A STUDY ON THE INFLUENCE OF ENVIRONMENTAL FACTORS IN RHEUMATOID ARTHRITIS

Satish Kumar[1], UshaKulangara Aravind[2]

[1]Research Scholar, ACESSD Mahatma Gandhi University, Kottayam, Kerala.
[2]Research Scientist, ACESSD Mahatma Gandhi University, Kottayam, Kerala.

ABSTRACT

BACKGROUND

Rheumatoid arthritis is a common rheumatological disorder of unknown cause. The development of rheumatological disorders like rheumatoid arthritis depends on the interaction between genetic background and number of environmental factors. Number of environmental factors have been implicated in the aetiology of rheumatic diseases which include infections like Epstein Bar Virus (EBV) Mycobacterium tuberculosis, Escherichia coli, Proteus mirabilis, and parvovirus B19. The other environmental factors include sunlight, cold climate, smoking, drugs and adjuvants, diet, exercise, occupation, radiation exposure, drinking water, psychological status, air pollution, chemicals, drugs, socioeconomic status, geographic location, hot and cold climate, occupation and alcohol.

MATERIALS AND METHODS

Cross sectional observational study. The sample selected was of 152 patients with rheumatoid arthritis fulfilling the ACR-EULAR 10 criteria. The tools used were clinical profile, 2010 ACR–EULAR 10 criteria, serology and acute phase reactants. The data was analyzed using SPSS-8 software.

RESULTS

In the study, most of the rheumatoid arthritis patients were females. In the study, the majority of the patients with rheumatoid arthritis resided in high ranges, were smokers and non-alcoholics. Rheumatoid arthritis is common in patients taking non-vegetarian diet, manual labours, those with low level of education and low socio-economic status. Most of the patients had aggravation of symptoms following exposure to cold and stress.

CONCLUSION

In the study, most of the rheumatoid arthritis patients were females. Environmental factors like smoking, alcoholism, diet, occupation, educational status, socioeconomic status, place of residence, climatic conditions and stress significantly influenced the occurrence and progression of symptoms in rheumatoid arthritis patients.

KEYWORDS

Rheumatoid Arthritis, Environmental Factors.

BACKGROUND

Rheumatoid arthritis is a systemic auto immune disease with primary involvement of synovium followed by polyarticular inflammation and joint damage.[1]

Epidemiology

RA affects 0.5-3% of the population world-wide, with a peak prevalence between the ages of 30 and 50 years. Before menopause, rheumatoid arthritis is 2-3 times more common in women with an equal sex incidence thereafter. In Rheumatoid arthritis activation of synovial T cells occur by an unknown agent. The exact aetiology of rheumatoid arthritis is not yet identified. There occurs chronic synovitis due to rheumatoid factor associated with macrophage stimulation causing production of IL8, IL1, TNFα, granulocyte macrophage stimulating factor and chemokines.

Pathology

Rheumatoid Arthritis is characterized by synovitis (inflammation of the synovial lining of joints, tendon sheaths or bursae). There occurs infiltration of synovium by plasma cells, lymphocytes and macrophages with secretion of pro-inflammatory cytokines and autoantibody production with formation of immune complexes. A pannus is produced by the synovium proliferating and growing over the surface of the cartilage. The articular cartilage and sub chondral bonds are destroyed by the pannus producing erosions in the bone. Rheumatoid factors (RhF) are antibodies directed against the Fc portion of immunoglobulin. Synovitis is maintained by the production of rheumatoid factor by the plasma cells which aggregate together and forms immune complexes.

Clinical Features

The presentation is usually with insidious onset of pain, swelling of small joint of hand and feet with early morning stiffness. The affections of the joints in early rheumatoid arthritis is –MCP joint affected, IP joint of thump, PIP joint of fingers, wrist and metatarsophalangeal joints.[2] There is spindling of the fingers caused by swelling of the proximal interphalangeal joints. The metacarpophalangeal and wrist joints are also swollen. In advanced disease there is weakening of joint capsule, causing joint instability, subluxation (partial dislocation) and deformity. Multiple joint involvement: elbows, wrist, knee ankles, Carpometacarpal joints, cervical spine is seen in patients. Joint effusions and wasting of muscles around the affected joints are early features. Less common presentations are 'explosive' (sudden onset of widespread arthritis), palindromic (relapsing and remitting monoarthritis of different large joints), or with a systemic illness with few joint symptoms initially. Periarticular features of RA include tenosynovitis, bursitis, wasting of muscles and nodule formation. Patients with rheumatoid arthritis have increased atherosclerosis which may due to increased systemic inflammation and patients with rheumatoid arthritis have increased risk of infections and osteoporosis.

