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Evaluation of Serum β2-microglobulin in Egyptian Patients with Systemic Lupus Erythematosus

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Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by alternating periods of activity and remission. Evaluation of the clinical activity of SLE is important for choosing the correct treatment. Current blood biomarkers for assessing SLE activity are not highly sensitive or specific to changes in disease activity. Therefore, the search for clinically useful markers of its activity is ongoing. This study aimed to evaluate serum beta-2 microglobulin (β2-MG) level in SLE patients and its relation to different clinical manifestations, laboratory parameters and disease activity using systemic lupus disease activity index (SLEDAI). The study included 40 SLE patients, divided according to SLEDAI into two groups: 20 active SLE patients with SLEDAI ≥4 and 20 inactive SLE patients with SLEDAI < 4. Also, 20 ages and sex matched apparently healthy individuals formed a control group. Serum β2-MG levels (mg/L) were measured by MININEPHPLUS. Furthermore, laboratory investigations and fundus examinations were performed. The study revealed a significant increase in serum β2-MG level in SLE patient groups (mean 6.77 ± 1.83 and 2.59 ± 0.43 mg/L), compared with the controls (0.82 ± 0.20mg/L, *P*=0.000), and its level increased in the active SLE group (mean 6.77 ± 1.83 mg/L) than in the inactive group of patients (mean 2.59 ± 0.43 mg/L). Serum β2-MG levels were significantly higher in SLE patients with arthritis, cutaneous and/or mucosal manifestations, Lupus nephritis, and cardiac manifestations but not in patients suffering from hematological, neurological or ocular manifestations. In active SLE patients, serum β2-MG levels correlated positively with SLEDAI, and ESR and correlated negatively with C3 and C4 complement. In conclusion, determination of β2-MG concentration in SLE patients may be helpful in assessing the disease activity as its serum level was higher in SLE patients especially those with active lupus and correlated with certain clinical and laboratory parameters.

Systemic lupus erythematosus (SLE) is an autoimmune disease with periods of flares and remissions, leading to chronic inflammation of numerous tissues and organs. The pathogenesis of SLE is complex and associated with excessive activation of T and B cells, apoptosis impairment, and inadequate immune complex clearance. Excessive B cell activation results in the overproduction of auto antibodies, which combine with chromatin, creating immune complexes and inducing inflammation [1]. The treatment for SLE accompanies the degree of disease activity and, thus, determining this activity level is very important, even though difficult. Systemic lupus erythematosus disease activity is assessed by many serological markers as anti-dsDNA, C3 and C4 complement components and anti-C1q antibodies [2]. However, C3 consumption and positive anti-dsDNA are not present in all SLE manifestation but only associated with specific lupus manifestations. Moreover, negative results could be noted in early stages of the disease, or after medical

treatments as well as in clinical remission [3]. Disease activity may also be reflected by circulating levels of various pro- and anti-inflammatory cytokines including interferon-a (IFN-a). Studies have reported positive correlations between disease activity measured by SLEDAI score and by pro-inflammatory cytokines such as interleukin (IL)-6, IL-18, and IFN-a as well as the anti-inflammatory cytokine IL-10 [4]. IL-18 may induce production of IL-8 and therefore also reflect disease activity. These cytokines have been suggested to play key roles in the immunopathogenesis of SLE [5]. Commonly used inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein are also nonspecific and unreliable in diagnosis of SLE activity. Generally, the CRP level is not elevated in patients with SLE, even with active disease, unless the patient has significant arthritis or infection [6]. On the other hand, composite measurements such as the SLE Disease Activity Index (SLEDAI) and the British Isles Lupus Assessment Group index (BILAG), which combine laboratory and clinical findings, are time-consuming and not easily applicable in daily practice. It consists of 24 weighted clinical and laboratory parameters of nine organ systems. The total possible score for all 24 descriptors is 105[3]. Therefore, the search for new SLE activity markers is ongoing.

