Original Article

The Association of Myositis Specific Antibodies in Patients with Inflammatory Myositis: Preliminary Data in Indian Patients

Natasha Vijay Negalur, Gayatri G. Ekbote, Dhiren N. Raval, Dhaval V. Tanna, Wasim S. Kazi, Muzaffar A. Bindroo, Durgarao J. Yadavalli, Rajiva Gupta

Department of Rheumatology and Clinical Immunology, Medanta - The Medicity Hospital, Gurugram, Haryana, India

Abstract

Context: Autoantibodies have a role in the diagnosis and prognosis in Autoimmune Inflammatory Myositis (AIM). **Aims:** The aim of this work was to study the prevalence and clinical correlation of myositis specific and associated antibodies (MSA and MAA) in AIM. **Setting and Design:** This was a cross-sectional observational study. **Methods and Materials:** Consecutive AIM patents were divided into groups as dermatomyositis (DM), polymyositis (PM), CTD-associated myositis (CTD-M), cancer-associated myositis (CAM) and juvenile myositis (JM). Their data along with serum samples were collected after obtaining informed consent. Sera was analyzed for IgG antibodies against Jo-1, PL-7, PL-12, EJ, SRP, Mi-2, MDA-5, TIF1γ, SAE1, SAE2, NXP2 and SSA/R052kD using the microELISA technique. The institutional ethics committee approved the study. **Statistical Analysis:** SPSS software (version 24.0) was used. *P* value < 0.05 was considered statistically significant. **Results:** There were 48 patients (DM = 19, PM = 19, CTD-M = 5, CAM = 2, JM = 3) included. MSA were positive in 37.5% patients. Antibodies against Mi-2 were present in 6 (12.5%), Jo-1 in 5 (10.4%), 2 (4.1%) each had PL-7 and SRP antibodies. One patient (2%) each had MDA-5, NXP2 and TIf1g antibodies. Jo-1 antibody was associated with mechanic's hands and ILD. There was a significant association of rash in the Mi-2 group with none of the patients having ILD. Malignancy screening was negative in NXP2 and TIF1g antibody-positive patients. Ro52 was the most common MAA (33.3%) and was associated with mechanic's hand. **Conclusion:** MSA was present in almost 40% of the cohort. Anti Jo-1 antibody was associated with mechanic's hands and ILD. None of the Mi-2 patients had ILD, which may point to a protective role of this antibody for ILD. The association of newer antibodies in Indian patients needs to be further studied in larger cohorts.

Keywords: Antibodies, Indian, MDA-5, myositis, myositis specific antibodies, NXP2, TIF1g

Introduction

Autoimmune inflammatory myositis (AIM) is a group of disorders characterized by muscle weakness and inflammatory damage of the muscle tissue on histology. It consists of polymyositis (PM), dermatomyositis (DM) (when associated with characteristic skin rashes), myositis associated with connective tissue diseases (CTD-M), juvenile myositis (JM), cancer-associated myositis (CAM) and inclusion body myositis (IBM).[1]

With antibodies being used as a criterion for a better classification system of AIM in the late 90s,[2] more and more newer antibodies are in search and have been found to date. These are divided as myositis specific antibodies (MSA), which are believed to be specific for AIM, and myositis associated antibodies (MAA), which can be seen in other connective tissue diseases as well. These antibodies have also earned a place as a biomarker in AIM due to their diagnostic and prognostic properties.[3]

MSA is considered to have disease specificity. Most common among them are the antisynthetase antibodies (ARS). These target the cytoplasmic aminoacyl- tRNA synthetases, which catalyze the binding of one amino acid to corresponding tRNA during protein synthesis and comprises of anti-Jo-1 (histidyl-tRNA synthetase), anti-PL7 (threonyl), anti-PL12, (alanyl), anti-EJ (glycyl), anti-OJ (isoleucyl), KS (asparaginyl), Zo (phenylalanyl) and Ha (tyrosyl). These are the most common antibodies, occur in almost one-third of the patients and are associated with ILD, arthritis, mechanic's hands and Raynaud's phenomenon.[4,5] Anti Mi-2 antibody recognizes the nucleosome remodeling histone-deacetylase (NuRD) nuclear protein complex involved in chromatin remodeling. This antibody is more common in DM and is associated with photosensitive rashes, less ILD predominance and lower frequency of cancer.[4,6,7] Recently sub-grouped as immune-mediated necrotizing myositis, in which there is a paucity of inflammation but widespread necrosis on histology, the anti-SRP and anti HMGCR antibodies are associated with refractory and severe disease.[6,8] Anti SRP is a Signal Recognition Protein, which plays a role in regulating the translocation of proteins across the

