

REVIEWS

Rheumatic disease in elderly population, how different from the conventional presentations?

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Abstract

Better healthcare facilities and therapeutic advances have contributed to a steep rise in geriatric population in India and all over the world. Hence the focus of medical/healthcare field has shifted to the management of chronic diseases seen in the elderly population. Rheumatologic diseases in elderly can be divided into: 1) diseases that primarily occur in the elderly population and 2) diseases usually occurring in the young decade and progress with age or have a late onset variant. The review mainly focuses on the late onset variants of various diseases including their difference from the conventional presentations and their diagnostic and therapeutic challenges in the elderly population.

Keywords: Rheumatic disease, systemic lupus erythematosus, geriatric population, rheumatic arthritis

Introduction

The United Nations defines a country as 'ageing' when the proportion of people >60 reaches 7% and India qualifies as an ageing nation, as per this definition. In 2000, the estimated proportion in the country was 7.7% and is expected to reach 12.6% by 2025. Thus with more mouths to feed and less hands to earn, there is an increasing burden on the resources of the country.¹

The number of elders suffering from chronic debilitating disorders increases with increase in lifespan.² Rheumatic musculoskeletal problems are a major cause of morbidity in elderly population. The prevalence of musculoskeletal problems reported in a study in elderly population from rural and urban areas of north India was 65.7% in males and 75.4% in females.³ The rheumatic diseases in elderly can be broadly divided into two (table 1). Rheumatic diseases in elderly can also have an early onset with major clinical impact.

The major therapeutic and diagnostic challenges encountered in geriatric population include:

1. Increase in the prevalence of autoantibodies with age.
2. Markers of inflammation such as erythrocyte

sedimentation rate (ESR) and c-reactive protein (CRP) have high normal values in the elderly, which may impair their effectiveness in identifying systemic inflammation.⁴

3. Diagnostic criteria used for these diseases have been developed based on the clinical and literature evidence in younger population and they may not be accurate in the elderly population.⁵
4. Therapeutic challenges in the elderly such as polypharmacy, comorbid conditions and even normal alterations in physiology, which affect the pharmacokinetics, pharmacodynamics, and adverse effects of many medications have to be considered before choosing the optimal therapeutic approach.⁶

The present review discusses various late-onset rheumatologic diseases, their differences from routine presentations, and the effective clinical approach to diagnose and manage them.

Rheumatoid arthritis

Rheumatoid arthritis (RA), the most common autoimmune inflammatory arthritis, typically manifests as a chronic, symmetrical, polyarthritis involving both large and small joints of hands and feet. The peak age of incidence is between 35 to 55 years. Late-onset rheumatoid arthritis

Table 1: Classification of rheumatic diseases in elderly population

Diseases primarily occurring in elderly population	Late onset diseases with varied presentation in elderly
Polymyalgia rheumatica Giant cell arteritis Osteoarthritis Crystal arthritis Paraneoplastic syndromes Generalized pain syndromes Osteoporosis	Rheumatoid arthritis Systemic lupus erythematosus Seronegative spondyloarthropathy Systemic sclerosis Gout

(LORA) has been defined as onset of RA after the age of 60 years.⁷ However, 65 years has been taken as the age cut-off.^{8, 9} LORA has a prevalence of around 2% in RA patients.^{5, 10} Most studies suggest that the female predominance reduces from 2-3:1 in early onset RA to 1.5:1 to 1:1 in LORA.^{11, 12}

Genetics

Literature evidence substantiates the association between human leukocyte antigen-D related (HLA-DR) genes and RA susceptibility and severity. HLA-DR phenotypes are similar in early onset RA (EORA) and LORA. However, the frequency of HLA-DRB1*0401, which is a more severe variant, is less common and HLA-DRB1*0101 is more common in the LORA.¹² Patients with seronegative LORA exhibit increased frequency of DRB1*13/*14 gene, which is also observed in isolated cases of polymyalgia rheumatica (PMR).¹³

