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RESEARCH ARTICLE

EPIDEMIOLOGICAL AND SEROLOGICAL STUDIES ON RHEUMATOID ARTHRITIS

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ABSTRACT

Back ground: Rheumatoid Arthritis (RA) is an inflammatory, autoimmune disease that causes pain, joint stiffness especially in the morning and loss of function. Although there are many forms of arthritis, of those commonly known, rheumatoid arthritis is the most serious and the second most common (after osteoarthritis). It can occur at any age but is more common in persons over the age of 30 years and affects women more often than men. It currently effects about 1-2% people worldwide. In India the prevalence of RA is approximately 0.75 - 1%. Very few studies have been focused on risk factors of RA in Andhra Pradesh therefore the aim of the present study was to find out the genetic and non-genetic factors responsible for the occurrence of rheumatoid arthritis in Andhra Pradesh.

Methods: The study includes 125 RA patients and 110 normal age and sex matched individuals as controls from Eluru, West Godavari district. The epidemiological data was taken from the study and control groups in a pre-designed questionnaire and analyzed by online free calculator (quantpsy.org.).

Results: In the present study age, gender, occupation, economic status, area of living, food habits, smoking, tobacco chewing, alcohol consumption, family history, height and weight shows association with RA, whereas community, religion, education, age of onset, symptoms, other abnormalities, treatment type, Body Mass Index (BMI), physical condition, ABO blood groups and Rh blood groups does not shows any association with RA.

Conclusions: To conclude with, the results of the present study were in agreement with the literature in the field.

INTRODUCTION

Rheumatoid Arthritis (RA) is an inflammatory, autoimmune disease that causes pain, joint stiffness especially in the morning and loss of function. Although there are many forms of arthritis, of those commonly known, rheumatoid arthritis is the most serious and the second most common (after osteoarthritis). It can occur at any age but is more common in persons over the age of 30 years and affects women more often than men. Classification criteria for RA was first proposed by the American Rheumatism Association (ARA) in 1958 (Ropes *et al*., 1958). The 1958 ARA criteria was revised in 1987 by the American College of Rheumatology (ACR) **(**Arnett *et al*., 1988). This criteria has also been modified for use in population studies (Symmons *et al*., 2002).The 2010 criteria emerged as a joint initiative of America and European workers and were published simultaneously in the ACR and EULAR journals. It affects 0.5-1% of population all over the world (Lawrence *et al*., 1998). The estimated prevalence of RA in developing countries is variable.

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Studies from Nigeria, (Silman *et al*., 1993) Indonesia (Darmawan *et al*., 1992) and Africa (Brighton *et al*., 1988) showed lower prevalence than that reported from the western countries, while the prevalence of RA in India (0.75%) (Malaviya *et al.*, 1993) is similar to that reported in white population from Manchester (0.8%) (MacGregor *et al*., 1994). In the urban population of Southern Pakistan, Karachi, the prevalence of RA is reported to be 0.14%, (Hameed *et al.,* 1995), whereas in Northern Pakistan the estimated prevalence is 0.55% (Farooqi and Gibson, 1998). Although rheumatoid arthritis is regarded as an autoimmune disease, details of its pathogenesis remain unclear. It is probably a multifactorial disease which occurs when several risk factors occur simultaneously. Rheumatoid Arthritis is a systemic disease, meaning that many parts of the body are affected. The disease can affect the skin, eyes, nerves and mouth. In more severe cases rheumatoid arthritis affects the lungs, heart and blood. Symptoms of the disease first being in the small joints of the fingers, wrist, feet, with warm, swollen, and tender joints that are painful and difficult to move. There is often stiffness in the morning that lasts for several hours or more. There is no single test for diagnosing rheumatoid arthritis. The disease is difficult to diagnose with certainty in its early stages because symptoms

vary considerably and overlap with other forms of arthritis. (The symptoms of pain and stiffness, often with fatigue also occur with some other forms of arthritis). Diagnosis is generally based on clinical assessment, laboratory tests and X-rays. Treatment of RA includes medication, education and self – management, physical therapy, surgical support, health-care services and other support. Very few studies have been focused on risk factors of rheumatoid arthritis in Andhra Pradesh, therefore the main objective of the present study isto assess the epidemiological profile of the rheumatoid arthritis patients that contributes to the onset of the disease and to evaluate the correlation between Body Mass Index (BMI) with occurrence of the disease.

