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Role of T-helper/T-Cytotoxic Cells as Biomarkers of Lupus Nephritis

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Abstract

Systemic lupus erythematosus is typical systemic autoimmune disease described by various, multisystem involvement & production of array of autoantibodies. Lupus nephritis is prevalent & severe manifestations of SLE affecting forty–seventy percent of all SLE studied cases & is significant reason for morbidity & hospital admissions. T lymphocytes have pivotal role in development of autoimmune disease & subsequent damage to target organs. Aim to determine the role of T-helper (CD3+\CD4+), T-cytotoxic (CD3+/CD8+) lymphocytes in peripheral blood as biomarkers for diagnosis of lupus nephritis. Research was conducted on100 individuals including fifty SLE studied cases (Group I) diagnosed according to 2012 Systemic Lupus International Collaborating Clinics criteria and 50 matched healthy control individuals (Group II). There was remarkably significant decrease in mean ± SD of CD4% in group I (42.8 ± 12.3) when compared with group II (60.5 ± 8.0) with (p-value < 0.001).There was remarkably significant increase in mean ± SD of CD8% in group I (49.9 ± 12.3) when compared with group II (32.5 ± 5.8) with (p-value < 0.001).There was remarkably significant increase in mean ± SD of double negative % in group I (6.29 ± 1.49) when compared with group II (3.33 ± 0.96) with (p-value < 0.001).There was remarkably significant reduction in mean ± SD of CD4 / CD8 ratio in group I (0.95 ± 0.52) when compared with group II (1.94 ± 0.57) with (p-value < 0.001).Double negative % can significantly diagnose SLE cases with p value <0.001, AUC 96.2%, sensitivity 86% & specificity 96% when using cutoff point 4.95%.CD4%/CD8% ratio can significantly diagnose SLE cases with p value <0.001, AUC 91.4%, sensitivity 90% & specificity 82% when using cutoff point 1.5. CD4%/CD8% ratio and double negative T cells can be used as diagnostic test for SLE patients developing lupus nephritis.

Keywords: CD4, CD8, SLE (Systemic lupus erythematosus), (lupus nephritis), T-helper/T-cytotoxic, biomarkers.

1. Introduction

Systemic lupus erythematosus is classical systemic autoimmune disease described by diverse, multisystem involvement & production of array of autoantibodies. SLE can involve almost any organ and clinical features in individual studied cases can be quite variable, ranging from mild skin & joint involvement to severe, organ /life-threatening disease. This is usually the result of autoantibody and immune complex mediated tissue damage [1]. Lupus nephritis (LN) frequent & serious manifestations of SLE affecting forty–seventy% of all SLE studied cases & is major reason for morbidity & hospital admissions [2]. Despite adequate immunosuppressive therapy ten-thirty percent of LN studied cases progress to end-stage renal disease & require renal replacement treatment. While overall survival in SLE patients at 10 years is approximately 92% it decreases to 88% in those with LN [3]. Proteinuria can take long time to normalise during follow-up, making it difficult to distinguish between proteinuria caused by irreversible damage to glomerular capillaries and ongoing LN activity [4]. Existence of periglomerular infiltrating CD8+ T-cells, in particular, has been shown to correlate with histologic activity, clinical severity, & poor prognosis of LN [5]. Thus, T-cell subsets study at peripheral blood is essential to improve diagnostic accuracy & sensitivity of lupus renal disease, prognostic stratification, monitoring, therapy response, & detection of early renal flares.

2. Patients and Methods

This research was carried out on 50 SLE (Group I) studied cases diagnosed according to 2012 Systemic Lupus International Collaborating Clinics criteria and 50 matched healthy subjects as control group (Group II).
Patients were recruited from Rheumatology outpatient clinic & inpatient ward of Internal Medicine department at Al zahraa University Hospital during time from July 2020 to October 2021.

The cases studied were separated into: Group I a: twenty-five *patients* diagnosed as lupus but without clinical or lab evidence of lupus nephritis. Group I b: 25 patients with active lupus nephritis which was either biopsy proven or defined by high disease activity.

2.1 Exclusion criteria

Other autoimmune disease, Diabetes mellitus and pregnancy

2.2 Methods

The individuals involved were subjected to the following:
History: with particular stress on birth date, gender, period of disease, presence of fever, malaise, weight loss, anorexia, hair fall, skin lesion, photosensitivity, joint pain, eye, renal, hematological and CNS related complaints. Examination: for the presence of skin, eye, cardiovascular, respiratory, renal, neuropsychiatric and hematological manifestations was done.

