

## AN ETIOLOGICAL CORRELATION OF *NIQRIS* WITH GOUTY ARTHRITIS

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### ABSTRACT

Gout, “the king of diseases and the disease of kings”,<sup>[1]</sup> was one of the earliest disorders to be recognised as a clinical entity. It was first identified by the Egyptian in 2640 BC, and written evidence of disease found to Hippocratic writings dates back to 400BC.<sup>[2,3]</sup> The most accurate early description of an acute attack of gout was made by Sydenham, an English physician, written about himself in 1683.<sup>[1,2]</sup> Crystal from tophi were first described during the 18<sup>th</sup> and 19<sup>th</sup> centuries, and in the mid-20<sup>th</sup> century the role of excess urate production and impaired excretion in the pathogenesis of Hyperuricaemia were reported. Finally, McCarty and Hollander showed that crystals from the synovial fluid of patients with gout were composed of monosodium urate.<sup>[2]</sup> Present study has been designed to study the aetiological correlation of Gout with *Niqris*.

### INTRODUCTION

Disease *Niqris* (gout) is well known in Unani system of Medicine also according to Ibn-e-Habal ‘*Niqris*’ originated from the word ‘*Anquroon*’ which means big toe of foot, because this disease usually starts with the involvement of this particular joint and hence the disease has been named after this joint.<sup>[3,4,5]</sup> Gout comes from the Latin ‘*Gutta*’ which means ‘Drop’ (Noxa) with reference to the mediaeval “flowing down of humoured”. Which justify the ancient belief about disease matter i.e. humours falling down drop by drop into the joint.<sup>[6,7,8]</sup> Ismail Jarjani have described that as *Mavad-e-fazooni* (morbid humours) which gets accumulate in the small joints and tendon, if it cause pain and inflammation in small joints called as *Niqris*. It occurs mainly in greater toe. Ankle joint and the joint of toes may also be involved.<sup>[9]</sup>

Pathophysiological factor of Gout is *Akhlat-e-Fuzlia* According to Ibn Sina the *Madda* of *Niqris* can be pure *Dam* (blood) or can be combination of *Damvi-Balghami* or *Damvi Safravi* or *Damvi-Saudavi* or pure *Balghami* or it can be *Balgham-e-Murra*. But majority of ancient physician accepted that *Balghami-Murra* is the main cause of *Madda-e-Niqris*, and then is can be pure *Balghami*, *Dam*, *Safra* respectively. Rarely the cause of *Madda-e-Niqris* can be *Sauda*. Nowadays, gout is

probably the best understood and most manageable of all common systemic rheumatic diseases.<sup>[10]</sup> frequently. It causes recurrent attacks of acute arthritis and sometimes can lead to chronic arthropathy, tophi depositions, and renal disease. Gout is a disorder of purine metabolism and result from urate crystal deposition in and around the joints caused by long standing hyperuricaemia.<sup>[10]</sup>

Acute arthritis is the most frequent early clinical manifestation of gout. Usually only one joint is affected initially but polyarticular acute gout can occur in subsequent episodes. The metatarsophalangeal joint of the first toe is often involved, but tarsal joints, ankles and knees as also commonly affected. Especially in elderly patients or in advanced disease, finger joints may be involved. The first episode of acute gouty arthritis frequently begins at night with dramatic joint pain and swelling. Joints rapidly become warm, red, and tender, with a clinical appearance that often mimics cellulites. After many acute mono- or polyarticular attacks, a proportion of gouty patients may present with a chronic nonsymmetric synovitis.<sup>[2,10,12,13]</sup>

So, gout is a major public help with this reason i have started correlation between *Niqris* and Gout with the help of classical Unani and modern literatures, research articles, and other online sources on the basis of causes clinical features pathogenesis.

## MATERIAL AND METHODS

Review material collected from the different ancient Unani and modern books, Dissertation, online authentic research Journals & different websites and summarized with the help of computer.

## LITERATURE REVIEW

The name “Gout” was coined by a monk named *Randolphus* of Bucking in the 13<sup>th</sup> century from the Latin word “Guuta” (which translates into “Drop”).<sup>[14]</sup> Randolphus thought that gout resulted from the excess of one of the four humours that maintained health. This drop was thought to flow into the joint, causing pain.

