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RESEARCH ARTICLE

AGE-ASSOCIATED B CELLS (ABCs) AND AUTOIMMUNITY AMONG EGYPTIAN FEMALES

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Abstract

Background: A particular population of B cells, named age-associated B cells (ABCs), was found at a higher frequency in healthy autoimmune-prone mice and in elderly women with rheumatoid arthritis.

Aim: We aimed at estimating the percentage of ABCs in females with 2 autoimmune disorders in comparison to healthy females and males. We also aimed at identifying any increase in their percentage with age, gender or disease activity.

Materials and Methods: Our study included 45 females having systemic lupus erythematosus (SLE) and 30 females having rheumatoid arthritis (RA). 63 healthy females and 60 males, served as control groups. Flowcytometric analysis was done to estimate the percentage of ABCs positive for CD19, CD11b and CD11c collectively, using MACSQuant Analyzer 10.

Results: The percentage of ABCs in SLE patients (mean ± SD = 0.22% ± 0.33) was significantly higher than that in RA patients (mean ± SD = 0.06 ± 0.13) and both healthy females (mean ± SD = 0.06% ± 0.1) and males (mean ± SD = 0.07% ± 0.1) with p values of 0.033, 0.021 and 0.011 respectively. However, their percentage was comparable between healthy females and healthy males, with p value = 0.818. Moreover, their percentage was found to increase with age, showing a statistically significant positive correlation, p <0.001.

Conclusion: ABCs were found to be significantly higher among SLE patients, but not RA patients, increasing with age in both healthy and autoimmune patients, but without sex predilection. Their percentage correlates positively but insignificantly with disease activity and damage indices.

INTRODUCTION

The normal function of the immune system is to protect the host against infection. Failure of the immune system to recognize its own cells and tissues as 'self' results in organ damage, leading to organ malfunction and causing autoimmune disease. It is well known that females are more predisposed to many autoimmune diseases than males. Estimates indicate that 78% of individuals affected with autoimmune diseases are women, though the reason for this sex bias is not completely understood (Rubtsov et al., 2010).

For some time, it has been known that, the basic immune response differs between males and females. Females respond to infection, vaccination and trauma with increased antibody production, whereas inflammation is

usually more severe in males resulting in an increased mortality in men and protection against infection in women (Straub, 2007). Although no sex- or age-associated differences were observed in T cells or dendritic cells, there is growing evidence that a population of cells contained within the B cell pool expresses immune-stimulatory activity and is involved in clinical autoimmunity (Jacob and Stohl, 2010). The principal mission of B lymphocytes is considered to reside in immunoglobulin production; yet an effector role for these cells in regulating immune activity has been repeatedly noted with the recent success of B cell depletion therapy in autoimmune diseases. However, clear identification of the B cells that possess this function has remained a mystery (Zouali, 2008).

The two most obviously and most intensively studied factors, that can be involved in the female bias among autoimmune diseases, are differences in sex hormones and genes differentially present on sex chromosomes. As far as sex hormones are concerned, it is well documented that the severity of rheumatoid arthritis and multiple sclerosis decreases during pregnancy (Confavreux, 1998). Additionally, animal studies revealed that gonadectomy affects the severity and/or onset of autoimmune diseases in mice (Gubbels Bupp et al., 2008). Immunoglobulin secretion and the numbers of immunoglobulin-secreting B cells are also affected by the levels of sex hormones (Lu et al., 2002). However, no significant differences in sex hormone levels between autoimmune patients and healthy controls have been reported, indicating that there must be additional factors explaining the overall female bias in many autoimmune diseases (Rubtsova et al., 2012).

As for chromosomal composition, since females have two X chromosomes and males have only one; genes located on this chromosome might differ in their expression level between males and females. To avoid these differences in the expression levels, one X chromosome in females is inactivated (lyonized). However, it has been reported that lyonization of the X chromosome is not complete, both in mice and humans, resulting in over-expression of some of these genes from partially non-lyonized parts of the X chromosome, which can contribute to autoimmune disease in females. In particular, it has been proposed that the X chromosome-encoded Toll-like receptor (TLR) 7 gene might be one of the genes with differential expression levels in female versus male cells that might trigger autoimmunity (Rubtsova et al., 2012).