2.3 Laboratory investigations that were done for the studied group of patients:

Blood samples were collected on ethylene diamine tetra-acetic acid anticoagulant for: Complete blood counting using an automated hematology analyser sysmex K x21N (Kobe, Japan). Erythrocyte sedimentation rate (ESR) was performed using modified Westergren method. Immunophenotyping of preiphral blood, lymphocytes was done by flowcytometry on Becton Dickinson FACs caliber using a panel of monoclonal antibodies included: Fluorescein isothiocyanate conjugated: CD3, phycoerythrin conjugated: CD4 and Peridinin chlorophyll protein conjugated: CD8. To estimate the percentage of T-helper (CD3+/CD4+) & T-cytotoxic (CD3+/CD8+) & double negative ($CD4^-/CD8^-$) lymphocytes of peripheral blood. Laboratory tests: Blood samples collected on plain tubes, left to clot and sera was used for the following using automated

chemistry analyzer Cobas c 311 system, Germany, Roche for: Renal function examinations containing (blood urea, serum creatinine, serum uric acid & protein: creatinine ratio). Liver enzymes and function examinations containing (serum alanine aminotransferase, aspartate aminotransferase & serum albumin). Renal function examinations were performed using chemistry analyzer Cobas c 311 system, Germany, Roche for C- reactive protein was performed using Cobas Integra 400 plus, Germany, Roche. Anti-nuclear antibodies & Anti deoxyribonucleic acid (Anti ds-DNA) antibodies by indirect immuno-fluorescence technique. C3 and C4 levels (was performed using radial immuno diffusion). eGFR was calculated using CKD-EPI formula

Complete urine analysis & twenty-four h urinary protein using colorimetric method (micrototal protein (MT-P) pyrogallol – Red).

The assessment of disease activity state of SLE studied cases was done by applying SLEDAI, & every patient received score, which is sum of scores assigned to specific symptoms & laboratory parameters. Lupus disease activity is assessed by global score (0-105), extra-renal score (zero-eighty-nine) & renal score (zero-sixteen). Renal score consists of four components, pyuria, hematuria, proteinuria, & urinary casts; each weighed with four points. Greater score usually shows more severe disease.

Assessment of renal disease by renal biopsy: Renal pathology will be identified in some cases according to revised International Society of Nephrology & Renal Pathology Society 2003 classification of lupus nephritis (Bajema et al., 2018). Ethical consideration: researcher took into consideration basic principles of biomedical ethics for participant studied cases. Patients provided free & voluntary written informed consent. Studied cases were informed of their absolute right to participate in or withdraw from research at any time. Personnel privacy & data confidentiality were protected.

2.4 Statistical analysis

The Statistical Program for Social Science version 24 was used to analyse the data. The quantitative data were presented as mean SD. The frequency & percentage of qualitative data were used. Following exams were carried out: Mann–Whitney when comparing 2 means, the U test was used (for abnormal distributed data). One-way analysis of variance (ANOVA) is used when comparing more than 2 means (for normally distributed data). When comparing more than 2 means, use the Kruskal Willis test (for abnormally distributed data). When comparing non-parametric data, Chi-square test was used. For data correlation, Pearson's correlation coefficient (r): test was used. post-hoc test was used to make multiple comparisons among variables.

3. Results

Total of 50 SLE patients (Group I) , 25 of them were diagnosed SLE without LN (Group I a) & 25 were SLE with LN (Group I b) & 50 matched healthy control individuals (Group II) were included in our final analysis.

As show in table 1 indicates that there is no statistically significant variation (p-value > 0.05) among the studied groups in terms of gender or age.

As show in table 2 there was a significant decrease in mean ± SD of RBCs in group I (3.9 ± 0.7) when compared with that of group II (5.5 ± 4.2) with (p-value < 0.001). decrease in mean ± There was a significant SD of Hb in group I (11.2 ± 1.9) when compared with group II (13.1 ± 0.9) with (p-value < 0.001). There was a significant decrease in mean ± SD of PLTs in group I (239.8 ± 94.8) when compared with group II (294.3 ± 71.8) with (p-value = 0.008). There was a significant increase in mean ± SD of ESR in group I (54.2 ± 41.9) when compared with group II (4.3 ± 1.6) with (p-value < 0.001). There was remarkable significant increase in mean ± SD of CRP in group I (12.5 ± 7.2) when compared with

group II (1.5 ± 0.6) with (p-value < 0.001). No variation among group I & group II as regard WBCs (p-value > 0.05).

