RMD Open
Rheumatic & Musculoskeletal Diseases

SHORT REPORT

The effects of alcohol consumption and its associations with disease activity among 979 patients with inflammatory arthritis

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To cite: Turk M, Murray K, Alammari Y, *et al*. The effects of alcohol consumption and its associations with disease activity among 979 patients with inflammatory arthritis. *RMD Open* 2021;**7**:e001510. doi:10.1136/rmdopen-2020-001510

Received 8 November 2020
Revised 15 March 2021
Accepted 22 March 2021

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ABSTRACT

Objective The role of alcohol in inflammatory disease remains debated. This study explores the relationship between alcohol and disease activity in patients with inflammatory arthritis.

Methods Patients attending a rheumatology clinic between 2010 and 2020 were prospectively followed. Information on demographics, alcohol use, smoking habits and disease outcome measures were collected from these patients. Statistical analysis included univariate and multivariate linear and binary logistic regressions, Mann-Whitney U tests and one-way analysis of variance with Tukey's honest significant difference (HSD) test.

Results Of the 979 analysed patients, 62% had rheumatoid arthritis (RA), 26.7% had psoriatic arthritis (PsA) and 11.2% had ankylosing spondylitis. Mean DAS28-CRP (Disease Activity Score 28 - C-reactive protein) in RA and PsA at 1 year was 2.96±1.39, and 64.2% of patients were in remission (DAS28-CRP ≤2.6 or BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) ≤4). Both male gender and risky drinking (>15 units of weekly alcohol) were significantly associated with remission. Compared with women, men had an OR of 1.8 (1.1, 2.5) (p=0.034) for any alcohol consumption and 6.9 (4.7, 9.1) (p=0.001) for drinking at least 15 weekly drinks. When adjusted for gender, there was no association between alcohol and disease activity. Yet, when adjusted for alcohol consumption, gender still significantly influenced disease activity.

Conclusion While it may appear that alcohol is linked to remission in inflammatory arthritis, when adjusted for gender, it is not. Men with inflammatory arthritis drink significantly more than women and have less severe disease activity.

Key messages

What is already known about this subject?

- Alcohol may have an effect on disease activity in inflammatory arthritis.

What does this study add?

- When controlling for gender, alcohol consumption is not associated with decreased disease activity in this cohort.

How might this impact on clinical practice?

- Physicians should continue to advise their patients with IA against excessive alcohol consumption.

INTRODUCTION

Alcohol is the seventh leading risk factor for both disability adjusted life years and deaths worldwide and 7% and 2% of age-standardised male and female deaths, respectively, are wholly attributable to alcohol.[1] Alcohol abuse has been linked to pathogenic changes to the liver, pancreas, central nervous sytem, cardiovascular system, gut and other systems.[2]

It has also been associated with immune changes by impacting immune responses throughout the body. Chronic alcohol use can create a sensitising effect to toll-like receptor 4 activation, whereby a proinflammatory effect is seen immediately following alcohol consumption.[3] This effect is followed by a sustained anti-inflammatory effect that can last hours.[4] Repeated and habitual alcohol consumption can cause tolerance to the lipopolysacchiride-tumour necrosis factor alpha activation, which has a long-term attenuative response on this proinflammatory pathway.[3] Alcohol can also activate anti-inflammatory cytokines to further dampen the general innate immune responses.[5]

Inflammatory arthritis refers to a variety of conditions including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS).[6] While alcohol may be generally immunosuppressive, its effects on inflammatory arthritis remain poorly understood.

Studies disagree as to whether alcohol has an effect on the incidence or risk of inflammatory arthritis.[7–9] One study linked alcohol consumption to increased radiological progression, however others associate drinking with milder disease activity.[10–12] This study examines the effects of alcohol consumption and its associations with remission and disease activity among 979 patients with inflammatory arthritis. Of the patients 64.2% were in remission.

METHODS

Study design

Patients with inflammatory arthritis attending a single centre rheumatology ambulatory care between 2010 and 2020 were prospectively followed. Demographics (gender, age, diagnosis), medications, disease activity (Patient Global Health Visual Analogue Score), swollen joint count (SJC), tender joint count (TJC), CRP, erythrocyte sedimentation rate, Disease Activity Score 28 CRP (DAS28-CRP)) and antibody status (rheumatoid factor (RF) and anti-cyclic citrullinated peptide (ACPA) serology) were recorded. DAS28-CRP <2.6 was classified as remission as per (EULAR) criteria.[13] In AS, a BASDAI Score of ≤4 was considered remission.[14] Patients were presented with an infographic of the UK standard drink guidelines and asked to report on their usual alcohol consumption. High-risk alcohol consumption was defined as >14 units weekly, as per UK guidelines.[15] While patients had varying disease durations, they were often unknown. However, patients were treatment-naïve at presentation to our clinic.

