Assessment of autoimmune rheumatic diseases activity during pregnancy

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Abstract

Background: Autoimmune rheumatic diseases (ARDs) are chronic problems that disproportionately impact females of childbearing age.

Objective: To evaluate the effect of pregnancy on rheumatic disease activity

Patients and Methods: This prospective study was conducted on (70) pregnant patients aged from 18 to 35 years old. They were divided into four groups; (30) with Rheumatoid arthritis, (20) with SLE, (10) with Systemic Sclerosis and (10) with Ankylosing Spondylitis. Routine baseline investigations, auto antibodies and imaging.

Results: There were significant differences between the current study groups as regards the history of hormonal therapy ($p<0.001$); family history of rheumatic disease ($p=0.037$). There was statistically significant higher RBCs ($p<0.001$), Hb ($p=0.006$), WBCs ($p<0.001$), platelets count ($p<0.001$) and HCT ($p<0.001$) value in RA patients versus other patients groups. The acute phase reactant was significant in AS patients; also both ALT and AST were significantly higher in AS patients ($p<0.001$).

RA patients had (Anti-CCP +) and (RF +) in 80% of cases and other 20% were negative , SLE had (ANA+) in all cases , Low (C3-C4) in 87.5% , (RF +) in 12.5% of cases , in SS all cases had (ACA +) ,(Anti-SCL70 +) and in AS all cases had (HLA-B27 +) .

Conclusion: The present study pointed to the importance of tight disease control and diagnosis before and during pregnancy as well as the importance of disease activity assessment

Keywords: Ankylosing spondylitis; Autoimmune rheumatic diseases; Rheumatoid arthritis;Systemic lupus erythematosus; Systemic sclerosis.

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Introduction

Autoimmune rheumatic diseases (ARDs) are a cluster of distinguishable abnormalities with clinical, laboratory, and autoimmune symptoms in common. Their basic pathobiological revelation is the emergence of an overly self-reactive, antigen-driven immune response. According to clinical and scientific investigations, their exact pathophysiology is caused by genetic propensity **(David et al., 2018)**, environmental profanities such as infectious diseases, biological and physical agents, hormone levels **(Shukla et al., 2018)**, and mentally taxing life occasions **(Skopouli and Katsiougiannis et al., 2018).**

ARDs, particularly systemic inflammatory rheumatic diseases such as rheumatoid arthritis [RA], systemic lupus erythematosus [SLE], ankylosing spondyloarthritis [AS], antiphospholipid syndrome [APS], and systemic sclerosis, are lifelong, autoimmune systemic conditions more common in women of childbearing age **(Wallenius et al., 2014).**

During pregnancy, the hormonal environment undergoes major changes. Raises in free steroid hormones like glucocorticoids, progesterone, and estrogens alter the function of immunocompetent cells like B cells, T cells, and monocytes. As a result, clinical signs of immune rheumatic diseases alter regarding the disease's key pathogenic course. Some improve, whereas others remain stable or aggravate during pregnancy **(Ostensen et al., 2011).**

One of the critical problems in SLE is the threat of disease activity flare-up throughout pregnancy. Previous research demonstrated changeable flare values in the range of 25 and 65 percent **(Carvalheiras et al., 2010)**.

The course of (RA) often changes during pregnancy. Approximately 50% of pregnant women with RA have low disease activity, with 20% to 40% remission in the third trimester. However, nearly 20% have low or moderate to high disease activity during pregnancy and may require further treatment **(Krause and Makol, 2016).**

The excellence of pregnancy outcomes for patients with inflammatory rheumatic diseases is optimized by developing a personalized plan to control disease activity using a "treatment-to-target" strategy. Patients who are pregnant or planning to become pregnant should be closely monitored for obstetrics and rheumatism in an interdisciplinary setting, with risk stratification based on the severity of maternal illness and the patient's antibody status **(Giles et al., 2019).**

The present study aimed to evaluate the effect of pregnancy on rheumatic disease activity.

Patients and methods

Study population: This prospective study was conducted on (70) pregnant women suffering from acute rheumatic diseases aged from 18-35 years attending the outpatient clinic of Physical Medicine& Rheumatology & Rehabilitation and Gynecology& Obstetric Department of Qena University Hospital, South Valley University, Qena, Egypt

They were classified into four groups according to the type of rheumatic disease:

I. Thirty (30) pregnant women with rheumatoid arthritis patients were diagnosed according to the 2010 ACR/EULAR criteria for the classification of rheumatoid arthritis **(Aletaha et al., 2010).**

II. Twenty (20) pregnant women with (SLE) patients were diagnosed according to the 2019 EULAR/ACR classification criteria for SLE **(Aringer et al., 2019).**

III. Ten (10) pregnant women with systemic sclerosis patients diagnosed according to ACR/EULAR 2013classification criteria **(Nihtyanova et al., 2014).**

IV. Ten (10) pregnant women with ankylosing spondylitis patients have been diagnosed according to The Assessment in Spondyloarthritis International Society (ASAS) classification criteria for axial spondyloarthritis **(Rudwaleit et al., 2011).**

Patients were excluding if they have one of the following criteria:

- Male patients
- Non pregnant females
- Age under 18 or above 35 years old
- Rheumatic diseases other than the study type

- Diabetes mellitus, endocrine diseases, and infectious diseases

Ethical clearance

A written consent was taken from all participants in the study.

