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An Explicit Appraisal on Gouty arthritis

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ABSTRACT

Gout is the most customary variety of incendiary arthritic condition which occurs when uric acid crystals accumulate in the joints, and is often kindred with hyper-uricaemia, also called crystal-induced arthritis. Gout has reported an upsurge in recent decades influencing approximately two percent of the citizenry at some place in their lives. The present review deals with Gout which includes its general description, history, etymology, definition, purine metabolism, its aetiology and associated factors, clinical features, complications, diagnosis and investigations, differential diagnosis, prognosis and management. The disorder has been considered for the study keeping in mind the dire need of the hour to understand the disease so as to find some safe, sure and permanent cure effective for the same.

Key Words: *Gout, Purine Metabolism, Podagra*

INTRODUCTION

Gout is a known disorder of Purine metabolism which was familiar amidst Egyptians as PODAGRA (foot pain) since 2640 B.C[1]. Gout has been described as "King of the diseases"[2]. Hippocrates, the father of modern medicines is approbated for the initial clear and clinical elucidation of Gout in the 5th century as the "unwalkable ailment" with its five aphorism cited in Table no 1[3].

Table 1 Five Axioms of Hippocrates on Gout

Aphorism	Details
VI-28	Baldness or having gout is rare in Eunuchs
VI-29	A woman takes gout after menopause
VI-30	A juvenile does not acquire gout before lovemaking
VI-40	In gout infection, inflammation abates within 40 days
XI-55	Gouty affections swing into action in spring and autumn

Gout between 1st and 6th century A.D.- A Roman representative entitled Seneca perceived the part of genetics in gout by the end of first century A.D. He observed that women were fetching gout much increasingly, purportedly based on women's feuding with men in living lavish lifestyles[4]. Simultaneously, Galen narrated 'tophi' as the exposition of abiding gout. Alexander of Tralles in

6th century uncovered Hermodactyl (a provenance of Colchicine's) while discerning for a laxative and was the first to employ it to manage gout[5].

Gout in 19th and 20th century A.D.- Alfred Baring Garrod elucidated his famous 'thread investigation' in 1848, a first semi-quantitative chemical test for the estimation of Uric acid in urine or serum was clinically undertaken[6]. Garrod narrated that, "the plonked Urate of soda may be counted as the cause, and not the upshot, of the gouty inflammation". Later, in 1899, Freudweiler demonstrated that acute gout could be expedited by the intra-articular inoculation of Sodium Urate microcrystals and revealed the genesis of tophi after subcutaneous inoculation of Urate crystals. These investigations were missed for a long time till paper publication by McCarty and Hollander[7], which exhibited Monosodium Urate crystals from the synovial fluid of subjects anguishing from gout. Their report enumerated the manoeuvre of indemnified polarized light microscopy to scrutinize joint fluid for crystals, and this strategy was eventually used to pin-point Calcium pyrophosphate dehydrate crystals in synovial fluid from the joints of patients with chondrocalcinosis and 'pseudogout'[8].

Gout in 21stcentury- In 21st century, gout was the most prevailing inflammatory arthritis in men over 40 years of age amongst all races[9]. This is accountable to aspects such as dietary modifications, escalating longevity, sub-clinical renal impairment and increased use of diuretics and other drugs causing hyper-uricaemia. A recent investigation pin-pointed gout as a benchmark of growing risks for metabolic syndrome, non-insulin-dependent diabetes mellitus (NIDDM) and adverse cardiovascular outcomes[10], and this composed a momentous concern within the milieu of pandemic of NIDDM and coronary heart diseases. Increase in mortality from coronary heart disease has been reported amidst men with gout compared to controls. In the gleam, increasing intake of fructose-rich drinks as compared to diet soft drinks has been kindred with increasing the menace for gout[11]. The clement lifestyles that incline to gout are also menace for maximum cardiovascular diseases. However, a presumptive study on consumption of coffee proposed that it seems to defend against the evolution of gout. This safeguarding up-shoots with the number of coffee cups consumed per day, with maximum protection at six cups, regardless of caffeine content [RR = 0.41; 95% CI (0.19–0.88)][12].

