in rural sub-Saharan Africa: Evidence from the Gilgel Gibe growth and development study, Ethiopia. *Spine*. 2011; **36**:213-219.
17. Fernández-de-las-Peñas C, Hernández-Barrera V, Alonso-Blanco C, *et al*. Prevalence of neck and low back pain in community-dwelling adults in Spain: a population-based national study. *Spine.* 2010; **29**:98-102.
18. Strine TW, Hootman JM. US national prevalence and correlates of low back and neck pain among adults. *Arthritis Rheum*. 2007; **57**:656-665.
19. Diomandé M, Tano M, Kouakou ESCL, Djaha KJM, Eti E, Kouakou MN. Cervical myelopathy: epidemiological and clinical characteristics in University Hospital Center in Cocody, Abidjan, Côte d'Ivoire. *Rev Med Madag*. 2015; **5**:501-504.
20. Ahanogbé KMH, Beketi KA, Kpelao E, Moumouni A, Doléagbénou K, Egbohou P. Cervico-arthrosic myelopathies operated in Togo, anterior approach: yes but not always. *Neurochirurgy*. 2018; **64**:238-239.
21. Alihoun T, Sakho Y, Gaye M, Fondo A, Ndoye N, Ba MC, Badiane SB. Our experience with cervical arthrosis myelopathy in Dakar (Sénégal). *Afr J Neurol Sci*. 2017; **35**:32-40.
22. Oniankitan O, Kakpovi K, Agoda-Koussema LK, Tagbor KC, Fianyo E, Houzou P, *et al.* Cervical spondylodiscitis in hospital outpatients in Lomé (Togo). *Tunis Med*. 2014; **92**: 567-569.
23. Lamini NE, Moyikoua R, Moussounda GS, NtsibaH, Bileckot R. Diagnosis of Pott's disease in the rheumatoly department of the university teaching hospital of Brazzaville. *Health Sci Dis*. 2019; **20**:53-56.

24. Gbané-Koné M, Ouali B, Coulibaly AK, Diomandé M, Yao JC, Eti E, *et al*. Cervical involvement in Pott's disease: epidemiological and radiological aspects of 26 cases in Abidjan. *Mali Med*. 2015; **30**: 15-18.
25. Oniankitan O, Bagayogo Y, Fianyo E, Koffi-Tessio VES, Kakpovi K, Tagbor KC, *et al.* Spondylodiscitis at hospital outpatient clinic in Lomé, Togo. *Med Trop*. 2009; **69**:581-582.
26. Maftah M, Lmejjati M, Mansouri A, El Abbadi N, Bellakhdar F. Pott's disease in 320 cases. *Med Maghreb.* 2001; **90**:19-22.
27. Ben Taarit C, Turki S, Ben Maiz H. Spondylodiscites infectieuses étude d'une série de 151 cas. *Acta Orthop Belg*. 2002; **68**: 381-387.
28. Tekaya R, Hamdi W, Azzouz D, Bouazziz M, Jaafoura MH, Ladeb MF, *et al.* Cervicobrachial neuralgia revealing a cervical neurofibrosarcoma (MPNST). *Rev Neurol*. 2008; **164**:82-86.

Shoulder pain: epidemiological, clinical and therapeutic aspects at Ignace Deen National Hospital in Conakry, Guinea

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Abstract

Background: Shoulder pain is a frequent reason for consultation in medicine.
Objective: To describe the epidemiological, clinical and therapeutic characteristics of shoulder pain in the Ignace Deen National Hospital of Conakry, Guinea.
Design: This was a prospective study of descriptive type with a duration of one year from June 1, 2020 to June 1, 2021.
Methods: All patients who consulted the Rheumatology and Physical Medicine Department for shoulder pain were included in this study.
Results: We collected 1561 patients who consulted during the study period, of whom 217 (13.9%) had shoulder pain with an average age of 51.2 years. There was a predominance of women in 114 (52.5%) of the cases with a sex ratio (M/F) of 0.9. Housewives were the most affected 73 (33.7%) of cases. Pain was severe in 41% of patients with a VAS of 7/10. Rotator cuff injuries were the most common in 146 (67%) and the treatment was dominated by the combination of level I and II analgesics in 113 (52%) and physical therapy in 136 (62.7%) of cases.
Conclusion: Shoulder pain was frequent in the most active segment of the population, with a female predominance. It is often intense and of mechanical type evolving towards chronicity and accompanied by a functional impotence, the treatment remains conservative associated with the taking of analgesic.

Key words: Pain, Shoulder, Conakry, Guinea

Introduction

Painful shoulder refers to any pain originating from the joint itself or its surrounding tissues[1] . Limitation of shoulder movement due to pain, stiffness or weakness can result in significant disability and affect a person's ability to perform daily activities and work[1, 2]. Shoulder pain is a common symptom, with an estimated prevalence of 16-26%[2,3]. It is the third most common cause of musculoskeletal consultation in primary care, and approximately 1% of adults consult a general practitioner each year for new shoulder pain[1]. It is one of the most common symptoms for which patients consult rheumatology, physical medicine and general medicine, it is called scapulalgia or Omalgia[4].

Shoulder pain has common clinical characteristics[5]. There is no consensus on the diagnostic criteria and clinical evaluation, which complicates the choice of treatment[6]. To our knowledge, little data is available on shoulder pain in Black Africa. The objective of this study was to describe the epidemiological, clinical, paraclinical and therapeutic characteristics of shoulder pain at the Ignace Deen CHU National Hospital in Conakry, Guinea.

Materials and methods

This was a prospective descriptive study of one year duration, from June 1, 2020 to June 30, 2021, conducted in the Rheumatology and Physical Medicine Department of the Ignace Deen National Hospital, CHU of Conakry, Guinea. All patients presenting with Spontaneous onset shoulder pain were included.
The following data were collected:
(i) Demographic age, sex, profession
(ii) Comorbidities (stroke, diabetes, hypertension)
(iii) Duration of pain, its location,

radiation and intensity (evaluated by the visual analog scale)

(iv) The presence of swelling, amyotrophy, increase in local heat was noted.

Shoulder examination included the following manouvers:

The combined mobility test were used for all patients, Neer test, Hawkins, yocum, Clairon's test and painful arc test have been used for the evaluation of impingement and Rotator cuff syndrome.

Jobe's and painful arc test used for tendonitis/ bursitis, and, for the tears syndromes, Geber's test and Lift off test were used. Adhesive capsulitis external rotation combined mobility test were used. Gleno humeral arthritis /AC joint arthritis and Instability, The combined mobility test were used.

(i) Erythrocyte Sedimentation Rate (ESR) in mm/h, C-Reactive Protein (CRP) in mg/l, rheumatoid factors (RF), uric acid.

(ii) Joint fluid examination for cells bacteria and microcrystals.

(iii) Imaging, standard radiography and ultrasound.

(iv) Functional disability was assessed by the Constant score[16].

(v) Therapeutic data: analgesics of level I and II of the World Health Organization (WHO), general and local corticotherapy, colchicine, antibiotic therapy.

(vi) The software, EPI info 7.2. 2. was used for data analysis. A value of $p<0.05$ is considered statistically significant

Patients were recruited with informed consent and anonymity, and we obtained the approval of the ethics committee of the Ignace Deen National Hospital for this study.

Results

All demographic and clinical results are presented in Table 1. Of the 1561 patients who presented to our combined departments 217 (13.9%) had shoulder pain.The average age of our patients was 51±14 years (21-82 years) with a slight female predominance 114 (52.5%). Housewives were the most affected 73 (33.7%). Diabetes was the most common comorbidity 67 (30.9%) cases. The mean time to consultation was 20 ± 17 weeks (range : 1 and 96). Pain was chronic in 137 (63.1%), progressive in 174 (80.2%), mechanical in 134 (61.7%) patients. The anterior aspect of the shoulder was by far the most common location (18:85.7%) with radiating to the neck in 52 (24%) of the cases. The average visual analogue scale was 7.34 ± 2 (4 - 10/10).

Table 1: Sociodemographic and clinical characteristics of patients

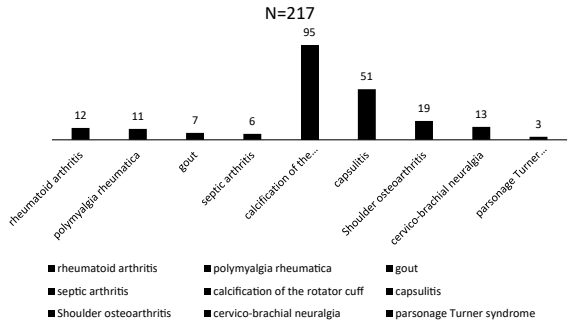
Socio-demographic data	(%)
Mean age at diagnosis (SD)	51.2 ± 14.25
Sex: female, n (%)	114 (52.5%)
Clinical data	
Average time to consultation in weeks	20 ± 17.4
Average VAS	7.34 ± 2
Profession	n (%)
Driver	25 (11.5)
Farmer	12 (5.5)
Pupil/Student	11 (5.1)
Housewife	73 (33.7)
Merchant	25 (11.5)
Civil servant	61 (28.1)
Sportsman	10 (4.6)
History	
High blood pressure	28 (12.9)
Rheumatological disease	57 (26.3)
Diabetes	67 (30.9)
stroke	51 (23.5)
Type of pain	
Inflammatory	63 (29.1)
Mechanical	134 (61.7)
Neuropathic	20 (9.2)
Progression	
Progressive	174 (80.2)
Location	
Anterior	186 (85,7)
Internal	91 (42)
Posterior	89 (41)
External	106 (48.9)
Radiation	
Cervical spine	52 (24)
Thoracic spine	6 (2,8)
Upper arm	26 (12)
Forearm	11 (5)
Hand	26 (12)
None	96 (44.2)
Evolution	
Acute	80 (36.9)
Chronic	137 (63.1)

VAS: Visual Analog Scale; Hypertension: high blood pressure; Stroke: cerebrovascular accident

Table 2: Tests and clinical maneuvers performed in our patients

Tests and maneuvers	(%)
Rapid mobility test	168 (77.4)
Neer's test	35 (16.1)
Hawkins sign	14 (6.5)
Yocum sign	15 (6.9)
Jobe maneuver	14 (6.5)
Limitation of external rotation	49 (23)
Paw test	12 (5.5)
Bugle sign	7 (3.2)
Automatic return sign	1 (0.5)
Geber's test	8 (3.7)
Belly Press-test	2 (0.9)
Sign of Popéyé	2 (0.9)
Fulcrum test	2 (0.9)
Apprehension to the backward push	2 (0.9)
Sign of the Furrow	1 (0.5)
Sign of the anteroposterior tiroi	1 (0.5)

Figure 1: Distribution of patients by aetiology



The results of the various tests of shoulder movement and function are shown in Table 2. CRP was positive in 100/207 tests performed (46.08%) with a mean of 42 mg/l (10 - 135), rheumatoid factors was positive in 11 (10.3%) patients, hyperuricemia was noted in 15 (14%) patients. Seventy-two patients underwent joint puncture plus cytobacteriological analysis and search for microcrystals. *Staphylococcus aureus* was detected in 15 (20.8%).

