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Original article

A study of (IL-23R) Genetic Variant (rs11805303) in Egyptian Patients with Rheumatoid Arthritis

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Abstract:

Objective: to study the relationship between RA disease and the IL-23R genetic variation (rs11805303) in a group of Egyptian patients diagnosed as rheumatoid arthritis and its association with disease activity. **Patient and Methods:** One hundred participants, ranging in age from thirty to sixty years old, 56 of whom had RA and 44 of whom were apparently healthy matched in age and sex with patients. All participants were genotyped using PCR/RFLP for the genetic variation (rs11805303). Data were analyzed through Kruskal–Wallis and Mann–Whitney, chi-square ($\chi 2$), Monte Carlo tests and logistic regression. **Results:** The prevalence of the rs11805303 TT genotype was 21.4% in RA patients, which is greater than in controls (2.3 %). A much greater association with RA was in the CT genotype (1.77 times) and the TT genotype (5.25 times) compared to the CC genotype. **Conclusion:** The study found that compared to apparently healthy controls, RA patients are more likely to have the IL-23R rs11805303 TT genetic variation. Additionally, greater levels of anti-CCP were associated with the TT genotype, but higher levels of acute phase reactants and disease activity scores are associated with the CC genotype.

Key words: Relevant Search Terms; PCR-RFLP; Interleukin 23 receptor; Rheumatoid Arthritis

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Introduction

The tiny synovial joints, often in a symmetrical pattern, are the primary targets of the chronic inflammatory illness known as rheumatoid arthritis (RA). For RA to be diagnosed, symptoms must persist for at least six months [1]. Damage to bone and cartilage is caused by the proliferation of synovial cells, which is triggered by a complex network of cytokines and cells [2].

At least in ACPA+ individuals, the development of autoantibodies years before to clinical symptoms suggests that the adaptive immune system plays a significant role in the early pathogenesis of RA. Inflamed joints have a high concentration of T cells, and some of these cells have been discovered to be autoreactive [3].

A member of the IL-12 cytokine family, IL-23 is a cytokine that promotes inflammation. Th17 cells, a subset of T lymphocytes involved in chronic inflammatory/autoimmune driven illnesses, cannot differentiate without IL-23. Clinical signs and experimental arthritic models have shown that Th17 cells play a significant role in the development of RA [3].

Parts 40 and 19 make up IL-23. Interleukin-23 receptor binding affinity is strong for the p19 subunit (IL-23R). The IL-23/IL-17 signal transduction pathway involves IL-23R. In contrast to antigen-presenting cells, inflammatory macrophages have the IL-23R gene and are stimulated to generate interleukin-1, tumour necrosis factor-alpha (TNF-α), and IL-23 when stimulated by IL-23. In an inflammatory state, particularly when TGF-β and interleukin-6 are present, IL-23 promotes the development and upkeep of CD4+ T helper 17 cells (Th17) (IL-6). When Th17 cells are activated, they release a variety of substances including granulocyte macrophage-colony stimulating factor, interleukin-17A, interleukin-22, IL-6, TNF-α, and interleukin-17F. (GM-CSF). Joint, bone, and cartilage systems are all vulnerable to harm from these pro-inflammatory cytokines. In addition to IL-17, IL-23 is involved in osteoclastogenesis and bone degradation by regulating T cell receptor activator of kappa B ligand (RANKL) expression and osteoclast tartrate-resistant acid phosphatase (TRAP) activity. Treatment with anti-IL-23 has been shown to protect against bone loss in recent investigations [4].

This research was set-up to examine the relationship between IL23R genetic variant (rs11805303) and rheumatoid arthritis disease in group of Egyptian patients and its association with disease activity.

Subjects and Methods

Subjects:

This case-control study was conducted on 2 groups:

Group I (patient group): total number of 56 rheumatoid arthritis patients, who were recruited from outpatient clinic of Rheumatology and Rehabilitation Department at Benha University Hospitals. Their age ranged from (30 -60) years old. Their median disease onset was 6.50 years. The gender breakdown was as follows: 75% female and 25% male. Their diagnosis was based on 2010 American College of Rheumatology/European league Against Rheumatism (ACR/EULAR) Rheumatoid Arthritis classification criteria. All patients included in the study were taking disease modifying antirheumatic drugs (DMARDs) as methotrexate, sulfasalazine, hydroxychloroquine and leflunomide. Complications were observed in 19 individuals and more common complications reported were lung fibrosis (7.1%) followed by corneal melting, herpes zoster, osteoporosis, peptic ulcer, recurrent bacterial infection, scleritis and aye dryness.