Clinical picture

As per earlier studies, LORA seemed to have higher frequency of abrupt onset, large joint predominant arthritis mimicking PMR, more benign course, and less IgM rheumatoid factor (RF) positivity.¹⁴ However later, larger studies have shown that upon adjusting the duration of disease, there is not much difference in the clinical picture, the severity of the disease, the progression of the disease, and in the amount of joint damage.¹⁵ The first difference to be noted in LORA when compared to EORA is the pattern of joint involvement- more commonly involves large joints such as shoulders, proximal interphalangeal joint (PIP), metacarpophalangeal joint (MCP) and metatarsophalangeal joint (MTP). Wrist, knee, and hip involvements are not different between the two groups. Secondly, classical rheumatoid hand deformities, interstitial lung disease and Sjögren's syndrome are significantly lower in LORA than in EORA; whereas weight

loss, myalgia, lymphadenopathy, PMR- like syndrome and neuropathy are more common.¹¹ Lastly, EORA patients tend to suffer more from RA-related comorbidities such as cardiovascular disease, chronic kidney disease, and osteoporosis.¹⁵

LORA has many similarities with PMR such as age, frequency of large joint involvement, and raised serum inflammatory markers, while PMR patients can have peripheral synovitis. LORA patients have a lower plasma viscosity and a lesser dramatic response to steroids.¹⁶ Pitting edema of the hands, similar to those found in remitting seronegative symmetrical synovitis with pitting edema (RS3PE) can be seen as an extra-articular manifestation of LORA, unlike in EORA, and tends to have a favorable prognosis.⁸

Investigations

Antibodies like serum rheumatoid factor (RF), anti-cyclic citrullinated peptide (ACPA), anti-nuclear antibody (ANA), anti-Ro, and anti-La occur in lesser frequency among patients with LORA compared to EORA.¹¹

Radiological changes

Similar to EORA, joint erosions in LORA can be damaging. Although earlier reports suggested less radiological damage in LORA, recent studies have shown that the duration of disease rather than the age at onset determines the degree of joint erosions (Fig.1).¹⁷ Serum RF, DR4 positivity, and elevated inflammatory markers at onset are associated with poor radiological outcome, irrespective of age of onset.⁹

Disease activity

In various studies, joint damage indices have been shown to be similar when adjusted for age.^{9, 17, 18} Yang *et al.* have reported that DAS 28CRP and clinical disease activity

index (CDAI) are similar between EORA and LORA. LORA patients tend to have a lower simplified disease activity index (SDAI) and better functional indices such as M-HAQ.¹⁹ Female sex and greater damage at presentation are associated with poor outcomes similar to EORA.⁹

Treatment

There are no separate treatment recommendations for this group. Non-steroidal anti-inflammatory drugs (NSAIDs), and disease modifying anti rheumatic drugs (DMARDs) remain the first-line of management with corticosteroids as bridging therapy. Methotrexate remains the most commonly used DMARDs. There is higher incidence of bone marrow aplasia.²⁰ Routine blood tests for cell counts, hemoglobin, and platelets are a must. For hydroxychloroquine (HCQ), baseline ophthalmologic evaluation followed by annual examination is recommended in the elderly. Biologics, especially anti-TNF, have shown good response in the management of elderly.²¹ Various studies have observed that DMARDs are used less frequently in the LORA group.^{18, 22} The probable reason could be earlier notion of LORA being more benign and increased number of age-associated co-morbidities. However, with more recent studies suggesting LORA to be as aggressive as EORA, it is prudent to use DMARDs as aggressively as in EORA, provided they are permissible with co-existing illnesses.^{15, 22} Due to the same reason, multidisciplinary treatment approach is recommended.