A particular population of B cells, named age-associated B cells (ABCs), bearing CD11b and CD11c, but not CD21, was found at a much higher frequency in aged female mice than in young females, or males of any age (Rubtsov et al., 2011 & Hao et al., 2011). Moreover, this population was found at a higher frequency in young healthy autoimmune-prone mice (Rubtsov et al., 2011) and also in elderly women with rheumatoid arthritis, scleroderma or common variable immunodeficiency with autoimmune symptoms (Rakhmanov et al., 2009 & Isnardi et al., 2010). Age associated B cells in mice secreted auto-antibodies upon stimulation in vitro. It has been reported that depletion of these cells in vivo resulted in a reduction of auto-reactive antibodies (Isnardi et al., 2010).

The growing presence of ABCs, coupled with their novel functional attributes, prompts consideration of their postulated contributions to the features of autoimmunity. Therefore, in our study, we aimed at estimating the percentage of ABCs in females with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), as examples of autoimmune disorders, in comparison to healthy females and males (not suffering from any autoimmune disorders). We also aimed at identifying any increase in this subpopulation of B lymphocytes in association with age, gender or disease activity in order to verify the recent findings on this new population of B cells that was found to be predominant in elderly females and to play a role in autoimmunity.

I. MATERIALS AND METHODS

A. Study Population:

Our comparative study was conducted on 75 females newly diagnosed with autoimmune disorders; 45 having SLE diagnosed based on the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus (Petri et al., 2012) and 30 having RA according to ACR/EULAR criteria 2010 (Aletaha et al.,) (all were positive for rheumatoid factor; RF). All patients were recruited from the Rheumatology outpatient clinic and ward of Alexandria Main University Hospital. Sixty three females and 60 males, not having any autoimmune disorders, served as control groups. Patients with other autoimmune diseases, hematological disorders, viral hepatitis B or C were excluded from the study.

All subjects enrolled in this study signed a written informed consent before participation. Details that might disclose the identity of the subjects under study were omitted. The study received approval from the Medical Ethics Committee of the Faculty of Medicine, Alexandria University and the practical work has been carried out in

accordance with the code of Ethics of the World Medical Association (1964 Declaration of Helsinki and its later amendments).

B. History Taking and Clinical Examination:

Personal history was taken from all participants, who were subjected to thorough clinical examination.

Disease activity assessment was done for SLE patients using SLE disease activity index (SLEDAI) (Bombardier et al., 1992), while DAS28 score was used in measuring disease activity in RA patients (Fransen et al., 2003). Regarding the damage index in patients with SLE, it was assessed using Systemic lupus international collaborating clinics/American College of Rheumatology (SLICC/ACR) damage index (SLICC/ACR) (Gladman et al., 1996).

C. Laboratory Investigations:

Peripheral venous blood samples were aseptically withdrawn by venipuncture into sterile vaccutainers; 2ml in serum separator vaccutainers and 3 ml in EDTA vaccutainers.

- **Routine Investigations:**

1. Complete blood picture (CBC), including hemoglobin (Hb) and platelets (plts).
2. Liver function tests; SGOT, SGPT and serum albumin.
3. Kidney function tests; blood urea nitrogen (BUN) and creatinine (Cr).
4. Erythrocyte sedimentation rate (ESR) & C reactive protein (CRP).

- **Specific Investigations for Autoimmunity:**

1. Anti-nuclear antibody (ANA) by immunoflourescence.
2. Anti-ds DNA by ELISA.
3. Anti-cyclic citrulinated peptide (Anti-CCP).
4. Rheumatoid factor (RF).
5. Coombs' test (for diagnosing autoimmune hemolytic anemia)

- **Immunological Investigations:**

1. Isolation of peripheral blood mononuclear cells (PBMNCs) from EDTA blood samples using density-gradient centrifugation (1800 rpm for 30 min) over Ficoll-Hypaque (Biochrom, Germany, Cat# L6113) (Fuss et al., 2009).
2. Viability of separated cells was tested by dye exclusion technique using trypan blue.
3. Flowcytometric analysis (i.e. immunophenotyping) of peripheral blood was performed to estimate the percentage of ABCs positive for all of the following monoclonal mouse antibodies (MoAbs), purchased from Immunostep, Spain:

