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The Relationship Between Serum Uric Acid, Creatinine, Urea, And Triglycerides Among Patients Diagnosed with Gout

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Abstract

Background: Gout is a systemic disease causes an increase in Uric acid in blood and tissues, the presence of lipid metabolism difficulties in gout patients has been variable and not always associated to gout and must be studied. Research objectives: This study aims to assess the relationship between serum uric acid, creatinine, urea, cholesterol, and triglycerides among subjects who are clinically diagnosed with gout. Method: A cross sectional study was conducted with recruiting subjects diagnosed with gout and testing them with specific laboratory tests such as renal function tests and total lipid profile in addition to their demographic data and clinical history with preliminary diagnosis for predominant disorders such as hypertension, diabetes mellitus, and thyroid dysfunction, for a period reaches 6 weeks, the study was conducted and the findings were extracted and analysed using SPSS version 21.0. Results: From total of 500 subjects who were readily diagnosed with gout, the mean age was 34±11.2 years old, among these subjects are and most of them were females (75%) and most of them (62.8%) had a history of gout,

and the laboratory data near to the borderline of normal ranges regarding serum triglycerides and cholesterol, the study results revealed that there is a significant relationship ($P < 0.05$) between gout Uric acid laboratory parameter and slightly elevated serum triglycerides level. Conclusion: Gout is mostly prevalent among females than males with mean age of late adulthood, in addition, there is a significant relationship between gout and hyperuricaemia and the elevation of triglycerides.

Keywords: Serum Uric Acid, Creatinine, Urea, Triglycerides, Cholesterol, Gout, Hyperuricemia.

*** Introduction**

Gout has been recorded in medical records from the early stages of medical writing and was also mentioned in the histories of individuals (Ortiz-Uriarte *et al*., 2023; Zhang *et al*., 2022). Gout is a systemic ailment resulting from the buildup of monosodium urate crystals (MSU) in the tissues of the body (Salah *et al*., 2021). Uric acid crystals can only occur when there are high levels of serum uric acid (SUA) that exceed a specific threshold (Wang *et al*., 2021; Shen *et al*., 2020). While hyperuricemia is the main pathogenic anomaly in gout (Russo *et al*., 2021), it is important to recognize that not all persons with hyperuricemia will develop gout or manufacture uric acid crystals (Liu *et al*., 2020). Only a small percentage, specifically 5%, of patients with hyperuricemia levels higher than 9 mg/dL really develop gout (Liang *et al*., 2020; Li *et al*., 2022). Genetic predisposition is considered to be a contributing factor to the incidence of gout (Oh and Moon, 2021).

MSU crystals possess the capacity to amass in many tissues, especially near the joints, leading to the creation of tophi. The main approach to diagnosing gout is recognizing the distinctive MSU crystals by extracting joint fluid or aspirating tophi. Early start of gout is characterized by a rapid inflammation of the joints (Liu *et al*., 2021). Renal stones and tophi are late-stage symptoms of the disease (Ran *et al*., 2021). The main goal in managing gout is to decrease serum uric acid (SUA) levels below the point where it can accumulate (He *et al*., 2022), which can be accomplished by making

changes to one's diet and taking drugs that lower uric acid levels. This results in the dissolution of MSU crystals (Ali *et al*., 2022), so preventing further attacks (Lu *et al*., 2022; Liang *et al*., 2021; Salah *et al*., 2021)

An overproduction of creatinine has been shown to increase the breakdown of S-adenosylmethionine and ATP, hence stimulating the production of uric acid. This study summarizes the findings of our analysis of urine creatinine and uric acid excretion in patients diagnosed with primary gout (Aiumtrakul *et al*., 2021).

Although vascular disease is frequently seen in persons with gout, the presence of lipid metabolism difficulties in gout patients has been variable and not always associated to anomalies. Several studies indicate a correlation between elevated levels of uric acid in the bloodstream (hyperuricemia) and elevated levels of both cholesterol (hypercholesterolemia) and triglyceride (hypertriglyceridemia) (Ran *et al*., 2021).

However, other research has discovered that the correlation exists solely with elevated levels of cholesterol or alone with elevated levels of triglycerides. Individuals with gout and high levels of triglycerides in their blood generally have reduced ability to tolerate carbohydrates (Oh and Moon, 2021). There are two potential reasons for the connection between gout and irregularities in glucose metabolism (Calabuig *et al*., 2023).