Statistical analysis

The data were analysed using SPSS V.26. Normally distributed continuous and ordinal data are given as mean±SD while other continuous data were presented as a median (range). Nominal data were given as numbers and percentages. Differences between means were calculated using one-way analysis of variance with Tukey's HSD. Mann-Whitney U tests were used to compare medians of non-normally distributed data. All factors that demonstrated an association within the univariate models of p≤0.20 were then used to create a multivariate model. Linear regression and binary logistic regression were to examine for associations as appropriate. Data were significant according to univariate analyses if p≤0.05. Linear regression data are presented as p values, r-squared values and β values (with 95% CIs). In logistic regression, a p value with an OR (with a 95% CI) are given.

RESULTS

Nine hundred and seventy-nine patients were included (table 1). These patients were representative of a standard rheumatology outpatient clinic. Of all patients, 65.7% were female and 77.3% completed secondary school. RA was the most common diagnosis (62.0%). Of these patients with RA, 367 (69.8%) were RF-positive and 199 (63.4%) were ACPA-positive.

Mean DAS28-CRP in RA and PsA was 2.96±1.39. Diagnosis had a significant effect on alcohol consumption at baseline. Patients with PsA had a median (IQR) weekly consumption of 4 (0–12) units. In comparison to AS, patients with RA had significantly lower alcohol

Table 1 Patient characteristics

	Total	RA	PsA	AS
	n=979	549 (62.0%)	237 (26.7%)	100 (11.2%)
Age, years	51±13.2	54.09±12.62	46.39±12.18	46.49±11.5
Female	578 (65.7%)	389 (70.9%)	138 (58.2%)	27 (27%)
Highest education level				
Primary school	78 (22.7%)	70 (28.5%)	8 (8.2%)	
Secondary school	151 (43.9%)	120 (48.8%)	31 (31.6%)	
University	115 (33.4%)	56 (22.8%)	59 (60.2%)	
Smoking status				
Never	262 (39.5%)	130 (36.1%)	65 (42.5%)	42 (42%)
Ex	232 (35.1%)	133 (36.9%)	55 (35.9%)	28 (28%)
Current	167 (25.3%)	97 (26.9%)	33 (21.6%)	30 (30%)
Alcohol, weekly units	4 (0–8.75)	2 (0–6)	4 (0–12)	6 (2–12)
HAQ Score	0.996±0.715	1.25±0.68	0.855±0.63	0.354±0.404
Early morning stiffness (minutes)	60 (15–120)	60 (15–120)	30 (10–60)	90 (15–225)
Low disease activity*	258 (64.2%)	155 (59.0%)	54 (71.1%)	67 (67%)

*Low disease activity DAS28-CRP of <2.6 (RA and PsA) or BASDAI ≤4 (AS).
AS, ankylosing spondylitis; DAS28, Disease Activity Score 28; HAQ, Health Assessment Questionnaire; ;PsA, psoriatic arthritis; RA, rheumatoid arthritis.

Table 2 Logistic regression analysis for high-risk alcohol use

Variable	P	OR (95% CI)
Diagnosis		
RA	0.008	0.2 (0.1 to 0.7)
AS	<0.0001	4.5 (2.0 to 10.0)
PsA	NS	NS
Male gender	0.001	6.9 (2.4 to 19.4)
Low disease activity*	0.038	6.1 (1.0 to 37.6)

*Low disease activity defined as DAS28-CRP ≤2.6 for patients with RA or PsA and as a BASDAI ≤4 for patients with AS.
AS, ankylosing spondylitis; DAS28, Disease Activity Score 28; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

consumption with medians of 6 (2–12) and 2 (0–6) units, respectively (p<0.0001). Based on linear regression (online supplemental table 1), baseline Health Assessment Questionnaire (HAQ) Scores were inversely related to alcohol consumption (p<0.0001, R^2=0.079, β=−3.7 (-5.0,–2.4)).

