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IN
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"SERUM URIC ACID LEVELS IN PATIENTS WITH CHRONIC NONSPECIFIC MUSCULOSKELETAL PAIN"

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Dr. TUMARADA V A M K RAJA

ABSTRACT

Background:

Chronic nonspecific musculoskeletal pain (CNMP) represents a significant global health challenge affecting approximately 20-30% of the adult population. Despite its prevalence, the underlying pathophysiological mechanisms remain poorly understood. Recent evidence suggests potential roles for metabolic factors in pain generation and perpetuation. By contrasting cases with healthy controls and assessing related demographic and clinical factors, this study sought to determine the link between serum uric acid levels and CNMP.

Methods:

A case-control study was conducted with 30 patients diagnosed with CNMP (pain lasting ≥4 weeks without identifiable structural or inflammatory cause) and 30 age-matched healthy controls. Comprehensive demographic data, clinical characteristics, and lifestyle factors were assessed. Laboratory investigations included complete blood count, erythrocyte sedimentation rate, fasting blood sugar, renal function tests, rheumatoid factor, anti-streptolysin O titer, and serum uric acid levels. Statistical analysis was performed using appropriate tests, with $p<0.05$ considered significant.

Results:

The case and control groups showed similar age distribution, with most participants in the 21-40 years bracket (46.7% vs. 53.3%). All participants had normal BMI (18.5-24.9 kg/m²). Significantly, 60% of CNMP patients exhibited hyperuricemia (men >7 mg/dl, women >6 mg/dl) compared to none in the control group ($p<0.001$). Serum creatinine levels were higher in cases compared to controls (0.8±0.1 vs. 0.67±0.1

mg/dl, p<0.001) while remaining within normal clinical ranges. Most CNMP patients (83.3%) reported pain duration of 4 weeks, with 96.7% describing moderate intensity. Nearly all cases (96.7%) were negative for rheumatoid factor, and all were negative for anti-streptolysin O titer. No significant differences were observed in hematological parameters, dietary patterns, smoking, or alcohol consumption between groups.

Conclusion:

This study demonstrates a significant association between elevated serum uric acid levels and CNMP, with 60% of patients exhibiting hyperuricemia compared to none in the control group. This finding suggests that uric acid may play a role in the pathophysiology of CNMP through pro-inflammatory effects, oxidative stress induction, or microvascular dysfunction. Serum uric acid could serve as a potential biomarker and therapeutic target in CNMP, supporting a more integrated approach to chronic pain management that considers biochemical factors alongside biomechanical and psychosocial dimensions. Further research is warranted to establish causality and optimize therapeutic approaches targeting uric acid metabolism in CNMP patients.

Keywords:

Chronic nonspecific musculoskeletal pain; Hyperuricemia; Uric acid; Allopurinol; Pain management; Inflammation; Oxidative stress; Case-control study.

ABBREVIATIONS

ASLO	-	Anti-streptolysin O
BMI	-	Body Mass Index
CNMP	-	Chronic Nonspecific Musculoskeletal Pain
DAMP	-	Damage-Associated Molecular Pattern
ESR	-	Erythrocyte Sedimentation Rate
FBS	-	Fasting Blood Sugar
GABA	-	Gamma-Aminobutyric Acid
Hb	-	Hemoglobin
IL-1β	-	Interleukin-1 Beta
IL-18	-	Interleukin-18
NADPH	-	Nicotinamide Adenine Dinucleotide Phosphate
NLRP3	-	NOD-like Receptor Protein 3
RF	-	Rheumatoid Factor
ROS	-	Reactive Oxygen Species
SD	-	Standard Deviation
TLC	-	Total Leukocyte Count

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INTRODUCTION

Chronic nonspecific musculoskeletal pain (CNMP) represents a significant global health challenge, affecting approximately 20-30% of the adult population worldwide.[1] This debilitating condition is characterized by persistent pain lasting more than three months, without clear pathological or anatomical causes that fully explain the severity and chronicity of the symptoms.[2] The complex nature of CNMP poses substantial challenges in both diagnosis and management, leading to considerable healthcare utilization, reduced quality of life, and significant socioeconomic burden.

The pathophysiology of CNMP involves multiple interconnected mechanisms, including central sensitization, altered pain processing, and various biochemical alterations. Among these biochemical factors, serum uric acid (SUA) has emerged as a potential marker of interest in recent years.[3] Traditionally associated with gout and cardiovascular diseases, emerging evidence suggests that SUA levels may play a more extensive role in pain mechanisms and inflammation than previously recognized.

Uric acid, the end product of purine metabolism, serves as both an antioxidant and a pro-oxidant in the human body, depending on its concentration and the cellular environment.[4] Under physiological conditions, it acts as a powerful antioxidant, contributing approximately 60% of the total plasma antioxidant capacity. However, elevated levels of SUA can trigger oxidative stress and promote inflammatory responses through various pathways, including the activation of the NLRP3 inflammasome and the production of pro-inflammatory cytokines.[5]

Recent studies have suggested a potential association between elevated SUA levels and various pain conditions, including fibromyalgia, chronic widespread pain, and other musculoskeletal disorders.[6] The proposed mechanisms include uric acid's role in oxidative stress, mitochondrial dysfunction, and the generation of reactive oxygen

species (ROS), which may contribute to peripheral and central sensitization in chronic pain conditions.

The relationship between SUA levels and pain perception is complex and potentially bidirectional. Chronic pain conditions may influence lifestyle factors and physical activity levels, which in turn can affect uric acid metabolism. Additionally, the stress response associated with chronic pain may lead to hormonal and metabolic changes that impact SUA levels.[7] Understanding these interactions is crucial for developing more effective therapeutic strategies for CNMP management.

The clinical significance of monitoring SUA levels in CNMP patients extends beyond its potential role as a biomarker. Some studies have suggested that interventions targeting uric acid metabolism might offer therapeutic benefits in certain chronic pain conditions.[8] However, the evidence base remains limited, and there is a clear need for more comprehensive research to establish the precise nature of the relationship between SUA levels and CNMP.

The socioeconomic impact of CNMP cannot be understated. The condition leads to substantial healthcare costs, reduced workforce productivity, and decreased quality of life for affected individuals. In the United States alone, the annual economic burden of chronic pain is estimated to exceed $600 billion, surpassing the combined costs of cancer, heart disease, and diabetes.[9] Understanding the role of biochemical markers like SUA could potentially lead to more targeted and cost-effective treatment approaches.

Current management strategies for CNMP primarily focus on symptom control through pharmacological interventions, physical therapy, and psychological support. However, the effectiveness of these approaches varies significantly among patients, highlighting the need for more personalized treatment approaches based on individual patient characteristics and biochemical profiles.[10] The identification of reliable

biomarkers, such as SUA, could potentially aid in patient stratification and treatment selection.

The investigation of SUA levels in CNMP patients represents an important step toward understanding the biochemical aspects of chronic pain conditions. While previous studies have examined SUA levels in specific pain conditions, comprehensive research focusing on its role in CNMP is limited. This knowledge gap necessitates further investigation to determine whether SUA levels could serve as a useful biomarker for disease severity, progression, or treatment response in CNMP patients.

Given the complex nature of CNMP and the potential role of SUA in pain mechanisms, this study aims to investigate the relationship between serum uric acid levels and chronic nonspecific musculoskeletal pain. The findings could contribute to our understanding of the biochemical basis of chronic pain and potentially inform future therapeutic strategies. Additionally, this research may help identify whether SUA monitoring could serve as a useful tool in the clinical assessment and management of CNMP patients.

AIM & OBJECTIVES

Objectives:

1. To assess the correlation of serum uric acid levels and chronic nonspecific musculoskeletal pain

REVIEW OF LITERATURE

URIC ACID

"Uric acid, $C_5H_4N_4O_3$, 7,9-dihydro-1H-purine-2,6,8(3H)-trione, molecular mass 168 Da."11

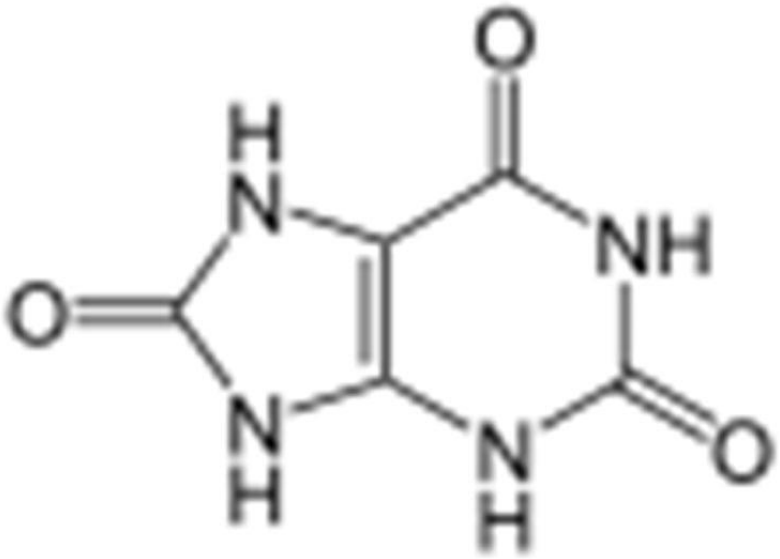


Figure 1: structure of Uric Acid

Production

The end product of purine metabolism, which produces vital biologic components such DNA, RNA, ATP, GTP, c-AMP, and NADH, is uric acid, a weak acid.[12]

Endogenous sources, such as nucleic acid degradation and de novo purine production, account for the great bulk of serum UA. An estimated 500–600 mg of purines are produced endogenously each day, whereas 100–200 mg of exogenous purines are consumed through diet.[13]

Organ meats (particularly the liver and kidneys), anchovies, beans, sardines, yeast, and beer are among the foods high in purines.[12]

Consuming fructose-rich items can enhance serum UA synthesis via accelerating adenosine triphosphate (ATP) decomposition, even though they are not a direct source of purines.[14]

Xanthine oxidase is an essential enzyme that catalyses the conversion of purines to UA in humans and is a target of multiple medications. The liver, the primary organ for UA synthesis, has the largest concentration of it. But other organs like the intestines, kidneys, lungs, heart, brain, muscles, and arteries also contain xanthine oxidase.[12, 15]

"It's interesting to note that human UA catabolism differs from that of other mammals. While most other mammals manufacture uricase, which converts UA into more easily excreted allantoin, UA is the end result of purine metabolism in humans. According to one theory, the uricase-coding gene has been lost over evolution in order to sustain the elevated blood pressure required to maintain an upright posture".[16]

The liver, intestines, muscles, kidneys, and vascular endothelium are the primary sites for the synthesis of uric acid (Fig. 2).