β2-microglobulin (β2-MG) is a small low molecular-weight protein (11 kDa) known as the light-chain molecule of the major histocompatibility complex (MHC) class I antigens. It is found on the surface membrane of all nucleated cells. It is particularly abundant on immunocompetent cells, including activated T and B lymphocytes and macrophages. Serum β2-MGG level is reported to be determined mainly by the turnover of these cells [7]. In healthy individuals β2-MG is normally detected in low levels in several body fluids including serum, urine, tears and synovial fluid. Furthermore, its route of elimination is exclusively through the kidney [8]. Serum β2-MG level is reported to be elevated in a variety of medical diseases such as chronic kidney disease, lymphoproliferative diseases, autoimmune diseases and in some viral infection as cytomegalovirus and Human Immunodeficiency Virus (HIV). Therefore, its elevated circulating levels have been found as a result of increased turnover of the activated macrophages and lymphocytes or decreased glomerular filtration rate [8].

Recently, few studies showed the relationship between SLE disease activity and β2-MG blood circulating levels. However, as yet, studies for evaluating the serum β2-microglobulin as a marker for the diagnosis of SLE disease and for monitoring of lupus activity seems limited [8]. Accordingly, this study aimed to evaluate and investigate serum β2-MG levels in Egyptian SLE patients and to correlate these levels with disease activity using SLEDAI, laboratory parameters as well as some disease manifestations.

Patients and Methods

This cross-sectional study was carried out on 40 SLE patients (eight males and 32 females) fulfilling 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE [9]. They were divided according to Systemic Lupus Disease Activity Index (SLDAI) score into two groups: 20 active SLE patients with SLEDAI $\geq$ 4 and 20 inactive SLE patients with SLEDAI < 4, selected from the Rheumatology outpatient Clinic and inpatient of the Rheumatological unit of Internal Medicine Department, and Rheumatology and Rehabilitation Department of Al-Zahraa University Hospital. The study protocol was reviewed and approved by Al-Azhar University Ethics Committee (approval number 201911231, November 2019).

The SLE patient's ages ranged from 20-40 years with mean of 30.50 ± 5.21 years for active SLE group and 30.65 years ± 5.07 for inactive SLE group. Their disease duration range was 1-7 years with mean 2.95 ± 1.90 for active SLE group and 3.55 ± 1.79 for inactive SLE group. They were compared to 20, sex, age and (BMI) matched apparently healthy individuals as a control group. Those with history of any malignancy, lymphoproliferative disorders, chronic kidney disease, Age <18 years, other autoimmune disease rather than SLE, drug-induced lupus erythematosus, pregnancy or associated infections were excluded.

After obtaining oral consents, all patients and controls were subjected to full medical history taking and through clinical examination with stress on duration of the disease and SLE manifestations besides assessment of the SLE disease activity using SLE disease activity index (SLEDAI) scoring. The patients were referred to an ophthalmologist for fundus examination. Body mass index (BMI) was measured as body weight (kg) divided by body height squared (m2).

All individuals underwent measurement of WBCs, Hb, and platelet count, using fully automated cell counter Sysmex KX21N, kits of Siemens (Germany), ESR using the Westergreen method and CRP by latex agglutination (Kit of OMEGA Diagnostics LTD. Omega House, Hillfoots Business Village. Alva FK12 5DQ, Scotland, United Kingdom). Urea, creatinine, albumin and lipid profile were measured on Cobas C311analyzer (Roche Diagnostic, Germany). C3 and C4 were evaluated by means of Radial Immuno Diffusion, kit was supplied by Biocientifica S. A. (Argentina). ANA and Anti-dsDNA were analyzed by means of Indirect Immunofluorescence Technique using Hep2 and Crithidialuciliae respectively, as the substrate. Kit for ANA was supplied by Inova Diagnostics (Inc., San Diego, CA 92131) and Kit for Anti-dsDNA was supplied by Diasorin Inc.-USA. All the above-mentioned techniques were performed according to the relevant manufacturer's instructions. Also, 24 hours urine was collected for assessment of proteinuria.

