POS1169 THE INFLAMMATION INDUCED BY MONOSODIUM URATE AND CALCIUM PYROPHOSPHATE CRYSTALS DEPENDS ON OSMOLARITY AND AQUAPORIN CHANNELS.

T. W. Chirayath[1], N. Pham[1], C. Duranton[2], I. Rubera[2], A. Gauffenic[1], M. Cohen Solal[1], A. Latourte[1], T. Bardin[1], P. Richette[1], F. Lioté[1], H. K. Ea[1]. *[1]UNIVERSITY DE PARIS, INSERM UMR 1132 (BIOSCAR), HOSPITAL LARIBOISIERE, PARIS, France; [2]University of Nice-Sophia Antipolis, Laboratoire de Physiomedecine Moléculaire CNRS-UMR 7370, NICE, France*

Background: The inflammation induced by monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals is driven by interleukin (IL)-1β production. This later relies on NLRP3 inflammasome which can be activated by variation of ion concentration.
Objectives: To assess the role of osmolarity and water flux in MSU and CPP crystal-induced inflammation.
Methods: In vitro, THP1 monocytes were stimulated by pyrogen-free synthetic MSU and CPP crystals in iso-, hypo- or hyperosmotic media. Cytokine production was quantified by ELISA in cell culture supernatants. Cell size was measured using video microscopy. The role of aquaporin channels was assessed by pharmacological inhibitor (mercury chloride, HgCl2). In vivo, murine air pouch model was used. MSU and CPP crystals were injected in air pouch of mice treated or not with HgCl2 or mannitol. Osmolarity of mouse sera and patient synovial fluids (SF) were measured using freezing point osmometer. The size of cells collected from SF was assessed with imageJ software.
Results: MSU and CPP crystal-induced IL-1β production was substantially reduced by HgCl2 treatment (MSU 4900 vs 880 pg/ml; CPP 10500 vs 980, p<0.0001) or when cells were cultured in hyperosmotic medium. MSU and CPP crystals induced a transient increase in cell size which was 1.6 and 1.5 bigger after 30 and 100 min of stimulation by MSU and CPP crystals, respectively. After 150 min of stimulation, cell size decreased to their baseline size. Cell size increase was abolished by HgCl2 or hyperosmotic medium. In vivo, MSU and CPP crystal-induced inflammation (assessed by cell infiltration, IL-1β and CXCL2 production in air pouch lavage) was drastically reduced by HgCl2 or mannitol treatment. The serum osmolarity was higher in mannitol-treated mice than untreated mice (320 vs 300 mmosm/L). In patients, cells collected from SF during CPP or MSU crystal-induced flares had a bigger size than cells collected from osteoarthitic SF. The osmolarity of MSU or CPP crystal-containing SF was lower than the osmolarity of osteoarthritic SF (270 vs 310 mmosm/L). Finally, the IL-1β concentration in SF was strongly correlated with cell size and SF osmolarity.
Conclusion: These results suggest that the variation of osmolarity plays central role in MSU and CPP crystal-induced inflammation. Deciphering how crystals modulate osmolarity will identify new therapeutic targets.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2022-eular.3571

POS1170 ASYMPTOMATIC URATE-CRYSTALS DEPOSITS IN PATIENTS WITH STAGES 3-5 CHRONIC KIDNEY DISEASE DETECTED BY ULTRASOUND

E. Calvo-Aranda[1], L. Barrio Nogal[2], B. A. Blanco Cáceres[3], M. Novella-Navarro[4], D. Peiteado[4], J. Arroyo Palomo[3], E. De Miguel[4], A. Prada Ojeda[2], L. Sala Icardo[2], M. T. Navio Marco[1], M. Vázquez Díaz[3], C. M. Gomez-Gonzalez[1], R. Alcazar Arroyo[5], J. A. Martin Navarro[5], M. Vaga Gallardo[6], M. Fernandez Lucas[7], M. E. Diaz Dominguez[7]on behalf of GEACSER. *[1]Hospital Universitario Infanta Leonor, Rheumatology, Madrid, Spain; [2]Torrejón University Hospital, Rheumatology, Torrejón de Ardoz, Spain; [3]Hospital Ramón y Cajal, Rheumatology, Madrid, Spain; [4]La Paz University Hospital, Rheumatology, Madrid, Spain; [5]Hospital Universitario Infanta Leonor, Nephrology, Madrid, Spain; [6]La Paz University Hospital, Nephrology, Madrid, Spain; [7]Hospital Universitario Ramón y Cajal, Nephrology, Madrid, Spain*

