Association of Serum Uric Acid with Chronic Diseases

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Uric acid occurs widely in nature in the form of its salts. It is found in plants as well as in animals. It is a white or yellowish white, odorless and tasteless substance, which may assume crystal or powder form.
The normal daily excretion of uric acid is 0.2-3.0 grams. However, this may vary with diet and pathological conditions such as gout. It is also present in the blood and, like many other substances; it is in dynamic equilibrium within the human body. Unfortunately, this equilibrium may change and result in elevated levels of uric acid in the blood, a condition known as hyperuricemia. Such condition has an important association with chronic illnesses in adults. These include gout, diabetes, arteriosclerosis, coronary heart diseases, renal diseases and several others.

This review article explains such associations and shows that hyperuricemia and obesity are associated with each other as well as with several other disorders in adulthood.

Introduction

History:

Uric acid (الحمض البولي) was discovered in 1776 by Von Scheele as a constituent of urine and bladder stone. He named it "Uric Acid" as well as "Bladder Stones Acid". Description of uric acid appeared occasionally in the literature during the eighteenth century. It was successfully synthesized by Horbizewski in the 1880's for the first time. He prepared it by fusing glycine with urea by heating 3,3,3-trichlorolactic acid with urea, but the complete description of the properties and synthesis of uric acid were achieved in the twentieth century (22).

Uric acid occurs widely in nature in the form of its salts. It is found in plants as well as in animals. Uric acid (2,6,8(1.3.9) purine trione), a white or yellowish white, odorless and tasteless substance which may assume crystal or powder form, it's a member of the purines and xanthines. In the human body, it is the end product of the metabolism of purines and their derivatives, notably the nucleic acids. It is used for the commercial

preparation of allantoin, alloxan, alloxantin, parabnic acid and other derivatives and occasionally in medicine (22).

The normal daily excretion of uric acid is 0.2-3.0 grams. However, this may vary with diet and pathological conditions such as gout (22). It is also present in the blood and, like many other substances; it is in dynamic equilibrium within the human body. Unfortunately, this equilibrium may change and result in elevated levels of uric acid in the blood, a condition known as hyperuricemia.

Uric Acid and Disease

Elevated level of serum uric acid (SUA) has an important association with chronic illnesses in adults. These include gout, diabetes, arteriosclerosis, coronary heart diseases, renal diseases and several others.

Gout (النقرس):

Gout is a condition characterized by perversion of purine metabolism, by an excess of uric acid in the blood, by attacks of acute arthritis and by the formation of chalky deposits in the cartilages of the joints consisting mostly of urates. It is also known as podagra, especially when affecting the big toe. Earlier in history, it was known as the disease of the rich and the overindulgent (2). Several studies associated gout with high levels of uric acid (2, 24, 25, 30, 36).

In Japan, the Somo wrestlers are known to be very obese as a result of their special daily diet, which contains twice the amount of calories of the average Japanese person. The mean serum urate among 95 wrestlers was found to be 6.1 mg per 100 ml, which was significantly higher than the controls. In addition, 45.3% of the wrestlers exhibited urate values over 7.0 mg per 100 ml compared to 6.8% among controls, and 6.3% of the wrestlers

but none of the controls had gout. Taking into consideration that the prevalence of gout in Japan was 0.10% the incidence of the disease among the wrestler group was quite high (31).

A study of 2,283 men and 2,844 women found that the prevalence of gouty arthritis increased as the level of SUA ascended. For example, among 1,281 men with serum SUA under 6 mg percent, 8(0.62%) developed gouty arthritis; among the 790 men with 6.0-6.9 mg percent level, 15(1.9%) developed the disease, and among the 50 men with 8.0 mg percent level or above, 19 men (48%) developed gouty arthritis. This yields a prevalence of 3.02% among men of age 30-59 years, but among women of the same age the prevalence was only 0.4% (15).

In the Framingham study, a group of adults, age 30 years and above, was followed for 12 years. The prevalence of gout was found to be 1.1% in the group who initially had uric acid levels under 6.0 mg percent and about 10% among those who had levels above 6.0 mg percent (30). Thus the occurrence of gout among asymptomatic hyperuricemics seemed to be rare. This agrees with the conclusion of other studies (11, 15). They also supported the idea that there are other factors associated with gout together with elevated levels of SUA. The study of the Somo wrestlers may be evidence that obesity is a possible cofactor in the presence of gout.