As show in table 3 there was remarkable significant decrease in mean ± SD of CD4% in group Ia (41.4 ± 14.5) when compared with group II (60.5 ± 8.0) with (p-value < 0.001). There was remarkable significant increase in mean ± SD of CD8% in group Ia (51.3 ± 14.01) when compared with group II (32.5 ± 5.8) with (p-value < 0.001). There was remarkable significant increase in mean ± SD of double negative % in group Ia (6.3 ± 1.2) when compared with group II (3.33 ± 0.96) with (p-value < 0.001). There was remarkable significant decrease in mean ± SD of CD4 / CD8 ratio in group Ia (0.94 ± 0.63) when compared with group II (1.94 ± 0.57) with (p-value < 0.001).

As show in table 4 there was remarkable significant decrease in mean ± SD of eGFR in group Ib (39.01 ± 12.4) when compared with group II (106.7 ± 9.0) with (p-value < 0.001). There was remarkable significant increase in mean ± SD of protein/Creat ratio in group Ib (1.09 ± 1.24) when compared with group II (0.1 ± 0.0) with (p-value < 0.001). There was remarkable significant increase in mean ± SD of 24-hour urine protein in group Ib (675.7 ± 694) when compared with group II (74.3 ± 13.4) with (p-value < 0.001). There was remarkable significant decrease in mean ± SD of C3 in group Ib (77.9 ± 26) when compared with group II (138.2 ± 10.3) with (p-value < 0.001). There was remarkable significant decrease in mean ± SD of C4 in group Ib (22 ± 11.2) when compared with group II (29.8 ± 4.7) with (p-value < 0.001).

As show in figure 1 and2 there was remarkable significant increase in mean ± SD of double negative % in group Ib (6.3 ± 1.7) and group Ia (6.3 ± 1.2) when compared with group II (3.33 ± 0.96) with (p-value < 0.001). There was significant decrease in mean ± SD of CD4 / CD8 ratio in group Ib (0.96 ± 0.39) and group Ia (0.95 ± 0.63) when compared with group II (1.94 ± 0.57) with (p-value < 0.001).

As shown in Table 5, there was a highly statistically significant decrease in the mean ± SD of CD4 / CD8 ratio in group Ib (0.95 ± 0.38) when compared with group II (1.94 ± 0.57) with (p-value < 0.001).

As table 6 there was a highly statistical significant decrease in the mean ± SD of CD4% in group Ib (44.2 ± 9.6) and group Ia (41.4 ± 14.6) when compared with group II (60.5 ± 8) with (p-value < 0.001) .There was a highly statistical significant increase in the mean ± SD of CD8% in group Ib (48.5 ± 10.3) and group Ia (51.3 ± 14) when compared with group II (32.5 ± 5.8) with (p-value < 0.001).

As show in table 7 in the lupus nephritis group, Pearson correlation test showed that CD4% was negatively correlate with CD8% with p value <0.001 & positively correlated with CD4 percent/CD8percent ratio with p value <0.001, while CD8% negatively correlated with CD4percent/CD8percent ratio with p value <0.001. Double negative% was negatively correlated with C4 level with p value 0.044.

As show in table 8 in the SLE cases, Pearson correlation test showed that CD4% is positively correlated with CD4/CD8% ratio and 24 hours urinary protein with p value <0.001 and 0.001, and negatively correlated to CD8% with p value <0.001. CD8% was negatively correlated with CD4%/CD8% ratio, 24 hours urinary protein and C4 with p values <0.001, <0.001, & 0.02. CD4%/CD8% ratio was directly correlated to 24 hours urinary protein with p value <0.001.

Double negative% can significantly diagnose LN cases with p value <0.001, AUC 96.2%, sensitivity 86% & specificity 96% when using cutoff point 4.95%.

As show in figure 5 CD4%/CD8% ratio can significantly diagnose LN cases with p value <0.001, AUC 91.4%, sensitivity 90% & specificity 82% when using cutoff point 1.5.

Table 1: Comparisons among group I & group II with regard to age and sex

		Group I (n = fifty)		Group II (n = fifty)		Stat. test	P-value
Gender	Male	8	16%	10	20%	$X^2 = 0.27$	0.603 NS
	Female	42	84%	40	80%		
Years old	Mean	35.8		34.8		T = 0.64	0.520 NS
	±SD	8.8		7.5			

S = Significant, HS= highly significant, NS= non-significant

Table 2: Comparisons among group I & group II as regards chemistry laboratory tests

		Group I (n = 50)	Group II (n = 50)	MW	P-value
WBCs (x10³/ul)	Mean	7.2	7.3	1113	0.345 NS
	± SD	3.1	1.9		
RBCs (million/ul)	Mean	3.9	5.5	252.5	< 0.001 HS
	± SD	0.7	4.2		
Hb (g/dl)	Mean	11.2	13.1	495.5	< 0.001 HS
	± SD	1.9	0.9		
PLTs (x10³/ul)	Mean	239.8	294.3	866	0.008 S
	± SD	94.8	71.8		
ESR (mm/h)	Mean	54.2	4.3	56.5	< 0.001 HS
	± SD	41.9	1.6		
CRP (mg/L)	Mean	12.5	1.5	40	< 0.001 HS
	± SD	7.2	0.6		

S = Significant, HS= highly significant, NS= non-significant

Table 3: Comparisons among Group Ia & Group II as regard studied markers.

