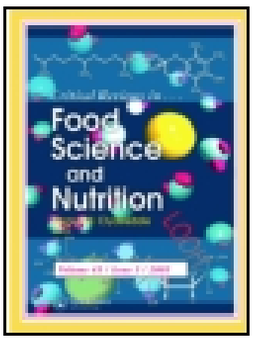

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REVIEW

The role of alcohol consumption in pathogenesis of gout

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ABSTRACT

Alcohol is recognized a risk factor for increased uric acid and gout flare. The aim of the study was to review the literature in order to find out what is the role of alcohol consumption in pathogenesis of gout. A search in PubMed, Google Scholar, Medline Complete database was performed in January 2021. The databases were searched with the phrases: "uric acid and alcohol," "alcoholic beverages and gout," "hyperuricemia and alcoholic beverages consumption" published between 2000 and 2021. A total of 2642 results were found. The 99 non-duplicate citations were screened. Then 81 articles were excluded after abstract screen. After that 18 articles were retrieved. Eventually 15 articles were included for systematic review. Several authors see the positive correlation between beer or distilled spirits consumption and gout. Some include wine to the list of triggers of gout. Others state that moderate wine consumption protects from gout attacks due to antioxidants and phytoestrogen content. Majority noticed the relationship between episodic alcohol consumption and gout attacks. Episodic alcohol intake triggers gout attacks, regardless of type of alcohol. Thus, individuals with established gout and pre-existing risk factors should limit all types of alcohol intake to prevent gout episodes.

KEYWORDS

Alcohol; hyperuricemia; gout; risk factors

Introduction

No one is sure who first invented wine, ale, beer, or spirits. The historians confirm that societies have enjoyed alcoholic beverages throughout recorded history. Wine was mentioned in the Bible and documents from ancient Rome. In the Middle Ages, drinking beer was recommended for children and pregnant women in order to avoid waterborne diseases as it was made with boiled water. For older adults, a drink before a meal may enhance appetite (Tulchinsky and Varavikova 2014). There are numerous examples of the use of alcohol as an anesthetic, myorelaxant, and central nervous system depressant in the history of medicine (Thompson et al. 2017; Arout et al. 2016). Moderate drinking may lower the risk of heart disease among people with risk factors for cardiovascular disease (especially men over 45 and women over 55 years of age) (Goel, Sharma, and Garg 2018). The crucial term here is "moderation": no more than one drink daily for a woman and no more than two drinks daily for a man (Oppenheimer and Bayer 2020). The World Health Organization (WHO) and most national guidelines typically quantify one drink (one unit or one equivalent of alcohol) as 10 g of ethanol. However, the metric used as a "standard measure" can vary across countries. Most countries across Europe use this 10 g of pure ethanol as an unit of alcohol, however this can vary with several countries adopting 12 or 14 g per unit (http://www.who.int/gho/en/, ● ● ●). We must remember that alcohol provides calories: 7 calories per 1 g of ethanol plus the ones from sugar and added juices. In one beer there is 150 calories, 1 glass of wine 100 calories, 1 shot of a distilled spirit 100 calories (Duyff 2017). Alcohol interferes with nutrient absorption. Moreover alcohol is a diuretic, which increases urine output and leads to dehydration. Everyone who enjoys alcoholic beverages should drink plenty of water too (Duyff 2017).

The Dietary Guidelines for Americans enumerate the risks related to consumption of alcoholic beverages: hypertension, stroke, cancer, motor vehicle crashes, violence, other injuries, and suicide. During pregnancy drinking increases the risk for birth defects. Moderate drinking increases the risk of breast cancer in women (Duyff 2017).

Repeated alcohol use produces physical, psychological, and social dependence. Rapid withdrawal leads to withdrawal syndrome with possibility of delirium. In alcoholics, encephalopathies and cardiomyopathies, liver cirrhosis, and pancreatitis are common (Duyff 2017).

