Review Article

Disease burden of rheumatic diseases in India: COPCORD perspective

Arvind Chopra *
Center for Rheumatic Diseases, Pune, India

ABSTRACT

The maiden WHO ILAR COPCORD (community oriented program for control of rheumatic diseases) Bhigwán (1996–2014) demonstrated that musculoskeletal (MSK) pain was the commonest self-reported ailment in the community, soft tissue rheumatism, ill-defined MSK symptoms and osteoarthritis (OA) were the predominant disorders and about 10% cases suffered from inflammatory arthritis. The burden of rheumatoid arthritis (RA) was high with point prevalence of 0.7%. Bone and joint decade (BJD) India conducted several standardized and uniform surveys (2004–2010) all over India and collected data from over 55,000 persons at 12 sites. The pooled age sex adjusted (India census population 2001) prevalence reported by the recent surveys was — RA (0.34), OA knees (3.34), undifferentiated inflammatory arthritis (0.22), Spondyloarthritis (0.23), ankylosing spondylitis (0.03), psoriatic arthritis (0.01) soft tissue rheumatism (1.39), gout (0.05) lupus (0.01); prevalence percent in parenthesis. Several forms of collagen vascular disorders and vasculitis are described in hospital based case series. Musculoskeletal infections including tuberculosis remain an important clinical burden. The 2006 India Chikungunya epidemic has put an additional burden of chronic MSK pain and arthritis. The recently launched national health programs pertaining to non-communicable diseases, rural and women health does not even mention rheumatic diseases thus there is urgent need to study the burden of rheumatic diseases and its impact on society.

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Musculoskeletal pain and arthritis (MSK) are as old as the human civilization and a major community burden.1,2 Rheumatic diseases find mention in the pre-biblical texts of Ayurveda.3 They cause immense morbidity in terms of poor quality of life, loss of function and productivity and further cause significant socioeconomic burden. Several inflammatory rheumatic diseases cause premature atherosclerosis, vascular complications and early death. All this is difficult to measure. The overall disease burden is likely to be underestimated.4 In India, community based arthritis camps are popular but not suitable to estimate disease burden.5

Some population based initiatives over the last four decades in India have provided prevalence estimates. The earlier (nineteen seventies and eighties) surveys focused on rheumatoid arthritis (RA) and lupus.6,7 In 1996, the maiden WHO ILAR COPCORD (community oriented program for

* Center for Rheumatic Diseases, 1988 Convent St., Camp, Pune 411001, India.
E-mail address: crdp@vsnl.net.
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control of rheumatic diseases) India was launched.8 The survey of over 7000 persons was completed in village Bhigwan in Pune district followed by a long term planned program of providing rheumatology services and collecting further incidence and risk factor data which has continued till date (2015).8–11 This survey data of RA and osteoarthritis knees was used by the WHO to project the likely burden in South East Asia.12 Subsequently, another COPCORD survey was completed in the Lucknow region but a comprehensive report is not yet published.13 The Bhigwan model was adopted by the Bone and Joint Decade (BJD) India to carry out several surveys all over India from 2004 to 2010 (Fig. 1) and over 55,000 persons were screened and several observations presented and published.34–37 More recently, Indian Council Medical Research (ICMR) completed a 30,000 urban and rural population survey at three sites (Delhi, Jodhpur and Dibrugarh) using a Bhigwan COPCORD based protocol.22

The Bhigwan COPCORD demonstrated for the first time that (i) MSK pain was the most common self-reported ailment in the community (ii) soft tissue rheumatism, ill-defined MSK pain and OA were the predominant rheumatic disorders (iii) about 10% community cases were classified as inflammatory arthritis.9,10 Several differences were reported between urban and rural areas in the Pune COPCORD study.19 RA and other inflammatory arthritis, soft tissue rheumatism, osteoarthritis and gout were much more prevalent in Bhigwan.19 Several publications have compared the Indian data with other COPCORD surveys.3,11

The BJD India sponsored surveys (Fig. 1) used well described sites chosen by preference and convenience sampling, and a uniform standardized protocol. The objective was to recognize the spectrum of rheumatic diseases in India and further estimate a burden of disease. Both urban and rural sites were chosen. Table 1 describes the age sex adjusted (India census population 2001) prevalence of rheumatic disorders reported by the Bhigwan study and the recently completed BJD India COPCORD survey.19,20