Standard radiography was performed in 71 (32.7%) patients, with signs of shoulder osteoarthritis found on 19 (26.8%) images. Ultrasound examination of 122 patients (56%) showed 95 (43.7%) cases of calcific tendinopathy of the rotator cuff. Adhesive capsulitis in 51 (23.5%) cases and omarthrosis in 19 (8.7%) cases.

There were 57 cases of specific rheumatic diseases, rheumatoid arthritis 16 (28%); polymyalgia rheumatica 11(5,06%), shoulder osteoarthritis 19 (8,7%); gout 7 (3.3%); remitting seronegative symmetrical synovitis with pitting edema 2 (3.5%) (Figure 1).

The treatment of patients was essentially based on the combinations of non-steroidal anti-inflammatory drugs and tramadol in 113 (52%) patients; general corticosteroid therapy in 55 (25.3%) and local corticosteroid therapy in 6.9% of cases; antibiotic therapy was prescribed in 28 (12.9%) of cases, and physiotherapy was used in 136 (62.7%) patients. The mean Constant index score in our series was 76.69 ± 13.49 (extremes 43 and 99).

Discussion

This study show as 13.9% frequency of shoulder pain among patients presenting to the Rheumatology and Physical Medicine Departments of the Ignace Deen National Hospital in Conakry, Guinea.

Jellad *et al*[7] reported a prevalence of 21.3% of shoulder pain. In the Physical Medicine Department of the University Hospital of Monastir in Tunisia. The lower rate in this study could be explained by a different selection process where we excluded cases of traumatic origin and also by the fact that in our setting many patients prefer to treat themselves at home.The lifetime prevalence of shoulder pain is 70%, and about 50% of people with shoulder pain will experience pain for more than a year[8].. However, other studies estimate the prevalence of shoulder pain to be between 6.9% and 26% depending on the population studied[2].

In this study these various shoulder conditions tend to affect the most active segment of the population, mainly women, cause chronic mechanical pain which is often intense and disabling.

The average age of our patients was 51.2 ± 14.25, with a predominance in the age range of 46 to 60 years. Maestroni *et al*[9] found a mean age of 49.6 ± 11.6. Thiel *et al*[10] and Farshid *et al*[11] in 2016 reported a mean age of 52.15 ± 11.82 and 52 ± 17 respectively. Indeed, there is a high exposure to wear and tear of shoulder structures after 40 years of age with an increase in the incidence of occurrence of shoulder pain with increasing age.

The results of this study are in agreement with the data in the literature[12,13], there was a predominance of women with a sex ratio of 0.9. This female predominance in our study could be explained by the simple fact that women have a greater sensitivity to pain[14-16] and also that they perform enough activity mobilizing the upper

limbs, particularly in household and daily tasks in our context of a developing country. This also corroborates the predominance of housewives in our study.

In this study, pain was severe in 41% with a mean VAS of 7.34. However, Farshid *et al*[17] and Azanmasso *et al*[13] reported a mean VAS of 5.3 ± 1.7 and 6.1 ± 2.7 respectively. This high pain intensity in our study could be explained by the fact that most of our patients neglect their pain and come at an advanced stage and wait until they have functional discomfort with mobilization to consult.

The combined rapid mobility test was positive in 77.4%. This could be due to the fact that the combined mobility test is the first test performed in front of any shoulder pain and it allows the detection of a limitation related to a shoulder injury and therefore the preferred test. Moreover, among the specific tests, the Neer test was the most positive in 16.1% of cases, which could be explained by the predominance of subacromial impingement in rotator cuff pathologies.

During our study, 52.6% of our patients underwent an ultrasound examination; our results are in disagreement with those of Smith *et al*[12] who used MRI in 76.7% of cases. This could be explained by the high cost of MRI in our context and also by the low income of the patients.

Rotator cuff injuries were the most common in 146 (67%). This was reported by Jellad *et al*[7] in 2011 who reported a predominance of rotator cuff pathologies with a frequency of 76.4%. In the same sense, Windt *et al*[8] stated that about 75% of shoulder pain is related to rotator cuff pathology. In fact, the diagnosis of rotator cuff damage is primarily clinical and due to the fact that in our context of developing countries we have a limited technical platform that does not allow access to the latest techniques of paraclinical exploration of the shoulder (arthrography, MRI). The treatment of our patients was essentially based on analgesics, in particular the combination of level I and II in 52.1% of cases, and physical therapy in 62.7% of cases for pathologies of abarticular and mechanical origin. For patients whose pain was of inflammatory origin, we combined analgesics, corticoids, antibiotics and colchicine or an immunosuppressant depending on the aetiology. For shoulder pain of neurological origin, we combined analgesics with tricyclic antidepressants.

Adhesive capsulitis (frozen shoulder) was our second most common diagnosis in 51 patients of whom 35 were diabetic.

The functional disability of our patients was evaluated by the Constant score with a mean of 76.69. Azanmasso *et al* [13] reported a mean score of 72.4 ± 18.87. There is a correlation found between age and the Constant score (P value = 0.01). The older the patient, the greater the impact of pain on quality of life.

Our study is one of the few studies to focus on shoulder pain in our context. Based on the frequency of consultation and the clinical characteristics of shoulder pain, it has allowed us to have a better knowledge of the pathologies involved and the therapeutic attitude to adopt in the face of shoulder pain. However, it must be emphasized that the relatively short duration of the study did not allow for the follow-up of patients over time and the evaluation of long-term therapeutic effectiveness.

Conclusion

This study showed that shoulder pain was frequent in the elderly, with a predominance of the female sex. It is often intense of mechanical type evolving most often towards chronicity and accompanied by a functional impotence, the treatment remains conservative associated with the taking of analgesic with a favorable evolution in the major part of the cases.

Declaration of interest

The authors declare that they have no conflict of interest.

References

1. Sarquis LMM, Coggon D, Ntani G, Walker-Bone K, *et al.* Classification of neck/shoulder pain in epidemiological research: a comparison of personal and occupational characteristics, disability, and prognosis among 12,195 workers from 18 countries. *Pain.* 2016; **157**(5) :1028-1036. doi: 10.1097/j.pain.0000000000000477.
2. Luime JJ, Koes BW, Hendriksen IJM, Burdorf A, Verhagen AP, Miedema HS, *et al.* Prevalence and incidence of shoulder pain in the general population; a systematic review. *Scand J Rheumatol*. 2004; **33**(2):73-81.
3. Master S, Burley S. Shoulder pain. *Aust Fam Physician*. 2007; **36**:414-416.
4. Patel RM, Gelber JD, Schickendantz MS. The weight-bearing shoulder. *J Am Acad Orthop Surg.* 2018; **26**(1):3-13. doi: 10.5435/JAAOS-D-15-00598.
5. Naidoo S, Kromhout H, London L, Naidoo RN, Burdorf A. Musculoskeletal pain in women working in small-scale agriculture in South Africa. *Am J Ind Med*. 2009; **52**(3) :202-209. doi: 10.1002/ajim.20662.

6. Greenberg DL. Evaluation and treatment of shoulder pain. *Med Clin North Am*. 2014; **98**(3):487-504. doi: 10.1016/j.mcna.2014.01.016.
7. Jellad A, Bouaziz MA, Salah S, Migaou H, Salah ZB. Epidémiologie de l'épaule douloureuse en milieu de médecine physique et réadaptation ambulatoire. *J de réadaptation M*éd. 2011; **31**:59-64.
8. Van Der Windt DA, Koes BW, de Jong BA, Bouter LM. Shoulder disorders in general practice: incidence, patient characteristics, and management. *Ann Rheum Dis.* 1995; **54**(12):959–964.
9. Maestroni L, Marelli M, Gritti M, Civera F, Rabey M. External rotator strength deficits in non-athletic people with rotator cuff related shoulder pain are not associated with pain intensity or disability levels. *Musculoskeletal Sci Practice*. 2020; **48:**: 102-156.
10. Libardoni TC, Armijo-Olivo S, Bevilaqua-Grossi D, de Oliveira AS. Relation between intensity of neck pain and disability and shoulder pain and disability in individuals with subacromial impingement symptoms: a cross-sectional study. *J Manipulative Physiol Ther*. 2020; **43**(7):691-699. doi: 10.1016/j.jmpt.2019.01.005. Epub 2020 Aug 26. PMID: 32861520.
11. Bagheri F, Ebrahimzadeh MH, Moradi A, Bidgoli HF. Factors associated with pain, disability and quality of life in patients suffering from frozen shoulder. *Arch Bone Jt Surg*. 2016; **4**(3):243-247. PMID: 27517070; PMCID: PMC4969371.
12. Smith A, Rathi S, Pavlora N, Littlewood C, Corneil D, Haines T, *et al.* Self-reported management among people with rotator cuff related shoulder pain: An observational study. *Musculoskeletal Sci Practice.* 2021; **51**: 102-305.
13. Azanmasso H, Zahi S, Kpadonou TG, Dedjan, Lola A, Alagnide E, *et al.* Caractéristiques des troubles musculosquelettiques de l'épaule du patient diabétique au Maroc. *J de réadaptation M*éd. 2014; **34**: 66-72.
14. Riley JL, Robinson ME, Wise EA, Myers CD, Fillingim RB. Sex differences in the perception of noxious experimental stimuli: a meta-analysis. *Pain*. 1998; **74**:181–187.
15. Ge HY, Madeleine P, Arendt-Nielsen L. Sex differences in temporal characteristics of descending inhibitory control: an evaluation using repeated bilateral experimental induction of muscle pain. *Pain*. 2004; **110**:72–78.
16. Lucas P. Epaule hémiplégique mécanique *Kinesither Rev.* 2017; **17**(182):4–8.
17. Farshid N, Akshat S, Navindran N, Ulvi U B, Allan M. Does irrigation of the subdiaphragmatic region with ropivacaine reduce the incidence of right shoulder tip pain after laparoscopic cholecystectomy? A prospective randomized, double-blind, controlled study. *Am Surg.* 2014**;** **80**(1): E17-18.