Serum β2-MG levels were estimated by nephelometry technique using MININEPH PLUS instrument and MININEPH^{TM} Human β2-Microglobulin Kite supplied by the Binding Site Group Ltd (8 Calthorpe Roag, Edgbaston, Birmingham, B15 1QT, U.K.), LOT No. 417663-1 according to the manufacturer's instructions. The approximate measuring range is 0.75-12.0 mg /L and the sensitivity limit for serum samples is 0.2 mg/L.

The nephelometry is a light scattering technique. The determination of soluble antigen concentration by nephelometric method involves a reaction with the antibody bound to a latex particle to form insoluble complexes. When light is passed through the suspension formed, a portion of the light is scattered and detected by a photodiode. The amount of light scattered is directly proportional to the specific protein concentration in the test sample. Concentrations are automatically calculated by reference to a calibration curve stored within the MININEPHPLUS instrument.

Statistical Analysis

The collected data were analyzed using the statistical package for social sciences, (SPSS Inc., Chicago, Illinois, USA) version 20. Quantitative data were expressed as mean± SD while Qualitative data were expressed as number and percentage. Chi-Squared (x2), t test, ANOVA and Pearson correlation coefficient (r) were used when required. Receiver operating characteristics (ROC) analysis was used to note the sensitivity and specificity of tested marker. *P*-value <0.05 was considered significant.

Results

Demographic data of patients and control groups are presented in (Table 1) and Laboratory investigations among SLE patients are presented in (Table 2).

Table 1. Comparison between patients and control as regard demographic data.

		Active SLE	Inactive SLE	Controls	*P*-value
		No. = 20	No. = 20	No. = 20	
Age (Years)	Mean±SD	30.50 ± 5.21	30.65 ± 5.07	30.35 ± 4.40	NS
	Range	20 – 40	20 – 40	20 – 40	
Sex	Female	16 (80.0%)	16 (80.0%)	16 (80.0%)	NS
	Male	4 (20.0%)	4 (20.0%)	4 (20.0%)	
BMI (kg/m2)	Mean±SD	24.00 ± 1.72	24.75 ± 2.00	24.45 ± 1.93	NS
	Range	21 – 27	21 – 28	21 – 28	

P>0.05 is not significant(NS).

Table 2. Comparison between patients and control as regard laboratory data.

		Active SLE No. = 20	Inactive SLE No. = 20	*P*-value
Disease duration (years)	Mean±SD	2.95 ± 1.90	3.55 ± 1.79	NS
	Range	1 – 7	1 – 7	
ESR (mm/hr)	Mean±SD	113.95 ± 13.24	54.60 ± 10.85	0.000
	Range	89 – 130	39 – 88	
CRP	Negative	16 (80.0%)	20 (100.0%)	0.035
	Positive	4 (20.0%)	0 (0.0%)	
C3(mg/dl)	Mean±SD	82.20 ± 21.98	104.90 ± 9.40	0.000
	Range	45 – 123	93 – 135	
C4(mg/dl)	Mean±SD	21.10 ± 6.76	26.95 ± 2.35	0.001
	Range	13 – 35	24 – 32	
ANA	Negative	0 (0.0%)	0 (0.0%)	NA
	Positive	20 (100.0%)	20 (100.0%)	
Anti dsDNA	Negative	4 (20.0%)	18 (90.0%)	0.000
	Positive	16 (80.0%)	2 (10.0%)	
SLEDAI	Median (IQR)	15.5 (10 - 18)	1 (0 - 2)	0.000
	Range	4 – 24	0 – 3	
WBC(×103/mm3)	Mean±SD	6.05 ± 2.28	6.48 ± 1.75	NS
	Range	2.7 – 10	3 – 9	
Hb(g/dl)	Mean±SD	11.93 ± 1.29	12.64 ± 0.89	NS
	Range	9 – 13	9.8 – 14	
Platelet(×103/mm3)	Mean±SD	277.70 ± 115.29	246.35 ± 106.02	NS
	Range	40 – 421	80 – 378	
Urea(mg/dl)	Mean±SD	24.35 ± 4.60	26.60 ± 4.98	NS
	Range	20 – 33	21 – 34	
Creatinine (mg/dl)	Mean±SD	0.70 ± 0.21	0.80 ± 0.22	NS
	Range	0.5 – 1.3	0.5 – 1.3	
Albumin(g/dl)	Mean±SD	3.69 ± 0.47	4.06 ± 0.16	0.002
	Range	2.8 – 4.3	3.8 – 4.4	
24hr ptn	Median (IQR)	900 (650 - 2000)	30 (30 - 95)	0.000
	Range	130 – 4000	20 – 140	
TG (mg/dl)	Mean±SD	173.75 ± 29.06	154.80 ± 21.95	0.025
	Range	138 – 231	98 – 193	
TC (mg/dl)	Mean±SD	188.40 ± 24.27	166.50 ± 25.04	0.008
	Range	158 – 233	118 – 200	
LDL(mg/dl)	Mean±SD	108.90 ± 13.90	98.80 ± 6.99	0.006
	Range	94 – 132	89 – 118	
HDL(mg/dl)	Mean±SD	40.85 ± 3.36	42.10 ± 2.63	NS
	Range	34 – 46	37 – 45	
eGFR(ml/min/1.73 m2)	Mean±SD	90.35 ± 3.57	93.75 ± 3.13	0.003
	Range	82 – 98	89 – 99	

