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Assessment of Anti-Myeloperoxidase Antibodies, Cholesterol and LDL-C in Serum of Sudanese Patients with Systemic Lupus Erythematosus: A pilot study

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Abstract: Background: *Immunological dysfunction, especially the secreation of antinuclear antibodies (ANA) are main feature of the Systemic lupus erythematosis (SLE) disease. Increased atherosclerosis in patients with SLE due to oxidative stress anti myeloperoxidase antibodies.* ***Aim:*** *This study aims to assess serum anti-myeloperoxidase antibodies, cholesterol and LDL-C levels in Sudanese Patients with Systemic lupus erythematous (SLE) in Khartoum State.* ***Materials and methods****: This cross-sectional study was conducted in Military Hospital, in Khartoum State (Sudan),. Fifty Sudanese Patients with SLE and fifty healthy individual were enrolled in this study. The anti-Myeloperoxidase antibodies was measured by cobas and the levels of serum cholesterol and LDL-C were measured by using Mandray.* ***Results:*** *The result found that,62% of patients at age less than 40 years , 86% of patients were females, 10% of patients were exposed to sun, while 90% of patients were not exposed to sun, 6% of patients had current medication and 20 % had chronic medication. The result of serum anti-myeloperoxidase antibodies (MPO) among study groups showed that, 18% of patients had positive result, while 82% of patients had negative result.100% of control had negative result. There was significant increased in LDL- C level in patients with SLE compared to control group , while there was insignificant different in cholesterol level in both study group. The odds ratios of cholesterol, and LDL-C levels and duration of disease among patients group were 0.5 and 0.6 respectively (P ≥0.05). The result showed that, 54% of patients had duration of disease more than 5 years.* ***Conclusion:*** *This study concluded; anti-MPO antibodies are found in patients with SLE, the level of LDL-C is elevated in patients with SLE.*

Keywords: Systemic lupus erythematosis; anti-Myeloperoxidase antibodies; antinuclear antibodies; LDL-C; Cholesterol

1- Introduction

Systemic lupus erythematosus (SLE) is the classical systemic chronic autoimmune disease, characterized by varied clinical manifestations and production of numerous autoantibodies. Myocardial infarction, cerebrovascular events and subclinical atherosclerosis are increasingly recognized as serious complications of SLE [(1),]

Patients with SLE have a higher prevalence of subclinical atherosclerosis and a higher risk of CV events compared to the general population [(2)]. The estimated prevalence of CVD in the SLE population is between 6 and 10%, with an annual incidence of 1.3–1.5% [(3).] . Recently, it has been widely esteemed that premature atherosclerosis is a chiefly prominent characteristic of the disease, especially in women [4] . Other factors concerned in the progress of SLE include changed cytokine levels, altered sex hormones metabolism, improved apoptosis, and high levels of oxidative stress [5] . Numerous of the auto-antibodies produced in SLE reveal preference for oxidized substrates, including oxidized myeloperoxidase (MPO), double stranded DNA (dsDNA) and phospholipids. Oxidative stress anti myeloperoxidase and anti-phospholipid antibodies have also been occupied in the increased atherosclerosis in patients with SLE [6] .

It was emphasized that the most common abnormality in SLE is ldecreased HDL levels, since HDL, levels are known to be inversely related to coronary artery disease (CAD) risk and importantly, hypertriglyceridemia itself is also recognized as an independent risk factor in women . Together, these data suggest that SLE itself promotes a proatherogenic lipid profile [(7)] . Accordingly; this study aimed to assess anti myeloperoxidase antibodies and some atherogenic lipid profile in Sudanese patients with SLE.

2. MATERIALS AND METHODS

This cross-sectional study was conducted during the period from September to November 2019. The study was approved by committee of Clinical Chemistry Department in Faculty of Medical Laboratory Science at Alneelain University.

Fifty Sudanese SLE Patients who admitted to Military Hospital in Khartoum State (43 of them were females and 7 were males) were recruited as cases and fifty apparently healthy individuals were enrolled as controls (41 of them were females and 9 of them

were males). The case and control groups were age-matched with mean age of 31.5 years. Pregnant or lactating women, patients with liver or kidney diseases, patients who are treating with phototherapy or any immunosuppressive drugs were excluded.

After obtaining informed consent from all participants; the demographic data was collected by using questionnaire. About 2.5 ml of random venous blood was collected from the arm of each participant into plain container, after formation of clot at room temperature, the samples were centrifuged for 10 minutes at 3000 rpm then the serum was obtained and analyzed.

The anti-myeloperoxidase antibodies (AMP) were measured by Cobas and the levels of serum total cholesterol and LDL-C were measured by using Mandray. Pathological and normal control sera were used to assure accuracy and precision of results.