Diabetes (السكري):

Diabetes is a disorder of carbohydrate metabolism in which sugars in the body are not oxidized to produce energy due to lack of insulin. As a result, a high concentration of sugar appears in the blood (Hyperglycemia) and in the urine afterwards. Thirst, loss of weight and excessive production of urine are symptoms of diabetes mellitus. Diabetes has been found to be associated with hyperuricemia in several studies (11, 15, 25, 31).

A case-control study of subjects with elevated SUA found the relative risk of developing gout or diabetes among the cases to be 10.8 times greater than the controls (10). Moreover, diabetes was reported in 28% of gouty subjects, and family history of diabetes in as high as 42% of gouty subjects (15). Clinical diabetes was found on admission in four of the 240 subjects with a uric acid concentration of 7.0 mg per 100 ml or more at any time (total 1.7%, men 1.4% and women 3.7%) (15). Similar results were found in the Framingham population, where the prevalence of diabetes in the population at risk was 2.1% (Men 2.6% and women 2.0%) (15).

Hypertension (ضغط الدم العالي):

Hypertension has been associated with high levels of SUA in several studies (11, 28, 34, 36).

One study concluded that elevated level of SUA is an independent and significant contributory risk factor to the development of arterial hypertension (36). Another study proposed that antihypertensive therapy may cause hyperuricemia in hypertensive patients (8); but others have found elevation in SUA in 27-38% of untreated hypertensive patients (28). These same studies revealed that antihypertensive therapy significantly increases the likelihood of finding hyperuricemia in hypertensive patients (28).

Coronary Heart Disease (مرض القلب التاجي):

In several studies, heart disease has been associated with high levels of SUA (11, 25, 24).

One researcher noted an association between an elevated level of SUA and cardiovascular complications (14). The analysis of the Framingham data has also shown that the incidence of ischemic heart disease is increased in persons with elevated SUA, regardless of the existence of gouty arthritis

whose presence was found to be associated with a tow-fold increased risk of coronary artery disease (16). As a result of a multivariate analysis of the data from Evans County Study, which were obtained from a survey of 2,530 persons of at least 15 years of age, there was evidence indicating a significantly increased incidence of ischemic heart disease and hypertension with increasing SUA levels (19).

An elevated level of SUA is associated with a number of definite and suspected cardiovascular risk factors. This association may account for the increase of ischemic heart disease in those who have elevated levels of SUA (36).

Renal Diseases (امراض الكلى):

Renal stones and urinary calculus have been associated with high levels of uric acid in the blood (5, 15, 30, 35, 36, 11). In a study of 240 subjects who had SUA value of 7mg /100ml or more, 12 subjects were found to have clinical evidence of renal disease (15). In the same study, urinary calculi were detected in 32 subjects (13.3% of the group). Another study examined 207 consecutive patients seen in a kidney clinic, of whom 22 (10.6%) were diagnosed with uric acid stones (23). A third study reported that renal tubular damage may be a reflection of hyperuricemia in older patients, since tubular secretion accounts for virtually all uric acid cleared by the kidneys (13).

Arteriosclerosis (تصلب الشرايين):

Atherosclerosis, one form of arteriosclerosis, is an arterial disease characterized by thickening and loss of elasticity of the arterial walls resulting from plaques of fatty and calcium deposits on the walls of the blood vessels.

A study of 437 cases of peripheral vascular disorders, including arteriosclerosis, arterial thrombosis, diabetes and thrombophlebitis; 39% of the patients were hyperuricemic (20). Another study of 10,000 patients found that the mean SUA was 5.5 mg per 100 ml among those considered to have no clinically significant abnormalities; 6.4 mg per 100 ml among those with peripheral arteriosclerosis and thrombophlebitis; and 6.7 mg per 100 ml among patients with cerebral vascular insufficiency (11).

Miscellaneous Associations of Hyperuricemia:

The association of hyperuricemia with several other disorders that have not already been discussed is worth of mentioning for the sake of completeness.