MATERIALS AND METHODS

The present study was carried out with 125 rheumatoid arthritis patients (33 males and 92 females) and 110 non-rheumatoid arthritis individuals (46 males and 64 females) as controls with age above 27 years during the period April 2014 – October 2014from general hospital in Eluru, West Godavari district. The personal information regarding Age, Sex, Community, Religion, Education, Occupation, Economic status, Area of living (rural or urban), Food habits, Smoking habit, Alcohol habit, Age of onset, Symptoms, Other disease association, Treatment, Height, Weight, BMI, Physical condition and Blood groups, were obtained in a pre-designed questionnaire at the time of interview. The data was analyzed by online free calculator (quantpsy.org.).

RESULTS

The age of disease onset presents a peak in the fifth decade of life according to the majority of epidemiological studies. Some more recent studies suggest a later onset of the disease, (Riise *et al*., 20001; Gabriel *et al*., 1999; Aho *et al.,* 1998; Drosos*et al.,* 1997; Symmons *et al*., 1994; Doran *et al*., 2002; Soderlin *et al.,* 2002; Guillemin *et al*., 1994). Table 1 represents the distribution of screened cases with respect to biological and behavioral characteristics along with relative risk and 95%CI. The odds ratio p-value is statistically significant with age, gender and education of RA and non-RA people. Age, gender and education shows association with RA as highly significant chi-square p-value was obtained. Socioeconomic factors appear to influence the course and the outcome of RA rather than the risk of developing RA. Occupation, educational level, marital status, and social group have been studied as possible risk factors for disease susceptibility, or predictors for disease severity and outcome. The results of these studies are conflicting mainly as concerning the impact of socioeconomic factors on the risk of developing RA. However, the data available suggest an association of adverse socioeconomic status with worse prognosis of the disease (MacGregor and Silman , 2003; Silman and Hochberg, 2001). The odds ratio p-value is statistically significant with occupation, economic status, area of living and food habits of RA and non-RA people. Highly significant chi-square p-value shows association of RAwith occupation, economic status, area of living and food habits. Smoking is likely to influence both the risk of developing RA and the course of the disease. The increased risk of RA associated with smoking has been suggested in cross-sectional as well as in longitudinal studies.

Table 1. Distribution of screened cases with respect to biological and behavioral characteristics along with relative risk and 95%CI

