§ Number of PT with a target tophus at baseline was small. # Wilcoxon test with H0: Mean ranks in categories are equal

Abstract FRI0235 – Table 2. Mean sUA at M6 and 12 by occurrence of GF and GFRT

Mean sUA mg/dL (95% CI) M6	p-value#	Mean sUA (95% CI) M12	p-value#
GF Yes	5.94 (5.80–6.07)	5.92 (5.79–6.06)	
GF No	5.71 (5.51–5.92)	5.91 (5.64–6.17)	
Difference	0.22 (–0.01–0.47)	0.01 (–0.28–0.31)	0.91
GFRT No	5.91 (5.79–6.03)	5.93 (5.80–6.05)	
GFRT Yes	5.530 (5.23–5.83)	5.83 (5.41–6.25)	
Difference	0.38 (0.06–0.71)	0.09 (–0.34–0.53)	0.65

T-test with H0: No difference in means

Conclusions: These results confirm that sUA on target <5–6 mg/dl is essential for TR, and longer the control better the TR. The lower mean sUA levels for PT with GF and GFRT was observed at M6 and not at M12, maybe owing to the fact that flares are common during the first months of ULT initiation and then taper off and urate deposits were more fragile and not completely dissolved. Also M6 and 12 may not be optimal to observe statistically significant differences between treatments with respect to TR, GF and GFRT.

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FRI0236

ASSOCIATIONS BETWEEN COMORBIDITY AND URATE DEPOSITION IN SUBJECTS WITH ASYMPTOMATIC HYPERURICEMIA: A PILOT STUDY

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Background: Hyperuricemia is common and along with comorbidities, is increasing in prevalence. Though often asymptomatic and hence, under diagnosed, it may be associated with subclinical urate deposition. Ultrasound (US) imaging can detect urate deposition in individuals with asymptomatic hyperuricemia (ASU).

Objectives: To evaluate the association of comorbidities with urate deposition via US in ASU.

Methods: ASU was defined as serum urate (sUA) >6 mg/dl; sUA <6 mg/dl served as controls. Demographic (age, gender, BMI), comorbidity (CM – [hypertension (HTN), hyperlipidemia (HLD), diabetes mellitus (DM), cardiovascular (CVD) and renal disease (CKD)], diuretic/aspirin use, dietary data (alcohol, red meat, seafood) were collected. Ultrasonography (US) of joints (knee/MTP), tendons (triceps, quadriceps/patella, Achilles) was performed via standard procedure, OMERACT parameters of urate deposition documented, and images read by an Expert ultrasonographer blinded to sUA category. Correlations between sUA levels and MSK urate deposition with comorbidities, medication and dietary risk factors were analysed by 2-stage multivariable logistic regression model with propensity score weighting.

Results: Of 95 predominantly non-Hispanic Blacks (mean age 59.7 years, BMI ~32 kg/m²), ASU subjects (n=71, median sUA=8.0) were older men, with more frequent HTN, CVD, CKD, alcohol ingestion versus controls. In multivariate analyses adjusting for demographic characteristics, BMI, CKD, and alcohol use were positively associated with sUA >6 mg/dl; while HTN, CVD, and CKD were positively associated with sUA >8 mg/dl. Adjusting for comorbidities, sUA >8 mg/dl was significantly associated with urate deposition at knee (OR=3.20; p=0.03), quadriceps and Achilles tendons (OR=4.14; p<0.01), OR=9.51; p<0.01, respectively) but not at 1 st MTP (OR=2.14; p=0.06). A sUA >6 mg/dl alone, however, did not predict urate deposition.

Conclusions: Presence of HTN, CVD and CKD are associated with higher levels of sUA and increases the risk of urate deposition in ASU patients. Identifying a subset of ASU patients that may benefit from urate lowering therapy requires

further stratification and long term follow up for incident gouty arthritis in order to alter current urate lowering treatment guidelines.

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FRI0237

PEGLOTICASE TREATMENT SIGNIFICANTLY DECREASES MEAN ARTERIAL BLOOD PRESSURE IN PATIENTS WITH CHRONIC GOUT

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Background: There are significant correlations between serum uric acid (sUA) and blood pressure (BP) in individuals with and without gout.¹ Limited data suggest that lowering sUA may decrease BP², but no consistent effect has been noted.³ Recent guidelines suggest the need for more aggressive management of increased BP.⁴

Objectives: To determine the impact of persistent, very low sUA levels on BP in subjects with chronic refractory gout treated with pegloticase, a recombinant uricase conjugated to polyethylene glycol approved for chronic refractory gout that decreases sUA to <1 mg/dL.

Methods: This analysis used results from two, 6 month randomised clinical trials (RCTs) in which subjects were treated with 8 mg pegloticase every 2 or 4 weeks (q2w or q4w) or placebo.⁵ sUA responders maintained sUA <6 mg/dL.⁵ Sitting BP was measured at each visit and estimated glomerular filtration rate (eGFR) was determined at baseline and after 3 and 6 months.

