RMD Open
Rheumatic & Musculoskeletal Diseases

REVIEW

Pain in autoimmune inflammatory myopathies: a scoping review

Valérie Leclair ,[1] Harmony Tsui,[2] Marie Hudson[1]

To cite: Leclair V, Tsui H, Hudson M. Pain in autoimmune inflammatory myopathies: a scoping review. *RMD Open* 2023;**9**:e002591. doi:10.1136/rmdopen-2022-002591

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/rmdopen-2022-002591).

Received 18 July 2022
Accepted 26 August 2022

[1]Division of Rheumatology, Jewish General Hospital and Lady Davis Institute, McGill University, Montreal, Quebec, Canada
[2]Department of Medicine, McGill University, Montreal, Quebec, Canada

Correspondence to
Dr Valérie Leclair;
valerie.leclair@mcgill.ca

ABSTRACT

Background Pain is considered a priority for research by adult patients with autoimmune inflammatory myopathy (AIM) and their families. Our aim was to review the literature for studies reporting on pain in adult AIM and to summarise their findings.

Methods A scoping review was conducted searching for studies in PubMed and MEDLINE including more than five adult patients with AIM and assessing pain using a patient-reported outcome measure. Study population characteristics, pain measurement and clinical correlates of pain were extracted using a standardised protocol.

Results The search strategy identified 2831 studies with 33 meeting inclusion criteria. Most studies used visual analogue scales (n=14) and/or the Medical Outcomes Study 36-Item Short Form Bodily Pain Scale (n=17). Frequency of pain and/or myalgias ranged from 64% to 100%. Subjects with AIM had significantly more pain than the general population and comparable pain to other chronic rheumatic diseases. Insufficient results were available to identify significant clinical correlates of pain in AIM.

Conclusion This review suggests that the burden of pain in AIM is considerable. Still, due to the heterogeneity and low quality of the evidence, significant knowledge gaps persist. Studies are needed to characterise pain trajectories of patients with AIM.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

⇒ Pain in autoimmune inflammatory myopathy (AIM) is considered a high priority for research by patients and their families. However, little is known about the pain experience in AIM.

WHAT THIS STUDY ADDS?

⇒ Based on patient-reported outcomes measures, the burden of pain in AIM is considerable. Important gaps in the literature were identified notably concerning clinical correlates of pain in AIM.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY?

⇒ Longitudinal studies are needed to characterise the pain experience in AIM including predictors of severity and clinical correlates to identify possible pain mechanisms and offer targeted management to patients.

INTRODUCTION

Autoimmune inflammatory myopathies (AIMs) are rare chronic autoimmune diseases characterised by muscle inflammation and weakness. Major AIM subsets are dermatomyositis (DM), antisynthetase syndrome, overlap myositis, immune-mediated necrotising myositis, sporadic inclusion body myositis and polymyositis (PM).[1 2] AIM in adults is rare, with an estimated incidence of 20 cases per million per year and a prevalence of 30 cases per 100 000 individuals.[3] AIMs are functionally impairing and, when compared with other systemic autoimmune rheumatic diseases, associated with greater impairment in health-related quality of life.[4] After conducting multiple surveys with patients, their families and physicians, the Outcome Measures in Rheumatology Myositis Special Interest Group listed pain as one of five highest priorities for research in AIM while emphasising the paucity of data on the subject.[5–8] With the aim to better characterise the pain experience in AIM, we searched the literature for studies reporting on pain in adult AIM and summarised their findings in this scoping review.

METHODS

This review was conducted using the Arksey and O'Malley framework[9] and guided by the methodology from recent scoping reviews.[10] It included the following five key phases: (1) research question identification; (2) relevant studies identification; (3) study selection; (4) data charting; and (5) collating, summarising and reporting results. The following question guided the review: what is known about the burden of pain in adult AIM? The comprehensive search was implemented on 15 February 2022, in PubMed and MEDLINE with limitation to English and French languages and human studies. No limits were placed on date or type of studies. The search query was built to capture articles that addressed the specific

Table 1 Pain measures in AIM compared with the general population

Study	AIM subsets	Pain severity*		P value
		AIM	General population	
SF-36 BP (additive 0–100, norm-based mean 50, SD 10); lower score, more pain				
Sultan *et al*[26]	DM, PM, OM	Mean: 55	Mean: 90	<0.001
Ponyi *et al*[28]	DM, PM, OM	Mean±SD DM: 54±18 PM: 58±20 OM: 66±18	Mean: 78	<0.001
Sadjadi *et al*[29]	IBM	Mean±SD 69±27	Z-score: −0.2	Non-significant
van de Vlekkert *et al*[35]	DM, OM, NS, NAM	Mean: 42†	Mean: 80	<0.05
Goreshi *et al*[23]	DM	Norm-based Mean: 50	Norm-based Mean: 52	Non-significant
Regardt *et al*[32]	DM, PM	Mean: 58	Mean: 70	0.023
Xu *et al*[43]	DM, PM, IBM, NAM, NS	Mean±SD 63±26	Mean±SD 77±25	<0.001
Cleary *et al*[21]	DM, PM, OM, IBM	Median (IQR) 78 (45–95)	Median (IQR) General population: 95 (82–100)	0.08
Feldon *et al*[22]	DM, PM, IBM, adult JDM	Norm-based Mean±SE 43±0.28	Norm-based Mean±SE 49±0.21	<0.0001
Poulsen *et al*[36]	DM, PM	Mean±SD 60±26	Median (IQR) 100 (72–100)	<0.001
NHP score (0–100); higher score, more pain				
Chung *et al*[19]	DM, PM	Mean±SD 30±32	Mean±SD RA: 49±34 OP: 33±36 OA: 41±27 General population: 6	N/A

*If not shown, measure of dispersion not provided.
†Baseline values at entry in the cohort.
AIM, autoimmune idiopathic myopathy; DM, dermatomyositis; IBM, inclusion body myositis; JDM, juvenile dermatomyositis; N/A, not available; NAM, necrotising autoimmune myopathy; NHP, Nottingham Health Profile; NS, non-specific; OA, osteoarthritis; OM, overlap myositis; OP, osteoporosis; PM, polymyositis; RA, rheumatoid arthritis; SF-36 BP, 36-Item Short Form Bodily Pain.

topics of pain, patient-reported outcome measures (PROMs), and autoimmune inflammatory myopathies or idiopathic inflammatory myopathies.