Extra-Articular Manifestations of Rheumatoid Arthritis Include

Fever, Fatigue, Weight loss, Sjogren's syndrome, Scleromalacia perforans, Carpal tunnel syndrome, Cord compression, Polyneuropathy, Felty's syndrome (RA, splenomegaly, neutropenia), Anaemia caused by Chronic disease, Hypersplenism, Haemolysis, Thrombocytosis, Rheumatoid nodules, Pleural effusion, Fibrosing alveolitis Rheumatoid pneumoconiosis (Caplan's syndrome), obliterative bronchiolitis, pericarditis pericardial effusion, Raynaud's syndrome, amyloidosis, leg ulcers, generalised weakness

Management

Rheumatoid Arthritis is treated using NSAIDS, DMARDS, biologics, and corticosteroids. Slow release NSAIDS preparations produce dramatic relief of pain and inflammation. DMARDS (disease modifying drugs) are to be used early in the disease to prevent long term inflammation of the joints. In patients with mild to moderate rheumatoid arthritis sulphasalazine and HCQS are used. Methotrexate is usually used in more active disease. Leflunomide acts by blocking T cell proliferation and is used along with methotrexate. Other drugs used in the rheumatoid arthritis include azathioprine, gold and pencillamine. TNFα blocking agents are used in patients who have active disease despite adequate treatment with at least two DMARDs, including methotrexate.

Biologics that inhibit the action of tumour necrosis factor- (e.g. etanercept, a soluble TNF-α receptor fusion protein that binds TNF-α; and adalimumab, a fully human anti-TNF monoclonal antibody to TNF) are now being used in the management of RA.

Corticosteroids are used to suppress disease activity i.e. (inflammation) but may produce GI bleed, drug induced diabetes, osteoporosis and pushing syndrome on long term use.

Prognosis

The prognosis is variable. After 10 years 10% of patients will be severely disabled and 25% will have minimal if any symptoms. Other patients lie between these two extremes.

Need and Significance of the Study

It is seen that rheumatological disorders are common in people who live in cold climatic areas and it's a common observation that aggravation of almost all rheumatological disorders occur during winter or during rainy season in Kerala and South India. Similar observations have been made in western countries.

Estimate of heritability suggest that genetic factors are responsible for at least 50% of the risk of developing RA. This means that gene-environment interactions and environmental factors could explain the rest. Evidence suggests that environmental factors important in RA may act years before clinical disease become apparent, Occupation and environment can modify joint diseases particular osteoarthritis, e.g. bass player's thumb, Zulu dancer's hip. Achilles tendinitis of long-distance runners and prepatellar bursitis in housemaid's knee are other examples of occupation-related rheumatism. Enthesopathies like lateral and medical epicondylitis of elbow (syn. Tennis elbow and golfer's elbow) are common in Indian household workers. Factory workers inhaling metal and polymer fumes can get fever associated with arthralgia. Environmental factors lead to the progression and aggravation of signs and symptoms of rheumatological diseases.

Although rheumatological diseases are generally more common in adults they can occur in childhood e.g. Juvenile rheumatoid arthritis. Both RA and SLE can occur in very young children and this supports the possibility that important environmental factors must be present during or before this time.

Rheumatological disorders are very common in the Indian population and cause a lot of disability. In India 8-9% of adult population suffer from one of the rheumatological disease and the degree of affection may vary from mild to severe with marked disability. In this context the study will help in understanding the influence of environmental factors in the causation and progression of rheumatological disease and identify how to modify the environmental factors and life style which can help in preventing the causation and progression of rheumatological diseases.