A study of the New Haven Community associated the high levels of SUA with polycythemia, which is an excess of the red corpuscles in the blood (3). This result was confirmed by another study (11). Hyperuricemia is seen in various endocrine disorders such as hyperthyroidism and hyperparathyroidism, as well as in chronic lead poisoning, chronic beryllium poisoning and sarcoidosis (11).

Among patients with sickle cell anemia, hyperuricemia was found to be frequent in adults (6). In a study of 95 patients with sickle cell anemia, aged 17 months to 45 years, hyperuricemia was present in 4 of 28 (14.3%) children, and in 26 of 67 (39.0%) adults (7). The frequency of hyperuricemia increased to 45% in sickle cell anemia patients between 21 and 30 years of age (7).

In another study, elevated levels of SUA were associated with higher hemoglobin levels, higher serum calcium levels, total protein values, albumin levels, psoriasis and alcoholism (36).

SUA was found to be significantly lower among smokers than non-smokers (11).

Hyperuricemia was also described in mongolism, in patients with peripheral neuropathy and several disorders of the eye (11).

Uric Acid, Genetics and Environment:

The genetic and environmental factors influencing the levels of SUA have been investigated in several occasions. One study showed that the level of SUA in siblings of gouty patients was significantly higher than the siblings of the controls, but the genetic hypothesis of dominant inheritance could not be tested because the uric acid values of the siblings fitted a normal distribution (17). These observations were confirmed by the studies of Blackfoot and Pima Indians (33). The frequency distribution of uric acid was described to be normal (Gaussian) in the general population (11). In addition, it was observed that the intrapair variance of uric acid was significantly greater in dizygotic than in monozygotic twins (18). In a similar study of 51 monozygotic twin pairs (16 males and 35 females) and 61 dizygotic twin pairs (11 males, 20 females and 30 of unlike sex), the intrapair variance in uric acid levels among female dizygotic twin pairs was significantly higher than those among monozygotic female twin pairs (4). In contrast, this difference among males was not significant (4). This may imply that the genotype exerts a significant effect on normal SUA levels particularly in females.

In the two previous studies, it was concluded that environmental as well as genetic factors act as determinants of uric acid levels. This conclusion was based on the observation that the intrapair variance among monozygotic twin pairs who were living apart was significantly higher than that among monozygotic twin pairs who were living together (4, 18).

In a study of the familial aggregation of SUA levels of 6,000 subjects from the Tecumseh Community Health Study, the investigators found the frequency distribution curve to be normal with a mean score of 4.5 mg per 100 ml and standard deviation of 1.0 mg per 100 ml (12). Some degree of skewness toward high values was observed without any suggestion of bimodality (12). The analysis showed evidence for interaction between genetic and environmental factors in determining the SUA phenotype. In other words, the study suggested that multi-factorial inheritance with additive gene action interact with environmental factors to produce SUA phenotype (12).

Serum Uric Acid and Body Fatness:

Obesity is an excessive accumulation of body fats, which consist of inner fat deposits and subcutaneous or outer deposits. During adolescence, subcutaneous fat is redistributed away from the extremities and towards the trunk (27). There are different types of obesity, depending on the body distribution of fat also referred to as "fat patterning" (27). A scale to distinguish the different types of obesity was established, which includes hypergynoid, gynoid, intermediate, android and hyperandroid (37). The first two are characterized by the localization of fat on the lower part of the body. These two types are more common in women than in men. The android and hyperandroid obesities, opposite of the preceding types, are characterized by the localization of fat on the upper part of the body. These two types are more frequent among males, but they are also seen in females particularly around menopause (37). Elevated SUA levels and diabetes are associated with obesity only of the android types and not the gynoid types of obesity (37). Thus, studying fat patterning and body fatness in relation to SUA is an important issue, especially during adolescence, since body fat

patterning in adulthood appears to manifest itself beginning in adolescence (27). The redistribution process takes place in both sexes, but more rapidly in males than in females. For this reason it is called a masculinizing process (37).