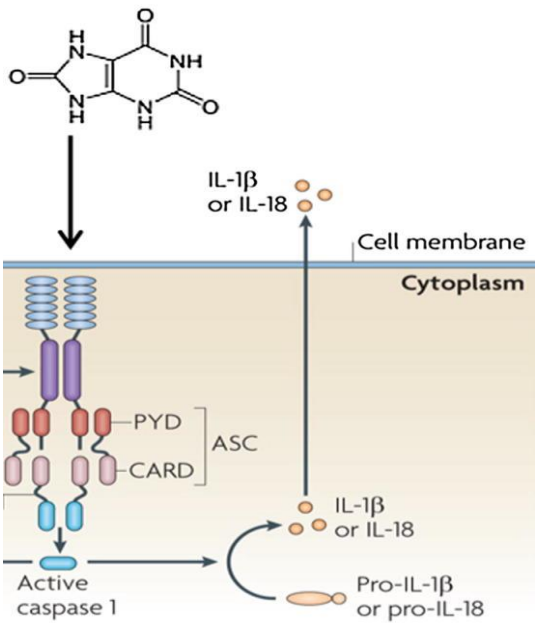


Figure 2: Synthesis of Uric Acid

PHYSIOLOGICAL FUNCTIONS OF URIC ACID

Antioxidant

"About 90% of filtered uric acid is reabsorbed, suggesting that it plays a significant physiological role. The majority of serum uric acid is freely filtered in renal glomeruli. In humans, uric acid accounts for more than half of blood plasma's antioxidant capability. Uric acid is a potent antioxidant and scavenger of peroxynitrite and reactive oxygen species (ROS). [17] Normal human and animal cells' cytosols contain high concentrations of uric acid, particularly in the liver, vascular endothelial cells, and human nasal secretions, where it functions as an antioxidant".[18]

"Endothelial function

A recent report revealed, for the first time, that extremely low levels of serum uric acid, caused by loss-of-function mutations of SLC22A12, which encodes blood vessels and kidney proximal tubular cells transporter, URAT1, cause endothelial dysfunction in vivo. This is in contrast to studies showing that uric acid can compromise the integrity of vascular endothelial cells. [19]The idea that uric acid causes kidney and cardiovascular disorders by compromising endothelial integrity and function was contested by this and other studies. In fact, uric acid may play essential functions in tissue healing by scavenging oxygen free radicals, promoting progenitor endothelium cells, and starting the inflammatory process required for tissue repair".[20]

Potent mediator of type 2 immune responses

Mice that received injections of the most used therapeutic adjuvant, alum (aluminium hydroxide), showed elevated levels of uric acid in their peritoneal cavities. [21, 22] "Uric acid is required and sufficient for the generation of antibody immunological responses to ovalbumin, according to experiments that involved injecting mice intraperitoneally with the innocuous protein ovalbumin or ovalbumin + alum along with

0 or 50 units of uricase. [22] It was shown that the alum's established T helper 2 (Th2) adjuvanticity was achieved by cell damage that resulted in the development of uric acid, which serves as a warning signal that encourages the production of dendritic cells originating from inflammatory monocytes. [21, 22] These results demonstrate how important uric acid is in triggering protective antibody responses to the several human vaccinations that use alum as an adjuvant".

In the airways of mice and individuals with asthma who were exposed to allergens, uric acid production was also seen. It seems to be essential for the development of Th2 cell immunity, airway eosinophilia, and bronchial hyperreactivity to inhaled innocuous proteins and house dust mite allergen. Furthermore, strong type 2 immunity was produced by administering MSU crystals along with inhaled innocuous proteins. By activating phosphoinositol 3 (PI3)-kinase and spleen tyrosine kinase (Syk), uric acid adjuvanticity was demonstrated. As a result, uric acid was found to be a crucial trigger and enhancer of allergic inflammation in vivo. [22]

In order to "direct the immune environment towards the type 2 axis and hypersensitive inflammation, barrier epithelial cells can be stimulated to produce type 2 cytokines like thymic stromal lymphopoietin (TSLP), interleukin (IL)-25, and IL-33 by allergens, which are frequently proteases, specifically cysteine proteases, and the cysteine peptidases papain and bromelain. According to recent research, uric acid is released when tissue cells, particularly the barrier epithelial cells, are stressed and damaged by allergens and cysteine peptidases like papain. One important factor that controls the development of type 2 immune responses to cysteine peptidase allergens is uric acid, which has been demonstrated to stimulate epithelial cells for the production of TSLP and IL-33 but not IL-25. [23] In vivo exposure of mice to particulate pollutants and the cysteine peptidase-containing house dust mite caused an increase in uric acid

production and release by mucosal cells and mediated allergic sensitisation, which was demonstrated to be inhibited by uricase. Uric acid is constitutively secreted by human and mouse airway epithelial cells. In fact, like ATP (adenosine triphosphate), HMGB1 (high mobility group box 1), IL-33", and other alarmins, uric acid is now known to be a significant and powerful modulator of type 2 immune responses that include mast cells, eosinophils, basophils, innate lymphoid cells, and epithelial cells".[21, 22]

Resistance to parasites

"Type 2 immune responses are necessary for the immune system's defence against several helminth parasites. [24] The role that uric acid plays in the establishment of protective type 2 immune responses against nematodes is unknown. Cysteine peptidases, including papain, Schistosoma mansoni cathepsin B1 (SmCB1), cathepsin L3 (SmCL3), and Fasciola hepatica cathepsin L1 (FhCL1), have been shown to produce reproducible and highly significant ($P < 0.0001$) reductions of 50–65% in challenge S. mansoni and Schistosoma haematobium infection through the production of polarised (papain, SmCL3, FhCL)- or predominant (SmCB1) type 2 responses that include the release of TSLP, IL-4, IL-5, and IL-13, as well as the production of IgG1 antibodies. The master cytokine of innate and adaptive type 2 immune responses, TSLP, is released when papain or helminth cysteine peptidases that are supplied subcutaneously interact with epithelial cells. [25] The produced type 2 cytokines drive the immune system to the type 2 immunological arm during challenge infection by recruiting and activating innate lymphoid cells 2, eosinophils, basophils, and mast cells. They also aid in the generation of IgG1 antibodies against the cysteine peptidase. The moving schistosome larvae are harmed by the combination of eosinophils, basophils, mast cells, and basic toxic proteins, proteoglycans, proteases, peroxidases, and extracellular traps. The endothelial cells in the blood capillaries are undoubtedly more severely damaged. It has been

demonstrated that damage to the capillary endothelium causes uric acid to be released and to build up around the growing blood flukes. These findings are consistent with the theory that, in the absence of an adjuvant, the establishment of type 2 immunity against cysteine peptidases requires endogenous uric acid. [21, 22] The discovery of increased uric acid concentrations in the liver and lung of immunised and unimmunized schistosome-infected animals is completely consistent with research demonstrating that uric acid is constitutively present in normal cells, particularly vascular endothelial, intestinal, and liver cells, and that its concentration rises in response to cell damage and after being released from dying cells. [23]

Type 2 immune effectors and cytokines harm hepatocytes in the liver sinusoids as worms proliferate, consume blood, and excrete and emit cysteine peptidases, which causes uric acid to be released. Non-alcoholic fatty liver disease (NAFLD) has been linked to uric acid, which has been shown to play a causal role in fatty liver by increasing the synthesis of fatty acids and releasing unsaturated fatty acids, particularly arachidonic acid, from cell membranes and lipid depots. [26] Uric acid acts as a substrate for the enzyme cyclooxygenase and inhibits the activity of lipoxygenases because of its potent antioxidant qualities. Since arachidonic acid has been demonstrated to be an efficient schistosomicide both in vitro and in vivo in mice, hamsters, and children infected with S. mansoni, it is therefore permitted to reach the parasites and mediate their death".[27]

Defense against neurological and autoimmune diseases

Supporting "evidence showed that patients with multiple sclerosis had low plasma uric acid levels, which resulted in a reduction in antioxidant molecules. High uric acid levels can prevent peroxynitrites and ROS, which are thought to be the cause of myelin degeneration in multiple sclerosis (MS), although gout patients hardly ever

exhibit MS symptoms. Numerous studies have shown a link between MS illness and low serum uric acid levels. [28] According to a recent meta-analysis of published data, patients with multiple sclerosis exhibited lower serum uric acid levels than healthy controls. This suggests that low serum uric acid levels could be a biomarker for multiple sclerosis. Neurological problems were also linked to low plasma uric acid levels,[29] Parkinson's and Alzheimer's disease, lichen planus, an autoimmune inflammatory disease of the mucocutaneous tissue, and Pemphigus vulgaris, an autoimmune disorder marked by blistering and sores (erosions) of the skin and mucous membranes, were all linked to low salivary uric acid levels".[30]

HYPERURICEMIA

DEFINITION

An increased "serum uric acid level, often more than 6 mg/dL in women and 7 mg/dL in men, is referred to as hyperuricemia".[31]

EPIDEMIOLOGY

"Uric acid levels can rise 10 to 15 years before gout symptoms appear, and asymptomatic hyperuricemia is thought to affect up to 21% of the general population and 25% of hospitalised patients. Since hyperuricemia is very common in the general population and asymptomatic in 90% to 95% of cases", it does not signify a pathogenic state. As both developed and emerging nations embrace Western diets and lifestyles, the prevalence of hyperuricemia is rising globally. 32 Pacific Islanders have especially high levels of hyperuricemia. 33 Because oestrogen protects against hyperuricemia and because women can develop hyperuricemia after menopause, men have greater rates than women. [34]

There are regional and population-specific variations in the prevalence of hyperuricemia. Over the past four decades, the incidence of HU has risen consistently

worldwide, with larger prevalences in Asian nations such as Taiwan (10–52%), India (~25.8%), Japan (20–26%), and China (6–25%) compared to the USA (21-22%), Brazil (13%) and Italy (9–12%).[35]

ETIOLOGY

Uric Acid Overproduction

- Purine-rich foods include "certain fish and shellfish (anchovies, cod, tuna, sardines, herring, mussels, prawns, lobster, codfish, scallops, trout and haddock), alcohol (particularly beer), bacon, beef, lamb, turkey, veal, venison and organ meats."
- Because fructose is metabolised by the liver via the aldolase reductase route, it results in hyperuricemia. Particularly dangerous and linked to childhood and teenage obesity are high-fructose corn syrup and full-sugar sodas. [36]
- Purine metabolism errors include over activity of phosphoribosylpyrophosphate (PRPP) synthetase and hypoxanthine-guanine phosphoribosyltransferase (HPRT or HGPRT) deficiencies.
- High cell turnover or breakdown, such as in myeloproliferative illnesses, polycythaemia vera, Paget disease, psoriasis, tumour lysis, haemolysis, rhabdomyolysis, chemotherapy, and lymphoproliferative diseases.

Decreased Uric Acid Excretion

- Acute or chronic kidney illness, sarcoidosis, hyperparathyroidism, hypothyroidism, Bartter syndrome, Down syndrome, acidosis (such as lactic acidosis or ketoacidosis), hypovolemia, and medications or toxins (such as diuretics, niacin, pyrazinamide, ethambutol, cyclosporine, beryllium, salicylates, lead, and alcohol).[37]

Diuretic-induced Hyperuricemia

- A dose-dependent form of hyperuricemia and potentially even gout are common side effects of thiazide and loop diuretics. Through volume depletion, they frequently promote renal uric acid reabsorption directly or indirectly. [38]
- Diuretics increase the relative risk of gout by nearly 80%. [39]
- Patients experiencing flare-ups of gout are advised to take an alternative or concurrent antihypertensive, "such as an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker, particularly losartan".[40]
- Xanthine oxidase inhibitors, such allopurinol, are used to treat the majority of individuals with diuretic-induced gout. However, there is no need for treatment if the patient has no symptoms.

PATHOPHYSIOLOGY

Clinical Manifestations

Uric acid "can build up in the blood and tissues due to gout, a metabolic disease. As a result, crystals of urate monohydrate precipitate inside a joint". Gout can appear in peripheral joints like the big toe because crystal deposition is accelerated in cold and acidic environments. In a 4:1 male to female ratio, gout is more common in men. [41]

Uric acid precipitates in the urine in uric acid nephrolithiasis, which is most frequently caused by "metabolic syndrome and acidic urine. Hypovolemia, hyperuricosuria, and acidic urine are the main risk factors for uric acid nephrolithiasis. Uric acid levels exceeding 800 mg/day in men and 750 mg/day in women are referred to as hyperuricosuria. Five to ten percent of all urinary stones are uric acid stones, which can also contain calcium".[42]

Even after controlling for the comorbidities of diabetes and obesity, hypertension is associated with hyperuricemia. After controlling for other comorbidities, a large cross-sectional investigation revealed a direct correlation

between blood uric acid levels and hypertension, even at levels deemed to be "within the normal range (≥5.3 mg/dL for males and ≥4.3 mg/dL for women). The renin-angiotensin system, oxidative stress, endothelial inflammation, endothelin-1 activation, and nitrous oxide reduction are some of the mechanisms via which hyperuricemia can result in hypertension" [43]

Additionally, there is a strong correlation between obesity and hyperuricemia, and some investigations indicate that obesity contributes to hyperuricemia. Two hypothesised processes are (1) the liver producing uric acid due to free fatty acids from visceral adipose tissue and (2) the renal tubules excreting less uric acid and salt due to adipocyte dysregulation. "Urate-lowering medications may prevent the onset of hypertension in teenagers, according to small clinical trials; nevertheless, because of its severe side effects, this is not advised as a treatment". [44]

Additionally, hyperuricemia is strongly linked to renal and cardiac disorders. It is challenging to establish cause and effect, nevertheless, because the risk variables for the three disease states significantly overlap. "Urate-lowering medications are not recommended for the primary prevention of kidney disease because a prospective research revealed that they did not slow the development of CKD and were instead linked to worse kidney outcomes".[45]

Mechanisms of Hyperuricemia

Purine degradation produces uric acid (2,6,8 thiopurine-C5H4N4O3). Uric acid circulates in the ionised form of urate at the physiological pH of 7.4. "Purine metabolism mostly takes place in the liver, although it can also happen in any tissue that has xanthine oxidase, like the heart or lungs. The kidneys eliminate roughly two-

thirds of the body's total uric acid production, while the intestines absorb the remaining one-third. 90% of the ureate is reabsorbed in the proximal tubule after it has been filtered and released by the kidneys. Because uricase converts urate to the more water-soluble allantoin, other mammals have significantly lower levels of uric acid. However, this enzyme does not operate in humans or higher primates". [46]

Uric acid "production is accelerated by purine-rich meals, endogenous purine production, and rapid cell breakdown. Particularly, beer raises uric acid levels because it contains a lot of purines. Phosphoribosylpyrophosphate (PRPP) synthetase activity and a malfunction in the regulating enzyme hypoxanthine-guanine phosphoribosyltransferase (HPRT) can both speed up the body's natural production of purines. Rhabdomyolysis, haemolysis, psoriasis, myeloproliferative diseases, and tumour lysis are examples of conditions that cause an accelerated breakdown or turnover of cells".[47]

Urate Transport in the Kidney

90% of people have hyperuricemia as a result of poor urine excretion, which mostly takes place in the kidneys. Reduced tubular secretion, increased tubular reabsorption, and lower glomerular filtration all contribute to underexcretion.