ESR: Erythrocyte Sedimentation Rate; CRP: C Reactive Protein; ANA: Anti-Nuclear Antibodies; Anti-dsDNA: Anti Double Stranded DNA. TC: total cholesterol; TG: triglyceride; HDL-c: high-density lipoprotein-cholesterol; LDL-c: low-density lipoprotein cholesterol. *P*>0.05 is not significant(NS).

The most frequent clinical presentations among active SLE patient group at the time of taking samples were proteinuria, photo sensitivity, oral ulcer, pericardial effusion, then arthralgia representing (85%), (75%), (75%), (65%) and (60%) respectively and the least frequent clinical presentations were neurological manifestation, coronary artery disease forming 0% for both. Visual changes were observed in 3% in the form of retinal changes, retinal hemorrhages, serous exudate or hemorrhage in the choroid and optic neuritis (not due to hypertension, infection, or drugs) (Table 3).

Table 3. Clinical data of systemic lupus erythematosus patients in both active and inactive SLE groups

		Active SLE		Inactive SLE		*P*-value
		No.	%	No.	%	
Fatigue	No	11	55.0%	15	75.0%	NS
	Yes	9	45.0%	5	25.0%	
Fever	No	12	60.0%	16	80.0%	NS
	Yes	8	40.0%	4	20.0%	
Malar.rash	No	10	50.0%	18	90.0%	0.006
	Yes	10	50.0%	2	10.0%	
Photosensitivity	No	5	25.0%	11	55.0%	NS
	Yes	15	75.0%	9	45.0%	
Oral ulcer	No	5	25.0%	15	75.0%	0.002
	Yes	15	75.0%	5	25.0%	
Alopecia	No	18	90.0%	20	100.0%	NS
	Yes	2	10.0%	0	0.0%	
Retinopathy	No	19	95.0%	20	100.0%	NS
	Yes	1	5.0%	0	0.0%	
Visual change	No	17	85.0%	20	100.0%	NS
	Yes	3	15.0%	0	0.0%	
Keratoconjunctivitis	No	16	80.0%	20	100.0%	0.035
	Yes	4	20.0%	0	0.0%	
Arthralgia	No	8	40.0%	10	50.0%	NS
	Yes	12	60.0%	10	50.0%	
Arthritis	No	14	70.0%	20	100.0%	0.008
	Yes	6	30.0%	0	0.0%	
Plural Effusion	No	18	90.0%	20	100.0%	NS
	Yes	2	10.0%	0	0.0%	
Interstitial pulmonary fibrosis (IPF)	No	19	95.0%	20	100.0%	NS
	Yes	1	5.0%	0	0.0%	
Pulmonary hypertension	No	18	90.0%	17	85.0%	NS
	Yes	2	10.0%	3	15.0%	
Pericardial effusion	No	7	35.0%	19	95.0%	0.000
	Yes	13	65.0%	1	5.0%	
Coronary Artery Disease (CAD)	No	20	100.0%	20	100.0%	NA
	Yes	0	0.0%	0	0.0%	
Proteinuria	No	3	15.0%	20	100.0%	0.000
	Yes	17	85.0%	0	0.0%	
Cast	No	10	50.0%	20	100.0%	0.000
	Yes	10	50.0%	0	0.0%	
Neurological manifestation	No	19	95.0%	20	100.0%	NS
	Yes	1	5.0%	0	0.0%	
Mesenteric vasculitis	No	20	100.0%	20	100.0%	NA
	Yes	0	0.0%	0	0.0%	
Pancreatitis	No	18	90.0%	20	100.0%	NS
	Yes	2	10.0%	0	0.0%	
Anemia	No	14	70.0%	19	95.0%	0.037
	Yes	6	30.0%	1	5.0%	
Leucopenia	No	15	75.0%	18	90.0%	NS
	Yes	5	25.0%	2	10.0%	
Thrombocytopenia	No	16	80.0%	16	80.0%	NS
	Yes	4	20.0%	4	20.0%	