One potential explanation is that the main correlation lies between gout and anomalies in carbohydrate metabolism, while the correlation with hyperlipidaemia is of secondary importance. An alternative explanation is that the lipid anomaly is the primary culprit, whereas the problems of urate and glucose metabolism are secondary to it (Salah *et al*., 2024). This result partially explains the diversity in the correlation between hyperuricemia and hyperlipidaemia.

However, the variation in the selection of gouty individuals across different research is also a probable factor contributing to the diverse spectrum of explanations for their gout (Lu *et al*., 2022).

Consequently, it is improbable that a person who has a lower-than-normal urate excretion will experience the same abnormalities in lipid metabolism as someone who excessively generates urate (Russo *et al*., 2021). Previous research has not investigated the association between creatinine and uric acid metabolism. (Ortiz-Uriarte *et al*., 2023; Zhang *et al*., 2022). Therefore, this study aimed to assess the relationship between serum uric acid, creatinine, urea, cholesterol, and triglycerides among subjects who are clinically diagnosed with gout.

*** Materials and Methods**

*** Study Design**

A cross sectional study was conducted on some selected patients diagnosed with gout for 6 weeks.

*** Population and Outcomes measurements**

A stratified sampling techniques with random method was used to recruit cases with only gout. A total number of 400 patients with gout were selected, they were diagnosed with gout either clinically or with other medical and clinical investigations such as X-ray, laboratory parameters and all patients with acute hyperuricemia, cardiovascular diseases, metabolic disorders, or other comorbidities were excluded.

All data of these subjects must be recorded, starting from their demographic data such as age, gender, history of gout, uric acid, Creatinine and urea are metabolic byproduct of muscular activity that is eliminated from the bloodstream by the kidneys and excreted in urine at a consistent pace, serum triglycerides, and cholesterol levels.

The Measurement of these kidney functions were carried out by glomerular filtration rate (GFR) which is defined as a measure of the volume of blood that is filtered by the glomeruli per unit of time, specifically per minute. and Creatinine clearance to exclude any cases of renal failure.

<u>The formula used to evaluate the eGFR</u>

$107.904 \times (\text{Creatinine in mg/dL}) - 1.009 \times (\text{age}) - 0.02 \times (0.67 \text{ if female})$ (Lee *et al*., 2010).

*** Uric acid, Urea, and Creatinine levels**

The primary focus of investigation was the amounts of serum uric acid (SUA), urea, and creatinine. During the morning, venous blood samples were obtained following an overnight period of abstaining from food. The measurement of serum uric acid (SUA)and other markers using a Hitachi automatic analyzer 7600-210, employing a colorimetric enzymatic approach as invented by Liddle *et al*. (1959). The levels of serum uric acid (SUA) were categorized into five groups for both males and females. One group was for individuals with hyperuricemia (SUA levels > 7.00 mg/dL for men; > 6.00 mg/dL for women20,21), and the remaining four groups (Q1, Q2, Q3, and Q4) were based on quartiles within the normal range specific to each sex. The quartiles for SUA levels were as follows: < 4.80 mg/dL, 4.80–5.49 mg/dL, 5.50–6.09 mg/dL, 6.10–6.99 mg/dL for males; and < 3.70 mg/dL, 3.70–4.19 mg/dL, 4.20–4.79 mg/dL, 4.80–5.99 mg/dL for women. The urea levels which were measured by method of Bonsnes and Taussky (1945) which were tested as follows: - For both men and women, the normal range is 17 - 43 mg/dL or 2.8 - 7.2 mmol/L. For women under 50 years old, the normal range is 15 - 40 mg/dL or 2.6 - 6.7 mmol/L. - For women over 50 years old, the normal range is 21 - 43 mg/dL or 3.5 - 7.2 mmol/L. - For men under 50 years old, the normal range is 19 - 44 mg/dL. While creatinine levels according to the severity of chronic kidney disease can be assessed using a staging method that measures the glomerular filtration rate (GFR).

Stage 1: Glomerular Filtration Rate (GFR) of 90 or above, indicating normal kidney function.

Stage 2: Glomerular Filtration Rate (GFR) between 60 and 89

Stage 3a of kidney disease is characterized by a glomerular filtration rate (GFR) ranging from 45 to 59, indicating modest impairment of kidney function.

Stage 3b GFR 30 - 44 indicates the presence of mild renal disease.

Stage 4: Glomerular Filtration Rate (GFR) between 15-29, indicating severe renal failure.