Address for correspondence: Dr. Natasha Vijay Negalur, A4-501/502, Vikas Complex, Castle Mill Compound, LBS Road, Thane West, Maharashtra – 400 601, India.
E-mail: natashanegalur@gmail.com

Submitted: 03-Nov-2020 **Accepted:** 03-Nov-2020 **Published:** 21-May-2021

DOI: 10.4103/aian.AIAN_1151_20

endoplasmic reticulum. The HMGCR antibody recognizes the autoantigen target as 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR), the rate-controlling enzyme of the cholesterol-producing mevalonate pathway. It was originally reported to be significantly associated with statin exposure, with about 63–67% patients having a prior history of statin use.[9] Antibodies associated with cancer are the anti NXP2 and anti TIF1gamma. Nuclear matrix protein 2 (NXP2) or MJ antibody is involved in DNA repair. Children and young adults present with severe weakness with muscle atrophy, calcinosis, vasculitis and a DM phenotype; while in the elderly, it is associated with malignancy.[10-12] TIF1 gamma autoantibody primarily binds the nuclear transcription factor- transcription intermediary factor 1gamma (TIF1g), which is involved in cell differentiation and carcinogenesis. Patients present with a DM phenotype having severe skin involvement. An association with malignancy is seen in some patients.[10,13] Anti-MDA-5 antibody targets the Melanoma differentiation-associated gene 5 (MDA5) belonging to retinoic acid-inducible gene (RIG)-I receptor family involved in antiviral response. It is seen more in Asian population, associated with DM phenotype and is known to cause rapidly progressive ILD (RPILD).[14]

MAA, though not specific for AIM, have important considerations in diagnosis and can correlate with clinical features. Anti Ro antibody, usually Ro52 is seen in around 25-35% of the patients.[15-19] It is frequently associated with ARS antibodies and when occurs together has a poorer prognosis and increased risk of relapse.[6,20] Other MAA like anti-Ku antibody and anti Pm/Scl are associated with scleroderma overlap,[6,21] while Ku antibodies also have higher incidence of ILD that is steroid resistant.[22] Anti RNP or U1snRNP antibodies are seen in overlap conditions, predominantly mixed connective tissue diseases associated with milder myositis.

The objective of this study was to assess the prevalence of MSA and MAA in Indian AIM patients, as there is a paucity of data in this respect, and to correlate them with clinical features.

Subjects and Methods

This was a cross-sectional observational study that comprised patients with AIM. All consecutive AIM patents (satisfying the Bohan and Peter criteria, 1975)[1] attending the Rheumatology and Clinical Immunology department of our tertiary care hospital, from November 2016 to October 2017 were included prospectively after informed consent and divided into groups as dermatomyositis (DM), polymyositis (PM), CTD associated myositis (CTD-M), cancer-associated myositis (CAM) and juvenile Myositis (JM). CTD-M was defined as those patients with features of inflammatory myositis along with another CTD like SLE, Scleroderma, etc., Their clinical and laboratory data were collected by patient interviews and review of medical records. These included presence or absence of muscle weakness, pharyngeal muscle weakness as a sign of severity and skin rash including the gottron's sign, heliotrope rash, V-sign, shawl sign, calcinosis and non-specific rash. Mechanic's hand, arthritis, Raynaud's phenomenon and digital ulcers were recorded if present. Interstitial lung disease (ILD) was defined by features of lung fibrosis in high-resolution CT of chest &/ or restrictive physiology in pulmonary function tests. Patient's serum samples were collected after obtaining informed consent and stored at a temperature of -80 degree C. Sera was analyzed for IgG antibodies against Jo-1, PL-7, PL-12, EJ, SRP, Mi-2, MDA-5, TIF1γ, SAE1, SAE2, NXP2 and SSA/R052kD using the microELISA technique (BlueDriver Dot Myositis[12] SAE IgG kit). Their extended nuclear antigens (ENA) containing Ku, RNP and Pm/Scl were also recorded (Blue DriverQuantrix-ANA25 Screen IgG kit D-tek). Results were read by the BlueScan scanner and value ≥10 was considered positive. The study was approved by the institutional Ethics committee.