P>0.05 is not significant(NS).

The median SLEDAI of active SLE patients was 15.5 with a range from 4 to 24, While, the median SLEDAI of inactive SLE patients was 1 with a range from 0 to 2. The majority of active SLE patients had moderate to severe disease activity (Figure 1).

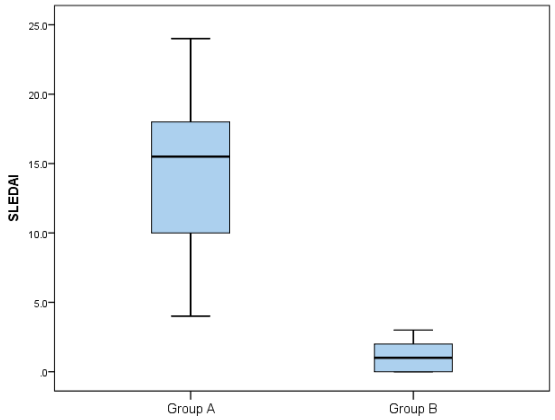

Figure 1. The mean SLDAI in both active and inactive SLE patients groups.

In the active SLE patient group (Group A), a significant increase in serum β2-MG levels (6.77 ± 1.83) was observed in comparison to (Group B), inactive SLE patients and (Group C), the control group (2.59 ± 0.43 and 0.82 ± 0.20, respectively) (*P*=0.000). Also, serum β2-MG levels were higher in inactive SLE patients when compared with controls (*P*=0.000) (Figure 2).

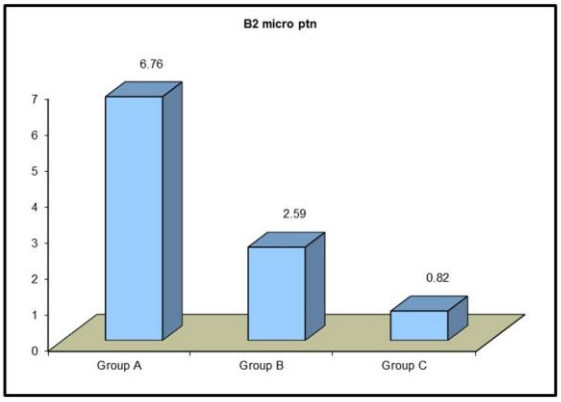

Figure 2. Comparison between SLE patient groups (Group A & B) and the control group (Group C) as regards serum β2-MG level.

In the active SLE patient group, there was a significant positive correlation between β2-MG levels and SLEDAI (r =0.862, *P*<0.001), and ESR (r =0.577, *P*<0.001). Furthermore, in the same group, a significant negative correlation was observed between serum β2-MG levels, C3 (r =0.612, *P*<0.001) and C4 titer (r =0.461, *P*=0.041). While in the inactive SLE group, β2-MG levels were positively correlated only with SLEDAI (r =0.651, *P* < 0.001) (Tables 4). SLE patients who were positive for anti-dsDNA had higher β2-MG serum levels (mean 6.77 ± 2.13 mg/L) when compared to those negative for anti-dsDNA (mean 2.96 ± 0.99mg/L) (*P* = 0.000).