Knee pain in outpatient at the National Hospital Ignace Deen, Conakry, Guinea

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Abstract

Background: Knee pain is a common complaint in primary care.
Objective: The aim of this study was to determine the profile of knee pain at the Ignace Deen National Hospital (HNID) in Conakry, Guinea.
Design: This was a two year descriptive prospective study.
Methods: All patients who had consulted for a knee pain were included.
Results: Knee pain represented 4.1% of the reasons for consultation. The average age was 53.8 years with extremes of 4 and 88 years. We noted a female predominance at 53.83% with a sex ratio H/F: 0.8. Axial disorders of the lower limbs accounted for 58.6% of knee pain risk factors. The mean intensity of pain (VAS) was 58.2mm with extremes of 20 and 80mm. Standard radiography was the most performed balance (63.4%). Knee osteoarthritis was the most common condition in 50.9% of cases. The level I analgesic treatment was the most prescribed at 69.7%. The average Lequesne index was 6.7 with extremes of 1 and 15.
Conclusions: Knee pain remains a public health problem, particularly in developing countries. In our study the risk factors were dominated by age, overweight and axial deformities with a female predominance. Knee pain is becoming increasingly important in Guinea. This study has enabled us to identify the various knee pathologies that are most frequent in our context and has the merit of being one of the first studies to describe the profile of knee pain in sub-Saharan Africa.

Key words: Knee pain, Knee osteoarthritis, Outpatient, Guinea

Introduction

Knee pain is defined as pain in the knee area, either mechanical or inflammatory in origin. Knee pain is a common complaint in primary care and is more common in physically active people than in sedentary populations[1]. The prevalence of knee pain is 22.7% in the general population and 7.2% in adolescents[2-4]. These numbers differ between studies, reaching up to 6% of all primary care consultations[5]. In Africa, in Togo in 2015, the reported frequency of knee pain was 23%[6]. In South Africa, a study of high school basketball players found a prevalence of 13% and 16% respectively for girls and boys[7]. In Cameroon, in a study of knee osteoarthritis, 100% of patients presented with knee pain[8]. Thus the aim was to determine the profile of knee pain at the Ignace Deen National Hospital in Conakry.

Materials and methods

This was a prospective descriptive study lasting two years from 1st October 2018 to 31st September 2020, conducted in the Rheumatology and Physical and Rehabilitation Medicine Departments of the Ignace Deen National Hospital which are reference centers for the management of musculoskeletal pathologies in Guinea. Our study included all patients seen for knee pain. All patients with traumatic knee pain or post-surgical origin and patients with knee prostheses were excluded.

The following data were collected;

Age, sex

Risk factors: Deformity of the lower limbs; intense sports activity involving lower limb action eg running; history of knee trauma; carrying of heavy loads; wearing of high-heeled shoes, kneeling at work.

The ratio of weight (kg) to height squared (m²) was used to calculate the body mass index; overweight was

defined as a Body Mass Index (BMI) greater than 25 kg/m² and obesity BMI greater than 30 kg/m².

Clinical data: Date of onset and duration of symptoms location of pain and intensity using 100 mm: Visual Analog Scale (VAS) minimal VAS 10-30 mm; moderate 30- 50 mm; intense 50-70 mm and very intense greater than 70. Clinical examination patello-femoral joint (Rabot sign) , patellar tap for joint fluid lower limb deformities (genu valgum varum and recurvatum and flexion deformity periarticular lesions Iiotibial band syndrome prepatellar popliteal and pes anserinus/crows foot bursa.

Laboratory investigations C-reactive protein; CRP sedimentation rate; (SV) uric acid; cyclic antibodies citrullinated peptides and rheumatoid factor RF. Aspiration and examination of fluid from swollen knee joint for cell count monosodium urate and calcium pyrophosphate dihydrate crystals gram stain and culture for bacteriae standard radiography and ultrasonography. Knee osteoarthritis classified according to the Kellgren and Lawrence scale. Analgesics non steroidal anti inflammatory drugs disease modifying drugs for RA and standard drugs for gout, physiotherapy was employed where appropriate. Quality of life was assessed with the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) and Lequesne index. Informed consent was obtained from the patients before they were subjected to our questionnaires. All data were collected on a survey form and processed by Epi Info. For categorical variables the Chi-square test was calculated and any difference associated with a probability value (p) less than 0.05 was considered statistically significant.

Results

During the study 208/5024 patients presented with knee pain, (4.1%.), socio demographic and clinical details are listed in Table 1. Of these 208 patients, 112 (53.8%) were women. The average age was 53.8±16.5 years axial deformities of the lower limbs were found in 122 (58.6%) patients carrying heavy loads 69 (33.1%) patients and a family history of knee pain in 40 patients (19.2%). The mean duration to diagnosis was 10.5 ± 21.8 months Bilateral knee pain was noted in 107 (51.4%) patients with a progressive onset in 163 (78.3%) patients anterior knee pain was located in 170 (81.7%) patients. The average VAS was 58.2±10.4mm, severe in 94 (45.1%) patients and moderate in 70 (33.6%). The average BMI was 25.7± 3.3 kg/m² with approximately one third of patients were (30.7%) overweight and 9.1% obese. Standard knee radiography was performed in 162 patients (77.8% of cases); joint fluid analysis in 86 (41.3%) patients. Bacteriae and a raised white cell count were found in 10 (11.6%) joint fluids Microcrystals were found in 32 (15.3%) patients with calcium pyrophosphate dehydrate crystals in 14 (6.6%) patients and monosodium urate crystals in 18 (8.7%) patients. The most common diagnosis was osteoarthritis in 106 (50.9%) patients followed by rheumatoid arthritis in 28 (13.4%) patients and gout in 22 (10.5%) (Table1). The Kellgren and Lawrence OA classification grades were grade II 25.9%, grade III 17.3% and grade IV 7.7% of cases: NSAIDs: were used in 34.6%; paracetamol: 23%; NSAIDs + paracetamol: 12%); Corticosteroid injection infiltration (46.6% of cases); slow-acting anti-rheumatic and antibiotics (in 33.6% and 14.4%respectively). The mean Lequesne index was 6.7±2.1 range `1-15 functional disability was moderate in 111 patients (53.3% of cases) and severe in 58 patients (27.8% of cases). The mean WOMAC index was 44.7±12 range 14 -76.. Risk factors associated with knee pain are presented in Table 2. Age, gender and axial limb deformities were statistically significant in the chi-square test.

Table 1: Distribution of patients according to socio-demographic and clinical data

Variables	All patients (N = 208)
Socio-demographic data	
Gender, female, n (%)	112 (53.8)
Age at diagnosis Mean (SD years)	53.8±16.5
Deformity of lower limbs, n (%)	122(58.6)
BMI at diagnosis Mean ± SD	25.7 ± 3.3
Clinical data	
Mechanical pain, n (%)	142 (68.2)
Bilateral, n (%)	107 (51.4)
Mechanism of onset, unknown, n (%)	180 (86.5)
VAS, mm mean ±SD	58.2 ± 10.4
Mean time from first symptoms to consultation (months)	10.5 ± 21.8
Physical sign, Rabot sign, n (%)	152 (73)
X-ray, n (%)	162 (77.8)
CRP[a] (mg/dl) mean± SD	40 ± 26.3
SV[b] (mm/hour) mean± SD	28.2± 5
Uric acid (mg/dl) mean ± SD	2.6±1.6
Joint fluid microcrystals, monosodium urate, n (%)	18 (8.7)
Kellgren and Lawrence, grade II, n (%)	54 (25.9)
Level I analgesic, n (%)	145 (69.7)
Corticosteroid infusions, n (%)	97 (46.6)
Physical therapy, n (%)	16 (7.6)
Lequesne Index	6.7±2.1
WOMAC[c] Index	44.7±12.4

[a]CRP C-reactive protein[b] SV sedimentation rate
[c]WOMAC Western Ontario and McMaster universities osteoarthritis index

Figure 1: Distribution of patients by diagnosis

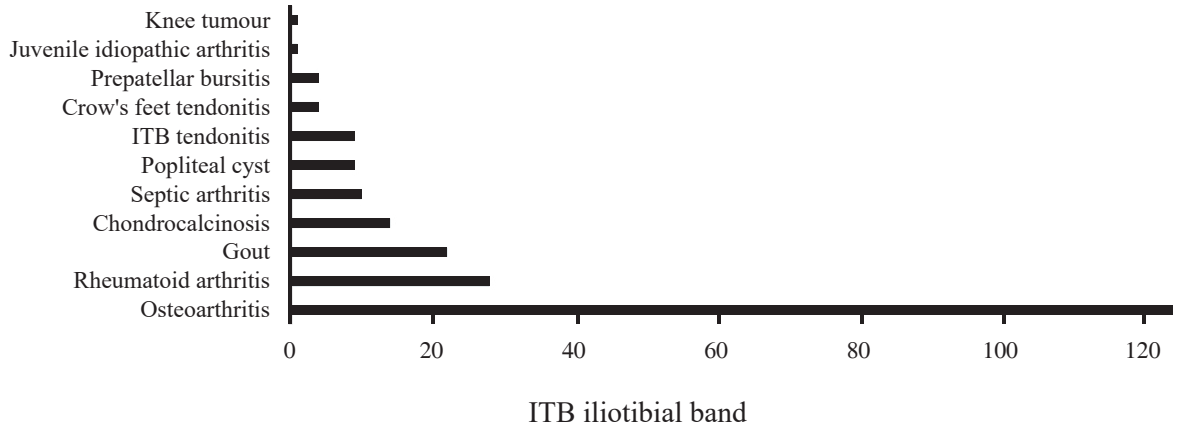

Table 2: Factors associated with knee pain (chi-square test)

Variables	Frequency	P-value
Gender		
Female	112 (53.8%)	0.06
Male	96 (46.1%)	
Age range (years)		
4 - 23	10 (4.8%)	
24 - 43	55(26.4%)	
44 - 63	95 (45.1%)	0.03
64 - 83	47 (22.6%)	
>83	2 (0.9%)	
Body mass index		
Underweight (<18.5)	1 (0.4%)	
Normal weight (18.5 - 24.99)	57 (27.4%)	
Overweight (25 - 29.99)	64 (30.7%)	0.035
Obese (>30)	19 (9.1%)	
Risk factors		
Deformity of the L[l]a	122 (58.6%)	0.005
Heavy load carrying	69 (33.1%)	
Intense sports activity	10 (4.8%)	
Menopause	22 (10.5%)	
Wearing high-heeled shoes	20 (16.8%)	
Obesity	19 (9.1%)	
Knee-jerk work	2 (0.9%)	

[a]L I Lower limb

Discussion

This study shows that knee pain occupies an important place in outpatient population at the Ignace Deen National Hospital with a frequency of 4.1%. Overweight, limb deformities and carrying heavy loads were the main risk factors found in our study. This was a hospital-based study involving only patients seen in the Rheumatology, Physical and Rehabilitation Medicine Departments, which are the two reference centers for the medical management of musculoskeletal pathologies in Guinea.