**Between 17<sup>th</sup> and 18<sup>th</sup> century AD: Gout microscopy, symptomatology and uric acid:** Around 1679, Antoni van Leeuwenhoek described the microscopic of tophi as follows: “I, observed the solid matter which to our eyes resembles chalk, and saw to my great astonishment that I was mistaken in my opinion, for it consisted of nothing but long, transparent little particles, many pointed at both ends about<sup>10</sup>, axes of the globules in length. I can’t better describe that by supporting that I saw with naked eye pieces from a horse-tail cut to length of one sixth of an inch”. This observation is consistent with modern microscopy of uric acid crystals, today, and presence of uric acid crystal in joint aspirates in a criterion for the diagnosis of gout.

In 1683, Thomas Sydenham gave a detailed description of the symptomatology of the acute disease, based on his personal experience both as a physician and a gout sufferer. He wrote: “the patient goes to bed and sleeps quietly until about two in the morning when he is awakened by a pain which usually seizes the great toe, but sometimes the heel, the calf of the leg or the ankle. The pain resembles that of a dislocated bone and this is immediately succeeded by chillness, shivering and a slight fever the pain which is mild in the beginning grows gradually more violent every hour so exquisitely painful as not to endure he weight of the clothes not the shaking of the room from a person walking briskly therein.

In 1734, William Stukeley described the crystal from a tophaceous joint and 42 years later, uric acid was identified by Scheele (a Swedish chemist). In 1763, colchicine was rediscovered by Prof. Baron von Störck in Vienna. Wollaston confirmed in 1797 that tophi consisted of uric acid deposit, 30 using tophi from his own ear. It was almost a century later that McCarty and Hollander used polarised microscopy to confirm that joint fluid of gout sufferers contains monosodium urate.

**Gout in the 19<sup>th</sup> and 20<sup>th</sup> centuries:** It was not until 1859 that Sir Albert Baring Garrod hypothesised that “Urate deposit is the cause and not an effect of Gout”. He advocated a diet low in purine rich food for the treatment

of gout. Between 1894 and 1897, Haig was reported to have conducted several experiments on himself (being a gout sufferer), to show that hyperuricaemia could be lowered by lowering the intake of purine-rich diets, and similarly Freud Wailer proved that injecting urate into joints and subcutaneous tissues precipitated gout and tophi respectively.<sup>[14]</sup>

In 1931, Sir Archibald Garrod suggested that gout should be included in the class of in-born error of metabolism. By 1940s aspirin was used for the treatment of gout. The year 1951 was the introduction of probenecid and by 1963, allopurinol was used for the treatment of gout.<sup>[15]</sup> George Hitchings and Gertrude Elion were awarded the Noble Prize for developing allopurinol, azathioprine and other drugs in 1988.

**Gout in the 21<sup>st</sup> century:** An old disease with a new challenge. In the 21<sup>st</sup> century gout remains the most common inflammatory arthritis in men over 40 years old and the incident is on the increase across all races.<sup>[16,17]</sup> This is attributable to factors such as dietary changes, increasing longevity, sub-clinical renal impairment and increase in the use of diuretics and other drugs causing hyperuricaemia. A recent study identified gout as an indicator of increased risks for metabolic syndrome, non-insulin dependent diabetes mellitus (NIDDM) and adverse cardiovascular outcomes,<sup>[18]</sup> and this constitutes a serious concern within the context of a global epidemic of NIDDM and coronary heart diseases. An increase in all cases of mortality from coronary heart disease has also been found among men with gout compared to controls.<sup>[19]</sup> In the same light, increase in servings of fructose-rich drinks in contrast to diet soft drinks has been associated with increased risk for gout.<sup>[20]</sup>

### Unani Concept of *Niqris*

Various physicians have defined Gout in various ways as follows:

**Ali-Ibn-Abbas-Al Majoosi** (930-994) have defined the pain which occurs in the joints of both legs or single leg and sometimes in wrist joint or elbow joint and mainly in the joints of great toe is to be known as *Niqris*.<sup>[21]</sup>

**Ismail Jarjani** (11<sup>th</sup> century AD) has defined the gout as *Mavad-e-Fazooni* (Morbid humours) which gets accumulated in the small joints, if it causes pain and inflammation called *Niqris*. It occurs mainly in greater toe. Ankle joint and the joint of toes may also be involved.<sup>[22]</sup>