Table 4. Correlation between serum β2-MGlevels and all parameters in patient's groups.

	β2-microprotein			
	Active SLE		Inactive SLE	
	r	*P*-value	r	*P*-value
Age	-0.165	NS	-0.142	NS
BMI	-0.080	NS	0.120	NS
Disease duration	-0.189	NS	-0.177	NS
ESR	0.577**	0.008	-0.097	NS
C3	-0.612**	0.004	-0.144	NS
C4	-0.461*	0.041	0.130	NS
SLEDAI	0.862**	0.000	0.651**	0.002
WBC	0.056	NS	0.134	NS
Hb	0.042	NS	-0.013	NS
Platelet	0.201	NS	0.005	NS
Urea	-0.098	NS	-0.004	NS
Creatinine	0.005	NS	0.104	NS
Albumin	-0.183	NS	0.422	NS
24hr ptn	0.196	NS	0.127	NS
TG	0.401	NS	0.045	NS
TC	0.256	NS	-0.001	NS
LDL	0.196	NS	-0.139	NS
HDL	-0.300	NS	0.234	NS
eGFR	0.367	NS	-0.022	NS

ESR: Erythrocyte Sedimentation Rate; CRP: C Reactive Protein; ANA: Anti-Nuclear Antibodies; Anti-dsDNA: Anti Double Stranded DNA. TC: total cholesterol; TG: triglyceride; HDL-c: high-density lipoprotein-cholesterol; LDL-c: low-density lipoprotein cholesterol. *P*>0.05 is not significant(NS).

β2-microglobulin serum levels were significantly higher in patients with arthritis, cutaneous and/or mucosal manifestations (*P*= 0.001), Lupus nephritis (*P*= 0.001), and cardiac manifestations of SLE (*P*= 0.00). No statistically significant deviation of β2-MG concentration was found in patients suffering from hematological manifestations, neurological or ocular manifestations (Table 5).

Table 5 serum β2-MG levels in SLE patient's groups with various clinical manifestations.

		β2-micro ptn		*P*-value
		Mean±SD	Range	
Fatigue	No	4.15 ± 2.34	2.10 – 8.90	NS
	Yes	5.65 ± 2.54	2.30 – 8.60	
Fever	No	4.15 ± 2.32	2.10 – 8.90	0.037
	Yes	5.92 ± 2.53	2.30 – 8.60	
Malar.rash	No	3.86 ± 2.12	2.10 – 8.90	0.001
	Yes	6.58 ± 2.30	2.80 – 8.60	
Photosensitivity	No	3.70 ± 1.96	2.10 – 7.80	0.041
	Yes	5.33 ± 2.62	2.10 – 8.90	
Oral ulcer	No	3.20 ± 1.31	2.10 – 5.90	0.000
	Yes	6.16 ± 2.52	2.30 – 8.90	
Alopecia	No	4.68 ± 2.55	2.10 – 8.90	NS
	Yes	4.55 ± 0.64	4.10 – 5.00	
Retinopathy	No	4.58 ± 2.44	2.10 – 8.90	NS
	Yes	8.60 ± 0.00	8.60 – 8.60	
Visual change	No	4.48 ± 2.43	2.10 – 8.90	NS
	Yes	7.13 ± 2.20	4.60 – 8.60	
Keratoconjunctivitis	No	4.46 ± 2.45	2.10 – 8.90	NS
	Yes	6.65 ± 2.14	4.60 – 8.60	
Arthralgia	No	4.64 ± 2.64	2.10 – 8.90	NS
	Yes	4.71 ± 2.42	2.10 – 8.60	
Arthritis	No	4.14 ± 2.22	2.10 – 8.60	0.001
	Yes	7.73 ± 1.59	4.60 – 8.90	
Pleural Effusion	No	4.61 ± 2.48	2.10 – 8.90	NS
	Yes	6.05 ± 3.04	3.90 – 8.20	
Interstitial pulmonary fibrosis (IPF)	No	4.68 ± 2.52	2.10 – 8.90	NS
	Yes	4.60 ± 0.00	4.60 – 4.60	
Pulmonary hypertension	No	4.77 ± 2.50	2.10 – 8.90	NS
	Yes	4.00 ± 2.54	2.20 – 8.20	
Pericardial effusion	No	3.52 ± 1.98	2.10 – 8.60	0.000
	Yes	6.82 ± 1.85	3.40 – 8.90	
Proteinuria	No	3.00 ± 1.37	2.10 – 8.60	0.000
	Yes	6.95 ± 1.71	4.10 – 8.90	
Cast	No	3.64 ± 1.81	2.10 – 8.20	0.000
	Yes	7.79 ± 1.39	4.90 – 8.90	
Neurological manifestations	No	4.58 ± 2.44	2.10 – 8.90	NS
	Yes	8.60 ± 0.00	8.60 – 8.60	
Pancreatitis	No	4.50 ± 2.42	2.10 – 8.90	0.048
	Yes	8.05 ± 0.64	7.60 – 8.50	
Anemia	No	4.45 ± 2.54	2.10 – 8.90	NS
	Yes	5.73 ± 2.10	2.70 – 8.60	
Leucopenia	No	4.55 ± 2.52	2.10 – 8.90	NS
	Yes	5.29 ± 2.43	2.50 – 8.60	
Thrombocytopenia	No	4.78 ± 2.59	2.10 – 8.90	NS
	Yes	4.29 ± 2.15	2.40 – 8.20	