SPSS software (version 24.0) was used for statistical analysis. Descriptive analysis of quantitative data was expressed as means and standard deviation. Ordinal data was expressed as absolute number and percentage. The student *t*-test was used for comparison of quantitative parameters. A value of $P < 0.05$ was considered statistically significant.

Results

Demographic profile

There were 48 patients in the cohort (M: F = 12: 36) with a median age of 43.5 years (range 4 to 75 years) and median disease duration of 33 months (range 1-300 months). Nineteen of them were DM, 19 were PM, 5 were CTD-M, 2 were CAM and 3 were JM. Table 1 depicts the demographic details of the cohort.

Autoantibodies

58.3% were ANA positive and MSA were positive in 37.5% of the cohort, MSA being mutually exclusive. Antibodies against Mi-2 were present in 6 patients (12.5%), Jo-1 antibodies in 5 (10.4%), 2 (4.1%) patients each had PL-7 and SRP antibodies. One patient (2%) each had MDA-5, NXP2 and TIf1g antibodies. Mi-2 antibodies were seen only in DM and JM group. MAA were seen in 39.5% of the cohort with antibodies against Ro, RNP and PM/Scl seen in 16 (33.3%), 2 (4.1%) and 1 (2%) respectively. None of the patients in the cohort had Ku antibody.

Although there were no overlapping antibodies within the MSA and MAA groups, 8 patients with MSA overlapped Ro52. Table 2 depicts the antibody prevalence in the different groups.

MSA and MAA associations with various clinical manifestations

Jo-1 antibody was associated with a higher frequency of mechanic's hands and ILD and the difference was statistically significant. There was also a higher frequency of arthritis although the difference compared to Non Jo-1 group was not statistically significant. There was no increased frequency of rash, Raynaud's phenomenon or digital ulcers whereas 20% of the group did not have muscle weakness (although this patient had elevated muscle enzymes and myopathic changes in EMG).

Table 1: Demographic data of the cohort

	DM (*n*=19)	PM (*n*=19)	CTD-M (*n*=5)	CAM (*n*=2)	JM (*n*=3)
Gender (M: F)	4:15	7:12	0:5	1:1	0:3
Median age in years (range)	44 (22-70)	42 (22-75)	37 (29-52)	45 (42-48)	17 (4-19)
Median Disease duration in months (range)	30 (1-120)	24 (1-300)	36 (12-180)	66 (36-96)	72 (1-84)

Table 2: Antibody prevalence in the different groups

	Total (*n*=48) %	DM (*n*=19) %	PM (*n*=19) %	CTD-M (*n*=5) %	CAM (*n*=2) %	JM (*n*=3) %
Myositis specific antibodies (MSA) %						
Mi-2	6 (12.5)	4 (21)	0 (0)	0 (0)	0 (0)	2 (66.6)
Jo-1	5 (10.4)	1 (5.2)	4 (21)	0 (0)	0 (0)	0 (0)
Non Jo-1 antisynthetase (PL-7)	2 (4.1)	0 (0)	0 (0)	1 (20)	1 (50)	0 (0)
NXP2	1 (2.0)	1 (5.2)	0 (0)	0 (0)	0 (0)	0 (0)
TIF1 gamma	1 (2.0)	0 (0)	1 (5.2)	0 (0)	0 (0)	0 (0)
SRP	2 (4.1)	0 (0)	2 (10.5)	0 (0)	0 (0)	0 (0)
MDA-5	1 (2.0)	1 (5.2)	0 (0)	0 (0)	0 (0)	0 (0)
SAE1	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
SAE2	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Myositis associated antibodies (MAA) %						
Ro52	16 (33.3)	5 (26.3)	7 (36.8)	3 (60)	1 (50)	0 (0)
PM-Scl	1 (2.0)	0 (0)	1 (5.2)	0 (0)	0 (0)	0 (0)
RNP	2 (4.1)	0 (0)	0 (0)	2 (40)	0 (0)	0 (0)
Ku	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
ANA	28 (58.3)	12 (63.1)	8 (42.1)	5 (100)	1 (50)	2 (66.6)
Negative MSA and MAA	19 (39.5)	10 (52.6)	7 (36.8)	0 (0)	1 (50)	1 (33.3)