**Shaikh-ur-Raees** (980-1030) stated that gout or *Niqris* started from the heel and later spreads to other joints and may affect even the viscera of the body.<sup>[23]</sup>

**Dawwod Zareer Antaqui** (1541) defines *Niqris* as a type of joint pain in which the disease matter enters into the intra articular space causing pain. The articular

structure is replaced by the matter of gout. Mostly it occurs in the big toes which get inflamed.<sup>[10]</sup>

### Classification in contemporary literature

#### ▪ Dorland's classification:

1. Latent gout
2. Oxalic gout
3. Polyarticular gout
4. Rheumatic gout
5. Saturning gout

#### ▪ Primary and Secondary gout

Gout can be classified as primary or secondary, depending on the presence or absence of identified cause of hyperuricaemia.<sup>[24,25]</sup> Thus, primary gout is not a consequence of an acquired disorder or the result of a congenital defect. Other conditions often accompany primary gout, including obesity, alcohol consumption, hypertension and hypertriglyceridemia, which should be carefully assessed.<sup>[24,25,26]</sup> Secondary gout is the consequence of use of specific drugs or develops in the course of other disorders such lead intoxication, renal failure,<sup>[24,25]</sup> and particularly in the rare familial juvenile hyperuricaemic nephropathy and the autosomal dominant medullary cystic kidney.

Gout is associated with use of several drugs, including diuretics, low-dose aspirin, and drugs often used in open organ transplantation.<sup>[27]</sup> Diuretics are one of the most important causes of secondary hyperuricaemia, which arises through a combination of volume depletion and decreased renal tubular secretion of uric acid.<sup>[28]</sup> However development of gout might depend on condition for which diuretics are prescribed rather than as a result of drugs.<sup>[29,30]</sup> Aspirin has a bimodal effect on renal processing of uric acid. At high doses (>3 g per day) aspirin is uricosuric, but at low doses (<1 g per day), it causes uric acid retention.<sup>[31]</sup> Hyperuricaemia and gout are common complaints of organ transplantation. Hyperuricaemia develops in about half and gout in 10% of recipient of solid organ transplants.<sup>[32,33]</sup> Immunosuppressive agents, such as ciclosporin and tacrolimus, prescribed for the transplant recipients have a key role in induction of hyperuricaemia and gout.<sup>[27,34,35]</sup>

There are two purine enzyme abnormalities result in uric acid overproduction, which leads to precocious uric acid nephrolithiasis and gouty arthritis mentioned in literature; one is hypoxanthine-guanine phosphoribosyltransferase (HGPRT) deficiency, characterised by hyperuricaemia with hyperuricosuria and continuum of neurological manifestations. HGPRT deficiency is inherited as a recessive x-linked trait, and generally only male children and adults are affected. Lesch-Nyhan syndrome corresponds to almost complete HGPRT deficiency. Hyperuricaemia-related renal and articular symptoms are present early in life in all patients deficient in HGPRT and are not related to severity of the enzyme defect. By contrast, neurological symptoms

including dystonia, mild-to-moderate mental retardation, and self-mutilation depend on the degree of enzyme deficiency. Serum concentration and urinary excretion of rate are greatly raised in these patients.<sup>[26]</sup> Another cause of hyperuricaemia with purine overproduction is phosphoribosylpyrophosphate synthetase (PRPS) super activity. Super activity of PRPS is an X-chromosome-linked inborn error, with increased enzyme activity associated with hyperuricaemia, gout, and uric acid nephrolithiasis. In this disorder gout develops mainly in male children and adolescents, and affected individuals might show abnormal neurodevelopment.<sup>[36,37]</sup>

### Classification of *Niqris* (Gout) in Unani literature:

Unani Physicians are classified the *Niqris* according to conditions of disease, involvement of organs and severity of symptoms.