The data was analyzed by using Statistical Package for Social Sciences (SPSS) version 21. Values were expressed as percentages and Mean ± SD. Independent T-test was used for comparison between groups and P-value less than 0.05 was considered to be statistically significant.

3. RESULTS

Hundred participants were enrolled in this study; 50 SLE patients, 31 (62%) of patients at age less than 40 years, while 19 (38%) at age more than 40 years, as in figure (1). 43 (86%) of them were females and 7 (14%) were males, as in figure (2) Fifty healthy participants serve as control group (41 females and 9 males).

10% of patients were exposed to sun, while 90% of patients were not exposed to sun, 6% of patients had current medication and 20 % had chronic medication as in table (1).

The result of serum Anti-Myeloperoxidase Antibodies (MPO) among patients showed that 18% of patients had positive result, while 82% of patients had negative result as in table (2) .

The results revealed that there is no statistical difference in total cholesterol level between patients and control group but there is a significant increase in the LDL-C level of patients when compared to healthy individuals (Table 3).

The duration of disease is not considered risk factor for cholesterol and LDL-C levels in patients with SLE , odds ratios of cholesterol, and LDL-C levels and duration of disease among patients group were 0.5 and 0.6 respectively ($P \geq 0.05$) as in table (4).

54% of patients had the disease for more than 5 years while 46% of them had the disease duration for less than 5 years, as in figure (3) .

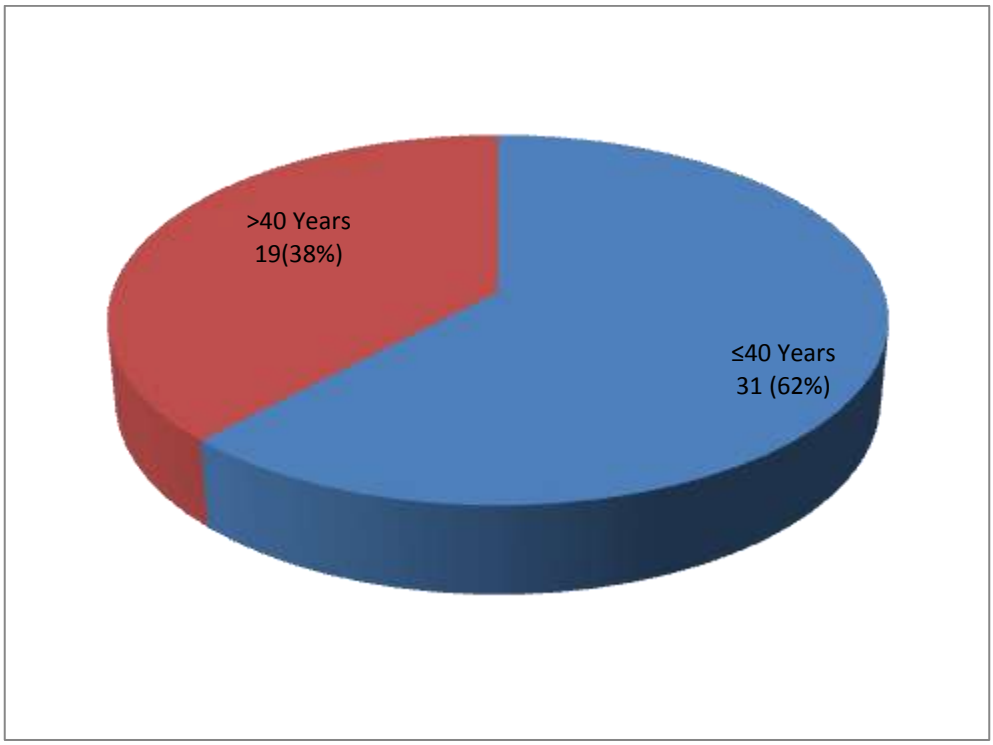

Figure (1)) Distribution of SLE patients according to age.