Prognosis

LORA patients tend to have a higher remission rate than younger-onset RA (YORA).⁹ The rate of radiological progression, extra-articular manifestations, and disease-related comorbidities are similar when adjusted for the duration of disease.¹⁵

Spondyloarthritis

The group seronegative spondyloarthritides (SpA) share certain unique features: absence of RF and subcutaneous nodules, involvement of the axial skeletal system, especially the sacroiliac joints, similar genetic background, and HLA B27 as the most common shared gene. SpA includes ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), inflammatory bowel disease (IBD)-related arthritis, and undifferentiated spondyloarthritis (USpA). The recently developed (Assessment of SpondyloArthritis international Society criteria (ASAS) for axial SpA include patients with back pain ≥ 3 months and age at onset < 45 years.²³ Hence the general notion is that

onset of SpA does not occur beyond 45 years. But it must be remembered that the classification criteria are meant to create a uniform cohort for research activity and do not exclude the diagnosis of SpA beyond the age of 45 years. Unlike LORA, late onset SpA (LOSpA) does not have a clear cut age cut-off and most series consider 45-50 years as the cut off.²⁴⁻²⁸

There are case reports or case series of almost all types of SpA, but epidemiologic studies on the prevalence of LOSpA are limited. The total incidence rate of AS was found to be 7.3 per 100,000 person-years; the incidence rate after 55 years was 2.2/100,000 person years in a population-based descriptive study from USA.²⁹ Data from the German AS Society demonstrated that 6% of AS patients had onset of symptoms after 40 years. Around 7.9% of AS patients in a study from Turkey had the disease onset after 50 years.³⁰ The Spanish (Registry of Spondyloarthritis of the Spanish Society of Rheumatology (REGISPONSER) data showed that 44 (3.5%) out of 1257 patients with AS had their disease onset after 50 years.²⁷ In the largest cohort of the Brazilian registry involving 1424 patients with SpA, the onset after 45 years was noted in 151 patients (10.6 %), and after 50 years in 81 patients (5.8 %).³¹ Disease onset was rarer after 55 years. From Asia, the only published data from Taiwan showed an incidence of 3.5% of LOSpA in a cohort of 546 SpA patients.³² PsA is more common in the elderly than believed. In 2009, Wilson *et al.* published time trends in a group of 147 incident PsA patients over 30 years (90 men and 57 women) meeting the CASPAR criteria.³³ Among the study cohort, the disease onset reported after the age of 50, 60, and 70 years were 48 (32.6%), 23 (15.6%), and 10 (9.3%) respectively.

Clinical features

There is no difference between late- and early-onset of AS according to sex and family history of SpA.²⁷ LOSpA patients show more frequent involvement of the cervical spine and peripheral arthritis of both upper and lower limbs as presenting manifestations than early-onset SpA.²⁷ There is lesser incidence of low backache and hip involvement in LOSpA.³² LOSpA patients have a higher incidence of mixed forms (axial and peripheral joint disease) during the course of the disease.²⁷ Radiological progression, disease activity, non-hip surgical interventions, and prevalence of extra-articular manifestations are similar between early- and late-onset SpA.³⁴

Late-onset USpA has the same wide spectrum of

manifestations as in early onset USpA including enthesitis, dactylitis, and uveitis in various combinations.²⁸ It can mimic PMR, RS3PE (Remitting Seronegative Symmetric Synovitis with Pitting Edema), and even reflex sympathetic dystrophy at onset.^{28, 35-37}

Late-onset PsA presents more commonly with peripheral manifestations than axial. Unilateral sacroiliitis and silent axial involvement is more common than bilateral sacroiliitis, while isolated axial disease is less compared to early onset PsA. They also tend to present early, and have more erosive and rapid radiological progression after initial 2 years. They have a lower frequency of family history and HLA-B27 positivity.²⁸

Late-onset ReA is not very common. Amor *et al.* had estimated 13% of ReA arthritis to be late onset. Dubost *et al.* had found only 4 out of 105 SpA patients to have ReA.³⁸

Diagnostic criteria

There are no diagnostic criteria for late onset SpA. The ASAS criteria for axial and peripheral SpA, which have been recently validated in >45 years of age, await validation for use in LOSpA. The radiographic criteria have been less useful in the late onset SpA, considering the age-related changes in the sacroiliac joints.³⁸ Nevertheless, the inclusion of MRI in ASAS criteria will enable the diagnosis of LOSpA with more certainty. CASPAR criteria for PsA have similar sensitivity in both early- and late-onset PsA.²⁸