The reference lists of included studies were manually searched to identify any further studies not captured by the search. A 'snowball' technique was adopted in which citations within articles were searched if they appeared relevant to the review.[10] Papers were eligible for inclusion if they were full-length articles in English or French language including (1) pain assessment by at least one PROM and (2) more than five adult subjects with AIM. Titles and abstracts were reviewed for eligibility. Titles for which an abstract was not available and/or for which the screening decision was uncertain were reviewed via a search for keywords in their full text.

Data from included papers were extracted including author(s), year of publication, publication type, main topic of the study and data relevant to the specific objectives of this scoping review, that is, (1) characteristics of study population included, (2) pain measurement using a PROM and (3) clinical correlates of pain if included in the study. Data were compiled in a tabular format and qualitatively summarised. A quantitative meta-analysis was not planned as it was anticipated that the data collected would be too heterogenous for this type of analysis.

RESULTS

Studies characteristics

The search strategy identified 2831 studies and, after exclusion of duplicates and ineligible papers, 33 studies including pain measures in adult subjects with AIM were included in this review (see flowchart in online supplemental figure 1).[11–43] The characteristics of the

Table 2 Pain measures in AIM compared with other neuromuscular or rheumatic diseases

Study	AIM subsets	Pain severity*		Findings
		AIM	Disease comparators	
SF-36 BP (additive 0–100, norm-based mean 50, SD 10); lower score, more pain				
Sadjadi *et al*[29]	IBM	Mean±SD 69±27	Mean±SD FSHD: 67±24 MyoDys: 75±25 CMT 1: 69±26 Various NMDs: 63±26	Comparable burden of pain with IBM and other NMDs
Goreshi *et al*[23]	DM	Norm-based Mean: 50	Norm-based Mean: SLE: 43 CLE: 54	
Feldon *et al*[22]	DM, PM, IBM, adult JDM	Norm-based Mean±SE 43±0.28	Norm-based Mean±SE RA: 42±0.85	Comparable burden of pain with RA
NHP score (0–100); higher score, more pain				
Chung *et al*[19]	DM, PM	Mean±SD 30±32	Mean±SD RA: 49±34 OP: 33±36 OA: 41±27	Less pain in AIM compared with RA and OA (p<0.002)
INQOL score; higher score, more pain				
Rose *et al*[33]	DM, PM, IBM	Mean±SD PM/DM: 70±20 IBM: 46±29	Mean±SD LGMD: 45±26 FSHD: 40±23 MyoDys: 41±27 Various NMDs: 35±23	More pain in DM/PM compared with NMD

*If not shown, measure of dispersion not provided.
AIM, autoimmune idiopathic myopathy; SF-36 BP, 36-Item Short Form Bodily Pain; CLE, cutaneous lupus erythematosus; CMT 1, Charcot-Marie-Tooth type 1; DM, dermatomyositis; FSHD, facioscapulohumeral dystrophy; IBM, inclusion body myositis; INQOL, Individualised Neuromuscular Quality of Life Questionnaire; JDM, juvenile dermatomyositis; LGMD, limb–girdle muscular dystrophy; MyoDys, myotonic dystrophy; NHP, Nottingham Health Profile; NMD, neuromuscular disease; OA, osteoarthritis; OP, osteoporosis; PM, polymyositis; RA, rheumatoid arthritis; SLE, sytemic lupus erythematosus.

studies included are summarised in online supplemental table 1. The papers included originated from Europe (n=24),[11–17 19 20 24–26 28–32 35–38 40] USA (n=7),[18 21–23 33 41 42] South America (n=1)[34] and Australia (n=1)[43] with years of publication ranging from 1999 to 2021. Most of the studies were cross-sectional (n=11) or cohort (n=9) studies. One study had a case–control design (n=1)[36] and one was prospective (n=1).[13] There were five open-label studies,[11 12 14 24 34] five randomised controlled trials (RCTs)[15 20 29 30 37] and one randomised single-blinded trial[39] using pain as an outcome measure. Almost half of studies used unidimensional pain intensity measurement, namely, visual analogue scale (VAS) or numerical rating scale (n=15).[11 13 17 23–25 27 30 31 36–39 41 42] The rest of the studies used multidimensional pain measurements including the Medical Outcomes Study 36-Item Short Form Bodily Pain (SF-36 BP) or 12-Item Short Form Bodily Pain (n=17),[11 12 16 21–23 26–30 32 34–37 40] the Borg Rate of Perceived Pain Scale (n=1),[14] the Health Assessment Questionnaire–Pain Index (n=1),[18] the Individualised Neuromuscular Quality of Life Questionnaire (INQOL, n=1),[33] the Nottingham Health Profile (NHP, n=3)[15 19] and the Short Form McGill Pain Questionnaire (n=1).[20]

Frequency of pain

Few of the studies included in the review provided estimates of the frequency of pain in their population. In a 2010 RCT including 62 patients with early AIM, 81% of the participants had myalgias at baseline.[44] In a small cohort study of eight patients newly diagnosed with AIM, 100% had pain at baseline.[25] In a 2020 US survey-based study (n=381), myalgias were reported in 64% of participants, being more frequent with increased numbers of flares per year.[18] A German study reporting on cross-sectional clinical characteristics of patients with AIM from 1997 to 2017 showed a decreasing frequency of moderate to severe pain (53% in 1997 compared with 25% in 2017).[13] However, the patient populations were quite different between those two time points with the 2017 cohort having a longer disease duration and lower disease activity compared with the 1997 cohort, making it difficult to draw meaningful conclusions.