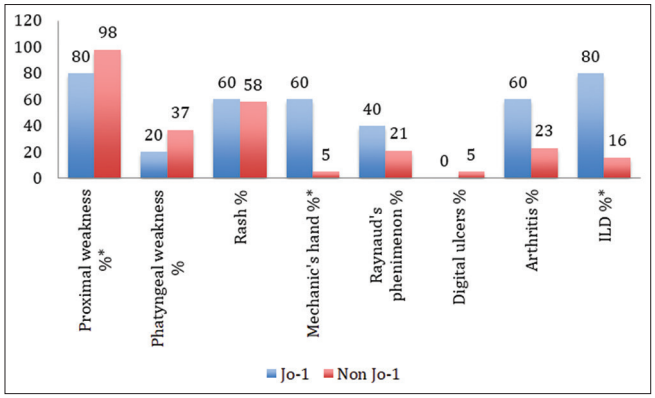

Figure 1: Clinical manifestations of Jo-1 vs Non Jo-1 groups. * statistically significant difference

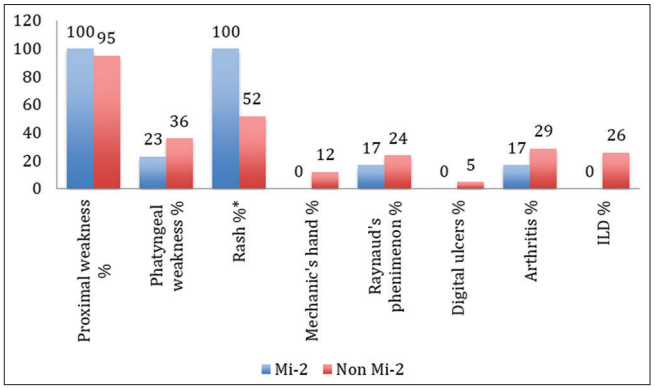

Figure 2: Clinical manifestations of Mi-2 vs Non Mi-2 groups. * statistically significant difference

A significant association of skin rash, which was present in all the patients, was found in the Mi-2 group. There was also a lower frequency of arthritis, Raynaud's phenomenon and mechanic's hands in this group, although it was not significant. None of the Mi-2 patients had ILD or lung involvement.

The lone patient who had MDA-5 antibody had amyopathic DM with refractory rash, mechanic's hands, digital and vasculitic hand ulcers, Raynaud's phenomenon and arthritis. He, however, did not have lung involvement.

One patient had NXP2 antibody with pharyngeal weakness and rash while the single patient with TIF1 gamma antibody had PM phenotype. Malignancy screening was negative in NXP2 and TIF1g antibody-positive patients.

Two patients had malignancy, one of which had a monoclonal gammopathy and was MSA and MAA negative but ANA positive. The other patient had malignant myxoid fibrous histiocytoma of thigh and was positive for PL-7 and Ro52 antibodies.

Among the MAA, Ro52 was the most commonly present antibody and had a higher frequency of mechanic's hand. 12%

of the patients had no muscle weakness while all patients who did not have Ro antibody had this feature, the difference being statistically significant. 45% of Ro positive patients had ILD and frequencies of the same were higher in the Ro vs non-Ro group, but the difference was not statistically significant. Table 3 and Figures 1, 2, and 3 depict clinical association of MSA and MAA.

