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Title page

A clinical and radiographic comparison of patients with psoriatic arthritis from different ethnic backgrounds

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Abstract (228 words)

Background

There are few papers concerning ethnic differences in disease expression in psoriatic arthritis (PsA), which may be influenced by a number of genetic, lifestyle and cultural factors.

Objectives

To compare clinical and radiographic phenotype in people of South Asian (SA) and North European (NE) origin with a diagnosis of psoriatic arthritis.

Methods

This was a cross-sectional observational study recruiting patients of SA and NE origin from two hospitals in a well defined area in the North of England.

Results

58 SA, and 48 NE patients were recruited. SA patients had a more severe clinical phenotype with more tender (med 5 v 2) and swollen (med 1 v 0) joints, more severe enthesitis (med 3 v 1.5), more patients with dactylitis (24% v 8%), more severe skin disease (med PASI 2.2 v 1) and worse disease activity, as measured by the composite psoriatic arthritis disease activity score (mean PASDAS 4.5 v 3.6). With regards to patient completed measures SA patients had worse impact with poorer quality of life and function (mean HAQ 0.9 v 0.6; mean PsAQoL 10.8 v 6.2; mean SF36-PCS 33.5 v 38.9). No significant differences in current methotrexate and biologic use were found.

Conclusions

SA patients had a worse clinical phenotype and worse impact of disease, , than NE patients. Further studies are needed to confirm and explore the reasons behind these differences.

Key words: psoriatic arthritis, rheumatoid arthritis, ethnic differences, outcomes

Key messages :

1. South Asian patients with psoriatic arthritis have a worse clinical phenotype than North European patients.
2. South Asian patients also have more patient reported impact of disease .
3. Use of methotrexate and biologic drugs is similar across ethnic groups.

Introduction

Spondyloarthritis (SpA) encompasses a group of diseases which include psoriatic arthritis (PsA), ankylosing spondylitis (AS), reactive arthritis, enteropathic arthritis and undifferentiated spondyloarthropathy. Ethnicity has been implicated as a factor contributing to differences in disease expression, clinical manifestations and prognosis in SpA and rheumatoid arthritis (RA) (1, 2). Studies have found that SpA runs a different course in non-white Caucasians, Asians and Africans as compared to White Caucasian populations (1). Moreover the association between HLA-B27 and SpA was found to be different across these different populations (1). Observational studies have found that RA patients with a South Asian (SA) background reported more pain and disability as compared to North European RA patients, despite similar levels of inflammation, number of swollen joints and the same incidence of rheumatoid factor positivity in both groups. There were also fewer erosions seen in SA RA patients(2).

PsA is an inflammatory arthritis, which occurs in the presence of psoriasis, and is the second most common type of arthritis, after rheumatoid, accounting for 10-15% of patients seen in early arthritis clinics (3). Both RA and PsA have significant impact on function and quality of life (4). PsA was considered a milder disease than RA (5), but recent evidence refutes this (4, 6).

The purpose of this study was to compare clinical manifestations and impact of PsA in people of SA and NE ethnicity seen in two clinics in the North of England. Our hypothesis was that disease activity and structural damage would be less in the SA population whereas disease impact would be similar to that seen in the NE population.

Methods

Patients over the age of 16 with a consultant diagnosis of PsA attending rheumatology out-patient clinics at St. Luke's Hospital, Bradford and Dewsbury Hospital, Dewsbury between January 2011 and December 2013 were invited to participate. Patients were classified by ethnic group according to their self-reported indication, and their ancestry: those classified as of SA origin were required to have at least 3 grandparents born in Pakistan or India and patients who classified as of North European origin were required to have at least 3 grandparents born in northern Europe. Exclusion criteria included age less than 16 and any other rheumatic diagnosis. Informed written consent was obtained at the study visit before any study information was collected.

Study assessments

Clinical assessments included; 78 tender joint count, 76 swollen joint count, the Leeds enthesitis index, a 20-digit tender dactylitis score, the modified nail psoriasis index, the psoriasis area and severity index (PASI) score and physician global, skin and arthritis visual analogue scores. Physicians were asked to record if they thought that the patient was in minimal disease activity (MDA). As a disease activity score the PASDAS was calculated: the PASDAS is a composite score which includes assessments of patient and physician global scores, a tender and swollen joint count, enthesitis and dactylitis, the C-reactive protein (CRP) and the physical function subscale of the SF36 (7). Radiographs of hands and feet were not specifically obtained for this study but any radiographs taken within 12 months of the study visit were read for erosion and joint space narrowing using the modified Sharp-van der Heidje (SVDH) method (8). Unblinded radiographs were read by two observers (PSH and FM) working in tandem and using a consensus scoring method.