Table 3 Studies reporting on age, sex, AIM subsets, disease activity/course and pain

Study	Disease duration (years)	Disease activity	Pain severity*	Findings
SF-36 BP (additive 0–100, norm-based mean 50, SD 10); lower score, more pain				
Sultan *et al*[26]	N/A	Active disease 21%	Mean 55	Significantly higher pain in chronic progressive illness compared with relapsing–remitting course (p<0.05), no difference between active and inactive disease
Ponyi *et al*[28]	Median (range) 8.9 (3.0–22.8)	Active disease 13%	Mean±SD DM: 54±18 PM: 58±20 OM: 66±18	No significant differences in pain between AIM subsets or disease course. No correlation with disease activity. Predictors of more pain: female (β=−15.5, p=0.00), disease duration <5 years (β=−14.2, p=0.001), arthralgias (β=−11.6, p=0.005) and compression fracture/AVN (β−23.9, p=0.002)
Sadjadi *et al*[29]	Mean±SD 4.4±3	N/A	Mean±SD 69±27	No significant correlation of pain with age or disease duration, moderate correlation with Beck Depression Inventory scores (values not reported)
Goreshi *et al*[23]	N/A	CDASI (0–100): 20±11	Norm-based Mean: 50	No significant correlation between pain and PtGA (r=0.296, p=0.67)
Regardt *et al*[32]	Mean±SD 6.8±5.5	N/A	Mean±SD All: 58 DM:55 PM: 58	No significant differences in pain between sex or AIM subsets
Xu *et al*43	Median (IQR) 5 (2.5–7.4)	VAS score (0–100) Median (IQR) PhGA: 17 (5–31) PtGA: 29 (11–49)	Mean±SD 63±26	No significant differences in pain with age, sex, disease duration or AIM subsets; pain correlated weakly with MMT-8 (r=0.30, p=0.03) and moderately with PtGA (r=−0.62, p<0.001); no significant correlation with PhGA
van de Vlekkert *et al*[35]	Median* baseline: 0.3	Early active disease	Mean 42	No difference in pain between AIM subsets
Landon-Cardinal *et al*[40]	Mean±SD DM: 3±2 IMNM: 9±8 OM: 3±4	VAS score (0–10), mean±SD DM PhGA: 3±2 IMNM PhGA: 2±2 OM PhGA: 3±3	Mean±SD All: 65±26 DM: 55±24 IMNM: 71±24 OM: 63±28	No significant difference in pain at baseline between AIM subsets
HAQ-Pain Index (0–3); higher score, more pain				
Christopher-Stine *et al*[18]	Mean±SD 8±7	In year prior, no flare 22%, 1–3 flares 47%, >4 flares 26%	Mean±SD 1.04±0.87	Higher mean±SD HAQ-Pain Index scores with increased flare frequency (no flare 0.69±0.83, 1–3 flares 1.02±0.84, >4 flares 1.52±0.78 (p<0.001))
INQOL score; higher score, more pain				
Rose *et al*[33]	N/A	N/A	Mean±SD PM/DM: 70±19 IBM: 46±29 All NMD: 42±27	Pain in NMD significantly correlated (p<0.01) with anxiety (r=0.33), depression (r=0.41) and many IPQ-R domains: identity (r=0.43), consequences (r=0.3), illness coherence (r=0.23), timeline cyclical (r=0.32) and emotional (r=0.35)

Continued

Table 3 Continued

Study	Disease duration (years)	Disease activity	Pain severity*	Findings
NHP score (0–100); higher score, more pain				
Chung *et al*[19]	Mean (range) DM: 7 (1–26) PM: 7 (1–27)	Acute cases excluded	Mean±SD All: 30±32 DM: 30±31 PM: 31±33	Worse energy scores were associated with worse pain (β =0.2, p=0.03)
VAS score (0–100); higher score, more pain				
Mahler *et al*[31]	Median (IQR) 4 (2.5–6.5)	VAS score (0–100) Mean±SD PhGA: 55±8	Mean±SD 21±21	After rituximab treatment, pain not significantly reduced while disease activity improved.
Opinc *et al*[38]	<1 year: 13% 1–5 years: 40% >5 years: 47%	N/A	Mean±SD DM: 37±28 PM: 39±29 OM: 38±33 IBM: 22±27	Pain in IBM significantly lower than other AIM subsets (p<0.05). Mean myalgia value (VAS, 0–10) significantly lower in IBM (3±2) compared with DM (4±2), PM (4±2) and OM (4±2) (p<0.001).

*If not shown, measure of dispersion not provided.
AIM, autoimmune inflammatory myopathy; DM, dermatomyositis; HAQ, Health Assessment Questionnaire; IBM, inclusion body myositis; IMNM, immune-mediated necrotising myopathy; INQOL, Individualised Neuromuscular Quality of Life Questionnaire; IPQ-R, Illness Perceptions Questionnaire-Revised; MMT-8, Manual Muscle Testing-8; N/A, not available; NHP, Nottingham Health Profile; NMD, neuromuscular disease; OM, overlap myositis; PhGA, Physician Global Assessment; PM, polymyositis; PtGA, Patient Global Assessment; SF-36 BP, 36-Item Short Form Bodily Pain; VAS, visual analogue scale.