Ethical approval code :

SVU-MED-PRR022-1-21-1-114

Study procedure

. A detailed history taking: personal history, obstetric history, smoking status, detailed history of general health condition, therapeutic history of hormonal treatment and family history of RD.

1. Physical examination:
   - General (vital signs: pulse, blood pressure, and temperature) and overall well-being
   - Musculoskeletal examination (inspection, palpation, range of motion, and presence of deformity)
2. Routine baseline investigations:

- Complete blood count
- ESR
- Urine analysis(clarity, ketone, protein, acetate, bacteria, crystals, casts, WBCS, RBCS)
- Liver enzymes tests; AST, ALT
- Kidney function tests; serum urea and serum Creatinine

Autoantibodies

- **Rheumatoid factor (RF)**:

Test principle: The RF semiquantitaive test RF Latex Test cat no. 320-100**: Cortez Diagnostics, Inc. Woodland Hills, California, USA**

- **Anti-double-stranded DNA:** according to the manufacturer instructions use anti-dsDNA ELISA Kit. Catalog Number: MBS269122. Bio Source, Inc San Diego, CA, USA
- **C3 ELISA kit:** Human Complement C3 ELISA Kit (ab108823) Sandwich (quantitative assay). Cambridge Biomedical Campus, Cambridge, CB2 0AX, UK
- **C4 ELISA Sandwich (quantitative) kit using MyBiosource, Inc. (USA). Catalog No: MBS2502561**
- **HLA B27:** AccuPower® Bioneer, Inc. Oakland, CA. HLA-B27 Real-Time PCR Kit Catalog No: HLB-1111
- **Human Scleroderma 70 Antibody (Anti-SCL70)** ELISA Kit, qualitative indirect assay; Catalogue No: abx055784. Abbexa Ltd., Cambridge Science Park, Cambridge, UK
- **Anti-Centromeres ELISA (IgG) Test:** Catalogue No: CMB-100; Alpha Diagnostic Intl. Inc. San Antonio, Texas USA.

Imaging

- Abdominal and obstetric ultrasound by an obstetrician to assess (fetal biometry, placental localization, amniotic fluid index)
- Musculoskeletal ultrasound for assessment of joints

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using numbers and percentages. The Shapiro-Wilk test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). The significance of the obtained results was judged at the 5% level.

The used tests were

1. Chi-square test: for categorical variables, to compare different groups
2. Monte Carlo correction: correction for chi-square when more than 20% of the cells have an expected count of less than
3. One way ANOVA test: for normally distributed quantitative variables, to compare between more than two groups and Post Hoc test (Tukey) for pairwise comparisons
4. Kruskal Wallis test: for abnormally distributed quantitative variables, to compare between more than two studied groups and Post Hoc (Dunn's multiple comparisons test) for pair-wise comparisons

Results

The comparison between the four studied groups was presented in (**Table.1**); there were insignificant differences between study groups as regard to age**.**

As regards Therapeutic history of hormonal TTT ($p < 0.001$), Family history of RD there were significant differences between study groups ($p = 0.037$) **(Figs 1, 2, 3).**

Table 1. Age among the studied cases of the four groups

Age (years)	Group 1 (n = 30) RA	Group 2 (n = 20) SLE	Group 3 (n = 10)SSC	Group 4 (n = 10)AS	F	p
Min. – Max.	18.0 – 34.0	18.0 – 35.0	18.0 – 33.0	19.0 – 33.0	0.025	0.995
Mean ± SD.	25.87 ± 4.67	25.90 ± 4.88	26.30 ± 4.60	26.10 ± 4.68		
Median (IQR)	25.50(22.0 – 29.0)	25.0(22.5 – 29.5)	26.50(24.0 – 30.0)	26.50(22.0 – 30.0)		