Discussion

This was a study done to assess the prevalence of MSA and MAA and their association with clinical characteristics in a cohort of 48 Indian patients of AIM over a 1-year period. Sixty point four percent patients had MSA &/or MAA positive. This figure was lower than in the other Indian cohort where 75% had positive antibodies,[15] while it was around half in other cohorts.[18,19]

Our study had equal number of DM and PM patients, but Mi-2 antibodies were only seen in the DM and JM group, which is consistent with other studies where the predominant antibody in DM subgroup was Mi-2.[15,17,18,23]

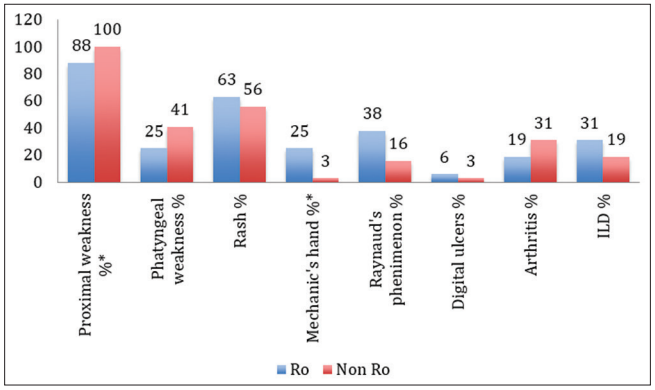

Figure 3: Clinical manifestations of Ro vs Non Ro groups. * statistically significant difference

Both the patients in the CAM group did not have antibodies typically associated with malignancy like NXP2 and TIF1gamma,[6,10] while those with these antibodies did not have any evidence of malignancy. One of the reasons for this may be the cross-sectional nature of the study and the lack of long term follow up where cancer may have developed at a later date in these patients. Younger age of the patients (between 35-50 years) may be a possible reason for the same.

Anti Ku antibody was not encountered in this study probably due to smaller size of the CTD-M group.

MSA and MAA antibody distribution was more or less comparable with other cohorts [Table 4][15-19,23,24] with the exception of lower prevalence of Mi-2 than the older Indian, PLANLAR group and Mexican cohorts. These cohorts, however, had a higher prevalence of DM compared to other groups accounting for the higher Mi-2 ratio.

Anti-Jo-1 antibodies along with other antibodies that target the aminoacyl t-RNA synthetases like PL-7, PL-12, OJ, EJ, KS and Zo are collectively known as antisynthetase antibodies (ARS). These antibodies, especially Jo-1 are found to be associated with certain features like fever, Raynaud's phenomenon, mechanic's hands, arthritis and ILD together called as the antisynthetase syndrome.[25] In our study also, Jo-1 was associated with mechanic's hands and ILD. This finding is consistent with other studies depicting the same.[15,17,18,24] Frequency of Jo-1 antibodies in our study was also higher in the PM group compared to the DM group consistent with the literature.[18,19,25]

All patients with Mi-2 antibody had skin rash and were either encountered in the DM or the JDM group. None of the patients

Table 3: Myositis Antibody distribution according to clinical features

	Proximal muscle weakness (%) (*n*=46)	Pharyngeal muscle weakness (%) (*n*=17)	Rash (%) (*n*=28)	Mechanic hands (%) (*n*=5)	Raynaud's (%) (*n*=11)	Digital Ulcer (%) (*n*=2)	Arthritis (%) (*n*=13)	ILD (%) (*n*=11)	Total
Myositis Specific Antibodies									
MI-2	6 (13)	2 (11.7)	6 (21.4)	0	1 (9)	0	1 (7.6)	0	6
JO-1	4 (8.6)	1 (5.8)	3 (10.7)	3 (60)	2 (18.1)	0	3 (23)	4 (36.3)	5
NON JO-I ARS (PL-7)	1 (2.1)	0	2 (7.1)	0	2 (18.1)	0	0	1 (9)	2
SRP	2 (4.3)	0	0	0	0	0	0	1 (9)	2
MDA-5	0	0	1 (3.5)	1 (20)	1 (9)	1 (50)	1 (7.6)	0	1
NXP2	1 (2.1)	1 (5.8)	1 (3.5)	0	0	0	0	0	1
TIF1g	1 (2.1)	0	0	0	0	0	0	1 (9)	1
SAE1	0	0	0	0	0	0	0	0	0
SAE2	0	0	0	0	0	0	0	0	0
Myositis Associated Antibodies									
RO52	14 (30.4)	4 (23.5)	10 (35.7)	4 (80)	6 (54.5)	1 (50)	3 (23)	5 (45.4)	16
PM SCL	1 (2.1)	0	0	0	0	0	0	1 (9)	1
RNP	2 (4.3)	1 (5.8)	1 (3.5)	0	2 (18.1)	1 (50)	2 (15.3)	2 (18.1)	2
Ku	0	0	0	0	0	0	0	0	0