P>0.05 is not significant(NS).

Serum β2-MG had a good diagnostic value of disease activity (AUC=1.000); at serum β2-MG cutoff value of 3.6, with sensitivity of 100% and specificity of 100% (Figure 3).

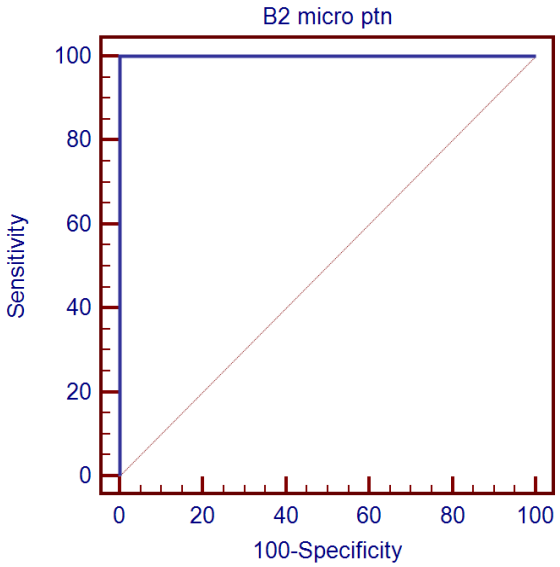

Figure 3. Receiver operating characteristic: Sensitivity and specificity of serum β2-MG in diagnosis of SLE disease activity LE disease activity

Discussion

SLE is a multisystem autoimmune disease with a wide spectrum of clinical manifestations characterized by remissions and exacerbations. Considerable importance has been attached recently to early detection of SLE exacerbation and to monitoring its activity. The search for sensitive markers of the disease activity continues to enable anticipation of exacerbation at the preclinical stage. The significance of β2-MG in monitoring SLE activity has been highlighted lately [8].

Serum β2-MG is filtrated through glomeruli, and most of it is reabsorbed in the proximal tubules of the kidneys under normal condition. Its level in serum increases with increasing β2-MG production and decreasing renal function. The normal upper limit of serum β2 MG level corresponds to a GFR of 65.0 [10]. In our patients, in both active and inactive groups, the eGFR was higher than 65.0 mL/min/1.73 m2with mean of 90.35 ± 3057 and 93.75 ±3.13, respectively. Thus, the level of serum β2-MG is considered not to be affected by renal function in our patients [3].