The average age at time of diagnosis of our patients was 53.8 years similar to 55 years as reported by Ouédraogo *et al* [9] in Burkina Faso but lower than 58.9 years as reported by Lukusa *et al*[10]

in Congo. Knee pain is associated with an active population linked to injuries due to overwork or knee trauma[11–14]. Our female prevalence at 53.8% is lower than Togo (63%)[15], but much higher on the other hand, than Niger where a male predominance of 61.8% with a sex ratio of 1.62[16]. The predominance of women with knee pain is in part explained by changes at the menopause and excess weight[9,17,18].

The most common cause of pain was mechanical (68.2%) similar to that detected in Madagascar[17] and due mainly to degenerative causes associated with osteoarthritis. We recorded a wide range of intraarticular and periarticular disorders but osteoarthritis was the most common (50.9%) and reflecting worldwide data[20 -23].

Risk factors were dominated by age (p=0.03), overweight (p=0.035), and deformities of the lower limbs (p=0.005). Ouédraogo *et al*[9] in 2008 in Burkina Faso found a mean BMI of 29.5, while Lukusa *et al*[10] in Congo found a mean BMI of 27.9. All these factors contribute to increased biomechanical stress on the knee[19].

In our study the mean VAS was 58.2 severe in almost half and moderate in one third of patients. Samison *et al*[17] reported pain of moderate intensity in 75.5% of cases with a mean VAS of 57.9 mm. However, Owonayo *et al*[24] in Togo reported moderate pain in 31.9% of patients.

In our study, moderate disability was the most frequent with a mean Lequesne index of 6.7±2.1 This is different from the data of Akinpelu *et al*[25] who in their 2009 study on osteoarthritis found extremely severe disability in 35.1% and Ouédraogo *et al*[9] who reported a frequency of 49.2% of very severe disability. This difference could be explained by a moderate Kelgren/Lawrence grade II in our study and the fact that the majority of our patients were active and consulted sooner before disability became severe and hindered their professional activities

Study limitations

The limitations of our study were the size of the sample and the difficulties in performing certain complementary examinations such as MRI. However, this study has the merit of being the first study on the profile of knee pain in Africa.

Conclusion

Knee pain remains a public health problem, particularly in developing countries. In our study the risk factors were dominated by age, overweight and limb deformities with a female predominance. Osteoarthritis was the most frequent aetiology. Further studies are needed to better characterize the profile of these patients in Africa.

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References

1. Kermode T, Cornuz J, Zufferey P, Pasche O. Gonalgies: que faire en médecine de premier recours? [Knee pain in ambulatory practice]. *Rev Med Suisse*. 2014;**10**(452):2238 - 40.
2. Smith BE, Selfe J, Thacker D, Hendrick P, Bateman M, Moffatt F, *et al*. Incidence and prevalence of patellofemoral pain: A systematic review and meta-analysis. *Plos One.* 2018; **13**:0190892.
3. Tuite M, Daffner R, Weissman B, Bancroft L, Bennett D, Blebea J, *et al*. ACR appropriateness criteria acute trauma to the knee. *J Am Coll Radiol*. 2012; **9**:96–103.
4. Florent Gamain. Analyse de pratiques professionnelles concernant la prescription d'IRM du genou dans une population ambulatoire présentant une gonalgie. *Médecine Humaine et Pathologie*. 2018. □dumas-01878787□.
5. Jackson JL, O'Malley PG, Kroenke K. Evaluation of acute knee pain in primary care. *Ann Intern Med.* 2003;**139**:575.
6. Adigo, A, Adjénou KV. Apport de l'IRM dans le diagnostic des pathologies du genou. Revue du CAMES. *Science de la Santé.* 2015; **3**(1): 85.
7. Louw Q. Prevalence of anterior knee pain among young South African basketball players. *South Afr J Physiother* 2003; **59**:20–23.
8. Doualla-Bijaet M, Ngandeu M, Farikou I, Namme Luma H , Tafam Gueleko E , Temfack E *et al.* Aspects cliniques et radiographiques de l'arthrose des genoux à Douala (Cameroun). *J Afr Imag* Méd. 2014; **6**(3):41-49.
9. Ouedraogo Dd, Séogo H, Cissé R, Tiéno H, Ouédraogo T, Nacoulma I, *et al*. Facteurs de risque associés à la gonarthrose en consultation de rhumatologie à Ouagadougou (Burkina Faso). *Med Trop.* 2008; **68**:597- 599.
10. Lukusa A, Malemba J-J, Lebughe P, Akilimali P, Mbuyi-Muamba J-M. Clinical and radiological features of knee osteoarthritis in patients attending the university hospital of Kinshasa, Democratic Republic of Congo. *Pan Afr Med J*. 2019; **34**:29.

11. Job-Deslandre C. Démarche diagnostique des gonalgies chez l'enfant et l'adolescent. *Rev Rhum* 2006; **73**:603–608.
12. Fernandez-Lopez J, Laffon A, Blanco F, Carmona L**.** Prevalence, risk factors, and impact of knee pain suggesting osteoarthritis in Spain. *Clin Exper Rheumatol*. 2008; **26**: 324-332.
13. Legré-Boyer V, Boyer *ET*. Examen clinique d'un genou douloureux. *Rev Rhum Monogr.* 2016; **83**:133–137
14. Aagesen A, Melek M. Choosing the right diagnostic imaging modality in musculoskeletal diagnosis. *Prim Care Clin Off Pract*. 2013; **40**:849–861.
15. Agoda-Koussema LK, Oniankitan O, Abalo GA, Ouro-Kefia DD, N'Dakena KG. Radiographie standard dans les gonalgies non traumatiques aux CHU Tokoin et Campus de Lome. *Mali Med*. 2012; TOME XXVII No. 1: Page 3.
16. Assadeck H, Daouda MT, Djibo FH, Maiga DD, Omar EA. Prevalence and characteristics of chronic pain: Experience of Niger. *Scand J Pain.* 2017; **17**:252–255.
17. Samison LH, Randriatsarafara FM, Ralandison S. Joint pain epidemiology and analgesic usage in Madagascar. *Pan Afr Med J*. 2017; **26**: 77. doi: 10.11604/pamj.2017.26.77.11215. PMID: 28491208; PMCID: PMC5410003.
18. Jones B, Covey C, Marvin Sineath J**.** Nonsurgical management of knee pain in adults. *Am Fam Physician*. 2015; **92**:875–883.
19. Green ST. Syndrome fémoropatellaire : prise en charge clinique. *EMC – Kinésithérapie*. 2005; **1**:101–111.
20. Battu V. Pathologies du genou : appareillage. *Actual Pharm*. 2017; **56**:55–8.
21. Jamard B, Verrouil E, Mazières B. Formes cliniques de la gonarthrose. *Rev Rhum.* 2000; **67**:149–153.
22. Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, *et al.* Prevalence of knee symptoms and radiographic and symptomatic knee osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. *J Rheumatol*. 2007; **34**(1):172-180.
23. Xu X, Yao C, Wu R, Yan W, Yao Y, Song K, *et al*. Prevalence of patellofemoral pain and knee pain in the general population of Chinese young adults: a community-based questionnaire survey. *BMC Musculoskelet Disord*. 2018; **19**:165.
24. Owonayo O, Eyram F, Agoda-Koussema LK, Sika VE, Cyrille TK, Prénam H, *et al.* Facteurs de risque de la gonarthrose en consultation rhumatologique à Lomé (Togo). *Mali Médical.* 2009; **24** (2):.
25. Akinpelu AO, Alonge TO, Adekanla BA, Odole AC. Prevalence and pattern of symptomatic knee osteoarthritis in Nigeria: A community-based study. *The Internet J Allied Health Sci Practice*. 2009; **7**(3): Article 10.

Profiles of Sjögren's syndrome in rheumatologic consultation in Guinea

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Abstract

Background: Sjögren Syndrome (SS) is a chronic autoimmune epithelitis, characterised by lymphocytic infiltration of the exocrine glands, mainly lacrimal and salivary. It is the second autoimmune disease after Rheumatoid Arthritis (RA). This connectivitis has not been studied extensively in sub-Saharan Africa.
Objective: To determine the epidemiological, clinical, paraclinical and therapeutic characteristics of SS in Guinea.
Design: Descriptive cross-sectional study.
Methods: The study involved all hospitalised and/or consulted patients in the Rheumatology Department of the Ignace Deen National Hospital, Conakry, Guinea from 1st March 2019 to 31st August 2020. Patients with Sjogren's syndrome meeting the 2002 AECG criteria were included in the study. Patients were divided according to the presence of primary Sjögren's syndrome (SSp) or secondary Sjögren's syndrome (SSs).
Results: Thirty-one patients recruited, who included 27 (87.1%) women, for a hospital prevalence of 3.9%. The middle age was 53.2 ± 14.6 years. The average diagnostic delay of SS was 6 ± 3.1 years. Clinic manifestations were dominated by ocular and oral sicca syndrome (100%), and arthralgia (77.4%). Neither renal involvement nor cutaneous vasculitis was noted in this study. However, one case of lymphomatous transformation was reported during regular follow-up. The immunological profile showed SSA-positive antibodies in 19.4% of cases and SSB-positive antibodies in 32.3% of cases. Schirmer's test was positive in 15 (48.4% patients. Labial Salivary Gland Biopsy (LSGB) was contributive in 17 (54.8%) patients, of which eight were at stage 3 of Chisholm and Mason (25.8%) and nine were at stage 4 of Chisholm and Mason (29.0%). SSp was diagnosed in 38.7% of patients against 61.3% with SSs, mainly in a context of RA (78.9%). Therapeutically, all patients received hydroxychloroquine and 74.2% of patients were treated by methotrexate. The ESSPRI score at admission showed unbearable symptoms in most patients and the ESSDAI score showed moderate disease activity in 38.5% of cases.
Conclusion: Sjögren Syndrome (SS) was frequent in hospital consultations and dominated by secondary SS. More detailed studies would make it possible to better describe all aspects.

Key words: Sjögren syndrome, Connectivitis, ESSPRI, ESSDAI, Sub-Saharan Africa, Guinea

Introduction

Sjögren Syndrome (SS) is a chronic connective tissue disease in which we observe progressive and irreversible damage to the exocrine glands, mainly the salivary and lachrymal glands[1]. It is, after Rheumatoid Arthritis (RA), the second most common autoimmune disease with an estimated frequency between 0.3 to 5%[2]. SS can present in two forms: it is classified as primary Sjögren syndrome (SSp) when it is isolated, and secondary Sjögren syndrome (SSs) when it is associated with another autoimmune disease[3,4]. SS has a strong female propensity with a sex ratio of 9F / 1H and a peak frequency estimated around 50[1, 2]. SS is accompanied by the expression of autoantibodies. Anti-SSA/Ro and anti-SSB/La antibodies play a role in the diagnosis of the disease and in predicting of their outcomes[5]. Patients with isolated anti-SSB antibodies are reported to have a relatively low frequency of the most severe organ

damage[6]. Treatment is primarily aimed at reducing symptoms and avoiding complications[7]. Systemic treatment is only used in cases of extra-glandular involvement[8,9]. New guidelines have been developed by the European League Against Rheumatism (EULAR) for the management of local and systemic manifestations[10]. Studies in sub-Saharan Africa reported low prevalence of Sjögren's syndrome with 2.4% in Burkina Faso [11] and 4.4% in Senegal[12]. The objective of this study was to determine the prevalence of Sjögren's syndrome in Conakry, Guinea.