Variables	RA 125 (%)	Non-RA 110 (%)	Chi-Square value	P-value	Relative risk 95% CI
Age Group			12.923	0.000**	0.000**
≤ 45	32 (25.6%)	52 (47.2%)			(0.2137-0.6407)
>45	93 (74.4%)	57 (51.8%)			
Gender			6.233	0.012*	0.013*
Male	33(26.4%)	46 (41.8%)			0.288-0.864
Female	92 (73.6%)	64 (58.1%)			
Education			4.123	0.042*	0.042*
≤Primary	70 (56%)	47 (42.7%)			(1.017-2.8614)
>Primary	55 (44%)	63 (57.2%)			
Type of occupation			4.699	0.030*	0.031*
Sedentary	38 (30.4%)	20 (18.1%)			(1.0611-3.6408)
Active	87 (69.6%)	90 (81.8%)			
Economic status					0.016*
Below average	100(75.2%)	64 (56.1%)			(1.181-5.394)
Average	13 (10.4%)	21 (19.1%)	13.45	0.001**	
Above average	12 (0.96%)	25 (22.7%)			0.002**
					(1.527-6.936)
Area of living			3.85	0.049*	0.050*
Urban	66(52.8%)	44 (40%)			(0.999-2.818)
Rural	59 (47.2%)	66 (60%)			
Food habits			5.399	0.020*	0.047*
Veg	16 (12.8%)	27 (24.5%)			(1.007-2.939)
Non-veg	109 (87.2%)	83 (75.4%)			
Smoking status			7.903	0.004**	0.006*
Users	33 (26.4%)	13 (11.8%)			(0.185-0.754)
Non-users	92 (73.6%)	97 (88.1%)			
Tobacco chewing			12.077	0.000**	0.001*
Users	30(24.1%)	8 (0.72%)			(0.108-0.568)
Non-Users	95 (76.1%)	102 (43.4%)			
Alcohol consumption			4.75	0.029*	0.031*
Users	34(27.2%)	17 (15.4%)			(0.255-1.937)
Non-users	91 (72.85)	93 (84.55)			
Family history			5.6	0.017*	0.021*
Positive	7 (21.2%)	41 (44.5%)			(1.177-7.570)
Negative	26 (78.7%)	51 (55.4%)			

The association appears to be dose-dependent, and is most clear for heavy smokers. The severity and outcome of RA appears also to be influenced by smoking, although it is not clear which clinical characteristics of the disease are related to smoking. An increased risk for seropositive disease is related to smoking habits (Wilson and Goldsmith, 1999; Harrison, 2002). The odds ratio p-value shows statistically significant result with smoking, chewing and alcohol consumption of RA and non-RA people. Highly significant chi-square p-value shows association of RA with smoking, chewing and alcohol consumption. A family history of rheumatoid arthritis has been shown to be a risk factor for developing the disease in a number of studies. Recent research suggests that a positive family history in first degree family relatives is strongly linked to the early appearance of significant radiographic (x-ray) joint damage (Rojas-Villarraga *et al*., 2009). The condition is strongly associated with the inherited tissue type Major Histocompatibility Complex (MHC) antigen HLA-DR4 (most specifically DR0401 and 0404).

The odds ratio p-value is statistically significant with family history of RA. Significant chi square p-value shows association between RA and family history. In most large-scale studies, obesity is estimated from body mass index (BMI; [kg]/height [m²]). BMI may not accurately reflect the amount of body fat in persons with RA (Stavropoulos-Kalinoglou *et al.,* 2007; Elkan *et al.,* 2009), however, because rheumatoid cachexia may occur with little or no weight loss; therefore an individual may have a BMI within a normal range, but may have greater fat mass than suggested by the BMI.

Table 2 demonstrates the distribution of RA people according to Body Mass Index (BMI). The odds ratio p- value and chi-square p-value shows insignificant results with RA and BMI.

Table 3 displays the distribution of RA and non- RA people according to Body Mass Index (BMI). The odds ratio p- value and chi-square p-value shows insignificant results with body mass index of RA and non- RA people.

Table 4 shows the distribution of RA and non- RA people according to ABO blood Groups. The odds ratio p-value and chi-square p-value shows insignificant results with RA and ABO blood groups.

Table 5 represents the distribution of RA and non- RA people according to Rh blood Groups**.** Theodds ratio p-value and chi-square p-value shows insignificant results with Rh blood groups of RA and non-RA people.

DISCUSSION

The age of onset of RA is most frequent during fourth and sixth decade of life, according to the majority of epidemiological studies. The mean age found in this study does not coincide with other studies of Syed *et al*., 2011, and Juliano *et al*., 2013,which shows increased mean age.This study shows significant association with RA regarding age and gender unlike the study of Ausaff Ahmed *et al*., 2014. In present study the odds ratio p-value is statistically significant with gender of RA and chi-square p-value shows association with gender of RA. RA is far more common in women than in men. The present study also follows the same trend which correlates with the studies of Goronzy*et al*., 1997;Kalpana *et al.,* 2009; Syed *et al*., 2011, whereas Hameed *et al*., 1995reported equal male to female ratio. In the present study education has not exhibits significant association with RA, unlike occupation which shows association with RA. In the studies of Olsson *et al*., 2004 and Ausaf Ahmed *et al*., 2014 reported that an association between type of occupation and the risk of developing RA has not been confirmed.