Patient completed measures included; the health assessment questionnaire (HAQ, the Bath Ankylosing spondylitis Disease Activity Index (BASDAI), the Ankylosing spondylitis Quality of Life tool (ASQol), the Psoriatic arthritis Quality of Life tool (PsAQol), the Short Form 36 (SF36) questionnaire and the Dermatology Life Quality Index (DLQI). In addition, patients were asked to complete four 100mm visual analogue scores for global disease, skin disease, arthritis and pain. Patients were also asked if they thought that their disease was well controlled (yes/no answer).

Statistics

No formal sample size calculation was undertaken in this cross-sectional observational study. Numbers are reported as mean or median according to distribution with appropriate statistical test for parametric and non-parametric data.

Results

Fifty-eight SA patients were recruited, 8 of whom were from Dewsbury. Forty-eight patients were of NE origin and all were recruited from Bradford. Due to historical immigration patterns in Bradford and Dewsbury most of the SA patients were either first generation immigrants or were born in the UK and had grandparents from a relatively well-defined area in North East Pakistan (Miapur). The majority of the NE patients were born in the UK or had grandparents born in the UK. There were no significant differences in age, gender, and duration of arthritis between groups, though the NE patients had a longer duration of psoriasis (Table 1).

Comparison of the two groups demonstrated a more severe phenotype in SA patients: more tender and swollen joints, more severe enthesitis (though fewer patients with enthesitis), more patients with dactylitis (though no difference in number of dactylitic digits in those with dactylitis), more severe skin disease and worse disease activity, as measured by the composite psoriatic arthritis disease activity score (PASDAS). In patients in whom recent hands and feet radiographs were available there was no difference in SVDH scores between the groups (Table 1) and, moreover, no difference between groups in the time interval between diagnosis and radiograph (mean time between diagnosis and radiograph for SA, 5.3y, and for NE 5.2y).

With regards to patient completed measures SA patients had worse impact with poorer quality of life and function (Table 1). In particular, SA patients had higher VAS scores (except for arthritis VAS), higher HAQ, higher PsAQoL, higher ASQoL, and worse scores on the physical function sub-scale of the SF36. Despite these differences, an equal proportion of patients in each group reported that they felt their disease was well controlled (Table 1).

Of note in Table 1 there is a discrepancy between those patients reporting that they thought their disease was well controlled and their disease activity categorisation by PASDAS score. Thus, in the SA group, 100% of those patients in the very low disease activity and low disease activity categories thought their disease was well controlled, but also 65% and 35% in the moderate disease activity and high disease activity categories respectively also thought their disease was well controlled. In the NE group the equivalent figures were 100%, 92%, 79% and 29% for the very low, low, moderate, and high disease activity categories respectively.

Current and past treatments were recorded (Table 2) but no significant differences between SA and NE patients were seen. In particular, a similar percentage of patients were currently taking methotrexate and biologic drugs. Further analysis examined the first date of methotrexate (in most cases the first disease modifying drug given) use in relation to the date of arthritis diagnosis but there was no difference between the SA and NE groups (mean time to MTX use for SA 214 days, for NE 215 days).

Discussion

This relatively small cross-sectional study is the first systematic study comparing the clinical phenotype, impact of disease, and treatment of patients with psoriatic arthritis from different ethnic backgrounds in the UK. Contrary to our study hypothesis, and based on studies in RA, SA patients had a more severe clinical phenotype and greater impact of disease, yet received similar treatment.

This study contrasts with that in a similar population with rheumatoid arthritis where it was found that NE patients had more severe disease but, in contrast, SA patients had greater impact of disease as measured by pain and loss of function (2). In that study the key factor in disease severity was the presence of the HLA-DRB ‘shared epitope’ haplotype. Unfortunately, such genetic data were unavailable for the current cohort, but genetic predictors of severity are less well established in PsA. In a Toronto cohort, HLA-B27 was one genetic marker associated with disease severity in PsA, but HLA antigens HLA-B39, and HLA=DQw3 were also associated with disease progression in the same cohort, while HLA-DR7 was "protective" (9) In the same cohort HLA-B39 was associated with progression in early disease (9). There are few population based data on HLA frequencies in SA, and particularly Pakistani, populations, though one small study suggested a low frequency (<3%) of the HLA-B27 genotype, and was a different sub-type (B*2707) (10). More recent genome wide studies have focussed more on susceptibility genes rather than disease severity genes. Nevertheless, hitherto unrecognised genetic factors may underline the differences we have observed.