The apical cell membrane's uric acid transporter 1 (URAT1) regulates proximal tubular reabsorption of uric acid. "Organic acids (lactate, acetoacetate, and beta-hydroxybutyrate), drugs (niacin, pyrazinamide, ethambutol, cyclosporin, and chemotherapeutic medicines), and decreased extracellular fluid volume that causes hyperuricemia can all stimulate this transporter. The best class of uricosuric drugs for treating hyperuricemia is URAT1 inhibitors. The GLUT9 transporter(GLUCOSE TRANSPORTER 9) then carries ureate into the renal interstitium".[48]

HISTORY AND PHYSICAL

History

Although “there is evidence that hyperuricemia is associated with the development of diabetes, hypertension, and heart disease, it is not a particular reason for medication on its own. The majority of asymptomatic patients with increased uric acid don't need long-term treatment. The patient may disclose a history of heavy alcohol use or a diet high in purines. A thorough evaluation of past medical history and current medications is necessary to look for any connections to elevated uric acid production or poor renal elimination of urate.

The two most prevalent conditions linked to hyperuricemia are gout and uric acid nephrolithiasis. The big toe (podagra) is frequently among the red, hot, swollen joints that the patient complains of during a gout episode. 49 Haematuria, or brownish urine; nausea and vomiting; renal colic, or severe, acute flank, stomach, or back pain that frequently radiates to the groin; and dysuria are the symptoms of nephrolithiasis. There may also be symptoms related to the urinary tract, such as fever, hazy urine, and frequent urination”.[50]

Physical Exam

Unless a patient exhibits signs of acute gout or uric acid nephrolithiasis, no particular physical examination results will point to hyperuricemia. The big toe is most affected by gout, but it can occur in any joint. Gout is characterised by erythematous, heated, and swollen joints. Gout typically only affects “one joint at a time. This manifests traditionally as "pain out of proportion to exam." Although there are no particular physical exam findings for nephrolithiasis, it may cause repeatable discomfort in the costovertebral angle”.

EVALUATION[51]

Laboratory Studies

- Elevated serum uric acid—normal levels might differ by gender and are usually less than 6.8 mg/dL. Hyperuricemia can be diagnosed with readings of 8 mg/dL or higher.
- A "urinalysis may reveal microscopic haematuria, uric acid crystals, and low urine pH (<5.5) if nephrolithiasis is present.
- On a low-purine diet, a 24-hour urine uric acid collection should ideally be less than 600 mg/day. Although hyperuricosuria is identified by a level above 800 mg/d, it is not indicated whether the aetiology is associated with increased uric acid synthesis or decreased excretion.
- A complete blood count (CBC) with differential, CMP, lipid profile, HgA1c, calcium, and phosphate levels are examples of further tests. When evaluating underlying illnesses such cancer, sickle cell disease, diabetes, and metabolic syndrome, these lab tests are helpful".
- Although x-ray results are not necessary to diagnose gout, take into account joint x-rays to assess any unexplained swelling.
- In individuals suspected of having uric acid nephrolithiasis, renal ultrasounds or noncontrast CT scans are recommended. The presence of stones may be obscured by the use of IV contrast.

CHRONIC MUSCULOSKETAL PAIN

Living with chronic pain

There are many different types of chronic musculoskeletal pain, and 20% of adults experience severe chronic pain, which is more common among "women and lower-income groups. While the 12-month prevalence of activity-limiting pain is believed to be between 2% and 14%, the 12-month prevalence of neck pain in the general population and working population is often between 30% and 50%. 52 Chronic whiplash-associated illnesses (1.5%), chronic widespread pain (5%–10%), and neck–shoulder pain, including chronic trapezius myalgia (10%–20%), are the most common chronic pain syndromes in the population. Between 1% and 4% of people have fibromyalgia syndrome (FMS), a subtype of chronic, pervasive pain. About 10% of people have chronic masticatory muscle pain, with women making up two-thirds of those affected". [53]

Patients with various pain disorders report widespread negative outcomes, such as severe pain, weakness, depressed symptoms, sleep issues, sick leave, diminished emotional well-being, and a general loss of enjoyment of life. A measure of nonfatal health consequences from illnesses and injuries is years lived with a disability. In the world, 21% of years spent disabled were due to pain disorders. Iron deficiency anaemia, neck discomfort, and severe depressive disorder were the next most common causes of years spent disabled, after low back pain.[54]

Biopsychosocial model of pain

Physical, emotional, psychological, and social variables all affect and interact with acute and chronic pain, and a biopsychosocial paradigm is being used more and more in clinical practice. It is believed that the biopsychosocial paradigm increases the possibility of creating more effective interventions and treatments. To further maximise

gains for patients with chronic pain, assessment methods based on active neurobiological pain mechanisms—the bio component of the biopsychosocial model of pain—are currently absent.[55]

The Classification of Chronic Musculoskeletal Pain[56]

"According to the 10th edition of the International Classification of Diseases (ICD-10), musculoskeletal pain is the collective term for symptoms related to established pathological disorders that impact the musculoskeletal" system or connective tissue, as well as unknown pathologies at certain places. The former is prevalent as autoimmune inflammatory arthritis (RA) and osteoarthritis (OA). In the latter type, "back pain" or "periarticular pain" are more prevalent. The ICD-10 assigns the diagnostic code for the condition, not the pain code, to pain that has a recognised cause. Nonetheless, it would be preferable to assign a pain code to patients who seek assistance solely for pain relief rather than to treat an underlying illness. In contrast, the coding system for ICD-10 does not include composite code. "Chronic primary musculoskeletal pain and chronic secondary musculoskeletal pain are the two key categories into which the ICD-11 divided CMPs. Chronic primary musculoskeletal pain, which includes chronic non-specific low back pain and chronic widespread pain, is characterised as persistent pain in the muscles, bones, joints, or tendons that is accompanied by substantial emotional distress or functional disability and cannot be directly linked to a recognised disease or damage process. One type of CMP that results from a recognised illness is chronic secondary musculoskeletal pain, which is frequently caused by multiple primary factors: Chronic local or systemic inflammatory diseases brought on by infection, crystal deposition, autoimmune, or autoinflammatory processes; structural alterations in the local musculoskeletal system; and musculoskeletal issues brought on by neurological disorders, like Parkinson disease's

muscular hypertonicity. In order to give more precise epidemiological studies of diseases marked by musculoskeletal pain, this new categorisation integrates the underlying mechanisms of early musculoskeletal disorders with chronic pain. Multimodal therapy of chronic pain will be necessary as a result of the classification shift, which will enable patient-centered management rather of only pathophysiology driven by disease".

Neurobiological alterations in chronic pain

A complicated, integrated sequence of peripheral and central processes leads to acute pain. In cases of chronic or intermittent pain, acute pain mechanisms may not always hold true. Pace et al. divided chronic pain into two categories: 1) neuropathic pain, and 2) nociceptive/inflammatory pain. According to Mense and Gerwin, there are additional variations in the clinical presentation of pain that is localised to the skin and muscles, such as in regards to pulse responses and nausea. The primary focus of this review is nociceptive/inflammatory muscular discomfort. Because of the potential for significant plastic changes in the pain transmission system as well as adjustments to environmental and psychological factors, chronic pain is more complicated than acute pain. [57] A nociceptor is described as "... a high-threshold sensory receptor of the peripheral somatosensory nervous system that is capable of transducing and encoding noxious stimuli" in the International "Association for the Study of Pain's taxonomy. Nociceptive information is transmitted via small diameter, slowly conducting skeletal muscle afferent nerve fibres, free nerve endings of group III (Aδ), and group IV afferent (C) fibres, which must be activated to produce pain. These nociceptors are sensitive to chemicals emitted from tissues that have undergone different kinds of deterioration and distortion. Nociceptors react to a variety of stimuli, including temperature, noxious mechanical stimuli, nerve growth factor (NGF), H+, serotonin (5-HT), bradykinin

(BKN), glutamate, substance P (SP), adenosine triphosphate (ATP), potassium (K+), and others. The nociceptors are affected by a mixture of molecules known as the "soup" of inflammation or trauma. Because plastic modifications, such peripheral sensitisation, can happen, the nociceptor is not a static detector. Because a sensitised nociceptor has a lower activation threshold, typically harmless stimuli can activate it. Studies primarily on animals have shown that the process of peripheral sensitisation involves H+, nitrogen oxide (NO), K+, ATP, NGF, tumour necrosis factor alpha (TNF-α), interleukin 6 (IL-6), prostaglandin E2 (PGE2), and glutamate. Thus, several chemicals, such as 5-HT, glutamate, and K+, seem to have both sensitisation and algesic effects. 57 Research also indicates that some compounds have anti-inflammatory properties, such as endogenous opioids, fatty acid metabolites (such as prostaglandins, leukotoxins, resolvins, protectines, endocannabinoids, and N-acylethanolamines [NAEs]), and specific cytokines (such as IL-10, IL-4, IL-13, and IL-1 receptor antagonists). Certain nociceptors' receptors, such as G protein-coupled receptors, receptor tyrosine kinases, and ionotropic receptors/ion channels, are affected by the algesic and sensitising chemicals. The sensitive area may enlarge in tandem with sensitisation". There have also been reports of quiet nociceptors being activated. It's possible that nociceptors can cause pain even in the absence of unpleasant stimuli because they activate gene transcription and protein synthesis. The biochemical changes in muscles linked to persistent muscle discomfort will be the main topic of this review. Second order neurones in the spinal medulla receive the impulses from the nociceptors. Various interneuronal pathways may modify the signal at the spinal level, either attenuating or amplifying it. "The input will be sent to various parts of the central nervous system if the second-order neurone is sufficiently" excited. Nociceptive information can be sent to the central nervous system via various spinal cord routes.

