folia medica

Folia Medica 65(5):770-774
DOI: 10.3897/folmed.65.e91075

Original Article

Diabetes Mellitus as a Risk Factor and Comorbidity in Gout

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Received: 30 July 2022 ♦ **Accepted:** 12 Aug 2022 ♦ **Published:** 31 Oct 2023

Citation: Rotaru L, Groppa L, Russu E, Chișlari L, Codreanu C, Spinei L, Arnaut O, Cornea C. Diabetes mellitus as a risk factor and comorbidity in gout. Folia Med (Plovdiv) 2023;65(5):770-774. doi: 10.3897/folmed.65.e91075.

Abstract

Introduction: Metabolic disorders are a public health issue because of the complications they cause, but they are also a major risk factor for the onset of gout.

Aim: The current study set out to demonstrate clinically how the clinical-paraclinical evaluation methodology had advanced as well as to assess comorbidity in gout patients using diabetes mellitus (DM). We also wanted to examine the pancreatic dysfunction in gout patients of different ages (by assessing the glucose and glycolated Hb analyses).

Materials and methods: Two hundred gout patients (mean age, men 60±8.0 years, women 63±9.0 years) were included in a descriptive, cross-sectional study. The diagnosis of gout was made according to the classification criteria for gout according to ACR and EULAR 2015. The raw data were analyzed using SPSS v. 26.0.

Results: In the study, type 2 diabetes mellitus (DM2) was encountered with a comparable frequency among both middle-aged and elderly patients (33.8% and 41.8%, respectively, p=0.26). In only 15% of cases, DM2 preceded the development of gout (in 3% with the beginning and 12% with late onset), while the developmental age of the DM2 prior to gout was comparable (50.9±2.8 years in age group 1 and 55.1±6.9 years in age group 2). We found that elderly people experience gout much more frequently (up to 41%) when DM2 is present. However, DM2 is not considered a predictor of gout.

Conclusions: In gout patients under the age of 59 inclusive, the mean age at diabetes onset is significantly lower than the age (37.49.6 years) at which diabetes develops in the general population. Early onset of diabetes is associated with early development of gout.

Keywords

gout, comorbidity, diabetes mellitus

INTRODUCTION

Gout is a condition marked by the buildup of sodium monourate crystals in various tissues and organs and the onset of inflammation that results from this in people with hyperuricemia (HU) brought on by environmental and/or genetic factors.[1-4]

Comorbid pathology is a condition that often occurs in old age.[5-8] Currently, the concept of comorbidity is considered as the presence of concomitant pathogenetically related diseases that have a reciprocal effect on the evolution of the other, complicating the management of the patient and aggravating his prognosis.[1,3,9,10] Even Paracelsus said that in an organism weakened by gout, "embryos of other

diseases" can develop.[6,9,11] The association of gout with cardiovascular pathology, chronic kidney, and metabolic diseases is generally recognized.[8,10,12-16]

The relationship between HU and DM was revealed most completely: a meta-analysis of 11 studies showed a significant increase in the risk of developing DM among patients with HU (1.41; 95% CI 1.23-1.58) after adjusting for traditional risk factors (age, BMI, smoking, and alcohol). Several studies have reported an increase of 1.13 in the relative risk of DM (95% CI 1.06-1.20) for every 1 mg/dl increase in uric acid (UA).[3,7,9,17-21] A meta-analysis of 25 studies conducted between 1972 and 2013 involving a total of 97824 people also showed an increase in the relative risk of DM (1.15; 95% CI 1.06-1.20) for 1 mg/dl increase in UA.[19-23]

AIM

Evaluation of comorbidity through diabetes mellitus and clinical substantiation of the improvement of the methodology of clinical-paraclinical evaluation of patients with gout.

MATERIALS AND METHODS

This descriptive, cross-sectional study included 200 patients with gout (mean age, men 60±8 years and women 63±9 years). The study was conducted in accordance with the requirements of the Ministry of Health for "Clinical and financial-economic research" within the postdoctoral research program in the discipline of Rheumatology and Nephrology at Nicolae Testemitanu State University of Medicine and Pharmacy.

We extracted clinical and paraclinical data and treated gout patients from the database of the Departments of Arthrology, Rheumatology, and Nephrology at Timofei Mosneaga Republican Clinical Hospital, a total of 658 gout patients observed between 2015 and 2022. Of these, 276 patients who met the study's criteria were chosen, with 200 of them being included in the statistical analysis. The diagnosis of gout in the database was made in accordance with the classification criteria for gout according to ACR and EULAR 2015.[6,8] These patients were divided into two groups based on their age at the onset of gout: those aged up to and including 59 years (group 1, n=150) and those aged 60 years and older (group 2, n=50). The data were analyzed using SPSS v. 26.0.

RESULTS

The patients (n=200) were divided into two groups, depending on the patient's age at the onset of gout: group 1 included patients who were up to 59 years of age inclusive (n=150) and group 2 consisted of patients aged 60 years and older (n=50). The ratio of men to women in group 1 (124 men, 83% and 26 women, 17%) and 37 men (74%) and 13 women (26%) in group 2 had no significant differences (p=0.18). The mean age of patients at the time of examination in group 1 was 57.9±11.3 years, in group 2 – 73.3±4.4 years (p<0.1).