In this study, we found that serum levels of β2-MG were significantly higher in active SLE patients when compared with inactive SLE patients and controls (P=0.000). Moreover, serum β2-MG levels were positively correlated with SLEDAI (r =0.862, $P< 0.001$), and ESR (r =0.577, $P < 0.001$) but negatively correlated withC3 (r =0.612, $P < 0.001$) and C4 titer (r =0.461, $P = 0.041$) in these patients. In line with our findings, Żychowska *et al.*, [8] reported similar results and concluded that elevated serum β2-MG levels in SLE patients was correlated with disease activity marker such as SLEDAI-2K, anti-dsDNA antibodies titer, andC4 component and considered serumβ2-MG levels as a useful biomarker of lupus activity. Hermansen *et al.*, [11] studied 26 SLE patients and recorded the relationship between β2-MG level and disease activity scored according to SLEDAI, C3 component and daily proteinuria. They also demonstrated a significant correlation between the serum level of β2-MG and cytokines responsible for SLE pathogenesis: IL-6, IL-8, IL-10, IL-18, IFN-α.11. Similar results were also found by Skare *et al.*, [12] in a group of 129 SLE patients, β2-MG serum levels correlated with SLEDAI, anti-dsDNA antibodies, and C3.

The reason for elevated β2-MG levels in SLE patients is poorly understood. Some

authors suggested that this increase might result from the increased lymphocytes turnover in autoimmune disease, or the presence of immune complexes formed by β2-MG and anti-β2-MG antibodies which have a larger size, they cannot be removed by the kidneys so, raising the serum levels of β2-MG and giving additional reason for this elevation.

Determination of serum anti-dsDNA titre and complement levels (C3, C4) are the most common and useful tests available for assessing disease activity and predicting flares in SLE. However, both these tests have limitations in that elevated anti-dsDNA antibodies and hypocomplementemia do not occur in all patients and their correlation with disease activity is not absolute [3]. In this study, in the group with active SLE, anti-dsDNA was positive only in 16 patients (80%) with concurrent flares and negative in 4 patients (20%). Also, complement components C3 and C4 showed normal levels in some patients of the active group. Decrease in C3 andC4 titers were observed in 55% and 60% of the disease flares, respectively. On the other hand, serum β2-MG level was clearly high in all of the 20 patients with active status of SLE. These data suggest that the measurement of β2-MG is superior to anti-dsDNA and complement components (C3, C4) and seems to be a useful addition to the laboratory tests that can help in assessment of disease activity of SLE.

When serum β2-MG levels were compared to clinical manifestations of SLE, higher levels of β2-MG were observed in SLE patients with manifestation of arthritis, cutaneous and/or mucosal manifestations, lupus nephritis, and cardiac manifestations of SLE but no significant deviation of β2-MG concentration was found in patients suffering from hematological manifestations, neurological or ocular manifestations. This is in accordance with Żychowska *et al.*, [8] who found higher β2-MG levels in SLE patients with musculoskeletal system involvement, but they also found higher β2-MG levels in SLE patients with hematological symptoms and vasculitis. The study conducted by Kim *et al.*, [13] on 100 SLE patients, reported increased serum β2-MG levels in 97% of patients, and mostly observed in patients with serositis, oral erosions and symptoms of lupus nephritis.

An experimental study on mice diseased with SLE that lacks β2-MG revealed differences in the clinical presentation of the disease (higher percentage of mice with cutaneous symptoms, with a lower percentage of kidney disease). These results indicate a possible impact of β2-MG levels on the clinical course of SLE [14].

In our study, ROC curve displayed that β2-MGlevel had a good diagnostic value for detection of disease activity with 100% sensitivity and specificity of 100% at cutoff value of 3.6. Hence, it may be considered as an accurate and sensitive marker for diagnosis of SLE lupus activity, however, more studies are needed to confirm such high sensitivity and specificity.

In conclusion, Serum β2-microglobulin level was significantly elevated in active SLE patients and was superior to other lupus activity markers in detecting patients with flares, but further studies on larger patient population are needed.

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