MS* REGISTER

Exploring pain associated with multiple sclerosis (MS) and its relationship with anxiety, depression, and physical disability.

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AIM

An analysis to explore the relationship between pain, anxiety, depression and physical disability in multiple sclerosis (MS).

INTRODUCTION

Multiple sclerosis (MS) is an autoimmune condition that affects the brain and spinal cord, with a typical onset age between 20 and 40 [1-3].

Pain is a common symptom in people with MS and can be categorised as mild, moderate, or severe. Pain can cause serious disability along with a reduced average life expectancy in people living with MS. Despite the wide prevalence of pain in MS ranging from 29 – 92% [4], there exists a substantial gap in the report of pain in MS with a consistent focus on fatigue [5-8]. Even though fatigue could be a main contributor to pain presence, pain in itself, is not a unidimensional outcome of MS and has shown to be largely dominant in impacting higher levels of anxiety, depression, disability, reduced quality of life and sleep problems [9-11].

As a result, the key justification for this analysis is to present a comprehensive and detailed assessment of pain in MS and its relationship with anxiety, depression, and physical disability.

METHODOLOGY

A longitudinal cohort was selected from the UKMSR that includes the population's demographics and symptoms [12]. Pain was measured using a numeric rating scale with 0 indicating 'mild pain', 1 indicating 'moderate pain', and 2 indicating 'severe pain'.

Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS). HADS total score ranges from 0 – 21 with scores < 8 indicating 'no anxiety/depression', 8 – 10 indicating 'mild anxiety/depression', 11 -14 indicating 'moderate anxiety/depression', and 15 – 21 indicating 'severe anxiety/depression' [13].

The level of disability was scored using the Multiple Sclerosis Impact Scale 29-physical sub-score (MSIS29 – Phys, with a total score range of 0-100) [14].

Statistical analysis was performed using R. The sample and summarised data were described using descriptive statistics (mean and standard deviation). Summary tables describing the characteristics of the study population were created using Tableone in R.

RESULTS

	Pain severity			
	Mild	**Moderate**	**Severe**	**Significant value (p-test)**
n	553	1237	546	
Age (mean (SD))	54.06 (12.15)	56.98 (11.42)	58.11 (11.59)	<0.001
Onset Age (mean (SD))	37.72 (10.97)	39.74 (10.60)	40.00 (11.22)	0.017
Diagnosis Age (mean (SD))	41.61 (11.14)	44.09 (10.60)	44.87 (11.12)	<0.001
MSTypeNow (%)				<0.001
PPMS	74 (13.4)	175 (14.1)	109 (20.0)	
RRMS	347 (62.7)	617 (49.9)	219 (40.1)	
SPMS	132 (23.9)	445 (36.0)	218 (39.9)	
MSAtDiagnosis (%)				<0.001
PPMS	72 (13.0)	168 (13.6)	100 (18.3)	
RRMS	444 (80.3)	938 (75.8)	370 (67.8)	
SPMS	21 (3.8)	73 (5.9)	47 (8.6)	
Unknown	16 (2.9)	58 (4.7)	29 (5.3)	
Gender = FEMALE/MALE (%)	418/135 (75.6/24.4)	959/275 (77.7/22.3)	412/133 (75.6/24.4)	0.481
HADS anxiety baseline (mean (SD))	7.64 (4.06)	8.87 (4.35)	10.17 (4.49)	<0.001
HADS depression baseline (mean (SD))	6.67 (3.66)	8.29 (3.99)	9.80 (4.23)	<0.001
MSISPhys baseline (mean (SD))	40.24 (22.93)	53.07 (22.45)	63.86 (21.03)	<0.001

Table 1: Demographic and clinical characteristics of the population stratified by pain severity.

As shown in Table 1, a higher percentage of people living with primary progressive MS (PPMS) experience severe pain compared to other MS types (relapsing-remitting MS (RRMS) and secondary progressive MS (SPMS). Additionally, as the level of pain severity increases, levels of anxiety (7.64 v 10.17), depression (6.67 v 9.80), and disability (40.24 v 63.86) all increase as well.

	FEMALE	MALE	p
N	2171	685	
Age (mean (SD))	55.73 (11.90)	58.90 (11.71)	<0.001
Onset Age (mean (SD))	38.09 (10.92)	41.86 (10.79)	<0.001
Diagnosis Age (mean (SD))	42.42 (10.93)	45.96 (10.88)	<0.001
MSTypeNow (%)			<0.001
PPMS	231 (11.1)	184 (28.4)	
RRMS	1146 (54.9)	232 (35.9)	
SPMS	710 (34.0)	231 (35.7)	
MSAtDiagnosis (%)			<0.001
PPMS	229 (10.5)	188 (27.4)	
RRMS	1693 (78.0)	406 (59.3)	
SPMS	116 (5.3)	50 (7.3)	
Unknown	133 (6.1)	41 (6.0)	
Gender = FEMALE/MALE (%)	2171/0 (100.0/0.0)	0/685 (0.0/100.0)	<0.001
Pain severity (mean (SD))	1.01 (0.68)	1.00 (0.70)	0.65

Table 2: Demographics and clinical characteristics of the study population stratified by gender.