Comparisons with the general population

Comparisons of pain measures with the general population were done in 11 studies (table 1). In nine of those, subjects with AIM had significantly more pain than the general population.[19 21 22 26 28 32 35 36 43] Subjects included in those studies generally had established stable disease except for one RCT comparing the use of high-dose prednisone to dexamethasone in early disease (<6 months disease duration) where SF-36 BP scores in untreated subjects with AIM at study entry were severely impaired.[35] In seven studies using an additive scoring of the SF-36 BP, the mean or median bodily pain (BP) scores in the subjects with AIM ranged from 42 to 78 compared with 70 to 100 in the general population (with lower numbers indicating more pain).[21 26 28 32 35 36 43]

Comparisons with other rheumatic or neuromuscular diseases

Comparisons of pain measures with other neuromuscular or rheumatic diseases were reported in five studies (table 2).[19 22 23 29 33] In a large survey-based study including 1715 patients with AIM with a median disease duration of 9.2 (IQR 5–14) years, the burden of pain using the SF-36 BP was comparable to rheumatoid arthritis.[22] A study including only female patients with DM/PM (n=113) recruited through a national support group with a mean (range) disease duration of 7 (1–27) years reported less pain in AIM using the NHP compared with female patients with rheumatoid arthritis and osteoarthritis.[19] In a cross-sectional study using the INQOL, patients with DM/PM reported more pain compared with various other neuromuscular diseases.[33] In that study, patients with inclusion body myositis (IBM) had burden of pain similar to other neuromuscular diseases, which was also the case in an RCT in IBM (n=60) where prerandomisation SF-36 BP scores were comparable to previously published scores in facioscapulohumeral dystrophy, myotonic dystrophy and Charcot-Marie-Tooth type 1.[29 45 46]

Clinical characteristics and disease course

Studies reporting on age, sex, AIM subsets, disease activity/course and pain are summarised in table 3. Sex differences were assessed in three studies.[28 32 43] In a cross-sectional study assessing grip strength and health-related quality of life in established DM/PM (n=31), women had lower mean SF-36 BP scores (more pain) compared with men (52 vs 65) although not reaching statistical significance.[32] In a cohort study of patients with DM, PM and overlap myositis (OM) (n=87), being female was a predictor of lower SF-36 BP scores (more pain; β −15.5, p=0.000).[28] A cross-sectional study including patients with DM, PM, immune-mediated necrotising myopathy (IMNM), IBM and non-specific myositis (n=50) found no sex differences in SF-36 BP scores.[43] Two studies reported no difference in SF-36 BP scores based on age, although results were not shown.[29 43]

Pain measures were stratified by AIM subsets in six studies,[19 28 32 33 38 40] and comparison of pain measures by AIM subsets were reported in six studies.[28 32 35 38 40 43] While most of these studies reported no statistically significant difference in pain measures between AIM subsets, a survey-based study showed lower mean±SD pain intensity using VAS in IBM (22±27, p<0.05) compared with DM (37±28), PM (39±29) and OM (38±33).[38] Similarly, in a cross-sectional study on health-related quality of life in chronic neuromuscular diseases, pain measured using

the INQOL score was lower in IBM compared with DM/PM (46±29 vs 70±19).[33] In a cohort study assessing physical activity in AIM, although non-significant, baseline mean±SD SF-36 BP scores were lower in DM (more pain, 55±24) than in IMNM (71±24) or OM (63±28).[40]

Few studies reported pain measures in patients with early active AIM.[15 25 30] Baseline pain scores in an RCT comparing high-dose prednisone to dexamethasone in early AIM reported very low median SF-36 BP scores in untreated subjects with AIM with improvement at 18 months (32 vs 72).[35] This contrasts with the results of a cross-sectional study that found disease duration more than 5 years to be a predictor of lower BP scores (more pain; β= −14.2, p=0.001). Of note, this study specifically included subjects with a follow-up of at least 3 years introducing a survivorship bias that may explain this discrepancy. In IBM, no correlation between pain and disease duration was reported by Sadjadi *et al*.[29] As for the impact of disease activity on pain, vague or broad inclusion criteria and heterogenous populations made interpretation of the results, and comparison of the studies difficult. Nonetheless, some studies suggested that uncontrolled disease (progressive course or frequent flares within 1 year) was associated with more pain.[18 26] Interestingly, a cross-sectional study found SF-36 BP scores to be correlated with Patient Global Assessment (r=−0.62, p<0.001) but not with Physician Global Assessment (r=−0.14, p=0.35).[43] Finally, a cross-sectional study explored associations between different domains of the NHP and found that low levels of energy were associated with more pain (β=0.2, p=0.03). Similarly, SF-36 BP scores were moderately correlated with Beck Depression Inventory scores in IBM.[29] These results align with those of Rose *et al*, who reported that pain in neuromuscular diseases including AIM correlated with anxiety, depression and illness perception.[33]

Muscle strength, endurance, functional disability and physical activity

Studies reporting on muscle strength, endurance and functional disability are summarised in table 4. Studies assessing pain in relation to muscle strength and endurance showed weak or no correlations.[16 24 28 32 36 43] Functional disability measured using the Health Assessment Questionnaire–Disability Index was moderately correlated with pain in two cross-sectional studies.[28 42] Similarly, lower SF-36 BP scores were reported in patients with AIM with higher disability scores measured by the modified Rankin score.[35]

Twelve studies reporting pain measures in physical activity interventions (n=10)[11 12 14 15 20 24 27 34 37 39] or monitoring (n=2)[40 41] are summarised in table 5. For most of the physical activity interventions, there was no significant change in pain preintervention and postintervention. However, two studies noted improvement of pain after physical activity interventions.[12 34] An open-label study of 13 patients with mildly active DM/PM following a 12-week low-intensity resistance exercise programme showed improvement in mean±SD SF-36 BP scores after the intervention (59±11 vs 87±15, p=0.002).[34] Interestingly, different pain measures generated conflicting results in some of those studies. In an RCT randomising participants to a 4-week standardised hospital-based exercise programme or standard or care, no significant differences in SF-36 BP scores at 3, 6 or 12 months were reported, while pain intensity measured with a VAS was significantly improved at 12 months in the intervention group (mean VAS±SD 36±37 vs 5± 11) while remaining stable in the control group.[37] In a small study of 10 patients with AIM following a home exercise programme for a 12-week period, median SF-36 BP scores worsened at 12 weeks (88 (range 25–100) vs 51 (range 31–100)), while the VAS for pain intensity remained stable.[11]

DISCUSSION

This scoping review of 33 studies reporting on pain measures in AIM indicates that the burden of pain in subjects with AIM is greater than that of the general population and comparable to other chronic rheumatic diseases such as rheumatoid arthritis. However, it is important to note that pain was rarely the primary focus of the studies included. In addition, the studies were mostly small, single-centre studies with ill-defined populations and methodology that were at high risk of bias. This review highlights areas where research could help better characterise the pain experience in AIM.