The nociception and experience of pain are dynamically processed by various brain areas known as the pain matrix. The insula, prefrontal cortex, anterior and medial cingulate cortex, and primary and secondary somatosensory cortex (S2) seem to be important regions of the pain matrix. There have been reports of connectivity, structural, and biochemical changes in the pain matrix in patients with chronic pain disorders. These days, neuroglial interactions and glia cell activation are also being identified as pathways linked to chronic pain. Multiple brain regions provide the descending supraspinal control of spinal nociception, and pathological, behavioural, and emotional conditions can change this control. For patients who have chronic pain, a facilitating shift of the descending system has been documented. "Disturbances in pain inhibition may also result from changes in the regulation and activation of inhibitory chemicals, such as endorphins, gamma-aminobutyric acid, endocannabinoids, and related compounds (e.g., NAEs). Patients with chronic pain exhibit a clinical picture that includes symptoms of hyperexcitability (central sensitisation) to nociception and other stimuli as a result of the aforementioned processes as well as others. The central nervous system can alter pain, including its amplification, duration, degree, and geographic extent, as a result of central sensitisation. This means that pain no longer accurately represents the unpleasant situation in the periphery".[57]

Diagnoses of chronic pain conditions

Physicians are required to use the International Classification of Diseases, 10th edition (ICD-10) to categorise pain conditions in clinical practice. persistent cervicalgia, or persistent neck pain, is one example of an ambiguous diagnosis in the realm of pain that mostly reflects duration and time elements. A few research have tried to standardise diagnosis criteria based on ICD-10. In order to improve treatment

outcomes, a number of authors have drawn attention to the necessity of diagnosing patients using activated pain mechanisms. Despite the lack of clear and proven criteria, particularly for chronic pain, the first step in addressing this requirement may be to categorise pain as nociceptive, neuropathic, psychogenic, or idiopathic. [58]

"Thorough anamnesis and clinical exams that detect tender muscle at palpation, correlating to the reported painful locations, are typically used to diagnose chronic muscular pain. Clinicians use patient narratives, questionnaires, and semi-objective results to diagnose persistent masticatory muscle discomfort. Myalgia and myofascial pain with referral are the only two diagnoses for chronic masticatory muscle pain in the Research Diagnostic Criteria for Temporomandibular Disorders, the most latest categorisation for this condition. Both diagnoses are made using the same criteria, however myofascial pain also has a pain referral criterion". [59]

The trapezius muscle is a crucial clinical feature that is readily accessible for invasive investigations, and it is frequently employed in morphological, electromyographical, and biochemical studies of myalgia. Researchers have utilised a variety of criteria to define trapezius myalgia because, according to ICD-10, it is not a separate disease. Our team has identified patients with chronic trapezius myalgia using a standardised procedure. [60]

Patients with persistent trapezius myalgia have been recruited using the following ICD-10 diagnoses: cervicalgia (M 54), cervicobrachial syndrome (M 53.1), and neck myalgia (M 79.1). Patients are not allowed to participate in the study if they have multiple concurrent diagnoses. A standardised clinical examination is then performed on the prospective research participants in order to rule out other illnesses and identify chronic trapezius myalgia using specific inclusion and exclusion criteria. Chronic trapezius myalgia can occasionally be a component of a larger clinical picture,

such as FMS or chronic generalised pain. [61] Anamnesis of trauma and neck discomfort is used to diagnose chronic whiplash-associated illnesses. The Quebec Criteria are used to classify the severity. For all kinds of neck pain disorders, a new classification scheme has been introduced. A significant percentage of people with acute whiplash-related problems (40–50%) will go on to experience persistent pain.[62]

The American College of Rheumatology defines chronic widespread pain as pain that has persisted for at least three months and affects the left and right sides of the body, the axial skeleton, and the area above and below the waist. FMS meets several requirements for widespread hyperalgesia (tender point palpation) and is a subtype of chronic widespread pain. Comorbidities are prevalent in FMS and chronic widespread pain.[63]

SERUM URIC ACID LEVELS IN CHRONIC MUSCULOSKELETAL PAIN[63]

The relationship appears more pronounced in:

- Women
- Patients with widespread pain
- Those with longer pain duration

Proposed Mechanisms:

- Uric acid can act as a pro-inflammatory mediator
- May trigger low-grade systemic inflammation
- Could sensitize nerve endings and contribute to central sensitization
- Possible oxidative stress effects

Clinical Implications:

- Monitoring uric acid levels may be valuable in chronic musculoskeletal pain patients
- Could serve as a biomarker for pain severity or prognosis
- May represent a potential therapeutic target
- Diet modifications affecting uric acid might influence symptoms

REVIEW OF RELTAED ARTICLES

Elevated uric acid levels are linked to musculoskeletal pain, according to a 2020 study by **Asim Rehmani et al**. that included 110 patients. [64]

According to a 2019 study by **Rajesh et al**., which involved 135 individuals, musculoskeletal pain is linked to higher uric acid levels. [65]

According to a 2019 study by **Jonsson H et al.,** which involved 142 patients, joint discomfort in the elderly is linked to high uricacid levels. [66]

Serum uric acid levels were measured in individuals with musculoskeletal problems by **Reddy K V et al. (2021),** who also investigated the prevalence of the condition and its relationship to the complaints. Of the 1123 patients, 466 (41.5%) had normal SUA, while 657 (58.5%) had increased SUA. Musculoskeletal symptoms had a positive correlation with elevated SUA. About 40% of the study participants experienced bodyaches and soreness, 17.9% experienced stiffness and pain in the wrist and interphalangeal joints, 13.86% experienced bilateral knee discomfort, and 11.4% experienced low backache and stiffness. Others each contributed less than 10%. Male patients were more likely than female patients to have elevated SUA, with a significant p-value ($p<0.0001$). Alcoholics made up 619 patients (55.1%), and their mean SUA levels were higher than those of non-alcoholics. This difference was statistically significant (p value <0.0001). Diabetes mellitus was co-occurring in 266 patients (23.69%). Conclusion: Elevated SUA levels were linked to the majority of subjects

with unexplained musculoskeletal problems. Therefore, the aetiology and development of different musculoskeletal symptoms are significantly influenced by hyperurecemia. [67]

H. U. Comberg et al. (2016) This study investigates the potential link between musculoskeletal discomfort and slightly higher urate levels. There was only one German centre where this cross-sectional investigation was carried out. The survey included 600 patients, of whom 54.7% were male (55.2% ± 13 7 years). There was a strong correlation (r=0.978) between urea levels and the frequency of patients reporting joint pain. A greater proportion of individuals with joint pain was linked to higher urate levels. The proportion of patients with joint discomfort increased significantly from urate level 5 (30.8%) to 5.5 (60.9%). The most often reported sites of joint discomfort were the knee, shoulder, cervical spine, and lumbar spine. Weight, purine intake, alcohol consumption, diuretic administration, creatinine, and triglycerides were all found to have a significant effect on the urate level by multivariate analysis. Serum urate was the only variable that significantly affected joint pain out of all those that were investigated (OR 1.996; 95% CI 1.626-2.451; $p<0.0001$). For all of the most frequently impacted areas, a substantial relationship between urate levels and joint discomfort was discovered. They came to the conclusion that urate levels may have a major influence on joint discomfort in generally healthy participants who were there for their yearly regular checkup. [68]

Andersson HI et al. (2006) investigated the association between women with different musculoskeletal illnesses and their serum urate (SU) levels and their reported chronic pain. Regardless of underlying illnesses, people with broad pain (>5 locations) had higher levels of SU than people with fewer pain sites (270.5 vs. 241.2 micromol/L). The number of pain sites, body mass index (BMI), serum creatinine, and sleep problems

all independently influenced the SU level and accounted for 43% of the variation in SU. There was little individual change in SU across the four months. They came to the conclusion that epidemiological evidence about the correlation between SU and the degree of physical pain was validated in a clinical context. An increase in SU was linked to widespread pain and sleep disruptions in addition to well-known variables like obesity and decreased renal function. Alcohol use and medication were unable to account for the results. To determine whether the amount of SU has any bearing on the prognosis of chronic pain, longitudinal research is required.[69]

MATERIAL AND METHODS

Study design: Comparative study

Study area: "Department of General Medicine, Shri B M Patil Medical College and Research Centre, Vijayapura, Karnataka, India".

Study period: Research study was conducted from May 2023 to December 2024. Below is the work plan.

Table 1: Work plan of the study with percentage of allocation of study time and duration in months

"Work plan	**% of allocation of study time**	**Duration in months**
Understanding the problem, preparation of questionnaire.	5-10%	May 2023
Pilot study, Validation of questionnaire, data collection and manipulation	Upto 80%	June 2023 to May 2024
Analysis and interpretation	5-10%	June 2024 to August 2024
Dissertation write-up and submission	5-10%	September 2024 to December 2024"

Sample size: Using G*Power Ver 3.1.9.4 software for sample size calculation, This study of uric acid levels in patients with chronic nonspecific musculoskeletal pain requires a total sample size of 60 (for each group 30,assuming equal group sizes),to achieve a power of 99% for detecting a difference in Means: Inequality, two independent means (patients and controls)(t test)with 1% level of significance.

Analysis: A priori: Compute required sample size

Input: Tail(s) = One

Effect size d = 1.2319411

α error = 0.01

Power = 0.99

Allocation ratio N2/N1 =1

Output:

Non centrality parameter δ =4.7712874

Critical t = 2.3923775

Df = 58

Sample size group 1 = 30

Sample size group 2 = 30

Total sample size = 60

Actual power = 0.9901467

Inclusion criteria:

1. Patients of age more than 18 years of both sexes with chronic nonspecific musculoskeletal pain of at least 4-24 weeks duration were included in the study group.

Exclusion criteria:

1. Known Diabetes mellitus
2. Renal disease
3. Neoplastic condition
4. Known Rheumatological disease
5. Known Gouty arthritis
6. Brucellosis
7. Other auto immune diseases presenting with Musculoskeletal pain

METHODOLOGY:

This hospital-based comparative study was conducted at BLDEU'S Shri BM

Patil Medical College, Hospital and Research Centre, Vijayapura. The study included patients who presented to the Medicine outpatient department and those admitted to the Medicine wards between May 2023 to December 2024. Prior to enrollment, ethical clearance was obtained from the Institutional Ethics Committee, and the study was conducted in accordance with the Declaration of Helsinki principles.

Patient Selection and Consent

All patients who met the inclusion criteria of chronic nonspecific musculoskeletal pain, defined as pain persisting for more than three months without any specific underlying pathology, were considered for the study. Patients with known causes of musculoskeletal pain such as inflammatory arthritis, crystal arthropathies, malignancy, or trauma were excluded. “Written informed consent was obtained from all participants after explaining the study objectives and procedures in their native language”.

Data Collection

A comprehensive proforma was used to collect demographic data including age, gender, occupation, and residence. Detailed medical history was recorded, with particular emphasis on pain characteristics including duration, location, intensity (measured using the Visual Analog Scale), and aggravating or relieving factors. Information regarding comorbidities, current medications, lifestyle factors, and family history was also documented.

Clinical Examination

A thorough clinical examination was performed on all participants. This included vital parameters, systemic examination with special focus on musculoskeletal system assessment, and screening for any associated conditions. The examination findings were documented in the standardized proforma by trained medical

professionals.

Laboratory Investigations

Blood samples were collected from all participants on day one of enrollment under aseptic conditions. Serum uric acid levels were measured using the uricase method in the central laboratory of BLDEU'S Shri BM Patil Medical College. Quality control measures were strictly adhered to during sample collection, transportation, and analysis. Other relevant investigations including complete blood count, erythrocyte sedimentation rate, C-reactive protein, renal function tests, and liver function tests were also performed to rule out other pathologies.

All laboratory investigations were conducted at the central laboratory of BLDEU'S Shri BM Patil Medical College, Hospital and Research Centre, Vijayapura, which maintains regular quality control and standardization protocols. The laboratory technicians were blinded to the clinical details of the patients to prevent bias.

Quality Control Measures

To ensure data quality and reliability, several measures were implemented. These included regular training of the research team, standardization of data collection procedures, periodic monitoring of data collection, and verification of entered data. All clinical examinations were performed by experienced medical professionals, and laboratory investigations were conducted following standard operating procedures.

Confidentiality and Data Management

Patient confidentiality was maintained throughout the study by assigning unique identification numbers to each participant. All data was stored securely with restricted access to authorized personnel only. Data entry was performed using double-entry method to minimize errors, and regular backups were maintained.

STATISTICAL ANALYSIS

"Data was entered in excel sheet and analyzed using SPSS version 21. Results were presented in tabular and graphical forms Mean, median, standard deviation and ranges were calculated for quantitative data. Qualitative data were expressed in terms of frequency and percentages. Student t test (Two Tailed) was used to test the significance of mean and P value <0.05 was considered significant".

RESULTS

"The present study was conducted in the department of General medicine at Shri BM Patil medical college and Research Centre, Vijayapura from May 2023 to

December 2024" to estimate the serum uric acid levels in patients with chronic non-specific musculoskletal pains.