Table 2. Distribution of RA people according to Body Mass Index (BMI)

BMI Category	Male n=33 (%)	Female n=92 (%)	Total n=235 (%)	Odds Ratio	95% CI	P Value
Healthy weight	8 (24.2%)	20 (21.7%)	28 (22.4%)	1	---	--
Under weight	1 (03.0%)	-	1(8.0%)	0.138	0.005 – 3.743	0.239 NS
Over weight	21 (63.6%)	54 (58.6%)	75 (60.1%)	1.028	0.392 – 2.693	0.954 NS
Obese	3 (09.0%)	18 (19.5%)	21 (16.8%)	2.400	0.550 – 10.457	0.243 NS
Mean	8.25	23				
SD	8.995	22.538				
Chi-Square – (4.541), df – (3),P- Value – (0.208 NS)						
**P≤0.01 – Highly Significant; *P≤0.05 – Significant; NS – Not Significant						

**P≤0.01 – Highly Significant; *P≤0.05 – Significant; NS – Not Significant

Table 3. Distribution of RA and non- RA people according to Body Mass Index (BMI)

BMI Category	RA n=125 (%)	Non-RA n=110 (%)	Total n=235 (%)	Odds Ratio	95% CI	P Value
Healthy weight	28 (22.4%)	33 (30.1%)	61 (25.9%)	1	---	--
Under weight	1 (8.0%)	5 (0.45%)	6 (0.25%)	4.242	0.467 – 38.493	0.199 NS
Over weight	75 (60.1%)	56 (50.9%)	131 (55.7%)	0.633	0.343 – 1.167	0.143 NS
Obese	21 (16.8%)	16 (14.5%)	37 (15.7%)	0.646	0.284 – 1.471	0.298 NS
Mean	31.25	27.5				
SD	31.330	22.218				
Chi-Square – (5.573), df – (3),P- Value – (0.134 NS)						

**P≤0.01 – Highly Significant; *P≤0.05 – Significant; NS – Not Significant

Table 4. Distribution of RA and non- RA people according to ABO blood Groups

Blood groups	RA n=125 (%)	Non-RA n=110 (%)	Total n=235 (%)	Odds Ratio	95% CI	P Value
A	26 (20.8%)	23 (20.9%)	49 (20.8%)	1	---	----
B	30 (24.1%)	26 (23.6%)	56 (23.8%)	0.979	0.454 – 2.112	0.958 NS
AB	28 (22.4%)	32 (29.2%)	50 (21.2%)	1.291	0.606 – 2.752	0.506 NS
O	41 (32.8%)	39 (35.4%)	80 (34.1%)	1.075	0.527 – 2.191	0.841 NS
Chi-Square -- (0.684), df – (3), P- Value -- (0.876NS)						

**P≤0.01 – Highly Significant; *P≤0.05 – Significant; NS – Not Significant

Table 5. Distribution of RA and non- RA people according to Rh blood Groups

Rh Blood group	RA n=125 (%)	Non-RA n=110 (%)	Total n=235 (%)	Odds Ratio	95% CI	P Value
Rh+	102 (81.6 %)	95 (86.3%)	197 (83.8%)	1	-	-
Rh-	23 (18.4%)	15 (13.6%)	38 (16.1%)	0.700	0.345 – 1.421	0.323NS
Chi-Square -- (0.979), df – (5), P- Value -- (0.322NS)						