The mean age at the onset of gout in group 1 was 42.9±9.8 years, in group 2 – 65.5±4.7 years (p<0.1). The duration of the disease in group 1 was 2 times longer than in group 2: 15.0 years (range 9.4-18.8 years) versus 7.8 years (range 5.3-10.0 years) (p<0.1).

The mean age of detection of DM2 did not have significant differences between the groups. Significantly earlier, the occurrence of coronary heart disease in group 1 was observed: the average age of manifestation of coronary heart disease in 19 patients was 48.4±6.9 years, and in 26 patients of group 2 – 59.1±5.0 years (p<0.1).

The chronic course of arthritis was initially assessed in 4 (8%) patients of group 2, while in group 1, the initial chronification of the gouty process was observed in only 2 people (1.3%) (p=0.0017).

In the study, DM2 was encountered with a comparable frequency among both middle-aged and elderly patients (33.8% and 41.8%, respectively, p=0.26%). In only 15% of the cases, DM2 preceded the development of gout (in 3% with the beginning and 12% with late onset), while the developmental age of the DM2 prior to gout was comparable (50.9±2.8 years in group 1 and 55.1±6.9 years in group 2). Gout has been found to occur much more often in the elderly in the presence of DM2, reaching 41%.[3,6,9-11] However, DM2 is not considered a predictor of gout.

A high comorbid background in patients with gout today is a close topic for attention. As the study showed, if in middle age there were 2 concomitant diseases, in the elderly they were 4. Only 2 (1%) patients with gout, middle-aged men, did not have concomitant diseases.

The study made it possible to determine the most common combinations of diseases: hypertension and nephrolithiasis at an early age occurred in 78.8% of cases, at the same time 82.9% of the elderly patients had hypertension and coronary artery disease. The results we obtained lead to the conclusion that the accumulation of diseases of the circulatory system, the main cause of death in the older age groups is a characteristic feature of gout of the elderly and requires special attention.[15,17-19,22]

The results of the study show that gout has not only a pronounced comorbid background, but also a high risk of developing concomitant pathology: cardiovascular disease, nephrolithiasis, chronic kidney disease, DM2, which has recently been demonstrated in various studies.[2,6,9,12]

DISCUSSIONS

The frequency of diseases directly associated with gout: DM2, urolithiasis, and chronic kidney disease (CKD), does not differ in the groups, which indicates the possible closeness of the pathogenetic mechanisms of these diseases with

gout. It is noted that the frequency of hypertension practically does not differ in groups, which may also indicate a pathogenetic link between them and gout.

Recently, a hypothesis has been presented regarding a decrease in the clearance of uric acid (UA) and the development of hyperuricemia due to the direct effect of hyperinsulinemia on the kidneys.[8-10] Currently, the high frequency of occurrence of gout in DM2 is explained not by the effect of DM2 on increasing the risk of developing gout, but by the action of 2 factors associated with diabetes: obesity, hypertension, chronic heart failure, CKD, the administration of diuretics and low doses of aspirin, the frequency of which in the patients we have examined is quite high.[1,3,8-10]

In an extensive long-term study, it was shown that the presence of DM2 reduces the risk of further development of gout by 41% compared to type 1 diabetes mellitus (DM1) (73% in DM1 and 39% in DM2) regardless of age, smoking, alcohol consumption, renal failure and coronary artery disease. At the same time, a more severe course of DM2 as a result of more pronounced blood glucose is associated with a lower risk of developing gout, and the risk of further development of gout gradually decreases inversely proportionally to the duration of the course DM2.[12,17,21,22]

According to some studies, out of 472 middle-aged gout patients (46.8±14.4 years), and the average duration of the disease of 5.3±2.9 years, 12 (2.5%) relatively young patients did not have concomitant pathology.[3,8,14,15,17] The average age of the patients in our study was significantly higher, and the duration of gout was 2 times longer, which significantly reduced the chances of detecting gout without concomitant diseases.

The risk reduction mechanism is explained by the uricosuric effect of glucose with an increase in blood glucose levels above 10 mmol/l.[3,8,10,19] However, as the study showed, the frequency of DM2 in patients with gout is comparable and quite high, since insulin resistance and hyperuricemia are pathogenetically linked as components of the metabolic syndrome, and the frequency of detection of metabolic syndrome and insulin resistance in patients with gout does not depend on age.[3,7,10,20]

The average number of comorbidities was 2 times higher in group 2 – 2.0 (2.0; 3.0) and 4.0, respectively, (3.0;5.0) (p<0.1).

Only 2 (1%) patients in group 1 had no comorbid pathology: both were men, aged 56.7 years at the time of the examination with onset at 47.1 years, and at the age of 37.6 years at the time of the examination with an onset of 28.1 years. The highest number in group 1 had 2 comorbidities (25, 35.2%). In group 2, 58% had 4 or 5 comorbidities. One patient in group 1 and 8 in group 2 had all 6 comorbid gout diseases.