There are large geographical differences in alcohol consumption: across North Africa and the Middle East alcohol consumption is particularly low – close to zero. It is connected with religious do's and dont's. Alcohol intake across Europe is highest at around 15 L per person per year in the Czech Republic, Lithuania, and Moldova. Behind the Eastern European countries are Western European countries – including Germany, France, Portugal, Ireland, and Belgium – where average alcohol consumption is 12–14 L per person per year. Outside of Europe the only other country in this category is Nigeria (Ritchie 2018). Per capita alcohol consumption has decreased by about one half in

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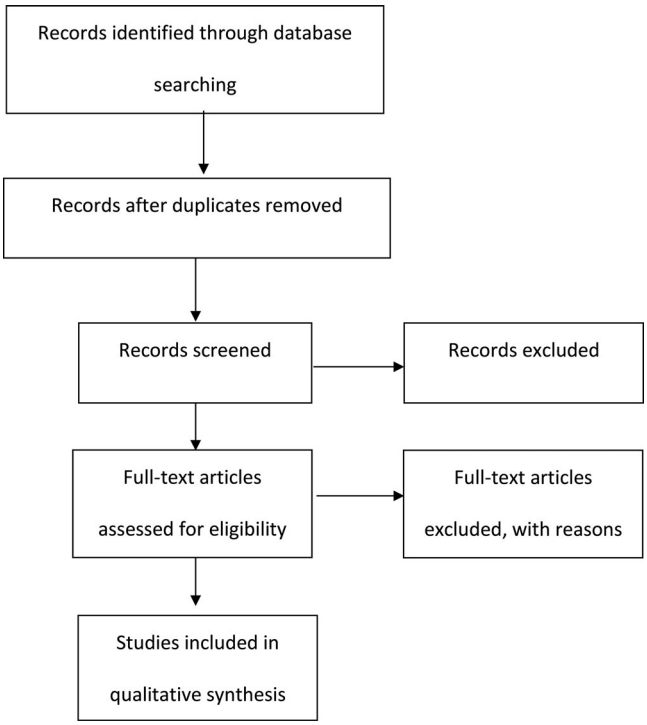

Figure 1. PRISMA flow diagram.

traditional wine-producing and wine-drinking countries such as Italy and France during the past few decades. During the same period it has doubled in the United Kingdom and Denmark. Alcohol consumption systematically increases in China (Ezzab and Riboli 2013). Per capita alcohol consumption in Poland is 12 L/year (Wojtyniak and Goryński 2018).

Globally, alcohol consumption causes 2.8 million premature deaths per year and 3.9% of the global burden of disease (Ritchie 2018; Ezzab and Riboli 2013).

Alcohol consumption is associated with numerous diseases including gout attacks. It is commonly believed that gout is a self-inflicted condition that is socially embarrassing and the focus of humor (Duyck, Petrie, and Dalbeth 2016). Hyperuricemia (HU) is considered the precursor of gout, which is the most common inflammatory arthritis in adult men.

In humans, uric acid (UA) is the final product of purine metabolism. It helps to maintain arterial blood pressure to guarantee sufficient blood flow through the brain and distal parts of the body in the erected position. Western diet is high in purines. In consequence, serum UA concentration gets too high. Other mammals produce an enzyme uricase, which converts UA into allantoine. Humans miss it, so they have the growing problem of HU. About 70% of UA is removed from the body with urine and 30% is removed via the gastrointestinal tract. HU is serum UA concentration >6 mg/dL (360 mmol/L). Among reasons of HU are underexcretion (90% of cases) and overproduction (10%). HU may result from exogenous factors (lifestyle – alcohol overconsumption, diet high in meat, fructose, corn sirup, obesity, and use of thiazide diuretics) as well as endogenous [male gender, old age, diabetes mellitus, metabolic syndrome, kidney failure, cardiovascular disease (CVD), arterial hypertension (AH), inflammatory diseases, genetic purine metabolism disorders, stroke and oxidative stress]. It is estimated that 30% of patients with HU have clinical symptoms of gout (Widecka et al. 2017).

According to American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR), gout is diagnosed if there was an episode of arthritis or bursitis at least once or natrium ureate crystals were identified in the joint, bursa, or tophus. Clinical symptoms that are taken into consideration are I metatarsophalangeal (MTP) joint, ankle, or other MTP except for MTP II involvement, erythema, tenderness, difficulty in walking, minimum two typical gout attacks, quick onset of the arthritis (<24 h), improvement within up to 14 days, remission between attacks, detection of calcium ureate deposits in ultrasound or computed tomography examination, and serum UA concentration >6 mg/dL (360 mmol/L) (Neogi et al. 2015; Richette et al. 2017).