Objectives of the Study

1. To study the influence of environmental factors among individuals with rheumatoid arthritis based on-
   a. Gender
   b. Locale
   c. Smoking habits

d. Alcoholism
e. Diet

2. To compare the influence of external environmental factors among individuals with rheumatoid arthritis disorders based on
   a. Occupational status
   b. Educational status
   c. Socio-economic status

3. To study the influence of a. cold climate b. stress based on aggravation of symptoms in rheumatoid arthritis

Hypothesis

1. There will be no influence of environmental factors in rheumatoid arthritis
2. There will be no difference in the prevalence of rheumatoid arthritis between males and females.
3. There will be no difference in the prevalence of rheumatoid arthritis based on occupation, education and socio-economic status.
4. Rheumatological disorders will be more common in older age group compared to younger patients.

MATERIALS AND METHODS

The study was Quasi experimental in nature and the study design was cross sectional observational. The population was patients with rheumatological disorders attending the rheumatology clinic the sample of present study consists 152 patients with rheumatoid arthritis attending the rheumatological clinic at Medical College, Kottayam, Kerala from the district of Kottayam, Ernakulam, Idukki, Pathanamthitta and Alappuzha.

Independent variable was environmental factors and the Extraneous variables are age, sex, birth, weight, educational status and place of residence.

The tools like Baseline proforma, Observational check list along with standardized instruments like weighing machine and measuring tape were used for collecting the anthropometric measurements of the patients Feedback schedule were also administered among patients under gone treatment. The data were analysed using simple percentage analysis.

Study Design

Cross sectional observation study.

Inclusion Criteria

- All patients diagnosed with rheumatoid arthritis according to 2010 ACR-EULAR classification criteria.
- Patients with no previous history of long-term treatment for other chronic illness.
- Patients with more than 10 years period of residence in particular geographic area.
- Patients had smoking habit more than 10 years.

- Patients had duration of consumption of alcohol was taken as more than 10 years with more than 3 drinks weekly.

Exclusion Criteria

- Patients with other co-morbid medical illness.
- Patients undergoing treatment for other co-morbid medical problems.

Analysis and Interpretation of Data-

I. Prevalence of Rheumatoid Arthritis in the Study

a. Prevalence of rheumatoid arthritis patients based on gender

The number and percentage of patients with rheumatoid arthritis were calculated and tabulated as shown below.

Gender	Rheumatoid Arthritis	
	Number	Percentage
Male	40	26.31
Female	112	73.69
Total	152	100
Table 1. Number and Percentage of Patients with RA based on Gender		

Out of 152 patients with rheumatoid arthritis 40 patients (26.31%) were male patients where as 112 patients (73.69%) were female patients.

b. Distribution of Rheumatoid Arthritis Patients based on the Geographic Area/Locale of Residence

The total of RA patients from geographic area/locale of residence were subjected to percentage analysis base on gender and tabulated as shown below.

Place of Residence	Number of Patients	Percentage
High ranges	70	46.05%
Plains	38	25.00%
Coastal area	44	28.94%
Table 2. Number and Percentage of RA patients based on the Geographic Area of Residence		

Out of the 152 patients with rheumatoid arthritis 70 patients (46.05%) resided in the high ranges and hilly ranges whereas 38 patients (25%) resided in the plains and lowlands. 44 patients (28.94%) came from the coastal area.
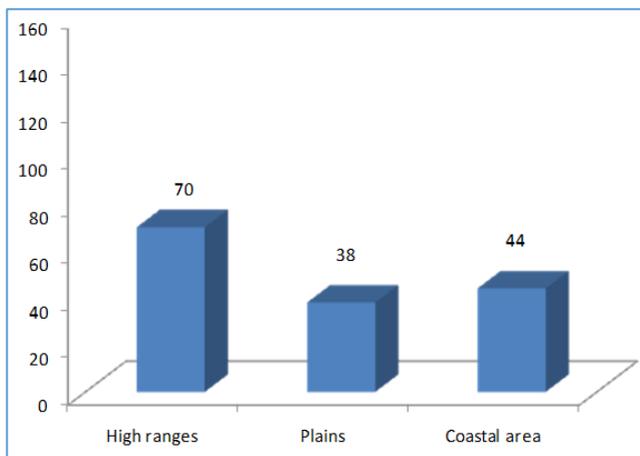
Figure 1. Number of RA Patients Based On Geographical Area of Residence

c.   Distribution of Rheumatoid Arthritis Patients with/without Smoking Habits based on Gender

The total of RA patients with/without smoking were subjected to percentage analysis base on gender and tabulated as shown below.