		Group Ia (n = 25)	Group II (n = 50)	MW	P-value
CD4%	Mean	41.4	60.5	154	< 0.001 HS
	± SD	14.5	8.0		
CD8%	Mean	51.3	32.5	129	< 0.001 HS
	± SD	14.01	5.8		
Double negative %	Mean	6.3	3.33	24.5	< 0.001 HS
	± SD	1.2	0.96		
CD4 \ CD8 ratio	Mean	0.94	1.94	136.5	< 0.001 HS
	± SD	0.63	0.57		

Table 4: Comparisons between Group I b & Group II as regards other laboratory data.

		Group I b (n = 25)	Group II (n = 50)	MW	P-value
eGFR	Mean	39.01	106.7	0.0	< 0.001 HS
	± SD	12.4	9.0		
Protein/ Creat	Mean	1.09	0.1	0.0	< 0.001 HS
	± SD	1.24	0.0		
24 h urine protein	Mean	675.7	74.3	0.0	< 0.001 HS
	± SD	694.0	13.4		
C3 (mg/dl)	Mean	77.9	138.2	0.0	< 0.001 HS
	± SD	26.0	10.3		
C4 (mg/dl)	Mean	22.4	29.8	383.5	< 0.001 HS
	± SD	11.2	4.7		

Table 5: Comparisons between Group I b and Group II as regard studied markers.

		Group I b (n = 25)	Group II (n = 50)	MW	P-value
CD4%	Mean	44.2	60.5	154	< 0.001 HS
	± SD	9.6	8.0		
CD8%	Mean	48.5	32.5	129	< 0.001 HS
	± SD	10.3	5.8		
Double negative %	Mean	6.29	3.33	24.5	< 0.001 HS
	± SD	1.74	0.96		
CD4 \ CD8 ratio	Mean	0.95	1.94	136.5	< 0.001 HS
	± SD	0.38	0.57		

Table 6: Comparison between group I (a,b) and group II as regards the markers studied.

		Groups			f	P-value
		Group I b (n = 25)	Group I a (n = 25)	Group II (n = 50)		
CD4%	Mean	44.2	41.4	60.5	36.4	< 0.001 HS
	± SD	9.6	14.6	8.0		
CD8%	Mean	48.5	51.3	32.5	41.8	< 0.001 HS
	± SD	10.3	14.0	5.8		
Double negative %	Mean	6.3	6.3	3.3	69.3	< 0.001 HS
	± SD	1.7	1.2	1.0		
CD4 \ CD8 ratio	Mean	0.96	0.95	1.94	40.6	< 0.001 HS
	± SD	0.39	0.63	0.57		