None of the studies included in this review formally explored the relationship between disease activity and pain in AIM using comprehensive disease activity measures. Potential non-inflammatory pain contributors such as comorbidities (eg, fibromyalgia) or disease damage (eg, muscle dysfunction/atrophy) are often overlooked and can complicate disease activity assessment. Correlations between pain and biological markers of disease activity would be helpful to generate hypotheses about the possible mechanisms of pain in AIM. For example, a histopathological study by Noda *et al* showed that fasciitis rather than myositis was associated with myalgia in their cohort of 54 Japanese patients with AIM.[47] Additionally, patients who present with pain and myopathic features should be carefully assessed for AIM mimickers such as toxic, infectious and metabolic myopathies. Future studies on structural abnormalities including, but not limited to, the muscle (eg, joint, skin, nerves, Raynaud's disease) would be important to identify possible structures involved in pain generation in AIM.

Interestingly, some of the data reported in this review suggest sex differences in the AIM pain experience. This aligns with the literature in inflammatory arthritis such as rheumatoid arthritis and spondyloarthropathies, where female patients consistently report higher levels of pain than male patients.[48] Animal studies have also shown that there are important sex differences in pain processing.[49 50] This notion should be kept in mind when planning future epidemiological or mechanistic studies on pain in AIM

Table 4 Studies reporting on muscle strength, endurance and functional disability and pain

Study	Disease duration (years)*	Disease activity	Pain severity*	Findings
SF-36 BP (additive 0–100, norm-based mean 50, SD 10); lower score, more pain				
Ponyi *et al*[28]	Median (range) 8.9 (3.0–22.8)	Active disease 13%	Mean±SD DM: 54±18 PM: 58±20 OM: 66±18	Pain correlated weakly with MMT8 (higher scores, stronger; r=−0.27, p=0.01) and moderately with HAQ-DI (higher scores, more limitation; r=0.52, p<0.001)
Regardt *et al*[32]	Mean±SD 6.8±5.5	N/A	Mean All: 58 DM:55 PM: 58	Pain not significantly correlated with grip strength or hand mobility
Xu *et al*[43]	Median (IQR) 5 (2.5–7.4)	VAS score (0–100) Median (IQR) PhGA: 17 (5–31) PtGA: 29 (11–49)	Mean±SD 63±26	Pain weakly correlated with MMT-8 (higher score, stronger; r=0.30, p=0.03)
van de Vlekkert *et al*[35]	Median Baseline: 0.3 Scheduled visit at 18 months from baseline	At inclusion: early AIM with active disease 18 months: remission 33%, polyphasic 33%, chronic course 35%	Mean Baseline: 42 18 months: 70 Last follow-up*: 65	Pain worse with higher disability measured with the modified Rankin score
Poulsen *et al*[36]	Median (IQR) 6.7 (4.1–13)	VAS score (0–10) Median (IQR) PhGA 4.4 (2.2–6.7)	Mean±SD 60+26	Pain not associated with MMT-8 (higher score, stronger; β=0.09, p=0.88) in multiple linear regression
Alexanderson *et al*[16]	Fixed visit 1 year after diagnosis	VAS score (0–100) Median (IQR) PhGA: 10 (4–24) PtGA: 27 (7–49)	Median (IQR) 74 (51–74)	BP scores weakly correlated with FI2 (higher scores, less limitation; r=0.36, 95% CI 0.05 to 0.61). No significant correlation with MMT-8 (higher score, stronger; r=0.20, 95% CI −0.12 to 0.49)
VAS score (0–100); higher score, more pain				
Heikkila *et al*[24]	Mean±SD 6.4±6.1	68% stable medication for >3 months, 27% immunosuppression reduction in previous month	Mean±SD 26±27	Pain moderately correlated with Functional Index (higher scores, less limitation; r=−0.52, p<0.01) at baseline
Baschung Pfister *et al*[17]	Median (IQR) 1.5 (0.3–4.5)	Acute 19% Subacute 15% Chronic 67%	Median (IQR) 14 (0–31)	Pain weakly correlated with Myositis Activity Profile (higher score, more limitation; r=0.38, 95% CI 0.10 to 0.62)
Saygin *et al*[42]	Mean±SD 3±4.2	VAS score (0–10) Mean±SD 3.1±2.3	Mean±SD 2.7±2.6	Pain moderately correlated with PROMIS PF-20 (higher score, less limitation; r=−0.60, p<0.0001), SF-36 PF-10 (higher score, less limitation; r=−0.62, p<0.0001) and HAQ-DI (higher score, more limitation; r=0.60, p<0.0001)

*If not shown, measure of dispersion not provided.