Stage 5: GFR below 15 (near or at the point of renal failure, frequently

necessitating dialysis or kidney transplantation)

*** Triglycerides and total cholesterol levels**

After fasting for at least 14 hours, venous blood was collected to determine the serum levels of triglycerides and cholesterol. The measurements were conducted using the methods described by Carlson and Wadstrom (1959) and Liese *et al*. (1952).

*** Statistical analysis**

The data were analysed and interpreted through use of the application of Statistical Package for Social Sciences (SPSS), version 26.0 the descriptive data were analysed using Frequency, percentage, mean, and standard deviations while the inferential data were analysed using simple Linear Regression.

*** Results**

This study recruited cross sectionally 500 subjects who were readily diagnosed with gout, the mean age34±11.2 years old, among these subjects are and most of them were females (75%) and most of them (62.8%) had a history of gout (Figure 1 and 2) and (Table 1).

Figure 1 The gender distribution among the subjects in this study

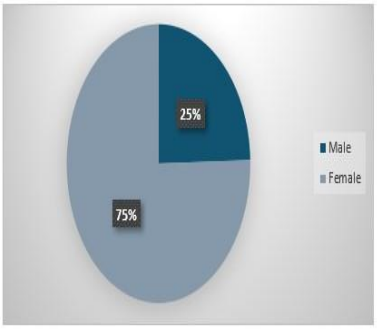
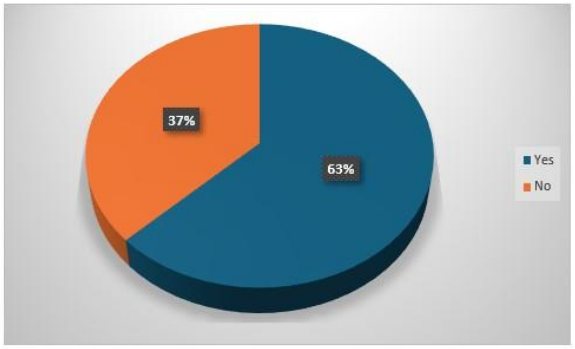


Table 1 The demographic data retrieved among the selected cases (n=500)

Data	Frequency (n)	Percentage (%)
Age		
Mean±S.D	**34±11.2**	
Gender		
Male	123	**24.6**
Female	377	**75.4**
History of gout		
Yes	314	**62.8**
No	186	**37.2**

Figure 2 History of gout among cases in this study



Regarding the clinical data, the mean systolic blood pressure

was 118±12 mmHg and diastolic 76±3.1 mmHg. While their mean blood glucose level was 106±12.1 mg/dl and thyroid functions revealed a normal functionality among all subjects (T4= 9.2±1.1 µg/dL and T3= 142±21.4 ng/dL) (Table 2).

Table 2 The clinical data retrieved among the selected subjects (n=500)

CLINICAL DATA	MEAN±S.D
Blood pressure (Sys/Dias)	118/76±12/3.1
Blood glucose	106±12.1
T4	9.2±1.1
T3	142±21.4

Table 3 The laboratory findings of lipid profile

Laboratory results	Mean±S.D
Total cholesterol	171±12.4
Triglycerides	188±2.1
HDL	97±12.3
LDL	55± 1.6

According the the recorded laboratory findings, most of cases in this study showed a normal HDL and LDL while they are clinically free of hyperlipidaemia and hypertriglyceridemia in spite of the laboratory data near to the borderline of normal ranges. Regarding the renal function tests, the subjects showed a high level of serum uric acid and normal Urea, creatinine and electrolytes (Table 3 and 4).

Table 4 The laboratory findings of renal function tests

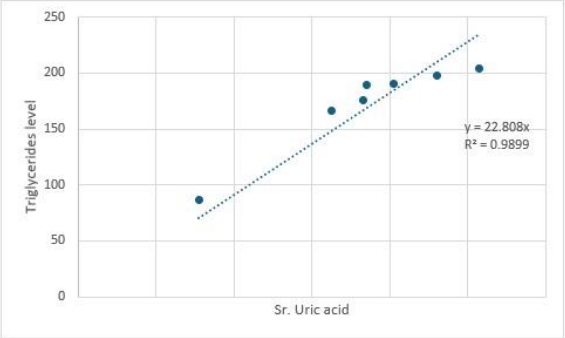
Laboratory results	Mean±S.D
Sr. Uric acid	**7.4±1.1**
Sr. Urea	**18±2.4**
Sr. Creatinine	**1.04±0.22**
Sr. Sodium	**121±1.34**
Sr. Potassium	**3.5±0.4**

The study findings revealed that there is a significant relationship ($P < 0.05$) between gout Uric acid laboratory parameter and slightly elevated serum triglycerides level, in addition, the demographic data such as age, gender, and history of gout has a significant relationship to gout and hypertriglyceridemia ($p < 0.05$) (Table 5).