**P≤0.01 – Highly Significant; *P≤0.05 – Significant; NS – Not Significant

There are conflicting reports as to whether formal education is associated with the incidence and prevalence of rheumatoid arthritis (Vliet Vlieland *et al*., 1994). An association between type of occupation and the risk of developing rheumatoid arthritis has not been confirmed. There is some evidence of an association between organic dust exposure and the incidence of rheumatoid arthritis in men (Olsson *et al.,* 2004). Socioeconomic factors affect the course and outcome of RA but do not seem to influence the risk of developing RA. In the present study the economic status shows association with RA. There are conflicting reports that socio-economic level is associated with the development of rheumatoid arthritis, however, the condition is more prevalent among lower socio-economic groups (Jacobi *et al*., 2003). Low socio-economic status has been linked with the progression of the disease (Symmons, 2003; Bankhead *et al.,* 1996). Most of the studies conclude that RA is more prevalent to the developed countries (Malaviya *et al*., 1993). RA is rare in undeveloped and rural areas (Symmons, 2002), and the incidence of RA is higher among groups residing in urban areas. As a result, urbanization and air quality have been proposed as risk factors for the condition (Bankhead *et al*., 1996) although reports of such an association are conflicting (MacGregor *et al*., 1994; Lau *et al*., 1993). In the present study that RA cases of rural areas were higher than urban areas which correlates with the study of Ausaf Ahmed *et al*., 2014.

Food habits of the present study shows association with RA. Mediterranean diet as a whole has also been reported as a lifestyle factor reducing the risk of developing RA, and protecting against severe course of the disease. These observations could partly explain the geographical variations of the disease occurrence, and severity (Skoldstam *et al*., 2003; Cleland *et al.,* 2003). Among environmental factors, smoking has by far the strongest association with RA. Smoking increases susceptibility to RA and adversely affects the clinical course of the disease, as shown by cross sectional and longitudinal studies (Costenbader *et al*., 2008).

In the present study smoking and alcohol shows association with RA. Moderate consumption of alcohol has been shown to protect against the development of rheumatoid arthritis in women (Ollier *et al.,* 2001), although other reports demonstrate no association between alcohol consumption and the risk of rheumatoid arthritis (Cerhan *et al*., 2002). In the present study odds ratio p-value is statistically significant with family history. Significant chi-square p-value shows association between RA and family history. A family history of rheumatoid arthritis has been shown to be a risk factor for developing the disease in a number of studies. Recent research suggests that a positive family history in first degree family relatives is strongly linked to the early appearance of significant radiographic (x-ray) joint damage (Rojas-Villarraga *et al.,* 2009). The condition is strongly associated with the inherited tissue type Major Histocompatibility Complex (MHC) antigen HLA-DR4 (most specifically DR0401 and 0404).

In most large –scale studies, obesity is estimated from body mass index (BMI; weight [kg/ height [m^2]). BMI may not accurately reflect the amount of body fat in persons with RA (Stavropoulos *et al*., 2007; Elkan *et al.,* 2009),however, because rheumatoid cachexia may occur with little or no weight loss; therefore, an individual may have a BMI within a normal range, but may have greater fat mass than suggested by the BMI. In the present study the odds ratio p-value and chi-square p-value shows insignificant results with RA and body mass index.

Conclusions

In the present study age, gender, occupation, economic status, area of living, food habits, smoking, tobacco chewing, alcohol consumption, family history, height and weight shows association with RA, whereas community, religion, education, age of onset, symptoms, other abnormalities, treatment type, BMI, physical condition, ABO blood groups, Rh blood groups

does not shows any association with RA. There has been considerable recent interest in understanding the epidemiology of RA. There have been several population studies in many different countries around the world, and observations of differential occurrence (with time, between populations and between the gender) has stimulated a number of analytical studies looking for both genetic and environmental risk factors. Future studies will benefit from advances in molecular biology techniques to aid with the identification and characterization of potential new genes for RA susceptibility. These studies, as already described, have revealed some tantalizing clues that will require further follow-up in years to come.

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