IQR: Inter quartile range; SD: Standard deviation; F: One-way ANOVA test

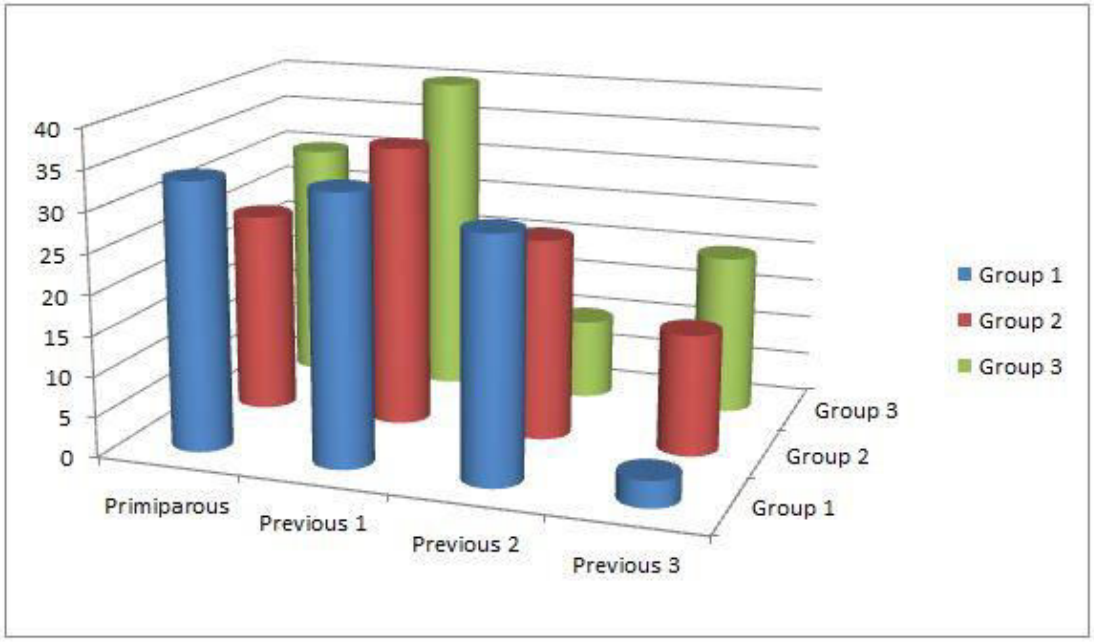

Fig.1. Obstetric history in the studied four groups

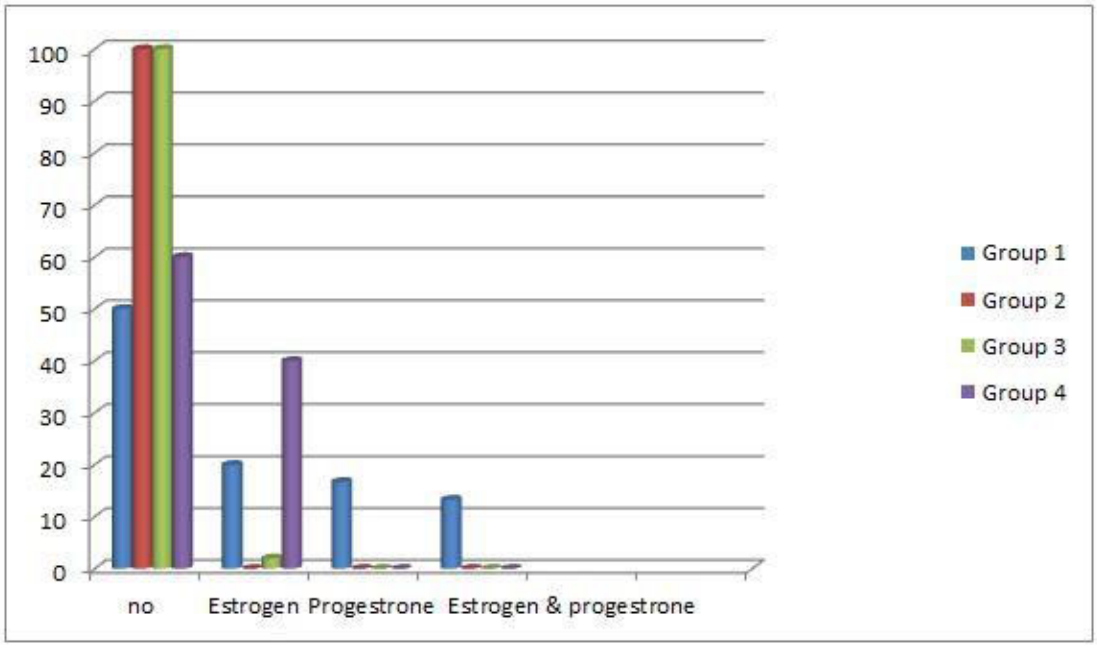

Fig.2. Therapeutic history of hormonal TTT in the studied groups

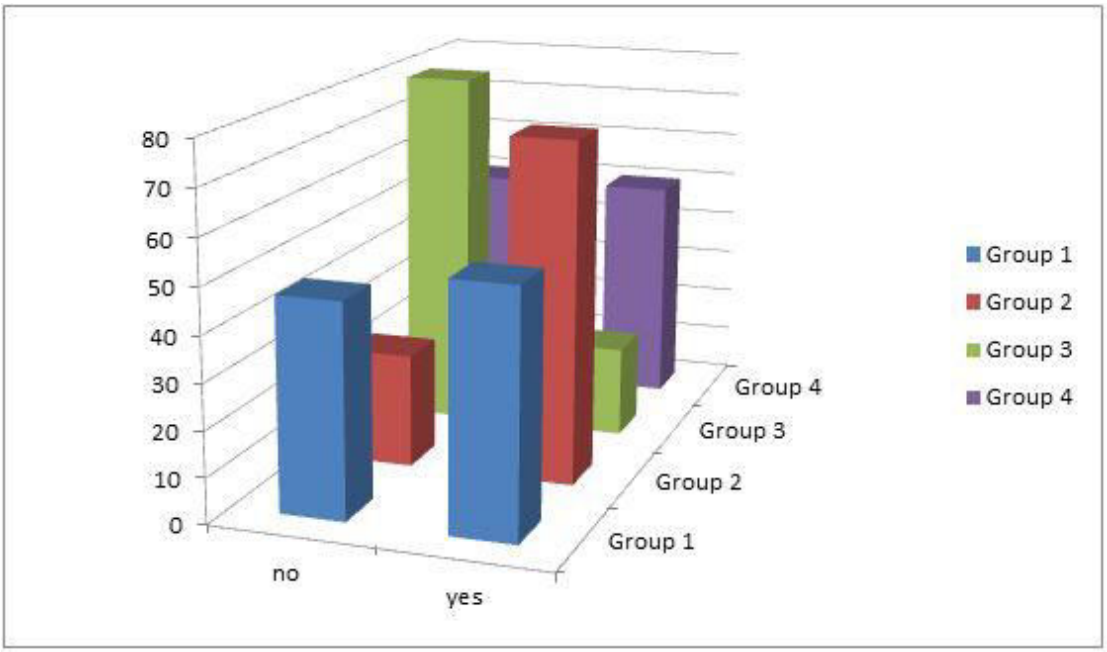

Fig.3. Family history of RD among the studied group

As regards heart rate there was significantly higher in group 3 versus other groups. **(Table. 2)**