Alcohol is recognized as a risk factor for increased UA in the blood serum and gout flare. Chronic and single doses of alcohol lead to an increase in the concentration of UA in the blood. Its excretion by the kidneys is reduced. UA is sent through the renal glomeruli, but alcohol is reabsorbed in the proximal tubule with slight secretion in the distal tubule. Lactic acid resulting from alcohol poisoning limits the latter process. Lactate inhibits the secretion of UA in the distal tubule and thus reduces its excretion in the urine (Ndrepepa 2018).

In addition, alcohol increases the synthesis of UA by accelerating the transformation of nucleotides while inhibiting the excretion of oxopurines in the urine.

The aim of the study was to review the literature to answer the question: what is the role of alcohol consumption in pathogenesis of gout? How does the type of beverage matter?

Material and methods

Standard up-to-date criteria were followed for review of the literature data. A search for English-language articles in the PubMed, Google Scholar, and Medline Complete database was performed in January 2021. The databases were searched with the phrases: “uric acid and alcohol,” “alcoholic beverages and gout,” “hyperuricemia and alcoholic beverages consumption” published between 2000 and 2021. A total of 2642 results were found. The 99 non-duplicate citations were screened. Then 81 articles were excluded after abstract screen. After that 18 articles were retrieved. Three articles were excluded after data extraction. The aim was to find studies assessing alcoholic beverages and their role in the pathogenesis of gout. Eventually, 15 articles were included for systematic review (Figure 1).

Results

The relationship between high-alcohol intake and HU is shown in several studies (Table 1).

Table 1. Analysis of 15 studies about the influence of alcohol consumption on the risk of gout.

No.	Source	country	Population size	Study design	The risk of gout
1	Choi et al. 2004	USA	47,150 (100% males); gout cases 730	Observational study; biennial questionnaires 12 years (1986–98)	1.32 (95% CI 0.99–1.75) for alcohol consumption 10.0–14.9 g/day 1.49 (1.14–1.94) for 15.0–29.9 g/day 1.96 (1.48–2·60) for 30.0–49.9 g/day 2.53 (1.73–3.70) for ≥50 g/day (p for trend <0.0001).
2	Choi and Curhan 2004	USA	14,809 participants (6932 men and 7877 women) age ≥20 years after excluding participants who self reported gout or were taking allopurinol or uricosuric agents ($n = 446$)	Observational study; assessed twice: in 1988 and 1994	Beer 0.46 mg/dL [95% CI 0.32, 0.60] (p for trend <0.01) Liquor 0.29 mg/dL [95% CI 0.14, 0.45] (p for trend <0.01) wine 0.04 mg/dL [95% CI −0.20, 0.11] (p for trend =0.6)
3	Gaffo et al. 2010	USA	3123	Observational study; follow-up at 20 years	Significant associations between higher SU concentrations and greater beer intake were observed among men and women, with more pronounced and consistent associations for women. An association between greater liquor intake and higher SU concentrations was only seen for men at the year 20 evaluation. Wine intake was not associated with SU in either sex and total alcohol was associated with higher SU concentrations in both men and women. The magnitude of the associations between alcoholic beverages intake and SU was modest (≤0.03 mg/dl/alcoholic beverage serving).
4	Sugie et al. 2005	Japan	Performed using data from 715 men employed as office workers	Observational study; cross-sectional survey	Odds ratio (OR) of hyperuricemia (serum uric acid = 7.0+ mg/dL) was 2.89 (95% confidence interval [CI]: 1.46–5.71) for subjects who consumed 50+ g/day of ethanol, and 2.64 (95% CI: 1.33–5.24) for subjects who consumed 25–49 g/day. Compared with subjects who drank Japanese sake, subjects who drank beer (OR = 1.24, 95% CI: 0.55–2.80) or shochu (OR = 1.06, 95% CI: 0.44–2.51) did not have a statistically significant difference in risk for hyperuricemia.
5	Cea Soriano et al. 2011	UK	The incidence of gout based on 24,768 newly diagnosed gout patients among a cohort of 1,775,505 individuals aged 20 to 89 years between 2000 and 2007	Observational study	The risk factor of gout: excessive alcohol intake (that is, more than 42 units per week), ORs of 3.00 (95% confidence interval (CI))
6	Lyu et al. 2003	Taiwan	Between 1998 and 1999, e recruited and conducted face-to-face interviews with patients from outpatient clinics in Taipei who had incident gout ($n = 92$) and with their healthy coworkers (controls; $n = 92$).	Observational study	Alcohol was a strong risk factor for gout but not purine consumption
7	Williams 2008	USA	28,990 male runners.	Survey	The risk of gout increased with higher alcohol intake [per 10 g/day; relative risk (RR): 1.19; 95% CI: 1.12, 1.26; $p < 0.0001$], The RR per 10 g alcohol/day consumed as wine (1.27; $p = 0.002$), beer (1.19; $p < 0.0001$), mixed drinks (1.13; $p = 0.18$) was not significantly different from each other. Consumption of >15 g alcohol/day led to 93% greater risk of gout than abstainers
8	Lee 2013	South Korea	Gout patients newly diagnosed between January 1, 2007, and December 31, 2008, and matching controls; the study was	Case–control study	Gout was associated with drinking ≥1drink/week ($p < 0.001$), drinking ≥1 bottle of *soju*/session ($p < 0.001$).