Females, from infancy through childhood and adolescence tend to have slightly more subcutaneous fat than males. Until age thirteen, subcutaneous fat increases in both sexes, but afterwards, with the adolescence growth spurt, it starts decreasing on the extremities in males and continues to increase in females. In both sexes, there is an increase of fat on the trunk during this period. Males are always leaner on the average than females, but the sex difference becomes more marked by late adolescence (26).

Elevated levels of SUA have been positively associated with obesity (9, 15, 24, 25, 28, 29).

The Somo wrestlers study showed clear evidence of the relationship between obesity and elevated levels of SUA (31). Moreover, a study of a population sample of 1,462 women aged 38-60 years, that separated the women with overweight and compared them to the rest of the population sample, found SUA to be significantly higher in the overweight group ($p<0.001$) (32).

In the Tecumseh Community Health study of 5,967 subjects, relative weight was computed by a regression formula taking into account actual weight, height, biacromial and bicristal diameters of the body. The prevalence rate of hyperuricemia was 3.4% among subjects whose relative weight was at or below the 20^{th} percentile; 5.7% among those from the 21^{st} to the 79^{th} percentile; and 11.4% among those with relative weight at or above 80^{th} percentile (28). Another study of 460 persons of various body weights found a linear relationship between SUA values and weight, starting from

80 kg, with a highly significant correlation coefficient between SUA and weight for both males and females (21).

The previous review leads to a conclusion that obesity and elevated levels of SUA are associated with each other as well as with several other disorders in adulthood. Although most of these disorders are very rare in adolescence, it is conceivable that elevated SUA levels could be precursors to later development of the chronic diseases mentioned above.

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עבמקהבך, ושק ום וטוש בסקסזכם גשדבזוו

וורקש

חומצת השתן נפוצה בטבע בצורת המלחים שלה. היא נמצאת בצמחים ובחיות. היא חומר לבן או צהבהב- לבן, נטול-ריח וחסר-טעם אשר נראה בצורת קריסטל או אבקה.

הצואה היומיומית הטבעית של החומצה בגוף היא 0.2-3.0 גרם. זה יכול להשתנות עם תזונה ומצב פתולוגי כמו צינית. החומצה נמצאת גם כן בדם בשיווי משקל דינמי בגוף האדם. למרבה הצער, שיווי משקל זה משתנה כתוצאה לעליית רמת חומצת השתן בדם, וזה גורר למצב עודף חומצת השתן בדם. למצב זה קשרים משמעותיים עם מחלות כרוניות בגיל הבגרות. מחלות אלה כוללות צינית, סוכרת, טרשת, מחלות לב, מחלות כליה ואחרות.

מאמר זה מסביר את הקשרים האלה ומראה שעודף חומצת השתן בדם ועודף משקל הם קשורים האחד לשני ולמספר גדול של מחלות בגיל הבגרות.

علاقة الحمض البولي في الدم بالأمراض المزمنة

سليم زيداني، محاضر للتربية الصحية والبحث

ملخص

يوجد الحمض البولي في الطبيعة على شكل ملح. من الممكن أن نجده في النبات أو الحيوان. وهو مادة بيضاء تميل الى الصفار، لا طعم لها ولا رائحة وتأخذ شكل بلورات أو مسحوق.

الافراز اليومي الطبيعي للحمض البولي هو 0.2–3.0 غراما. من الممكن أن يختلف هذا حسب الغذاء والوضع الباثولوجي للانسان مثل مرض النقرس. والحمض موجود ايضا في الدم، ومثله مثل الكثير من المواد الاخرى، فهو في توازن ديناميكي في الجسم. ولسوء الحظ، من الممكن لهذا التوازن ان يختل نتيجة ارتفاع مستوى الحمض البولي في الدم. ولهذه الظاهرة علاقة متينة مع العديد من الأمراض المزمنة عند البالغين مثل: النقرس، السكري، تصلب الشرايين، مرض القلب التاجي، أمراض الكلى والعديد غيرها.

هذه الدراسة تفسر تلك العلاقة وتظهر أن ارتفاع مستوى الحمض البولي في الدم والسمنة لهما علاقة قوية ببعضهما البعض وبالعديد من الامراض الاخرى في جيل البلوغ.