Table 5 The relationship between Sr. Uric acid, Urea, Creatinine as represented to gout triglycerides

Variables	Co-variate	P value
Sr. Uric acid		**0.03**
Sr. Urea	Triglycerides	**0.11**
Sr. Creatinine		**0.32**
Triglycerides	Age	**0.07**
	Gender	**0.002**
	History of gout	**0.001**

Figure 3 The regression line for estimating the relationship between gout and triglycerides level



The previous figure showed that there is a positive regression between gout represented in sr. uric acid and triglycerides level (R^2 = 0.9899).

*** Discussion**

This study aimed to assess the relationship between serum uric acid, creatinine, urea, cholesterol, and triglycerides among subjects who are clinically diagnosed with gout. In this study, from total of 500 selected subjects with gout and the majority of them were females and with mean age 32 years old, which is in agreement with Kuo *et al*. (2015) study, who reported that the male to female ratio typically ranges from 3 to 4 males for every 1 female. While it is in contrast to Singh and Gaffo (2020) study, who reported that gout has a higher prevalence in men compared to women, with a ratio ranging from 3:1 to 10:1. The occurrence and frequency of gout rise with each successive decade of life, resulting in a prevalence of 11-13% and an incidence of 0.4% in those aged 80 years and above.

According to the recorded laboratory findings, most of cases in this study showed a normal HDL and LDL while they are clinically free of hyperlipidaemia and hypertriglyceridemia in spite of the laboratory data near to the borderline of normal ranges. Regarding the renal function tests, the subjects showed a high level of serum uric acid and normal Urea, creatinine and electrolytes, to revela that there is a significant relationship ($P < 0.05$) between gout Uric acid laboratory parameter and slightly elevated serum triglycerides level, it is in alignment with Hou *et al*. (2019) study, who found that from overall prevalence of hyperuricemia was 62.3 cases per 1000 person-years. In the univariate analysis, those with hypertriglyceridemia had a 2.353 times higher risk of developing hyperuricemia compared to those with normal triglyceride levels. The

95% confidence range for this risk was calculated to be between 2.011 and 2.754. Additionally, men had a 1.86 times higher risk of hyperuricemia compared to women, with a 95% confidence interval ranging from 1.634 to 2.177. Upon controlling for potential confounding factors, the relative risk (RR) of TG at Q2, Q3, and Q4 was found to be 1.445 (95% confidence interval [CI]: 1.114, 1.901), 2.075 (1.611, 2.674), and 2.972 (2.322, 3.804), respectively.

The study findings reported that there is a positive regression between gout represented in sr. uric acid and triglycerides level (R^2 = 0.9899), which agrees with Lin *et al*. (2019) study, who found from a total of 68 people diagnosed with gout were observed. Out of the total, 21 individuals belonged to the normal cholesterol group, 13 belonged to the increased cholesterol group, 21 belonged to the normal triglyceride group, and 13 belonged to the elevated triglyceride group. The outcomes of the independent sample test conducted on the two groups are as follows: The occurrence of gout attacks differs significantly between the group with normal cholesterol levels and the group with high cholesterol levels over three months, six months, and one year (P=0.001). The frequency of gout attacks is significantly different between the normal triglyceride group and the raised group after three months, six months, and one year (P=0.018; P=0.016; 1, P=0.003).

This positive relationship and the demographic data such as age, gender, and history of gout has a significant relationship to gout and hypertriglyceridemia ($p < 0.05$) is also affirmed by Zhang *et al*. (2020) study, who reported the results of the multiple linear regression analysis indicate that there is a significant and positive association between TG levels and both SBP and DBP in both men (SBP: $P = 0.001$; DBP: $P = 0.002$) and women (SBP: $P = 0.002$; DBP: $P = 0.000$). Additionally, SUA levels are significantly and positively associated with SBP in both men (SBP: $P = 0.013$) and women (SBP: $P = 0.028$), regardless of other factors that may influence the results. After accounting for various factors that

could influence the results, there was no evidence of a relationship between serum uric acid and triglyceride levels on systolic blood pressure (SBP) or diastolic blood pressure (DBP) in both men and women.