### Table 1 — Standardized prevalence (percent, 95% confidence interval) of rheumatic diseases in COPCORD Bhigwan (n = 4092) and BJD India COPCORD (n = 56,541) surveys.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>COPCORD Bhigwan 1996</th>
<th>BJD India COPCORD 2004–2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>0.67 (0.57, 0.79)</td>
<td>0.34 (0.08, 0.79)</td>
</tr>
<tr>
<td>Undifferentiated arthritis</td>
<td>0.76 (0.64, 0.89)</td>
<td>0.22 (0.05, 0.68)</td>
</tr>
<tr>
<td>Spondyloarthitis</td>
<td>0.30 (0.23, 0.39)</td>
<td>0.23 (0.05, 0.68)</td>
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<tr>
<td>Ankylosing Spondylitis</td>
<td>0.10 (0.06, 0.15)</td>
<td>0.03 (0.02, 0.05)</td>
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<tr>
<td>Osteoarthritis, any form</td>
<td>6.25 (5.9, 6.60)</td>
<td>4.39 (3.3, 5.61)</td>
</tr>
<tr>
<td>Osteoarthritis knee</td>
<td>4.42 (4.14, 4.71)</td>
<td>3.34 (2.43, 4.47)</td>
</tr>
<tr>
<td>Gout</td>
<td>0.13 (0.08, 0.19)</td>
<td>0.04 (0.03, 0.05)</td>
</tr>
<tr>
<td>Soft tissue rheumatism, any form</td>
<td>3.77 (3.51, 4.05)</td>
<td>1.31 (0.77, 2.11)</td>
</tr>
<tr>
<td>Ill defined symptoms, nonspecific arthralgias</td>
<td>6.25 (5.29, 6.59)</td>
<td>4.25 (3.23, 5.53)</td>
</tr>
<tr>
<td>Lupus &amp; other connective tissue disorders</td>
<td>NI</td>
<td>0.02 (0.01, 0.03)</td>
</tr>
</tbody>
</table>

Note: Prevalence was adjusted for age-sex distribution with India population census 2001; rheumatic diseases diagnosis was clinical; COPCORD: community oriented program for control of rheumatic diseases; n: number population; NI: not identified.

1. **Soft tissue rheumatism (STR)**

Soft tissue rheumatism (STR) encompasses diverse conditions with a broad classification system based on anatomy (tendon, fascia, bursa etc.) and pathophysiology (inflammatory, degenerative etc.).22 These are very common but neglected disorders in the community. Though psychological factors and trauma play an important role, occupational overuse and/or misuse contribute significantly in our setting of modest living and intense labor to make the ends meet. Using an Indian version of health assessment questionnaire, Bhigwan COPCORD described a significant functional impact of STR.10,24 Fibromyalgia, a diffuse form of chronic MSK pain, was found to be rather uncommon except in the Lucknow COPCORD Survey (3.8% urban and 4.5% rural).25

2. **Osteoarthritis (OA)**

OA was the second most common disorder in COPCORD4,9,19 (Fig. 1). Radiographic work up is critical to the diagnosis but grossly limited in community surveys. Using clinical criteria often causes an overestimate.4 Knee and back pains are very common in the community and doctors may overzealously attribute them to OA.4,10,11 The prevalence of OA knees and spine was found high in the urban and rural setting (Table 1); nodal and erosive forms of generalized OA were reported.19 OA hip was rather uncommon.19

3. **Rheumatoid arthritis (RA)**

COPCORD surveys in the Asia Pacific region have provided a much lower prevalence of RA than the widely quoted global

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**Fig. 1** — Diagnostic break-up (Percent) in the WHO Bhigwan (India) COPCORD survey 1996.
In India, the prevalence (Fig. 2) varied widely. In Bhigwan COPCORD, the adjusted point prevalence of RA was 0.55% (95% confidence intervals, 0.3–0.7) as per the ACR 1988 criteria and 0.7% based on clinical diagnosis; this was considered unusually high for a rural study. Also, a strikingly high prevalence (1639 per 100,000 population) in the young women (30–44 years) as compared to the rest of the World was observed in this rural population. After a ten year follow up in village Bhigwan (assuming geometric growth pattern; adult population about 4545), the period prevalence and incidence of RA was 1.17% and 0.044% (44/100,000) respectively.

The multisite India COPCORD surveys (Fig. 1) used a clinical approach and demonstrated a standardized prevalence of 0.34% (Table 1) and this is likely to be a robust projection. There were few differences reported for RA in Indian patients (i) an earlier onset in younger women (ii) lesser extent of extra-articular features, including subcutaneous nodules (iii) lower frequency of rheumatoid factor (RF). The Bhigwan COPCORD data on RA showed prevalence of RF as 41%, anticyclic Citrullinated Peptide as 60%, radiological erosions as 54%. The RF prevalence was similar to data from other Indian sites.