   - **PE Anti-human CD19** [labeled with phycoerythrin (PE) fluorochrome, emitting red fluorescence, Ref. Cat: 19PE1-100T], for identification of human B lymphocytes bearing CD-19 antigen and constituting approximately 10% of peripheral blood lymphocytes.
   - **PerCP Anti-human CD11b** [labeled with Peridin-cholophyll-protein complex (PerCP), emitting orange fluorescence, Ref. Cat: 11BPP-100T]. This Mo Ab is directed against the CD11b antigen (MO-1) located on the alpha-M chain of Lymphocyte Function-associated Antigen-1 (LFA-1) complex, expressed on monocytes, granulocytes and natural killer cells (NK-cells).
   - **FITC Anti-human CD11c** [labeled with fluorescein isothiocyanate (FITC), emitting green fluorescence, Ref. Cat: 11CF3-100T], for identification of human receptor for interleukin-2 (IL-2R). CD11c expression is restricted to leucocytes mainly of myeloid lineage, with highest expression on macrophages.

This analysis was done using MACSQuant Analyzer 10 (Miltenyi, Biotec Germany). Age associated B cells are those cells which are positive for the three CDs (clusters of differentiation); CD 19, a B lineage marker, and both CD 11b and CD 11c are defining markers as stated by Rubstov et al, 2011.

D. Statistical Analysis of the Data: (Binu et al., 2014)

Statistical analysis was carried out using IBM SPSS software package version20.0. F for ANOVAtest and Kruskal Wallis test was done regarding the normality of the data. Correlations between two quantitative variables were assessed using Spearman coefficient. All variables were described using the mean and standard deviation A statistical significance level of 95% ($p<0.05$) was considered for all statistical analysis.

II. RESULTS

IIa. Subjects' Demographic Data

Our study included 75 females with autoimmune diseases; 45 females suffering from SLE (mean age: 24 years, range 13 - 36) and 30 females suffering from RA (mean age: 35 years, range 19 - 60). Sixty three healthy females (mean age: 38 years, range: 14 - 56) and 60 healthy males (mean age: 47 years, range 18 - 65) were also included in the study as healthy control groups. The mean age of SLE at diagnosis was significantly lower than that of the other 3 groups included in our study; RA patients, healthy males and females, p <0.001. [Table 1]

IIb. Patients' Clinical Data

The 3 most common presenting symptoms among the 45 SLE patients, included in our study, were; arthralgia &/or arthritis (100%), anemia (51.1%) and Raynaud's phenomenon (46.8%). In RA patients, DAS 28 activity score ranged between 3.26 and 6.9 with a mean ± SD of 4.64 ± 1.73.

IIc. Routine Laboratory Investigations

Regarding routine laboratory investigations done for all autoimmune patients, anemia and thrombocytopenia were significantly more marked among SLE patients (Hb = 9.5gm/dl ± 1.5, plts=$178.1x10^3$/cmm ± 117.1) than RA patients (Hb = 11.6gm/dl ± 0.95, plts=$351.3x10^3$/cmm ± 131) with p value <0.001 for both parameters. Erythrocyte sedimentation rate (ESR) was also significantly higher among SLE patients (91.7mm ± 35.2) than RA patients (57.8mm ± 34.5) in the first hour, with p value = 0.0006. Serum creatinine and CRP were higher in SLE patients (Cr = 1.1mg/dl ± 1.1, CRP = 20.6 mg/L ± 37.2) than RA patients (Cr = 0.77mg/dl ± 0.2, CRP = 17.1 mg/L ± 13.7) but without significant difference between both groups, p=0.327 & 0.0579 respectively.

Anti DNA titre (positive if >75) ranged between 18 and 542 IU/ml among SLE patients, with a mean of 192 IU/ml and a median of 127 IU/ml. Complement 3 (normal level= 0.8-1.8 g/L) and 4 (normal level= 0.16-0.4 g/L) ranged between 0.1 - 1.2 g/L and 0.09 – 0.77g/L respectively among SLE patients, with a mean of 0.61 g/L for C3 and 0.25 g/L for C4.