Background: One in ten patients with hyperuricemia may develop gout over time, with urate deposition sometimes asymptomatic. Recent reviews support ultrasound (US) to assess asymptomatic hyperuricemic (AH) patients to detect gout lesions, showing double contour (DC) and tophus the highest specificities and positive predictive values. Hyperuricemia and gout are common in chronic kidney disease (CKD), especially with glomerular filtration rate (GFR) <60, and are associated with worse prognosis. US gout lesions have been found more frequently in AH (up to 35%) than in normouricemic (NU) patients, but evidence is scarce in CKD.
Objectives: To assess the prevalence of urate deposit in stages 3-5 CKD detected by US, and to investigate if there are differences between AH and NU patients.
Methods: Case-control study, recruiting patients aged ≥18 years with AH and stages 3-5 CKD in 4 hospitals from January 2020 to December 2021. Controls were patients with stages 3-5 CKD and NU. Exclusion criteria: previous diagnosis of gout, tophi. Hyperuricemia was defined as serum uric acid (sUA) >6.8 mg/dl, documented at least twice during the last 12 months. A standardized US exam of the knees and bilateral first metatarsophalangeal joints was performed to assess patients for DC/tophus as defined by OMERACT. Demographic, clinical and laboratory data were recorded. A descriptive analysis was performed using SPSS. Pre-clinical gout (PCG: DC and/or tophus) was considered as outcome variable. Chi-square and Fisher's exact test were used for qualitative variables, and Mann-Whitney U test for quantitative variables; significant threshold p<0.05.
Results: Forty-four patients with stages 3-5 CKD (59.6% stage 3, 19.1% stage 4, 21.3% 5) were recruited, 35 AH and 9 NU. Hyperuricemia was associated with a higher prevalence of US findings, with significant differences between cases (AH) and controls (NU): PCG 19 vs 1 (p=0.023), DC 13 vs 1, and tophus 11 vs 0. No significant differences were found in demographic variables, comorbidities and treatments. sUA levels, were higher in patients with PCG (8.3±1.4 vs 7.6±2.2; p=0.36), and these patients also showed lower GFR (31.4±14.1 vs 33.7±16.9; p=0.62). Patients with PCG also showed a non-significant trend towards shorter duration of CKD [6.3±5.7 vs 8.3±4.9 years; p=0.1] and younger age (66.4±15.1 vs 70.0 ±11.0; p=0.30).
Conclusion: We found an outstanding prevalence of asymptomatic urate deposits in our cohort of patients with stages 3-5 CKD, that is higher in hyperuricemic than in normouricemic patients. The prevalence of DC and tophus in our cohort of AH patients with stages 3-5 CKD was higher than that reported in AH patients in studies conducted in general population (37% vs 16-31% and 31% vs 16%, respectively). Early diagnosis of pre-clinical gout by ultrasound might change therapeutic approach in CKD.
REFERENCES:
[1] Robinson PC, *et al*. Longitudinal development of incident gout from low-normal baseline serum urate concentrations: individual participant data analysis. BMC Rheumatol. 2021;5(1):33.
[2] Jing J, *et al*.; GCKD Study Investigators. Prevalence and correlates of gout in a large cohort of patients with chronic kidney disease: the German Chronic Kidney Disease (GCKD) study. Nephrol Dial Transplant. 2015;30(4):613-21.
[3] Stack AG, *et al*. Gout and the risk of advanced chronic kidney disease in the UK health system: a national cohort study. BMJ Open. 2019;9(8):e031550.
[4] Stewart S, *et al*. Prevalence and discrimination of OMERACT-defined elementary ultrasound lesions of gout in people with asymptomatic hyperuricaemia: A systematic review and meta-analysis. Semin Arthritis Rheum. 2019;49(1):62-73.
[5] Christiansen SN, *et al*. Ultrasound for the diagnosis of gout-the value of gout lesions as defined by the Outcome Measures in Rheumatology ultrasound group. Rheumatology 2021.
[6] Peiteado D, *et al*. Value of a short four-joint ultrasound test for gout diagnosis: a pilot study. Clin Exp Rheumatol 2012.
Acknowledgements: Special thanks to the Nephrology and Rheumatology departments of the 4 participating centers.
Disclosure of Interests: Enrique Calvo-Aranda Speakers bureau: Menarini, Grünenthal, Laura Barrio Nogal: None declared, Boris Anthony Blanco Cáceres: None declared, Marta Novella-Navarro: None declared, Diana Peiteado: None declared, Jaime Arroyo Palomo: None declared, Eugenio de Miguel: None declared, Alejandro Prada Ojeda: None declared, Luis Sala Icardo: None declared, maria teresa navio marco: None declared, Mónica Vázquez Díaz: None declared, Claudia Maria Gomez-Gonzalez: None declared, Roberto Alcazar Arroyo: None declared, Juan Antonio Martin Navarro: None declared, Marco Vaga Gallardo: None declared, Milagros Fernandez Lucas: None declared, Martha Elizabeth Diaz Dominguez: None declared
DOI: 10.1136/annrheumdis-2022-eular.4045