Group II (control group): there were 44 apparently healthy control individuals from general population who were

matched in age and gender (P≥0.05). Their mean age was 47.77 ±9.35 years. Their age ranged from 31 to 60 years. They were 28 females and 16 males. This case control study was conducted from October 2022 to September 2023, the research was carried out with the blessing of the Ethical Committee of Benha Faculty of Medicine {M.S:7-10-2022}. An informed written consent was obtained from each participant before enrolment in the study. Patients were not eligible for participation in the trial if their reports showing other autoimmune diseases.

Sampling:

Under strict aseptic circumstances, eight millilitres of each participant's venous blood were collected and allocated as follows:

In an EDTA vacutainer, 2 mL of whole blood were drawn and used for the complete blood count (CBC). While another 2 ml were frozen at -20ºC for future DNA extraction. Two millilitres of that blood sample was transferred to the Na citrate tube for the ESR. The other two millilitres were kept in a plain vacutainer until it coagulated. After 15 minutes of centrifugation at 1500 rpm and the serum was separated.

Methods:

All patients were subjected to**:**

Full medical history, physical examination (joints for swelling and tenderness), evaluation of disease activity using the 'gold standard' in RA diagnosis, the disease activity score 28 (DAS 28 score), calculated by numbering swollen joints and tender joints, estimation of ESR and CRP, Global assessment of health by means of a questionnaire is marked by the patient (marking a scale of 0 to 100). The results from the above observations were then put into a complex mathematical formula,

DAS28 = 0.56*sqrt (tender 28) + 0.28*sqrt (swollen 28) + 0.70*ln (ESR) + 0.014*GH.

The DAS28 range from (0.49 to 9.07) [5].

High disease activity (score >5.1), moderate disease activity score (3.2 to 5.1) and low disease activity (score<3.2) [6].

Laboratory test:

Complete blood count (CBC) was measured by using Sysmex XS-800, Rheumatoid factor (RF) and C-reactive protein (CRP) were measured by nephelometry, Erythrocyte sedimentation rate (ESR) was measured by Westergren technique, Anti-cyclic citrullinated peptide (anti CCP) was measured by using chemiluminescence enzyme immunoassay, Liver function (ALT-AST) and kidney function (serum urea -serum creatinine) had been measured by Dialab chemical analyzer.

Molecular investigation:

Genetic Details of the SNP rs11805303, an intron variation with the variant allele T, were examined using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique with a minor allele frequency (MAF) of 0.38 (T) in accordance with the 1000 Genomes Project. It is situated on the IL23R gene's chromosome 1.

Using the Quick-DNATM Miniprep plus Kit 50 preps (Catalogue No: D4068) (Lot No: 210376) from Zymo-Spin TM Technology, genomic DNA was extracted from EDTA blood leucocytes and then amplified by polymerase chain reaction (PCR).

The following ingredients were used in the final volume of 25 µl: 12.5 µl of PCR Master Mix from Intron Biotechnology in Korea, 1.5 µl of forwarding primer from Eurofins in Europe, 1.5 µl of reverse primer from the same source, 3µl of template DNA, and 6.5µl of nuclease-free water. The PCR reaction was conducted in this volume. The following conditions were followed for conducting polymerase chain reaction (PCR) in a thermal cycler manufactured by Applied Biosystems and manufactured in Singapore: One minute of denaturation at 95 degrees Celsius. For 35 cycles, denaturation at 95 °C for 15 sec,

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annealing at 66 °C for 20 sec, and extension at 72 °C for 10 sec.

Analytic Jena Company of Taiwan's Biometra gel electrophoresis and Alpha Innotech Corporation's UV light trans-illumination were used to identify the amplification products, namely the existence of the amplification band at 490 bp. Thermo Scientific Fast Digest (Mn1I) from Enzymomics, Korea, with Cat No: R055S, was used to digest the PCR amplification products for 120 minutes at 37 °C. On a 2% agarose gel, the DNA bands could be seen. The CC genotype presents with three bands at 150,490 and 570 bp, the CT genotype with four bands at 150,490, 520, and 570 bp, and the TT genotype with a mutation presents with three bands at 150,490 and 520 bp (figure 1).