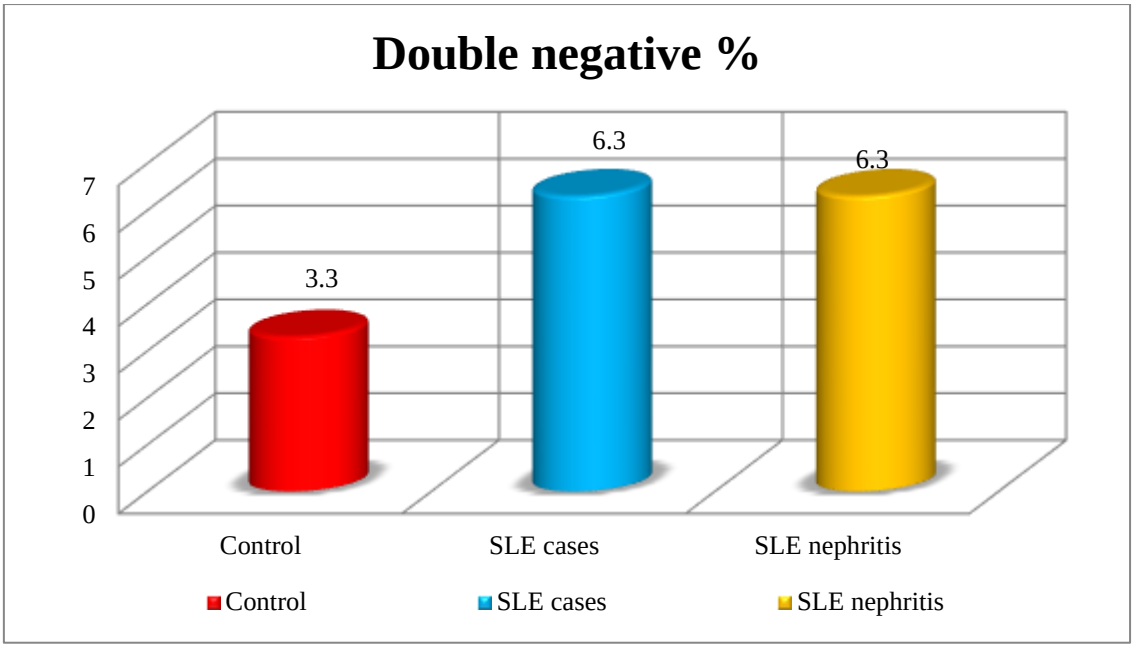

Figure 1: Comparisons between studied groups as regard double negative %.

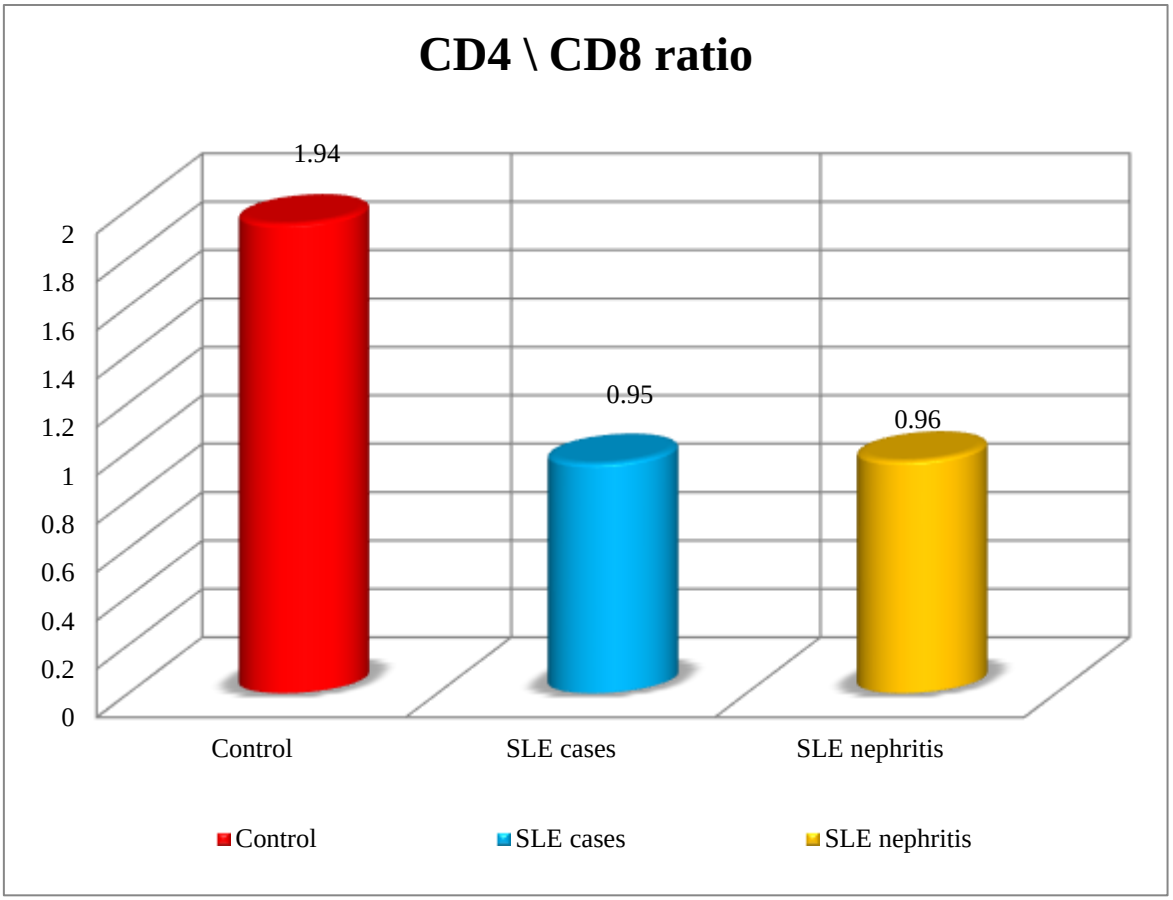

Figure 2: Comparisons between studied groups as regards CD4/CD8 ratio.