POS1171 TRIPLE THE RATE OF EMERGENCY ROOM VISITS AND HOSPITALIZATIONS FOR GOUT AMONG US BLACKS VS WHITES – 2019 NATIONWIDE ANALYSIS

C. Yokose[1,2], N. Mccormick[1,2], N. Lu[3], A. Joshi[4], L. Jackson[5], M. Kohler[1], J. Yinh[1], Y. Zhang[1], K. Saag[5], H. Choi[1,2]. *[1]Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America; [2]Massachusetts General Hospital, Clinical Epidemiology Program, Mongan Institute, Boston, United States of America; [3]Arthritis Research Canada, n/a, Vancouver, Canada; [4]Massachusetts General Hospital, Clinical and Translational Epidemiology Unit, Mongan Institute, Boston,; [5]University of Alabama at Birmingham, Division of Clinical Immunology and Rheumatology, Birmingham, United States of America*

Background: Gout is a highly prevalent inflammatory arthritis with increasing global disease burden in recent years.[1,2] Gout prevalence has been reported to be higher among Blacks compared to Whites,[3] and that they are less likely to receive allopurinol in outpatient care.[4] The potential nationwide impact of these racial disparities on emergency department (ED) visits and hospitalizations is unknown.

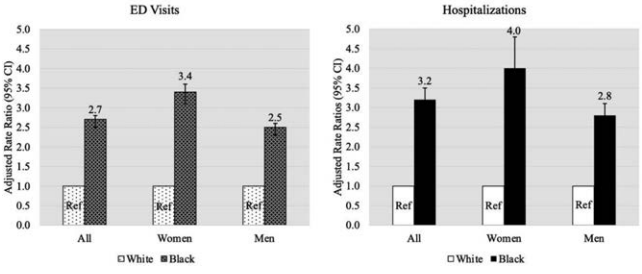
Objectives: To examine the contemporary racial disparities in ED visits and hospitalizations with a primary discharge diagnosis of gout in the US (2019).
Methods: We compared ED visits and hospitalizations between Blacks and Whites in the latest data (2019) from the US National Emergency Department Sample (NEDS) and National Inpatient Sample (NIS). We focused on encounters for which the primary diagnosis was gout based on ICD codes (M1A.xx, M10.xx). We calculated annual population rates of ED visits and hospitalizations for gout (per 100,000 US adults) using the 2019 US census adult population (>18 years) according to race.
Results: There were a total of 160,759 ED visits and 9,560 hospitalizations among White and Blacks with a gout diagnosis in the US in 2019. The mean age (58.2 years vs. 56.5 years) and male proportion (78.0% vs. 74.8%) tended to be higher among Whites, while more Blacks tended to live in the South (40.7% vs. 66.5%) and reported a median household income of < $50,000 (30.7% vs. 57.1%). Compared to Whites, Blacks had 2.7- and 3.2-fold higher rates of gout ED visits and hospitalizations, respectively, after adjusting for age, sex, payer, region, and