The pattern of rheumatological disorders and its management in rural population of central India

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Abstract---Background: India is home to the world's second largest population. Rheumatology is an emerging specialty in India. We looked at publications in the field of rheumatology from India from over the past six years using Scopus and Medline databases. Despite rheumatologic disorders affecting 6.0%-24.0% of the population, rheumatology in India is still in its infancy. So, we studied the pattern of rheumatological disorders and its management in rural population of central India. Material and Methods: A cross sectional study was done for a period of 18 months on 100 people attending inpatient and outpatient from General Medicine and Orthopaedics departments of Uttar Pradesh University of Medical Sciences, Saifai, India. All patients of age 12 years and above coming to UPUMS with history

suggestive of Rheumatological disorders were included in the study. Results: Out of 100 studied patients 85.0%were in age group 31-40 years with female predominance (72.0%). Hypertension was the commonest comorbidity followed by hypothyroidism and diabetes. Rheumatoid arthritis (49.0%) was the most common disease followed by Osteoarthritis (20.0%), Spondyloarthritis (18.0%) and Systemic lupus erythematosus (7.0%). The difference between joint examination in different rheumatic disease was statistically insignificant (p>0.05). The difference between the auto antibodies (vitamin-D, RF and anti-CCP antibody) was statistically insignificant in different rheumatic diseases (p>0.05). Conclusion: The prevalence of RD is substantially high among Indian women above 35 years demanding attention of health care providers. Inflammatory joint diseases are mostcommon in a specialised rheumatology clinic, followed by degenerative joint and spine diseases, soft tissue rheumatism, and metabolic bone diseases.

Keywords---rheumatological disorders, osteoarthritis, rheumatoid arthritis, inflammatoryjoint diseases.

Introduction

Rheumatoid Disease is a chronic debilitating systemic inflammatory condition, whose cause remains elusive, with the dominant manifestation marked by a symmetric, additive erosive polyarthritis involving the small and large synovial joints apart from other systemic features. Erosive arthritis with resulting deformities add to the disability and poor quality of life of these patients, with a high mortality related to accelerated atherosclerosis associated with this prolonged inflammatory state. There has been rapid progress in the treatment for Rheumatological Disorders over the last couple of decades, with newer understanding of its pathogenesis and the development of targeted therapy in the form of monoclonal antibodies against cytokines and their receptors, and newer small molecule inhibitors targeting intracellular cytokine pathways.[1]

Female population constitutes a big strength with the advancement of age and is more prone to the onslaught of various chronic diseases. Few studies have documented that females are suffering more of musculoskeletal and rheumatic complaints especially with theadvancement of age.[2] The presentation of various RD however remains varied and complex.

The first studies to identify rheumatic diseases at a community level emanated from a suburban area near New Delhi in the early 1990s. The prevalence of musculoskeletal complaints in general, rheumatoid arthritis, spondyloarthropathy and SLE were studied. The first study identified a prevalence of 8.5% for musculoskeletal complaints, amongst more than 44,000 people studied. The most common cause was related to non-specific musculoskeletal complaints (2.07%), followed by osteoarthritis (1.89%). With regards to inflammatory rheumatic diseases, 0.75% had rheumatoid arthritis and 0.36% seronegative spondyloarthropathy.[3] The second study screened over 52,000 people for lupus (using both

clinical criteria and antinuclear antibodies) and projected a population prevalence of 3 per 100,000.[4]

The issues facing the practice of rheumatology in India have been elucidated in a recent article[5] by Handa, an ex-president of the APLAR. Briefly, lack of adequate manpowerand training facilities, staggering costs of therapy and unique problems like burden of infectious diseases challenge adequate management of rheumatic diseases in the country.