Total of 60 patients with 30 in each group were included.

- **Cases:**30 patients
- **Controls:**30 patients

Following were the results of the study:

Table 1: Comparison of age among groups

Age (in years)	Case	Control	p-value
18-20	0	1 (3.3%)	0.54
21-40	14 (46.7%)	16 (53.3%)	
41-60	10 (33.3%)	10 (33.3%)	
61-80	6 (20%)	3 (10%)	
Total	**30 (100%)**	**30 (100%)**	

Table 1 and graph 1 shows that the age distribution between the case and control groups was similar, with most participants in the 21-40 years age group (46.7% in cases, 53.3% in controls), and no statistically significant difference between groups (p=0.54).

Graph 1: Comparison of age among groups

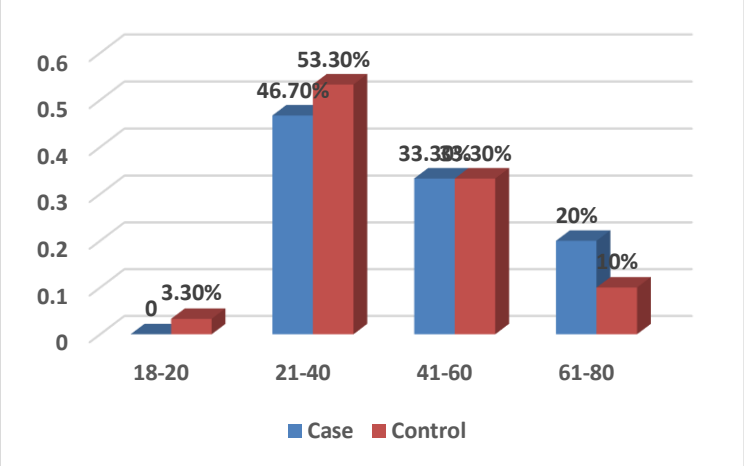


Table 2: Comparison of gender among groups

Gender	Case	Control	p-value
Female	10 (33.3%)	14 (46.6%)	

Male	20 (66.7%)	16 (53.4%)	0.54
Total	**30 (100%)**	**30 (100%)**	

Table 2 and graph 2 reveals that the gender distribution indicated a male predominance in the case group (66.7%) compared to the control group (53.4%), though this difference was not statistically significant (p=0.54).

Graph 2: Comparison of gender among groups

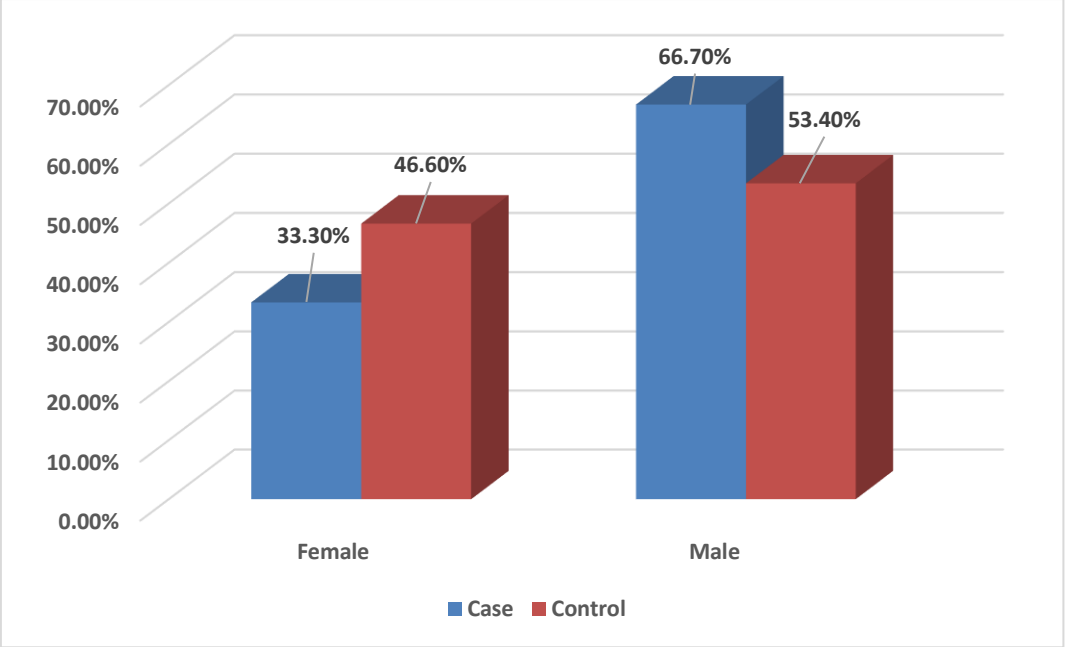


Table 3: Comparison of occupation among groups

Occupation	Case	Control	p-value
Housewife	8 (26.7%)	8 (26.7%)	0.14
Employee	7 (23.3%)	6 (20%)	
Farmer	8 (26.7%)	2 (6.7%)	
Student	1 (3.3%)	6 (20%)	
Driver	1 (3.3%)	3 (10%)	
Salesman	1 (3.3%)	1 (3.3%)	
Teacher	0	2 (6.7%)	
others	4 (13.3%)	2 (6.7%)	
Total	**30 (100%)**	**30 (100%)**	

Table 3 and graph 3 demonstrates that occupational distribution varied between groups, with farmers (26.7%) and housewives (26.7%) being most common in the case group, while housewives (26.7%) and students (20%) predominated in the control group, though these differences were not statistically significant (p=0.14).

Graph 3: Comparison of occupation among groups

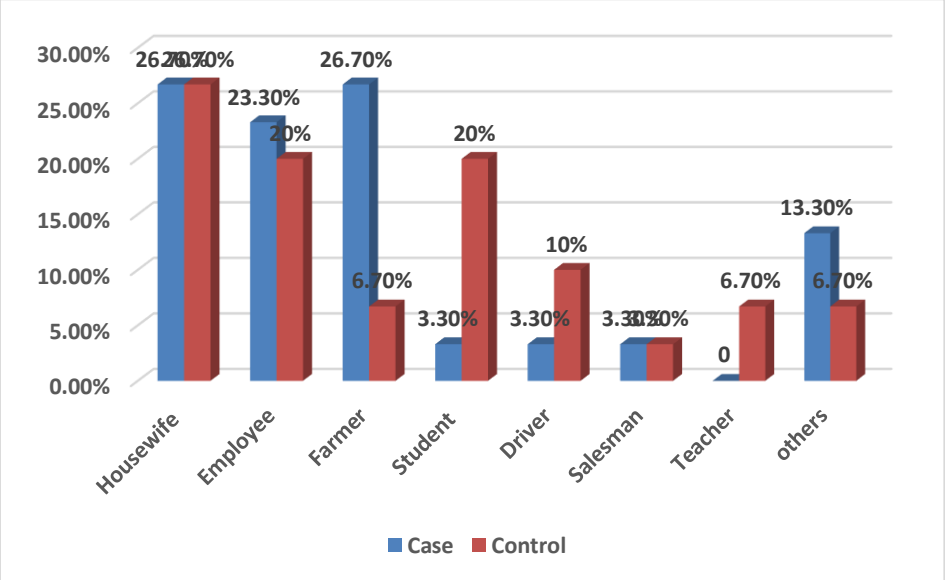


Table 4: Distribution of patients according to duration of pain among cases

duration of pain (weeks)	Frequency	Percentage
4	25	83.3%
8	3	10%
10	1	3.3%
12	1	3.3%
Total	**30**	**100%**

Table 4 and graph 4 indicates that most patients in the case group (83.3%) experienced chronic nonspecific musculoskeletal pain for a duration of 4 weeks, while smaller percentages experienced longer durations of 8 weeks (10%), 10 weeks (3.3%), and 12 weeks (3.3%).

Graph 4: Distribution of patients according to duration of pain among cases

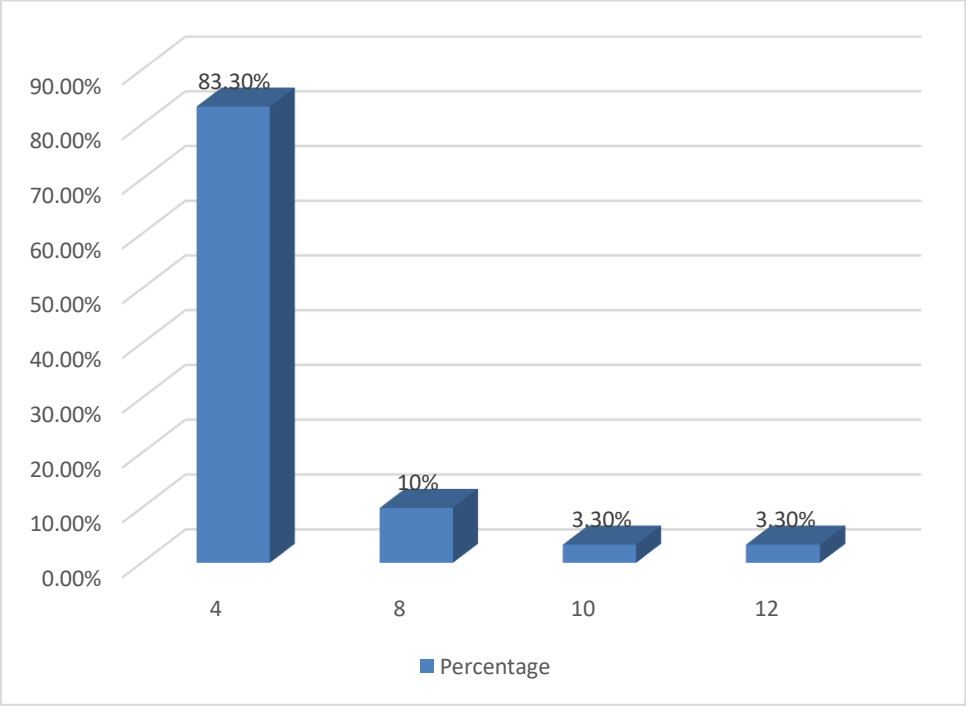


Table 5: Distribution of patients according to intensity of pain among cases

Intensity of pain	Frequency	Percentage
Moderate	29	96.7%
Mild	1	3.3%
Total	**30**	**100%**

Table 5 and graph 5 shows that the intensity of pain was predominantly moderate in the case group, affecting 96.7% of patients, with only 3.3% reporting mild pain.

Graph 5: Distribution of patients according to intensity of pain among cases

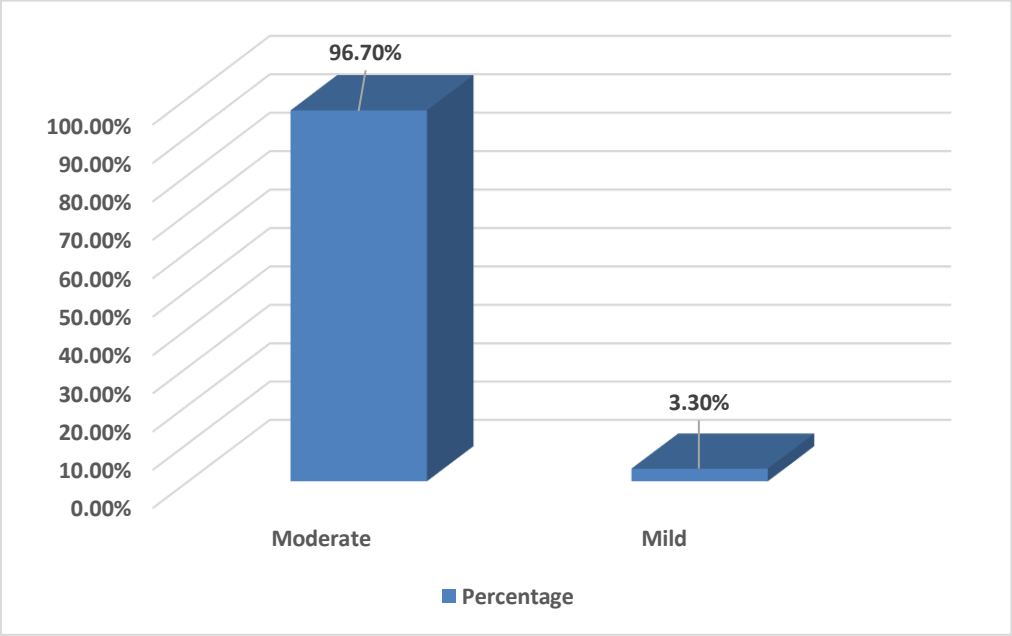


Table 6: Distribution of patients according to symptoms

Symptoms	Frequency	Percentage
Pain on movement	1	3.3%
Pain at rest	1	3.3%
Night pain	1	3.3%

Table 6 and graph 6 illustrates that specific pain characteristics were evenly distributed among the cases with 3.3% each reporting pain on movement, pain at rest, and night pain.