household income (Table 1 & Figure 1). Black women, in particular, had 3.4- and 4.0-fold higher rates of ED visits and hospitalizations compared to White women, while the corresponding rate ratios for men were 2.5 and 2.8, respectively. The mean costs per gout ED visit were similar for Blacks compared to Whites (adjusted difference, -$7.6 [95% CI, -25.4 to 1.0]), while hospitalizations were more costly (adjusted difference, $1,055.3 [95% CI, 553.1 to 1557.5]). The duration of ED visits and hospitalizations was also higher among Blacks than Whites (adjusted difference of 0.41 days [95% CI, 0.19 to 0.63] and 0.59 days [95% CI, 0.25 to 0.94], respectively).

Table 1. Racial Disparities in Emergency Department Visits and Hospitalizations with Primary Diagnosis of Gout in 2019

	Emergency Department Visits		Hospitalizations	
Race	White	Black	White	Black
All	68011965	24521330	19851043	4519150
Visits, N	88810	71949	6200	3360
Rate per 100,000	130.6	293.4	31.2	74.4
Rate Ratio (95% CI)*	1.0 (ref)	**2.81 (2.63, 3.00)**	1.0 (ref)	**3.08 (2.79, 3.40)**
Rate Ratio (95% CI)**	1.0 (ref)	**2.66 (2.50, 2.82)**	1.0 (ref)	**3.17 (2.86, 3.50)**
Women	37851369	14363031	11039093	2647105
Visits, N	19567	18163	1770	1145
Rate per 100,000	51.7	126.5	16.0	43.3
Rate Ratio (95% CI)*	1.0 (ref)	**3.68 (3.39, 3.99)**	1.0 (ref)	**4.01 (3.40, 4.73)**
Rate Ratio (95% CI)**	1.0 (ref)	**3.36 (3.11, 3.62)**	1.0 (ref)	**4.02 (3.39, 4.78)**
Men	30156101	10156573	8809815	1871620
Visits, N	69228	53783	4430	2215
Rate per 100,000	229.6	529.5	50.3	118.3
Rate Ratio (95% CI)*	1.0 (ref)	**2.59 (2.42, 2.78)**	1.0 (ref)	**2.66 (2.36, 3.00)**
Rate Ratio (95% CI)**	1.0 (ref)	**2.47 (2.32, 2.64)**	1.0 (ref)	**2.77 (2.45, 3.14)**

*Adjusted for age and sex for all, adjusted for age for sex-specific rate ratios**Adjusted for age, sex, payment, region, and household income

Figure 1. Racial Disparities in Emergency Department Visits and Hospitalizations with Primary Diagnosis of Gout in 2019



Conclusion: These latest national data indicate that ED visits and hospitalization due to gout are both 3 times higher among Blacks than Whites; this disparity was particularly prominent among women with gout. Higher risk of developing gout[3] and suboptimal care[4] both translate to these avoidable costly healthcare utilizations, calling for improved primary prevention and gout care.

