Introduction
Musculoskeletal (MSK) disorders are fairly prevalent and have a significant impact on the functional ability of the individual, as well as on healthcare costs. The common disorders that contribute substantially to the burden of such disorders are osteoarthritis, low-back pain/backache, osteoporosis and rheumatoid arthritis (RA).

Inflammatory arthritides are led by RA. The estimated prevalence of RA is approximately 0.5%-1%. However, studies from the Pima Indian population showed significantly higher incidence and prevalence estimates for RA. The reported estimated prevalence of RA in northern Pakistan is 0.55%. Other connective tissue disorders have a variable prevalence. Ankylosing spondylitis (AS) prevalence varies with the prevalence of human leukocyte antigen B27 (HLA B-27). The exact prevalence of AS in Pakistan is largely unknown as studies pertaining to this are scarce. The mean AS prevalence per 10,000 population is considered to be 23.8 cases in Europe, 16.7 in Asia, 31.9 in North America, 10.2 in Latin America and 7.4 in Africa. Systemic lupus erythematosus (SLE) is 2 to 4 times more prevalent in non-white populations across the globe. Varying prevalence of SLE, ranging between 30-50 per 100,000 population has been reported among Asian countries. The prevalence of SLE in Indian population is comparatively low, reported at 3.2 per 100,000 population.

The current study was planned to study the frequency, demographic features, associated co-morbidities and extra-articular manifestations in patients with different rheumatological disorders.

Patients and Methods
The retrospective study was conducted at the Rheumatology Clinic of Jinnah Postgraduate Medical Centre (JPMC), Karachi, and comprised prospectively collected data of patients who presented between February 2004 and February 2014. The Rheumatology Clinic is the first and only public-sector facility for rheumatic diseases in the province of Sindh. Patients from other provinces of the country also seek treatment here.

Patients with degenerative joint diseases like osteoarthritis and osteoporotic fractures were excluded and so were those with the primary diagnosis of fibromyalgia. All cases with definitive diagnosis of inflammatory rheumatological diseases were registered. Validated diagnostic criteria were used for the diagnosis.

Data for all the registered cases were recorded in a pre-designed structured proforma that included all perspectives of history, examination, laboratory
investigations, co-morbidities, treatment and follow-up records. Data was analysed using SPSS 17. For descriptive statistics like gender, disease, co-morbidities and extra-articular features, frequency and percentages were calculated, while means and standard deviations were calculated for age and duration of disease.

Results
Of the 603 patients whose data was analysed, 460 (76.3%) were females, and 143 (23.7%) were males, with a female-to-male ratio of 3:1. The overall mean age of the patients was 35.2±12 years. The most affected age group was between 21-40 years i.e 367 (60.86%) patients, shown in Figure-1.

The commonest disorder was RA seen in 458 (76%) patients, followed by SLE in 42 (7%), AS in 32 (5.3%), mixed connective tissue disease (MCTD) in 22 (3.6%), systemic sclerosis in 12 (2%), juvenile RA (JRA) in 7 (1.2%), and antiphospholipid antibodies (APLA) in 6 (1%) patients. Miscellaneous disorders contributed 0.2-1% patients individually. These include inflammatory myopathies in 5 (0.9%) patients, psoriatic arthritis in 4 (0.7%), Takayasu’s arteritis in 3 (0.5%), overlap syndrome in 3 (0.5%), Sjogren’s syndrome in 2 (0.3%), gout in 2 (0.3%), Behcet’s disease in 1 (0.2%) and Still’s disease in 1 (0.2%) patient (Figure-2).

In terms of ethnic distribution, 264 (44.1%) patients were immigrant Urdu-speaking, 89 (14.8%) Sindhi, 65 (10.8%) Punjabi, 118 (19.6%) Pathan, 17 (2.8%) Balochi, 9 (1.5%) Gujrati, 21 (3.5%) Hindko, 12 (2.0%) Saraiki, 5 (0.8%) Gilgity, and 1 (0.2%) was an Egyptian.