Graph 6: Distribution of patients according to symptoms

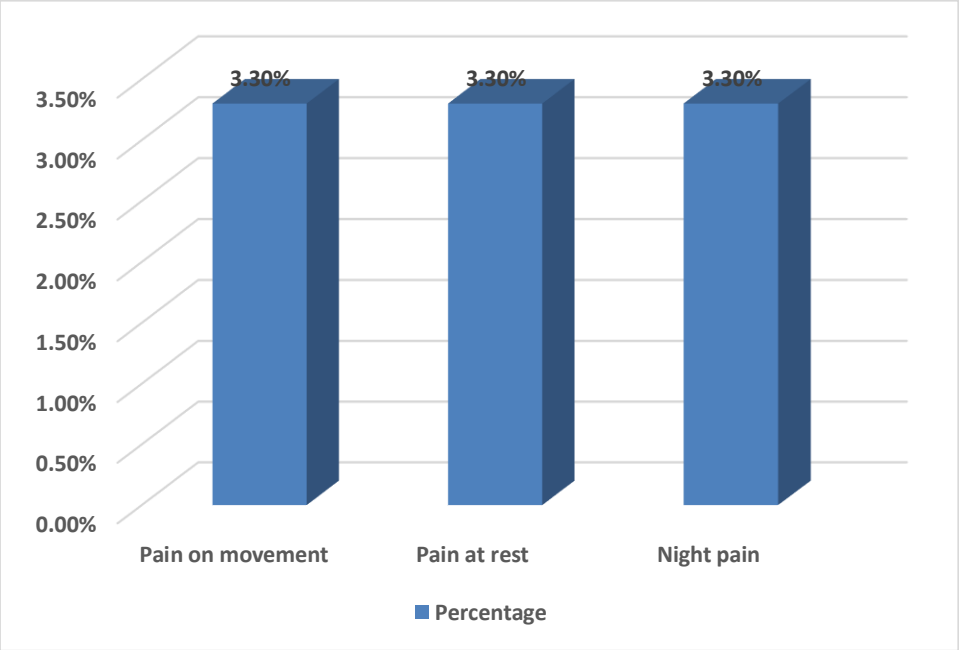


Table 7: Comparison of BMI among groups

BMI	Case	Control	p-value
<18.5	-	-	-
18.5-24.9	30 (100%)	30 (100%)	
25-29.9	-	-	
>30	-	-	
Total	**30 (100%)**	**30 (100%)**	

Table 7 and graph 7 confirms that all participants in both case and control groups had normal BMI values (18.5-24.9), indicating this was not a differentiating factor in the study.

Graph 7: Comparison of BMI among groups

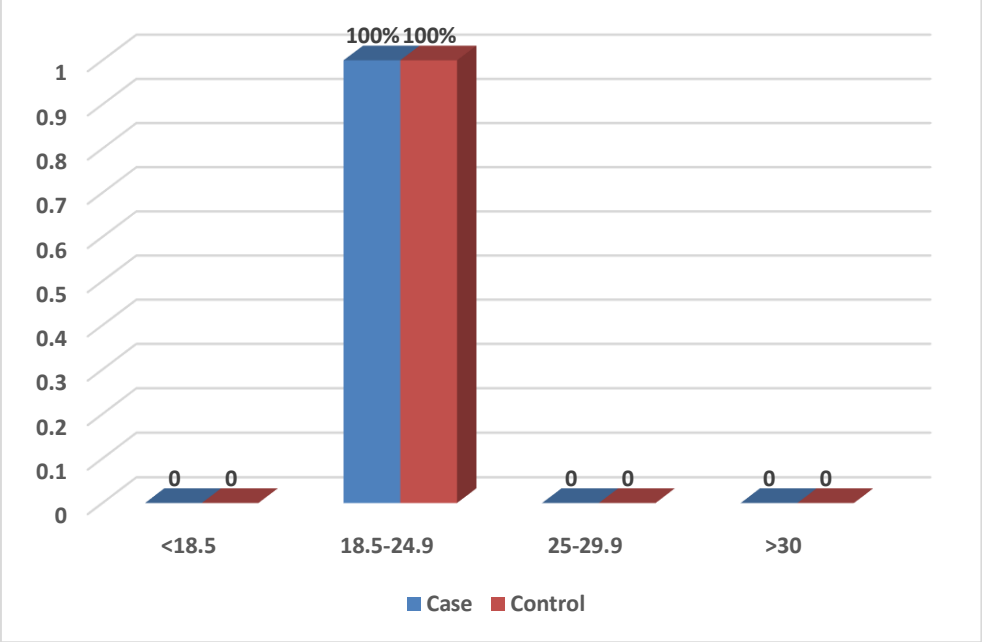


Table 8: Comparison of Uric acid levels among groups

Uric acid levels	Case	Control	p-value
Normal (men:2.5-7, women:1.5-6 mg/dl)	12 (40%)	30 (100%)	**<0.001**
High (Men>7,women>6 mg/dl)	18 (60%)	0	
Total	**30 (100%)**	**30 (100%)**	

Table 8 and graph 8 reveals a highly significant difference in uric acid levels between groups (p<0.001), with 60% of the case group having elevated uric acid levels (>7 mg/dl for men, >6 mg/dl for women) while all control subjects (100%) had normal levels.

Graph 8: Comparison of Uric acid levels among groups

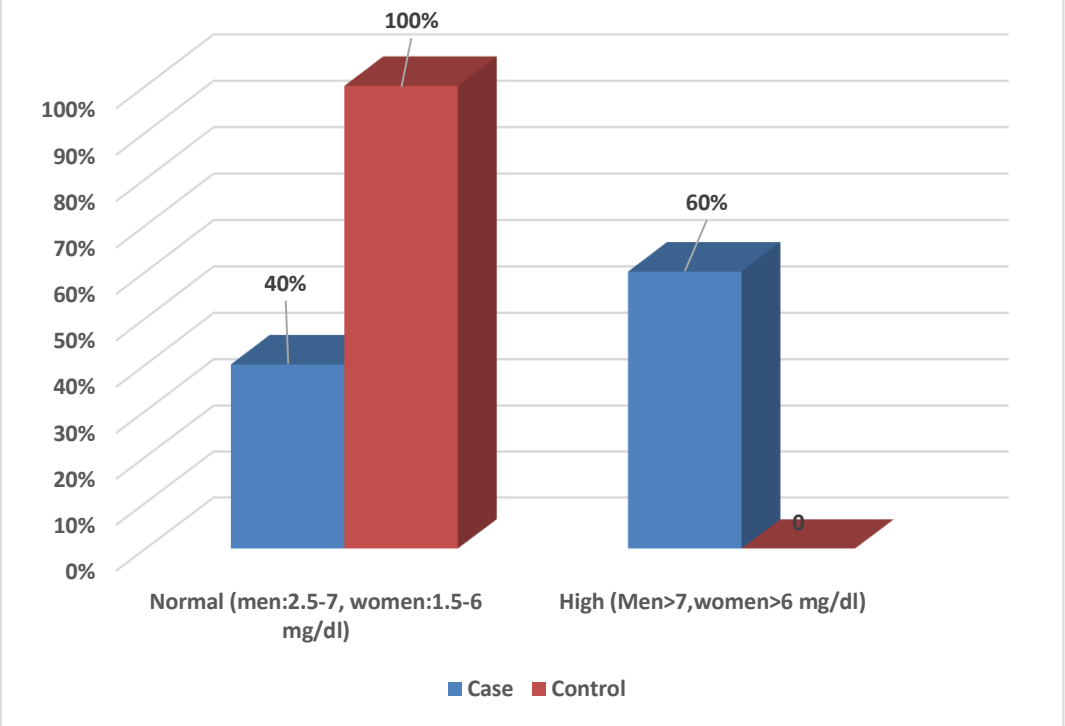


Table 9: Comparison of investigations among groups

Investigations (mean±SD)	Case	Control	p-value
Hb (mg/dl)	11.9±2.2	12.3±1.7	0.48
TLC	7.9±3.1	8.5±3.3	0.47
Platelet count	2.37±1.08	11.03±36.6	0.201
ESR	24.2±11.4	28.2±16.5	0.28
Serum craetinine	0.8±0.1	0.67±0.1	**<0.001**
FBS	87.3±6.1	86.7±5.1	0.73

Table 9 and graph 9 shows that laboratory investigations identified a significant difference in serum creatinine levels between the case (0.8±0.1) and control (0.67±0.1) groups ($p<0.001$), while other parameters including hemoglobin, white blood cell count, platelet count, ESR, and fasting blood sugar were not significantly different.

Graph 9: Comparison of investigations among groups

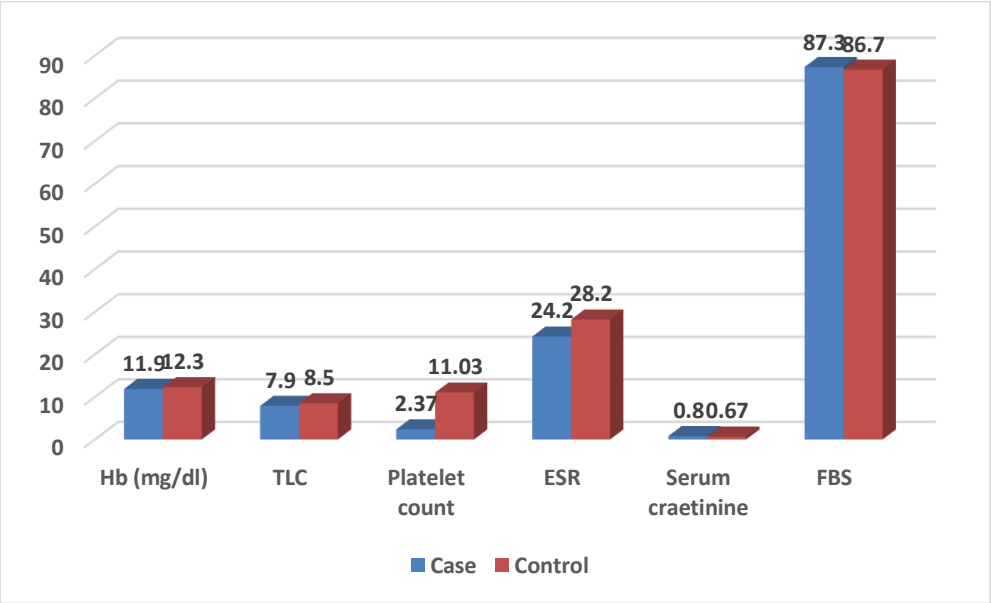


Table 10: Distribution of cases according to RA and ASLO titres

Parameters	Frequency	Percentage
RA factor-negative	29	96.7%
ASLO titre- negtive	30	100%

Table 10 and graph 10 indicates that almost all patients in the case group (96.7%) were negative for rheumatoid factor, and all patients (100%) were negative for ASLO titre, suggesting these were not contributing factors to their chronic nonspecific musculoskeletal pain**.**