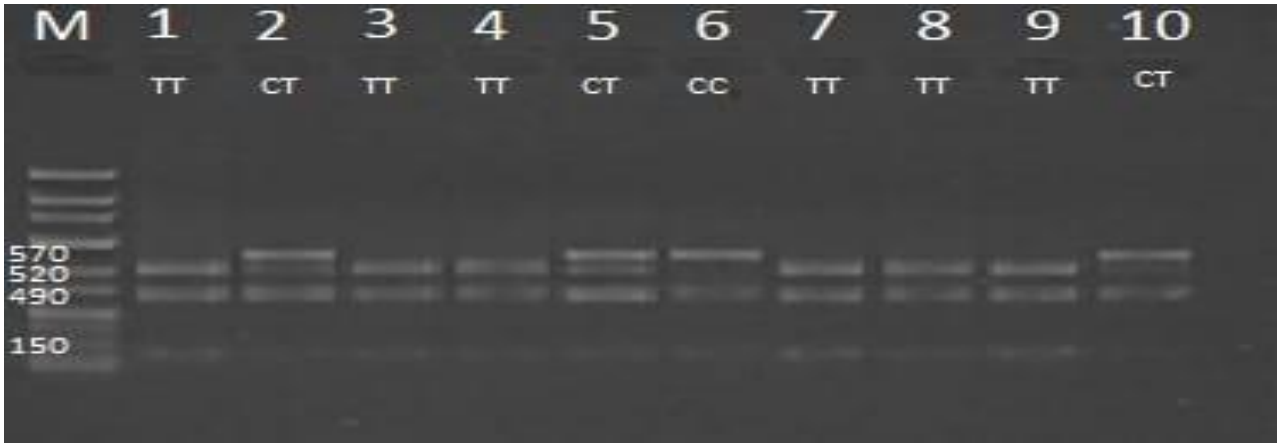

Fig.1: Results of agarose gel electrophoresis for PCR-RFLP components. A PCR marker (50-1000 bp ladder) is shown on the left lane. Lane6: homozygote CC (150,490,570bp). Lane2, 5, 10: heterozygote CT (150,490,520,570bp). TT homozygote in Lane 1, 3, 4, 7, 8, and 9 (150,490,520bp).

Statistical analysis

Statistical data were analysed using SPSS 25.0. (IBM SPSS Statistics 25 software Armonk, NY: IBM Corp). The data's normality was checked using the Shapiro-Wilks test. The quantitative parametric data was analysed using the One Way ANOVA (F) test and the Student T test, and the results were shown as the mean and standard deviation (SD). We used the Kruskal-Wallis test in conjunction with the Mann Whitney U test to compare the groups' quantitative non-parametric data, which was reported as median. The frequency and percentage (%) of qualitative variables were reported, and they were analysed using the Chi-square test and the Monte Carlo test. Statistical significance was determined by a two-tailed P value less than 0.05. Logistic regression is also used to estimate the relationship between a dependent variable and one (univariate) or more (multivariate) independent variables.

Results

The studied rs11805303 single-nucleotide polymorphism (SNP) is located within IL23R gene on chromosome 1 and consists of the reference allele, C, and an alternative allele, T. The current study on rs11805303 showed that genotypes in cases as well as control groups was in Hardy-Weinberg Equilibrium (HWE) (i.e. no significant differences were found between observed and expected counts in each group) (Table 1).

In terms of genotype and allele distribution, the two categories could not be more different. The association of RA was much increased in those with the CT and TT genotypes compared to the CC genotype. People with the TT genotype had a substantially increased with RA, according to the recessive model study. The analysis of the alleles showed that the T allele was associated with rheumatoid arthritis, with an Odds ratio of 3.38. (Table 2).

RA patients had significantly elevated ESR levels and CRP levels than the control group ($p < 0.001$). Regarding RF, 89.3% of RA patients had a positive RF test. The median positive RF level for RA patients was 64 U/L. Regarding anti-CCP, 85.7% of RA patients had a positive anti-CCP test. The median positive anti-CCP level for RA patients was 210 U/L. The results shows that 7.1% of RA patients had a low DAS 28 score, 39.3% of RA patients had a moderate DAS 28 score, and 53.6% of RA patients had a high DAS 28 score. The mean DAS 28 score for RA patients was 5.35 ± 1.15.