There was a significant higher abnormal fetal biometry among group 3 followed by group 2 followed group 1, and regarding placental localization or amniotic fluid index there were insignificant differences between study groups. . **(Table .3)**

As regards musculoskeletal examination there were significant differences between study groups as regards inspection and palpation, but as regards the range of motion, type of deformity, and the number of tenders or swelling joints there were insignificant differences between study groups **(Figs 4, 5)**.

Table 2. Comparison of vital signs of the in the studied group

Vital signs	Group 1 (n = 30) RA	Group 2 (n = 20) SLE	Group 3 (n = 10)SSC	Group 4 (n = 10)AS	F	p
Temperature						
Min. – Max.	37.10 – 37.50	37.10 – 37.70	37.10 – 37.50	37.10 – 37.60	2.595	0.060
Mean ± SD.	37.29 ± 0.13	37.40 ± 0.17	37.27 ± 0.13	37.33 ± 0.16		
Median (IQR)	37.30(37.2 – 37.4)	37.40(37.3 – 37.5)	37.25(37.2 – 37.4)	37.30(37.2 – 37.5)		
HR (Beats/min.)						
Min. – Max.	70.0 – 99.0	75.0 – 99.0	88.0 – 114.0	78.0 – 87.0	9.792*	<0.001*
Mean ± SD.	87.83 ± 8.90	88.65 ± 7.58	101.60 ± 9.19	83.40 ± 4.65		
Median (IQR)	88.0(87.0 – 98.0)	87.0(87.0 – 98.0)	101.0(95.0 – 110.0)	87.0(78.0 – 87.0)		
p_0		0.985	<0.001*	0.445		
Sig. bet. Grps.		p_1=0.001*,p_2=0.347,p_3<0.001*				
Respiratory rate						
Min. – Max.	16.0 – 22.0	14.0 – 26.0	16.0 – 23.0	16.0 – 25.0	1.822	0.152
Mean ± SD.	18.40 ± 1.48	19.60 ± 4.37	18.70 ± 2.31	20.70 ± 3.20		
Median (IQR)	18.0(18.0 –	18.50(16.0 –	18.0(17.0 –	21.50(18.0 –		

	19.0)	24.0)	20.0)	23.0)		
Blood pressure						
Systolic (mmHg)						
Min. – Max.	110.0 – 130.0	110.0 – 142.0	110.0 – 150.0	110.0 – 140.0	0.451	0.718
Mean ± SD.	121.77 ± 4.42	124.05 ± 11.02	124.10 ± 10.86	124.50 ± 10.48		
Median (IQR)	120.5 (120.0 – 125.0)	120.0 (116.5 – 134.5)	121.0 (120.0 – 128.0)	121.0 (117.0 – 135.0)		
Diastolic (mmHg)						
Min. – Max.	73.0 – 89.0	70.0 – 100.0	70.0 – 100.0	70.0 – 92.0	0.176	0.912
Mean ± SD.	81.97 ± 3.90	81.95 ± 8.41	83.60 ± 8.46	82.0 ± 6.88		
Median (IQR)	82.50(80.0 – 85.0)	80.0(76.5 – 89.5)	83.0(80.0 – 88.0)	81.50(78.0 – 88.0)		

F: One way ANOVA test, Pairwise comparison between every 2 groups was done using Post Hoc Test (LSD), (Tukey); p_0: p-value for comparing **Group 1** and each; other groups; p_1: p-value for comparing **Group 2** and **Group 3**; p_2: p-value for comparing **Group 2** and **Group 4**; p_3: p-value for comparing **Group 3** and **Group 4**