Table 4: Prevalence of MSA and MAA in various cohorts

	Indian cohort (current study)	Indian cohort 2016[15]	PLANLAR myositis study group 2020[16]	Greek cohort 2019[17]	Brazil cohort 2013 [18]	Dutch cohort 2019[24]	Mexican cohort 2013[23]	Italian cohort 2010[19]
No. of patients	48	124	210	95	222	187	95	208
Patient groups	DM, PM, CTD-M, CAM, JM	DM, PM, JDM, CTD myositis	DM, PM, JDM	DM, PM, ADM, JDM, IBM	PM, DM	IIM	PM, DM, JDM	PM, DM, JDM. Overlap myositis, CAM
Antibodies tested	Jo-1, PL-7, PL-12, EJ, SRP, Mi-2, MDA-5, TIF1γ, SAE1, SAE2, NXP2, Ro52, Ku, RNP, Pm/ Scl 75/100.	Mi2, SRP, Jo1, PL7, PL12, EJ, OJ, Ku, Pm-Scl 100, Pm-Scl 75 and Ro52	mi-2, Jo-1, Ro, Pm/Scl	Jo-1, PL-7, PL-12, EJ, OJ, Mi-2 alpha, Mi-2 beta, TIF1γ, MDA5, NXP2, SAE1, SRP, PM-Scl100, PM-Scl75, Ku, and Ro-52.	Jo-1, Mi-2, SRP, PL-7, PL-12, OJ, EJ, Ro52, Ku, Pm/scl75, Pm/scl100	Jo-1, SRP, EJ, OJ, Mi-2α, Mi-2β, TIF1-γ, MDA5, NXP2, SAE1, PL-12, PL-7, Ku, PM/Scl-75 and PM/ Scl-100	Mi-2, TIF1c, NXP2, SAE1, SRP, Jo-1, PM-Scl, Ro/SSA-52, RNP	Jo-1, non Jo-1 ARS, Mi-2, SRP, Ro52, Ku, pm/scl
Method	Line blot	Line blot	Line blot	Line blot	Line blot	Line blot	Immunoprecipitation/ ELISA	Line blot
Myositis Specific Antibodies								
MI-2	12.5	20.9	38.5	12	8.1	7.5	35	4
JO-1	10.4	11.3	11.9	22	18.9	10.2	4	21
NON JO-I ARS	4.1	12.1	NA	6	8.6	8	ND	4
SRP	4.1	4.8	NA	13	3.2	5.9	3	0
MDA-5	2.0	ND	NA	1	ND	5.4	ND	ND
NXP2	2.0	ND	NA	4	ND	2.1	3	ND
TIF1g	2.0	ND	NA	7	ND	7	11	ND
SAE1	0	ND	NA	6	ND	1.1	2	ND
SAE2	0	ND	NA	ND	ND	ND	ND	ND
Myositis Associated Antibodies								
RO52	33.3	36.3	17.6	30	36.9	ND	21	24
PM SCL	2.0	14.5	7.5	13	5	12.4	3	4
RNP	4.1	0	NA	ND	ND	ND	3	ND
Ku	0	10.5	NA	6	4.1	4.3	ND	5

ND-Not Done. NA- Not Available

in this group had ILD, which is consistent with the other Indian study[15] although low prevalence of lung involvement has been seen in earlier studies.[6,23]

In our study, due to low positive rates of NXP-2, TIF1gamma and MDA-5, no robust associations could be computed. Although all these antibodies are said to have a DM phenotype,[4] the patient with TIF1gamma had PM.