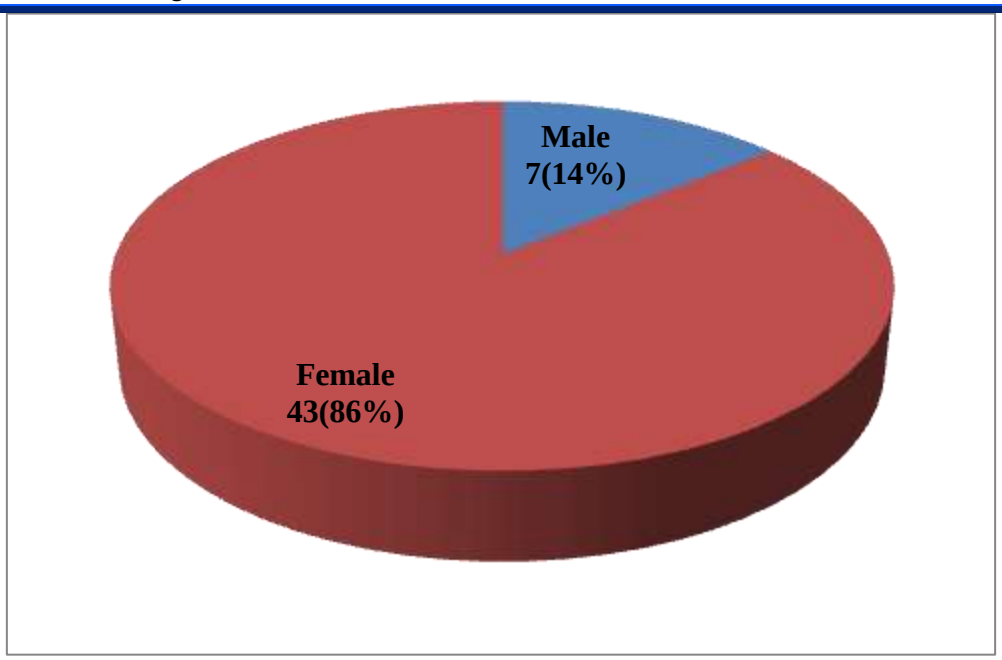

Figure (2)) Distribution of SLE patients according to Gender.

Table (1) : exposure to sunlight ,current medication and chronic medication among case group.

Variables	Case	
	Yes	No
Sun Exposure	5 (10%)	45 (90%)
Current Medication	3 (6%)	47 (94%)
Chronic Medication	10 (20%)	40 (80%)

Chi-Square test

Table (2) Serum Anti-myeloperoxidase Antibodies (MPO) among study groups

		AntiMyeloperoxidase			P-value
		positive	Negative	Total	
sample	case	9(18%)	41(82%)	50	
	control	0	50(100%)	50	0.02
Total		9	91	100	

Chi-Square test

Table (3) mean comparison of Cholesterol and LDL-C in case versus control group

Parameters	Case (Mean ±SD)	Control (Mean ±SD)	*P-value*
Cholesterol (mg/dL)	174 ± 25	173 ± 14	0.8

LDL-c(mg/dL)	121 ± 11	116 ± 9.2	0.03

Results given in mean ± SD , P. value ≤ 0.05 is considered significant.

Independent sample T-test was used for comparison.

Table (4): Odds ratio of total cholesterol mg/dl, LDL-C mg/dl and duration of disease among patients group

				duration of disease (years)			p. value	Odd ratio	Odd ratio
				more than five	less than five	Total			
Total cholesterol mg/dL		less than 200mg/dL	Count	13	27	40			
			% within total cholesterol mg/dL	32.5%	67.5%	100.0%	0.302	0.5	0.5
		200-239 mg/dL	Count	5	5	10			
			% within total cholesterol mg/dL	50.0%	50.0%	100.0%			
Total			Count	18	32	50			
			% within total cholesterol mg/dL	36.0%	64.0%	100.0%			
LDL mg/dL	100-129 mg/dL	Count		13	26	39			
within LDL/C mg/d l		%		33.3%	66.7%	100%			
	130-159 mg/dL	Count		5	6	11	0.459	0.6	
within LDL mg/dL		%		45.5%	54.5%	100%			
	Total	Count		18	32	50			
within LDL mg/dL		%		36.0%	64.0%	100%			

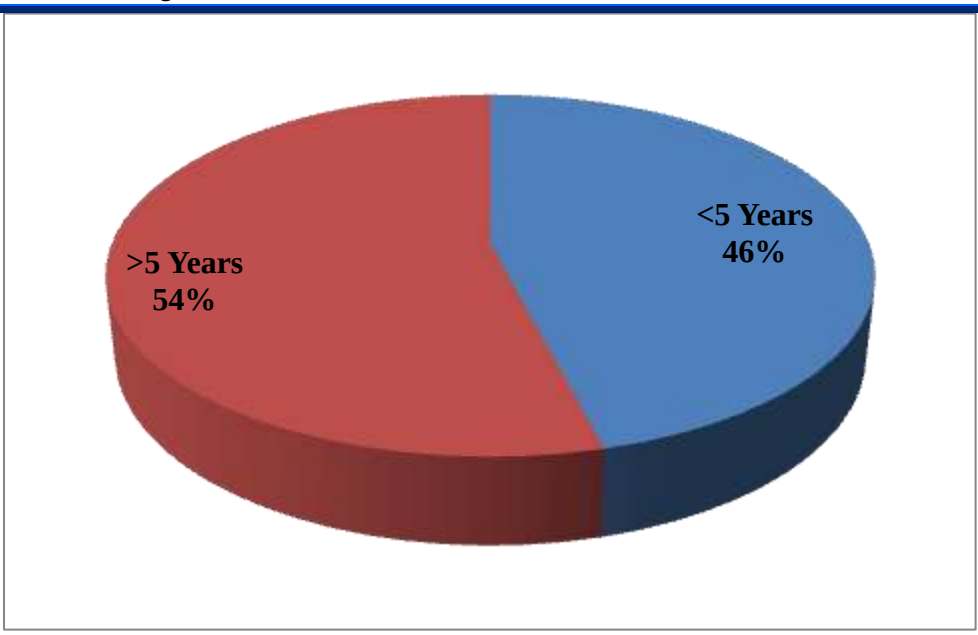

Figure (3): Duration of SLE disease.