History of therapy- History of therapy is also significant. For selective management of gout Colchicine was used as powerful purgative which was derived from autumn crocus (*Colchicum autumnale*), > 2000 years ago by Greece. Colchicine's was applicable for the management of acute gout, but it could cause severe gastrointestinal side effects. Due to the huge impact of Thomas Sydenham ('the British Hippocrates'), who refused all purgative medications as being too harmful for use, Colchicine was not used for managing gout for about 150 years until its rediscovery in 1763 by Professor Baron Von Stoerk in Vienna[13]. For treatment of acute gout, the drugs of solution in

modern era is Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) whereasCcyclo-oxygenase-2 inhibitors and intra-articular or systemic Corticosteroids are less incessantly used to manage acute ambush in patients with relative contraindications to NSAIDS[14]. Uricosuric agents, which augment the renal clearance of Urate, were initially used at the end of 19th century[15]. The first Xanthine Oxidase inhibitor Allopurinol was developed for the management of hyper-uricaemia by Hitchings and Elion. In 1988 they were awarded with Nobel Prize in medicine for developing Allopurinol, Azathioprine and five other drugs. Since then, Allopurinol become the uttermost incessantly used Uric acid lowering drug clinically. Xanthine Oxidase inhibitors, acts by impeding the conglomeration of Uric acid from Hypoxanthine and Xanthine & effectual in diminishing plasma and urinary Urate levels and it reverses the development of tophaceous deposits[16]. Infusion of recombinant fungal Uricase has been found beneficial in patients with malignancies, for prevention of acute Uric acid nephropathy due to tumour lysis[17]. It converts Urates to soluble and comfortably excreted compound i.e. Allantoin. But due to its short half-life and inherent immunogenicity limits, its protracted use is not recommended for management of chronic gout. Phase III trials of a PEGylated, recombinant Porcine Uricase for chronic treatment of gout are directly undertaken.

ETYMOLOGY: Gout word is derived from a Latin word “gutta” means a drop[18]. The disease was pondered to be produced by bubbles of viscous humors exuding from the blood into the joints, which is nearer to the modern scientific view.

DEFINITION: Gout constitutes a class of heterogeneous metabolic dysfunctions denoted by supplanting of Monosodium Urate crystals in the tissue from hyperuricemic body fluids, which includes-

1. An elevated serum Urate levels i.e. hyper-uricaemia.
2. Recurrent attacks of acute arthritis, in which Monosodium Urate monohydrate crystals are demonstrable in synovial fluid leucocytes.
3. Deposition of tophi (aggregates of MSUM crystals) particularly all over the joints, sometimes leads to deformity. Deposition of tophi is commonly seen in soft tissues especially in the twirl of ear, great toe, feet, joints of hand and olecranon[19].

EPIDEMIOLOGY: The pervasiveness of gout fluctuates between populations but is approximately 1–2%, with a considerable 5:1 male dominance. It is the most customary inflammatory arthritis in men and older women. The risk of gout is directly proportional to age and serum Uric acid (SUA) levels whose magnitude is higher in men and is associated with body weight. Proportion is higher in some ethnic groups (such as Maoris and Pacific islanders). Hyper-Uricaemia can be elucidated as serum Uric acid proportion more than 2 standard deviations over the mean for the population. Gout has become more customary recently analogous with increased longevity and the higher preponderance of metabolic syndrome,

of which hyper-Uricaemia is an indispensable component. Although hyper-uricaemia is an unconventional risk factor for renal disease, hypertension, vascular disease and cardiovascular events, only a splinter group of hyper-Uricaemic people develop gout. There is presently no corroboration to reinforce the use of Urate-lowering therapy in asymptomatic hyper-Uricaemic patients[20].

RISK FACTORS FOR THE GOUT:

Age and sex— Gout becomes customary with increasing age. In men the delineated prevalence fluctuates from < 0.5% in those aged under 35 to over 7% over 75 yrs of age. It is scarce in premenopausal women but increases to 2.5 – 3.0% in those crossed over 75. The later age of outbreak in women may be related to the Uricosuric upshots of oestrogens.

Obesity — Relative risk of gout increases with rising body mass index (BMI). Compared to people with a BMI of 21 – 25, those with BMI of > 35 are four times as likely to prosper gout.

Diet — Each additional daily segment of meat per day raises the menace of gout by 20%. Purine - rich vegetables do not causes gout, while eating more dairy products diminishes the risk of conquering the disease. Fructose present in soft drinks may increase the menace of conquering gout.