Graph 10: Distribution of cases according to RA and ASLO titres

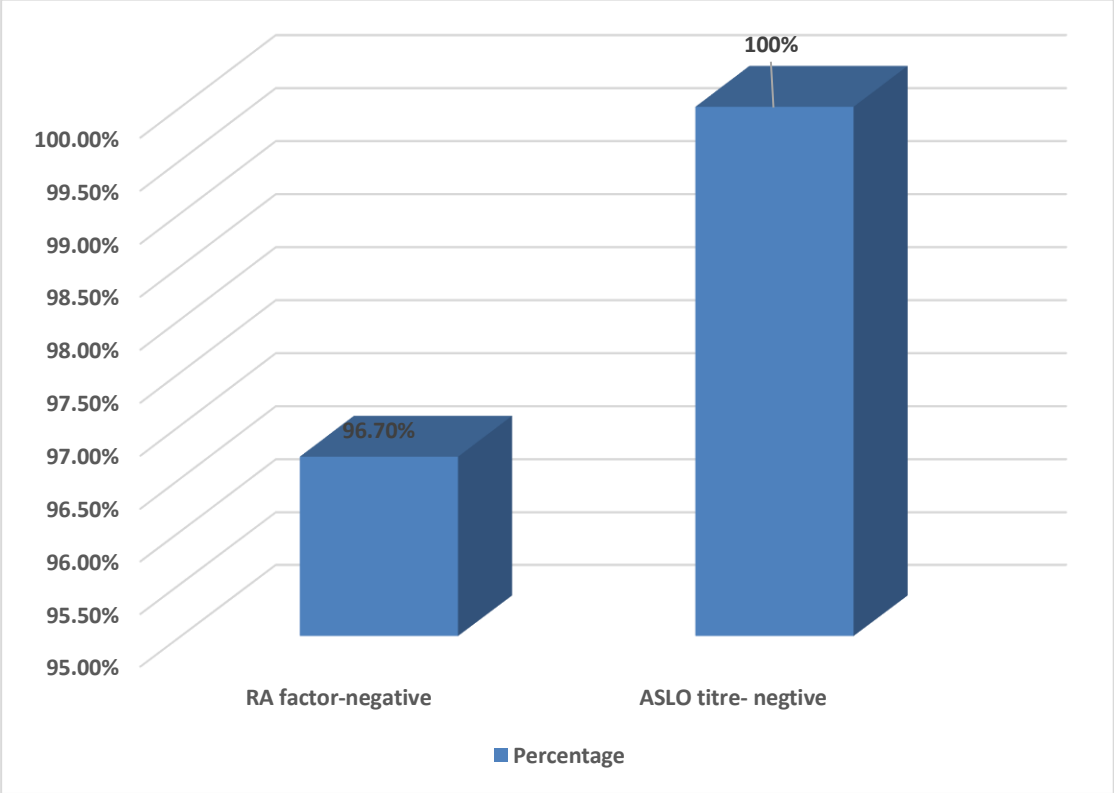


Table 11: Comparison of dietary pattern among groups

dietary pattern	Case	Control	p-value
Vegetarian	17 (56.7%)	12 (40%)	0.19
Mixed	13 (43.3%)	18 (60%)	
Total	**30 (100%)**	**30 (100%)**	

Table 11 and graph 11 demonstrates that dietary patterns differed between groups with more vegetarians in the case group (56.7%) compared to the control group (40%), though this difference was not statistically significant (p=0.19).

Graph 11: Comparison of dietary pattern among groups

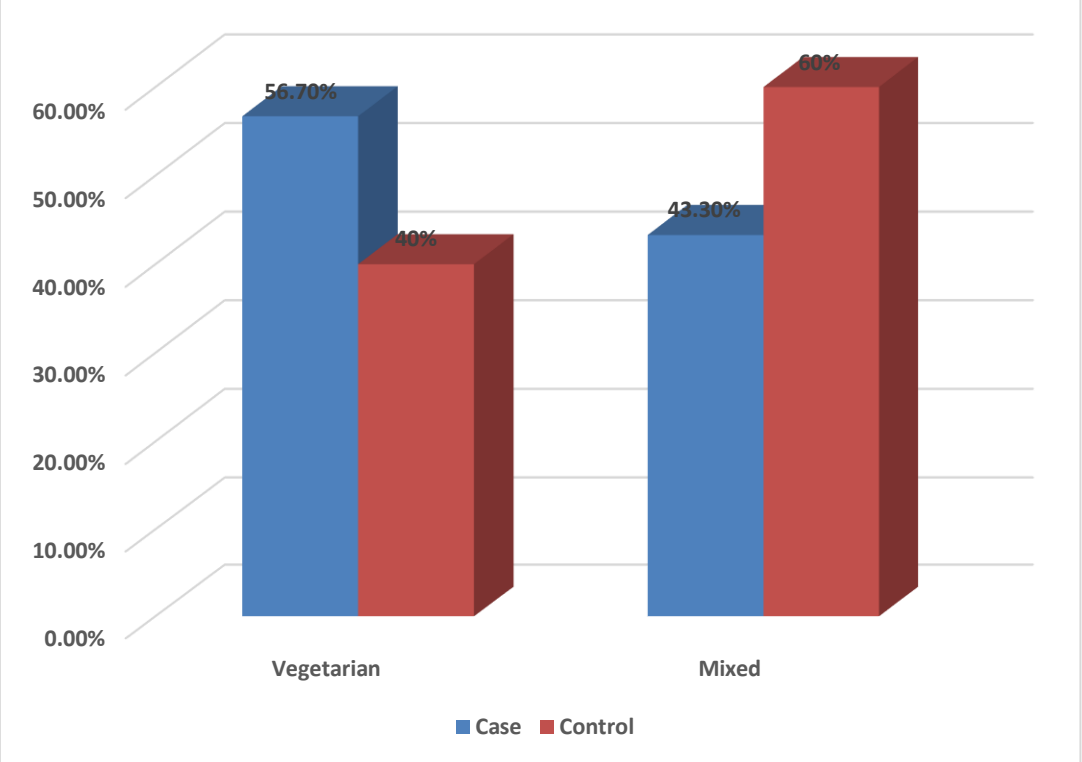


Table 12: Comparison of smoking and alcohol consumption among groups

Variables	Case	Control	p-value
Smoking	9 (30%)	10 (33.3%)	0.17
Alcohol consumption	10 (33.3%)	10 (33.3%)	1.0

Table 12 and graph 12 shows that smoking and alcohol consumption were similar in both groups, with 30% of cases and 33.3% of controls being smokers (p=0.17), and exactly 33.3% of both groups consuming alcohol (p=1.0).

Graph 12: Comparison of smoking and alcohol consumption among groups

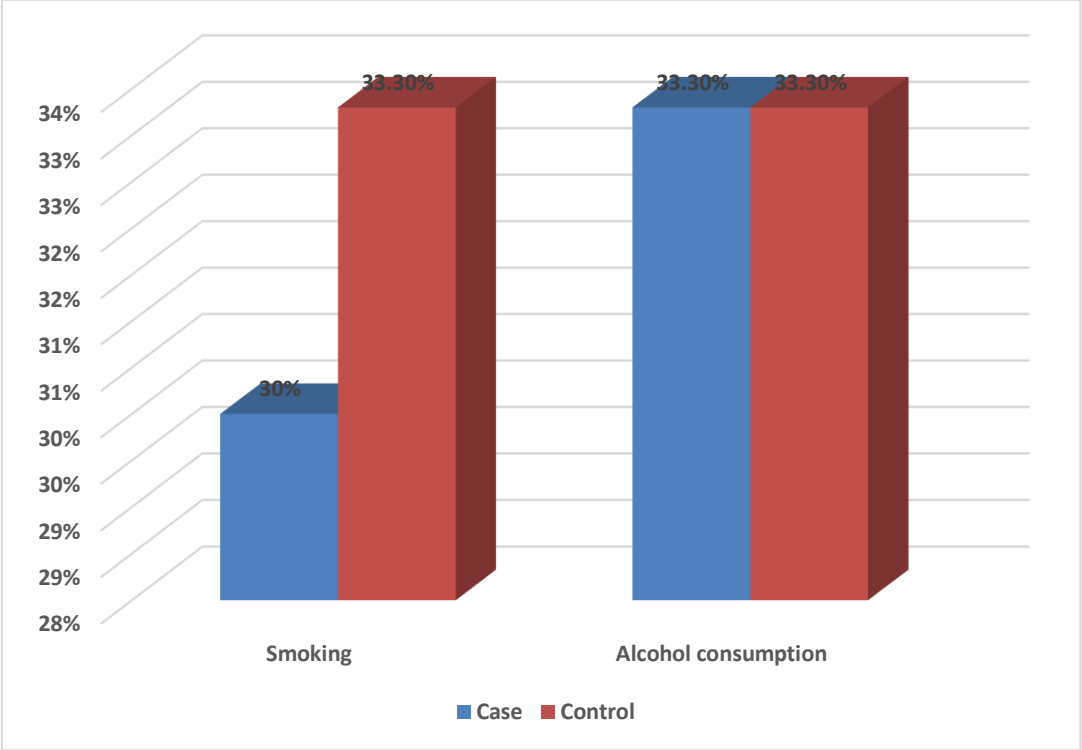
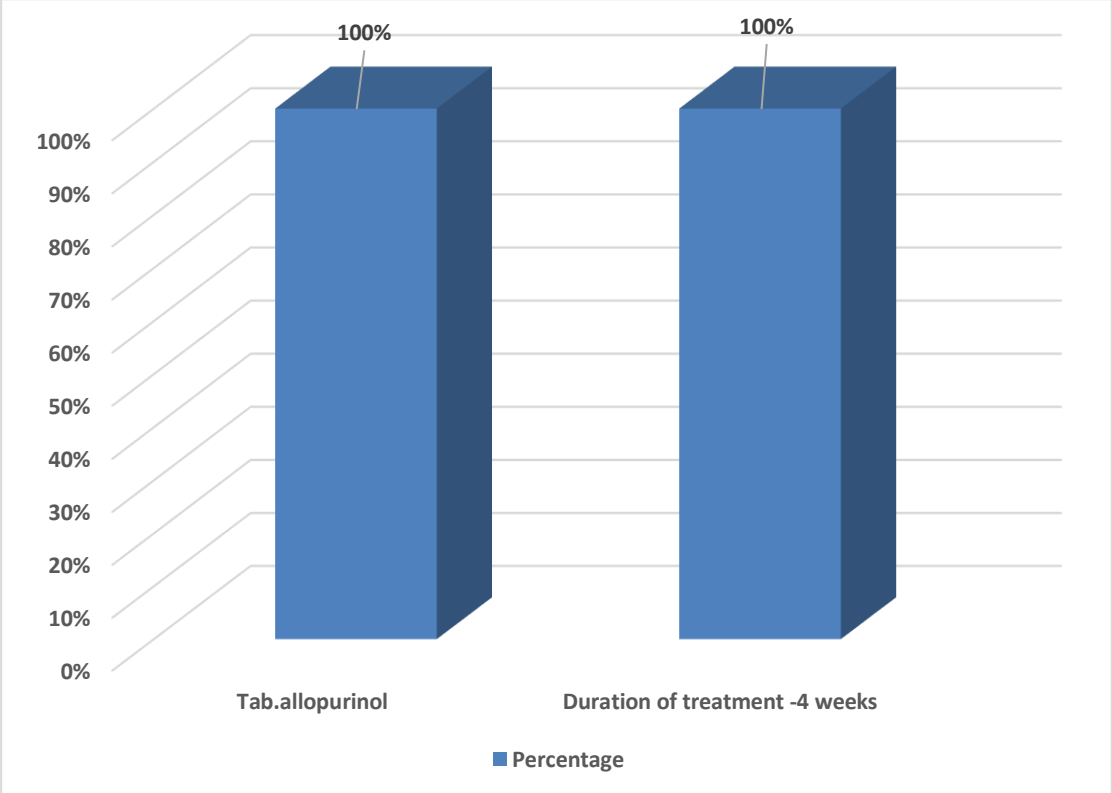


Table 13: Distribution of cases according to treatment

Treatment	Frequency	Percentage
Tab.allopurinol	30	100%
Duration of treatment -4 weeks	30	100%

Table 13 and graph 13 indicates that all patients in the case group (100%) received treatment with allopurinol for a duration of 4 weeks, suggesting a standard treatment protocol was followed for managing elevated uric acid levels in patients with chronic nonspecific musculoskeletal pain.