Materials and methods

This was a descriptive cross-sectional study over 18 months, from November 1st, 2017 to May 31st, 2019. The study involved all hospitalised and/or consulted patients in the Department of Rheumatology of the Ignace Deen National Hospital in Conakry, Guinea, diagnosed with primary or secondary Sjögren's Syndrome meeting the criteria of the American European Consensus Group (AECG) of 2002[5]. The data collected were:

(i) Epidemiological (age, sex, diagnostic delay, medical history).
(ii) Clinical (fatigue, xerostomia, xerophtalmia, arthritis, arthralgia, saprodontia, dysguesia, neurological involvement).
(iii) Paraclinical including biological features (Erythrocyte sedimentation rate, C reactive protein, serum protein electrophoresis, complete blood count, rheumatoid factor, Ro/SSA, La/SSB antibodies, anti-CCP, Schirmer test). The labial salivary gland biopsy specified the degree of salivary gland infiltration (Grade 3 or 4 of Chisholm and Mason scoring system).
(iv) *Therapeutic:* Hygiene and dietary measures, symptomatic and background treatment.
(v) *Evolutionary*: The disease activity was evaluated by the ESSDAI (Eular Sjögren Syndrome Disease Activity Index). The functional impact was assessed by the ESSPRI (Eular Sjögren's Syndrome Patient Reported Index). For ESSDAI, a score of 0 indicated remission, a score between 1 to 4 (inclusive) indicated low activity, a score between 5 to 13 (inclusive) indicated moderate activity and a score of 14 or more indicated high activity. For ESSPRI, we defined mild symptomatology for a score of 0 to 5 and unbearable symptomatology for a score of 6 to 10.

The data were analysed with Epi Info 7.1.5.2. The results were expressed in number, frequency, median ± standard deviation and median.

Results

The study included 31 cases of SS out of 799 patients, for a hospital prevalence of 3.9%. Majority of patients were female (n=27, 87.1%) with a sex ratio of 6/1. The mean age was 53.2 ± 14.6 years. The average diagnostic delay was 6 ± 3.1 years (range 0.5 and 25 years). The main clinical manifestations are shown in Table 1. Secondary SS was associated to rheumatoid arthritis (n=15, 78.9%), systemic lupus erythematosus (n=2, 10.5%), Biermer's disease (n=1, 5.3%) and leucoderma (n=1, 5.3%). Xerophthalmia, xerostomia and joint involvement (arthritis and arthralgia) were observed in all our patients. Fatigue was almost constant (90.3%). Four patients presented a peripheral neurological involvement. Neither renal involvement nor cutaneous vasculitis was noted. However, a case of lymphomatous transformation was reported during regular follow-up.

Table 1: Clinical characteristics of patients suffering from Sjögren's syndrome

	No.	(%)
Medical history		
High blood pressure	8	25.8
Family history of rheumatic disease	6	19.4
Diabetes	4	12.9
Renal failure	2	6.5
Clinical features		
Xerostomia	31	100
Xerophthalmia	31	100
Fatigue	28	90.3
Arthralgia	24	77.4
Saprodontia	21	67.8
Arthritis	7	22.6
Dysguesia	7	22.6
Neurological involvement	4	16.1
Types of Sjögren's syndrome		
Primary Sjögren's syndrome	12	38.7
Secondary Sjögren's syndrome	19	61.3

Inflammation blood test was positive with an accelerated ESR (80.6%), a positive CRP (67.6%) and hypergammaglobulinemia (25.8%). Immunological features were also positive: RF (58.1%), anti-CCP (29.0%), Ro/SSA antibodies (19.4%) and La/SSB antibodies (32.3%). Fifteen patients had a positive Schirmer test (48.4%). The labial salivary gland biopsy was contributive to the diagnosis for 17 patients (54.9%) with 8 at grade 3 (25.8%) and 9 at grade 4 (29.0%) from Chisholm and Mason scoring system. These main paraclinical features are shown in Table 2.

Table 2: Paraclinical characteristics of patients with Sjögren's syndrome

	No.	(%)
ESR accelerated	25	80.6
CRP positive	21	67.8
Anaemia	19	61.3
Schirmer's test positive	15	48.4
Polyclonal hypergammaglobulinemia	8	25.8
Hyperleukocytosis	6	19.3
Immunology		
Rheumatoid factor positive	18	58.1
La/SSB positive	10	32.3
Anti-CCP positive	10	29.0
Ro/SSA positive	6	19.4
Labial salivary gland biopsy		
Grade 3	8	25.8
Grade 4	9	29.0

ESR: Erythrocyte Sedimentation Rate; CRP: C Reactive Protein; Anti-CCP: anti-Cyclical Citrullinated Peptide

Hygiene and dietary measures were prescribed for 38.7% of patients (sufficient hydration, regular dental hygiene and control, non-cariogenic diet). Most patients were treated with DMARDs, in particular hydroxychloroquine (100%) and methotrexate (74.2%), while 67.7% of patients received oral route and / or local corticosteroids either as monotherapy or in association with DMARDs. None of the patients received biotherapy due to its unavailability in our region. The outcome of the treatment was considered favorable for the majority of our patients. However there was a case of death. The majority of our patients had a favourable evolution under treatment. There was one case of death. These results are shown in Table 3.

Table 3: Treatment and evolution of patients suffering of Sjögren's syndrome

	No.	(%)
Hydroxychloroquine	31	100
Methotrexate	23	74.2
Oral and local corticosteroids	21	67.7
Hygiene and dietary measures	12	38.7
Analgesics	10	36.3
Evolving modalities		
Stabilization	26	83.9
Relapse	4	12.9
Complication	1	3.2

The ESSPRI score at admission showed unbearable symptomatology in most patients (Table 4) and the ESSDAI score showed moderate disease activity in 38.5% of cases (Table 5).

Table 4: ESSDAI features outcome measures in patients with Sjögren's syndrome

	Median	Standard deviation
Dryness		
[0 – 5]	2.4	± 1.8
[6 – 10]	6.5	± 0.7
Fatigue		
[0 – 5]	4.5	± 0.7
[6 – 10]	7.8	± 1.3
Pain		
[0 – 5]	2.5	± 2.1
[6 – 10]	7.6	± 1.1

Table 5: ESSDAI results in patients with patients with primary Sjögren's syndrome

	No	(%)
Remission	3	23,1
Low activity	4	30,7
Moderate activity	5	38,5
High activity	1	7,7

Median: 5.3 ± 5.6
Range: 0 and 19

Discussion

The study reported 31 cases of SS over a period of 18 months. Despite some methodological bias linked to the small sample, the hospital-based study and the under-equipped laboratories, it appears that Sjögren's syndrome represents a relatively low number of consultation in our series (3.9%) which is lower to the literature reported [12,14]. This relative rarity could be explained in our context by a lack of knowledge of this pathology due to the lack of specialists (internists, rheumatologists, etc.) and the difficult access to diagnostic means, particularly immunological, which are expensive for the population. The mean age (53.16 ± 14.6 years) was similar to those of Diallo *et al*[12] in Senegal (50 years old) and Rihani *et al*[15] in Morocco (48 years old). It differs from the data reported in France[16] where the mean age was 65 years. This relative youthfulness in African studies only reflects the general demography of developing countries. The female predominance in this study (n=27, 87.1%) is classic in SS as noted in African and Western studies [12,16-18] and could be explained by a hormonal involvement. However, this predominance attenuates at the older ages with an equal number of cases between men and women[4].

A long average diagnostic delay was also reported in Algeria[19] (7.5 ± 5.1 years) and in Senegal[12] (7 years). It could be the result of various factors including the delay in the consultation, the lack of knowledge of the disease by some practitioners, a limited technical platform. As noted in the study, the data collected in France[16] and in Senegal[12] showed a high frequency of sicca syndrome followed by articular involvement. The salivary and lachrymal glands are the main target of SS[4] and the joints are often involved in the extra-glandular manifestations of SS[20,21]. The frequent association between SS and rheumatoid arthritis (78.9%) is common[15,22,23]. Although lower than in the literature[15,24,25], the Schirmer test was positive in 48.4%. It remains the major diagnostic tool for dry eye. The results of the LGSB were lower than those found in 2020 in Senegal[14]. This could be explained by the fact that in that study, LGSB was more accessible as it was performed in the same hospital. Immunologically, autoantibodies were not systematically requested due to their high cost. The results found were inferior to those from Tunisia[26]. The use of low-dose corticosteroids for symptomatic treatment was justified by the high frequency of joint involvement in the study and corroborated the data of Benasr *et al*[27], where 100% of their patients received symptomatic treatment, including 63.5% of corticosteroids. Hydroxychloroquine, as first line of background treatment, was administered in only 18% of cases in the Moroccan study[15]. This difference may be due to the fact that hydroxychloroquine, which is more accessible in our context, allows the management of a wide range of extra-glandular manifestations and is preferred to methotrexate in women with a desire to have children. Contraception was a measure that was not adhered to by patients. The mean ESSPRI score is consistent with the Spanish data[28]. The use of this score as a predictor of health[29] and the ESSDAI score to assess systemic SS activity[30] highlighted the consequences of delay in consultation and delay in diagnosis.

Conclusion

Sjögren Syndrome (SS) was common in hospital consultations and dominated by secondary SS. The significant diagnostic delay underlines the need to sensitize practitioners in order to improve the prognosis of this condition. Larger cohort studies would give a better picture of this disease in Guinea.