There were significant differences in ESR (figure 2a), CRP, RF (figure 2b) levels and DAS 28 score between the IL-23R (rs11805303) genotype groups. Specifically, individuals with the CC genotype had significantly higher ESR, CRP and RF levels compared to those with the TT or CT genotype. The p-values for pairwise comparisons suggested that the difference between each of the two genotype groups was significant ($p<0.05$).

The results showed that there were significant differences in anti CCP levels between the IL-23R (rs11805303) genotype groups (Figure 3). The individuals with the TT genotype had significantly higher anti-CCP levels compared to those with the CC or CT genotype. The median anti-CCP in the TT genotype (370 U/L) was significantly higher compared to those with the CC (80 U/L) or CT genotype (210 U/L) (Table 3).

DAS score differed significantly according to IL23R polymorphism, with highest score was attributed to those carrying CC genotype, followed by those carrying CT genotype, and lastly those carrying TT genotype (median=6.57, 4.96, 4.30 respectively)

DAS 28 showed significant positive correlation with ESR, CRP, RF, significant negative correlation with anti CCP. Otherwise no significant correlations were found between DAS28 and other parameters(Table 4).

Regression analysis was conducted for prediction of DAS 28, using age, gender, family history, laboratory data and IL23 polymorphism as confounders. Higher ESR, CRP, RF, lower anti CCP and wild IL23 R polymorphism were associated with prediction of higher activity.

Regression analysis was conducted for prediction of complications, using age, gender, family history, laboratory data and IL23 polymorphism as confounders. None was considered as predictor of complications.

Table 1: Assessment of Hardy Weinberg equilibrium for (rs11805303) Gene polymorphism.

IL23R gene polymorphism	RA n = 56		Control n = 44	
	Observed	Expected	Observed	Expected
CC	20	18.3	29	29.5
CT	24	27.4	14	13.0
TT	12	10.3	1	1.45
P	0.350		0.645	

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Table 2: Association of IL-23R (rs11805303) among RA patients and control group

IL-23R (rs11805303)		RA n = 56 No(%)	Control n = 44 No(%)	P value	OR (95 % CI)
Genotypes	CC	20 (35.7%)	29 (65.9%)		Reference
	CT	24(42.9%)	14 (31.8%)	0.039*	1.77(1.03–3.03)
	TT	12(21.4%)	1(2.3%)	0.002*	5.25(1.81–15.22)
Dominant model	CC	20(35.7%)	29(65.9%)		Reference
	CT+TT	36(64.3%)	15(34.1%)	0.003*	3.48(1.52–7.97)
Recessive model	CC+CT	44(78.6%)	43(97.7%)		Reference
	TT	12(21.4%)	1(2.3%)	0.021*	11.73(1.46-94.14)
Alleles	C	64(57.1%)	72(81.8%)		Reference
	T	48(42.9 %)	16(18.2%%)	<0.001*	3.38(1.75–6.52)

Table 3: Association between IL-23R (rs11805303) and ESR, CRP, RF and DAS 28 score among RA patients.