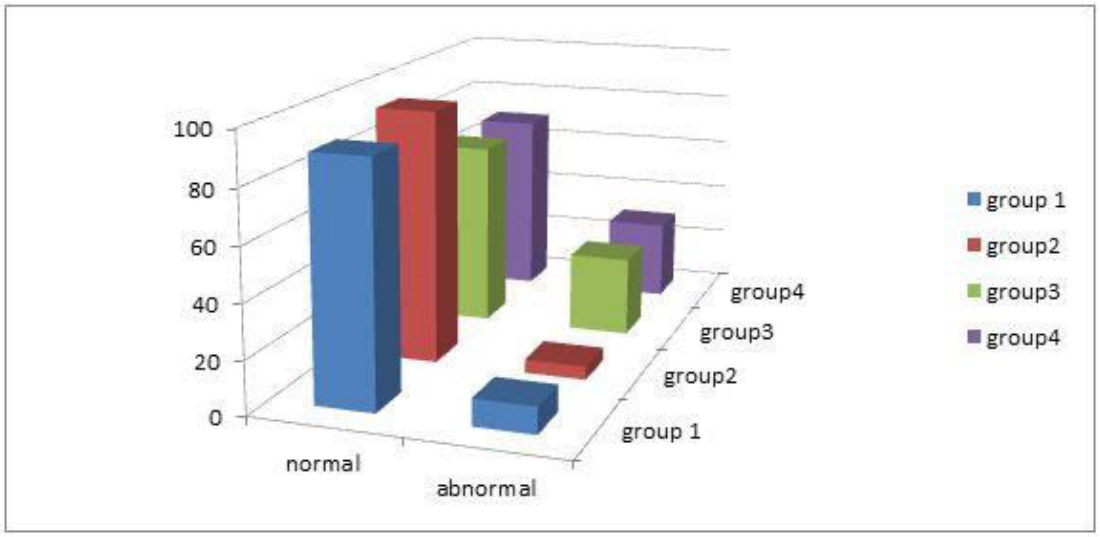

Fig.4. The range of motion of affected joints in the four studied groups

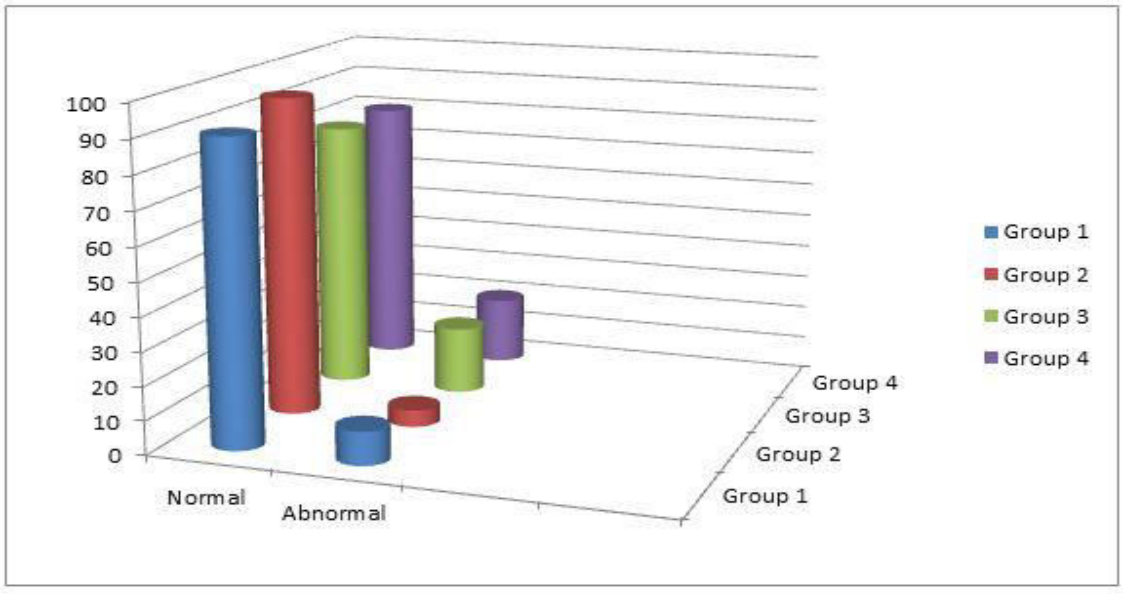

Fig.5. Deformity of joints in the four studied groups

Table 3. Obstetric examination findings of the studied groups

Obstetric examination	Group 1 (n = 30)RA		Group 2 (n = 20)SLE		Group 3 (n = 10)SSc		Group 4 (n = 10)AS		χ^2	^{MC}p
	No.	%	No.	%	No.	%	No.	%		
Fetal biometry										
Less than normal	7	23.3	7	35.0	6	60.0	0	0.0	9.488*	0.018*
Normal	23	76.7	13	65.0	4	40.0	10	100.0		
Placental localization										
Anterior position	18	60.0	10	50.0	7	70.0	6	60.0	3.551	0.887
Posterior position	11	36.7	10	50.0	3	30.0	4	40.0		
Placenta accrete	1	3.3	0	0.0	0	0.0	0	0.0		
Amniotic Fluid index										
Normal	24	80.0	16	80.0	7	70.0	10	100.0	3.247	0.400
Oligohydramnios	6	20.0	4	20.0	3	30.0	0	0.0		

MC: **Monte Carlo** χ^2: **Chi-square test**

As regards CBC between groups there was significantly higher RBCs, Hb, WBCs, platelets, and HCT value in group 1 versus other groups **(Table 4).** As regards ESR there was a significantly higher abnormality in group 4 followed by group 3 versus other groups **(Table 5)**.