Treatment

The treatment of LOSpA is similar to early onset SpA. NSAIDs are the first-line therapy. But the response is less when compared to early onset SpA.²⁵ Elderly patients should be closely monitored for side effects such as gastric ulcers and renal damage. Corticosteroids are used more frequently in late-onset SpA, but there is no clinical trial-based evidence.²⁵ DMARDs are used based on the data available on early-onset SpA. Sulfasalazine is the preferred DMARD, especially in peripheral SpA. Side effects, such as agranulocytosis is more common in the elderly. Other DMARDs are less commonly used. There are no trials of anti-TNF agents in LOSpA. Anti-TNF agents seem to be less effective and have higher rate of infections in the late-onset group.³⁹

Outcome

Age at onset does not seem to affect the prognosis and

LOSpA should be treated as early-onset disease with precautions for comorbidities.²⁸

Systemic lupus erythematosus

It is an autoimmune disease with multi-system involvement and variable presentations. As a result, recent trends have been to identify subsets of patients with SLE. One such subset, which was ignored initially, comprises of patients with age of onset of disease after the 5th decade. As such there are a number of studies published on late-onset SLE, but there is not much data from Asian countries. The onset of SLE among the Asian SLE population beyond the age of 50 years is reported to be 4-10%.⁴⁰⁻⁴² Though SLE is more common in females, the female preponderance reduces in late-onset disease.⁴²⁻⁴⁵ This drastic change is due to the absence of female sex hormones in elderly patients.^{42, 46} There was an increased prevalence of HLA-DQA1*0103 in Chinese patients with late-onset disease. These findings suggest that a subgroup of late-onset patients may experience milder disease and that the risk conferred by the HLA-DQA1*0103 may be significant.⁴⁷

Clinical features

The disease is more insidious in onset and the period of onset to diagnosis varies from 12-24 months.^{40, 45} The clinical features are usually mild and comparable with early-onset disease.^{40, 42, 48-51} In contrast to early-onset disease, these patients present with more non-specific symptoms such as weight loss, arthralgia, myalgia, weakness and fatigue. Diagnosis is difficult, as these symptoms mimic general aging problems. These patients fulfill very few American College of Rheumatology criteria for SLE at diagnosis. The cutaneous involvement is less, while cytopenia is common.^{52, 53} Major organ involvement in the form of central nervous system (CNS), renal, and cardiopulmonary manifestations occur less frequently compared to early onset SLE. (Table 2).^{42, 45, 51} Despite this fact, long-term prognosis in patients with renal involvement is not necessarily better, since they tend to accrue more renal damage and experience a decreased overall survival.^{44, 49}

Immunological features

Patients with late-onset SLE may have a different autoantibody profile compared to patients with young-onset disease. Late-onset SLE is characterized by a lower frequency of anti-RNP and anti-Sm antibodies, a variable frequency of anti-dsDNA antibodies, hypocomplementemia and, a higher frequency of RF, anti-Ro, and anti-La

Table 2: Cumulative clinical and immunological features of late-onset SLE in Asian population