Among the MAA, Ro antibody was the most predominant in the cohort and in the various subgroups. Ro antibody was positively associated with mechanic's hands possibly because they also had ARS antibodies (3/5) as compared to those with Ro positive alone or along with Non-ARS antibodies (1/11). Ro antibodies are known to be frequently associated with Jo-1 antibodies and the combination has an increased risk of mechanic's hands, malignancy, lower functional status and poor prognosis.[6] Ro antibody in combination with MDA-5 antibody was also found to have worse ILD and poor survival in Japanese DM patients.[26] However, in our study, the lone patient with MDA-5 had Ro positivity but no lung involvement.

PM/Scl antibody is frequently associated with scleroderma and overlap diseases,[21] but in our cohort, it was seen in a single patient who did not have any overlap features and was phenotypically PM.

Both the patients with RNP antibody had overlap with scleroderma and ILD.

It was interesting to note that although there were some overlaps between Ro antibodies and MSA, the MSA were mutually exclusive.

The strengths of this study were the use of newer antibodies in the Line blot assay like MDA-5, NXP-2, TIF1gamma, SAE1/2 which have not been previously used in another Indian study. There was also a relatively short time of storage of samples (less than 12 months) to prevent denaturation. This study was limited by a relatively smaller sample size and the unavailability of HMGCoR antibody in the line blot test kit.

Conclusion

About 60% of patients had positive antibodies (MSA/MAA or both) with MSA being present in almost 40% of the cohort. Anti Jo-1 antibody was associated with mechanic's hands and ILD while Mi-2 antibodies were associated with skin rash. None of the Mi-2 patients had ILD, which may point to a protective role of this antibody for ILD. Ro antibody was also associated with mechanic's hands confirming western data. The association of newer antibodies like TIF1gamma, NXP2 and MDA-5 in Indian patients needs to be further studied in larger cohorts. Clinical associations of MSA and MAA may further help in disease classification, management and prognosis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Bohan A, Peter JB. Polymyositis and dermatomyositis. N Engl J Med 1975;292:403-7.
2. Targoff IN, Miller FW, Medsger TA Jr, Oddis CV. Classification criteria for the idiopathic inflammatory myopathies. Curr Opin Rheumatol 1997;9:527-35.
3. Satoh M, Tanaka S, Ceribelli A, Calise SJ, Chan EK. A comprehensive overview on myositis-specific antibodies: New and old biomarkers in idiopathic inflammatory myopathy. Clin Rev Allergy Immunol 2017;52:1-19.
4. Ghirardello A, Doria A. New insights in myositis-specific autoantibodies. Curr Opin Rheumatol 2018;30:614-22.
5. Monti S, Montecucco C, Cavagna L. Clinical spectrum of anti-Jo-1-associated disease. Curr Opin Rheumatol 2017;29:612-7.
6. Betteridge Z, McHugh N. Myositis-specific autoantibodies: An important tool to support diagnosis of myositis. J Intern Med 2016;280:8-23.
7. Liang L, Zhang YM, Chen H, Ye LF, Li SS, Lu X, *et al*. Anti-Mi-2 antibodies characterize a distinct clinical subset of dermatomyositis with favourable prognosis. Eur J Dermatol 2020. doi: 10.1684/ejd.2020.3750.
8. Pinal-Fernandez I, Casal-Dominguez M, Mammen AL. Immune-mediated necrotizing myopathy. Curr Rheumatol Rep 2018;20:21.
9. Mammen AL, Chung T, Christopher-Stine L, Rosen P, Rosen A, Doering KR, *et al*. Autoantibodies against 3-hydroxy-3-methylglutaryl-coenzyme A reductase in patients with statin-associated autoimmune myopathy. Arthritis Rheum 2011;63:713-21.
10. Ceribelli A, Isailovic N, De Santis M, Generali E, Fredi M, Cavazzana I, *et al*. Myositis-specific autoantibodies and their association with malignancy in Italian patients with polymyositis and dermatomyositis. Clin Rheumatol 2017;36:469-75.
11. Albayda J, Pinal-Fernandez I, Huang W, Parks C, Paik J, Casciola-Rosen L, *et al*. Antinuclear matrix protein 2 autoantibodies and edema, muscle disease, and malignancy risk in dermatomyositis patients. Arthritis Care Res (Hoboken) 2017;69:1771-6.
12. Aouizerate J, De Antonio M, Bader-Meunier B, Barnerias C, Bodemer C, Isapof A, *et al*. Muscle ischaemia associated with NXP2 autoantibodies: A severe subtype of juvenile dermatomyositis. Rheumatology (Oxford) 2018;57:873-9.
13. Hida A, Yamashita T, Hosono Y, Inoue M, Kaida K, Kadoya M, *et al*. Anti-TIF1-γ antibody and cancer-associated myositis: A clinicohistopathologic study. Neurology 2016;87:299-308.
14. Li L, Wang Q, Wen X, Liu C, Wu C, Yang F, *et al*. Assessment of anti-MDA5 antibody as a diagnostic biomarker in patients with dermatomyositis-associated interstitial lung disease or rapidly progressive interstitial lung disease. Oncotarget 2017;8:76129-40.
15. Srivastava P, Dwivedi S, Misra R. Myositis-specific and myositis-associated autoantibodies in Indian patients with inflammatory myositis. Rheumatol Int 2016;36:935-43.
16. González-Bello Y, Garcia-Valladares I, Reyes-Pérez IV, García-Cerda D, Medrano-Ramírez G, Navarro-Zarza JE, *et al*. Myositis-specific antibodies and myositis-associated antibodies in patients with idiopathic inflammatory myopathies from the PANLAR Myositis study group. J Clin Rheumatol 2020. doi: 10.1097/RHU.0000000000001350.
17. Zampeli E, Venetsanopoulou A, Argyropoulou OD, Mavragani CP, Tektonidou MG, Vlachoyiannopoulos PG, *et al*. Myositis autoantibody profiles and their clinical associations in Greek patients with inflammatory myopathies. Clin Rheumatol 2019;38:125-32.
18. Souza FH, Shinjo SK. Myositis-specific and myositis-associated autoantibody profiles and their clinical associations in a large series of patients with polymyositis and dermatomyositis. Clinics (Sao Paulo) 2013;68:909-14.
19. Ghirardello A, Rampudda M, Ekholm L, Bassi N, Tarricone E, Zampieri S, *et al*. Diagnostic performance and validation of