		IL-23R (rs11805303) CC N = 20 (%) №	CT N = 24 (%) №	TT N = 12 (%) №	Test	P	Pairwise
ESR (mm/h)	Mean ± SD.	103.15 ± 15.49	53.75 ± 14.16	22.83 ± 4.88	H= 47.729	<0.001*	P2<0.001* P3<0.001* P4=0.002*
	Median	110.0	50.0	23.50			
	Min. – Max.	85.0 – 129.0	30.0 – 80.0	15.0 – 30.0			
CRP (mg/L)	Mean ± SD.	86.40 ± 19.70	38.18 ± 13.68	16.80 ± 11.59	H= 38.134	<0.001*	P2<0.001* P3<0.001* P4=0.019*
	Median	96.0	48.0	12.0			
	Min. – Max.	48.0 – 96.0	12.0 – 48.0	12.0 – 48.0			
DAS 28 score	Low	0(0.0%)	0(0.0%)	4(33.3%)	X^2= 42.480	MC <0.001*	P2<0.001* ^{MC}P3<0.001* ^{MC}P4=0.001*
	Moderate	0(0.0%)	14(58.3%)	8(66.7%)			
	High	20(100.0%)	10(41.7%)	0(0.0%)			
	Mean ± SD.	6.64 ± 0.43	5.0 ± 0.31	3.91 ± 0.76	F= 134.23	<0.001*	P2<0.001* P3<0.001* P4<0.001*
	Median	6.57	4.96	4.30			
	Min. – Max.	5.90 – 7.60	4.60 – 5.50	2.80 – 4.54			
RF (U/L)	Mean ± SD.	97.60 ± 31.32	46.96 ± 17.11	19.43 ± 4.28	H= 36.348	<0.001*	P2<0.001* P3<0.001* P4=0.002*
	Median	100.0	56.0	16.0			
	Min. – Max.	64.0 – 128.0	24.0 – 64.0	16.0 – 24.0			
Anti CCP (U/L)	Mean ± SD.	83.25 ± 14.54	219.0 ± 52.81	382.3 ± 92.85	F= 75.186	<0.001*	P2<0.001* P3<0.001* P4<0.001*
	Median	80.0	210.0	370.0			
	Min. – Max.	65.0 – 110.0	110.0 – 300.0	230.0 – 529.0			

* X2: Chi-Square, * SD: Standard Deviation, * Min: Minimum, * Max: Maximum, Myrtle Beach, F: Analysis of variance test, H: Kruskal Wallis test. Part P: Analyzing the various IL-23R (rs11805303) genotypes. First, we will compare the various IL-23R (rs11805303) genotypes. Then, we will compare CC and CT. Third, we will compare CC and TT. Finally, we will compare CT and TT. **: Significance is maintained when the p-value is less than 0.05.

Table 4: Correlation of DAS 28 score with other parameters.

	DAS.28	
	Correlation coefficient	**p**
Age	-0.224	0.097
Onset	-0.122	0.372
Hemoglobin	-0.079	0.561
WBC	-0.038	0.781
Platelets	0.057	0.676
ESR	0.785	<0.001
CRP	0.689	<0.001
RF	0.671	<0.001
Anti CCP	-0.753	<0.001
ALT	0.027	0.841
AST	0.004	0.979
Urea	-0.022	0.871
Creatinine	0.158	0.245

