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Body mass index, serum rheumatoid factor and c-reactive protein among individuals with rheumatoid arthritis in Kano Metropolis

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ABSTRACT

Background: Rheumatoid arthritis (RA) is becoming a global health menace associated with joints swelling, pain, stiffness, and progressive loss of function of extremities etc. This study aimed at evaluating the Body Mass Index (BMI), Serum Rheumatoid Factor (RF) and C-Reactive Protein (CRP) among RA Patients in Kano Metropolis.

Methods: A total of 111 participants comprising 74 Rheumatoid Arthritis patients and 37 apparently healthy controls were recruited for this study. Exactly 29 were males while 44 were females aged between 25 to 75 years. Using standard techniques, BMI was calculated using the weight and height taken from the participants. Blood samples were collected for serum RF and CRP and were analysed using Enzyme linked immunosorbent assay technique. Statistical Package for Social Sciences version 21 was used for the analysis of data.

Results: Our findings reveal that, females recorded higher percentage frequency of 45 (60.8%) while males recorded a lower percentage frequency of 29(39.2%) of RA patients with the ratio of 1.55:1, the higher percentage frequencies of 35(47.3%) was observed in overweight BMI patients of between 25- 29.9 kg m^{-2}. The mean serum value of RF was significantly ($p = 0.00$) higher in case group (4.4 ±1.5 ng/ml) compared with the control group (2.0 ±1.5 ng/ml) and also the mean serum value of CRP was significantly ($p = 0.00$) higher in case group (13.0 ±5.0 mg/L) compared with the control group (5.5±5.0 mg/L). A significant positive correlation was established between serum RF and CRP ($r = 0.48$, $p=0.00$).

Conclusion: Our findings show increased RF and CRP in RA case group. Quantitative evaluation of immunological parameter such as RF, CRP and BMI monitoring may aid in proper management of RA patients.

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Keywords: Body Mass Index, C-reactive protein, Enzyme linked immuno-sorbent assay, Immunology, Rheumatoid Factor

INTRODUCTION

Globally, Rheumatoid arthritis has been found to be one of the most prevalent connective tissue diseases and the most common inflammatory arthritis which has been on the rise in sub-sahara Africa particularly Nigeria (Dawman *et al.,* 2012), thus leading to increase medical intervention for this burden (Lwin *et al*., 2020). It is a severe, progressive, systemic inflammatory disease of unknown cause (Cojocarua *et al.,* 2010). Rheumatoid arthritis has been found to be easily complicated by vasculitis with systemic manifestations (Romanowska-Prochnicka *et at.,* 2013; Guo *et al.,* 2018). The most significant clinical symptom is an inflammation of the synovial membranes which causes a painful swelling of the articulations and the ankylosis (Grassi *et al.,* 1998). Early identification, accurate diagnosis and treatment are important in achieving control of this disease and subsequent prevention of joint injury, disability among others (Heidari, 2011). The prevalence of rheumatoid arthritis has been estimated to be 1-2 percent of the adult population

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(Carmona *et al.,* 2002; Lawrence *et al.,* 2008; Turesson and Matterson, 2014), and the morbidity and mortality it causes are a consequence of local and systemic inflammatory processes that damage cartilage, bone and soft tissue, as well as blood vessels and viscera (Niewold *et al.,* 2007). Certain risk factors such as genetic and environmental factors have been shown to be associated with a greater risk of rheumatoid arthritis; some of which are modifiable, while others are not (Deane *et al.,* 2017; Xu and Lin, 2017).

The body mass index (BMI), is the measurement of the relationship between weight and height (kg/m^2), it is a routing indicator used in measuring anthropometric indices associated with obesity or underweight in adults (Isah *et al*., 2020a). Numerous factors affecting arthritis among which are BMI need to be further explored (Feng *et al.,* 2019). In the developed world, overweight/obesity has been implicated with increased prevalence of metabolic episode, rheumatoid arthritis among others (Zhang *et al.,* 2014), but this has become exponentially alarming also in sub-Sahara Africa (Chukwuonye *et al.,* 2013).

