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Gender Differential in the Prevalence of Rheumatoid Arthritis

Dr. Ausaf Ahmad, Prof T. B. Singh

Division of Biostatistics, Department of Community Medicine, IMS, BHU

Abstract: ***Background and Objectives: Rheumatoid Arthritis(RA) is an auto-immune disease in which body mistakenly considers some parts of its own system as pathogens and attacks them. Prevalence of approximately 0.75% in India. About 40% diseased become work disabled within 5 years from onset of symptoms. The objectives of this paper are (i) to find the positivity rate among clinically suspected cases and (ii) to find out the epidemiological risk factors for it. Method: The study is based on 290 clinically suspected RA patients. Cross-sectional study design was used. Clinically suspected cases were referred by different OPD's of Sir Sunderlal Hospital for screening. Blood samples were collected in plain vial from each patient and each sample were tested by the laboratory persons. Result: The overall prevalence of RA was observed 16.6% and aged upto 50 years and above 50 years prevalence was 15.4% , 20.6% respectively. The odds ratio was 1.426 with 95% CI(0.709-2.873) .The prevalence of this was 12.7% among male as compared to 18.9% in female where odds ratio was 1.597 with 95% CI(0.821-3.103). This prevalence among urban was 13.1% in comparison of 19.5% among rural. Conclusion: The finding of this study suggests that the proportion of diseased cases increased as age increases. Females are more prone for this disease as compared to male. The suspected cases having the family history had more chances to become diseased as compared to cases not having the family history of RA. This disease also affects the quality of life, disability increases.***

Keywords: epidemiological, cross-sectional, Rheumatoid arthritis

1. Introduction

The healthy human body is equipped with a powerful set of tools for resisting the onslaught of invading microorganisms (such as viruses, bacteria, and parasites). Unfortunately, this set of tools, known as the immune system, sometimes goes awry and attacks the body itself. These misdirected immune responses are referred to as autoimmunity.(National Institutes of Health,2012) In some cases, however, the cells of our immune system get out of control. They turn against the body itself and begin to destroy healthy tissue. This results in autoimmune disease Autoimmune diseases affect about five percent of people living in industrialized nations; over 80 of these "autoaggressive" diseases are now recognized.(sangha et al., 2000)

Rheumatoid Arthritis(RA) is an auto-immune disease in which body mistakenly considers some parts of its own system as pathogens and attacks them.(Li W et al.,2011) Epidemiological study of Rheumatoid Arthritis are dependent on the criteria used to define the disease.This is challenging, because no aetiological agent has been identified and there is no unique clinical or laboratory features that can be used to define the disease clearly.(Chronic diseases and health promotion,2011)The prevalence of rheumatoid arthritis (RA) varies between 0.3% and 1% worldwide and is more common in women and in developed countries.(Malaviya et al. 1993) Rheumatoid arthritis (RA) is a chronic systemic inflammatory illness with prevalence of approximately 0.75% in India.(Gabriel et al. 2003) It leads to irreversible joint damage and systemic complications. It is associated with substantial morbidity and increased mortality.(Gabriel et al. 1999.;Young et al. 2002) Patients with active RA suffer from significant decline in functional capacity. As many as 40% become work disabled within 5 years from onset of symptoms.(Aggarwal et al., 2006) Direct and indirect costs are also enormous.(Woolf A.et al., 2007)

RA affects everyone differently. Patients may find that their symptoms come and go with little pain, swelling or inflammation. Flare-ups can last for a few days to a couple of months. They probably won't be able to predict when they'll occur.

Rheumatoid arthritis, are the number one cause of early retirement, disability payments, and loss of employment.(Bräuer W, et al., 2002) The social and economic consequences for the individual are drastic even in the first years of the disease. Within seven years, up to 40 percent of patients are no longer able to work in their profession. (The Burden of Musculoskeletal Conditions at the start of the Millenium, 2003) According to the WHO, this percentage rises significantly as rheumatoid arthritis progresses: ten years after onset of the disease, nearly 60 percent of RA patients are no longer able to work.(Hemminki et al2009)