Table 4. CBC findings of the studied groups

CBC	Group 1 (n = 30) RA	Group 2 (n = 20) SLE	Group 3 (n = 10) SSc	Group 4 (n = 10) AS	F	p
RBCs						
Min. – Max.	4.21 – 4.81	3.70 – 4.50	3.90 – 4.70	3.80 – 4.30	9.394*	<0.001*
Mean ± SD.	4.39 ± 0.16	4.18 ± 0.25	4.33 ± 0.25	4.03 ± 0.19		
Median (IQR)	4.34(4.3 – 4.5)	4.20(4.1 – 4.4)	4.35(4.1 – 4.5)	4.0(3.9 – 4.2)		
p_0		0.004*	0.855	<0.001*		
Sig. bet. Groups.		p_1=0.251,p_2=0.251,p_3=0.010*				
Hb.						
Min. – Max.	9.70 – 10.90	7.90 – 10.60	8.50 – 10.90	8.50 – 10.20	4.580*	0.006*
Mean ± SD.	10.04 ± 0.31	9.63 ± 0.83	10.03 ± 0.78	9.33 ± 0.56		
Median (IQR)	9.90(9.8 – 10.2)	9.85(9.3 – 10.3)	10.25(9.4 – 10.7)	9.25(8.9 – 9.8)		
p_0		0.097	1.000	0.011*		
Sig. bet. Groups.		p_1=0.327,p_2=0.578,p_3=0.056				
WBCs.						
Min. – Max.	9.70 – 11.90	2.90 – 11.50	6.40 – 10.20	6.80 – 10.20	20.576*	<0.001*
Mean ± SD.	10.89 ± 0.51	7.78 ± 2.27	8.76 ± 1.34	8.92 ± 1.19		
Median (IQR)	10.90(10.8 – 11.2)	7.65(5.9 – 10.0)	9.10(7.7 – 9.7)	9.10(7.8 – 10.1)		
p_0		<0.001*	0.001*	0.002*		
Sig. bet. Groups.		p_1=0.295,p_2=0.176,p_3=0.994				
PLT.						
Min. – Max.	205.0 – 301.0	100.0 – 280.0	169.0 – 310.0	188.0 – 270.0	13.173*	<0.001*
Mean ± SD.	249.3 ± 23.18	183.3 ± 52.33	230.3 ± 43.26	213.1 ± 24.87		
Median (IQR)	244.5	179.5	230.5	207.5		

	(233.0 – 261.0)	(147.5 – 215.0)	(194.0 – 256.0)	(195.0 – 225.0)		
p_0		<0.001*	0497	0.044*		
Sig. bet. Groups.		p_1=0.009*,p_2=0.168,p_3=0.726				
HCT						
Min. – Max.	33.60 – 36.40	25.50 – 34.10	27.90 – 32.80	25.90 – 31.20	51.504*	<0.001*
Mean ± SD.	35.18 ± 0.87	30.60 ± 2.46	31.06 ± 1.72	28.77 ± 1.73		
Median (IQR)	35.10(34.6 – 35.8)	31.15(29.3 – 32.5)	31.70(29.6 – 32.4)	28.80(27.5 – 30.2)		
p_0		<0.001*	<0.001*	<0.001*		
Sig. bet. Groups.		p_1=0.894,p_2=0.035*,p_3=0.019*				
MCV						
Min. – Max.	76.80 – 80.20	74.80 – 84.70	74.70 – 81.30	72.90 – 78.10	9.067*	<0.001*
Mean ± SD.	78.52 ± 0.88	79.78 ± 2.95	77.94 ± 2.02	75.88 ± 1.77		
Median (IQR)	78.50 (77.9 – 79.3)	79.75 (77.9 – 82.1)	78.0 (76.8 – 79.1)	75.80 (74.4 – 77.6)		
p_0		0.127	0.848	0.002*		
Sig. bet. Groups.		p_1=0.082,p_2<0.001*,p_3=0.096				
MCH						
Min. – Max.	25.20 – 29.50	24.90 – 29.10	25.60 – 27.60	25.60 – 28.30	0.957	0.419
Mean ± SD.	27.01 ± 1.03	27.19 ± 1.18	26.57 ± 0.71	26.77 ± 0.85		
Median (IQR)	26.80 (26.5 – 27.7)	27.45 (26.8 – 27.9)	26.45 (25.9 – 27.3)	26.85 (25.9 – 27.3)		
MCHC						
Min. – Max.	31.60 – 34.80	30.90 – 36.10	29.50 – 35.10	28.90 – 33.10	6.992*	<0.001*
Mean ± SD.	33.04 ± 0.95	33.11 ± 1.42	32.49 ± 1.78	31.04 ± 1.34		
Median (IQR)	32.80 (32.6 – 33.7)	33.20 (32.2 – 34.1)	32.45 (31.1 – 33.9)	30.80 (29.9 – 31.8)		
p_0		0.997	0.652	<0.001*		
Sig. bet. Groups.		p_1=0.602,p_2=0.001*,p_3=0.066				

Table 5. ESR findings in the four studied groups

ESR	Group 1 (n = 30) RA		Group 2 (n = 20) SLE		Group 3 (n = 10) SSc		Group 4 (n = 10) AS		χ^2	^{MC}p
	No.	%	No.	%	No.	%	No.	%		
Normal	24	80.0	16	80.0	5	50.0	4	40.0	8.088*	0.041*
Abnormal	6	20.0	4	20.0	5	50.0	6	60.0		

χ^2: **Chi-square test**; MC: **Monte Carlo**

As regards urine analysis (protein, ketone, acetate, WBCs, and RBCs); urine protein was significantly higher in group 2, and urine WBCs were also significantly higher in group 1 versus other groups. As regards urine RBCs there was a significantly higher group 1 versus other groups **(Table 6)**.

There was a significantly higher liver enzyme among group 4 versus other groups **(Table 7)**.