One sixth of the world's population lives in India, and more than two-thirds of the entire population of India lives in rural areas. A few population-based studies have been conducted in rural India to assess the prevalence of rheumatic disorders and other musculoskeletal complaints. However, these have been conducted in relatively affluent or peri-urban rural areas,[6] while studies from rural agrarian communities in India are very rare.This is of the special interest, as these populations are even more likely to experience substantial burden of rheumatic disorders, as manual labour is the main source of income. This study was conducted in tertiary care hospital of inpatient practice at UPUMS, Saifai Etawah region of India, with an aim to audit the pattern of rheumatological disordersand its management in rural population of central India

Materials and Methods

This is a cross sectional study for 1½ year time period from January 2020 to June 2021 on patients attending outpatient department of General Medicine, admitted in Medicine ward and patients visiting orthopaedics OPD and IPD of UPUMS, Safai, Etawah. A total 100 adult patients greater than 12 years of age those were attending Outpatient Department and IPD for various Rheumatological Disorders were included in this study and other than this [patients were excluded from the study. All the patients were examined by an expert physician and supportive medical team, and then their routine clinical and radiological examinations were done on each patient.

Method of collection of data

Each patient's height and weight were measured and BMI was calculated. In all patients, blood pressure (BP) was measured in the sitting posture by the physician using mercury sphygmomanometer. If the patient's BP was elevated, two additional measurements was done, waiting a few minutes between measurements. All these information was entered into a database and was maintained for registry according to the unique hospital outpatient ID given to individual patient to avoid repetition of patient enrolment. Patients who met the inclusion criteria for selection of study were identified. The purpose of the study was explained to the patients and those who were willing to give consent were included in this study.

Patients who meet the study criteria was interviewed by a physician and the information was recorded. Patient interview consisted of demographic questions related to age, occupation, personal history (smoking, tobacco chewing, and alcohol consumption), family history of arthritis, existing comorbidities, drug

allergies, and duration of RD. Each and every data was compiled and documented using a standardized interview. Body height, body weight, hip and waist to hip ratio (WHR) was calculated according to recommendations of the world health organization (WHO). Data regarding complete blood count including haemoglobin level and peripheral blood smear, S. Creatinine, S. Urea, blood glucose (fasting and post prandial), HbA1c, lipid profile , liver function tests, vitamin b12 levels and rheumatological markers were obtained. Patients were observed for below mentioned rheumatological markers. The research procedure followed was in accordance with the approved ethical standards of the ethical committee of UPUMS, Saifai, Etawah.

Statistical analysis

Data was analyzed using Statistical Package for Social Sciences, version 23 (SPSS Inc., Chicago, IL). Results for continuous variables are shown as mean ± standard deviation (SD), whereas results for categorical variables are shown as number (percentage). Chi-square test and Fischer's exact test will be applied to measure association between categorical data. P value less than 0.05 will be considered statistically significant.

Ethical Considerations:

Ethical clearance with number 94/2019-20 was obtained and the permission to conduct the study was given by ethical committee of Uttar Pradesh University Of Medical Sciences. Patient informed consent was taken and medical records and patient data were maintained with confidentiality. The data was used only for the study.

Results

In the present study out of the total 100 studied patients the majority were in the age group 31-40 years (85.0%) followed by 9.0% less than and equal to 30 years and least 6.0% patients were more than 40 years of age. On our study female predominance (72.0%) was found. Only 28.0% were male patients. Majority 66.0% of patients were Graduate or more followed by 25.0% of patient's high school pass, only 7.0% of patients were had primary level education. Majority 44.0% of patients were doing service or job followed by 27.0% were from house held, and 19.0% of patients were running their business. Only 10% of patients were laborer. The mean age of patients was 35.65±3.94 years, mean weight, mean height and mean BMI was 60.72±7.53 kg, 158.72±7.17 cms and 24.17±3.32 kg/m². Blood investigation was done for all patients their finding were noted in table 1. The majority of the studied patients were having hypertension (29.0%) followed by hypothyroidism and diabetes mellitus with 15.0% each, and asthma (4.0%) whereas 32.0% were having no comorbidities.

Rheumatoid arthritis (49.0%) was the most common followed by Osteoarthritis (20.0%), Spondyloarthritis (18.0%) and Systemic lupus erythematosus (7.0%) whereas 6.0% were having other rheumatic diseases (Table 2). The mean duration of disease was 5.57±2.44 years, swollen (0-28) was 2.52±2.19 and tender (0-28) was 11.0±5.5, mean ESR was 29.16±6.42 and DSA-28 score was 4.51±0.84. The

difference between joint examination in different rheumatic disease was statistically insignificant (p>0.05). The RF and vitamin d level were maximum for Osteoarthritis 4.32±0.70 mg/dl and 16.41±4.36 mg/dl respectively while mean anti CCP antibody was maximum for spondyloarthritis (28.72±3.85 u/ml). The difference between the auto antibodies (vitamin D, RF and anti CCP antibody) was statistically insignificant in different rheumatic diseases (rheumatoid arthritis, osteoarthritis,spondyloarthritis, and systemic lupus erythematosus) (p>0.05).