Results: Serial BP measures were obtained in 173 subjects during the course of the RCTs. Significant reductions in mean arterial pressure (MAP) from baseline to 6 months were noted in q2w responders (p=0.0029) (figure 1), whereas reductions in MAP in other groups were not significant. Notably, 18/29 (62.1%) of q2w sUA responders experienced persistent reductions in MAP (p=0.01 compared to other groups). Changes in both systolic and diastolic BP paralleled the change in MAP. Of the q2w sUA responders exhibiting persistent decreases in MAP, there were no significant differences in baseline age, gender, race, body mass index, history of hypertension, gout duration, MAP, sUA, cholesterol, eGFR, or urinary UA/creatinine ratio compared with those who did not lower MAP. There were no significant changes in eGFR in sUA responders to pegloticase treatment over the course of the study and there was no significant correlation between change from baseline MAP and eGFR in these subjects (p=0.43).

Abstract FRI0237 – Figure 1. *Significantly different from baseline (GLM adjusted for multiple comparisons)

Conclusions: Responders to biweekly pegloticase experienced significant reductions in MAP that were independent of changes in renal function.

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FRI0238 THE LEVEL OF LEPTIN IN PATIENTS WITH GOUT AND ITS ASSOCIATION WITH THE GOUT ACTIVITY SCORE

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Background: Leptin is a cytokine-like hormone mainly produced by adipose tissue. Its role in inflammation, obesity, diabetes mellitus, and cardiovascular pathology is well known.² Most of these pathological conditions usually accompany gout, but role of leptin in gout remains on the discussion.

Objectives: To determine the level of leptin in patients with gout and evaluate its association with the disease activity.

Methods: Study involved 151 patients with gout (100% men), aged (mean $\pm$ SD) 52.4 $\pm$ 9.2 years, with a disease duration 8.9 $\pm$ 6.6 years. In 51 (33.7%) was diagnosed tophaceous gout. Control group was represented by 31 healthy subjects. Diagnosis of gout was based on the ACR/EULAR 2015 criteria. The disease activity was determined by the Gout Activity Score (GAS),² the intensity of the pain – by the visual analogue scale (VAS_{pain}). Leptin in serum was determined by ELISA.

Results: The level of leptin in patients with gout was 2 times higher compare to those in the control group (6.6 $\pm$ 4.3 vs 3.0 $\pm$ 1.4 ng/ml). The number of attacks in the last year was 3.9 $\pm$ 2.7, number of affected joints was 8.1 $\pm$ 5.4, and uric acid in serum (sUA) was 8.1 $\pm$ 2.0 mg/dl. Mean value of VAS_{pain} in gout patients was 5.4 $\pm$ 2.4 cm, and disease activity by GAS – 5.9 $\pm$ 2.1. Regarding GAS we divided our patients in three groups: low activity (GAS <25 th percentile), moderate activity (between 25th and 75th percentile) and high activity (>75 th percentile). In 36 patients with high disease activity (GAS >7.4) the level of leptin was the highest (11.7 $\pm$ 4.7 ng/ml), whereas in patients with moderate activity (GAS 4.5–7.4; n=77) and in patients with low disease activity (GAS <4.5; n=38) it was 5.3 $\pm$ 2.6 ng/ml and 3.9 $\pm$ 1.4 ng/ml, respectively. The difference in leptin levels between all groups was significant (p<0.01). The level of leptin correlated with the number of gout attacks (r=0.41), number of affected joints (r=0.55), sUA (r=0.39), VAS_{pain} (r=0.35), and GAS (r=0.69).

Conclusions: Association of increased leptin level with high gout activity may indicate possible pathogenic role of leptin in gout. GAS is reliable and sensitive clinical tool for determining disease activity in patients with gout.

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FRI0239 ABSOLUTE NUMBERS OF PERIPHERAL TH17 AND TH2 CELLS INCREASED IN PATIENTS WITH GOUT

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Background: Gout is generally considered as an acute or chronic inflammatory disease of the joints due to deposition of crystals of monosodium urate (MSU). However, crystals of MSU do not always elicit inflammation in joints, suggesting that the immunological basis is required for the development of gouty arthritis. Although T helper 17 (Th17) and regulatory T cell subsets in CD4 +T cells have been reported to play a key role in autoimmune diseases, their status in peripheral blood of gout patients are rare studied.

Objectives: Our present study is to explore whether the absolute numbers of peripheral CD4 +T subsets, especially Th17 cells and CD4 +CD25+FOXP3T regulatory (Treg) cells, is abnormal in gout.