*** Conclusion**

Gout is mostly prevalent among females than males with mean age of late adulthood, in addition, there is a significant relationship between gout and hyperuricaemia and the elevation of triglycerides, in addition to that, Serum triglycerides can be used as predictor for hyperuricaemia among subjects diagnosed with gout with high levels of serum uric acid. Several studies need to be performed to assess the relationship between other laboratory markers for gout and other chronic disorders parameters.

*** (Ethical standards and considerations**

a. Conflict of interest

Authors declare there is no conflict of interests.

b. Funding

This study did not obtain any funds or grants.

c. Ethical approval

An Institutional Review Board (IRB) approval was obtained with a number 1893-453a. Additionally, the study participants were provided with detailed information about the study methods, and then their written informed consent was obtained on cases.

* References

Aiumtrakul, N., Wiputhanuphongs, P., Supasyndh, O., & Satirapoj, B. (2021). Hyperuricemia and impaired renal function: a prospective cohort study. *Kidney Diseases*, *7*(3), 210-218.

Ali, F. A., Tahir, N. A. K., George, T. R., Ibrahim, A. A. K., Yakob, N. A. K., & Toma, M. E. Relationship between Uric Acid, Creatinine, Urea and Triglyceride Production in Gout.

Bonsnes R W, Taussky H H. On the colorimetric determination of creatinine by the Jaffe reaction. J Biol Chem 1945; 158: 581-91

Calabuig, I., Marty-Ané, A., Norberciak, L., Budzik, J. F., Legrand, J., Martínez-Sanchis, A., ... & Andrés, M.

(2023). Prediction of renal and cardiometabolic outcomes in gout during urate-lowering therapy by sonography. *International Journal of Rheumatic Diseases*, *26*(12), 2450-2459.

Carlson, L. A., and Wadstrom, L. B. Determination of glycerides in blood serum. Clin. Chim. Acta 4: 197, 1959.

He, Y., Xue, X., Terkeltaub, R., Dalbeth, N., Merriman, T. R., Mount, D. B., ... & Li, C. (2022). Association of acidic urine pH with impaired renal function in primary gout patients: a Chinese population-based cross-sectional study. *Arthritis Research & Therapy*, *24*(1), 32.

Hou, Y. L., Yang, X. L., Wang, C. X., Zhi, L. X., Yang, M. J., & You, C. G. (2019). Hypertriglyceridemia and hyperuricemia: a retrospective study of urban residents. *Lipids in health and disease*, *18*, 1-5.

Kuo, C. F., Grainge, M. J., Zhang, W., & Doherty, M. (2015). Global epidemiology of gout: prevalence, incidence and risk factors. *Nature reviews rheumatology*, *11*(11), 649-662.

Lee, C. S., Cha, R. H., Lim, Y. H., Kim, H., Song, K. H., Gu, N., ... & Kim, Y. S. (2010). Ethnic coefficients for glomerular filtration rate estimation by the Modification of Diet in Renal Disease study equations in the Korean population. *Journal of Korean medical science*, *25*(11), 1616.

Li, Q., Shao, X., Zhou, S., Cui, Z., Liu, H., Wang, T., ... & Yu, P. (2022). Triglyceride-glucose index is significantly associated with the risk of hyperuricemia in patients with diabetic kidney disease. *Scientific Reports*, *12*(1), 19988.

Liang, J., Jiang, Y., Huang, Y., Huang, Y., Liu, F., Zhang, Y., ... & Gu, J. (2021). Comorbidities and factors influencing frequent gout

attacks in patients with gout: a cross-sectional study. *Clinical Rheumatology*, *40*, 2873-2880.

Liang, J., Jiang, Y., Huang, Y., Song, W., Li, X., Huang, Y., ... & Gu, J. (2020). The comparison of dyslipidemia and serum uric acid in patients with gout and asymptomatic hyperuricemia: a cross-sectional study. *Lipids in health and disease*, *19*, 1-7.

Liddle L, Seegmiller J E, Laster L. The enzymatic spectrophotometric method for determination of uric acid. J Lab Clin Mtd 1959; 54: 903-13.

Liese, L., Abell, B., Levy, B., Brodie, B. B., and Kendall, F. E.: A simplified method for the estimation of total cholesterol in serum and demonstration of its specificity. J. Biol. Chem. 195:357, 1952.