Autoantibodies according to disease specificity, were significantly different between study groups as group 1 mainly had Anti-CCP + in and RF + in 80% of cases group 2 had ANA+ in all cases, Low C3-C4 in 87.5%, RF + in 12.5% of cases, in group 3 all cases had ACA +, Anti-SCL70 + and in group 4 all cases had HLA-B27 +, Anti-SCL70 + **(Table 8).**

Table 6. Urine analysis findings in the studied groups

Urine analysis	Group 1 (n = 30) RA		Group 2 (n = 20) SLE		Group 3 (n = 10) SSc		Group 4 (n = 10)AS		Test of Sig.	p
	No.	%	No.	%	No.	%	No.	%		
Clarity										
Turbid	6	20.0	4	20.0	2	20.0	1	10.0	χ^2= 1.164	^{MC}p= 0.993
Cloudy	6	20.0	4	20.0	2	20.0	3	30.0		
Clear	18	60.0	12	60.0	6	60.0	6	60.0		
Ketone										
Min. – Max.	0.60 – 1.10		0.40 – 0.90		0.50 – 1.20		0.50 – 0.80		F= 2.002	0.122
Mean ± SD.	0.73 ± 0.13		0.70 ± 0.16		0.77 ± 0.20		0.62 ± 0.12			
Median (IQR)	0.70(0.60 – 0.80)		0.70(0.60 – 0.80)		0.75(0.60 – 0.90)		0.60(0.50 – 0.70)			
Acetate										
Negative	19	63.3	16	80.0	7	70.0	8	80.0	χ^2= 1.960	^{MC}p= 0.645
Positive	11	36.7	4	20.0	3	30.0	2	20.0		
Protein										
Min. – Max.	110.0 – 170.0		115.0 – 340.0		110.0 – 166.0		112.0 – 140.0		H= 19.093*	<0.001*
Mean ± SD.	139.2 ± 15.01		180.3 ± 77.32		128.3 ± 18.94		121.5 ± 8.70			
Median (IQR)	137.0 (128.0 – 142.0)		152.0 (129.0 – 176.5)		121.0 (116.0 – 130.0)		119.5 (115.0 – 123.0)			
p_0			0.239		0.028*		0.002*			
Sig. bet. Groups.			p_1=0.003*,p_2<0.001*,p_3=0.482							
Bacteria										
None	21	70.0	14	70.0	8	80.0	8	80.0	χ^2= 0.665	^{MC}p= 0.888
Moderate	9	30.0	6	30.0	2	20.0	2	20.0		
WBCs										
Min. – Max.	2.0 – 21.0		1.0 – 11.0		2.0 – 11.0		1.0 – 4.0		H= 18.241*	<0.001*
Mean ± SD.	6.47 ± 3.71		5.05 ± 2.65		5.40 ± 2.46		2.50 ± 1.08			
Median (IQR)	6.0(4.0 – 7.0)		5.0(3.0 – 6.0)		5.0(4.0 – 6.0)		2.50(2.0 – 3.0)			
p_0			0.127		0.511		<0.001*			
Sig. bet. Groups.			p_1=0.604,p_2=0.004*,p_3=0.003*							

χ^2: Chi-square test; MC: Monte Carlo; H: Kruskal Wallis test; Pairwise comparison between every 2 groups was done using Post Hoc Test (Dunn's for multiple comparisons test)

Table 7. Liver enzymes findings in the studied groups

Liver enzymes	Group 1 (n = 30) RA	Group 2 (n = 20) SLE	Group 3 (n = 10) SSc	Group 4 (n = 10) AS	F	p
AST(U/L)						
Min. – Max.	18.0 – 33.0	34.0 – 50.0	30.0 – 50.0	33.0 – 46.0	81.807*	<0.001*
Mean ± SD.	22.87 ± 3.68	38.75 ± 4.29	38.40 ± 5.95	40.50 ± 4.22		
Median (IQR)	23.0 (21.0 – 24.0)	38.50 (36.0 – 40.0)	38.0 (34.0 – 41.0)	41.0 (38.0 – 44.0)		
p_0		<0.001*	<0.001*	<0.001*		
Sig. bet. Groups.		p_1=0.997,p_2=0.721,p_3=0.696				
ALT (U/L)						
Min. – Max.	16.0 – 24.0	48.0 – 61.0	45.0 – 62.0	45.0 – 61.0	450.784*	<0.001*
Mean ± SD.	20.33 ± 2.76	52.40 ± 3.23	52.50 ± 5.32	55.10 ± 5.02		
Median (IQR)	21.0	52.0	51.50	55.50		

	(17.0 – 23.0)	(50.0 – 53.0)	(49.0 – 55.0)	(53.0 – 59.0)		
p_0		<0.001*	<0.001*	<0.001*		
Sig. bet. Groups.		p_1=1.000,p_2=0.244,p_3=0.401				

IQR: Inter quartile range; SD: Standard deviation; F: One-way ANOVA test; Pairwise comparison between every 2 groups were done using Post Hoc Test (LSD), (Tukey)

Table 8. Autoantibodies specificity in the studied four groups

Autoantibodies	Group 1 (n = 30)RA		Group 2 (n = 20)SLE		Group 3 (n = 10)SSc		Group 4 (n = 10)AS		χ^2	^{MC}p
	No.	%	No.	%	No.	%	No.	%		
Negative	6	20.0	0	0.0	0	0.0	0	0.0	143.419*	<0.001*
ANA+	0	0.0	20	100.0	0	0.0	0	0.0		
ACA +	0	0.0	0	0.0	10	100.0	0	0.0		
Anti-CCP +	24	80.0	0	0.0	0	0.0	0	0.0		
HLA-B27 +	0	0.0	0	0.0	0	0.0	10	100.0		
RF +	24	80.0	1	12.5	0	0.0	0	0.0	59.799*	<0.001*
Low C3-C4	0	0.0	7	87.5	0	0.0	0	0.0		
Anti-SCL70 +	0	0.0	0	0.0	10	100.0	10	100.0		

χ^2: Chi-square test MC: Monte Carlo

Discussion

The clinical manifestations of the autoimmune rheumatic disease depend on its pathogenesis. Some improve spontaneously during pregnancy, while others continue to be active or relapse. Pregnancy results also depend on the severity and severity of the illness **(Ostensen et al., 2011).**

The comparison between the four study groups revealed an insignificant difference in the age of patients. In general, innate immune processes are becoming more active with age, whereas adaptive immune system function declines **(Chalan et al., 2015).**

Results of the personal history in our study revealed insignificant differences concerning the smoking history and obstetric history.