**Qustha Ibn Luqa** has described two types of *Niqris* according to accumulated *fuzulath* (*Khilt*):<sup>[11]</sup>

- One of them related to *Safra* that is '*murrah-safra*'
- Other one is related to *Balgham* that is '*Balgham Ghaleez*'

**Dr. Gulam Jeelani** classified *Niqris* as follow.<sup>[2]</sup>

#### 1. According to severity of symptoms.

- *Niqris* Har or Acute
- *Niqris* Barid or Chronic

#### 2. According to involvement of organ

- *Niqris ishvi* - Visceral gout
- *Niqris ikba* - Gonagra
- *Niqris ghair munthazim* - Irregular Gout
- *Niqris ul qadam* - Podagra
- *Niqris ul qatif* - Omega
- *Niqris ul warq* - Ischiagra
- *Niqris ul yad* - Chiagra

### Pathogenesis

Biologically significant hyperuricemia occurs when serum urate level exceed solubility (~6.8 mg/dL). Hyperuricemia is a common serum abnormality that does not always progress to gout. Humans generate about 250 to 750 mg of uric acid per day. The uric acid comes from dietary purines and the breakdown of dying tissues. The exact cause of gout is not yet known, although it may be linked to generic defect in purine metabolism. Uric acid, the most insoluble of the purine substances, is a trioxypurine containing three oxygen groups. The pathogenesis of gout starts with the crystallization of urate within the joint, bursa, or tendon sheath, which leads to inflammation as a result of phagocytosis of monosodium urate crystals; the disease is usually associated with an elevated concentration of uric acid in the blood.<sup>[38,39]</sup> Specially, uric acid is breakdown product of the purines like adenine, guanine, hypoxanthine and xanthine. Adenine and guanine are found in both DNA and RNA. Hypoxanthine and xanthine are not incorporated into the nucleic acids but they are important

intermediates in the synthesis and degradation of the purine nucleotides. Both undissociated uric acid and monosodium salt, the primary form of (MSU), are only sparingly soluble.

The amount of urate in the body depends in the balance between dietary intake, synthesis and excretion<sup>97</sup>. In people with primary gout, defects in purine metabolism lead to hyperuricemia that is high levels of uric acid in the blood. This can be caused by increased production of uric acid or abnormal retention of uric acid, or both. Urate in the blood can accumulate either through an overproduction or an under excretion of uric acid. Hyperuricemia results from the overproduction of urate found in 10% of gout patients and from under excretion of urate found in the remaining 90%.<sup>[40]</sup>

The majority of patients with endogenous overproduction of urate have the condition as result of salvaged purines arising from increased cell turnover in proliferation and inflammatory disorder, from pharmacologic intervention resulting in increased urate production and also from tissue hypoxia.<sup>[40]</sup>

The renal mechanism for handling urate is one of glomerular filtration followed by partial tubular reabsorption.<sup>[41]</sup> The final fractional excretion of uric acid in about 20% of what was originally filtered. Uric acid levels independently predict renal failure in patient with pre-existing renal disease. Hyperuricemia causes interstitial and glomerular changes that are independent of the presence of crystal, and the changes very much resemble what hypertensive changes would look like chronically. In addition, serum hyperuricemia is epidemiologically linked to hypertension and seems to be an independent factor for the development of hypertension.

#### **The pathophysiology of Nigris in Unani literature:**

The food substances which have been absorbed by *Quwat-e-jazeba* and retained by *Quwat-e-maseka* but have not been acted upon by *Quwat-e-Mughaiyyera* so that it can be absorbed by the digestive system and can become part of the body; instead it turned into toxic substances or can be called as *Fazil Akhlat*.<sup>[42]</sup> These toxic substances or *Fazil Akhlat* get deposited anywhere in the body and become the pathophysiological factor of gout. This *Akhlat Fazila* can be purely of *Damvi*, *Safravi*, *Balghami* or *Saudavi* type can be combination of any two *Akhlat* as sheikh stated in his book *Al qanoon Fit-Tib*: According to *Ibn Sina* the *Madda* of *Nigris* can be pure *Dam* or can be combination of *Damvi-Balghami* or *Damvi-Safravi* or *Damwi-Saudawi* or pure *Balghami* or it can be *Balgham-e-Murra*. But majority of ancient physician accepted that *Balgham-e-Murra* is the main cause of *Madda-e-Nigris*, and then it can be pure *Balgham*, *Blood* and *Safra* respectively. Rarely the cause of *Madda-e-Nigris* can be pure *Sauda*.<sup>[43]</sup>