Separately, the variants and frequency of the combination of concomitant diseases in representatives of groups 1 and 2 were considered. In group 1, the combination of DM, hypertension, and urolithiasis prevailed significantly (17 people, 23.9%), in 10 people (14.1%) gout was accompanied by hypertension, urolithiasis, and type 2 diabetes. Seven people had only DM and 6 people only hypertension. In 4 people (5.6%), a combination of gout with hypertension, coronary artery disease, urolithiasis and DM2 was found. The rest of the combinations of diseases of group 1 occurred with a frequency of less than 5%.

Most commonly, in group 2, there were patients with a combination of gout with hypertension, coronary artery disease, chronic heart failure (CHF), urolithiasis, and DM2 (19 people, 15%), in a significant number of patients gout was simultaneously combined with hypertension, coronary artery disease, CHF, urolithiasis and CKD (15 people, 12%). In 11 (8.5%) patients, there was a combination of gout simultaneously with hypertension, DM, CHF, and urolithiasis. In 9 (7%) people with hypertension, coronary artery disease, CHF and in 9 (7%) gout was combined with hypertension, DM, urolithiasis, and CKD. In 8 cases, hypertension and coronary heart disease were determined as comorbid diseases, and in 7 cases – DM and urolithiasis. All other combinations of comorbid diseases were determined with a frequency of less than 5%. Options for combinations of the most common (in more than 50% of cases) concomitant diseases in groups were considered.

Widely represented in different combinations of concomitant pathology in both groups and at the same time isolated cases of detection of gout without or with a concomitant disease of both young and old age indicate comorbidity as an integral part of gout.

CONCLUSIONS

1. Gout is associated with a pronounced comorbid background, increasing significantly in the elderly and developing earlier with the early onset of gout: the average number of concomitant diseases is 2 times higher in the group of patients with gout aged 60 years and older.
2. With age, the frequency of comorbidity for gout increases: alcohol consumption from 14 to 28%, consumption of foods saturated with purine from 51 to 68%, overweight and obesity from 58 to 76% in groups of patients with gout onset at the age of 59 years inclusive and 60 years and older.
3. The early age of the onset of DM is associated with the early development of gout: the average age of the onset of the DM in patients with gout development under the age of 59 years inclusive is significantly lower than that in the general population (37.4±9.6 years).

Acknowledgements

The authors have no support to report.

Funding

The authors have no funding to report.

Competing Interests

The authors have declared that no competing interests exist.

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Сахарный диабет как фактор риска и сопутствующая патология при подагре

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Дата получения: 30 июля 2022 ♦ **Дата приемки:** 12 августа 2022 ♦ **Дата публикации:** 31 октября 2023

Образец цитирования: Rotaru L, Groppa L, Russu E, Chișlari L, Codreanu C, Spinei L, Arnaut O, Cornea C. Diabetes mellitus as a risk factor and comorbidity in gout. Folia Med (Plovdiv) 2023;65(5):770-774. doi: 10.3897/folmed.65.e91075.

Резюме

Введение: Метаболические нарушения являются проблемой общественного здравоохранения из-за вызываемых ими осложнений, но они также являются основным фактором риска возникновения подагры.

Цель: Настоящее исследование имело целью клинически продемонстрировать развитие методологии клинико-параклинической оценки, а также оценить сопутствующую патологию у пациентов с подагрой и сахарным диабетом (СД). Мы также хотели изучить дисфункцию поджелудочной железы у пациентов с подагрой разного возраста (путём оценки анализов глюкозы и гликолированного гемоглобина).

Материалы и методы: Двести пациентов с подагрой (средний возраст: мужчины 60 ± 8.0 лет, женщины 63 ± 9.0 лет) были включены в описательное перекрёстное исследование. Диагноз подагры устанавливался в соответствии с классификационными критериями подагры согласно ACR и EULAR 2015. Исходные данные анализировались с использованием SPSS v. 26.0.

Результаты: В исследовании сахарный диабет 2 типа (СД2) встречался с сопоставимой частотой среди пациентов как среднего, так и пожилого возраста (33.8 % и 41.8 % соответственно, p=0.26). Лишь в 15 % случаев СД2 предшествовал развитию подагры (в 3 % с началом и в 12 % с поздним началом), при этом возраст развития СД2 до подагры был сопоставимым (50.9 ± 2.8 года в 1-й возрастной группах и 55.1 ± 6.9 года в возрастной группе 2). Мы установили, что пожилые люди гораздо чаще (до 41 %) страдают подагрой при наличии СД2. Однако СД2 не считается предиктором подагры.

Заключение: У больных подагрой в возрасте до 59 лет включительно средний возраст начала диабета значительно ниже возраста (37.4 – 9.6 лет), в котором развивается диабет в общей популяции. Раннее начало диабета связано с ранним развитием подагры.

Ключевые слова

подагра, сопутствующие заболевания, сахарный диабет