References

1. Patel R, Shahane A. The epidemiology of Sjogren's syndrome. *Clin Epidemiol*. 2014; **6**:247-255.
2. Westhoff G, Zink A. Epidemiology of primary Sjögren's syndrome. *Z Rheumatol*. 2010; **69**(1):41-49.
3. Ramos-Casals R, Brito-Zerón P, Sisó-Almirall A, Bosch X. Primary Sjögren syndrome. *BMJ*. 2012; **344**:3815-21.
4. Jonsson R, Vogelsang P, Volchenkov R, Espinosa A, Wahren-Herlenius M, Appel S. The complexity of Sjögren's syndrome: Novel aspects on pathogenesis. *Immunol Lett.* 2011; **14**1(1):1-9.
5. Brito-Zerón P, Ramos-Casals M, Bove A, Sentis J, Font J. Predicting adverse outcomes in primary Sjögren syndrome: identification of prognostic factors. *Rheumatol.* 2007; **46**(8):1359-62
6. Acar-Denizli N, Horváth IF, Mandl T, Priori R, Vissink A, Hernandez-Molina G *et al.* Systemic phenotype related to primary. Sjögren's syndrome in 279 patients carrying isolated anti-La/SSB antibodies. *Clin Exp Rheumatol.* 2020; **126 (**Suppl 126):85-94.
7. Saraux A, Pers J-O, Devauchelle-Pensec V. Treatment of primary Sjögren syndrome. *Nat Rev Rheumatol.* 2016; **12**(8):456-471.
8. Aeby M, Maurer B, Distler O. Le syndrome de Sjögren primaire, une maladie systémique : partie 2. *Forum Med Suisse*. 2017; **17**(48): 1063-66.

9. Vivino FB, Carsons SE, Foulks G, Daniels TE, Parke A, Brennan MT, *et al.* New Treatment Guidelines for Sjögren's Disease. *Rheum Dis Clin North Am.* 2016; **42**(3):531-551.
10. Ramos-Casals M, Brito-Zerón P, Bombardieri S, Bootsma H, De Vita S, Dörner T *et al*. EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies. *Ann Rheum Dis*. 2020; **79**(1):3-18.
11. Ouédraogo D-D, Korsaga-Somé N, Zabsonné Tiendrébéogo J, Tiéno H, Kaboré H, Niamba P, *et al.* Les connectivites en pratique hospitalière à Ouagadougou (Burkina Faso). *Med Sante Trop.* 2014; **24**(3):271-274.
12. Diallo S, Niasse M, Diaw CAB, Diallo R, Diouf C. Syndrome de Gougerot-Sjögren: étude préliminaire de 266 observations au Sénégal. *Revue du Rhumatisme.* 2016; **83**:266-267.
13. Vitali C, Bombardieri S, Jonsonn R, Moustopoulos HM, Alexander EL, Carsons SE, *et al*. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Ann Rheum Dis.* 2002; **61**(6):554-558
14. Garba MS, Niasse M, Conde K, Diouf C, Diallo S. Le Syndrome de Sjögren : aspects épidémiologiques, diagnostiques, thérapeutiques et évolutifs au CHU Aristide-Le-Dantec de Dakar, Senegal (2012-2016). *Bull Soc Pathol Exot.* 2020; **113**(3):136-142.
15. Rihani N, Echchilali K, Bouissar W, Moudatir M, Alaoui FZ, El Kabli H. Le syndrome de Sjögren primitif: expérience d'un service de médecine interne (139 cas). *Rev Med Interne*. 2015; **36**:154-155.
16. Meckenstock R, Sakarovitch B, Monnier S, Devred I, Greder-Belan A. Syndrome de Gougerot-Sjögren et co-morbidités dans une série de 41 patients. *Rev Med Interne*. 2019; **40**:128.
17. Mijiyawa M, Amanga K, Oniankitan OI, Pitché P, Tchangaï-Walla K. Les connectivites en consultation hospitalière à Lomé (Togo). *Rev Med Interne.* 1999; **20**(1): 13-17.
18. Bel Feki N, Fkihi A, Velmans N. Le Syndrome de Gougerot Sjögren. Une étude monocentrique de 66cas. *Rev Med Interne*. 2016; **37**:159-160.
19. Taharboucht S , Kessal F, Mammeri A, Hamrour F, Hatri A, Hocine O, *et al.* Les manifestations extra-glandulaires du Gougerot-Sjögren: une étude descriptive. *Rev med interne.* 2015; **36**:155-156.
20. Aeby M, Maurer B, Distler O. Le syndrome de Sjögren primaire, une maladie systémique : partie 1. *Forum Med Suisse.* 2017; **17**(47):1027-38.
21. Brito-Zerón P, Baldini C, Bootsama H, Bowman SJ, Jonsson R, Mariette X, *et al.* Sjögren syndrome. *Nat Rev Dis Primers.* 2016; **2**:16047.
22. Niasse M, Kane BS, Ndiaye AA, Ndao AC, Djiba B, Automne S, *et al.* Severity of the rheumatoid arthritis in sub-Saharan Africa: Study of 403 Senegalese Observations. *Open J Intern Med*. 2017; **7**(4):151-159.
23. Najah S, Lamrani F, Moudatir M, Ettaldi N, Jabbouri R, Alaoui FZ, *et al*. Le syndrome de Gougerot-Sjögren secondaire. 136 cas. *Rev Med Interne*. 2010; **31**:434.
24. Zhao Y, Li Y, Wang L, Li X-F, Huang C-B, Wang G-C, *et al*. Primary Sjögren Syndrome in Han Chinese: clinical and immunological characteristics of 483 patients. *Medicine*. 2015; **94**(16):660-667.
25. Chebbi W, Ben Salem W, Klii R, Kessomtini W, Jerbi S, Sfar MH. Syndrome de Gougerot-Sjögren primitif du sujet âgé : caractéristiques cliniques et immunologiques. *Pan Afr Med J.* 2015; **20**(8):1-7.
26. Ben Salem T, Tourgoti M, Ben Ghorbel I, Houman MH. Caractéristiques clinico-biologiques du syndrome de Sjögren primitif dans une population tunisienne : à propos de 84 cas. *Rev Med Interne*. 2017; **38**:184-185.
27. Benasr M, Jaziri F, Rouached L, Sami T, Ben Abdelghani K, Ben Abdallah T. Manifestations extraglandulaires du syndrome de Gougerot-Sjögren. A propos de 95 patients. *Rev Med Interne*. 2016; **37**:100.
28. Posso-Osorio I, Nieto-Aristizábal I, Soto D, Ariza C, Urbano M, Cañas AC, *et al.* Validación y adaptación al castellano del Índice Reportado por Pacientes conSíndrome de Sjögren del EULAR (ESSPRI-EULAR Sjögren's Syndrome PatientReported Index). *Rheumatol Clin.* 2020; **17**(5):300-304.
29. Ng WF, Mitchell S, Lendrem D, Bowman S, Price E, Pease C, *et al*. SAT0242 How good are the eular sjögren syndrome disease activity index (ESSDAI) and EULAR sjögren syndrome patients reported index (ESSPRI) in predicting health status in primary sjögren syndrome? *Ann Rheum Dis.* 2013; **71**(3):553-554.
30. De Wolff L, Arends S, Van Nimwegen JF, Bootsma H. Ten years of the ESSDAI: is it fit for purpose? *Clin Exp Rheumatol*. 2020; **38**(126):283-290.

Frequency of thyroid dysfunction among rheumatoid arthritis patients at the Kenyatta National Hospital, Nairobi, Kenya

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Abstract

Background: Rheumatoid Arthritis (RA) affects 0.5-1% of the adult population. A higher prevalence of thyroid dysfunction is observed in patients with RA compared to the general population.

Objectives: To establish the frequency of thyroid dysfunction among ambulatory RA patients and to describe the association between thyroid dysfunction and the patients' socio-demographic characteristics, clinical characteristics, level of disease activity, and their functional status.

Design: This was a cross-sectional descriptive study.

Methods: Adult patients on follow up for RA at the outpatient clinic were sampled. Sociodemographic data was recorded. The Clinical Disease Activity Index (CDAI) and Health Assessment Questionnaire (HAQ) scores were computed from examination findings and questionnaires respectively. A venous blood sample was analyzed for Thyroid-Stimulating Hormone (TSH), free triidothyronine (fT3), and free tetraiodothyronine (fT4). This data was analyzed to determine frequencies and associations.

Results: Seventy-six patients were recruited into the study. Sixty-one participants were female. The mean TSH level was 5.8Miu/L. The frequency of thyroid dysfunction was 47.4%. Overt hypothyroidism was the most common form of thyroid dysfunction at 39.5% while 6.6% had Sick Euthyroid. Majority of the participants, 75%, had low disease activity, mean CDAI was 11.6. Forty-one (53.9%) participants had no disability, mean HAQ was 0.5. Correlations between thyroid dysfunction and advancing age, duration of disease, level of disease activity, and functional disability did not attain statistical significance.

Conclusion: Thyroid dysfunction is common among patients with RA with no significant association found between thyroid dysfunction socio-demographic characteristics, clinical characteristics, level of disease activity, and functional status.

Key words: Thyroid dysfunction, Rheumatoid arthritis, Disease activity, Functional disability

Introduction

Rheumatoid Arthritis (RA) is a symmetric polyarthritis with a variety of systemic manifestations. In the general population thyroid dysfunction affects 1-10% of adults, with variations in geographical areas, age and sex[1]. The causes of thyroid dysfunction include; iodine deficiency, infections and autoimmune associated thyroid disease[2]. Thyroid dysfunction is more prevalent in patients with autoimmune diseases such as RA. This is attributed to overlap of autoimmune conditions that are initiated by loss of tolerance to self-antigens[3].

The burden of thyroid dysfunction among RA patients has been found to vary between 6-47% in various studies. The entire spectrum of thyroid dysfunction has been described, however, hypothyroidism occurs more frequently. Patients with thyroid dysfunction have higher RA disease activity scores and poorer functional status measured using the health assessment questionnaire[4,5].

The clinical manifestations of RA overlap significantly with the musculoskeletal manifestations of thyroid dysfunction. This overlap may mask the diagnosis of thyroid

dysfunction; patients with a diagnosis of RA who develop concurrent thyroid dysfunction may remain symptomatic despite optimal RA management, they will also have worse physical functional status[6].

Both RA and thyroid dysfunction are known risk factors for cardiovascular disease, their co-occurrence confers additional risk above that attributed to the conventional cardiovascular disease risk factors[5,6]. Identifying RA patients with thyroid dysfunction will support instituting more stringent risk factor modification in addition to the benefit of treating both conditions optimally.

This study sought to determine the frequency of thyroid dysfunction among RA patients. Additionally, we sought to describe the association between presence of thyroid dysfunction and patient's demographic characteristics, duration of RA disease, clinical disease activity scores and functional status.

Materials and methods

This was a cross sectional study conducted at the Kenyatta National Hospital outpatient rheumatology clinic. The study population comprised of male and female patients aged above 18 years who had a confirmed diagnosis of RA having met the 2010 ACR/EULAR classification criteria.

Following approval by the ethics committee of the University of Nairobi and the Kenyatta National Hospital, 76 patients were recruited to the study using consecutive sampling technique. Recruited patients provided written informed consent and had their demographic data and medical history including current management and duration of disease recorded. A general and musckuloskeletal examination was conducted and used to compute the Clinical Disease Activity Index (CDAI). The health assessment questionnaire was also administered to determine patients' functional status. ELISA was used to determine TSH, FT4 and FT3 levels.