The commonest presenting symptom was joint pain seen in 573 (95%) patients; the mean duration of disease being 3.2±2 years. Only 30 (5%) patients presented with other symptoms like rash, oral ulcers, photosensitivity, seizures, muscle weakness, digital gangrene, skin tightening, thrombo-embolic events such as stroke and deep vein thrombosis (DVT) etc.

Co-morbidities were seen in 82 (13.6%) patients; the commonest being hypertension (HTN) in 45 (7.4%), followed by diabetes in 10 (1.7%), hypothyroidism in 8 (1.3%), tuberculosis (TB) in 7 (1.2%), chronic hepatitis C in 5 (0.8%), asthma in 3 (0.5%), ischaemic heart disease in 2 (0.3%), hyperthyroidism in 1 (0.2%) and chronic hepatitis B in 1 (0.2%) patient.

Extra-articular features were present in 341 (56.7%) patients. The predominant ones included oral ulceration in 84 (13.9%), fatigue in 57 (9.5%), skin rash and alopecia in 40 (6.6%), dry mouth in 34 (5.6%), ocular dryness in 23 (3.8%) and photosensitivity in 20 (3.3%) patients. Other manifestations like respiratory symptoms were seen in 16 (2.7%) patients, Raynaud’s phenomenon in 15 (2.5%), skin tightening in 10 (1.7%), reduced mouth opening in 7 (1.2%), genitourinary complaints in the form of genital ulceration, urethral discharge or recurrent urinary tract infections (UTIs) in 13 (2.1%) patients. Psychosis was reported in 4 (0.7%) patients, headache in 4 (0.7%), eye symptoms in 3 (0.5%), skin discoloration in 3 (0.5%), stroke in 1 (0.2%) and DVT in 1 (0.2%) patient. Patients with sero-negative spondyloarthropathies had few extra-articular features. Among the 341 patients

Only 103 (17.1%) patients had earlier been on treatment with disease-modifying anti-rheumatic drugs (DMARDs) or steroids before registration in the Clinic. Treatment instituted at the Clinic included DMARD alone in 260 (42.6%) patients, combination of DMARDs and steroids in 155 (25.7%), immune-suppressive drugs in 16 (2.7%) and only non-
steroidal anti-inflammatory drugs (NSAIDs) in 20(3.3%) patients. Use of biological agents was limited because of cost constraint. Anti-tumour necrosis factor (TNF) therapy (etanercept) was used in only 2(0.33%) patients with AS, and anti-interleukin-6 (IL-6) (tocilizumab) in 1(0.16%) case of JRA.

**Discussion**

For provision of prompt and effective healthcare, knowing the disease prevalence and pattern is of paramount importance. Although, the facts regarding the rheumatological diseases in the developing countries are less well known, but epidemiological studies have shown that the spectrum of rheumatological disorders is similar across the globe. However, the impact of disease tends to be higher in developing countries due to a delay in diagnosis or lack of access to adequate healthcare facilities. We have provided an estimate of the burden of different rheumatological disorders in a dedicated Rheumatology service of a public-sector hospital. This reflects a snapshot of the growing burden of different rheumatological disorders in a multi-ethnic, low-income population representative of the entire country as can be seen from the various ethnicities reported in our study. These diseases constitute a major disease burden in a relatively young population. RA was the most common disorder, representing 76% of total rheumatological disorders, followed by SLE.

Studies have shown increased frequency of associated co-morbidities in rheumatoid and other musculoskeletal disorders, often with a poor outcome. HTN was the commonest co-morbidity in our patients. Increased frequency of HTN may be due to the immune-mediated inflammation in these conditions, which causes the release of inflammatory cytokines and plays a key role in atherosclerosis, hence leading to HTN and an increased cardiovascular (CVD) risk. Studies indicate a high prevalence of HTN and a 48% increase in the risk of CVD in patients with RA compared to the general population. Premature atherosclerosis is well-documented in SLE as well. An increased mortality has been reported in SLE patients, and the factors associated with high mortality include female gender, younger age, shorter duration of disease, and black/African American race.