Allama Qarshi explained that pure *Balgham* due to its consistency cannot penetrate and retained in joints unless *Balghami-e-Murra* mixed with it and bring about changes in the consistency of pure *Balgham* and make it easily penetrable into the joints so as to become the cause of gout. About *Balgham-e-kham* he wrote, *Balgham-e-kham* is the common use of joint pain. Blood enters into the joint either through a vessel or by any other means, but vessels are less in number near the joints hence *Madda-e-Nigris* will not spread, hence *Khilt-e-Dum* is less likely cause of gout. *Khilt-e-Safra* due to its hot temperature and high penetrative power gets infiltrate into nearby organs and hence cannot reach up to the joints and is therefore cannot be the cause of gout. *Khilt-e-sauda* due to its consistency cannot penetrate into joints, and hence cannot causes gout.<sup>[44]</sup> *Ismail Jarjani* and *Azam Khan* are agree with the philosophy of *Ibn Sina*.<sup>[22,45]</sup>

*Zakariya Razi* presented his view about gout in new fashion. He stated that *Balgham-e-kham*, which is little bit concentrated and is similar to pus is the cause of Gout. Hence, he wrote: Often the matter of disease (*Madda-e-Merz*) is *Dum*, but most of the time it is *Balgham-e-Safravi*. It is true that *Balgham* is a type of humour when mixed with raw matter becomes more concentrated and resemble pus and when remain located at one place for some time it become more concentrated and get solidified.<sup>[1]</sup>

As per the discussion of ancient medical scholars it is clear that the matter of disease is most of the time *Balgham* either in the form of *Balgham-e-khamor* *Balgham-e-Murra*. When *Quwat-e-Dafea* (Faculty of excretion) expelled this *Madda* or excess humour through urine some quantity it get excreted but some quantity get deposited in kidney or anywhere else in the body and produces pathological conditions, and during this course the quantity of this humour also increases in the blood as well as in urine.

#### **Pathogenesis of Nigris in Unani literature:**

Hippocrates regarded gout as being the result of an excessive accumulation of one of the bodily humours, probably phlegm that distended the affected joint painfully. The three famous surviving aphorisms of Hippocrates that refer to gout have often been quoted: "Eunuchs do not take the gout nor become bald". A woman does not take the gout unless her menses is stopped", and "A young man does not take the gout until he indulges in coitus". Hippocrates also believed that gouty affections rankled in the spring and in the autumn. An eminent Greek physician *Diocles of Carystus* (4<sup>th</sup> century CB) believed that gout was an inflammation caused by the concentration of humours on the nerves of the foot joints. He said that choleric humours created cold podagra, and phlegmatic ones warm pdagra.<sup>[46]</sup>

The eminent Greek physician Galen (130- CA. 215) based on Hippocrates quotes described tophi as the manifestation of longstanding gout and stated that a female body was unlikely to be affected by gout, arthritis, and pleurisy.<sup>[47]</sup>

Rufus of Ephesus (1<sup>st</sup> century CE) was the first to recognise the systemic complication as he wrote on the concept of visceral gout. He believed that the internal organs could become affected mortally by the gouty humour. He said that such sudden revulsion of the humours from the joints would provoke pulmonary or cerebral complications and renal failure resulting in death.<sup>[48]</sup>

Aretaeus of Cappadocia (2<sup>nd</sup> century CE) described the disease based on Hippocrates view, but he suggested first that the cause of gout could lie in the presence of specific toxic humour in blood rather than the imbalance of the four humours that maintained the human body in the health.

Ancient physicians also observed that gout affected not only humans but animals as well.

Oribaasius (C 320-400 CE), who was the personal physician of Emperor Julian the Apostate, mentions that gout affects the feet, while arthritis affected the hands, knees, elbow joints, buttocks, and shoulders.<sup>[49]</sup>

## DISCUSSION AND CONCLUSION

Though the exact terminology and complete clinical picture of gout had mentioned in the ancient books of Unani, also above references from these famous books are very close to modern description of the disease. Further the cause mentioned in these books, as admixing of blood with abnormal phlegm (*balghame shor merari*) pungent acidic fluid mixed with *fasaad-e-khoon* or altered blood and heredity, all of these correlates with causes mentioned in modern books, as a genetic or heredity cause, change in the biochemistry and the life style cause of blood with *Balgham-e-shor merari*, such as abnormal blood is sent towards the joints via peripheral circulation<sup>23</sup>.

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