Male gender was associated with a significant increase in alcohol consumption. Compared with women, men had an OR of 1.8 (1.1, 2.5) (p=0.034) for any alcohol consumption and 6.9 (4.7, 9.1) (p=0.001) for drinking at least 15 weekly drinks. The median (IQR) alcohol consumption was 6 (1–12) for men and 2 (0–6) for women (p<0.001). High-risk alcohol consumption was associated with EULAR low disease activity (OR=6.2 (3.6, 8.8) p=0.05) (table 2, online supplemental tables 2, 3).

When adjusted for gender, the association between alcohol and disease activity is lost, however this may reflect a statistical lack of power in our study. Yet, when adjusted for alcohol consumption, gender still significantly influenced disease activity. When controlling for gender, there was no association between high-risk drinking and remission (OR=5.6 (0.4–76.1)). However, when controlling for alcohol, male gender still had a significant association with remission in inflammatory arthritis (OR=6.1 (3.2–11.8), p<0.0001).

There was no significant correlation between alcohol consumption and methotrexate use, morning stiffness, CRP, TJC, SJC, age, radiographic erosions or smoking.

DISCUSSION

Patients with high alcohol consumption had significantly higher OR of DAS28-CRP remission and report significantly lower HAQ Scores, both suggesting lower disease activity. However, when adjusted for gender, alcohol was no longer related to disease activity. Gender was still predictive of disease activity regardless of alcohol use, suggesting the link between higher-risk drinking and lower disease activity was due to male gender.

There was no significant association between alcohol use and educational level in our cohort. This is in contrast to previous literature showing higher levels of consumption in more educated people.[16 17] The Alcohol Harm Paradox alludes to the finding that lower socioeconomic status groups suffer more alcohol-related problems, despite drinking less alcohol.[18] The male predominance in the AS cohort likely explains the increased alcohol consumption when compared with the mostly female RA cohort. Increased alcohol consumption is also associated with male gender and younger age groups in the UK.[18] The AS cohort is predominantly male and is slightly younger in age to the RA group, which could in part explain the higher rates of alcohol consumption therein. In addition, having lower disease activity may allow patients the energy to participate in more social events, some of which may include alcohol. Previous work has shown lower self-reported disease activity in women with RA who drink alcohol.[19] While we do not observe similar findings in our cohort, we used composite patient/physician assessments of disease activity to evaluate outcomes.

Previous work has compared alcohol consumption with erosive radiographic progression in RA. Nissen *et al* found an association between light alcohol consumption and less erosive damage within their cohort.[20] While we found no such association, we looked at the development of new erosions whereas their group analysed erosions using the Ratingen Score. Nevertheless, this discrepancy highlights the need for further investigations into alcohol's role in erosive changes.

A major strength of this study is the detailed description of a large cohort representative of patients with IA seen in everyday 'real-world' clinical practice. There were also no significant differences in age between the cohorts. We provide quantitative data on alcohol use. In contrast to prior studies, we perform detailed multivariate analysis and also adjust for confounders, highlighting the importance of the inter-relationship between alcohol and gender. We also compare gender-based ORs between high-risk drinkers instead of comparing those who drink any amount versus those do not drink.[12]

A potential weakness of this study is the use of self-reported alcohol consumption. The use of self-reported outcome measures is a limitation. This can lead to under-reporting of alcohol intake.[21] However, due to the difficulty of performing phlebotomy in non-clinic populations, self-report surveys are often used in assessing alcohol behaviours and have been validated.[22 23]

CONCLUSION

High-risk alcohol consumption and gender were associated with DAS28-CRP remission. When controlled for gender, the association with alcohol lost significance. However, when the model was controlled for alcohol, gender remained significantly associated with remission. This study highlights the importance of controlling for gender and other demographic information when assessing the effects of alcohol on disease activity. We suggest alcohol does not have an influence on disease activity, gender does.

Acknowledgements The authors thank the professional and research staff at the Bone and Joint Unit and the Centre for Rheumatic Diseases at St. Vincent's University hospital, Dublin, Ireland.

Contributors MT, KM and YA were responsible for study design, statistical analysis, manuscript writing and data entry. FY was involved in data entry. TJ and FY created the database and entered baseline data. DV conceptually designed the study. PG, LF, SM and FO contributed to recruitment and patient data. All authors approved the manuscript. The corresponding author had final responsibility for the decision to submit for publication.

Funding The study was funded by the Centre for Arthritis and Rheumatic Diseases.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval All data collection was fully in compliance with the Declaration of Helsinki and both the data collection and the analysis were approved by the St Vincent's University Hospital ethics committee.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Additional data are available in the online supplemental file.

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