ORIGINAL ARTICLE

Association of Family history with clinical presentation of rheumatoid arthritis patients in Saudi Arabia: A cross sectional study

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ABSTRACT

Objective: Rheumatoid arthritis (RA) is a chronic inflammatory, a multisystem disease characterized by progressive, irreversible joint and bone destruction leading to disability, loss of function, significant morbidity, and premature mortality. Family history of rheumatoid arthritis is a strong influence for RA. The aim of the study was to determine the relationship between family history and personality traits of patients with RA.

Methods: This cross-sectional observational study was carried out on 60 Saudi patients with newly or previously diagnosed RA according to the 2010 American College of Rheumatology‑European League Against Rheumatism Criteria.. They all were followed from the month of January 2017 to December 2020 in the Rheumatology Clinic of King Majmaah Hospital (KKMH).

Results: The mean age of the patients was 47.87 ± 11.55 years. The preponderance of all them included female 52 vs.8; female: male ratio, 6.5:1; 23.3% of the patients had a family history of RA. The incidence rates of extra-articular manifestations of RA and joint deformities were 18(30%) and 8 (13.3), respectively. The DAS28 score for 37 patients (61.7%) was between 3.2 and 5.1, and 23 patients (38.3%) had a score >5.1. Further, 66.7% and 78.3% of the patients were affirmative for rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) correspondingly.

Conclusion: Positive family history was more common among rural RA patients than among other RA populations. No significant association was observed between family history and characteristic features of the studied groups.

Keywords: Rheumatoid arthritis, Family history, Characteristics features, Saudi patients

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory, a multisystem disease characterized by progressive, irreversible joint and bone destruction leading to disability, loss of function, significant morbidity, and premature mortality (1, 2). The etiology of the ailment is unknown, but ranges from 0.5% to 1% in the general population, higher in women than men [3].

The familial clustering of RA suggests the fact that family members of patients with RA are more likely to have the disease due to genes and environmental factors that are common in families (4); so, family history should be considered regularly as part of the clinical work of patients with arthritis. One study reported that the family history of first-degree families with one or more RAs increased the risk of RA by about 3-fold [5].

Several studies have demonstrated that genetic components have an impact on an individual's susceptibility to developing RA (6), such as twin studies suggesting that RA is approximately 65% heritable (7). In addition, changes in the environment and lifestyle can affect conditions, including occupational airborne particles (8), smoking (9), and diet (10-12), thereby increasing the risk of RA. Links between gender and environmental risk factors may augment the risk of RA [13] and therefore augment to the familial aggregation of RA (14).

There is little data available on familial clustering among patients with RA in Saudi Arabia (SA). To the best of our acquaintance, no preceding study has examined the family history and characteristics of Saudi rural communities affected by RA. Therefore, the purpose of this study was to determine on the relationship between family history and characteristic features of patients with RA among the rural population of Majmaah province who visited Rheumatology Clinic of King Khalid Majmaah Hospital (KKMH).

MATERIALS AND METHODS

This observational cross sectional study was carried out among Saudi patients with RA.They were newly or previously diagnosed with RA and were examined in the Rheumatology Clinic at KKMH from January 2017 to December 2020. The study identified sixty percent of RA patients according to the 2010 American College of Rheumatology /European League Against Rheumatism Diagnostic Criteria [15]. The study was approved by the central assessment body of the Ministry of Health ,Saudi Arabia.

The patient's demographic characteristics and presence of extra-articular manifestations of RA (ExRA) and of joint deformities were evaluated using medical records. Family history was considered positive if at least one first-degree relative was diagnosed with RA. Laboratory blood tests, including rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) levels, were routinely performed on admission to the clinic.

In the study, patients with the DAS28 disease assessment scale (ESR specification) were assessed as follows: remission, DAS28 ≤2.6; low disease activity, 2.6 <DAS28 ≤3.2; moderate disease activity, 3.2 <DAS28 ≤5.1; and high disease activity, DAS28 >5.1.

The characteristic features of the patients with RA were statistically analyzed using IBM SPSS version 26 (IBM Corp., Armonk, NY, USA). Age was defined as mean ± SD. Pearson's chi-square and Fisher's exact tests were

used to observing associations between various study parameters. Statistical significance was set at $p < 0.05$.