(*continued*)

Table 1. Continued.

No.	Source	country	Population size	Study design	The risk of gout
			conducted using the nationwide database (National Health Insurance Corporation and National Health Screening Exam (NHSE) database), which included the healthcare records of 48.1 million individuals.		
9	Cheng et al. 2012	China	120 patients with gouty arthritis were surveyed and compared with 135 control population	Case–control study	Alcohol drinking increased the risk of gout (OR = 7.081)
10	Lin, Lin, and Chou 2000	China	223 asymptomatic hyperuricemic men initially studied in 1991–92 were reassessed in 1996–97.	Observational study	The 5-year cumulative incidence of gout was 18.83%. Excessive alcohol consumption, particularly if occasional, was the most important factor in the development of gout, even when the concentration of uric acid level was below 8 mg/dL.
11	Bhole et al. 2010	USA	2476 women and 1951 men. 304 cases of gout, 104 of them among women.	Data from the Framingham Heart Study (1950–2002)	The incidence rates of gout for women per 1000 person-years according to serum uric acid levels of <5.0 mg/dL was 0.8 and≥ 8.0 mg/dL was 27.3 Multivariate relative risks conferred by increasing alcohol intake (≥7 ounces of pure alcohol/week), ($p < 0.05$), for women.
12	Ndong et al. 2018	Gabon	85 patients, 54% men ($n = 46$) and 46% women ($n = 39$)	Adult men aged 19 years old and women older than 18 were hyperuricaemic or under treatment due to hyperuricemia.Only adults over 18 years with a request for uric acid tests have been retained.	Consumption of alcohol (OR = 13) was associated with gout and hyperuricemia.
13	Nakamura et al. 2012	Japan	3310 men; 529 incident cases of hyperuricemia	6-year prospective study; annual heath examinations	The hazard ratio (95% confidence interval) for hyperuricemia in drinkers compared with nondrinkers was 1.10 (0.85–1.42) for <10.0 drinks/week, 1.40 (1.07–1.84) for 10.0–19.9 drinks/week, 1.64 (1.23–2.21) for 20.0–29.9 drinks/week 1.98 (1.40–2.80) for ≥30.0 drinks/week
14	Yu 2008	China	2176 adults, 987 (45%) men, and 1189 (55%) women	Cross-sectional survey	Beer consumption was significantly associated with hyperuricemia in men, odds ratio was 1.49 for men who imbibed <1 drink daily, 1.56 for men who imbibed ≥1 drink daily, when compared with that for men who did not drink beer ($p = 0.035$). Adjusted OR for men who drank <5 cans of beer daily was 1.13, men who drank > or =5 cans daily OR was 1.28 compared with men who did not drink beer ($p = 0.003$).
15	Neogi et al. 2014	USA	724, 78% men, mean age 54 years; 1434 gout attacks during 1-year follow-up	Online study is an Internet-based case-crossover study	The risk of recurrent gout attack was 1.36 (95% CI, 1.00–1.88) and 1.51 (95% CI, 1.09–2.09) times higher for >1–2 and >2–4 alcoholic beverages

SU serum urate.

According to Choi et al. (2004), beer consumption shows the strongest association with the risk of gout: relative risk (RR) per 12-oz serving (359 mL) per day is 1.49; 95% with confidence interval (CI) 1.32–1.70. Consumption of spirits was also significantly associated with gout (RR per drink per day 1.15; 95% CI 1.04–1.28); however, wine consumption was not significantly associated with gout (RR per 4-oz serving per day 1.04; 95% CI 0.88–1.22).