4- Discussion

One of the common autoimmune diseases is systemic lupus erythematosis (SLE) . It range from 40 -100 per 100.000. The secretion of multiple auto antibodies against a variety of nuclear antigens is the main characteristic of SLE disease. In a subset of patients with systemic lupus erythematous (SLE), circulating anti-neutrophil cytoplasmic antibodies (ANCA) specific for myeloperoxidase (MPO) are present .In various types of SLE antibodies against MPO have been implicated [(8)].

This study represented their ages of SLE patients ranged from 16-46 years and 62% of SLE patients at age less than 40 years .This study is consistent with another result which found that, the age of SLE patients less than 45 years [(9)] .

The results of this study were pointed to high incidence of systemic lupus erythematosis (SLE) in female 43(86%) versus in male was 7(14 %) .This result agreed with result carried out by Ming-Hui Zhao *et al* ., who noted high incidence of systemic lupus erythematous (SLE) in female 83% versus 17% in male[(10)] , and disagreed with Gang Xin *et al*., who found the incidence of SLE Male/female is 62/59[(11)].Result in this study reported that, 10% of patients were exposed to sun, while 90% of patients were not exposed to sun. This may be due to the patient with SLE when exposed to sun , the sun cause damage in skin cell , because skin cell in SLE patients is very sensitive to light, this explain why the majority of patients with SLE were not exposed to sun, the dying cells are not cleared away completely. As a result the dying cells contents may be free, counting those found in their nuclei. These nuclear proteins (nuclear antigens) are mainly accountable for interacting with the immune system in patients with SLE , and this cause inflammation and injure to many parts of the body [(12) (13)]. The result found that 6% of patients had current medication and 20 % had chronic medication. This result parallel to another result which reported; 33.2% of patients with SLE used chronic medication [(14)] .The present findings observed Positive Anti-Myeloperoxidase antibodies in SLE patients as compared to healthy control (p value=0.001) similar with the another study , which found that, in sera from patients with SLE , there was a heterogeneous antibody response to MPO when compared to controls[(15)] .Van der Woude *et al*., reported , in patients with SLE we found circulating anti-MPO and anti-elastase antibodies [(16)], but this is in contrast to results reported by Nassherger *etal.*, who noted, the absence of anti-Myeloperoxidase antibodies in patients with SLE. [(17)]. Result of this study found, there was insignificant different in the mean level of cholesterol in patients with SLE compared to control group (p- value =0.8). This result disagreed with another result which found, the elevated level of cholesterol is significant in patients with SLE compared to control group (p-value=0.000) [(18).] . The level of serum LDL-C was significant increased in patients with SLE compared to control group (p-value=0.03).This result parallel to another result which showed, the level of LDL-C in patients with SLE is significant increased, the potential role of inflammation in modulating Lipoprotein Lipase (LPL) enzyme is emphasized by the current explanation of a significant losing-regulation of LPL activity enhanced by TNF-α, IL-1 and IFN-γ.18 The alteration of hepatic synthesis of a large array of proteins involved in lipoprotein metabolism is promotes by the acute phase , in coagulation and in the complement system [(19)] . Therefore, it seems reasonable to accept that , the specific alterations in the lipid profile induced by inflammatory conditions

of this disease itself. An promote production of these cytokines (IL6) is feature of SLE, particularly during active disease, and it supports their role in lupus dyslipoproteinemia [(20)].

Also another study done by Carvalho *etal .,* reported that; the traditional risk factors like dyslipidemia and the presence of anticardiolipin antibodies, contribute to the development of atherosclerosis[(21)].

Another study found high LDL-C and cholesterol levels in SLE patients, this may be due to .the levels of circulating TNF-α are raised in SLE and it correlates with active disease and lipids levels [(22)].

The duration of disease is not considered risk factor for cholesterol and LDL-C levels in patients with SLE , odds ratios of cholesterol, and LDL-c levels and duration of disease among patients group were 0.5 and 0.6 respectively ($P \geq 0.05$). This result disagreed with another result which found the odds ratios of cholesterol and duration of SLE disease in patients was 6.6 ($P<0.05$) .[(23)]

CONCLUSION Study confirmed anti-MPO antibodies are found in patients with SLE, the level of LDL-C is elevated in patients with SLE

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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