It is now accepted that those affected by these diseases must be genetically predisposed toward them. Many autoimmune diseases occur more frequently within families, and in some families there is an increased tendency toward autoimmune diseases.(Padyukov et al., 2004.) For some autoimmune diseases, such as rheumatoid arthritis and multiple sclerosis, the genetic component of the disease has already been scientifically verified.(Hafler et al., 2007; D'Netto et al., 2009; Padyukov et al 2004) In addition, environmental factors like eating habits and lifestyle always contribute to this predisposition to promote the development of an autoimmune disease. This means that not every "genetically burdened" individual is certain to become ill. As well as predisposition, there is generally a trigger. For example, smoking increases the risk of developing rheumatoid arthritis when there is a familial predisposition toward the disease.(Baron,1984) In addition, Cigarette smoking is known to influence oestrogen related conditions such as osteoporosis, onset of menopause, and oestrogen dependent

malignancies.(S Daniell,1976; Baron et al.,1986; Wing et al.,2006)Autoimmune disease causes the body to lose its capacity for immune tolerance, which makes it possible for a healthy body to differentiate between "foreign" substances and the body itself. Clearly, in these diseases the autoreactive cells, which are always also found in healthy individuals, are excessively activated. Or they escape from the control of the immune system.(Fehervari et al.,2007; . Vessey et al.,1987) Finally, scientists have hypothesized that pathogens may be the culprits that lead the immune system astray. The objectives of this paper are (i) to find the positivity rate among clinically suspected cases and (ii) to find out the epidemiological risk factors for it.

2. Materials and Methods

The present study is based on prospective cross-sectional cohort study design. In the present study 290 (110 male and 180 female) clinically suspected of rheumatoid arthritis patient were studied. Who were screened at UGC Advanced Immunodiagnostic Training and Research Centre, Department of Pathology, IMS, BHU, Varanasi, U.P. The cases were referred by different OPD's of Sir Sunderlal Hospital. Mostly screened subjects were from eastern Uttar Pradesh, western Bihar, Madhya Pradesh and Jharkhand. About 2-ml of blood samples were collected in plain vial from each patient and each sample were tested for diagnostic tests RF, CRP and AntiCCP by using RF-Latex, CRP Latex and ELISA method respectively by the laboratory person. The patients for rheumatoid arthritis were diagnosed according to –'The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis' Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of _6/10 is needed for classification of a patient as having definite RA)

	Score
A. Joint involvement	
1. Large joint.	0
2. 10 large joints	1
1_3 small joints (with or without involvement of large joints)	2
4_10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)	5
B. Serology (at least 1 test result is needed for classification)	
Negative RF *and* negative ACPA	0
Low-positive RF *or* low-positive ACPA	2
High-positive RF *or* high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)	
Normal CRP *and* normal ESR	0
Abnormal CRP *or* abnormal ESR	1
D. Duration of symptoms	
<6 weeks	0
≥6 weeks	1

*ACPA(anti-citrullinated protein antibodies) ,** ESR(erythrocyte sedimentation rate)

3. Statistical Analysis

Initially data of rural subjects has been presented in number and percentage and then data were cross- tabulated as male versus female and comparison with the age groups, food habit, type of occupation, family history, place of residence, education etc. Compute the prevalence of RA in rural and urban areas separately . Find out the association between different risk behaviour factors and positivity status. Also find out the chi-square and relative risk with 95% confidence interval. For the purpose of analysis SPSS version 16.0 was used.

4. Result and Discussion

Rheumatoid arthritis is believed to be associated with a family history of the disease and exposure to an environmental trigger, although the exact cause is unknown. A number of risk factors and determinants may contribute to the development and/or progression of rheumatoid arthritis according to national action plan(appendix A). 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; Solomon el al., 1975) although reports of such an association are conflicting (MacGregor et al 1994; Lau et al 1993). In this present study showed that number of registered clinically suspected RA cases of rural areas were higher in comparison to urban areas. Table 1 illustrate that total number of clinically suspected RA cases were 290. In which 168 were belong to rural areas and left were urban. Out of 168 rural study subjects, majority of subjects were female. In urban about 65% were female subjects. This favour the previous study of Gabriel et al. 2003 that female were more prone to RA. Lawrence et al.,1998 said that there are 2.5 times as many women as there are men with RA.

In present study percentage of female clinically suspected RA cases to total study subjects was approximately 59%. In fifty nine percent female subjects, we observed that 24% were RA cases according to ACR 2010 criteria(table 1 ,table 2). With comparison to the male study subjects was 41% In which fourteen percent were RA cases according to ACR 2010 criteria. Percentage difference between male to female RA cases is about ten. Table 3 illustrate that out of 290 study subject of all the age group screened at UGC Advanced