Drugs — Number of drugs can increase serum Urate; this is most commonly due to diuretics. Aspirin and salicylates at low doses diminish Urate excretion, but at high doses (4 – 6 g/day) they cause Uricosuric effect.

Alcohol— People taking >50 g alcohol per day are 2.5 times as likely to prosper gout. While there is a sturdy bond between beer intake and gout, there is only a weak bond between spirit intake and gout. Alcohol is catabolized to ketones which compete with Urate for excretion by the renal tubule. Beer usually contains considerable amounts of purines, from yeast, which are catabolized to Urate by gut bacteria. Alcohol increases the dose of Allopurinol required by decreasing the transformation of Allopurinol to its effectual metabolite, Oxipurinol.

Relationship between gout and Hyper-uricaemia- Hyper-uricaemia is mandatory for the development of gout. Crystal deposition occurs when serum is drenched with Urate ≥ 0.42 mmol/l. This may be different from some laboratories normal ranges, which are based on population norms. A few people with hyper-uricaemia are expected to evolve gout. For instance, the yearly incidence of gout is only 6% in people with a Urate of 0.60 mmol/l. Serum Urate can diminish during an acute attack, and patients on Urate - lowering medication can still be affected until crystal deposits have cleared from the joints. Thus, demonstrating a raised serum Urate is not an essential prerequisite for diagnosing gout.

Hyper-uricaemia and cardiovascular disease- There is a well-recognized relation between hyper-uricaemia and cardiovascular disease. It is not clear whether hyper-uricaemia is an unconventional risk component for cardiovascular disease. Thus, screening for hyper-uricaemia in people with more cardiovascular risk is not

indicated. However, assessing cardiovascular risk in people presenting with gout is worthwhile[21].

AETIOLOGY- Hyper-uricaemia can result from either overabundance or below excretion of Uric acid. Uric acid is end result of purine metabolism. The purine pool of body is derived from dietary sources. The formation of purine nucleotides such as Adenylic acid and Guanylic acid from preformed purines by the salvage pathway and de novo synthesis from Phosphoribosyl pyrophosphate (PRPP).

CLASSIFICATION OF HYPER-URICAEMIA AND GOUT- The development of Hyper-uricaemia may be caused by an excessive rate of Urate production, a decrease in the renal clearance of Uric acid or amalgamation of both events. Hyper-uricaemia and Gout may be classified as follows.

i. **Primary: -** It includes cases that appear to be innate, neither secondary to another acquired disorder nor a subordinate manifestation of an inborn error that leads initially to a major disease unlike Gout.

ii. **Secondary: -**That develop in the course of another disease or as a consequence of drug use.

iii. **Idiopathic: -** In which a more precise classification cannot be assigned.

CAUSES OF HYPER-URICAEMIA- Given in table no 2[22]

Table 2 Hyper-uricaemia: Causes and Classification

A. **Uric Acid Over-production**	A. **Uric Acid Under-excretion**
Primary Hyper-uricaemia ✡ **Idiopathic** ✡ **Increased Urate production** ✡ **Phosphoribosyl pyrophosphate synthetase over activity** ✡ **Hypoxanthine-guanine phosphoribosyl transferase deficiency**	**1. Primary Hyper-uricaemia** ✡ Idiopathic (influenced by gender and ethnicity) ✡ Familial Juvenile hyper-Uricemic nephropathy
Primary Hyper-uricaemia ✡ **Idiopathic** ✡ **Increased Urate production** ✡ **Phosphoribosyl pyrophosphate synthetase over activity** ✡ **Hypoxanthine-guanine phosphoribosyl transferase deficiency**	**2. Primary Hyper-uricaemia** ✡ Idiopathic (influenced by gender and ethnicity) ✡ Familial Juvenile hyper Uricemic nephropathy
3. **Secondary Hyper-uricaemia** ✡ **Excessive dietary purine intake** ✡ **High nucleotide turnover (psoriasis, myeloproliferative, lympho-proliferative diseases)** ✡ **Increased adenosine triphosphate (ATP) degradation (vigorous muscle exertion, Ethanol abuse, Fructose ingestion).**	**2. Secondary Hyper-uricaemia** ✡ Inhibition of Urate secretion (ketoacidosis, lactic acidosis) ✡ Drugs (low-dose salicylate, diuretics, Pyrazinamide, Ethambutol, Warfarin, Cyclosporine, Theophylline, Levodopa, Nicotinic acid, Alcohol) ✡ Lead nephropathy