Features	Shaikh <i>et al.</i> , 1995. ⁵¹ n- 17	Kwan ho <i>et al.</i> , 1998. ⁴² n- 25	Feng <i>et al.</i> , 2014. ⁴⁰ n- 195	Choi <i>et al.</i> , 2015. ⁴⁸ n- 25
	n (%)			
Malar rash	12 (70.6)	7 (28)	120 (61.5)	11 (44)
Discoid rash	12 (70.6)	0	120 (61.5)	4 (16)
Photosensitivity	-	2 (8)	120 (61.5)	11 (44)
Serositis	-	3 (12)	51 (26.2)	3(12)
Oral ulcers	5 (29.4)	5 (20)	120 (61.5)	2 (8)
Arthritis	9 (52.9)	21 (84)	122 (62.5)	13 (52)
Alopecia	8 (47)	4 (16)	-	2 (8)
Sicca syndromes	-	3 (12)	-	5 (20)
Raynaud's phenomenon	0	2 (8)	-	9 (36)
Fever	-	10 (40)	-	2 (8)
Myalgia	-	1 (4)	-	
CNS involvement	2 (11.8)	0	16 (8.2)	1 (4)
Nephritis	5 (29.4)	1 (4)	90 (46.2)	3 (12)
Pancytopenia	-	1 (4)	137 (70.3)	
Lymphopenia	11 (64)	11 (44)	94 (48.2)	19 (56)
Hemolytic anemia	1 (5.9)	5 (20)	-	6 (36)
Thrombocytopenia	6 (35)	5 (20)	63 (32.3)	5 (20)
ANA	14 (82)	25 (100)	178 (93.7)	24 (96)
Complements	11 (64)	-	-	13 (52)
Anti-dsDNA	10 (58.8)	21 (84)	111 (59)	7 (28)
Anti-Ro	1 (5.9)	15 (60)	-	13 (52)
Anti-La	1 (5.9)	2 (8)		6 (24)
Anti-Sm	0	6 (24)	42 (23)	4 (16)
Anti RNP	2 (11.7)	5 (20)	-	10 (40)
Rheumatoid factor	-	8 (32)	-	-

antibodies.^{40, 42, 44} The presence of anti-Ro and anti-La makes them more prone to develop Sjögren's syndrome.^{53,}

⁵⁴

Treatment

Guidelines are similar to that in the younger age group. Antimalarial agents, such as HCQ, should be prescribed to all patients as they decrease the frequency of flares and also improve survival.⁵⁵⁻⁶⁰ NSAIDs or low-dose glucocorticoids can be used; however, the diminished

renal reserve commonly seen in elderly individuals should be taken into account, particularly with regard to NSAIDs.⁴⁹ Moreover, the increased risk of developing osteoporosis and atherosclerosis should be considered.⁶¹ The involvement of main organs such as the kidneys, lungs, blood or the CNS may require high doses of glucocorticoids and the use of immunosuppressant drugs such as cyclophosphamide, azathioprine and mycophenolate mofetil. These drugs should be used with great caution.⁶²

Outcome

Despite the fact that patients with late-onset SLE have a mild disease with less major organ involvement, they do not have a better outcome than patients with disease with adult onset. These patients tend to accrue more damage than patients with disease onset at a younger age, probably due to the impact of age and associated comorbidities. These patients have more cardiovascular, ocular, musculoskeletal damage and higher chances of malignancy compared to conventional patients.⁶³ In fact, mortality rates have been found to be higher in these patients due to infections, with 5, 10 and 15-year survival rates being 80.4%, 56.5% and 31.7% respectively.^{40, 41, 43}

Gout

Gout is a heterogeneous disorder that results in the deposition of uric acid salts and crystals in and around joints and soft tissues. Elderly-onset gout (EOG) is appearance of gout after the age of 60 or 65 years and present with atypical findings. It has equal incidence in both sexes. Though it has been reported as the most common inflammatory arthropathy of the elderly, there is no epidemiological data. Its incidence among elderly has risen worldwide due to an increase in risk factors such as renal diseases, hypertension, coronary artery disease, metabolic syndrome, long-term diuretic use and a diet rich in purines.⁶⁴⁻⁶⁶

Clinical features

The clinical presentation is often polyarticular with insidious onset. The joint involvement can be symmetrical or asymmetrical. Small joint involvement occurs early in older females with gout.^{64, 66} There is early development of tophi and sometimes patients present with tophi at multiple atypical sites and sometimes in vertebral locations. Tophus is more associated with patients EOG with metabolic syndrome.⁶⁷ In a series of patients with late-onset gout, 25% of women (zero for men) had initial symptoms in the fingers. In these patients, gouty attacks were less painful and more frequently noted on interphalangeal joints affected by osteoarthritis, particularly on Heberden's nodes.⁶⁸ Diuretic use has been reported in over 75% of patients with late-onset gout (almost 100% in women). As a result, EOG can also be termed as 'diuretic gout'.⁶⁹