In the study published by Choi and Curhan (2004), it was found that serum UA levels decreased with increasing wine intake except for one who drank more than 1 serving per day. There was an inverse association between wine

intake and serum UA concentration (p for trend <0.001) and the difference per serving per day increase was –0.42 mg/dL (95% CI –0.62, –0.22).

In the study by Gaffo et al. in young adults, there was a significant association between high-serum UA concentrations and greater beer intake. The relationship was observed among men and women. The association was more pronounced for women. An association between liquor intake and elevated UA concentrations was seen in men at the year 20 of the evaluation. Wine intake was not associated with UA in men or women. Per each serving of alcohol, UA concentration increased by ≤0.03 mg/dL (Gaffo et al. 2010) .

In the study conducted by Sugie et al. in Japanese men, alcohol consumption was associated with an increased risk of HU and the increased risk did not vary according to the type of alcoholic beverage. Compared with subjects who drank Japanese sake (distilled spirit), subjects drinking shochu (Japanese beer) did not have a significant difference in risk for HU. Both sake and shochu increase the risk for HU but not gout (Sugie et al. 2005).

According to Cea Soriano, excessive alcohol intake (drinking more than 42 units per week) increases the risk of gout: odds ratio (OR) =3.00 (95% CI). Authors identified psoriasis, heart failure, hypertriglyceridemia, and cyclosporine therapy as additional risk factors for gout (Cea Soriano et al. 2011).

Lyu in his publication from 2003 concerning risk factors for gout concluded that consumption of alcohol, but not of purine is a significant risk factor for the disease. The author analyzed the correlation between systolic and diastolic blood pressure, waist-to-hip ratio, waist-to-height ratio, body mass index with the risk of gout. All the aforementioned factors were significantly higher in patients with gout than in controls. Family histories of gout and diabetes mellitus were also found to be strong risk factors for gout. Patients with gout ate vegetables and fruits significantly less often than controls. These analyses showed that high-alcohol intake strongly increased the risk of gout, but no association was found with purine intake (Lyu et al. 2003).

The risk of gout is lower in men who are physically active, maintain body weight within healthy range of body mass index, and consume diets enriched in fruit and low in meat and alcoholic beverages (Williams 2008).

According to Lee at al. who conducted their case–control study in South Korea in 2007 and 2008 among ≥40 years old citizens, gout was positively correlated with having ≥1 alcoholic drink per day ($p < 0.001$) or drinking ≥1 bottle of *soju* per session ($p < 0.001$) (Lee et al. 2013).

Cheng agrees that drinking alcohol was one of the most important risk factors contributing to gout (OR = 7.081) (Cheng et al. 2012).

Lin in the study of 223 asymptomatic patients with HU calculated the 5-year cumulative incidence of gout and it was 18.83% (42/223). Excessive alcohol consumption, particularly if occasional, was the most important factor in the development of gout, even when the concentration of UA concentration in the blood serum was <8 mg/dL (Lin, Lin, and Chou 2000).

Bhole et al. using prospective data from the Framingham Heart Study (1950–2002) analyzed the risk factors of gout in 2476 women and 1951 men. They documented 304 gout cases, 104 of them among women. The incidence rates of gout for women per 1000 person-years according to serum UA levels of <5.0 mg/dL was 0.8 and ≥8.0 mg/dL was 27.3, respectively (p for trend <0.0001). Multivariate relative risks conferred by increasing alcohol intake (≥7 ounces of alcohol/week) was 3.10 ($p < 0.05$) for women (Bhole et al. 2010).

Nakamura et al. conducted a study in 3310 men from Japan for 6 years. They obtained data about alcohol consumption including sake and shochu. Sake is a Japanese wine. Shochu is a Japanese distilled spirit. During the period, 529 incident cases of HU were recorded. Authors found a positive correlation between the number of alcohol equivalents consumed per week and the risk of HU and gout (Nakamura et al. 2012).

Yu demonstrated that beer intake is independently associated with increased risk of HU in men. Restricted beer intake may help prevent HU in the population (Yu et al. 2008).