autoantibody testing in myositis by a commercial line blot assay. Rheumatology (Oxford) 2010;49:2370-4.
20. Tatebe N, Sada KE, Asano Y, Zeggar S, Hiramatsu S, Miyawaki Y, *et al*. Anti-SS-A/Ro antibody positivity as a risk factor for relapse in patients with polymyositis/dermatomyositis. Mod Rheumatol 2018;28:141-6.
21. Oddis CV, Okano Y, Rudert WA, Trucco M, Duquesnoy RJ, Medsger TA Jr. Serum autoantibody to the nucleolar antigen PM-Scl. Clinical and immunogenetic associations. Arthritis Rheum 1992;35:1211-7.
22. Rigolet A, Musset L, Dubourg O, Maisonobe T, Grenier P, Charuel JL, *et al*. Inflammatory myopathies with anti-Ku antibodies: A prognosis dependent on associated lung disease. Medicine (Baltimore) 2012;91:95-102.
23. Petri MH, Satoh M, Martin-Marquez BT, Vargas-Ramírez R, Jara LJ, Saavedra MA, *et al*. Implications in the difference of anti-Mi-2 and -p155/140 autoantibody prevalence in two dermatomyositis cohorts from Mexico City and Guadalajara. Arthritis Res Ther 2013;15:R48. doi: 10.1186/ar4207.
24. Platteel AC, Wevers BA, Lim J, Bakker JA, Bontkes HJ, Curvers J, *et al*. Frequencies and clinical associations of myositis-related antibodies in The Netherlands: A one-year survey of all Dutch patients. J Transl Autoimmun 2019;2:100013.
25. Targoff IN. Update on myositis-specific and myositis-associated autoantibodies. Curr Opin Rheumatol 2000;12:475-81.
26. Temmoku J, Sato S, Fujita Y, Asano T, Suzuki E, Kanno T, *et al*. Clinical significance of myositis-specific autoantibody profiles in Japanese patients with polymyositis/dermatomyositis. Medicine (Baltimore) 2019;98:e15578. doi: 10.1097/MD.0000000000015578.