Extra-articular manifestations can occur at any point during the disease course in most rheumatological disorders and these may involve any system of the body, and their frequency has been reported to vary among different populations. Moreover, extra-articular involvement is seen frequently in patients with severe active disease, reflecting longstanding active inflammation and an associated increased mortality risk. In a United States study, extra-articular manifestations were seen in 42.7% of RA patients during a median follow-up of 11.8 years, while a study in Italy reported it in about 41% patients, either in the beginning or during the course of the disease.

In this era of DMARD and availability of biological agents for treatment of rheumatological disorders, the prevalence of extra-articular manifestations has declined, leading to a change in the natural course and presentation of the disease. A significant proportion of our patients had variable range of extra-articular features. Over 80% of our patients were treatment-naïve despite a mean duration of illness of 3.2 years. Hence, it is not surprising that extra-articular manifestations were seen in nearly 57% patients. In contrast, an earlier study from Pakistan reported only 3.47% of extra-articular manifestations in its RA cohort. Only 17% patients had received erratic DMARD or steroids before registration,
and hence any treatment was unlikely to have affected the frequency of extra-articular manifestations recorded at the first presentation in this clinic. Delayed presentation probably accounts for the fairly large number of patients with extra-articular features in the study. This might be due to poor ability to access healthcare, as well lack of availability of specific long-term healthcare services for rheumatological disorders. The high prevalence of oral ulcers as an extra-articular feature can be attributed to the additive effects of high intake of betel-nuts and oral tobacco or other addictions, as well as micro-nutrient deficiencies as confounding factors. Oral and ocular dryness can be a manifestation of secondary Sjogren's syndrome, seen commonly with RA. Kerato-conjunctivitis sicca has been reported in 11.6% patients with RA with symptoms of persistent oral or ocular dryness.23

Patients with MCTD in this study had variable combinations of SLE, systemic sclerosis (SSc) or RA at disease onset or during clinical course, with polyarthralgia being the commonest. SLE patients had a wide variation in clinical presentation, but the commonest clinical manifestation was joint involvement, ranging from mild arthralgia to non-erosive arthritis. This is comparable to the reported studies, which show arthritis as the commonest manifestation in SLE patients.24

Some non-specific features such as fatigue was also seen in a significant number of patients. Pain, fatigue and physical disability are important parameters with substantial effects on the quality of life. Although subjective fatigue has been reported in most musculoskeletal disorders, no clear relationship exists between fatigue and inflammatory activity. Psychosocial variables appear to be associated with RA-related fatigue.25,26 No patient presented to the clinic with an exclusive diagnosis of fibromyalgia. Other manifestations like gastrointestinal discomfort, ranging from simple heartburn to nausea and vomiting could be due to constant NSAIDs or DMARD therapy itself.

There is some published information from Pakistan about the prevalence of various rheumatological diseases from over 20 years ago, but the study population was not representative of the entire country.3 A set of patients from a public-sector hospital in Karachi is likely to represent all ethnicities of Pakistan and the disease pattern in them, as can be seen from this study. Moreover, the prevalence of diseases without a definite aetiology can change with the passage of time and changing circumstances. This meticulously maintained and reported long-term data may also contribute to a better understanding of rheumatological diseases and their impact on the lives of affected patients. Additionally, comparison of the disease pattern and demographic features with other studies from the same geographical region, as well as from the western countries, will enhance the understanding of the causal factors and triggers of these immune-mediated inflammatory disorders. The study emphasises the need for establishment of more rheumatology facilities in different hospitals of the country and allocation of appropriate resources for the same.

**Conclusion**

The sizeable cohort of patients with definite rheumatological disorders from a multi-ethnic, low-income group of patients in a public-sector hospital setting suggested that the pattern of inflammatory rheumatological diseases was similar as reported from the rest of the world. However, patients with chronic inflammatory disorders presented late, received delayed or piecemeal DMARD treatment due to poverty, lack of awareness, as well as rudimentary healthcare facilities for chronic rheumatological disorders. Dedicated centres for long-term comprehensive care of rheumatological diseases are required to ensure prompt diagnosis and adequate disease control for ensuring better health and quality of life.

**References**