Among RA patients, anti-CCP levels (normal level up to 20 U/ml) ranged between 19 and 497 U/ml, with a mean of 181.6 U/ml and a median of 89 U/ml, while rheumatoid factor (normal up to 8 U/ml) ranged between 8 and 54 U/ml, with a mean of 30.5 U/ml and a median of 31.2 U/ml.

The lymphocyte percentage in SLE patients was significantly lower (mean ± SD= 21.27% ± 11.47) than that of healthy males (28.8% ± 11.1) and healthy females (34.85% ± 12.17), with p= 0.002 and < 0.001 respectively, while that of RA patients (26.65% ± 4.27) was significantly lower than that of healthy females only with p value = 0.004. [Table 1]

IId. ABCs and Autoimmunity

Regarding the subset of B lymphocytes, termed ABCs, which are positive for CD 19, CD 11b and CD 11c collectively, their percentage in SLE patients (mean ± SD = 0.22% ± 0.33) was significantly higher than that in RA patients (mean ± SD = 0.06% ± 0.13), healthy females (mean ± SD = 0.06% ± 0.11) and healthy males (mean ± SD = 0.07% ± 0.14) with p values of 0.033, 0.021 and 0.011 respectively. However, there was no significant difference regarding their mean percentage between RA patients and both healthy control groups; whether females or males, with p values=0.721 and 0.812 respectively. [Table 2, Figures 1 & 2]

IIe. ABCs and Gender

The percentage of ABCs was comparable between healthy females (mean ± SD = 0.06% ± 0.11) and healthy males (mean ± SD = 0.07% ± 0.14), with p value = 0.818, as shown in table 2.

IIf. ABCs and Age

Moreover, their percentage was found to increase with age in all groups included in our study separately and collectively; SLE patients, RA patients, healthy females and healthy males, showing a statistically significant positive correlation, p <0.001. [Table 3]

IIg. ABCs and Disease Activity [Table 4]

Among SLE patients, there was a statistical significant negative correlation between the percentage of ABCs and serum levels of complement C3 (r = -0.454, p = 0.001) but not C4 (r = -0.281, p = 0.311). Moreover, we have found a statistically significant positive correlation between ABCs percentage and ANA titre (r = 0.613, p= 0.015,

but their correlation with anti-ds DNA, SLEDAI/105 and SLICC/ACR/47 was statistically insignificant, as shown in table 4.

Among RA patients, there was a statistically significant positive correlation between the percentage of ABCs and both rheumatoid factor (r = 0.392, p = 0.029) and anti-CCP levels (r = 0.57, p = 0.001). However, their percentage correlated positively but insignificantly with DAS 28 activity score, r = 0.054 and p = 0.772.

IIh. Other Significant Associations with ABCs

Moreover, the percentage of ABCs was significantly higher in SLE patients having anemia, thrombocytopenia and neurological deficits, with p value=0.025, 0.008 and <0.001 respectively, as shown in table 5.

Table (1): Comparison between the different studied groups according to age and lymphocyte percentage

	SLE Patients (n= 45)	RA Patients (n =30)	Female Controls (n= 63)	Male Controls (n= 60)	p
Age (years)	24 ± 6	35 ± 13	38 ± 14	47 ± 16	<0.001*
p_1		<0.001*	<0.001*	<0.001*	
p_2			0.982	0.022*	
Lymphocytes (%)	21.27 ± 11.47	26.65 ± 4.27	34.85 ± 12.17	28.81 ± 11.10	<0.001*
p_1		0.141	<0.001*	0.002*	
p_2			0.004*	0.804	

Normally quantitative data is expressed as (mean ±SD) and compared using F test (ANOVA), while abnormally quantitative data is expressed as median (min. – max.) and compared using Kruskal Wallis test.
p_1: p value for comparing SLE patients with each of the other 3 groups.
p_2: p value for comparing RA patients with female controls (FC) and male controls (MC)
*: Statistically significant at $p \leq 0.05$

Table (2): Comparison between the four studied groups according to ABC%

	SLE Patients (n= 45)	RA Patients (n =30)	Female Controls (n= 63)	Male Controls (n= 60)	p
ABC (%)	0.22 ± 0.33	0.06 ± 0.13	0.06 ± 0.11	0.07 ± 0.14	0.024*
P_1		0.033*	0.021*	0.011*	
P_2			0.721	0.812	
P_3				0.818	