Discussion

In the present study out of the total 100 studied patients the majority were in the age group 31-40 years (85.0%) and the mean age was 35.65±3.94 years with female predominance (72.0%). 66.0% were graduate and above, 44.0% were in service department. Our findings were consistent with the study performed by **Mittal G et al**[1] who reported that the comparable findings to the present study. Various other studies conducted in different settings have reported similar female predominance in their study varying between 76.7% and 87.0%.[7,8,9] **Jagdish RK et al**[10] and **Joshi VR et al**[6] findings were also consistent with the present study. The reasons for this feminine predominance in auto-immune diseases are not clear, though genetic (X-linked) factors and hormonal relation have been attributed.[11]

In our study on 100 patients the majority of the studied patients were having hypertension (29.0%) followed by hypothyroidism and diabetes mellitus with 15.0% each, and asthma (4.0%) whereas 32.0% were having no comorbidities. An Indian study from Tamil Nadu, India, reported higher incidence of HTN in 60.0% and DM in 26.7%.[12] **MittalG et al**[1] and **Kudial S et al**[13] reported that co-morbid condition present, with hypertension being the commonest followed by anemia, diabetes mellitus and other conditions. **Jagdish RK et al**[10] findings were also in accordance with our study. This indicates Rheumatological patients are at high risk of cardiac problem due to accumulation of risk factors and chronic inflammation leads to endothelial dysfunction and accelerated atherosclerosis.[14]

In the present study rheumatoid arthritis (49.0%) was the most common followed by Osteoarthritis (20.0%), Spondyloarthritis (18.0%) and Systemic lupus erythematosus (7.0%) whereas 6.0% were having other rheumatic diseases. Our findings were in accordance with **Jagdish RK et al**[10] who reported that among Inflammatory /autoimmune spine, joint and systemic diseases rheumatoid arthritis was most common followed by, spondyloarthritis, and Connective tissue diseases. Our findings were also similar to study of **Ranwa BL et al**[15] (RA 35.67%), **Miedema HS et al**[16] (RA was 26.5%) and **Zink A et al**[17] (RA 51%). Spondyloarthritidies(SpA) was found in 9% of cases which is comparable to studies by **Vanhoof K et al**[18] (SpA-7%) and **Miedema HS et al**[16] (AS was 5.1%, PsA was 3.6%). According to **Joshi VR et al**[6] depicted that among various sites, osteoarthritis of knee had the highest prevalence. The point prevalence of STR was 28.0%. Regional STR was more common (24.7%) than diffuse STR (4.9%)

In our study the mean duration of disease was 5.57±2.44 years, swollen (0-28) was 2.52±2.19 and tender (0-28) was 11.0±5.5, mean ESR was 29.16±6.42 and DSA-28 score was 4.51±0.84. The difference between joint examination in different rheumatic disease wasstatistically insignificant (p>0.05).

Combination DMARD therapy should be initiated when the disease activity score remains high, despite adequate MTX monotherapy, or at the very onset in a sub-group of patients with aggressive disease associated with high risk factors including, smokers, femalegender, high tender, and swollen joint counts, markedly elevated acute phase reactants, highdisease activity scores, marginal erosions on X-ray at baseline, high rheumatoid factor (RF)and anti-cyclic citrullinated peptide antibody (anti-CCP) titres and severe disability indicated by high health assessment questionnaire scores.[19] Various studies have concluded that combination DMARD therapy is effective in RA, with the strongest evidence in established RA for combinations of MTX + anti-TNF and/or SSZ/HCQ, given to patients who have partially responded to DMARD monotherapy.[20] **Mittal G et al**[1], reported MTX+ HCQ was the most frequently prescribed DMARD combination, in concurrence with two other Indian studies where this combination therapy was prescribed in more than 50.0% of RA patients.[21,12] Hence, in the Indian scenario, MTX + HCQ is the most frequently used combination of DMARDs. This is also the most popularly prescribed combination DMARD, in the USA and Canada. Consistent with our results, none of the other studies have reported use of biological/biosimilar DMARD (bDMARDs) or Janus Kinase Inhibitors (JAKinibs) at the treatment initiation. Most probable reason for this can be the high cost and the current recommendation of these agents only after failure of primary therapy with combination csDMARDs