Rheumatoid factor (RF) was the first autoantibody to be discovered in people with rheumatoid arthritis (Nell *et al.,* 2005), it is a family of autoantibodies directed to the Fc portion of IgG which are formed in RA patients by B cells synthesized in lymphoid follicles and germinal center-like structures that develop in inflamed synovium (Song and Kang, 2010). The hallmark of this disease are autoantibodies which developed in response to the body own tissue, and are characteristic of autoimmune diseases, such as rheumatoid arthritis (Shinji *et al.,* 2017). Despite the name, rheumatoid factor is not specific to rheumatoid arthritis, and there are many factors that can impact rheumatoid factor results (Ingegnoli *et al.,* 2013). Some conditions and medical procedures that can raise RF levels include: other autoimmune diseases, certain chronic infections, diabetes etc. It's important to note that once the RF level is elevated, it will often remain so even if the disease goes into remission (Ingegnoli *et al.,* 2013; Shinji *et al.,* 2017).

C-reactive protein (CRP) is a nonspecific acute phase reactant that is a member of the pentraxin proteins, which are pattern recognition proteins that are an integral part of the innate immune system (Pepys and Hirschfield, 2003). It is produced and synthesized in the liver in response to inflammatory cytokines and assists in complement binding and phagocytosis by macrophages. Thus, one of the major roles of CRP is the recognition and elimination of certain foreign pathogens, including endotoxemia (Sproston and Ashworth, 2018). CRP may also help in clearance of necrotic or apoptotic cell (Gershov, 2000), and it is a sensitive marker of systemic inflammation (Otterness, 1994). The goal of this study is to evaluate Body Mass Index, Serum RF and CRP among Rheumatoid Arthritis Patients in Kano Metropolis.

MATERIALS AND METHODS

Study Area and Population

This study was a case control study conducted at Aminu Kano Teaching Hospital and Abdullahi Wase Specialist Hospital in the Kano metropolis, Kano State, North-western Nigeria. A total of one hundred and one (111) participants were recruited. Seventy-four (74) were naïve for Rheumatoid arthritis while thirty-seven (37) were apparently healthy controls who were recruited into the study through convenience sampling in a cross-sectional pattern.

Males were 29 while females were 45 for the case group and the control group had 16 males and 21 female aged ranges 25 to 75 years. Patients with a history of any underlying autoimmune diseases like systemic lupus erythematosus, Sjogren syndrome, Hashimoto thyroiditis among others, patients who have commenced RA treatment were excluded in this study. Both clinical (Clinical history, Sign and symptoms) and laboratory (Uric acid, ANA, Anti-CCP and qualitative RA) investigation were used to confirmed those patients with rheumatoid arthritis. The controls were clinically examined by a physician, with or without a self-reported family history of RA. The BMI was determined using standard technique as described by WHO (2004). Relevant

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data was obtained using the clinical records and a detailed interviewer-based administered questionnaire. Participants provided written informed consent before being enrolled into this study.

Ethical consideration

This study was approved by the Ethical Committee of Aminu Kano Teaching Hospital Kano, with a Reference number NHREC/21/08/2008/AKTH/EC/2555 dated 23rd July, 2019 and Kano state Ministry of Health, with a Reference number MOH/Off/797/T.I/1447 dated 14th August, 2019. The participants were well informed about the purpose and the procedure of the study and a written informed consent was obtained from the participants before samples were collected. The study conformed to the provisions of the declaration of Helsinki (WMA, 2013).

Sample Collection and Laboratory Methods

Five (5 ml) of blood was collected via venipuncture from all participants into a plain vacutainer. The serum harvested was stored in cryotubes at -20°C until assayed. The sample were used for assay of RF and CRP by ELISA technique using reagents supplied by Kuancheng District, Changchun Jilin Province, China.

Statistical analysis

Data was analyzed using Statistical Package for Social Sciences version 21.0 (SPSS) statistical software. The Mean and Standard Deviation were computed and results were expressed as mean±SD. Student t-test was used to compare differences between means. Correlation was performed using Pearson's Correlation Coefficient. Statistical significance was set at $p<0.05$.

RESULTS

Table 1 shows the distribution of patients according to gender. The study population comprised of 45 (60.8%) females and 29 (39.2%) males, in a comparative ratio of 1.55:1 respectively.

Table 2 shows the distribution of case and control groups according to BMI. In the case group, the highest frequency of BMI was observed in Overweight with percentage frequency of 47.3% and the lowest frequency of BMI was observed in underweight and morbid obese with percentage frequency of 0%. In control, the higher frequency BMI was observed in normal body weight with percentage frequency of 48.7% and the lowest frequency of BMI was observed in underweight and morbid obese with percentage frequency of 0%. However, the mean value of BMI was not statistically significantly ($p<0.05$) in the patient group (29.8±5.10) when compared with the control group (26.3 ± 4.4).