$^{KW}\chi^2$: Chi square for Kruskal Wallis test
P_1: p value for Mann Whitney test for comparison between SLE patients and other groups
P_2: p value for Mann Whitney test for comparison between RA patients and other groups
P_3: p value for Mann Whitney test for comparison between female controls and male controls

Table (3): Correlation between ABCs (%) and age (years) in each group and in the total sample (n=201)

	Age (years)					
	Total sample (n=201)	SLE Patients (n = 45)	RA Patients (n = 30)	All Patients (n=78)	Female Controls (n = 63)	Male Controls (n = 60)

ABCs (%)	**r_s**	0.609*	0.650*	0.808*	0.683*	0.731*	0.678*
	p	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

r_s: Spearman coefficient
*: Statistically significant at $p \leq 0.05$
ABCs: Age associated B lymphocytes, RA: Rheumatoid arthritis, SLE; systemic lupus erythematosus

Table (4): Correlations between ABCs (%) and some laboratory and clinical parameters of SLE and RA.

	ABCs (%)	
	r	**p**
SLE Patients (n=45)		
ANA	0.613*	0.015*
Anti DNA [Normal up to 75 IU/ml]	0.032	0.911
C3 [Normal = 0.8-1.8 g/L]	-0.454	0.001*
C4 [Normal = 0.16-0.4 g/L]	-0.281	0.311
SLEDAI/105	0.436	0.104
SLICC/ACR/47	0.261	0.347
RA Patients (n=30)		
RF [Normal up to 8 U/ml]	0.392	0.029*
Anti-CCP [Normal up to 20 U/ml]	0.57	0.001*
DAS 28	0.054	0.772

r_s: Spearman coefficient
*: Statistically significant at $p \leq 0.05$
ANA: Anti-nuclear antibody, Anti DNA: Anti-deoxyribonucleic acid, C3: Complement 3, C4: Complement 4, SLEDAI/105: Systemic lupus erythematosus disease activity index, SLICC/ACR/47: Systemic lupus International Collaboration Clinic/ American College of Rheumatology, RF: Rheumatoid factor, CCP: Cyclic citrulinated peptide, DAS 28: Disease activity score on 28 joints for rheumatoid arthritis.

Table (5): Relation between ABCs (%) and some clinical parameters in SLE group (n=45)

	n	**ABCs (%)**
Anemia		
Absent	**21**	0.20 ± 0.25
Present	**24**	0.48 ± 0.52
p		**0.025***
Thrombocytopenia		
Absent	**30**	0.20 ± 0.28
Present	**15**	0.64 ± 0.54
p		**0.008***
Leucopenia		
Absent	**36**	0.34 ± 0.45
Present	**9**	0.33 ± 0.36
p		**0.970**
Neurological Deficits		
Absent	**39**	0.29 ± 0.44
Present	**6**	0.70 ± 0.11
p		**<0.001***

2ry Anti-Phospholipid Syndrome		
Absent	**39**	0.32 ± 0.46
Present	**6**	0.45 ± 0.16
p		**0.207**
Arthralgia/ itis		
Absent	**0**	-
Present	**45**	0.19 ± 0.35
Serositis		
Absent	**36**	0.28 ± 0.46
Present	**9**	0.57 ± 0.22
p		**0.078**
Raynaud's Phenomenon		
Absent	**24**	0.41 ± 0.52
Present	**21**	0.26 ± 0.30
p		**0.23**

Normally quantitative data is expressed as (mean ± SD) and compared using Student t-test, while abnormally quantitative data is expressed as median (min. – max.) and compared using Mann Whitney test.