Regarding the therapeutic history of hormonal TTT; there were significant differences between the current study groups (p<0.001). The effect of hormonal therapy on autoimmune rheumatic diseases was discussed previously; existing data from investigations imply that women with SLE who use hormone replacement therapy may have a slightly higher risk of mild/moderate relapses, but not of major relapses. Hormone replacement therapy does not appear to be associated with a higher risk of disease flare in rheumatoid arthritis and may effectively enhance disease activity **(Holroyd and Edwards, 2009).**

As regards the family history of rheumatic disease (RD); the highest percentage was (75%) in Group (2) patients followed by (53.3%) in rheumatoid arthritis patients then (50%) in Ankylosing spondylitis patients. Recently, the results of **Kronzer et al., (2021)** study revealed that a family history of various autoimmune and non-autoimmune co-morbidities was linked to a higher risk of RA. **Morin et al., (2020)** stated that first-degree family members of ankylosing spondylitis patients had a 20-fold increased risk of the disease.

Heart rate was significantly higher in Systemic sclerosis patients compared to other groups (p<0.001 **Bienias et al., (2010)** found that the heart rate turbulence was impaired in systemic sclerosis patients

In our study, painful joints were recorded in (5%) of SLE patients and painful ulcers in (5%) of patients. while, in the study of **Khan et al., (2017)**, arthritis was recorded in (78.1%) of SLE patients and body aches in (66.08%).

Fetal biometry was less than normal in (60%) of SS patients, (35.0%) of SLE patients, and (23.3%) of RA patients. Our results agreed with the study of **Rom et al., (2014)**, who found that a slightly smaller fetal size for mothers having RA at birth compared to unexposed children in this study, which may be related to a 1.5-fold increased risk of preterm birth. Children exposed to maternal preclinical RA had similar outcomes. Paternal RA, on the other hand, was not linked to reduced fetal growth or preterm birth.

The present study results showed significantly higher RBCs (p<0.001) , Hb (p=0.006), WBCs (p<0.001) , platelets count (p<0.001) and HCT (p<0.001) value in RA patients versus other patients groups.

The present study results showed ~~statistically~~ significantly higher RBCs, WBCs, platelets counts, HCT (p <0.001), and Hb (p=0.006) values in RA patients versus other patient groups. There were significantly higher MCV and MCHC (p <0.001) in SLE patients. **Mursal et al., (2016)** result demonstrated that MCH was significantly reduced in anemic rheumatoid arthritis patients in comparison with non-anemic rheumatoid arthritis patients with (P=0.003) while MCV & MCHC are within the normal range.

Results of the present study showed that the ESR was significantly higher in abnormality in Ankylosing spondylitis followed by Systemic sclerosis versus other groups. There was an agreement with **Kozaci et al., (2010).**

Regarding the urine analysis results, we found that urine protein was significantly higher in SLE (p<0.001), while urine WBCs and RBCs were significantly higher in rheumatoid arthritis patients. This was in agreement with **Lu et al., (2021)** found that pregnant women with SLE activity had significant 24-h urine protein.

Regarding the liver enzymes, our results showed that both ALT and AST were significantly higher in Ankylosing spondylitis patients in comparison to other groups (p<0.001). The incidence of liver enzyme elevation was 23.7% in AS patients **(Choi et al., 2020).** In SLE patients also, elevated liver enzymes were found in 81% of the cases **(Vaiphei et al., 2011).**

In the present study, autoantibodies were significantly different because of multiple disease specificities, between study groups as group 1 mainly had Anti-CCP + in and RF + in 80% of cases and the other 20% were negative, group 2 mainly had ANA+ in all cases, Low C3-C4 in 87.5%, RF + in 12.5% of cases, in group 3 all cases had ACA +, Anti-SCL70 + and in group 4 all cases had HLA-B27 +, Anti-SCL70 +

The anti-CCP was positive in 53.1% of RA patients and 4.7% of controls. The frequency of RF-T was 61.87% and 17.66% in RA patients and controls respectively **(Shakiba et al., 2014).** In **Arévalo et al., (2018)** study in AS patients, the prevalence of HLA-B27 was 83 percent

In the study **(Al-Mughales, 2022),** serum C3 and C4 components showed median values of 0.89 and 0.17

IU/ml, respectively, while rheumatoid factor was positive for 12.8% of the patients. Titers of ANA were higher in 82.4% of the patients. The ANA pattern was associated with many immune markers that have been linked to clinically meaningful consequences in SLE.

Conclusion

The present study pointed to the importance of ARDS control and diagnosis before and during pregnancy as well as the importance of disease activity assessment. Further larger prospective studies are needed. A multidisciplinary team (rheumatologists/internists, obstetricians, and neonatologists) should take care of patients during pregnancy.

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