AIM, autoimmune inflammatory myopathy; DM, dermatomyositis; FI2, Functional Index 2; HAQ-DI, Health Assessment Questionnaire–Disability Index; MMT-8, Manual Muscle Testing-8; N/A, not available; OM, overlap myositis; PhGA, Physician Global Assessment; PM, polymyositis; PROMIS PF-20, Patient-Reported Outcomes Measurement Information System physical function-20; PtGA, Patient Global Assessment; SF-36 BP, 36-Item Short Form Bodily Pain; VAS, visual analogue scale.

as ignoring the possibility of sex differences could lead to inconclusive or misleading results. Similarly, some of the studies included in this review suggested differences in pain measures when populations were stratified by AIM subsets. Disease subset classification in AIM is challenging and the subject of considerable debate in the field. However, as AIM phenotypes differ significantly based on clinical features and serological profiles, pain mechanisms and characteristics could as well. The studies included in this review in majority overlooked extramuscular features and their possible association with pain, and none considered autoantibody profiles. Some of the included studies also showed that muscle strength and endurance are not parameters that correlate well with pain.[16 24 28 32 36 43] Thus, researchers interested in pain in AIM should carefully select their study subjects and plan their analyses, paying particular attention to possible sex differences and heterogeneity in clinical phenotypes.

Finally, several of the studies included in this review used VAS as pain measure. The use of unidimensional scales for pain measurement has some limitations as it mostly reflects the sensory pain dimension and not the

Table 5 Studies assessing pain severity in relation with physical activity

Study (year)	Disease activity	Pain severity		Findings
		Baseline	Follow-up	
SF-36 BP (additive 0–100, norm-based mean 50, SD 10); lower score, more pain				
Alexanderson *et al*[11]	Inactive on stable treatment	SF-36 BP, median (range) 88 (25–100), VAS score (0–100) 13 (0–75)	12 weeks SF-36 BP median (range) 51 (31–100) VAS score (0–100) 9 (0–52)	BP only SF-36 domain that worsened after the 12 weeks exercise programme, discordance with VAS that remained stable
Alexanderson *et al*[12]	Early AIM with less than 3 months of immunosuppression	Median (range) 41 (0–84)	12 weeks Median (range) 72 (22–100)	BP scores significantly improved after exercise programme
Mattar *et al*[34]	VAS score (0–10), mean±SD Baseline: PhGA: 2.6±1.2 12 weeks: PhGA: 1.2±0.6	Mean±SD 59±11	12 weeks Mean±SD 87±15	Decreased pain after exercise programme (effect size 2.52, 46% improvement in BP score; p=0.002)
Landon-Cardinal *et al*[40]	VAS score (0–10), mean±SD	Mean±SD All: 65±26	Mean±SD All (V2)*: 76±21 All (V3)*: 73±23	Pain weakly correlated with physical activity at baseline (r=0.33, p<0.05) and follow-up (r=0.21, p<0.05).
	DM PhGA: 3±2			
	IMNM PhGA: 2±2			
	OM PhGA: 3±3			
Tiffreau *et al*[37]	Included in study if ongoing relapse	SF-36 BP Mean±SD Programme: 50±25 Control: 48±21 VAS score (0–100) Mean±SD Programme: 36±37 Control: 29±25	1 year VAS Mean±SD Programme: 5±11 Control: 33±36	No significant BP score differences between groups at 3, 6 and 12 months (figures only); discordance with pain VAS showing a significant reduction in the programme group (p=0.04)
VAS; higher score, more pain				
Heikkilä *et al*[24]	68% stable medication for >3 months, 27% medication tapered in previous month.	VAS score (0–100) Mean±SD 26±27	3 weeks Mean change (%) −2.8 (95%CI −11.7 to 6.2)	No change in pain after exercise programme
Varjú *et al*[27]	N/A	VAS score (0–100) Mean±SD Early recovery: 34±27 Chronic stage: 29±24	3 weeks Mean±SD Early recovery: 23±24 Chronic stage: 18±16	No change in pain after training in both groups
Wallace *et al*[39]	6MWD (m), mean±SD Group A: 327±92 Group B: 270±78	VAS score (0–10) Mean±SD Group A: 1±2 Group B: 1±3	12 weeks Mean±SD Group A: 0±3 Group B: 1±3	No change in pain after exercise programme
Rockette-Wagner *et al*[41]	VAS score (0–10), mean±SD PhGA: 3.1±2.3	VAS score (0–10) Mean±SD 2.7±2.6	N/A	Moderate negative correlation between pain and physical activity (r=−0.38 to −0.40, p<0.001)
NHP score (0–100); higher score, more pain				
Chung *et al*[20]	Stable patients with low disease activity per inclusion criteria	Mean±SD Creatine: 38±33 Placebo: 30±29	3 and 6 months N/A	Results not shown but no significant difference in pain reported in between or within groups at 3 or 6 months
Alexanderson *et al*[15]	Early AIM (<3 months' duration) improving on treatment per inclusion criteria	Median (IQR) Programme: 20 (14-29) Control: 0 (0–9)	24 weeks N/A	No significant difference in pain between or within groups at 24 weeks for pain
Borg scale (0–10); higher score, more pain				
Alexanderson *et al*[14]	VAS score (0–10), mean±SD Baseline: PhGA: 0.8±1 7 weeks: PhGA: 0.8±0.9	Median (range) 1.3 (0–3)	7 weeks Median (range) 1.3 (0–3)	Comment in the Discussion section that patients with arthritis may require load adjustment to avoid increasing pain

Continued

Table 5 Continued

*Mean±SD time between baseline and V1 was 94±12 days, and V1 and V2 was 96±17 days.
DM, dermatomyositis; IMNM, immune-mediated necrotising myopathy; 6MWD, 6 min walk distance; N/A, not available; NHP, Nottingham Health Profile; OM, overlap myositis; PhGA, Physician Global Assessment; PM, polymyositis; PtGA, Patient Global Assessment; SF-36 BP, 36-Item Short Form Bodily Pain; VAS, visual analogue scale.

affective aspect of pain. On the other hand, multidimensional tools that are more comprehensive take longer to administer. Moreover, as there is currently no consensus on how to measure pain in AIM, different tools are used, and their results are difficult to compare. As shown in this review, discordance is possible between unidimensional and multidimensional measures, and it is imperative that future studies address this important issue. There is a pressing need for systematic and standardised pain assessment in AIM to facilitate research and improve management of patients with AIM.