In the study of Noegi et al. from 2014 it was indicated that episodic alcohol consumption, regardless of type of alcoholic beverage, was associated with an increased risk of recurrent gout attacks, including potentially with moderate amounts. Authors suggest that individuals with gout should limit alcohol intake of all types to reduce the risk of recurrent gout attacks (Neogi et al. 2014).

Discussion

Results from observational studies analyzing the relationship between alcohol consumption and the risk of gout were conflicting. Some authors see the positive correlation between beer or distilled spirits consumption, and gout (Choi et al. 2004; Gaffo et al. 2010; Yu et al. 2013; Wang et al. 2013). Some include wine to the list of triggers of gout (Sugie et al. 2005). Some state that moderate wine consumption protects from gout attacks (Choi and Curhan 2004).

Many authors agree that episodic intake triggers gout attacks, even for moderate amounts and regardless of type of alcohol. Thus, individuals with established gout should limit all types of alcohol intake as a preventive strategy to reduce the risk for recurrent gout episodes.

In the meta-analysis of 12 articles prepared by Wang et al., alcohol consumption had been linked to the risk of gout. The pooled RR for highest compared to non-occasional alcohol drinking in every study was 1.98 (95% CI, 1.52–2.58). The RRs for ≤1 drink/day was 1.16 (95% CI, 1.07–1.25). For >1 to <3 drinks per day was 1.58 (95% CI, 1.50–1.66) and for ≥3 drinks per day when compared to non-occasional alcohol drinking was 2.64 (95% CI, 2.26–3.09) (Wang et al. 2013).

Ethanol intake has been shown to increase serum UA level via both decreased urate excretion (Drum, Goldman, and Jankowski 1981; Sharpe 1984; Vandenberg et al. 1994; Eastmond et al. 1995) and increased production (Faller and Fox 1982; Puig et al. 1991). Reduced renal urate excretion

occurs because of lactic acidosis associated with acute excessive alcohol intake. Moreover, the acidosis may be associated with fasting.

After drinking, alcohol is easily absorbed through the mucous membranes of the digestive tract and reaches the brain with blood very quickly. The rate of alcohol absorption depends on the rate of gastric emptying and the concentration of alcohol in the beverage. Drinking more concentrated alcohol in the fasted state leads to more rapid absorption of ethanol. The small polar molecules of ethanol are water soluble and readily cross the blood–brain barrier (Cederbaum 2012). The initial "lift" after alcohol use comes by dulling various brain centers. It results in impaired concentration, coordination, prolonged response time, blurred vision, and slurred speech. Alcohol interferes with normal sleep patterns.The concentration of alcohol in a tissue depends on water content in it. Due to higher fat content in females, alcohol has lower volume of distribution than in males. So women are at greater risk for problems related to alcoholism. The first-pass metabolism of alcohol occurs in the stomach. In alcoholics it is significantly decreased. The major enzyme responsible for alcohol metabolism is alcohol dehydrogenase in the liver (Chrostek and Szmitkowski 1996). Its activity is higher in males than females. The enzyme requires the cofactor nicotinamide adenine dinucleotide (NAD) and the products produced are acetaldehyde and reduced NAD (NADH). Nearly, 95% of consumed ethanol is metabolized to acetaldehyde. The rest is excreted with urine and exhaled with air via lungs. In ethyl alcohol metabolism, catalase and microsomal enzymes also participate. Dehydrogenase metabolizes 80–90% of ethanol (Chrostek and Szmitkowski 1996). Catalase plays a minimal role in vivo (van der Zel et al. 1991). Microsomal enzymes convert about 20% of the absorbed dose of ethanol (Lieber 1987). All the enzymes metabolize ethanol to acetylaldehyde. Depending on liver glycol reserves, alcohol consumption may lead to hyper- or hypoglycemia. The simultaneous increase in the activity of hepatic phosphorylase accelerates the process of glycogenolysis, reducing the glycogen content in hepatocytes. The increase in the NADH:NAD + ratio accompanying intoxication with ethanol acts to inhibit the glycolysis process by reducing the activity of glyceraldehyde:phosphate dehydrogenase. Thus, one may develop hyperglycemia after drinking alcohol (Shimomura and Wakabayashi 2015).The ethanol-induced hypoglycemia is generally seen in alcoholics or in hungry individuals who lack liver glycogen stores. The direct cause of hypoglycemia in these individuals is alcohol inhibition of gluconeogenesis in the liver. Increasing the NADH:NADF + ratio reduces the concentration of pyruvate and hexafluacetate, leading to a reduction in phosphoenolpyruvate synthesis. The concentration of this substrate is a rate-limiting factor for gluconeogenesis (Tetzschner, Nørgaard, and Ranjan 2018).