REFERENCES:

[1] Safiri et al., PMID 32755051
[2] Xia et al., PMID 31624843
[3] Chen-Xu et al., PMID 30618180
[4] Krishnan et al., PMID 18260174

Disclosure of Interests: Chio Yokose: None declared, Natalie McCormick: None declared, Na Lu: None declared, Amit Joshi: None declared, Lesley Jackson: None declared, Minna Kohler Speakers bureau: Lilly, Consultant of: Mymee, Novartis, Grant/research support from: Setpoint Medical, Janeth Yinh: None declared, Yuqing Zhang: None declared, Kenneth Saag Consultant of: Arthrosi, Atom Bioscience, Horizon Therapeutics, LG Pharma, Mallinkrodt, SOBI, Takeda, Grant/research support from: Horizon Therapeutics, SOBI, Shanton, Hyon Choi Consultant of: Ironwood, Selecta, Horizon, Takeda, Kowa, and Vaxart, Grant/research support from: Ironwood and Horizon
DOI: 10.1136/annrheumdis-2022-eular.4189

POS1172

RISK OF VENOUS THROMBOEMBOLISM AFTER GOUT FLARES

E. Cipolletta[1,2], G. Nakafero[2], M. Mamas[3], A. Avery[4], L. Tata[5], A. Abhishek[2].
[1]Polytechnic University of Marche, Department of Clinical and Molecular Sciences, Ancona, Italy; [2]University of Nottingham, Academic Rheumatology, Nottingham, United Kingdom; [3]Keele University, Keele Cardiovascular Research Group, Stoke-on-Trent, United Kingdom; [4]University of Nottingham, Division of Primary Care, Nottingham, United Kingdom; [5]University of Nottingham, Division of Epidemiology and Public Health, Nottingham, United Kingdom

Background: Several population-based cohort studies have reported an increased risk of venous thromboembolism (VTE) in gout patients. However, none of these studies has investigated the temporal relationship between gout flares and VTE.
Objectives: To explore whether gout flares increase the risk of VTE in the short-term using the self-controlled case series (SCCS) method.
Methods: We identified participants with incident gout from the Clinical Practice Research Datalink (CPRD). Participants having less than one year of registration in CPRD and patients with a history of VTE or anticoagulant prescription more than one year before the first gout consultation were excluded. Participants with at least one gout flare and a diagnosis of VTE were selected. VTEs and gout flares were ascertained using primary care data, hospitalisation and mortality records, using previously validated algorithms (positive predictive value of 94% for VTE [1] and 68-95% for gout flares [2,3]). SCCS method involves fitting a Poisson model conditioned on the number of VTEs, and it calculates the adjusted incidence risk ratio (aIRR) and its 95% confidence interval (95%CI) for each stratum of the "at-risk" period as compared with the "baseline" period (Figure 1). The analysis was adjusted for age and calendar season.

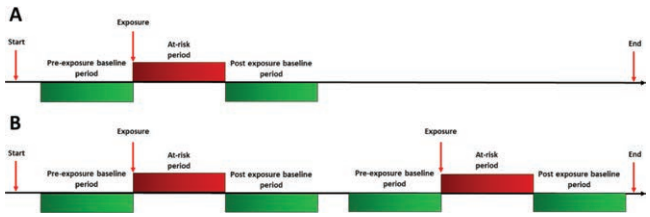


Figure 1. Schematic description of the observation period ("at-risk" and baseline periods).

The "at-risk" period (in red) was defined as the period following the exposure (the gout flare), and it was subdivided as follows: days 0-30, 31-60 and 61-120 after each gout flare. The baseline period (in green) consisted of a pre-exposure and a post-exposure period of 365 days each. The length of each period varied according to the occurrence of the next flare and its timing. Panel A and panel B provide a schematic representation of patients with a single observation period and with multiple "non-overlapping" observation periods, respectively. In such cases, the length of the "at risk" period was 120 days, while the length of the pre-exposure and post-exposure period was 365 days each.
Results: Among the 104,962 patients with an incident diagnosis of gout in CPRD between 1997 and 2020, we identified 2,678 VTE (4.0 events/1,000 person-years). There were 53 VTE (13.3 events/month) during the "at-risk" period and 143 (6.0 events/month) during the "baseline" period (crude incidence rate ratio, 1.75; 95%CI: 1.27-2.42). The rates were highest in the first month after gout flares and then fell progressively (Table 1). Sensitivity analyses were consistent with the main analysis (Table 1).