There is currently no evidence for differential responses solely based on disease duration, when leaving differences in baseline damage due to delayed treatment initiation aside. Indeed, trials on MTX-naïve patients with RA used different disease durations for inclusion, which ranged from a few months to several years, without appreciable differencesin outcomes on indirect comparison.[22]

Low disease activity also needs to be properly defined and measured. Measures that highly weigh C reactive protein or erythrocyte sedimentation rate (e.g., the disease activity score (DAS-28) may not convey sufficiently reliable results when used with agents that interfere with the acute phase response, such as anticytokine agents (especially interleukin (IL)-6 inhibitors) or Jak-inhibitors.[23]

Auto-antibodies findings in various Rheumatic diseases

In the present study the difference between the auto antibodies (vitamin D, RF and anti CCP antibody) was statistically insignificant in different rheumatic diseases (rheumatoid arthritis, osteoarthritis, spondyloarthritis, and systemic lupus erythematosus) (p>0.05). The RF and vitamin d level were maximum for Osteoarthritis 4.32±0.70 mg/dl and 16.41±4.36 mg/dl respectively while mean anti CCP antibody was maximum for spondyloarthritis (28.72±3.85 u/ml).

Mittal G et al[1] reported that all patients in their study also received vitamin D (vit- D) supplements. In a study conducted in 2012, vit-D deficiency was found to be highly prevalent in patients with RA, and was observed to be linked to disease severity. Vit-D deficiency has been related to diffuse musculoskeletal pain. Vit-D supplementation may be prescribed for prevention of osteoporosis along with some pain relief in patients with RA.[24] In another study, vit-D has been implicated in preventing the onset and RA pathogenesis and also promoting anti-inflammatory response.[25] **Pal CP et al**[26] also found knee and hip OA as the most prevalent and leading causes of disability. Their prevalence increases with age and generally affects women more frequently than men. Females are more prone toward vitamin D and calcium deficiency than males. Females in both urban and rural areas who do housework squat to work, a risk factor for development of OA. Metabolic bone diseases accounts for 13.6% of total patients in a study **Jagdish RK et al**[10] in which vitamin D deficiency was in 11.6% (8% patients having Vitamin D deficiency only and 3.6% patients with Osteomalacia) which contradict with reports by **Ritu G** and **Gupta A**[27] who showed the prevalence of vitamin D deficiency is 70.0-100.0% in general population of Indian subcontinent, this can be explained by the fact that our patients being hospital based and might have taken calcium and vitamin D supplementation.

Sulaiman W et al[28] from Malaysia reported 45.8% patients not aware of any NSAIDs side effect status in an established rheumatologic clinic, Current report by **Misra DP et al**[29] highlighted this problem also. There is a marked imbalance between number of rheumatologist and the concerned disease burden at present scenario. Despite rheumatologic disorders affecting 18.5%-23.9% of the population, rheumatology in India is still in its infancy. Therefore, there is a dare need of increasing awareness, training programmes for doctors in this developing field of medicine. With rising standards of care and outcomes, RA management has become increasingly complex over the last decade. Despite the availability of many efficacious agents, treatment strategies that have been developed, and outcomes assessments that allow effective follow-up, the high costs of novel therapies have limited the widespread use of these therapeutic options, creating a significant extent of inequity. Therefore, management recommendations on the approach to treating patients with RA have become increasingly useful in providing physicians, patients, payers, regulators and other healthcare suppliers with evidence-based guidance supported by the views of experts involved in many of these novel developments. Indeed, EULAR has recently updated the standardised operating procedures on the development of recommendations, which include cost aspects in addition to accounting for the assessment of evidence and expert opinion. [30]

Limitations of the study

- The few limitations to our study, are the small sample size assessed and the inclusion of all patients, both old as well as new, in the study which could confound the exact results.
- Additionally, the response was less among young males, labourers and literate individuals, possibly causing some selection bias; higher mobility of

this group might be the reason for their non-response.