RESULTS

This study included 52 women as well as 8 men who visited KKMH. The mean age of the patients was 47.87 ± 11.55 years, and the female-to-male ratio was 6.5:1; 14 patients (23.3%)had a family history of RA. The incidence rates of presence of ExRA and joint deformities were 18(30%) and 8 (13.3%), respectively. The DAS28 scores of 37 patients (61.7%) were between 3.2 and 5.1, and 23 patients (38.3%) had scores>5.1. Further, 40 (66.7%) patients were positive for RF, and 47 (78.3%), for anti-CCP antibodies. Table1 presents the clinical distinctiveness of the patients.

The Table 2 presents a comparison of various factors such as sex, ExRA, joint deformities, DAS28 score, and RF and anti-CCP status in the two RA groups (with and without a family history). We did not observe any significant differences between them.

Table 1: Characteristic features of rheumatoid arthritis population (N =60)

Parameter	n (%)
Mean age (years)	47.87 ± 11.55
Sex Female Male Female: Male ratio	 52 (86.7) 8 (13.3) 6.5:1
Family history of RA No Yes	 46 (76.7) 14 (23.3)
Extra-articular manifestation No Yes	 42(70) 18(30)
Joint deformities No Yes	 52 (86.7) 8 (13.3)
DAS-28 (%) Remission ≤2.6 Low 2.6 and ≤3.2 Moderate 3.2 and ≤5.1 High >5.1	 0 (0.0) 0 (0.0) 37 (61.7) 23 (38.3)
Rheumatoid factor (RF) Positive Negative	 40 (66.7) 20 (33.3)
Anti-cyclic citrullinated peptide (Anti-CCP) Positive Negative	 47(78.3) 13(21.7)

Table 2: Association between family history and characteristics features of patients with RA

Associations		Family history of RA patients		
Items	Overall N=60 (%)	Yes n=14(23.3)	No n=46(76.7)	p-value
Sex Female Male	 52 (86.7) 8 (13.3)	 12 (85.7) 2 (14.3)	 40(87) 6 (13)	0.904
Extra-articular manifestation No Yes	 42(70) (30)**18**	 10 (71.4) (28.6)**4**	 32 (69.6) **)**30.4**(**14	0.894
Joint deformities No Yes	 52 (86.7) 8 (13.3)	 13 (92.9) 1(7.1)	 39 (84.8) 7(15.2)	0.436
DAS-28 (%) ≤2.6 2.6 and ≤3.2 3.2 and ≤5.1 >5.1	 0 (0.0) 0 (0.0) 37 (61.7) 23 (38.3)	 0 (0.0) 0 (0.0) 12 (85.7) 2 (14.3)	 0 (0.0) 0 (0.0) 25 (54.3) 21 (45.7)	0.215
Rheumatoid factor (RF) Positive Negative	 40 (66.7) 20 (33.3)	 8(57.1) 6 (42.9)	 32(70) 14(30)	0.387
Anti-cyclic citrullinated peptide (Anti-CCP) Positive Negative	 47(78.3) 13(21.7)	 12 (85.7) 2 (14.3)	 35(76) 11(24)	0.443

DISCUSSION

We conducted this observational cross-sectional work to evaluate the connection between family history as well as characteristic features of RA patients who visited the rheumatology clinic at KKMH.

The outcome of this work displayed a considerably higher prevalence of Rheumatoid arthritis among women than men (female-to-male ratio, 6.5:1). The mean age of the patients was 47.87 ± 11.55 years. The findings are in concord with previously published reports (16, 17).

A genetic component has been implicated in RA patients (18–19) and may explain the high prevalence of a family history of rheumatic diseases (20). Although the exact mode of inheritance is still unknown, it has been proven that the likelihood of genetic heritability is close to 60% (21). The prevalence of RA among Caucasian populations is around 1% (22), and the incidence rate among women is 2–3-fold higher than that among men (23). Traditional marriage, especially between relatives, may promote the transmission of potential genes (20).

