Background: Psoriatic arthritis (PsA) and psoriasis are both strongly associated with impaired glycemic control and type 2 diabetes. The risk of developing type 2 diabetes is estimated to be ~40% higher in PsA compared to controls [1]. However, these observational findings are susceptible to bias from reverse causation: insulin resistance and impaired glycemic control are evident well over a decade before clinical onset of type 2 diabetes [2]. Therefore, whether impaired glycemic control is a cause or consequence of PsA is unclear. Testing this hypothesis using traditional observational designs is challenging since longitudinal assessments of glycemic control before PsA onset are often not available. Mendelian randomization (MR) is an epidemiologic method that provides evidence about putative causal relationships between modifiable exposures and disease outcomes using genetic variants as instrumental variables. MR is less likely to be affected by confounding or reverse causation than conventional observational designs because genetic variants are randomly allocated at conception.

Objectives: To estimate the effect of genetically predicted glycaemic traits - glycated haemoglobin (HbA1c), 2-hour glucose after oral glucose challenge (2hG), fasting glucose (FG), and fasting insulin (FI) - on risk of PsA and psoriasis compared to controls using two-sample MR.

Methods: We selected 320 independent (p<0.001) genome-wide significant (p<5x10^-8) variants as instruments for HbA1c from a UK biobank genome-wide association study (GWAS) of 344,182 individuals, and 14 variants for 2hG, 67 for FG and 38 for FI from up to 200,622 individuals from a MAGIC consortium meta-analysis that adjusted for body mass index. Genetic associations for PsA were obtained from a GWAS comprising 3,609 cases (majority fulfilling CASPAR criteria) and 9,192 controls. Psoriasis data were obtained from 5,278 cases (96% European, defined using ICD and phenotypes) and 650,391 controls from the UK biobank, FinniGen and BioBank Japan [3]. We used the inverse-variance weighted method to combine effect estimates from each variant using fixed-effect meta-analysis.

Results: Genetically predicted HbA1c increased risk of PsA (OR 1.18 per standard deviation (6.7 mmol/mol) increase in HbA1c; 95%CI 1.02, 1.36). 2hG (OR 1.55 per SD (0.6 mmol/L) increase; 95%CI 1.26, 1.89) and FG (OR 1.73 per SD (1.6 mmol/L) increase; 95%CI 1.35, 2.21) increased PsA risk (Figure 1). FI was not associated with PsA risk. 2hG was the only glycaemic trait significantly associated with psoriasis. (OR 1.21, 95%CI 1.04, 1.40).

Conclusion: This study provides supportive genetic evidence that impaired glycemic control increases risk of PsA. By contrast, estimates were smaller when comparing psoriasis against controls with confidence intervals including the null. Improving glycemic control may reduce PsA risk, although further studies are required to confirm these findings and to compare PsA directly against cutaneous only psoriasis.

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Acknowledgements: This work was supported by Versus Arthritis (grant number 21173, grant number 21754 and grant number 21755).

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2022-eular.408

Clinical aspects in Psoriatic Arthritis

POS0307

IMPAIRED GLYCEMIC CONTROL IS ASSOCIATED WITH INCREASED RISK OF PSORIATIC ARTHRITIS: MENDELIAN RANDOMISATION STUDY

S. S. Zhao 1, A. Barton 1, J. Bowes 1. 1The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom; 2The University of Manchester, Centre for Genetics and Genomics Versus Arthritis, Manchester, United Kingdom

Figure 1. Mendelian randomisation estimates of the effect of glycaemic traits on risk of psoriatic arthritis and psoriasis.

Clinical aspects in Psoriatic Arthritis

POS0308

EFFECT OF GUSKELUMAB ON SERUM BIOMARKERS IN PSORIATIC ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE OR INTOLERANCE TO TUMOR NECROSIS FACTOR INHIBITORS: RESULTS FROM THE COSMOS STUDY

G. Schett 1, W. Chen 2, S. Gao 2, S. D. Chakravarty 2, M. Shiwi 6, F. Lavié 1, E. Theander 1, M. Neuhold 1, L. Coates 1, S. Siebert 12, FAU Erlangen-Nürnberg,

Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, review, and approval of the abstract. No honoraria or payments were made for authors. Medicinal writing support was provided by Julia Zolotarova, MSc, MWC, of AbbVie.

Disclosure of Interests: None declared