Gender	Smokers		Non-smokers	
	Number	percentage	Number	Percentage
Male	32	80	8	20
Female	8	7.14	104	92.85
Table 3. Number and Percentage of RA patients with/without Smoking Habit				

Out of the 40 male patients 32 patients were smoker where as 8 patients were non-smokers. Among the female participants of the study 8 patients were smokers where as only 94 patients were nonsmokers.
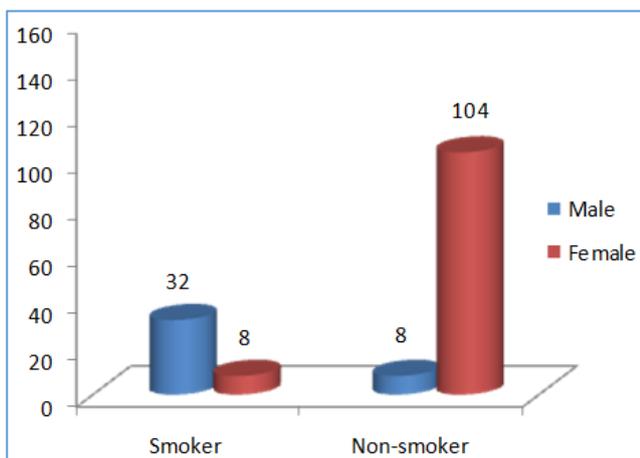

Figure 2. Number of RA Patients with/without Smoking Habit Based on Gender

d.   Distribution of Rheumatoid Arthritis Patients with/without Alcohol Consumption based on Gender

The total of RA patients with/without alcohol consumption were subjected to percentage analysis base on gender and tabulated as shown below.

Gender	Alcoholic		Non-alcoholic	
	Number	Percentage	Number	Percentage
Male	32	80	8	20
Female	10	8.92	102	91.07
Table 4. Number and Percentage of RA Patients with/without Alcoholic Consumption				

In the study 152 patients with rheumatoid arthritis of the 40 male patients 32 were alcoholic whereas 8 where nonalcoholic.
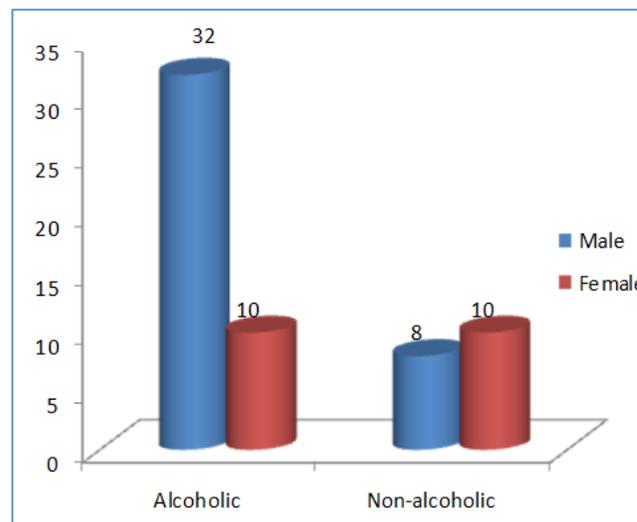

Figure 3. Number of RA Patients with/without Alcoholic Consumption based on Gender

e.   Distribution of Rheumatoid Arthritis Patients in the Study based on Dietary Habits

No. of Patients	Vegetarian	Non-Vegetarian	Mixed Diet
152	22(14.47%)	78(51.31%)	82 (53.94%)
Table 5			

Of the 152 rheumatoid arthritis patients 22 patients were vegetarians, 78 patients were non-vegetarian and in the rest 82 patients consumed mixed diet.

II.   Prevalence of Rheumatoid Arthritis Patients Based On External Environmental Factors

a.   Distribution of Rheumatoid arthritis patients based on Occupation status

The total of RA patients based on occupational status were subjected to percentage analysis base on gender and tabulated as shown below.