The well-known association of HLA DRB1* alleles (in particular *0401, *0404) and/or shared epitope with RA was largely derived from Caucasian studies. Similar observations were reported by the initial Indian studies on patients from tertiary hospitals. However, in contrast, only 8% patients of RA from Bhigwan COPCORD were positive for HLA DRB1*04, which was not significantly different from healthy controls. The odds ratio for HLA DRB1*1001 was significant (1.85). Subsequently, a comprehensive study based on COPCORD Pune population (urban and rural) validated the earlier Bhigwan findings and demonstrated significant association with shared epitope (mostly HLA DRB1*1001); other associated alleles were HLA DQA1*0103, DQB1*0201 and DPB1*0401.  

Fig. 2 — Standardized prevalence of rheumatoid arthritis (RA) in different population based survey sites: A Bone and Joint Decade India COPCORD (community oriented program control of rheumatic diseases) Study (2004–2010).
Tobacco consumption and smoking is a well-known risk factor in RA. COPCORD Bhigwan demonstrated rampant use of oral tobacco and showed a significant association (odds ratio 1.71 95% CI 1.44–2.04) with rheumatic MSK pain. This was further endorsed by urban COPCORD Pune (odds ratio 3.16 95% CI 2.88–4.05). However, a significant association between tobacco use and RA could not be demonstrated and this was possibly due to a relatively smaller sample size. Being an important public health preventive measure, tobacco use in all its forms, must be thoroughly condemned and stopped in patients suffering from RA and other inflammatory arthritis disorders.

RA is a recognized cause of premature atherosclerosis and coronary artery disease and related morbidity and mortality. In a cross sectional analysis of a case series of 60 fatalities, infections (23%) and cardiac disorders (40%) were the leading causes of death; other causes classified were 10% respiratory, 9% hepatic, 8% stroke and 10% miscellaneous. At least 30% deaths could be due to events associated with ischemic heart disease/myocardial infarction. Though detail medication in the 3 month period prior to death could not be confirmed in the large majority, at least half the cases were on long term methotrexate and low dose steroids.

4. Spondyloarthritis (SA)

A large spectrum of Spondyloarthritis are reported in Indian patients. An undifferentiated type characterized by a dominant asymmetric lower limb oligoarthritis and enthesitis (usually tendon-achilles) is the commonest type encountered in clinical practice. The latter are probably forme-fruste of the classical Reiter’s syndrome and are believed to be triggered by a wide array of gut and genitourinary related infections. A high frequency of HLA B27 was reported in patients of AS Delhi (92%), Chennai (83%) and Pune (73%); in healthy Indians it was 2.5% (Chennai), 6% (Delhi) and 9% (Pune).

Intriguingly, few COPCORD surveys reported psoriatic arthritis. A large sample based hospital study from South India reported a prevalence of 0.83% and described asymmetrical oligoarthritis (63%), symmetrical polyarthritis (32%), dominant distal interphalangeal (DIP) joint arthritis (25%) and predominant spondyloarthropathy (15%).

5. Systemic connective tissue disorders (CTD) & vasculitis

Very large population samples would be required to capture these relatively uncommon disorders. A point prevalence of 3 per 100,000 for SLE was reported in a Delhi survey. A crude incidence rate of 1 per 25,000 person years (4 per 100,000 populations per year) for SLE was found by the author in a long term follow up of Bhigwan COPCORD population. 21 cases of CTD were diagnosed amongst 68,273 inpatients during the period 1982–1986 in a large Armed Forces referral-teaching hospital in Pune providing an incidence of 0.03% in hospitalized patients.

Numerous hospital based series of systemic lupus erythematosus (SLE), scleroderma, mixed connective tissue disease, vasculitis have been published and the descriptions were generally similar to that reported from Western European and North American community.

SLE in India was comprehensively described based on non-standardized clinical data collected retrospectively from tertiary clinics. 63% and 32% patients of SLE from North and South India respectively reported neuropsychiatric manifestations. 65% of the SLE patients, often in the age group 20–30 years, were admitted with a neurological complication in an emergency setting.

Oral and ocular sicca is not too uncommon in patients with RA though the precise prevalence is not well reported. Amongst 24,500 cases seen over 20 years, only 3 cases were found to have primary Sjogren’s syndrome. However, a large series of Sjogren’s syndrome was recently presented (annual meeting of Indian Rheumatology Association 2012) from Vellore suggesting that the diagnosis was probably missed in clinical practice.