CONCLUSION

The burden of pain in AIM is considerable. However, due to the heterogeneity and low quality of the evidence available, significant knowledge gaps persist. Studies are needed to longitudinally characterise the pain experience in AIM, including predictors of severity and clinical correlates to identify possible pain mechanisms and offer targeted management to patients.

Contributors All authors have contributed to study conception, data collection, data analysis and interpretation, drafting of the article, critical revision of the article and final approval of the submitted version.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD

Valérie Leclair http://orcid.org/0000-0001-8643-6697

REFERENCES

1 Lundberg IE, Tjärnlund A, Bottai M, *et al*. 2017 European League against Rheumatism/American College of rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. *Ann Rheum Dis* 2017;76:1955–64.
2 Allenbach Y, Benveniste O, Goebel H-H, *et al*. Integrated classification of inflammatory myopathies. *Neuropathol Appl Neurobiol* 2017;43:62–81.
3 Meyer A, Meyer N, Schaeffer M, *et al*. Incidence and prevalence of inflammatory myopathies: a systematic review. *Rheumatology* 2015;54:50–63.
4 Greenfield J, Hudson M, Vinet E, *et al*. A comparison of health-related quality of life (HRQoL) across four systemic autoimmune rheumatic diseases (SARDs). *PLoS One* 2017;12:e0189840.
5 Regardt M, Basharat P, Christopher-Stine L, *et al*. Patients' Experience of Myositis and Further Validation of a Myositis-specific Patient Reported Outcome Measure - Establishing Core Domains and Expanding Patient Input on Clinical Assessment in Myositis. Report from OMERACT 12. *J Rheumatol* 2015;42:2492–5.
6 Park JK, Mecoli CA, Alexanderson H, *et al*. Advancing the development of patient-reported outcomes for adult myositis at OMERACT 2016: an international Delphi study. *J Rheumatol* 2017;44:1683–7.
7 Regardt M, Mecoli CA, Park JK, *et al*. OMERACT 2018 modified patient-reported outcome domain core set in the life impact area for adult idiopathic inflammatory myopathies. *J Rheumatol* 2019;46:1351–4.
8 Mecoli CA, Park JK, Alexanderson H, *et al*. Perceptions of patients, caregivers, and healthcare providers of idiopathic inflammatory myopathies: an international OMERACT study. *J Rheumatol* 2019;46:106–11.
9 Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;8:19–32.
10 Pham MT, Rajić A, Greig JD, *et al*. A scoping review of scoping reviews: advancing the approach and enhancing the consistency. *Res Synth Methods* 2014;5:371–85.
11 Alexanderson H, Stenström CH, Lundberg I. Safety of a home exercise programme in patients with polymyositis and dermatomyositis: a pilot study. *Rheumatology* 1999;38:608–11.
12 Alexanderson H, Stenström CH, Jenner G, *et al*. The safety of a resistive home exercise program in patients with recent onset active polymyositis or dermatomyositis. *Scand J Rheumatol* 2000;29:295–301.
13 Albrecht K, Huscher D, Callhoff J, *et al*. Trends in idiopathic inflammatory myopathies: cross-sectional data from the German national database. *Rheumatol Int* 2020;40:1639–47.
14 Alexanderson H, Dastmalchi M, Esbjörnsson-Liljedahl M, *et al*. Benefits of intensive resistance training in patients with chronic polymyositis or dermatomyositis. *Arthritis Rheum* 2007;57:768–77.
15 Alexanderson H, Munters LA, Dastmalchi M, *et al*. Resistive home exercise in patients with recent-onset polymyositis and dermatomyositis -- a randomized controlled single-blinded study with a 2-year followup. *J Rheumatol* 2014;41:1124–32.
16 Alexanderson H, Regardt M, Ottosson C, *et al*. Muscle strength and muscle endurance during the first year of treatment of polymyositis and dermatomyositis: a prospective study. *J Rheumatol* 2018;45:538–46.
17 Baschung Pfister P, de Bruin ED, Bastiaenen CHG, *et al*. Reliability and validity of the German version of the myositis activities profile (MAP) in patients with inflammatory myopathy. *PLoS One* 2019;14:e0217173.
18 Christopher-Stine L, Wan GJ, Kelly W, *et al*. Patient-Reported dermatomyositis and polymyositis flare symptoms are associated with disability, productivity loss, and health care resource use. *J Manag Care Spec Pharm* 2020;26:1424–33.
19 Chung YL, Mitchell HL, Houssien DA, *et al*. A comparative study of outcome in myositis and other musculoskeletal disorders assessed using the Nottingham health profile. *Clin Exp Rheumatol* 2001;19:447–50.
20 Chung Y-L, Alexanderson H, Pipitone N, *et al*. Creatine supplements in patients with idiopathic inflammatory myopathies who are clinically weak after conventional pharmacologic treatment: six-month, double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* 2007;57:694–702.
21 Cleary LC, Crofford LJ, Long D, *et al*. Does computed tomography-based muscle density predict muscle function and health-related