*: Statistically significant at $p \leq 0.05$

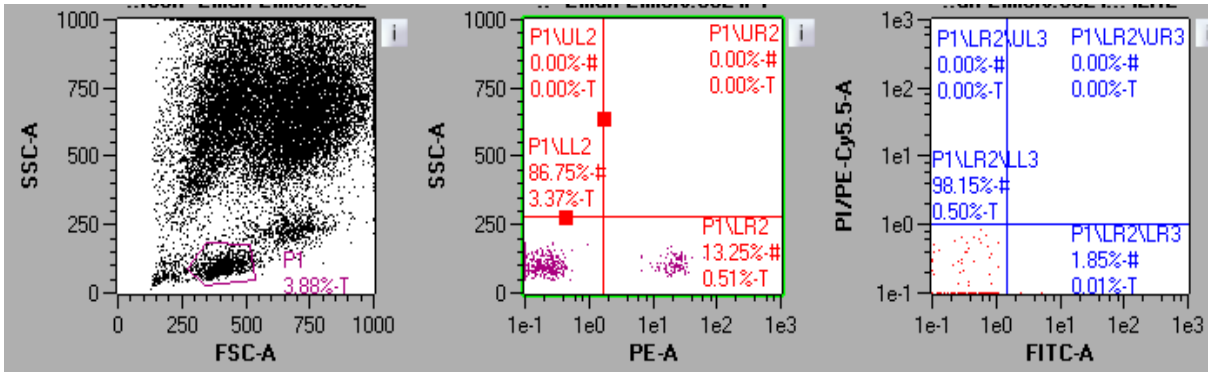

Fig (1): A control subject with 0% triple positive ABCs. Left diagram: lymphocyte gating. Middle diagram: CD 19 positive lymphocytes (PE labeled) on the X axis (13.25%). Right diagram: upper right quadrant shows cells positive for the 3 MoAbs; CD 19 (PE labeled), CD 11b (PerCP labeled) on the Y axis and CD11c (FITC labeled) on the X axis (0%).

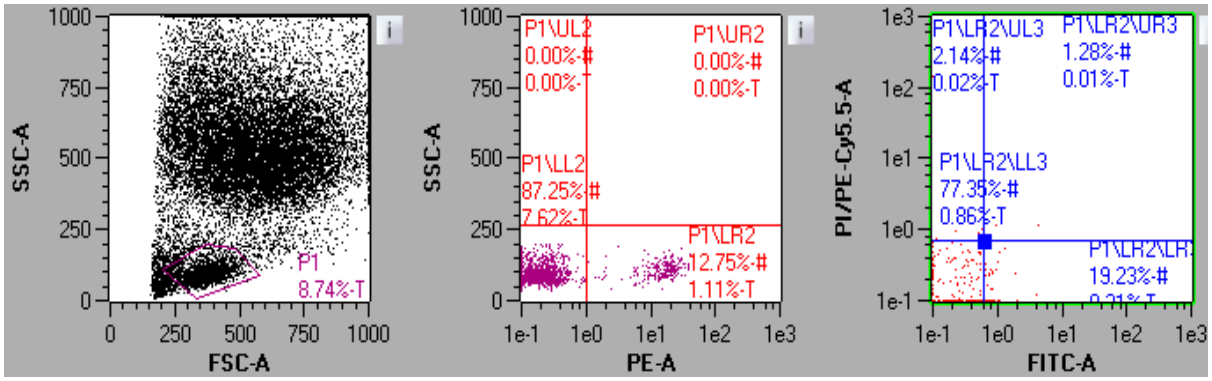

Fig (2): A patient having SLE with 1.28 % triple positive ABCs. Left diagram: lymphocyte gating. Middle diagram: CD 19 positive lymphocytes (PE labeled) on the X axis (12.75%). Right diagram: upper right quadrant shows cells positive for the 3 MoAbs; CD 19 (PE labeled), CD 11b (PerCP labeled) on the Y axis and CD11c (FITC labeled) on the X axis (1.28%).

III. DISCUSSION

The causes of depressed humoral immunity with aging are complex, and likely involve a B cell-intrinsic loss of responsiveness and alterations in antigen receptor diversity. And so, research has focused on understanding the basis for these defects, thus fostering detailed analyses of how developing and mature B cell populations change with age (Hao et al., 2012).

In our study, patients having SLE were significantly younger than RA patients. This significantly younger age is simply explained by the fact that all the patients were newly diagnosed and that young adult women are more likely to develop SLE , unlike RA which is more frequently seen in middle-aged women (West, 2008).

The percentage of ABCs was found to be more predominant among SLE patients than RA patients, healthy males or females. It has, also, been found to increase with age in all the studied groups; separately and collectively. However, their percentage was more or less the same in RA patients and healthy controls, whether males or females. This might suggest that ABCs play a significant role in the pathogenesis of SLE in particular, more than other autoimmune disorders.