Diagnosis

Clinically, the diagnosis of gout is similar to early-onset gout, based on clinical and laboratory findings. The identification of monosodium urate crystals (negatively

birefringent needle-shaped crystals) in synovial fluid, tissue or tophi through polarizing microscopy is the gold standard.⁷⁰

Treatment

The management of EOG is challenging and unsatisfactory owing to lower creatinine clearance and presence of multiple comorbidities. Considering the toxicity profiles, colchicine and NSAIDs should be used with care in older adults.⁷ NSAIDs with short plasma half-life (such as diclofenac and ketoprofen) are preferred, but these drugs are not recommended in patients with peptic ulcer disease, renal failure, uncontrolled hypertension or cardiac failure. Colchicine is poorly tolerated in the elderly. Intra-articular and systemic corticosteroids should be used for treating acute gouty flares in EOG with medical disorders contraindicating NSAID therapy. Urate-lowering drugs are indicated for the treatment of hyperuricemia and chronic gouty arthritis. Uricosuric drugs are poorly tolerated by most EOG patients and are associated with renal involvement. Allopurinol is the urate-lowering drug of choice, but its use in EOG is associated with an increased incidence of cutaneous and severe hypersensitivity reactions. To reduce this risk, it is recommended to start the dose with 50 to 100 mg on alternate days and increase to a maximum daily dose of about 100 to 300 mg, based upon the patient's creatinine clearance and serum urate level.^{72, 73} The newer urate lowering drug febuxostat is a better choice for elderly people. An analysis of 374 elderly gout subjects demonstrated that urate lowering therapy with febuxostat 80 mg or 40 mg once daily lead to significantly more subjects achieving a therapeutic goal of target serum uric acid than commonly used doses of allopurinol (200 or 300 mg). It was well tolerated, despite high rates of comorbidities and concomitant medication use.⁷⁴ There is no data on the use of interleukin 1 inhibitors in EOG. Asymptomatic hyperuricemia is not an indication for long-term urate-lowering therapy; the risks of drug toxicity often outweigh any benefit.⁷

Systemic sclerosis

Systemic sclerosis (SSc) is an uncommon multisystem autoimmune disease characterized by immune abnormalities, fibrosis of the skin and internal organs and an obliterative vasculopathy. It is a heterogeneous disease ranging from mild limited cutaneous features to widespread skin thickening. Whereas SSc affects adults across all ages, with peak age of onset between 40 to 50 years. The true incidence, prevalence and phenotype of

Table 3: Characteristic differences between early- and late-onset rheumatic diseases

Characteristics	Early onset	Late onset
Rheumatoid arthritis (RA)		
Onset	Usually between 35-55 years	After 60 years
Frequency	Most patients	2% of all RA patients
Female:male ratio	2-3:1	1.5-1:1
Genetics	HLA DRB1*0401 more common	HLA DRB1*0101 more common
Clinical feature	Insidious onset, small joint predominant with classical deformities	More frequently abrupt onset, large joint predominant, less commonly with deformities
Associated features	ILD and Sjögren's syndrome more common	Constitutional polymyalgia rheumatica like features more common
Antibodies	Rheumatoid factor and anti-cyclic citrullinated peptides more common	Less common
Spondyloarthritis		
Onset	Less than 45 years	More than 45-50 years
Frequency	More than 90%	Less than 10%
Joint involvement	More axial usually involving sacroiliac joints and lumbar spine	Cervical spine and peripheral joints are more commonly involved
HLA B27	More than 90% positive	Around 70%
Undifferentiated spondyloarthritis	Less common	More common
SLE		
Onset	Before 50 years	More than 50 years
Female: Male ratio	10:1	3.2-7.6:1
Disease nature	More acute	More insidious
Cutaneous features	More common	Less common
Cytopenias	Less common	More common
Major organ involvement (CNS/renal/cardiopulmonary)	More common	Less common
Autoantibodies	Anti-Sm and Anti-RNP are more common than elderly	Anti-Ro and Anti-La; rheumatoid factor more common
Gout		
Onset	Defined as onset less than 25 years Usual onset of gout in adults: 4th-6th decade	More than 60-65 years
Gender difference	More common in males	Equal sex distribution
Initial joints involved	Most commonly 1st MTP	Late-onset gout in females, 25% have initial involvement of interphalangeal joints
Tophi	Develop late	Develop early