Strengths of the study

This study will help primary care physicians get the data about the most commonly prescribed DMARD therapy in RA patients, and spread awareness about polypharmacy in RA, thus helping physicians make more aware choices about the RA drug prescriptions and limiting polypharmacy when not needed

Recommendations of the study

Cardio metabolic risk factors are predominately associated with rheumatological patients and therefore we suggest that proactive screening of these factors should be routinely done for prevention of complications.

Conclusion

The prevalence of RD is substantially high among Indian women above 35 years demanding attention of health care providers. This study provides an estimate of the pattern of rheumatic diseases in a tertiary institution with a newly started rheumatology clinic in Saifai. It can serve as a base-line research on which future researchers could build on as similar studies from India are scarcely available. A community study will however be more appropriate to determine the actual prevalence of rheumatic diseases in the community. We conclude that inflammatory joint diseases are most common in a specialised rheumatology clinic, followed by degenerative joint and spine diseases, soft tissue rheumatism, and metabolic bone diseases. Patients need more and more public awareness programme to increase their knowledge towards the rheumatology branch and commonly used medicines.

Results Table 1: Blood Investigation findings of patients

Variable	Mean±SD
Hb (%)	10.52±1.54
Platelet Count (10^5 cells/mm^3)	2.89±0.74
WBC (count)	7.32±1.97
RBS (mg/dl)	133.27±8.80
CRP (mg/l)	3.51±1.21
ESR (mm/1st hour)	29.16±6.42
Creatinine (mg/dl)	0.95±0.26
Serum calcium (mg/dl)	8.41±0.85
Serum Phosphate (mg/dl)	3.26±0.58
Uric acid	4.56±0.69
Vitamin D level	15.23±5.68
RF (mg/dl)	4.02±0.87
Anti CCP antibody (u/ml)	27.13±3.97

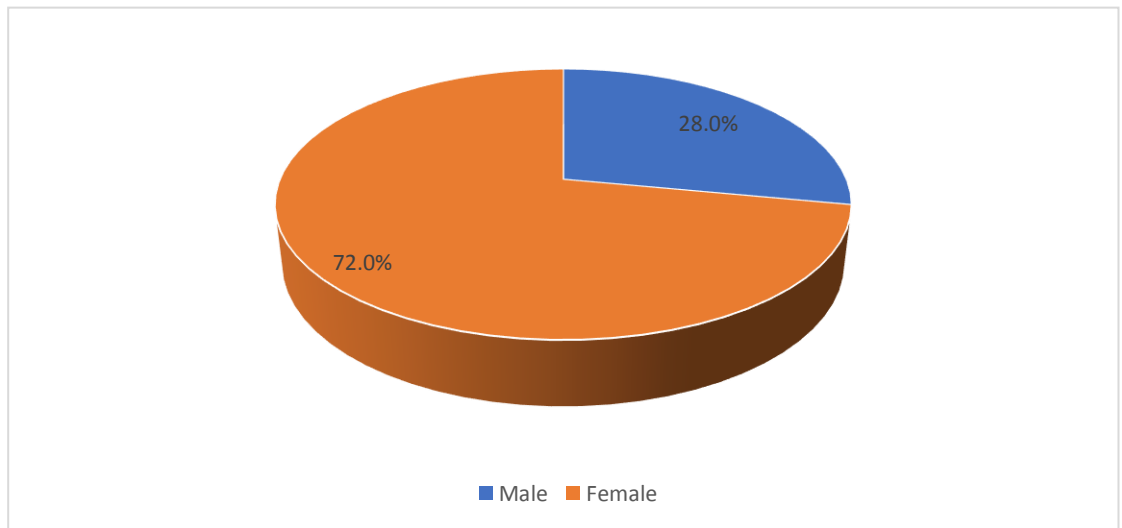**Table 2: Diagnose Rheumatic diseases**

Rheumatic diseases	Frequency (n-100)	Percentage
Rheumatoid arthritis	49	49.0%
Osteoarthritis	20	20.0%
Spondyloarthritis	18	18.0%
Systemic lupus erythematosus	7	7.0%
Others	6	6.0%