Table 7: Correlation between CD4, CD8, double negative% and CD4%/CD8% ratio with other laboratory findings in the lupus nephritis group

lupus nephritis		CD4%	CD8%	Double negative %	CD4%\CD8% ratio
CD4percent	r	1			
	P value	.			
CD8percent	r	-0.883-	1		
	P value	< 0.001	.		
Double negative %	r	0.131	-0.180-	1	
	P value	0.534	0.39	.	
CD4%\CD8% ratio	r	0.975	-0.953-	0.164	1
	P value	< 0.001	< 0.001	0.435	.
e GFR	r	0.065	-0.130-	-0.006-	0.087
	P value	0.757	0.535	0.977	0.68
protein \create	r	-0.129-	0.117	0.063	-0.112-
	P value	0.538	0.576	0.764	0.593
24 h protein in urine	r	0.056	-0.019-	-0.068-	0.04
	P value	0.79	0.927	0.748	0.848
C3	r	-0.069-	0.086	-0.226-	-0.086-
	P value	0.743	0.682	0.278	0.683
C4	r	0.003	0.063	-0.407-	-0.028-
	P value	0.991	0.767	0.044	0.894

Table 8: Correlation between CD4, CD8, double negative% and CD4%/CD8% ratio with other laboratory findings in the SLE group

SLE		CD4%	CD8%	Double negative %	CD4%\CD8% ratio
CD4percent	R	1			
	P value	.			
CD8percent	R	-0.968-	1		
	P value	< 0.001	.		
Double negative %	R	-0.030-	-0.057-	1	
	P value	0.886	0.788	.	
CD4%\CD8% ratio	R	0.995	-0.981-	0.021	1
	P value	< 0.001	< 0.001	0.92	.
e GFR	R	0.159	-0.180-	-0.085-	0.169
	P value	0.449	0.389	0.685	0.42
protien \creat	R	0.051	-0.108-	0.288	0.082
	P value	0.808	0.606	0.162	0.698
24 h protien in urine	R	0.64	-0.688-	0.099	0.652
	P value	0.001	< 0.001	0.638	< 0.001
C3	R	0.145	-0.254-	0.242	0.165
	P value	0.49	0.22	0.244	0.432
C4	R	0.351	-0.455-	-0.019-	0.365
	P value	0.085	0.022	0.93	0.072

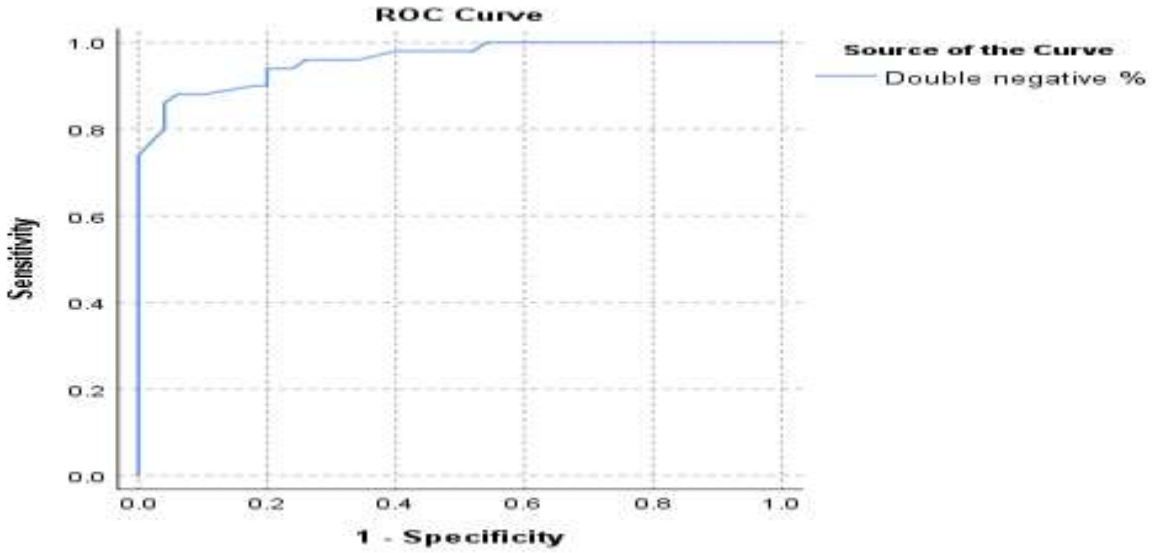

Figure 3: ROC curve showing the ability of double negative% in diagnosis of cases