The acetaldehyde is then oxidized to acetate. The acetate can be converted to CO_2, fatty acids, ketone bodies, cholesterol, and steroids. Oxidation of alcohol by cytochrome P450, especially CYP2E1, is a secondary pathway to remove alcohol from human body. Cytochrome P450 is induced by alcohol at high concentrations. Alcohol metabolism is increased in alcoholics without liver disease. Such metabolic tolerance to alcohol involves induction of CYP2E1 and faster regeneration of NAD (Cederbaum 2012).

Currently, alcoholic beverages are legal, easily available, and socially accepted in many countries.

Some authors suggest that certain nonalcoholic components that vary across these alcoholic beverages play an important role in serum UA level. One candidate for this nonalcoholic component is the variation in purine contents among the individual alcoholic beverages. Beer is the only alcoholic beverage acknowledged to have a large purine content, which is predominantly guanosine. Guanosine is more readily absorbed than other nucleosides, nucleotides, or bases. Thus, the effect of ingested purine in beer on the blood UA may be sufficient to augment the hyperuricemic effect of alcohol itself (Gibson et al. 1983; 1984). There may be other nonalcoholic offending factors, particularly in beer.

Wine is known to contain a number of nonalcoholic beneficial components. Phytonutrients such as resveratrol and tannins in wines give some benefits. Resveratrol (which is a flavonoid found in the skins and seed of grapes has properties similar to human estrogens and helps increase high-density lipiporoteins (HDL). Resveratrol stimulates clot dissolving ability of the body. Tannins inhibit platelet clotting (Frankel, Waterhouse, and Kinsella 1993; Booyse and Parks 2001; Rimm et al. 1996). Wines contain natural vasorelaxants (Fitzpatrick, Hirschfield, and Coffey 1993).

Because UA is considered an indicator for increased oxidative stress, nonalcoholic components in wine (polyphenols with antioxidant properties) (Frankel, Waterhouse, and Kinsella 1993; Booyse and Parks 2001; Maxwell, Cruickshank, and Thorpe 1994) may play a role in mitigating the impact of alcohol on serum UA levels. Nonetheless, moderate wine drinking may not increase serum UA levels. However, historically there were reports of gout attacks after wine consumption, although this may be related in part to lead contamination in the Roman era (Neogi et al. 2014).

Rasheed et al. described how alcohol influences the risk of gout via glucose and apolipoprotein metabolism. In the absence of alcohol exposure, genetic variants in the glucokinase (hexokinase 4) regulator (GCKR) and the gene encoding the complementation factor for the apolipoprotein B mRNA-editing enzyme (A1CF) have a stronger role in gout . They conducted the study on 2792 New Zealand European and Polynesian people with or without gout. The investigators revealed that the GCKR and A1CF genes influenced the risk of gout in the Europeans. At A1CF, alcohol exposure suppressed the risk of gout. At GCKR, alcohol exposure eliminated the genetic effect on gout. In the Polynesians, there was no evidence for interaction with alcohol in the risk of gout (Rasheed et al. 2017). In a study published in the XXth century in Taiwan, a high prevalence of gout among Taiwanese Aborigines was observed. The authors concluded that the race was the most significant risk factor associated with the risk of gout (Chang et al. 1997). Stamp in the study from 2013 also found racial background of gout. The participants were 751 citizens aged 20–64 years

Table 2. Alcohol content in different beverages (Duyff 2017).