Table 3, shows the Serum RF in case with RA compared with control subjects. The mean values of RF were statistically higher ($p=0.000$) in the case group with (4.4 ±1.5 ng/ml) when compared with the control group with (2.0 ±1.5 ng/ml). The higher concentration frequency of RF >3.0 ng/ml were observed in case group with percentage frequency 58(78.4%), while the lower concentration of between 0-3.0 ng/ml were observed in case

Table 1 Distribution of patients according to gender

Gender	Frequency	Percent (%)
Male	29	39.2
Female	45	60.8
Female to Male Ratio = 1.55:1		

Data presented as frequency and percent; %= percentage

Table 2 Distribution of Body Mass Index among the study participants

		Patient (n=74)		Control (n=37)	
Grade	BMI (Kg/m^2)	frequency	%	frequency	%
Underweight	<18	0	0	0	0
Normal	18-24.9	9	12.2	18	48.7
Overweight	25.0-29.9	35	47.3	16	43.2
Moderate Obesity	30.0-39.9	30	40.5	3	8.1
Morbid Obesity	>40	0	0	0	0
Mean±SD		29.8 ± 5.1		26.3 ± 4.4	p=0.133

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Table 3: Serum Rheumatoid factor and C-reactive protein in patients with Rheumatoid Arthritis compared with control subjects

	Patient (n=74)		Control (n=37)			
Variable	frequency	Percent	Frequency	Percent	t	p-value
Serum RF (ng/ml)						
0-3.0	16	21.6	37	100		
>3.0	58	78.4	0	0		
Mean±SD	4.4 ±1.5		2.0 ±1.5		11.145	0.0001
Serum CRP (mg/L)						
≤10	19	25.7	37	100		
>10	55	74.3	0	0		
Mean±SD	13.0 ±5.0		5.5±5.0		6.46	0.0001

f= Frequency, %= Percentage, t= student t-test, p≤ 0.05 (significant of t-test) for patient V's control analysis

Table 4: Correlation of Serum C-reactive protein and Serum Rheumatoid factor in Rheumatoid Arthritis patients

	RF ELISA Test			
Serum CRP	**0-3.0**	**>3.0**	**r#**	**p-value**
≤10	4	12	0.483	0.0001
>10	10	48		

*#=determined by Pearsons correlation; *p= Correlation is significant at ≤ 0.05 levels (2-tailed); r = strength of correlation; CRP=C reactive protein; RF=Rheumatoid Factor.*

group with percentage frequency16 (21.6%).

The mean values of CRP were statistically higher (p=0.000) in the case group with (13.0 ±5.0 mg/L) when compared with the control group with (5.5±5.0 mg/L). The higher frequency of CRP was observed in >10.0 mg/L with percentage frequency 55 (74.3 %), while the lower frequency was observed in ≤10 mg/L with percentage frequency 19 (25.7%) as shown in table 3.

There is significant positive (r =0.483, p=0.000). correlation between CRP and RF in RA patient as depicted in Table 4.

DISCUSSION

Rheumatoid arthritis is associated with inflammation of the synovial membrane of the joint and if left untreated, often leads to the destruction of bone and cartilage components of the joint and the resulting disability (Guo *et al.,* 2018). A variety of comorbidities associated with systemic inflammation contribute to the increase in mortality observed in RA patients (Kłodziński and Wisłowska, 2018). Although the pathophysiology of RA is not fully understood, the process usually involves dysregulated inflammation, with antigen presentation, T cell activation, and autoantibody production, all as mediators of the inflammatory process (Brito-Rocha *et al.*, 2019). However, quantitative diagnostic and specific approaches, such as RA and CRF, can be important in providing clinician with the accuracy of diagnosis and prognosis to reduce their suffering.

Our finding shows that, female had higher percentage frequency than the male with a ratio of 1.55:1, this is in line with the reports of van Vollenhoven (2009), Moneim *et al.* (2013) and Intriago *et al.* (2019). It is in disagreement with the study of Laivoranta-Nyman *et al.* (2001) who reported that, women's immune system are resilience and more responsive than that of males, leading to greater justification for autoimmune diseases or the physiological requirements of puberty, menstruation, pregnancy and breastfeeding (Azizi and Amouzegar, 2011), since women are more susceptible and sensitive to hormonal changes than men

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(Amalya, 2016; Isah *et al.*, 2018). Women are also more predisposed to autoimmune diseases, due to the higher level of anti-nuclear antibodies present in women. Furthermore, its might also be accredited to the X-chromosome, which has many genes related to the immune system (Isah *et al.*, 2020b).