PATHOPHYSIOLOGY: Uric acid is normally produced as an end product of the abasement of purine compounds. However, the solubility of the principal physiologic salt of Uric acid, monosodium Urate, in connective tissues is normally close to 7 mg/dL at 37° C, and Urate solubility declines progressively at cooler temperatures such as those in distal peripheral joints. Thus, in humans, “normal” serum Urate concentrations provide only a narrow safety

margin for Urate crystal deposition. Human beings, like other high mammals, lack Uric acid oxidase (Uricase), which oxidizes Uric acid to much soluble compound Allantoin. Significantly, not only do genetically engineered Uricase knockout mice demonstrate a marked increase in levels of serum Urate (from _1.0 to 11.0 mg/dL), but severe Uric acid nephrolithiasis with compromise of renal function in early life also develops. Miscible entire body Urate load is approximately 1.2 g (range, 800 to 1600 mg) in healthy men and about half this value in healthy women. Significantly, Urate synthesis averages around 750 mg/day in men, and dietary purine intake stimulates additional Uric acid production. Gastrointestinal excretion of Uric acid through bacterial Urate oxidation in the gut can remove a few hundred milligrams of Uric acid daily, but this elimination pathway has limited potential for adaptive increases in capacity. Renal Urate excretion in normal adult men ingesting a purine free diet averages approximately 400 mg/day, with the normal range being between 250 and 750 mg/day with a typical Western diet. Renal Urate excretion can increase substantially in adaptation to increased Uric acid generation. However, physiologic limits to renal excretion of Uric acid constrain the capacity of this Urate removal pathway, and excessive Uric acid filtration is nephrotoxic, as discussed later. Therefore, the majority of entire body Urate load is normally turned over daily, thus providing a narrow physiologic window for Urate balance with the potential for substantial expansion of total body Urate stores. Multiple social, environmental, and genetic factors influence Uric acid formation and removal. Hereditary occurrence of gout is reported in approximately 20% of affected patients. Family and twin studies suggest that both hyper-uricaemia and renal pick-up of Uric acid are polygenic traits. In a given individual, single and combined disorders of Uric acid formation and excretion can be responsible for hyper-uricaemia and gout. A splinter of patients with gout have Urate overproduction alone as the primary abnormality. The most common defect identifiable in patients with gout is renal under excretion of Urate via an undefined mechanism. Recent cloning of the key renal Urate reabsorption transporter URAT 1 may help in elucidating the molecular basis for this common observation.

CLINICAL FEATURES OF GOUT-_Gout generally occurs in four stages

- Asymptomatic Hyper-uricaemia
- Acute stage
- Intercritical Periods
- Advanced Gout

1-Asymptomatic Hyper-uricaemia- Hyper-uricaemia may be an incidental finding and may never lead to gout. Conversely, serum Uric acid levels may not be elevated during acute gouty arthritis. This is because ACTH released in response to stress is Uricosuric. Generally, asymptomatic hyper-uricaemia needs close observation with no active treatment. However, growing epidemiological and experimental evidence indicates that asymptomatic hyper-uricaemia is capable of directly promoting

hypertension and vascular disease. Severe over-production of Urate, as may occur with cytotoxic chemotherapy, is associated with high risk of acute renal failure and requires intervention.

2-Acute Stage- The big toe (first metatarsophalangeal joint) is the authoritative site for gout. One-third of patients may conquer their first attack at another site such as the in-step of the foot, ankle, knee, or hand joints. Classical description of Sydenham's enlists the essential clinical attributes used to discover a typical attack. The attack is acute, it starts in the night, the joint and surrounding tissues are swollen, hot, red, shiny and extremely painful. There is a mild fever with chills. Left untreated, the attack will start to improve in a week or two. The skin over the joint may subsequently desquamate. Atypical manifestations include tenosynovitis, bursitis, cellulitis or mild pain and discomfort without swelling, lasting a day or two. Acute gout in one joint may provoke migratory attacks affecting other joints over subsequent days (cluster attacks). Pauci or polyarticular gout attacks are more common in women, especially with diuretic use.