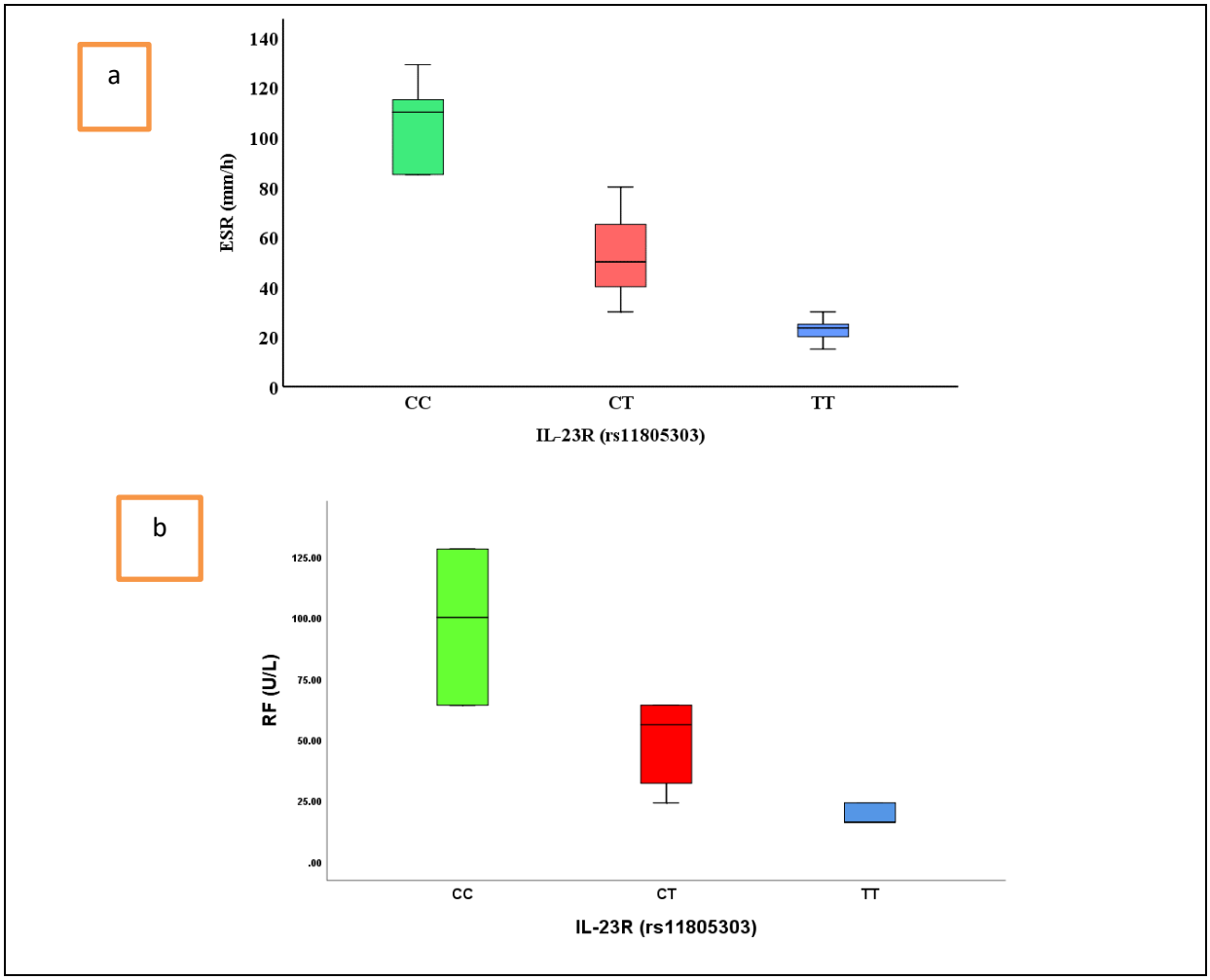

Fig 2a): Boxplot chart for association between IL-23R (rs11805303) and ESR among RA patients.
Fig 2b): Boxplot chart for association between IL-23R (rs11805303) and RF among RA patients.

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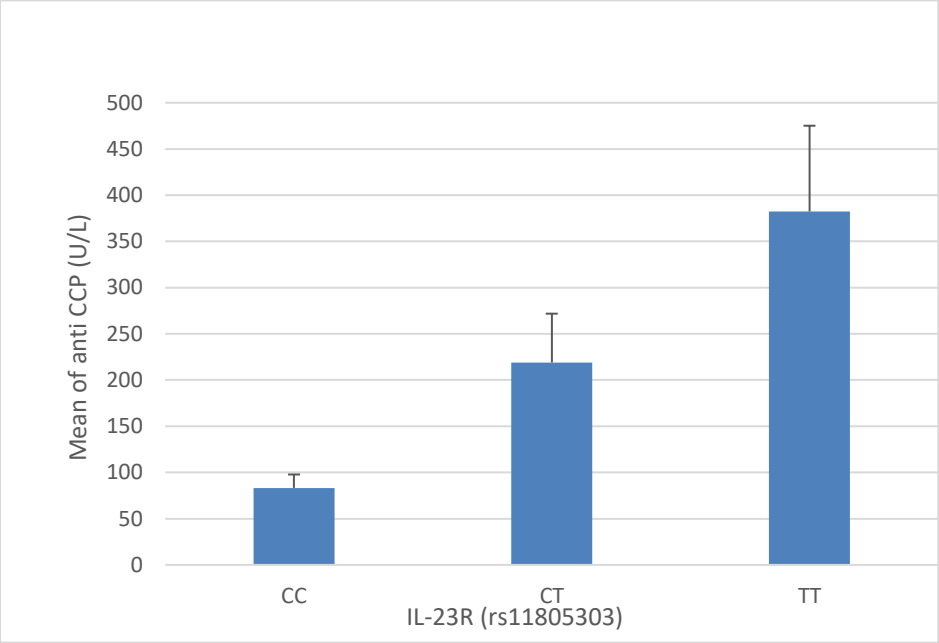

Fig. 3: Bar chart for association between IL-23R (rs11805303) and anti CCP among RA patients.