Several case series of vasculitis were published. The most frequent form is an undifferentiated or an overlap systemic necrotizing vasculitis. In a retrospective study from Mumbai, 100 patients (1.3%) were found to suffer from vasculitis amongst 7700 patients attending a rheumatology clinic. In this study, Henoch Schonlein purpura was the commonest disorder followed by medium vessel disease (polyarteritis nodosa, SLE) and large vessel disease (aortoarteritis, temporal arteritis); no case of polyangiitis with granulomatous (Wegener/WG) was reported. 0.9% cases in the latter study had RA which was quite similar to that reported from Delhi and Chennai. Several cases treated for pulmonary TB were actually found to be that of WG in case series from North India. Polyarteritis nodosa has been sparingly reported.

Takayasus’s arteritis or aorto-arteritis has been uncommonly reported and unlike elsewhere in the World is an important cause of renovascular hypertension in India. A large retrospective tertiary hospital based case series from South India identified only 5 patients of Takayasus’s arteritis. A task force of Indian rheumatologists recently recommended classification criteria and functional assessment in patients suffering from Takayasus arteritis.

30% Indians carry HLA B5 which is considered to be a marker for Behcet disease which per se seems to be uncommon in India. Though avascular necrosis, especially hip, is not too uncommon in clinical practice and an important cause for arthroplasty, the prevalence data is sparse.

6. Hyperuricemia and gout

It is generally stated that gout is probably less common in the Indians (Table 1) as compared to the Caucasians and we might be sharing this observation with several other Asian countries. In the ongoing Bhigwan COPCORD rural population (about 5000 adults) study, the author observed classical acute gout episodes in only 4 patients during a
closely monitored 10 years regular follow-up (unpublished). In a retrospective tertiary hospital study, 101 cases (95 males) amongst 20,000 patients attending rheumatology outpatients during the period 1989–2001 were diagnosed as acute gout. About 20% patients in the Chennai study had polyarticular onset. 20% patients in the Delhi study had renal calculi as compared to about 10% found amongst the Caucasians suffering from gout. Indian patients are predominantly under excretors of uric acid. Overall the pattern of Indian gout was similar to that seen in the Caucasians with some differences (1) lesser prevalence (35–75%) of classical first metatarsophalangeal affection as against about 90% in Caucasians (2) lesser (5–27%) prevalence of tophaceous gout as against about 35% in Caucasians.

With an increasing awareness and large data emerging on diabetes and other associated metabolic disorders in India, gout requires comprehensive evaluation based on population studies.

7. Infections

Infections are rampant in the Indian environment and a nuisance in rheumatology practice. Not only do we see primary infective arthritis, several infections are attributed to the drug induced immunosuppression. Of late, the concern for infections and tuberculosis has been further heightened with the increasing use biologic DMARDs and anti-tumor necrosis factor agents in particular.

Staphylococcus aureus, salmonella typhimurium, shigella shigae, brucella, mycobacterium tuberculosis and treponema pallidum infections were reported from a tertiary hospital rheumatology clinic. In this case series, Poncet’s disease was diagnosed in 0.23% patients.

Usually less than one-tenth of all patients of TB develop osteoarticular TB. TB of the spine and peripheral joints (usually monoarticular) is not too infrequent in our setting. With advanced imaging modalities (MRI) and newer mycobacterium detection methods (especially PCR), osteoarticular TB is being diagnosed early and often reported to be multicentric.

Leprous arthritis, usually a component of the lepra reaction, and mimicking seronegative RA or asymmetrical oligoarthritis, has been reported from rheumatology practice and needs a high index of clinical suspicion.

HIV is reported in case series to present a varied spectrum of rheumatic syndromes—from reactive arthritis to polymysitis like CTD profile.

The unprecedented Chikungunya (CHIKV) epidemic in 2006 in several regions of India led to several thousand patients suffering from chronic forms of rheumatic musculoskeletal pains. Several case series of musculoskeletal pain and arthritis following the acute episode were reported from central and South India. A wide spectrum of classifiable and undifferentiated rheumatic disorders was described. The phenotype was often similar to RA but invariably accompanied by significant soft tissue rheumatism (puffy feet, ankles, hands and wrists) and absence of RF and anti-CCP. In a clinic based case series, 66% naïve patients within 12 weeks of the acute phase showed elevated CRP (median value 15 mg/l, ELISA) but only 8% showed RF; 6% showed anti-CCP antibodies (second generation ELISA). Several known patients of RA, psoriasis and Reiter’s syndrome were described to develop an acute relapse following the acute phase.