This study indicates that, the higher frequency of bodyweight BMI of was observed in overweight cases with mean value showing no statistically significant (<0.05) difference when compared with the control group. This result is similar to the reports of Stavropoulos-Kalinoglou (2007), Turesson and Matterson (2014), Feng *et al.,* (2019), but disagreed with the report of Emily (2015) who reported that about two-third of people with RA are overweight or obese with regards to BMI. Liu *et al.* (2017) also demonstrated in contrast to our finding. In people with RA, excess body fat creates special complications in addition to its well-known role in increasing risk of heart disease, stroke and other conditions (Jagpal and Navarro-Millán, 2018).

Our finding shows that, the comparison between rheumatoid factor (RF) in patients with RA compared with control subjects revealed a statistically significant higher value ($p<0.05$). Our result is in agreement with the studies conducted by Nielsen *et al.* (2012), Ingegnoli *et al.* (2013), but in disagreement with the finding of Didier *et al.* (2018), who stated that RF are also used as a marker in other autoimmune condition like Sjogren syndrome, systemic lupus erythematosus, mixed connective tissue disease and non-autoimmune conditions, such as in chronic infections and old age among others not necessarily RA. Rheumatoid factor could be probably developed in humans as mechanism for helping remove immune complex from the circulatory system (Song and Kang, 2010).

Elevated RF concentration might indicate a *greater* possibility of *a patient having* RA, poorer prognosis of patients with RA as patients with higher RF levels tend to have more severe disease (Brito Rocha *et al.,* 2019;Tiwari *et al.,* 2020). Rheumatoid factor is a protein or antibodies that recognize the Fc portion of IgG molecules as their antigens leading to attack on healthy tissue in the body, it plays a fundamental role in the diagnosis and prognosis of patients with arthritis (Wilson, 2006; Song and Kang, 2010). Rheumatoid arthritis occurs when our immune system attacks the synovium, the lining of the membranes that surround the joints resulting in inflammation, thickens the synovium, which can eventually destroy the cartilage and bone within the joint. In some people, the condition can damage a wide variety of body systems, including the skin, eyes, lungs, heart and blood vessels (Catherine and Melissa, 2020).

C-reactive protein (CRP) revealed a statistically significant higher value ($p<0.05$) in patients when compared with the controls. This is in line with the studies conducted by Nancy *et al.* (2006); Brenda (2018) and Murphy *et al.* (2018). In contrary to the report of Aho *et al.* (2000), were they reported no elevation in CRP concentration in RA. This may be because CRP is an indicator for measurement of the immune-mediated inflammatory response, and also the most useful marker in systemic Rheumatoid Arthritis patients (Otterness, 1994; Pope and Choy, 2021). C-reactive protein shows high expression during inflammatory condition such as rheumatoid arthritis (Sproston and Ashworth, 2018). The immune system signals inflammation and the body immune system sends CRP through the bloodstream to the affected area to enable a robust combat of the immune system. Elevated CRP in the blood indicate chronic systemic inflammation (Brenda, 2018).

In our finding, significant positive correlation was observed between Rheumatoid factor and C-Reactive Protein. This is in conformity with the report of Murphy *et al.* (2018). An elevated concentration of CRP suggests more substantial systemic inflammation with increase in RF in *rheumatoid arthritis* (Arntz *et al.*, 2018; Branda, 2018). Aman *et al.* (2000) reported that, CRP and RF are useful immunological parameter affecting the prognosis of RA and the prediction achieved by the combination of elevated CRP and RF is of sufficient accuracy to be considered for clinical

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management when compare with one parameter. These might probably indicate that, increase in RF may subsequently results in increase CRP due to the increase in the autoantibody around the joints and extremities.

CONCLUSION

Based on this study's findings, it can be concluded that, females are more prone to RA than males, rheumatoid arthritis is more common among overweight patients, RA patients has increase concentrations of Rheumatoid factor and C-reactive protein. A significant positive correlation was established between serum Rheumatoid factor and C-Reactive Protein in this group of patients. Quantitative RF and CRP might be an important immunological and routine diagnostic analyte for the diagnosis and prognosis of rheumatoid arthritis patient.

COMPETING INTEREST

Authors declare that they have no competing interests.

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