Multiple histocompatibility complex (MHC) class II genes role has been investigated and the several studies

has shown an association between RA and HLA-DR4 and HLA-DR1 [24,25]. One study examined the interaction of HLA-DRB1 in patients with Saudi RA and concluded that DRB1 * 04 and DRB1 * 08 are predictors of RA susceptibility, whereas DRB1 *06 could have a protective effect in Saudis (17).

However, few studies have examined the family history of RA in the Saudi patient population. Our results showed that approximately one-quarter of the patients reported at least one first-degree relative affected by Rheumatoid arthritis. ExRA is all the conditions and symptoms that are not directly related to the locomotor system (26) and can involve other systems, such as heart, respiratory problems, kidneys, hematology, skin, eyes, kidneys, nerves and gastrointestinal tract. It occurs either in the beginning or at the time of the disease (27); Thirty percent of our patients had ExRA, which is in agreement with the numbers in other reports (28).

The deformities in hand is considered as a significant characteristic of RA, and differet types can occur simultaneously [29]. Deformities, painful joints and weakness in the grip can affect the functioning of everyday life and, ultimately, the inability to perform daily activities. [30]. It may too augment to the psychiatric ailments like distress or depression (31).This study included 13.3% patients with RA had hand deformities, inconsistent with the results of Pia, i.e., 59% (32).

The DAS28 score is a measure of disease activity in RA, which includes an asymptomatic evaluation of the patients, physical examination, and blood work. It is mainly used in treat-to-target strategies to assess the ailment action level and degree of reaction to management (33). Our results demonstrated around 60% of Rheumatoid arthritis suffered with moderate disease activity. The results were comparable to those of another study performed by Attar et al. (34)

At present, laboratory investigations like RF and anti-CCP status are significant in the identification of Rheumatoid arthritis. Though it has high sensitivity, the specificity of RF status is comparatively low for the reason that 50% of seropositivity is found in patients with other medical conditions such as connective tissue diseases and infectious diseases and in older individuals (35). In our study, 66.7% of the patients were positive for RF, analogous to the findings reported by Smolen (36).

Anti-CCP is one of the latest parameter for diagnosing RA. Specificity and sensitivity are assumed to be 98% and 68% respectively. Cheng et al. For example, drug therapy against CCP in RC patients is associated with bone loss, dysfunction, chronic disease, and functional impairment (38). In the current work, the anti-CCP antibody was detected in 47(78.3%) patients, consistent with the findings of Siheme (79.7%) (39).

Family aggregation is of clinical significance because it is commonly encountered in reviewing the family history of RA and is also useful for understanding the genetic link of the disease [40]. However, another study reported that combined data on family history with established environmental and genetic RA risk factors showed no part of the familial aggregation was explained by various non-genetic risk factors (4). In addition, a scientific review found no significant differences in clinical characteristics (seropositive serology in onset) between family and family RA. (41).

We compared the various clinical characteristics (sex, ExRA, joint deformities, and DAS28 score) of two RA groups, i.e., with and without a family history. No statistically significant differences between them were observed. These findings are consistent with those of Frisellet al. (41).

Two-thirds of patients with RA work specifically for RF or anti-CCP [4]. Clinical studies showed differences and similarities in the genetic risk factors for patients who are seropositive and seronegative for RA (42). In the middle of the last century, studies have reported stronger family reunification in seropositive sufferers than in seropositive patients. However, there are some reports that exhibit stronger family aggregation in patients.(43). The associations between RF, anti-CCP, and the presence or absence of family history among RA patients were compared in the study and no significant relationship was observed between serological status and family history. These findings are inconsistent with those of other studies (4).

Based on our findings, family history is one of the strongest risk factors for developing RA, may predict the disease course, and is an integral part of the workup and diagnosis of RA. However, in future studies, the number of investigated patients must be increased to confirm our findings and to accurately represent the entire population.

CONCLUSION

Positive family history was more common among rural RA patients than among other RA populations. However, the present work did not find any noteworthy correlation between family history and personality traits of the studied groups. Further studies with a large number of patients are needed to validate our findings**.**

Conflict of interest: The authors declare no conflicts of interest.

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