As shown in Table 2, males are reported to be older, have an older onset age and diagnosis age, and are more likely to have PPMS than their female counterparts.
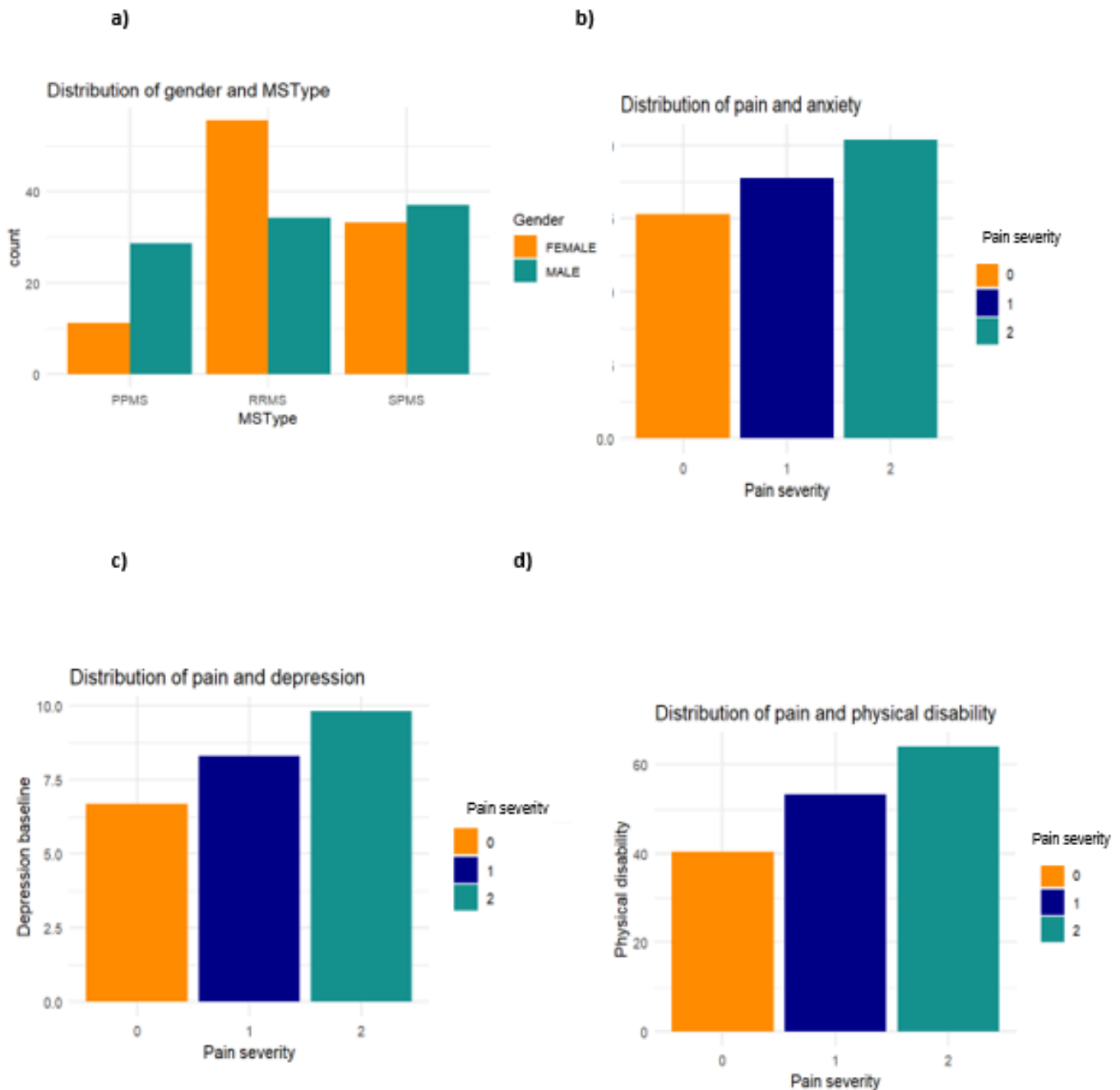
Figure 1: a) Distribution of gender and MSType b) Distribution of pain and anxiety c) Distribution of pain and depression d) Distribution of pain and physical disability.

As shown in Figure 1; b) baseline anxiety increases as pain severity increases, c) baseline depression increases as pain severity increases, d) physical disability increases as pain severity increases. Figure 1 a) also shows a higher rate of males experiencing PPMS and SPMS than females.

DISCUSSION
The results of this analysis reveal different levels of pain in patients with MS. Additionally, MS patients who experienced severe pain were more likely to have greater anxiety, depression, and physical disability. As a result, their daily activities which sum up their quality of life are reduced.

The findings of this analysis are consistent with the results of several studies on the intertwining of pain in MS with mood and physical disability [1,7]. Similarly, studies revealed severe pain as a predictor of increased physical disability, anxiety, and depression [7, 15-16]. This could be argued that the presence or severity of one symptom may amplify the presence or severity of the other. Essentially, it can be summarised from this analysis that increased pain intertwines with increased levels of depression, physical disability, and anxiety.

Table 3: Strengths and limitations of the analysis.

STRENGTHS	LIMITATIONS
Includes many men thus providing a unique opportunity to explore MS and pain in both genders. In contrast, many studies on Pain in MS included few male participants and tended towards female participants experiencing severe pain.	Symptoms data was only collected from 2018 onwards.

Overall, the results of this study help for better exploration of pain among people living with MS. The different levels of pain and their associations are necessary as their results would help for prioritised management and treatment of MS-related pain, anxiety, depression and physical disability.

CONCLUSION
Pain is a common symptom among people living with MS. While pain is largely prevalent in MS patients, it can also impact the levels of MS-related physical disability, depression, and anxiety. The different levels of pain experienced by participants highlight the importance of exploring pain and adequate intervention in the management and treatment of pain in MS patients.

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