3-Intercritical Stage- After the initial attack of gout, the second episode may never occur or occurs after several years. However, in most of the patients, the next few episodes occur within one year. The frequency of attacks and number of sites involved gradually increase with time.

4-Chronic Gout (Tophaceous gout)- Development of chronic tophaceous gout depends on uncontrolled hyper-uricaemia of long duration, usually more than 10. But tophi or chronic polyarthritis may occur as early as 3 years or as late as 40 years after the initial acute attack. Tophi appear as firm, nodular or fusiform swellings. In inflamed tophi, the overlying skin may be erythematous. In ulcerated tophi, white chalky material, the Urate crystals, may exude. The common locations of tophi are the great toe, feet, hand joints and olecranon. Tophi of helix of the ear, though classic is uncommon. The gout in elderly patients, especially women, may present differently compared to typical gout occurring in middle-aged men given in Table no 3[23].

Table 3 Typical gout versus elderly-onset gout

Feature	Typical Gout	Elderly Onset Gout
Age of onset	Peak in mid 40s	Over 65
Sex	M > F	M = F
Presentation	Acute monoarthritis; lower extremity (base of greater toe, instep of the foot)	Polyarticular upper and lower extremity (finger involvement more common than typical gout)
Tophi	Several years of attack	May occur early
Associated features	Obesity, hyper-uricaemia, hypertension, alcohol abuse	Renal insufficiency, diuretic use

COMPLICATIONS

1. Deposition of Urates in renal parenchyma that can leads to chronic Pyelonephritis and progressive renal failure.
2. Renal calculus causing renal colic (10%—20%).
3. Atherosclerosis.
4. Hypertension.

5. Hypertension and atherosclerosis may lead to coronary or Cerebro-vascular accidents.
6. Diabetes mellitus.
7. Acute tenosynovitis, bursitis and supraspinatus tendinitis.

PROGNOSIS- Acute gouty arthritis is self-limiting, prognosis is good if recurrence of acute attacks of gouty arthritis are often of long duration, patient has proper understanding of the disease and stick to preventive measures, keeps check on obesity, hypertriglyceridemia and hypertension. Prognosis is poor if there is frequent recurrence of attacks, patient does not stick to preventive measures and there is no check on associated diseases. Poor understanding of the disease, its consequences and lack of application of recommended treatment regimens by the patient. Other factors which indicate about poor prognosis are chronic infections, blood dyscrasias, and metabolic faults in diabetics or thyroid dysfunctions.

DIAGNOSIS

✡ Synovial fluid analysis—should be done to confirm gout even when clinical appearance is strongly suggestive; joint aspiration and corroboration of both intracellular and extracellular needle-shaped negatively birefringent MSU crystals by polarizing microscopy. Gram stain as well as culture should be carried out on all body fluids to eliminate infection. Crystals of MSU can also be illustrated in protracted joints or tophaceous deposits.

✡ Serum Uric acid—normal levels do not rule out gout.

✡ Urine Uric acid—excretion of >800 mg/d on regular diet in the absence of drugs suggests overproduction.

✡ Screening for menace factors or sequelae—urinalysis; serum creatinine, liver function tests, glucose and lipids; complete blood counts.

✡ If overabundance is suspected, measurement of erythrocyte hypoxanthine guanine phosphoribosyl transferase (HGPRT) and PRPP levels may be indicated.

✡ Joint x-rays—may display cystic changes, erosions with sclerotic margins in advanced chronic arthritis.

✡ If renal stones suggested, abdominal flat plate (stones often radiolucent), possibly IVP.

✡ Chemical analysis of renal stones[24].

TREATMENT- There is little sturdy data to inform the management of gout. Recommendations for the treatment are mainly based on clinical experience rather than randomized controlled trial evidence. There are now some suggested quality standards for the management of gout/hyper-uricaemia that can be used to audit practice, and the British Society of Rheumatology has produced guidelines for the treatment of gout.

ACUTE GOUT- The choice of drug treatment is dependent on the equilibrium of menace and benefits. Our view, backed by some empirical data, is that for many patients with acute gout a short course of oral steroids often provides the best balance of benefits and risks.

- ***NSAIDs —***

There is one small randomized controlled trial of NSAIDs compared to placebo for acute gout as given in Table no 4. Decades of clinical experience attest to the efficacy of these drugs for acute gout.