Discussion

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease manifested primarily as inflammatory arthritis, typically involving the small joints of the hands and feet. It can lead to severe disability and death [7]. It is a chronic inflammatory disorder caused by the interaction between genes and environmental factors that primarily involves synovial joints[1]. Interleukin-23 has been implicated in several autoimmune inflammatory disorders such as colitis, gastritis, psoriasis and arthritis, and as a novel pro-inflammatory cytokine, with close resemblance to IL-12. Although similar to IL-12 in both structurally and in the ability of memory T cells to increase interferon-γ (IFN-γ) production and proliferation, the ability of IL-23 to induce IL-17 provides a unique role compared with that of IL-12 in both the development and the maintenance of autoimmune inflammation[8].

The current study found that, RA patients had significantly elevated ESR levels than the control group (60.0 mm/h versus 12.50 mm/h) and elevated CRP levels than the control group; the mean positive CRP level for RA patients was 52.62 mg/L. A study done in 2023, revealed that ESR and CRP were significantly higher in RA patients than in control group [9]. The current study found that RA patients had significantly higher levels of RF and anti-CCP than the control group. The median positive RF level for RA patients was 64 U/L and ranged from 16 U/L to 128 U/L. The median positive anti-CCP level for RA patients was 200 U/L and ranged from 45 U/L to 529 U/L.

The current study found that 7.1% of RA patients had a low DAS 28 score, 39.3% of RA patients had a moderate DAS 28 score, and 53.6% of RA patients had a high DAS 28 score. The mean DAS 28 score for RA patients was 5.35 ± 1.15. The median DAS 28 score for RA patients was 5.12.

In 2020, it was revealed that 45.5% of the cases had demonstrated active disease (moderate or high disease activity) based on DAS-28-CRP scores, while 54.5% were

in low disease activity or remission. The remission rates after 1 year had increased to 79.6% (345 patients), while 9.7% (42 patients) and 10.6% (46 patients) had low disease activity and moderate disease activity, respectively [10].

The *IL23R* gene is present on chromosome 1p31 and the rs11805303 variant results in the substitution of the C wild-type allele to the T allele in the sixth intron of the *IL23R* gene. Regarding the distribution of genotypes and alleles between the two groups, individuals with the CT genotype and TT genotype had a significantly higher association with RA than those with the CC genotype, with Odds ratios of 1.77 and 5.25, respectively. The dominant model analysis, which combines CT and TT genotypes, also showed a significantly higher association with RA for individuals with these genotypes, with Odds ratios of 3.48.

Similarly, the analysis using the recessive model showed a significantly higher association with RA for individuals with the TT genotype. The analysis of the alleles showed that the T allele was associated with a significantly higher association with RA, with an Odds ratio of 3.38.

Similarly, in the study done in 2022 it was found that the genotypes with rs11805303 (TT), polymorphisms in the IL-23R gene were seen more often in RA patients than healthy controls which agreed with our results [4].

The current study revealed significant differences in ESR levels and CRP titter between the IL-23R (rs11805303) genotype groups. Specifically, individuals with the CC genotype had significantly higher ESR and CRP levels compared to those with the TT or CT genotype.

Similarly, Soysal et al., 2022 showed that CC genotype showed the highest level regarding ESR and CRP, when compared to CT and TT genotypes [4].

The current study revealed a significant difference in RF and anti CCP levels between the IL-23R (rs11805303) genotype groups. Specifically, individuals with the CC genotype had significantly higher RF levels compared to those with the TT or CT genotype. Conversely, the individuals with the TT genotype had significantly higher anti-CCP levels compared to those with the CC or CT genotype. The median anti-CCP in the TT genotype (370 U/L) was significantly higher compared to those with the CC (70 U/L) or CT genotype (210 U/L).

These findings were in agreement with other researchers in 2022, as they found that among RA patients, the highest titre of RF was associated with rs11805303 CC genotype, while the highest titre of anti CCP was associated with rs11805303 TT genotype. However, the findings were not statistically significant [4].

The current study found a significant association between IL-23R (rs11805303) genotype groups and the DAS 28 score. All patients in the CC genotype group had a high DAS 28 score. DAS 28 scores were moderate in 58.3% of the CT genotype group and high in 41.7%. In the TT genotype group, 33.3% had a low DAS 28 score and 66.7% had a moderate DAS 28 score. Higher DAS score differed significantly according to IL23R polymorphism, with highest score was attributed to those carrying CC genotype, followed by those carrying CT genotype, and lastly those carrying TT genotype. In agreement with other studies who found that RA patients with the CC genotype rs11805303 gene had more active disease scores [4].