The natural history of acute Chikungunya and its musculoskeletal sequel, and specific IgM and IgG antibody response and persistently elevated serum interleukin 6 were reported in a long term prospective rural community based large sample study from South Maharashtra during the 2006 epidemic. 4.1% and 1.6% community suffered from chronic musculoskeletal pains and arthralgia (mostly nonspecific and knee pains) at 1 and 2 years respectively. 5.8% cases in this community study tested seropositive for RF which was not higher than the seropositive RF in healthy Indians reported from the neighboring Bhigwan Pune COPCORD. Intriguingly, very few patients in the rural community study (Maharashtra) showed significant inflammatory arthritis beyond 6 months. A highly upregulated Th1 and Th2 cytokine phenotype was demonstrated during the acute illness which seemed to persist for several weeks (upto 24 weeks) beyond recovery and in those with chronic musculoskeletal pain and arthritis. In a community based controlled intervention trial of 24 weeks duration, the investigators failed to show any therapeutic advantage of chloroquine to treat early post CHIKV chronic MSK pains and arthritis.

Mathew et al (2011) described the post CHIKV chronic MSK and arthritis sequel in a 15 month observational study following a COPCORD survey in Kerala. The authors also used a validated Indian version of HAQ to document the functional impact and quality of life in patients suffering from chronic MSK pain and disorders following acute CHIKV.

An intriguing possibility of a distinct type of chronic post CHIKV arthritis was speculated but not yet confirmed. It needs to be determined whether post CHIKV arthritis per se can be erosive and progressive and lead to articular deformities. The author has observed some naive cases who developed erosive deformed knee and shoulder arthritis following acute CHIKV and required early arthroplasty. It is speculated that the incidence of rheumatic diseases has increased following the CHIKV epidemic but this remains to be investigated.

8. Juvenile idiopathic arthritis (JIA)

Several case series, mostly tertiary hospital based, were reported; polyarticular forms and enthesitis related arthritis were predominant (Table 2). The recently described ILAR classification system (Edmonton) were validated in a large case series from a community based rheumatology center. The role of hypermobility in musculoskeletal pains and arthralgia was described in large sample sizes studies. JIA is rather uncommon as compared to its adult counterpart and very few population based studies are reported Worldwide. The Bhigwan COPCORD survey reported a prevalence of 0.26 and
The current paper provides an overview of the spectrum of rheumatic disorders in the Indian community and an update on their likely prevalence. The Indian data is mostly based on the COPCORD initiative. Data on several other uncommon rheumatic disorders in the Indian community and an update on their likely prevalence. The Indian data is mostly based on the COPCORD initiative. Other studies have shown that the burden of rheumatic diseases in India is staggering, it is poorly recognized. To begin with, a large-scale population-based study is needed to assess the prevalence and burden of rheumatic diseases in India. Such a study would help in identifying the priority areas for the implementation of effective prevention and control strategies. The COPCORD initiative has provided a valuable framework for conducting such studies in different parts of the world.

Table 2 - Distribution of inflammatory disorders of childhood arthritis.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Lucknow 81 (n = 89)</th>
<th>Delhi 82 (n = 361)</th>
<th>Pune 83 (n = 272)</th>
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<tbody>
<tr>
<td>RA</td>
<td>14</td>
<td>24</td>
<td>9</td>
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<tr>
<td>OLA</td>
<td>34</td>
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<tr>
<td><strong>ILAR-JIA Subsets</strong></td>
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<td>Psoriatic arthritis</td>
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</table>

0.09 for juvenile chronic arthritis and rheumatic fever respectively.

9. Conclusions

Many more population surveys would be required to measure a true burden of rheumatic disorders. Evaluation of impact in terms of socioeconomics and functional ability should be carried out. Prevalence statistic is not a static measure. It needs to be repeated to know the changing patterns in epidemiology, risk factors and impact of health care interventions. In a billion plus population in India, a seemingly small prevalence translates into millions of patients.

The current paper provides an overview of the spectrum of rheumatic disorders in the Indian community and an update on their likely prevalence. The Indian data is mostly based on the COPCORD initiative. Data on several other uncommon disorders (example Handi-Godu disease and fluorosis and hypermobility) is currently sparse. The occupational overuse syndrome related to ‘prolonged and aggressive computer use and television viewing’ pertains mostly to musculoskeletal pains and arthralgia. It is on the increase and neglected in clinical practice. This enormous problem ought to be studied and preventive measures advocated.

Despite the fact that the burden of rheumatic diseases in India is staggering, it is poorly recognized. To begin with, a national community awareness and education drive should be initiated and spearheaded by the rheumatologists. Rheumatic disorders should be included in the Government health programs on non-communicable diseases.

Conflicts of interest

The author has none to declare.

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