Table 4 Proposed quality care indicators for gout management. Reproduced with permission from underwood (2006)

Treatment of Acute Gout
• Patients depicting symptoms of acute gouty arthritis who don't have notable renal impairment (creatinine clearance ≤ 50 ml/min or creatinine concentration ≥ 167 µmol/l) or peptic ulcer disease should be managed with one of the following:
• A non-steroidal anti-inflammatory drug
• Steroids or Adrenocorticotrophic hormone (systemic or intra - articular)
• Colchicine
Prevention of Recurrent Gout
Obese patients with gout (body index > 28), or who have one or more alcoholic drinks per day, should be advised to lose weight or decrease their alcohol consumption, or both
• Initially, one should use a low dose (< 300 mg/day) of Allopurinol in patients with major renal impairment.
• One should reduce the dose of Azathioprine or 6-mercaptopirine by at least 50% while recommending a combination of Xanthine oxidase inhibitor with Azathioprine or 6-mercaptopurine,
• While initiating a Urate- reducing drug in gout patient without major renal impairment (see definition above) or peptic ulcer disease, combination of a NSAIDs or Colchicine should be used to decrease the frequency of rebound gout attacks
• Asymptomatic hyper Uricaemic patient need not to be treated
• Uricosuric medications not to be used in patients with noteworthy renal deterioration or with known renal calculi
• Gout patients having tophaceous deposits, erosive changes on radiographs, or more than two attacks annually should be prescribed Urate-lowering treatment
• Patients with gout taking A xanthine oxidase inhibitor should check their serum Urate level at least once during first 6 months of repetitive use.
• Patients taking constant prophylactic oral colchicine who have noticeable renal impairment (see definition above) should check their full blood count and creatine kinase at least once every 6 months

Typically, high-dose NSAIDs, e.g. Indomethacin 50 mg TDS, are recommended, although there are no empirical data to support this. The only firm conclusion from comparative studies of NSAIDs is that pain reduction with Indomethacin or Etoricoxib are equivalent. If NSAIDs or COX - 2 inhibitors are used, a co - prescription of a proton pump inhibitor is usually indicated.

- ***Colchicine*** —

There is one small controlled trial of Colchicine compared to placebo for acute gout; everyone taking Colchicine developed diarrhoea and vomiting, frequently before pain relief. Severe diarrhoea when immobilized with acute gout can be an unpleasant experience. Other adverse reactions include bone marrow and neuromuscular dysfunction. Traditionally high doses of Colchicine are recommended; however, a lower dose of 0.5 mg three times a day is less toxic and can be adequately effective.

- ***Steroids /adrenocorticotrophic hormone (ACTH)***—

There are no controlled trials comparing steroids/ACTH with placebo for acute gout. One trial, in a Hong Kong emergency department, compared Indomethacin 150 mg/day with Prednisolone 30 mg daily for 5 days. Prednisolone was at least as effective as indomethacin. Among the patients that received indomethacin, 5% had a gastrointestinal haemorrhage and 11% were awowed to hospital for treatment of a serious adverse effect. Nobody in the control group had a haemorrhage or was admitted to hospital. A second trial, in Dutch primary care, compared naproxen 1 g/day with Prednisolone 35 mg per day and found effectiveness to be equivalent and a

similar incidence of adverse effects. Clinical experience supports the employment of intra - articular steroids, but septic arthritis must be positively excluded. Intra - articular injections in acute gout can be difficult and very painful, particularly in smaller joints.

- ***Analgesics —***

Gout is painful. Patients may need potent analgesic in addition to specific treatments. For some frail patients, just using analgesics may be appropriate.

- ***Other treatments —***

Experience and some controlled trial evidence suggest that some non - drug pain relief modalities such as the use of ice packs may give additional pain relief.

INTERCRITICAL AND CHRONIC GOUT- The mainstay of treatment for prevention of recurrent acute gout and chronic gout is reducing serum Urate enough to allow crystals to clear. Different authorities suggest < 0.30 mmol/l or <0.36 mmol/l as the therapeutic target. Asymptomatic hyper-uricaemia does not require treatment. Patients with two or more episodes of gout annually should be offered Urate - lowering medication. Starting Urate - lowering drugs during an attack may delay resolution and should be avoided as lowering serum Urate can trigger acute gout. An NSAID's, probably with a proton pump inhibitor, or colchicine should be co-prescribed for the first 3 months.