Methods: A total of 72 patients with gout (70 male/2 female) and 41 age-sexual-matched controls were recruited from the Second Hospital of Shanxi Medical University (from March 1 st in 2016 to July 30th in 2017). Of these, 72 patients were categorised as acute gout who had redness, swelling, warmth and pain at the same time (Group1; n=18) or as acute gout without redness and warmth (Group2; n=52). All patients fulfilled 2015 Gout classification criteria developed by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR). Patients with a history of other autoimmune diseases, nephropathy, cancer, infectious processes, or hematopathy were excluded. The detail medical histories were collected, comprehensive laboratory examinations were performed, and then the differences between the patients and controls were investigated. The concentrations of CD4 +T cell subsets (the absolute numbers of Th1, Th2, Th17 and Treg cells) in peripheral blood were measured by flow cytometry combined with internal standard beads and then the ratios of Th1/Th2 and Th17/Treg were calculated.

Results: The duration of their disease was 46.73 $\pm$ 54.92 (Group1), or 61.54 $\pm$ 70.51 (Group2) months. The white blood cells (WBCs) and neutrophils in gout blood were significantly higher than those in controls (P<0.01) and ESR in Group1 was obviously increased (p=0.033). Levels of Total T lymphocyte counts (CD3 +CD19-), Total B lymphocyte counts (CD3-CD19+) and Helper T cells (CD3 +CD4+) were increased in Group2 (all p<0.05). Nevertheless, there was no difference between Group1 and healthy controls. The absolute number of peripheral Th2 in gout (both Group1 and Group2) was higher than that in healthy controls (p=0.001). Most importantly, the absolute number of peripheral Th17 cells was significantly increased in gout patients in Group2 (p=0.006) while, in Group1, the absolute number of Treg cells decreased despite no statistical significance (P>0.05).

Abstract FRI0239 – Table 1. Lymphocyte subsets of Gout Patients & Normal Persons

	Group1	Group2	Normal	F	P-values
N	18	52	41		
Total T cells, CD3+CD19- (cell/ μ L)	1475.50(1234.50)	1538.43(894.50)	1360.59(488.84) ^a	4.954	0.084
Total B cells, CD3-CD19+ (cell/ μ L)	200.51(195.92) ^a	300.50(224.27)	191.04(103.48) ^a	13.610	0.001
Th cells, CD3+CD4+ (cell/ μ L)	783.34(527.75)	866.50(520.75)	625.84(187.63)	13.134	0.001
Ts cells, CD8+ T (cell/ μ L)	608.00(472.25)	600.83(336.00)	536.13(320.43)	1.220	0.543
Th/Ts, CD3+CD4+/CD8+ T	1.15(0.31)	1.50(0.91)	1.11(0.63) ^a	11.625	0.003
NK cells, CD3-CD16+CD56+ (cell/ μ L)	278.00(208.75)	311.70(187.58)	340.59(280.05)	2.780	0.249
T+B+NK cells, CD3+CD19-+CD3-CD19+ (cell/ μ L)	2148.00(1501.23)	2253.00(1006.00)	1918.47(739.66) ^a	6.093	0.048

a. Total B lymphocyte counts (CD3-CD19+) were increased in Group1 compared with Group2 (p=0.037);

c. Total T and B lymphocyte counts (CD3-CD19+) were increased in Group2 compared with healthy controls. (all p < 0.05)

Abstract FRI0239 – Table 2. CD4+ T cell subsets of Gout Patients & Normal Persons

	Group1	Group2	Normal	F	P-values
N	18	52	41		
Th1 cells, IFN- γ (cell/ μ L)	63.24(126.68)	115.03(183.53)	125.72(98.01)	1.610	0.447
Th2 cells, IL-4 (cell/ μ L)	12.92(16.62)	11.38(11.16) ^b	7.44(5.88) ^c	12.379	0.002
Th17 cells, IL-17 (cell/ μ L)	6.79(12.77)	11.07(9.37)	7.48(5.87) ^c	7.131	0.028
Treg cells, CD4+CD25+FoxP3+ (cell/ μ L)	23.62(28.06)	30.25(20.53)	30.22(16.72)	2.032	0.362
Th1/Th2, IFN- γ /IL-4	7.14(7.66)	8.95(14.49) ^b	16.17(20.13) ^c	16.288	0.000
Th17/Treg, IL-17/CD25+FoxP3	0.29(0.83)	0.40(0.43)	0.24(0.20) ^c	6.986	0.030

b. the absolute number of peripheral Th2 cells was significantly increased in gout patients in Group1 compared with healthy controls (p=0.012)

c. the absolute number of peripheral Th2 and Th17 cells was significantly increased in gout patients in Group2 compared with healthy controls (all p < 0.05)

Conclusions: The increase of peripheral Th2 and Th17 cells led to an imbalance of CD4 +T cell subsets may correlate with gouty inflammation in an undefined way. The elevation of Th2 and Th17 cells may serve as important reference indices for gout attack and a target of gout treatment. Moreover, Th17 may contribute to the persistence of the disease.

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