Occupation	Number	Percentage
Manual labours and technicians	90	59.21
Office workers	42	27.63
High officials	20	13.15
Table 6. Number and Percentage of RA Patients based on Occupation Status		

Out of the 152 patients with rheumatoid arthritis, 90 (59.21%) were manual labourers and technicians, 42 (27.63%) were office workers, and the rest 20 (13.15%) were high officials.
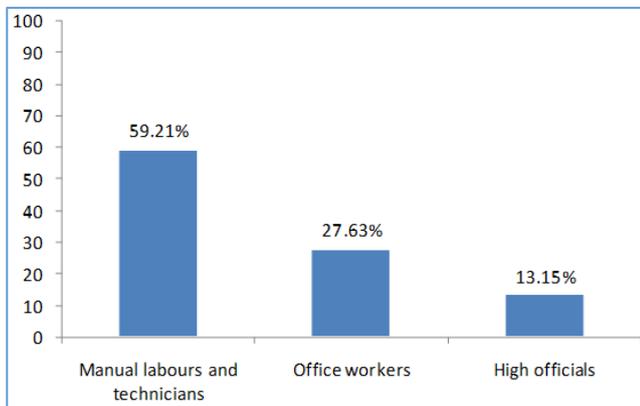

Figure 4. Occupation Status of RA Patients (Percentage)

b. Distribution of Rheumatoid Arthritis patients based on Educational Status

The total of RA patients based on educational status were subjected to percentage analysis and tabulated as shown below.

Education Status	Number	Percentage
Secondary	58	38
Higher secondary	61	40
Graduation	18	12
Post graduation & above	15	10
Table 7. Number and Percentage of RA patients based on Educational Status		

Out of 152 patients with rheumatoid arthritis 58 patients (38%) had studied upto 10th std., 61 patients (40%) had studied at pre-degree, 18 patients (12%) upto degree, and the rest 15 patients (10%) had post-graduation or higher qualification.
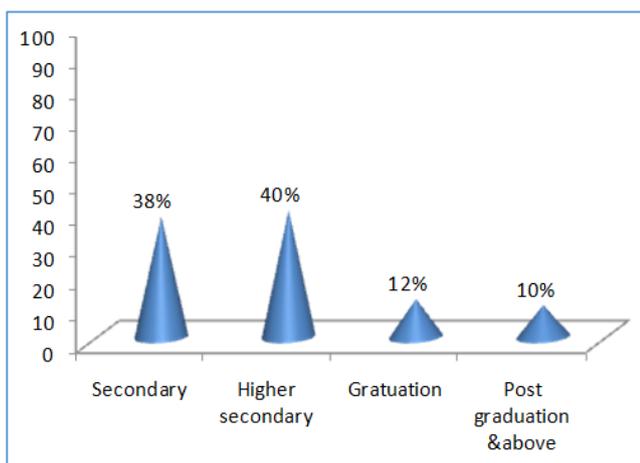

Figure 5. Education Status of RA Patients (Percentage)

c. Distribution of Rheumatoid arthritis patients based on socio economic status

The total of RA patients based on socio economic status were subjected to percentage analysis and tabulated as shown below.

Socio Economic Status	Number	Percentage
High	20	13.15
Middle	50	32.89
Low	82	53.94
Table 8. Number and Percentage of RA Patients based on Socio Economic Status		

Out of the 152 patients with rheumatoid arthritis, 20 (13.1%) belonged to high category, in middle socio-economic group 50 patients (32.89 %), and the rest 82 (53.94%) belonged to low socio-economic status.
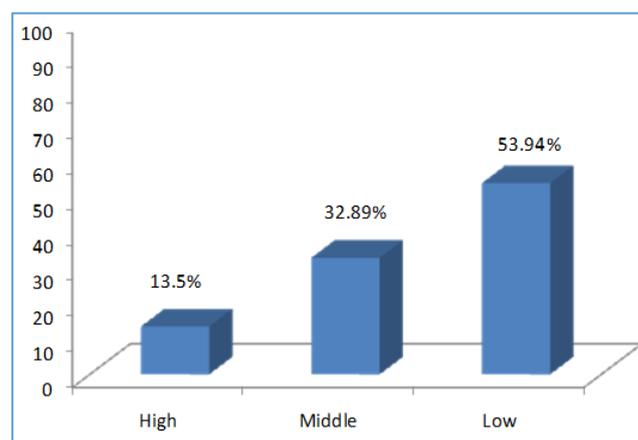

Figure 6. Socio Economic Status of RA patients (Percentage)

III. Distribution of rheumatoid arthritis patients based on aggravation of symptoms depending on a) climatic conditions, b) stress

a. Distribution of rheumatoid arthritis patients based on climate

The total of RA patients with/without exposure to cold were subjected to percentage analysis based on gender and tabulated as shown below.