- ***Medication Review —*** Consider stopping diuretics or any other drugs known to increase serum Urate.

- ***Lifestyle Interventions —***

Patients should be advised to: lose weight; reduce the amount of meat and fish eaten; reduce alcohol intake and avoid beer; increase intake of low-fat dairy products.

- ***Xanthine Oxidase Inhibitors —***

These prevent the purine breakdown products Xanthine and Hypoxanthine being converted into Urate. Allopurinol has been available for over 40 years. A new Xanthine oxidase inhibitor, Febuxostat, has been developed.

- ***Allopurinol —***

Allopurinol reduces serum Urate, but its action on recurrent gout is unclear. Only a few patients taking the typical dose of 300 mg/day achieve a target Urate of 0.36 mmol/l. Its dose should be titrated as per response, up to 900 mg/day. Allopurinol hypersensitivity may occur in up to 2% of patients; this can be severe or even fatal. Desensitizing regimens of Allopurinol can be tried in milder cases of hypersensitivity.

- ***Febuxostat —***

Over half of patients taking Febuxostat 80 mg achieve a Urate of < 0.36 mmol/l compared to one in five of those taking allopurinol 300 mg. However, Febuxostat does not seem to be more effective at reducing recurrent gout over 1 year. It may have a role in patients who can't take Allopurinol, either because of intolerance or because it is contraindicated.

- ***Uricosuric Drugs —***

Uricosuric drugs lower serum Urate by impeding its tubular reabsorption. There is no randomized controlled trial evidence supporting their use for

avoidance of recurrent gout. Only Sulfinpyrazone is generally available for the management of gout. Benzbromarone can also be used, but it is not universally available, and there are concerns about it causing liver problems. Historically, Probenecid has also been used. One should consider measuring urinary Urate before starting Uricosurics.

- ***NSAIDS And Colchicine —***

Both regular NSAIDs and Colchicine can be used to prevent recurrent gouty attacks but have no effect on serum Urate.

- ***Uricase drugs —***

Uricase drugs work by oxidizing Uric acid to the much soluble Allantoin. A number of these are currently under investigation. Their role, if any, in the management of gout is unclear.

- ***Other drugs —***

Several other drugs have, coincidentally, been found to have Urate - lowering effects. These include Losartan, Fenofibrate, Atorvastatin and Amlodipine. Although they are not licensed for the management of gout, they may have a role if other drugs cannot be tolerated or if they are otherwise indicated for patients with multiple pathology[25].

DISCUSSION

Gout is musculoskeletal disorder, having the incidence of 2-26 per 1000[26]. In a citizenry of 1000, 00 people, there will be about 30 new cases per year of gout. The rate of gout has raised in recent decades not only in America, also in developing countries. Gout is rare in children and pre-menopausal females in India. It effects males in their 40s and 50s and is common in female after menopause[27]. Gout, when it involves the big toe, then it is called as Podagra. It is a clinical entity usually distinguished by repeated episodes of acute incendiary arthritis – a red, hot, tender, swollen joint. The most habitually contrived joint is metatarsal phalangeal joint at the base of the big toe[28] (approximately 50% of the cases). Albeit, it can also exhibit tophi, kidney stones, or Urate nephropathy mainly produced by increased amount of Uric acid which crystallizes, and the crystal gets deposited in joints, tendons, and adjacent tissues. Present dietary habits like protein rich diet, consumption of alcohol and sedentary life style are the predisposing factor for causing the disease. In history, gout has been designated as rich man's disease also called as disease of king/lord, but in present era, it is not only limited to rich class of society but it is also affecting middle class people.

CONCLUSION

It may be concluded that Gout is predominantly a disease of males, usually having age >40 years. Females are protected from gout due to hormonal effect but after menopause, they also become prone to this disease. Most common factors that may be related to aetiogenesis of the disease are non-vegetarian diet, sedentary lifestyle, alcohol addiction which helps in precipitating gout attack. Increase in urbanization and affording capability of people can be said as main constituent factor in causation of the disease. Also faulty dietary habits and lack of exercise resulting in hypertension,

coronary artery disease, overweight or obesity are the main associated diseases in gout.

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