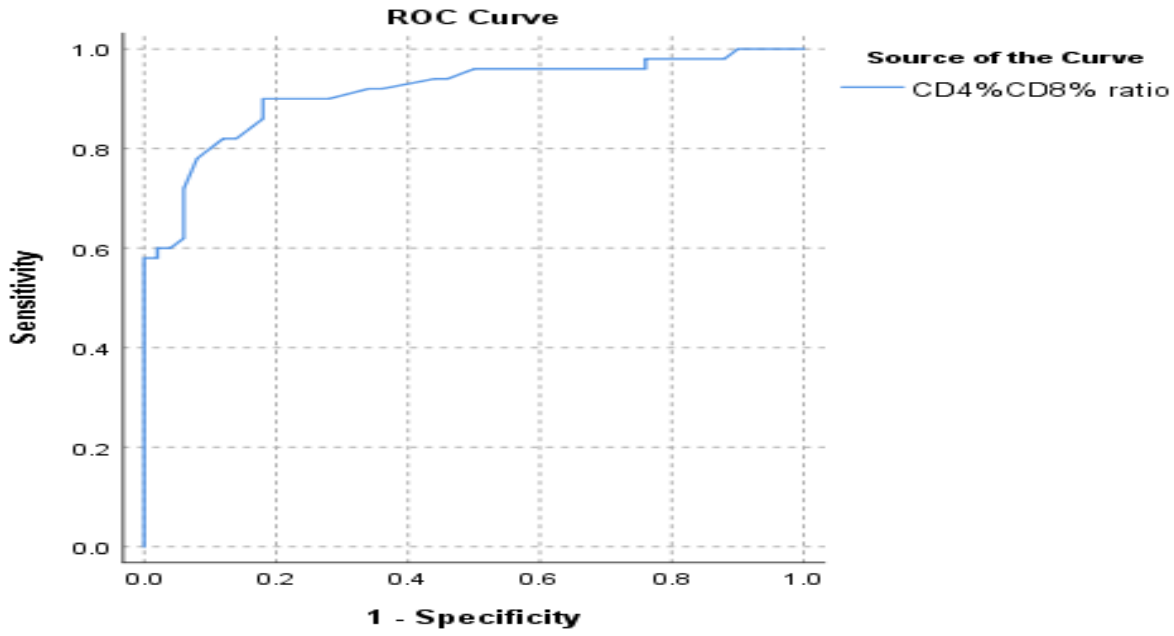

Figure 4: ROC curve viewing capability of CD4/CD8% ratio in diagnosis of cases

4. Discussion

Double negative (DN) T lymphocytes: were initially identified and characterized in lpr and gld mice (deficiency of either Fas or Fas ligand) in which lympho-proliferative syndrome developed due to impaired Fas-mediated apoptosis.[6].

However, a small population of αβ T cells which do not express both CD4 and CD8, termed "double negative" T (DNT) cells and have been considered to contribute to the pathophysiology of a series of autoimmune diseases [7].

Rise in double-negative (DN) cells has been observed in SLE studied cases. DN cells can be divided into several subsets, like TCR-, TCR-. They can be derived from CD4 (+) & CD8 (+) T lymphocytes, as well as from distinct cell lineage [8].

T cells are regulated by adhesion molecule CD44, which improves signal transduction via TCR/CD3 complex. In SLE studied cases, there is rise in CD44, which correlates with disease activity [9].

So, in current research we wanted to determine role of T-helper (CD3+\CD4+), T-cytotoxic (CD3+/CD8+) lymphocytes in peripheral blood as biomarkers for diagnosis of lupus nephritis & explore its relationship with other parameters of lupus disease activity.

We recruited 100 individuals including 50 SLE studied cases diagnosed according to 2012 Systemic Lupus International Collaborating Clinics criteria (group I), 25 of them were SLE without LN (group Ia) & 25 were SLE with LN (group Ib) & 50 matched healthy control individuals (group II).

In present study, females accounted for the majority of the included sample (80%).

These findings are consistent with most of the evidence available in literature of (Crispín et al 2010)[8] that reported higher incidence of SLE among females compared to males, specifically middle-aged females with incidence ratio females to males 9:1.

In the research we showed that there was decrease among study groups regarding RBCs count, Hemoglobin level, and platelet count between study groups.

These findings were reported also by Aleem et al 2014 [9] found that there was low hemoglobin level, low RBCs count and low platelet count in SLE patients.

In the study of Aringer 2019 [10] found that, pancytopenia is one of criteria for SLE (revised American College of Rheumatology classification).