quality of life in patients with idiopathic inflammatory myopathies? *Arthritis Care Res* 2015;67:1031–40.
22 Feldon M, Farhadi PN, Brunner HI, *et al*. Predictors of reduced health-related quality of life in adult patients with idiopathic inflammatory myopathies. *Arthritis Care Res* 2017;69:1743–50.
23 Goreshi R, Chock M, Foering K, *et al*. Quality of life in dermatomyositis. *J Am Acad Dermatol* 2011;65:1107–16.
24 Heikkilä S, Viitanen J, Kautiainen H. Rehabilitation in myositis: preliminary study. *Physiotherapy* 2001;87:301–9.
25 van der Meulen MF, Hoogendijk JE, Wokke JH, *et al*. Oral pulsed high-dose dexamethasone for myositis. *J Neurol* 2000;247:102–5.
26 Sultan SM, Ioannou Y, Moss K, *et al*. Outcome in patients with idiopathic inflammatory myositis: morbidity and mortality. *Rheumatology* 2002;41:22–6.
27 Varjú C, Pethö E, Kutas R, *et al*. The effect of physical exercise following acute disease exacerbation in patients with dermato/polymyositis. *Clin Rehabil* 2003;17:83–7.
28 Ponyi A, Borgulya G, Constantin T, *et al*. Functional outcome and quality of life in adult patients with idiopathic inflammatory myositis. *Rheumatology* 2005;44:83–8.
29 Sadjadi R, Rose MR, Group MS, Muscle Study Group. What determines quality of life in inclusion body myositis? *J Neurol Neurosurg Psychiatry* 2010;81:1164–6.
30 van de Vlekkert J, Hoogendijk JE, de Haan RJ, *et al*. Oral dexamethasone pulse therapy versus daily prednisolone in sub-acute onset myositis, a randomised clinical trial. *Neuromuscular Disorders* 2010;20:382–9.
31 Mahler EAM, Blom M, Voermans NC, *et al*. Rituximab treatment in patients with refractory inflammatory myopathies. *Rheumatology* 2011;50:2206–13.
32 Regardt M, Welin Henriksson E, Alexanderson H, *et al*. Patients with polymyositis or dermatomyositis have reduced grip force and health-related quality of life in comparison with reference values: an observational study. *Rheumatology* 2011;50:578–85.
33 Rose MR, Sadjadi R, Weinman J, *et al*. Role of disease severity, illness perceptions, and mood on quality of life in muscle disease. *Muscle Nerve* 2012;46:351–9.
34 Mattar MA, Gualano B, Perandini LA, *et al*. Safety and possible effects of low-intensity resistance training associated with partial blood flow restriction in polymyositis and dermatomyositis. *Arthritis Res Ther* 2014;16:473.
35 van de Vlekkert J, Hoogendijk JE, de Visser M. Long-Term follow-up of 62 patients with myositis. *J Neurol* 2014;261:992–8.
36 Poulsen KB, Alexanderson H, Dalgård C, *et al*. Quality of life correlates with muscle strength in patients with dermato- or polymyositis. *Clin Rheumatol* 2017;36:2289–95.
37 Tiffreau V, Rannou F, Kopciuch F, *et al*. Postrehabilitation functional improvements in patients with inflammatory myopathies: the results of a randomized controlled trial. *Arch Phys Med Rehabil* 2017;98:227–34.
38 Opinc AH, Brzezińska OE, Makowska JS. Disability in idiopathic inflammatory myopathies: questionnaire-based study. *Rheumatol Int* 2019;39:1213–20.
39 Wallace A, Pietrusz A, Dewar E, *et al*. Community exercise is feasible for neuromuscular diseases and can improve aerobic capacity. *Neurology* 2019;92:e1773–85.
40 Landon-Cardinal O, Bachasson D, Guillaume-Jugnot P, *et al*. Relationship between change in physical activity and in clinical status in patients with idiopathic inflammatory myopathy: a prospective cohort study. *Semin Arthritis Rheum* 2020;50:1140–9.
41 Rockette-Wagner B, Saygin D, Moghadam-Kia S, *et al*. Reliability, validity and responsiveness of physical activity monitors in patients with inflammatory myopathy. *Rheumatology* 2021;60:5713–23.
42 Saygin D, Oddis CV, Dzanko S, *et al*. Utility of patient-reported outcomes measurement information system (PROMIS) physical function form in inflammatory myopathy. *Semin Arthritis Rheum* 2021;51:539–46.
43 Xu A, Sun C, Metcalf R, *et al*. Health-Related quality of life and work impairment in idiopathic inflammatory myopathies in South Australia. *Int J Rheum Dis* 2021;24:809–14.
44 van de Vlekkert J, Hoogendijk JE, de Haan RJ, *et al*. Oral dexamethasone pulse therapy versus daily prednisolone in sub-acute onset myositis, a randomised clinical trial. *Neuromuscul Disord* 2010;20:382–9.
45 Boyer F, Morrone I, Laffont I, *et al*. Health related quality of life in people with hereditary neuromuscular diseases: an investigation of test-retest agreement with comparison between two generic questionnaires, the Nottingham health profile and the short form-36 items. *Neuromuscul Disord* 2006;16:99–106.
46 Kalkman JS, Schillings ML, van der Werf SP, *et al*. Experienced fatigue in facioscapulohumeral dystrophy, myotonic dystrophy, and HMSN-I. *J Neurol Neurosurg Psychiatry* 2005;76:1406–9.
47 Noda K, Yoshida K, Ukichi T, *et al*. Myalgia in patients with dermatomyositis and polymyositis is attributable to fasciitis rather than myositis: a retrospective study of 32 patients who underwent histopathological examinations. *J Rheumatol* 2017;44:482–7.
48 Barnabe C, Bessette L, Flanagan C, *et al*. Sex differences in pain scores and localization in inflammatory arthritis: a systematic review and metaanalysis. *J Rheumatol* 2012;39:1221–30.
49 Sorge RE, LaCroix-Fralish ML, Tuttle AH, *et al*. Spinal cord Toll-like receptor 4 mediates inflammatory and neuropathic hypersensitivity in male but not female mice. *J Neurosci* 2011;31:15450–4.
50 Fernandez-Zafra T, Gao T, Jurczak A, *et al*. Exploring the transcriptome of resident spinal microglia after collagen antibody-induced arthritis. *Pain* 2019;160:224–36.