Could the presence of co-morbidities have influenced the difference in disease impact found in this study? In a cross-sectional cohort one of the factors influencing disease impact was the presence of co-morbidities (11), though the magnitude of the effect was not large. Moreover, the co-morbidity index used in that study included obesity. In the current study the groups were matched for body mass index and hypertension, though not for diabetes. Unfortunately, the current study did not collect extensive data on co-morbidities so further analysis of this possible explanatory factor was not possible. It is worth noting, however, that other studies have not found a worse outcome associated with co-morbidities (12, 13).

The discrepancy between patient opinion of their disease control and disease activity categorisation by PASDAS highlights a previously reported mismatch using this composite outcome measure. The study by Fei et al found that 55% of people reporting that their disease control was acceptable (patient acceptable symptom state, PASS) had moderate disease activity according to the PASDAS, and 16.7% of those with high disease activity considered themselves to be in a PASS (14). The discrepancy between what is acceptable to the patient and what is measured by the PASDAS remains to be explained, particularly as the two major components of the PASDAS are the patient and physician global scores. In this study fully 87% of patients with a global VAS score of over 30 indicated that they thought their disease was well controlled (data not shown). It is possible therefore that, for some patients, the question about their disease control was answered more to reflect the *process* of their care, rather than their disease control.

Although the SA patients in this study had a more severe phenotype, the treatments used were the same across the two groups and time to first methotrexate use was similar between groups. In this study only a minority were thought to be in minimal disease activity by the treating physician. Although this study was undertaken before the publication of the TICOPA trial (15) it remains unexplained why patients not thought to be in MDA did not have their treatment escalated. One possibility is that the SA patients were, on the whole, satisfied with their disease control (Table 1). Another reason may have been reluctance to change or start new disease modifying treatment – we have previously shown higher discontinuation rates due to adverse events for SA patients in Bradford (16). Data on compliance and delay to diagnosis were not collected as part of this study.

The prevalence of PsA is 0.04% to 0.1% in the general population.(17) However, one systematic review suggests that there are wide variations in the prevalence of PsA in different countries; ranging from 20 to 420 patients per 100,000 in Europe and the USA respectively. Clearly, some of this variation will be due to the population screening method and some due to the case definition. With the availability and acceptance of the CASPAR criteria, future studies should provide more comparable prevalence and incidence figures. A Singaporean study suggests that Indian patients with psoriasis have twice the risk of developing PsA than Chinese patients, or the Singapore population as a whole, but data from Asia are limited.(18). PsA affects men and women almost equally in Caucasian population (19). Studies from Singapore, Hong Kong (20) (21) and Iran (22) confirm this, but a small Kuwaiti study found a predominance amongst females in a group of PsA patients (23).

There are several limitations to this study. This was a cross-sectional observational study where recruitment may have been influenced by several factors, including language, work availability, the reluctance of SA women to take part in ‘research’ appointments out with their normal clinic times. In addition, the study did not control for co-morbidities (such as metabolic syndrome, smoking and alcohol). A measure of the duration of symptoms before diagnosis and treatment would have been informative, and should be included in future studies, as delays may influence subsequent disease severity (24)

Current knowledge about PsA is largely based upon the results of studies of Caucasian populations. Studies performed across various other population groups suggest that there is some variation in disease characteristics by ethnic group, but these studies are generally of poor quality. This study has added, modestly, to that data. Ethnicity may be an important factor in determining the presentation and management of PsA but further, longitudinal, studies, controlling for such factors

as socioeconomic status, smoking, delay in diagnosis, and treatment response are needed to further explore these differences.

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Table 1. Demographics, clinical data and patient reported outcomes