Logistic regression analysis was conducted for the prediction of susceptibility to RA. IL23R CT and TT genotypes were significantly associated with susceptibility to RA. Similarly, in a recent study 2022, it was found that rs11805303 T allele increases the association with RA with a statistical significance when compared with healthy controls [4]

The rs11805303 SNP was thoroughly investigated in many diseases. The rs11805303 C allele was more frequent in

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patients with papulopustular lesions of Behçet disease [12].

Others found that the rs11805303 CC genotype and C allele of IL-23R were related to pulmonary TB(PTB). They suggested that IL-23R rs11805303 TT polymorphisms were associated with a decreased exposure to PTB in Chinese population [13].

On the other hand, T allele of the IL23R rs11805303 was found to be associated with cutaneous leishmaniasis (CL). Researchers identified the IL23R variant rs11805303 as a greater association to developing CL and provided a possible lead in the molecular involvement of the IL-23/IL-17 axis in the immunopathogenesis of the disease [11].

In addition, the T allele frequencies of rs11805303 were significantly higher among cerebral palsy patients and controls in Han Chinese. The inflammatory response and cytokine cascade are likely to play a role in the occurrence and development of CP [14].

Moreover, other studies confirmed the association of rs11805303 TT polymorphisms with ulcerative colitis [15, 16]

A significant increase in the carriage of the T allele of rs11805303 in the ankylosing spondylitis group compared with the controls in a Hungarian population, was observed [17].

IL-23R genetic variant in patients with RA was investigated and proved that the rs10489629 and rs7517847 polymorphisms of the IL-23R gene were of greater association for the development of RA in a European population[16].

IL23R gene SNPs including rs11209026, rs2201841, and rs10889677 were analyzed in Egyptian RA patients, and found the AA genotype variant of rs11209026 as a culprit factor in RA etiology, whereas others were not associated[18].

In a study done in 2019 revealed that genetic variations in the IL-23R could change the susceptibility to RA with the cytokine axis. The A allele in the IL23R gene rs1343151 SNP was related to higher association with RA while the C allele of the IL23R gene rs2201841 SNP significantly decreased the association with the disease[19].

It was showed that Identification of certain IL-23R genotypes conferring a predilection for RA not only elucidates the role of IL-23 in disease pathogenesis, but also indicates certain therapeutic managements as well. IL-23 antagonists available as monoclonal antibodies target cytokines and effectively attenuate IL-23-mediated diseases such as Crohn disease, psoriasis and sarcoidosis. Thus, IL-23 targeting monoclonal antibodies might offer enhanced anti-inflammatory effects in RA management[20].

Many researches have reported that some single nucleotide polymorphisms (SNPs) are related to the therapeutic response of several monoclonal antibody drugs including adalimumab, infliximab, rituximab, and tocilizumab, which target tumour necrosis factor (TNF), CD20 of B-cells, and interleukin (IL)-6. Biological therapies are now prescribed on a “trial and error” basis for RA patients. If appropriate drug treatment is not started early, long-term treatment outcomes may worsen and joint may deformed. Pharmacogenomic approaches that predict therapeutic responses for RA patients have the potential to significantly improve patient quality of life and reduce treatment costs[21].

The new therapy focuses on treatment of RA based on gene therapy, which is active only when the joint gets inflamed. It will prevent side effects of systemic application of drugs. Furthermore, the benefits of this treatment for the patient from a socio-economic perspective has been discussed, focusing on the quality of life of the patent and lower costs for the society[22].

To the best of our knowledge, this study is the first one that investigates the relationship between IL-23R rs11805303 gene polymorphism with acute phase

reactants, and DAS-28 in Egyptian population.

Limitations of the present study included the small sample size and that, no more studies were previously conducted on IL23 (rs11805303) genotype specifically.

Conclusions

Our findings suggest that IL-23R rs11805303 TT gene polymorphisms are seen more frequently in RA patients than healthy controls. Additionally, greater levels of anti-CCP are associated with the TT genotype, but higher levels of acute phase reactants and disease activity scores are associated with the CC genotype.

Conflict of interest:

None of the contributors decline any conflict of interest.

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