In the study of Hepburn et al 2010 [11] study showed that, anemia is found in almost 50% of SLE patients, mainly in the form of anemia of chronic disease (normochromic normocytic anemia).

In our study, ESR & CRP were greater among group I with p value <0.001 & <0.001.

This is agree with the study by Firooz et al. 2011 [12] as they found that, ESR and CRP are both inflammatory markers that are related to SLE activity and exacerbation.

In the current study, AST and ALT were significantly elevated among group I compared to group II with p values < 0.001.

These findings were supported by Yang et al. 2012 [13] as they investigated the liver functions among 198 SLE patients without liver disease and 154 healthy controls; they found that AST and ALT were significantly elevated among SLE and LN patients with p values 0.001.

In the present study, Complement C3 and C4 were significantly more consumed among group I with p value <0.001 & <0.001.

These findings are consistent with Narayanan et al, 2010 study as they demonstrated that C3 and C4 were consumed more commonly reported among SLE and LN patients compared to controls.

As well, Hussain et al. 2008 [14] research that conducted on fifty SLE studied cases and their outcomes found that level of C3 and C4 were more consumed among LN

group versus SLE group, specifically C4 which was more profoundly consumed versus C3.

In our study, ANA is highly significant positive in all group I cases by 100% and negative in group II.

This is confirmed by Leuchten et al. 2018 [15] as they revealed that positive ANA is essential for classification of SLE in new EULAR/ACR criteria.

In present study, Anti-ds DNA was positive in 82% of all group I and negative in 18% of them with highly significant negative result in all group II individuals.

This finding is enhanced by Conti et al. 2015 [16] as they found that anti-dsDNA antibodies are indicator for Systemic Lupus Erythematosus & seventy–ninety eight percent of studied cases test positive.

In current work, CD4% & CD4%/CD8% ratio was significantly lower among groupI than groupII. While CD8%, and Double negative**%** were greater among group I than group II with p value <0.001 each

These results are consistent with research reported by Matsushita et al. 2000 [17] whom investigated the CD4/CD8 ratio between 30 SLE studied cases versus 30 healthy controls, results revealed that CD4/CD8 ratio was lower among SLE patients than control, CD8 were significantly higher among SLE patients.

In our lupus nephritis cases renal, biopsy showed that 16% were LN class II, 44% were LN class III, 20% were LN class IV, 8% were class V, one case acute interstitial nephritis and 2 cases Membranous lupus nephritis.Weening et al. 2004 [18] showed that International Society of Nephrology/Renal Pathology Society 2003 classification of lupus nephritis was developed based on light microscopy, immunofluorescence & electron microscopy renal biopsy and mention all stages of lupus nephritis also.

Our outcomes showed that lupus nephritis group, Pearson correlation test showed that CD4% was negatively correlate with CD8% with p value <0.001 & positively correlated with CD4percent/CD8percent ratio p value <0.001, while CD8% negatively correlated with CD4percent/CD8percent ratio with p value <0.001. Double negative% was negatively correlated with C4 level with p value 0.044.

These results were consistent with the research conducted by Crispín et al. 2008 [19] whom reported that patients with LN had renal infiltration with double negative T cells, which increase production of IL-17 that led to renal damage and eventually to lupus nephrits.

As well, these findings were similar to You et al .2020 [20] who stated that double negative cells found positive relationship with twenty four-hour urine protein excretion levels, & inversely correlated with assessed glomerular filtration rate, they also reported the response to treatment and correlated it to the level of double negative cells.

This finding is similar to (Yuan et al. 2022 [21] they found that CD8+ found negative relationship with level of C3 and C4.

Sensitivity analysis of current research found that Double negative% can significantly diagnose SLE cases with p value <0.001, AUC 96.2%, sensitivity 86% & specificity 96% when using cutoff point 4.95%. As well, CD4%/CD8% ratio can significantly diagnose SLE cases with p value <0.001, AUC 91.4%, sensitivity 90% & specificity 82% when using cutoff point 1.5.

These results were comparable to outcomes of Handono et al. 2020 [22] whom reported that CD4/CD8 ratio was found to predict renal involvement among SLE patients (p = <0.001) with wide area of sensitivity & specificity (0.869). As well he reported that CD4/CD8 ratio can significantly diagnose SLE using a cut of 0.67 with sensitivity 71.4%, specificity 71.4% and AUC 71.8%.

5. Conclusion

In group I, CD4, & CD4/CD8 ratios were lower compared to group II, while CD8 and double negative T cells were greater among group I when compared to group II. In

lupus nephritis group, double negative% was negatively correlated with C4 level. CD4percent/CD8percent ratio & double negative T cells can be used as diagnostic test for lupus nephritis patients.

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