	South Asian	North European	Statistic (see legend for details	p
N	58	48		
Age (y) Mean (sd)	44.9 (13.7)	47.2 (13.8)	0.9+	ns
Sex	33M 25F	28M 20F	0.02¬	ns
Duration arthritis (y) Mean (sd)	11.5 (5.0)	11.1 (5.5)	0.3+	ns
Duration psoriasis (y) Mean (sd)	15.8 (7.5)	24.2 (15.1)	2.8+	0.01
Current smoker N (%)	1 (2)	9 (20)	13.4¬	0.001
BMI mean (sd)	29.8 (7.1)	29.2 (6.5)	0.4+	ns
Hypertension N (%)	19 (33)	17 (35)	0.1¬	ns
Diabetes N (%)	12 (21)	2 (4)	6.3¬	0.01
TJC (0-78) median (range)	5.0 (0 - 59)	2.0 (0 - 20)	2.8~	0.006
SJC (0-76) median (range)	1.0 (0 - 19)	0 (0 - 10)	2.6~	0.008
N (%) patients with enthesitis	18 (31)	18 (38)	0.5¬	ns
LEI in patients with enthesitis (0-6) median (range)	3.0 (1 - 6)	1.5 (1 - 4)	3.1~	0.002
N(%) patients with dactylitis	14 (24)	4 (8)	5.7¬	0.03
Dactylitis count in patients with dactylitis (0-20) median (range)	1.5 (1 - 3)	1.5 (1 - 2)	0.2~	ns
PASI (0-72) Median (range)	2.15 (0 – 39.3)	1.0 (0 – 17.6)	2.3	0.03
mNAPSI median (range)	2.0 (0 - 40)	2.0 (0 - 38)	0.6	ns
PASDAS (0-10) mean (sd)	4.63 (1.6)	3.53 (1.6)	3.2	0.002
PASDAS categories:				
Very low disease activity N (%)	2 (4)	7 (17)		
Low disease activity N (%)	8 (16)	13 (31)		
Moderate disease activity N (%)	20 (41)	15 (38)		
High disease activity N (%)	19 (39)	7 (17)		
MDA N(%)	23 (45)	30 (63)	15.3¬	0.0001
SVDH total score (0-520) Median (range)	2.0 (0 - 236)	2.0* (0 - 43)	0.9~	ns
Global VAS (0-100) Mean (sd)	51.9 (29.6)	38.9 (29.1)	2.2*	0.03
Arthritis VAS (0-100) Mean (sd)	50.6 (31.9)	40.9 (30.5)	1.6*	ns
Skin VAS (0-100) Mean (sd)	40.2 (32.4)	22.4 (25.1)	3.1*	0.002
Pain VAS (0-100) Mean (sd)	49.5 (30.4)	35.2 (27.4)	2.5*	0.01
Disease well controlled N (%)	31 (61)	31 (66)	11.0¬	0.004
BASDAI (0-10) Mean (sd)	4.9 (3.2)	3.8 (2.9)	1.9+	ns
HAQ (0-3) Mean (sd)	0.9 (0.8)	0.6 (0.7)	2.0+	0.05
PsAQol (0-20) Mean (sd)	10.8 (7.8)	6.2 (6.5)	3.0+	0.004
ASQoL (0-18) Mean (sd)	9.6 (6.9)	6.2 (5.6)	2.7+	0.01
SF36 – PCS (0-100) Mean (sd)	33.5 (12.4)	38.9 (11.6)	2.2+	0.03
SF36 – MCS (0-100) Mean (sd)	44.8 (11.3)	46.4 (11.9)	0.7+	ns
DLQI (0-30) Mean (sd)	6.3 (7.9)	4.2 (4.0)	1.5+	ns

BMI: body mass index, TJC: tender joint count, SJC: swollen joint count, LEI: Leeds enthesitis index, Dactylitis: tender dactylitis count, PASI: psoriasis area and severity index, mNAPSI: modified nail psoriasis severity index, PASDAS: psoriatic arthritis disease activity score, MDA: according to physician opinion patient is in minimal disease activity, SVDH: Sharp van der Heijde radiological score

VAS: visual analogue scale (0-100), BASDAI: Bath Ankylosing spondylitis Disease Activity Index, HAQ: Health Assessment Questionnaire, PsAQoL: Psoriatic arthritis Quality of Life Instrument, ASQoL:

Ankylosing spondylitis Quality of Life Instrument, SF36-PCS: physical component summary scale of the SF36, SF36-MCS: mental component summary scale of the SF36, DLQI: Dermatology Life Quality Index

+ t test statistic, ~ Mann Whitney test statistic, ¬ chi squared test, *For SA n = 38, for NE n = 33

Table 2. Treatment.

	South Asian n=58			European n=48		
	Never	Past	Current	Never	Past	Current
SAS	41 (71%)	13 (22%)	4 (7%)	31 (65%)	8 (17%)	9 (19%)
MTX	16 (28%)	13 (22%)	29 (50%)	18 (38%)	7 (15%)	23 (48%)
LEF	52 (90%)	2 (3%)	4 (7%)	46 (96%)	0	2 (4%)
Biologic	45 (78%)	3 (5%)	10 (17%)	39 (81%)	0	9 (19%)
Steroid	57 (98%)	0	1 (2%)	47 (98%)	1 (2%)	0
	Not current		Current	Not current		Current
NSAID	40 (69%)		18 (31%)	39 (81%)		9 (19%)

SAS: sulfasalazine, MTX: methotrexate, LEF: leflunomide, NSAID: non-steroidal anti-inflammatory drug

None of the comparisons for current drug use were significantly different between South Asian and North European patients

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