HLA: human leukocyte antigen; ILD: interstitial lung disease; SLE: systemic lupus erythematosus; CNS: central nervous system;

RNP: ribonucleoprotein; MTP: metatarsophalangeal joint

Characteristics	Early onset	Late onset
Systemic sclerosis		
Onset	Before 60 years	After 60 years
Frequency	More than 80%	Less than 20%
Raynaud's phenomenon and digital ulcers	More common	Less common
ILD and pulmonary hypertension	Common	More common
Conduction disorders	Less common	More common
Anti-centromere antibodies	Less common	More common
Mortality rate	Lower	Higher

ILD: interstitial lung disease

late onset SSc is not known. Only 6 studies have been published till date, out of which 2 are from Asia.⁷⁵⁻⁸⁰ Late-onset SSc constitute about 9-19% of the SSc patients.^{75, 77, 81} It is defined as disease onset beyond the age of 60 years and in some studies as disease beyond the age of 75 years.^{75, 79}

Clinical features

However, SSc is not an uncommon condition and it is rarely considered in elderly patients, Sometimes the disease is underdiagnosed due to several reasons. The skin changes may be overlooked either because they are minimal, possibly restricted to mild tethering of skin in the hands, or because they are considered as features of ageing. In the absence of skin changes, the diagnosis is less frequently considered especially in the elderly in whom multiple vague symptoms such as dysphagia, Raynaud's phenomenon and arthralgia are more frequently attributed to multiple pathologies rather than a multi-system disorder.⁸⁰

Late-onset SSc is usually diagnosed early and full spectrum of SSc symptoms are seen in patients with the following differences. Limited cutaneous disease is a more commonly seen variant in elderly patients.^{75, 78} These patients exhibit lower frequency of digital ulcers and Raynaud's phenomenon, and higher cardiopulmonary morbidity in the form of interstitial lung disease, pulmonary hypertension, heart conduction disorders and systemic hypertension.^{75-77, 81} Amongst the immunological variables, these patients are more anti-centromere (ACA) and RF positive, while ANA positivity is similar to early-onset SSc.^{76-78, 81} Due to more ACA and less digital ulcers, there is mild peripheral vascular involvement. Other factors that probably play a role include: the normal immune system senescence, aging-related changes of the skin's

microcirculation, more cold avoidance among the elderly and the fact these patients are more likely to be on drugs like aspirin and calcium channel blockers for their comorbidities.^{75, 76, 78}

Prognosis

The mortality rate is higher and median survival time from diagnosis has been found to be variable when compared to adult onset and early onset SSc.^{75, 78} These patients have more associated comorbidities, disabilities and higher chances of malignancy.^{77, 81}

Treatment

Principles of treatment remain same as for young onset. The treatment is individualized according to organ involvement and presence of comorbid conditions.

The differences between early and late onset rheumatologic conditions have been summarized in table 3.

Conclusion

Rheumatic diseases with late age of onset exhibit a clinical and immunological profile different from the conventional. Underdiagnosis of these diseases in elderly population is a major concern. Expert opinion of a rheumatologist should be sought in patients suspected with late-onset rheumatologic condition. Even though the diseases exhibit a mild clinical profile, the prognosis is not better due to the impact of age and associated comorbidities. The treatment principles remain the same as for young-onset diseases. But it is necessary to carefully assess the patient and associated comorbidities before initiating the treatment and not to overlook early complications.

Competing interests

The authors declare that they have no competing interests.

Disclosure

None

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