Type of drink	Ethanol content
Low-alcohol or reduced alcohol beer	<2.5%
Alcohol-free malt beverage	0%
Flavoured malt beverage (beer, lager, ale, porter, stout)	0.5–5.5%
Aperitif wine	15–24%
Dessert wine	14–24%
Table wine	7–14%
Low alcohol wine	<7%
Wine cooler	<7%
Near beer	<0.5%
Distilled spirits (80-proof)	40%

recruited by random selection from the electoral roll in New Zealand. Māori had a significantly higher prevalence of HU (SU > 0.40 mmol/L) compared with non-Māori (17.0% vs. 7.5%, $p = 0.0003$). A total of 57 participants had a history of gout, with a higher prevalence in Māori (10.3%) compared with non-Māori (2.3%, $p < 0.0001$). Participants with gout were more likely to have metabolic syndrome, diabetes, cardiac disease, or hypertension (Stamp et al. 2013). Maynard examined racial differences in gout incidence among black and white participants from the United States. The cohort was 23.6% black. The incidence rate of gout was 8.4 per 10,000 person-years (15.5/10,000 person-years for black men, 12.0/10,000 person-years for black women, 9.4/10,000 person-years for white men, and 5.0/10,000 person-years for white women; $p < 0.001$). In this US population-based cohort, black women and black men were at increased risk of developing gout during middle and older ages compared with whites, which appears, particularly in men, to be partly related to higher urate levels in middle-aged blacks (Maynard et al. 2014).

Kirshan also confirmed that African Americans have a higher prevalence of risk factors for gout than Caucasians (Krishnan 2014).

Prevalence of gout varies: it is 1.4% in the UK and Germany. The most common comorbidities are obesity (Annemans et al. 2008). Wang found that high shrimp consumption increases the risk of gout too (Wang et al. 2013). Other authors confirmed high meat consumption, use of diuretics, kidney disease, hypertension, family history of gout as addition risk factors for gout (Cheng et al. 2012; Lin, Lin, and Chou 2000; Bhole et al. 2010; Ndong et al. 2018). For women, the risk of gout is higher after menopause (Puig et al. 1991).

Alcohol content in beveraages differs (Table 2) (Duyff 2017). Rheumatologic guidelines recommend avoidance of alcoholic beverages in patients with gout (Richette et al. 2017).

Migliori wrote about anti-inflammatory effect of white wine and olive oil. It was evaluated in 10 healthy volunteers and in 10 patients with chronic kidney disease in a prospective, single blind, randomized, cross-over trial. Subjects were randomized to a 2-week treatment with white wine (4 mL/kg body weight of 12% alcohol wine, corresponding to 2–3 glasses/daily) and extra-virgin olive oil or extra-virgin olive oil alone. During the combined consumption of wine and olive oil, plasma levels of C-reactive protein and proinflammatory interleukin6 decreased significantly in both: patients with and without chronic kidney disease. No significant change was observed in those who consumed olive oil only. The results suggest an anti-inflammatory effect of that nutritional intervention (Migliori et al. 2015).

There is also data that consumption of vitamin C at the dose of 500 mg per day, ≥4 cups of coffee per day, ≥1serving of milk per day, and ≥0.5 serving of yoghurt per day reduce UA serum concentration and the risk of gout attack (Towiwat and Li 2015).

Despite variety of medicines that can be used for HU and gout treatment, lifestyle change remains the main advice for all patients with this health problem (Richette et al. 2017; Cicero et al. 2021).

As alcohol consumption is often accompanied by food overconsumption it is worth to mention the foods high in purines that increase the risk of HU and gout: meat and seafood (Clebak, Morrison, and Croad 2020). The patients with gout or HU are recommended to consume less than 400 mg of dietary purines per day. The purine content of foods is the highest in fish milt (375.4–559.8 mg/100 g of the product), meat or fish (19.0–385.4 mg/100 g), peas and seeds (19.6–67.1 mg/100 g). Foods containing more than 300 mg of purines/100 g include anchovy, cutlassfish (hairtail), cod milt, globefish milt, dried Chinese soup stock, dried yeast, a *Euglena* supplement and a *Lactobacillus* supplement (Kaneko et al. 2020). In a recent study conducted in China among adolescents, HU prevalence was 25.4% and it was more common among those with high intake of carbonate beverage and mutton (Lu et al. 2020). Chiu et al. in their prospective study examined the relationship between a vegetarian diet and gout. The lacto-ovo vegetarians participating in their study had the lowest UA concentration, followed by vegans, then nonvegetarians. The vegan diet is considered an ideal approach to gout management: it simultaneously reduces UA and inflammation, while preventing gout-associated comorbidities (Chiu et al. 2020).

Conclusion

Episodic alcohol intake triggers gout attacks, regardless of type of alcohol. Thus individuals with established gout and pre-existing risk factors should limit all types of alcohol intake to prevent gout episodes.

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