Table 3: Correlation of Joint Examination findings in various Rheumatic diseases

	Rheumatic diseases				P value
	Rheumatoid arthritis (n=49)	Osteoarthritis (n=20)	Spondyloarthritis (n=18)	Systemic lupus erythematosus (n=7%)	
Duration of disease (year)	5.69±2.29	5.75±2.75	5.22±2.46	4.43±1.72	0.613
Swollen (0-28)	2.61±2.04	2.80±2.14	2.50±2.68	1.86±1.68	0.748
Tender (0-28)	10.63±5.18	12.10±6.12	11.33±6.11	9.29±5.12	0.782
ESR	28.78±6.48	29.80±5.73	30.44±7.18	27.14±7.71	0.776
DSA-28 score	4.49±0.79	4.66±0.87	4.53±0.94	4.20±0.93	0.798

Table 4: Correlation of Auto-antibodies findings in various Rheumatic diseases

Auto-antibodies	Rheumatic diseases				P value
	Rheumatoid arthritis (n=49)	Osteoarthritis (n=20)	Spondyloarthritis (n=18)	Systemic lupus erythematosus (n=7%)	
Vitamin D level	15.09±5.85	16.41±4.36	13.80±6.03	15.57±7.70	0.689
RF (mg/dl)	4.05±0.86	4.32±0.70	3.84±0.93	3.54±0.82	0.223
Anti CCP antibody (u/ml)	27.51±4.09	25.55±3.05	28.72±3.85	25.57±4.04	0.095

Figure 1: Distribution of patients on the basis of sex

Figure 2: Diagnose Rheumatic diseases
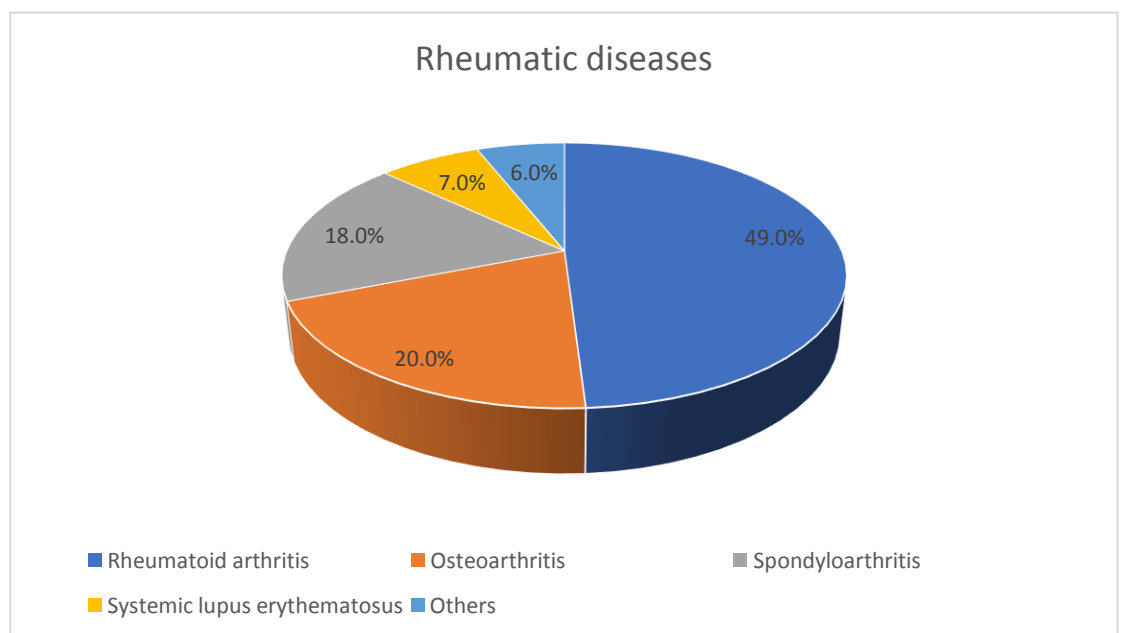
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