SPSS version 21.0 Chicago Illinois was used for data entry and analysis. The frequency of thyroid dysfunction was calculated as a percentage. The various types of thyroid function abnormalities were presented as percentages. Odds ratio was used to test the association between the presence of thyroid function abnormalities and patient demographic characteristics, disease activity scores, and functional status. P-values and 95% Confidence Intervals (CIs) were calculated where applicable. P-value <0.05 was considered statistically significant.

Results

Seventy-six patients were recruited out of the 86 patients screened during the study period. The mean age was of 41 years (range 18-78 years). Fifteen participants were male (19.7%) and 61(80.5%) participants were female. The male to female ratio was 1:4. Majority of participants (84.2%) had attained post-primary education and 73.7% were married.

Fifty five point three percent of the patients had the diagnosis of RA for 5 years or less. Thirty six point eight percent of patients had RA for 6 to 10 years while 7.9% had had RA for more than 10 years.

All the study subjects were on DMARDS while 44.7% were on steroids. None of the study participants were on biological agents.

The mean CDAI score was 11.6 (IQR 4-10). Low disease activity was the most prevalent at 75%. Only 2.6% were in remission. Almost twelve percent (11.8%) of the study population had high disease activity.

HAQ score mean was 0.5 (IQR 0.0-0.8). Eighty six point three percent of patients had mild to no disability while 8 (10.5%) participants were found to have high disease activity. The demographic and

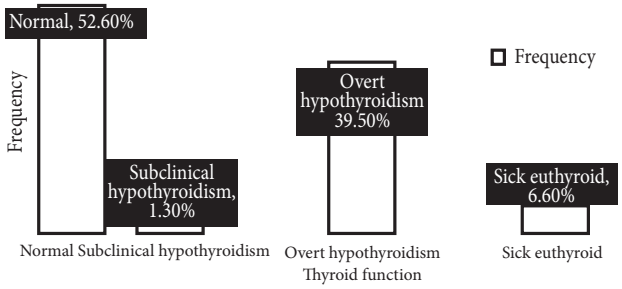
clinical characteristics of the study participants are depicted in Table 1.

Table 1: Participants sociodemographic and clinical characteristics

	Frequency N (%)
Age (years)	
≤30	7(9.2)
31-40	15(19.7)
41-50	22(28.9)
51-60	17(22.4)
>60	15(19.7)
Gender	
Male	15(19.7)
Female	61(80.3)
Education	
None	3(3.9)
Primary	9(11.8)
Secondary	44(57.9)
Tertiary	20(26.3)
Marital status	
Married	56(73.7)
Single	15(19.7)
Widowed	5(6.6)
Duration of disease	
<6	42(55.3)
6-10	28(36.8)
>10	6(7.9)
RA medication	
DMARDS	35(46.1)
DMARDS+steroids	34(44.7)
DMARDS+other	7(9.2)
Biological agents	0
CDAI	
Remission	2(3)
Low activity	57(75)
Moderate activity	8(10)
High activity	9(12)
HAQ score	
No disability	41(54)
Mild disability	25(33)
Moderate disability	2(3)
Severe disability	8(10)

The median TSH levels were 5.8 (IQR 4.1-7.5), higher than the laboratory reference range provided. The frequency of thyroid dysfunction was 47.4%. The majority of the patients 39.5% had overt hypothyroidism with only 1% having subclinical hypothyroidism. The distribution of thyroid function is depicted in Figure 1.

Figure 1: Distribution of thyroid function



Univariate analysis was done to interrogate the presence of correlations between thyroid dysfunction and various patient and disease characteristics: Age, sex, duration of disease, CDAI, and HAQ scores.

Participants that were less than 30 years old had three times the likelihood of having thyroid dysfunction compared to those above 60 years. This observation was however not significant, P-value 0.297.

Male participants had a higher likelihood of having thyroid dysfunction compared to females OR 1.3; this observation was not significant, P-value 0.6. Participants with a duration of disease >6 years were more likely to have thyroid dysfunction compared to those who had RA for less than 6 years OR 1.2 (P-value 0.6). The participants with low disease activity were less likely to have thyroid dysfunction compared to those with high disease activity OR 0.72, this observation was not significant P-value=0.72. Participants with severe disability had a marginally higher likelihood of having thyroid dysfunction compared to those with no disability; OR 1.2.

Table 2: Factors associated with thyroid dysfunction, univariate analysis

	Thyroid hormone abnormal				
	Yes	No	Total	OR (95% CI)	P-value
Age (years)					
≤30	4 (11.1)	3 (7.5)	7 (9.2)	2.67 (0.42-16.83)	0.297
31-40	6 (16.7)	9 (22.5)	15 (19.7)	1.33 (0.30-5.91)	0.705
41-50	11 (30.6)	11 (27.5)	22 (28.9)	2.00 (0.51-7.80)	0.318
51-60	10 (27.8)	7 (17.5)	17 (22.4)	2.86 (0.67-12.11)	0.154
>60	5 (13.9)	10 (25.0)	15 (19.7)		
Gender					
Male	8 (22.2)	7 (17.5)	15 (19.7)	1.35 (0.43 -4.18)	0.606
Female	28 (77.8)	33 (82.5)	61 (80.3)		
Duration of disease (years)					
<6	19 (52.8)	23 (57.5)	42 (55.3)		
6-10	14 (38.9)	14 (35)	28 (36.8)	1.21 (0.46 -3.16)	0.696
>10	3 (8.3)	3 (7.5)	6 (7.9)	1.21 (0.22 -6.7)	0.827
Drugs					
DMARDS	14 (38.9)	21 (52.5)	35 (46.1)	0.27 (0.05 -1.57)	0.144
DMARDS + steroids	17 (47.2)	17 (42.5)	34 (44.7)	0.40 (0.07 -2.35)	0.311
DMARDS + other	5 (13.9)	2 (5)	7 (9.2)		
CDAI					
0.0-2.8 (Remission)	0 (0.0)	2 (5.0)	2 (2.6)	-	
2.9-10.0 (Low activity)	27 (75.0)	30 (75.0)	57 (75.0)	0.72 (0.18-2.96)	0.720
10.1-22.0 (Moderate activity)	4 (11.1)	4 (10.0)	8 (10.5)	0.80 (0.12-5.40)	0.800
22.1-76.0 (High activity)	5 (13.9)	4 (10.0)	9 (11.8)		
HAQ					
0 (No disability)	18 (50.0)	23 (57.5)	41 (53.9)		
<0.3 (Mild)	13 (36.1)	12 (30.0)	25 (32.9)	1.38 (0.51-3.76)	0.523
0.3-1.8 (Moderate)	1 (2.8)	1 (2.5)	2 (2.6)	1.28 (0.07-21.86)	0.866
>1.8 (Severe)	4 (11.1)	4 (10.0)	8 (10.5)	1.28 (0.28-5.82)	0.751

Discussion

The association between RA and thyroid dysfunction has been envisaged for a long time and several studies have been done to quantify the co-occurrence. This is the first study in Kenya describing the frequency of thyroid dysfunction among RA patients.

This study investigated 76 RA patients who were attending the outpatient Rheumatology clinic at the KNH. The frequency of thyroid dysfunction was 47.4%. The predominant pattern of thyroid dysfunction was overt hypothyroidism at 39.5%, while one (1.3%) participant had subclinical hypothyroidism.

A wide range of thyroid abnormalities has been observed in various studies around the world. Our prevalence was higher than most studies reviewed. The differences in prevalence across various populations has been attributed to: Differences in assay techniques, presence of other goitrogens that alter thyroid function and the influence of medications such as steroids. Persistent inflammation characterized by high disease activity also causes thyroid dysfunction[7-9].

Nadeem *et al*[5] in India found that 42% of the patients studied had thyroid dysfunction. Unlike our observation, 37.9% of participants in Nadeem's study had subclinical hypothyroidism and only 3.6% had overt hypothyroidism.

In another study in India by Joshi *et al*[10] looking at the prevalence of hypothyroidism in RA demonstrated a prevalence of 38.4% which is similar to the prevalence of overt hypothyroidism in our study.

A study done in China by Li *et al*[11] in 2019 observed a prevalence of 32.3% thyroid dysfunction of which there was a predominance of overt hypothyroidism at 26.2%. In a Danish population of newly diagnosed RA patients, one study demonstrated a high rate of overt hypothyroidism among the proportion of participants who had thyroid dysfunction. The prevalence of overt hypothyroidism was 30.4%, 26% of the population had subclinical hyperthyroidism or hypothyroidism[12]. These studies had lower prevalence demonstrated than our study but were similar in that the majority of cases had overt hypothyroidism. SCH has been shown advance to overt hypothyroidism at an estimated rate of 1-4% per year[13].

The lack of standard reference ranges for interpretation of thyroid function results provides a possible explanation for the variations in prevalence reported. Different studies used different assay and laboratory specific reference ranges. ELISA and chemiluminescence are second and third generation thyroid hormone assays respectively. At the lower ranges of TSH for the detection of hyperthyroidism, chemiluminescence has been shown to have higher precision than ELISA. At the upper ranges of euthyroidism, these two immunoassays have comparable precision. In one study comparing the sensitivity of ELISA and chemiluminescence in the estimation of TSH, in patients with hypothyroidism, ELISA had a sensitivity of 96% compared to 100% for chemiluminescence. The sensitivity of ELISA makes it suitable for the detection of thyroid hormone abnormalities at baseline. In our study, we employed the ELISA technique which is appropriate for initial assessment of thyroid disorders[7,14].

Joshi and colleagues[10] in India while utilizing the ELISA method of thyroid hormone assay observed a high prevalence of 38% hypothyroidism. This is similar to the prevalence of overt hypothyroidism we demonstrated at 39.5%.

Mousa and colleagues[15] in a study on thyroid dysfunction in RA patients in Egypt utilized the ELISA method of thyroid hormone assay and observed a low prevalence of 8.3%. In another study in Jordan, thyroid dysfunction in a population of RA patients was determined by utilizing the ELISA method and a prevalence of 14.3% was observed[16]. These findings were low compared to the prevalence we observed despite utilizing the same assay technique.

Among the studies that utilized the chemiluminescence method of thyroid hormone assay, they also observed a wide variation in the prevalence of thyroid dysfunction. Nadeem and colleagues[5] demonstrated a high prevalence of thyroid dysfunction at 47% which was comparable to what we observed. In Italy a study by Atzeni and colleagues[17] utilizing this assay technique for thyroid hormones, observed a low prevalence of thyroid dysfunction at 7.1%. These varied results demonstrated even with similar assay techniques utilized suggest caution should be used in drawing comparisons.