Immunodiagnostic Training and Research Centre, 48(16.6%) were RA positive. The percent distribution of RA positivity were 5.1, 18.2, 16.9 and 33.3 in the age group 0-16, 17-40, 41-60, 61 and above years respectively, which shows highest percentage at the age group 60 and above(Chi-square =5.843, p>0.05). Some previous study exhibit assorted pattern of prevalence according to the age-groups, such as, in the study of symmons(2002), The incidence and prevalence of rheumatoid arthritis increase with age. Globally, the peak incidence of rheumatoid arthritis occurs between the ages of 55 and 64 years in women and 65-75 years in men and the age of onset is rising (Symmons 2002). The prevalence of rheumatoid arthritis increases with age and starts to decline at approximately 70 years of age (Linos et al 1980; Picavet and Hazes 2003). In addition to being a risk factor for the onset of rheumatoid arthritis, older-age onset of the condition is characterised by more rapid functional decline than younger-age onset (Symmons 2002). Positivity of female subjects were higher as compare to male subjects (Chi-square=1.87, p>0.05). This finding is concords with an added linked studies, for instance, Rheumatoid arthritis is more common among women than men, however, the ratio of female to male cases decreases with age (Kvien 2004). Female gender may have an impact on symptoms and functional outcome (Symmons 2002). The reason for the higher incidence and prevalence among women has not been established (Kvien 2004).).This study result related to female RA cases added previous studies, which found that the women have more risk than men to the development of RA.

Considered the clinically suspected cases according to their type of occupation, family history and education, which shows significant relation. Although in the study of Olsson et al., (2004) reported that 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 . The familial nature of rheumatoid arthritis suggests that genetic risk factors play a role in susceptibility to rheumatoid arthritis (Gabriel 2001). Based on twin studies, the genetic contribution to rheumatoid arthritis susceptibility is estimated to be 60% (MacGregor et al., 2000). Genetic variation in the human leukocyte antigen region is a contributing factor to the genetic risk of rheumatoid arthritis (Stastny 1978). There are conflicting reports as to whether formal education is associated with the incidence and prevalence of rheumatoid arthritis (Vliet Vlieland et al 1994; Gordon and Hastings 2003). An Australian study demonstrated that the prevalence of rheumatoid arthritis was lowest among those who attended university and highest among those leaving school before 15 years of age (Hill et al 1999). The identification of people at high-risk of developing rheumatoid arthritis and those with early features of the condition can provide a framework for improving the overall management of the disease (Woolf 2003).

Table 1: Showing the place of residence according to male and female Clinically suspected RA cases

Gender	Place of Residence		Total
	Urban	Rural	
Male	43(39.09%)	67(60.90%)	110
Female	79(43.88%)	101(56.11%)	180
Total	122	168	290

Table 2: Showing the distribution of RA cases verses Non-RA cases in male and female Clinically suspected RA cases

Gender		Place of Residence		Total
		Urban	Rural	
RA Cases	Male	5(35.7%)	9(64.29%)	14
	Female	11(32.4%)	23(67.65%)	34
Non-RA Cases	Male	38(39.6%)	58(60.42%)	96
	Female	68(46.6%)	78(53.42%)	146

Table 3: Percent distribution of screened cases with respect to biological and behavioral characteristics along with relative risk and 95% CI

Variables	RA(%)	Non-RA (%)	Chi-Square value	p-value	Relative Risk 95% CI
Age Group					
≤ 16	2(5.1)	37(94.9)	5.84	0.119	3.55 (0.91-21.29)
17-40	30(18.2)	135(81.8)			
41-60	13(16.9)	64(83.1)			3.29 (0.77-20.9)
>60	3(33.3)	6(66.7)			6.5 (0.95-52.21)
Gender					
Male	14(12.7)	96(87.3)	1.877	0.177	0.68 (0.36-1.23)
Female	34(18.9)	146(81.1)			
Food Habits					
Veg.	21(16.7)	105(83.3)	0.002	0.963	1.01 (0.58-1.77)
Non- Veg.	27(16.5)	137(83.5)			
Type of Occupation					
Sedentary	33(25)	99(75)	12.52	0.000	2.63 (1.45-4.89)
Active	15(9.5)	143(90.5)			
Family History					
Yes	12(32.4)	25(67.6)	7.744	0.005	2.28 (1.19-3.97)
No	36(14.2)	217(85.8)			
Place of Residence					
Urban	16(13.1)	106(86.9)	1.801	0.1796	0.68 (0.38-12.33)
Rural	32(19.0)	136(80.9)			
Education					
≤ Primary	19(23.7)	61(76.3)	8.915	0.0116	3.15 (1.33-7.99)
Primary to Inter.	22(18.8)	95(81.2)			
>Inter.	7(7.5)	86(92.5)			2.49 (1.07-6.26)
Milk Consumption					
Yes	21(14.3)	126(85.7)	1.108	0.292	0.757 (0.43-1.32)
No	27(18.7)	116(81.1)			

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