Total	Aggravation of symptoms on exposure to cold		No aggravation on exposure to cold	
	Number	percentage	Number	Percentage
152	140	92.10	12	7.89
Table 9. Distribution of Rheumatoid Arthritis Patients with/without Exposure to Cold				

Of the total 152 patients with rheumatoid arthritis 140 (92.10) had aggravation of symptoms following exposure to cold where as only 12 (7.89%) had no aggravation of symptoms following exposure to cold.
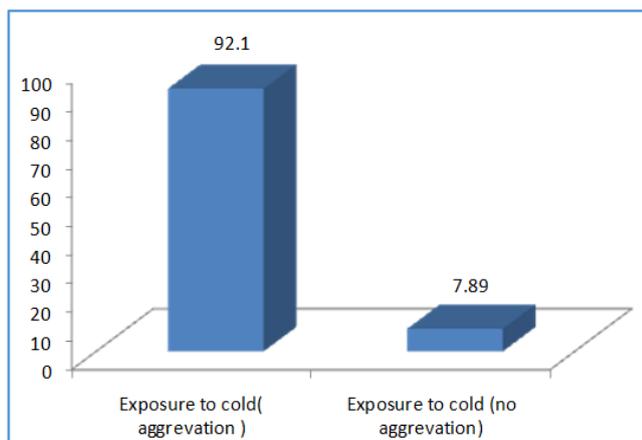
Figure 7. Number of RA Patients with /without Aggravation of Symptoms based on Exposure to Cold

b. Aggravation of Symptoms in Rheumatoid Arthritis Patients with Stressors

No. of Patients	Symptoms Aggravated		No Aggravation of Symptoms	
	No	%	No	%
152	132	86.84	22	14.47
Table 10				

Of the 152 rheumatoid arthritis patients who took part in the study 132 patients (86.8%) had aggravation of symptoms following stressors, and 22 patients (13.2%) reported no aggravation of rheumatological symptoms.

RESULTS

1. Out of 152 patients with rheumatoid arthritis 40 patients (26.31%) were male patients where as 112 patients (73.69%) were female patients.
2. Out of the 152 patients with rheumatoid arthritis 70 patients (46.05%) resided in the high ranges and hilly areas whereas 38 patients (25%) resided in the plains and lowlands. 44 patients (28.94%) came from the coastal area.
3. Out of the total 40 male patients 32(80%) patients were smokers where as 8 patients were nonsmokers. Among the female participants of the study 18 patients were smokers where as only 94 patients were nonsmokers.
4. In the study out of 40 male patients with rheumatoid arthritis 32 (94%) were alcoholics whereas 8 patients (20%) were nonalcoholic.
5. Of the 152 rheumatoid arthritis patients 22 patients were vegetarians, 78 patients were non-vegetarian and in the rest 52 patients consumed mixed diet.
6. Out of the 152 patients with rheumatoid arthritis, 90 (59.21%) were manual labourers and technicians, 42 (27.63%) were office workers, and the rest 20 (13.15%) were high officials.
7. Out of 152 patients with rheumatoid arthritis 58 patients (38%) had studied upto 10th std., 61 patients (40%) had studied upto pre-degree, 18 patients

(12%) up to degree, and the rest 15 patients (10%) had post-graduation or higher qualification.
8. Out of the 152 patients with rheumatoid arthritis, 20 (13.15%) belonged to high category, 50 (32.89 %) belonged to middle category and the rest 82 (53.94%) belonged to low socio-economic status.
9. Of the total 152 patients with rheumatoid arthritis 140 (92.10%) had aggravation of symptoms following exposure to cold whereas only 12 (7.89%) had no aggravation of symptoms following exposure to cold.
10. Of the 152 rheumatoid arthritis patients who took part in the study 132 patients (86.84%) and aggravation of symptoms following stressors, and 22 patients (14.47%) reported no aggravation of rheumatological symptoms with exposure to cold.