Their similar percentages among healthy males and females show no sex predilection. This is not conforming to the findings of Rubtsova et al, 2012 and Rubstov et al, 2011 who found a higher prevalence of ABCs in females.

Failure to inactivate the second X chromosome happens more frequently with age, potentially leading to elevated levels of TLR7 expression (located on X chromosome). Rubtsova et al suspected that this might explain the female-specific accumulation of ABCs and female-biased autoimmunity with age. Overall, their discovery that TLR7 expression affects autoimmune symptoms and the generation of ABCs, has shed some light on the phenomenon of the female-bias of some autoimmune diseases (Rubtsova et al., 2012). Moreover, Rubtsov et al, also, proved that TLR7 signaling is required for ABC development, since TLR7 knockout mice failed to accumulate ABCs, thus TLR7 signaling is apparently required to drive expansion and differentiation to the ABC phenotype. They also suggested that humoral autoimmune disease, which often emerges in young or middle aged adults, might be associated with premature increase of ABCs (Rubtsov et al., 2011). Several studies suggest the appearance of ABCs at early ages in autoimmune prone mice and in human patients suffering from autoimmunity (Rubtsov et al., 2011 & Rakhmanov et al., 2009 & Isnardi et al., 2010).

The nature of hematological affection of each disease; in SLE manifested by anemia and thrombocytopenia and in RA by thrombocytosis, explains the significant anemia and thrombocytopenia among SLE patients compared to patients with RA (Petri et al., 2012).

Though a positive but insignificant correlation existed between ABCs % and anti-ds DNA, SLEDAI/105 and SLICC/ACR/47 among our lupus patients, there was a statistical significant positive correlation with ANA titre and significant negative correlation with serum levels of complement C3, which may reflect an indirect evidence of association between ABCs and lupus activity as the usual pattern of complement activation in SLE involves the classical pathway, leading to low C3 and C4. However, a small percentage of SLE patients may demonstrate predominant alternative pathway activation (Merle et al., 2015), as evidenced by normal C4 but low C3 found in our study.

Since anemia, thrombocytopenia and neurological involvement are among the characteristics of lupus patients and are demonstrated in both the SLICC classification criteria and the disease activity index, the significantly higher percentage of ABCs in those patients expands their role or effect on disease activity or even the pathogenesis of SLE in an indirect way (Petri et al., 2012). We have also found a significant positive correlation between percentage of ABCs and both RF and anti-CCP levels among RA patients despite their relatively normal percentage among such patients.

Among the strong points in our research is that it is the first study addressing ABCs to be conducted on the Egyptian population. Moreover, all patients recruited were newly diagnosed with autoimmune disorders in order to eliminate the bias that might be caused by the effect of medications on cellular phenotypes. We also resorted to calculating ABC percentage and not their absolute number, due to the high prevalence of absolute and relative lymphocytopenia among SLE patients.

Among the main limitations of our study are the relatively small number of MoAbs used for immunophenotyping and ABCs determination, due to the limited multi-color detectors of the available flowcytometer. CD19 was used as a B lineage marker, CD11b and CD11c were used as defining markers, as recommended by Rubstov et al, 2011. More MoAbs could have been used to increase the specificity of the assay.

ABCs are thought to contribute to autoimmunity by the production of auto-antibodies, but this is probably not their only function. It is still unclear how ABCs affect other immune cells; in particular T cells, which is a subject of future research. Although ABCs are generated from follicular B cells, Hao et al reported that the exact process leading to their generation is still unknown (Hao et al., 2011).

While it is tempting to speculate that ABC-targeted approaches might improve some aspects of immunosenescence, further understanding of their origins and functional attributes is required before such possibilities can be critically evaluated (Hao et al., 2012). Many questions still remain about the appearance, functions of ABCs and their potential role in autoimmunity.

CONCLUSIONS

Age-associated B cells were found to be significantly higher in SLE but not all autoimmune disorders, as in rheumatoid arthritis, their percentage was comparable to normal values. Age associated B cells showed a statistically significant positive correlation with age in both healthy and autoimmune patients, but without a significant difference between both sexes. Their percentage correlated positively but insignificantly with disease activity and damage indices in SLE and RA.

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