While the local rate co-occurrence of thyroid dysfunction in the RA patient population and at the community level in Kenya is not known, comparisons can be made to prevalence in select population groups. Ngugi[18] in a study on patients with type 2 diabetes at the KNH, determined the presence of thyroid dysfunction by utilizing ELISA

assay thyroid hormones. This study described a prevalence of 60% which was higher than what we observed in our study. These findings may indicate that thyroid dysfunction is prevalent in the general population and hence more pronounced in these patient groups with other factors contributing to dysfunction. The high prevalence observed in both studies is expected because, in addition to being in the same geographical location and having exposure to common possible goitrogens, some of the pathogenetic mechanisms underlying the development of thyroid dysfunction in these patient populations such as chronic inflammation are similar[8]. Forty four point seven percent of our study participants were found to be on steroids at various doses. Glucocorticoids suppress thyroid hormone production leading to low FT4 and high TSH[9]. This may explain the high prevalence of thyroid dysfunction which we observed to be predominantly hypothyroidism.

Thyroid dysfunction, especially hypothyroidism has been found to occur in chronic inflammation. Cytokines elaborated during inflammation such as IL1 and IL6 suppress the hypothalamic-pituitary and thyroid axis. TSH action on the thyroid gland and peripheral conversion of T3 to T4 is inhibited directly by IL1 and to a lesser degree IL6. These cytokines are targets for biological agents in RA disease control which results in improvement in thyroid function[19]. Thyroid dysfunction as a disease of chronic inflammation was also evident in conditions that involve chronic sustained inflammation. Inflammation can impair thyroid tissue and cause thyroiditis directly and it can also promote hyperplasia of thyroid cells causing thyroid nodules. Thyroid nodules coexists with the elevated TSH[20].

Iron, selenium, and iodine deficiency are also known goitrogens that are prevalent in our region and may explain the high prevalence observed.

Thyroid hormone synthesis is influenced by iron deficiency which has been shown to reduce the activity of the heme-dependent thyroid hormones especially thyroid peroxidase. This has been noted to blunt the effects of iodine supplementation in areas of low iodine[21]. The prevalence of iron deficiency in the national nutritional survey of 2011 in Kenya which included 2851 participants was 18.4%. In this survey, the prevalence of iodine deficiency ranged from 19.1% among adult males to 30% among non-pregnant women. Salt is the main mode of supplementing iodine in Kenya it was hence significant to note that 48% of salt samples tested during this survey had lower than the recommended levels of iodine[22]. In an Indian study that included 50 newly diagnosed hypothyroid patients and 50 appropriate controls, Dahiya *et al*[23] observed that levels of ferritin and serum iron were low in those who were hypothyroid relative to the controls, P-value less than 0.005.

High concentrations of selenium are found in the thyroid gland where seleno-proteins are incorporated into iodinases in thyroid hormone synthesis. Selenium levels are dependent on diet and geographical areas. One study identified the risk of the inadequacy of dietary selenium at 22% across Africa[24]. In Istanbul a 9-month selenium supplementation study in patients with AITD on therapy with thyroxine was conducted, after the follow up period it was observed that there was the suppression of levels of TPOab by 26.2% to 30% P-value=<0.001[25]. This indicates an association between selenium deficiency and thyroid function.

Our study did not demonstrate a significant relationship between advancing age and having RA for a longer duration with occurrence of thyroid dysfunction. Presence of high disease activity and increasing functional limitation did not correlate significantly with occurrence of thyroid dysfunction.

Previous studies have however made some associations. In one case-control study in Canada that recruited 119 RA patients and 108 appropriate controls, age and thyroid disease were not significantly correlated. There was a significant correlation between thyroid dysfunction and duration of disease, P value=0.03[4]. Similarly, in India, a prospective study of 52 RA patients found no statistically significant relationship between advancing age and occurrence of thyroid function, P-value=0.99 but there was a correlation with duration of disease, P-value=0.33[10]. This study in India demonstrated an association between TSH levels and severity of RA, P-value=0.003. In contrast, another prospective study involving 385 RA patients in India did not find a correlation between thyroid dysfunction and severity of RA. For those who had SCH the P-value was 0.075 and among those with overt hypothyroidism P-value was 0.28[5].

A case-control study in Egypt involving 200 participants found that high TSH levels were associated with higher Modified Health Assessment

Questionnaire scores, P-value= 0.01. Similarly, high TSH was associated with high disease severity estimated using MDAS, P value=0.02[17].

The varied results on associations between thyroid dysfunction and patient demographics, disease severity, and functional disability, delineate the need for more investigation to further explore these associations.

Study limitations

(i) This study provides data on a one-time estimate of thyroid function whereas changes in thyroid hormone levels occur from time to time. However, this study provides a baseline assessment that will inform decisions on the need for screening of RA patients for thyroid dysfunction and further follow up schedule for those with established thyroid dysfunction.

(ii) There is no population data on the prevalence of thyroid dysfunction from which comparisons with the prevalence in our population could be drawn**.**

Conclusion

Thyroid dysfunction is prevalent among RA patients. No significant associations were found between thyroid dysfunction and advancing age, having RA for a longer duration, increasing severity of disease, and functional disability.

Recommendations

All patients with rheumatoid arthritis should be screened for thyroid dysfunction.

References

1. McInnes IB, Schett G. Cytokines in the pathogenesis of rheumatoid arthritis. *Nat Rev Immunol.* 2007; **7**(6):429–442.
2. Ogbera A, Kuku S. Epidemiology of thyroid diseases in Africa. *Indian J Endocrinol Metab*. [Internet]. 2011; **15**(6):82.
3. Jeong H, Baek SY, Kim SW, Eun YH, Kim IY, Kim H, *et al.* Comorbidities of rheumatoid arthritis: Results from the Korean National Health and Nutrition Examination Survey. *PLoS One*. 2017; **12**(4):1–15.
4. Shiroky JB, Cohen M, Ballachey M-L, Neville C, Shiroky CJB, Cohen M, *et al.* Thyroid dysfunction in rheumatoid arthritis: a controlled prospective survey. *Ann Rheum Dis Rheum Dis.* 1993; **52**(52):454–456.
5. Nadeem M, Khaliq A, Bhat MH, Mustafa F, Mushtaqe M. Spectrum of thyroid disorders in sero positive rheumatoid arthritis. *J Thyroid Disord Ther.* 2017; **06**(04).
6. Anwar S, Gibofsky A. Musculoskeletal manifestations of thyroid disease. *Rheum Dis Clin North Am* [Internet]. 2010; **36**(4):637–646.
7. Shamsian AA, Ghazvini K, Sokhtanloo M, Moghaddam MS, Vakili R. Which quantitative method in determination of the thyroid hormone levels is more consistent with the clinical symptoms of the thyroid disorders? *Comp Clin Path.* 2016; **25**(1):101–106.
8. Mancini A, Di Segni C, Raimondo S, Olivieri G, Silvestrini A, Meucci E, *et al.* Thyroid hormones, oxidative stress, and inflammation. *Mediators Inflamm.* 2016; **2016**:6757154. doi: 10.1155/2016/6757154.
9. Gamstedt A, Järnerot G, Kågedal B, Söderholm B. Corticosteroids and thyroid function. *Acta Med Scand.* 2009; **205**(1–6):379–383.
10. Joshi P, Agarwal A, Vyas S, Kumar R. Prevalence of hypothyroidism in rheumatoid arthritis and its correlation with disease activity. *Trop Doct.* 2017; **47**(1):6–10.
11. Li Q, Wang B, Mu K, Zhang J, Yang Y, Yao W, *et al.* Increased risk of thyroid dysfunction among patients with rheumatoid arthritis. *Front Endocrinol* (Lausanne). 2019; **10**(Jan):1–10.
12. Emamifar A, Marie I, Hansen J. Thyroid disorders in patients with newly diagnosed rheumatoid arthritis is associated with poor initial treatment response evaluated by disease activity score in 28 joints-C-reactive protein (DAS28-CRP) An observational cohort study. *Medicine.* 2017; **96** (43): e8357.
13. Kim YA, Park YJ. Prevalence and risk factors of subclinical thyroid disease. *Endocrinol Metab.* 2014; **29**(1):20–29.
14. Spencer CA. Assay of Thyroid hormones and related substances. *Endotext.* 2000; (January 2000). Available from: http://www.ncbi.nlm.nih.gov/pubmed/25905337.
15. Mousa AA, Ghonem M, Hegazy A, El-Baiomy AA, El-Diasty A. Thyroid function and auto-antibodies in Egyptian patients with systemic lupus erythematosus and rheumatoid arthritis. *Trends Med Res.* 2012; **7**(1):25–33.
16. Al N, Rn Z, Al M, Rn H. Thyroid dysfunctions among Jordanian patients with rheumatoid arthritis and systemic lupus erythematosus : A hospital-based study. *J R Med Serv.* 2013; **20**(1):37–42.

17. Atzeni F, Doria A, Ghirardello A, Turiel M, Batticciotto A, Carrabba M, *et al.* Anti-thyroid antibodies and thyroid dysfunction in rheumatoid arthritis: Prevalence and clinical value. *Autoimmunity.* 2008; **41**(1):111–15.
18. Ngugi R. Prevalence of thyroid dysfunction in ambulant patients with Type 2 diabetes attending diabetes clinics at Kenyatta National Hospital. 2014; [unpublished manuscript available on the internet], University of Nairobi Erepository. Available from: http://erepository.uonbi ac.ke/bitstream/handle/11295/75480.
19. Hermus ARMM, Linkels E, Klootwijk W, Kaptein E, Sweep CGJ, Visser TJ, *et al.* Thyroid axis of continuous infusion of interleukin-. *Society.* 2007; **135**(4): 71-81.
20. Li Z, Huang Y, Chen X, Wei C, Yang P, Xu W. The effect of inflammation on the formation of thyroid nodules. *Int J Endocrinol.* 2020: 9827349. doi.org/10.1155/2020/9827349.
21. Zimmermann MB. The influence of iron status on iodine utilization and thyroid function. *Annu Rev Nutr.* 2006; **26**(1):367–389.
22. Kenya National Bureau of Statistics. The Kenya National Micronutrient Survey. 2011;1–150.
23. Dahiya K, Verma M, Dhankhar R, Ghalaut VS, Ghalaut PS, Sachdeva A, *et al.* Thyroid profile and iron metabolism: Mutual relationship in hypothyroidism. *Biomed Res*. 2016; **27**(4):1212–25.
24. Hurst R, Siyame EWP, Young SD, Chilimba ADC, Joy EJM, Black CR, *et al.* Soil-type influences human selenium status and underlies widespread selenium deficiency risks in Malawi. *Sci Rep.* 2013; **3**(2):1–6.
25. Turker O, Kumanlioglu K, Karapolat I, Dogan I. Selenium treatment in autoimmune thyroiditis: 9-month follow-up with variable doses. *J Endocrinol.* 2006; **190**(1):151–156.

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