DISCUSSION

In the study conducted out of the 152 rheumatoid arthritis patients 40 were males whereas the rest 112 were females. This was similar to the study done by Harish et al in which, out of 100 symptomatic active cases, 26 were male, while 74 were female.[3] In our study out of the 152 patients with rheumatoid arthritis 70 patients (46.05%) resided in the high ranges and hilly areas whereas 38 patients (25%) resided in the plains and lowlands. 44 patients (28.94%) came from the coastal area which was contrary to the result of study conducted by Costenbader K H et al in US Where women who lived in the same region at birth into adulthood, the risk was highest among those living in the mid-west and northeast. Those living in the Northeast had as high as 45% elevated risk compared with those in the west if comparing the population at different time points of birth ages.[4] In our study out of the total 40 male patients 32(80%) patients were smokers where as 8 patients were nonsmokers and similar findings were got in the NHS study were a linear relationship between smoking and risk of rheumatoid arthritis whereby increasing doses of cigarettes (pack –years of smoking) was associated with an increased risk of RA.[5] In the study out of 40 male patients with rheumatoid arthritis 32 (94%) were alcoholic whereas 8 patients (20%) were nonalcoholic and similar findings were observed in the Henrik Källberg, et al study were alcohol consuming people had statistically significant risk of rheumatoid arthritis.[6] Of the 152 rheumatoid arthritis patients 22 patients were vegetarians, 78 patients were non vegetarian and in the rest 52 patients consumed mixed diet and similar observations where increased red meat and protein intake was associated with an increased risk of inflammatory arthropathy.[7] Out of the 152 patients with rheumatoid arthritis, 90 (59.21%) were manual labourers and technicians, 42 (27.63%) were office workers, and the rest 20 (13.15%) were high officials and similar observations where got in studies which showed patients whose occupation required manual labour the risk of rheumatoid arthritis was 20% more than non-manual workers. Out of 152 patients with rheumatoid arthritis 58 patients (38%) had studied upto 10th std., 61 patients (40%) had studied at pre-degree, 18 patients (12%) up to degree, and the rest 15 patients (10%) had post-graduation or

higher qualification and these results are similar population based case control study in Sweden (EIRA) in which the risk of RA in patients without university degrees was 40% higher compared with those with university degrees.[8] In the study of 152 patients with rheumatoid arthritis, 20 (13.15%) belonged to high category, 50 (32.89 %)belonged to middle category and the rest 82 (53.94%) belonged to low socio economic status and similar findings where got in the study conducted by Deng HO Yang where higher incidence of rheumatoid arthritis was found in patients with low socio economic status.[9]

Of the total 152 patients with rheumatoid arthritis 140 (92.10) had aggravation of symptoms following exposure to cold were as only 12 (7.89%) had no aggravation of symptoms following exposure to cold and similar results have been obtained in studies conducted by Pingling Zeng et al.[10]

Of the 152 rheumatoid arthritis patients who took part in the study 132 patients (86.84%) had aggravation of symptoms, following stressors, and 22 patients (14.47%) reported no aggravation of rheumatological symptoms and similar results have been observed in rheumatoid arthritis where stress exacerbates rheumatological diseases.[11]

CONCLUSION

The cause of development and progression of rheumatoid arthritis are multi factorial of which environmental factors are very important. In several studies, the association of rheumatoid arthritis and environmental factors have been under estimated, and more importance given to genetic aetiology. Genetically susceptible patients after exposure to a particular environmental factor can develop rheumatoid arthritis as the environmental factors may be cause for that particular rheumatological disorder. More knowledge about the environmental factors help in broadening our knowledge of how and to what extent these environmental factors are involved in the causation of rheumatoid arthritis and how alteration or manipulation of the environmental factors can help in preventing the causation and progression of rheumatoid arthritis. It will also help in gaining more knowledge about gene environmental interaction in cases of rheumatological disorders. Along with life style modification, modification of the other environmental factors, judicious use of drugs can go a long way in the better management of rheumatoid arthritis and preventing the exacerbation of symptoms.

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