Lin, L. I., Lu, Q. Q., Tao, J., Zhang, H. L., Tang, Y. J., Xin-Ya, L. I., & Zhu, Z. W. (2019). SAT0449 EFFECT OF CHOLESTEROL AND TRIGLYCERIDE ON THE FREQUENCY OF GOUT ATTACKS.

Liu, B., Zhao, L., Yang, Q., Zha, D., & Si, X. (2021). Hyperuricemia and hypertriglyceridemia indicate tubular atrophy/interstitial fibrosis in patients with IgA nephropathy and membranous nephropathy. *International urology and nephrology*, *53*(11), 2321-2332.

Liu, X. Y., Wu, Q. Y., Chen, Z. H., Yan, G. Y., Lu, Y., Dai, H. J., ... & Yuan, H. (2020). Elevated triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) ratio increased risk of hyperuricemia: a 4-year cohort study in China. *Endocrine*, *68*, 71-80.

Lu, C. C., Liu, Y. H., Lee, W. H., Chen, S. C., & Su, H. M. (2022). Associations of liver function parameters with new-onset hyperuricemia in a large taiwanese population study. *Nutrients*, *14*(21), 4672.

Oh, Y. J., & Moon, K. W. (2021). Presence of tophi is associated with a rapid decline in the renal function in patients with gout. *Scientific Reports*, *11*(1), 5684.

Ortiz-Uriarte, M., Betancourt-Gaztambide, J., Perez, A., & Roman, Y. M. (2023). Urate-Lowering Therapy Use among US Adults with Gout and the Relationship between Patients' Gout Treatment Status and Associated Comorbidities. *Rheumato*, *3*(1), 74-85.

Ran, Z., Xue, X., Han, L., Terkeltaub, R., Merriman, T. R., & Li, C. (2021). Decrease in Serum Urate Level Is Associated With Loss of Visceral Fat in Male Gout Patients. *Frontiers in Endocrinology*, *12*, 724822.

Russo, E., Viazzi, F., Pontremoli, R., Barbagallo, C. M., Bombelli, M., Casiglia, E., ... & Working Group on UricAcid and Cardiovascular Risk of the Italian Society of Hypertension. (2021). Association of uric acid with kidney function and albuminuria: the Uric Acid Right for heArt Health (URRAH) Project. *Journal of Nephrology*, 1-11.

Salah, A. N., Al-Otaibi, M. B., Al-dhmashi, A. S. F., & Mariee, A. A. (2024). Infection control practices and approaches in the dentistry field; a review. *Journal of Bioscience and Applied Research*, *10*(1), 42-58.

Salah, A. N., Elleboudy, N. S., El-Housseiny, G. S., & Yassien, M. A. (2021). Cloning and sequencing of lsaE efflux pump gene from MDR Enterococci and its role in erythromycin resistance. *Infection, Genetics and Evolution*, *94*, 105010.

Salah, A., El-Housseiny, G., Elleboudy, N., & Yassien, M. (2021). Antimicrobial stewardship programs: A review. *Archives of Pharmaceutical Sciences Ain Shams University*, *5*(1), 143-157.

Shen, J., Zhu, J., Si, S., Fu, Y., Mo, M., Xin, X., ... & Yu, Y. (2020). Uric acid fluctuation

had no effect on renal function among gout patients. *Nutrition, Metabolism and Cardiovascular Diseases*, *30*(10), 1833-1839.

Singh, J. A., & Gaffo, A. (2020, June). Gout epidemiology and comorbidities. In *Seminars in arthritis and rheumatism* (Vol. 50, No. 3, pp. S11-S16). WB Saunders.

Wang, Y., Wang, Y., Jia, X., Wang, Z., Li, X., Mu, L., & Zhang, B. (2021). The anti-inflammatory properties of HDLs are impaired in gout. *Clinical Rheumatology*, *40*, 1525-1531.

Zhang, L., Li, J. L., Guo, L. L., Li, H., Li, D., & Xu, G. (2020). The interaction between serum uric acid and triglycerides level on blood pressure in middle-aged and elderly individuals in China: result from a large national cohort study. *BMC cardiovascular disorders*, *20*, 1-11.

Zhang, Y., Chen, S., Yuan, M., Xu, Y., & Xu, H. (2022). Gout and diet: a comprehensive review of mechanisms