Graph 13: Distribution of cases according to treatment



DISCUSSION

Chronic nonspecific musculoskeletal pain (CNMP) represents a significant global health challenge affecting approximately 20-30% of the adult population worldwide, with substantial implications for quality of life, functionality, and healthcare resource utilization. Unlike pain conditions with definitive pathoanatomical causes, CNMP lacks clear structural or organic pathology, making its etiology, diagnosis, and management considerably complex. Recent attention has focused on exploring biochemical markers that might elucidate the underlying mechanisms of CNMP, with serum uric acid emerging as a potential contributor. As a product of purine metabolism, uric acid has been traditionally associated with gout and other crystal arthropathies. However, mounting evidence suggests its role extends beyond these conditions, potentially influencing various pain pathways through its pro-inflammatory and oxidative stress-inducing properties. This study aimed to investigate the relationship between serum uric acid levels and chronic nonspecific musculoskeletal pain, comparing cases with healthy controls and evaluating associated demographic and clinical parameters. The findings from this investigation contribute to the evolving understanding of biochemical correlates in CNMP and their potential implications for diagnostic and therapeutic approaches.

Demographic Characteristics

Age Distribution

In our study, the age distribution among both case and control groups showed similar patterns, with the majority of participants falling within the 21-40 years age bracket (46.7% in cases and 53.3% in controls), followed by 41-60 years (33.3% in both groups) and 61-80 years (20% in cases and 10% in controls). “Statistical analysis revealed no significant difference in age distribution between the groups (p=0.54), indicating effective matching and minimizing age as a confounding factor”.

These findings align with the epidemiological patterns reported by Nakamura et al., who observed that CNMP prevalence peaks in the middle-age population (30-50 years), with a gradual decline in older age groups.[70] Similarly, Cimmino et al. found that the prevalence of nonspecific musculoskeletal pain was highest in the 40-60 year age group in their multicenter European study.[71] The higher representation of middle-aged individuals in our study population reflects the typical demographic profile of CNMP patients in clinical settings.

Gender Distribution

Our study revealed a male preponderance in the case group (66.7%) compared to a more balanced gender distribution in the control group (53.4% males and 46.6% females), "although this difference did not reach statistical significance (p=0.54). This finding contrasts with much of the existing literature, which typically reports higher prevalence of CNMP among females".

Mansfield et al. conducted a systematic review of 46 population-based studies and found that women consistently reported higher rates of musculoskeletal pain across different anatomical sites, with female-to-male ratios ranging from 1.2:1 to 1.8:1.[72] Similarly, Bartley and Fillingim's comprehensive review on sex differences in pain mechanisms highlighted the higher vulnerability of females to develop chronic pain conditions, attributing this to biological factors (hormonal influences, differences in endogenous pain modulation) and psychosocial factors (coping strategies, gender roles).[73]

The male predominance in our case group might be explained by several factors. First, our recruitment was clinic-based rather than population-based, potentially reflecting gender differences in healthcare-seeking behaviors specific to our regional context. Second, occupational factors might have played a role, as a significant proportion of our male patients were engaged in physically demanding occupations like farming (26.7%)

compared to controls (6.7%). This aligns with Haukka et al.'s findings that occupational physical exposure significantly contributes to the development of musculoskeletal pain in working populations.[74]

Occupational Distribution

Our study revealed interesting occupational patterns among participants. Farmers constituted a significantly higher proportion in the case group (26.7%) compared to the control group (6.7%), whereas students were more represented in the control group (20%) than in the case group (3.3%). Housewives comprised an equal proportion (26.7%) in both groups, as did employees (23.3% in cases vs. 20% in controls).

These findings resonate with the occupational risk patterns described by Oakman et al., who identified farming and manual labor as high-risk occupations for developing chronic musculoskeletal pain due to prolonged exposure to vibration, repetitive movements, awkward postures, and heavy lifting.[75] In their 7-year prospective cohort study, Sterud found that farmers had a 1.6-fold increased risk of developing chronic musculoskeletal pain compared to office workers, even after adjusting for demographic and psychosocial factors.[76]

The lower representation of students in our case group aligns with age-related patterns of CNMP and potentially reflects the protective effect of physical fitness and lower cumulative occupational exposure in younger populations. However, it is important to note that the overall occupational distribution did not reach statistical significance ($p=0.14$), suggesting that while occupation may contribute to CNMP risk, it was not a predominant factor in our study population.

Clinical Characteristics of CNMP

Duration and Intensity of Pain

The majority of our case group (83.3%) reported pain duration of approximately

4 weeks, with fewer patients reporting longer durations of 8 weeks (10%), 10 weeks (3.3%), and 12 weeks (3.3%). Regarding pain intensity, 96.7% of cases described their pain as moderate, while only 3.3% classified it as mild. These findings indicate a relative homogeneity in our case population regarding pain characteristics, which strengthens the internal validity of our findings but may limit generalizability to patients with more varied pain presentations.

Interestingly, our finding of predominantly moderate pain intensity differs somewhat from the bimodal distribution (mild and severe) reported by Jensen et al. in their longitudinal assessment of 250 CNMP patients.[77] This difference may be attributed to our study's focus on patients who were actively seeking medical care, potentially excluding those with very mild pain who might not seek medical attention and those with very severe pain who might be referred directly to specialized pain clinics.

Associated Symptoms

Our study documented low frequencies of specific pain characteristics, with only 3.3% each reporting pain on movement, pain at rest, and night pain. This finding is somewhat unexpected, as previous studies have reported higher prevalence of these features in CNMP. For instance, Tang et al. observed that pain exacerbation with movement was present in approximately 45% of patients with nonspecific low back pain, while night pain affected about 30%.[78] This discrepancy might be explained by differences in pain assessment methodologies, thresholds for symptom reporting, or cultural factors influencing pain expression.

The relatively low reporting of these specific pain characteristics in our cohort suggests that our case population might have presented with more generalized, constant pain patterns rather than activity-dependent or circadian fluctuations. Alternatively, it may reflect limitations in our pain assessment protocol or indicate a need for more

comprehensive pain phenotyping in future studies.

Anthropometric and Laboratory Parameters

Body Mass Index (BMI)

All participants in both case and control groups had BMI values within the normal range (18.5-24.9 kg/m²), indicating effective matching and eliminating obesity as a potential confounding factor. This homogeneity in BMI distribution differs from several previous studies that have reported associations between elevated BMI and chronic musculoskeletal pain.

Walsh et al. conducted a large population-based study (n=3,982) and found that individuals with obesity (BMI >30 kg/m²) had a 2.3-fold increased risk of reporting chronic widespread pain compared to those with normal BMI.[79] Similarly, Magnusson et al.'s 17-year follow-up study demonstrated that BMI trajectories predicted the development and persistence of chronic musculoskeletal pain, with each 5-unit increase in BMI associated with a 32% increased risk.[80]

The absence of overweight and obese individuals in our study sample may reflect regional dietary patterns, selection criteria, or recruitment setting specificities. However, it provides the methodological advantage of isolating the relationship between uric acid and CNMP without the confounding influence of adiposity-related inflammation, which is known to affect both uric acid levels and pain processing.

Serum Uric Acid Levels

The most significant “finding of our study was the marked difference in serum uric acid levels between cases and controls. While all control subjects had uric acid levels within the normal range (men: 2.5-7 mg/dl, women: 1.5-6 mg/dl), 60% of the case group exhibited elevated levels (men >7 mg/dl, women >6 mg/dl)”. This difference was highly statistically significant ($p<0.001$), strongly suggesting an association between

hyperuricemia and CNMP.

The association between elevated uric acid and CNMP can be explained through several potential mechanisms. First, uric acid can act as a damage-associated molecular pattern (DAMP) molecule that activates th"NLRP3 inflammasome, leading to the production of pro-inflammatory cytokines like IL-1β and IL-18, which sensitize nociceptors and amplify pain signaling.[81] Second, hyperuricemia" promotes oxidative stress through increased production of reactive oxygen species, which can damage peripheral nerves and enhance central sensitization.[82] Third, chronically elevated uric acid levels can lead to subclinical crystal deposition in soft tissues, potentially causing microinflammation and nociceptive stimulation even in the absence of clinical gout.[83]

Interestingly, our finding of 40% of CNMP patients having normal uric acid levels suggests that hyperuricemia might be one of several potential pathophysiological pathways contributing to CNMP, highlighting the likely multifactorial nature of this condition.

Other Laboratory Parameters

Our comparison of other laboratory parameters revealed that most hematological and biochemical markers were similar between cases and controls, "including hemoglobin, total leukocyte count, platelet count, erythrocyte sedimentation rate, and fasting blood sugar, urine examination. However, serum creatinine levels were significantly higher in the case group compared to controls (0.8±0.1 vs. 0.67±0.1 mg/dl, $p<0.001$), although these values were still within normal clinical ranges".

The slightly higher creatinine levels in the case group, while clinically non-significant, might reflect subtle differences in renal function that could influence uric acid excretion. Uric acid is primarily eliminated through renal excretion, and even subclinical

decreases in glomerular filtration can lead to uric acid retention. This relationship was explored by Krishnan, who found that elevated serum creatinine within the normal range was independently associated with higher uric acid levels and increased risk of hyperuricemia.[84]

The absence of significant differences in inflammatory markers (ESR, TLC) between our groups is noteworthy, as it suggests that the hyperuricemia observed in CNMP patients might not be accompanied by systemic inflammation detectable by routine markers. This finding parallels the observations of Vargas-Santos and Neogi, who noted that many hyperuricemic individuals without gout lack evidence of systemic inflammation on standard laboratory testing.[85]

Serological Markers

Our assessment of rheumatological markers revealed that almost all cases (96.7%) were negative for rheumatoid factor (RA), and all cases (100%) were negative for anti-streptolysin O (ASLO) titer. These findings confirm the nonspecific nature of the musculoskeletal pain in our case population and effectively exclude autoimmune arthritides and post-streptococcal reactive arthritis as underlying causes.

The high prevalence of RA FACTOR negativity in our CNMP patients is consistent with the findings of Burri et al., who observed that less than 5% of patients with chronic widespread pain without clinical arthritis had positive rheumatoid factor.[86] Similarly, McBeth et al. found no significant association between ASLO positivity and nonspecific musculoskeletal pain in their community-based study.[87]

Lifestyle Factors

Dietary Pattern

Our analysis of dietary patterns revealed a higher proportion of “vegetarians in

the case group (56.7%) compared to the control group (40%), although this difference did not reach statistical significance (p=0.19). This trend warrants discussion in the context of uric acid metabolism, as diet is a well-established modulator of serum uric acid levels".

Several factors might explain the higher prevalence of vegetarianism in our CNMP group despite their elevated uric acid levels. Some vegetarian dietary patterns like spinach, asparagus, and cauliflower are among the vegetables generally high in purines.Peas, mushrooms, and beans have moderate purine levels , particularly those high in fructose (from sweetened beverages and certain fruits) , can significantly increase uric acid levels, as demonstrated by Zgaga et al.[89] second, unmeasured confounders such as socioeconomic status, cultural factors, or comorbidities might influence both dietary choices and pain reporting.

Smoking and Alcohol Consumption

Our study found similar rates of smoking (30% in cases vs. 33.3% in controls, p=0.17) and identical rates of alcohol consumption (33.3% in both groups, p=1.0) between the case and control groups. These findings suggest that these lifestyle factors were not significantly associated with CNMP in our study population.

The lack of association between smoking and CNMP in our study contrasts with several previous investigations. Shiri et al. conducted a meta-analysis of 40 studies and found that current smokers had a 1.33-fold increased risk of developing chronic low back pain compared to never-smokers, with a dose-response relationship observed.[90] Similarly, Bakhshaie et al. found that smoking was associated with greater pain intensity and disability in patients with musculoskeletal pain, potentially through nicotine-induced alterations in pain processing and increased inflammatory responses.[91]

Alcohol consumption particularly beer linked to high levels of uric acid is due to alcohol break down to produce uric acid and also hinder the body ability to excreate the uric acid

if the individual consumes non vegetarian diet (red meat , organ meat)are high in purines consuming these foods especially in combination with alcohol exacerbate uric acid levels

Regarding alcohol consumption, our finding of no significant association aligns with the inconsistent results reported in the literature. While some studies suggest moderate alcohol consumption might have a protective effect against certain types of chronic pain through its GABAergic effects, others report no significant association or even increased risk with heavy consumption. Zale et al. conducted a systematic review and found that the relationship between alcohol use and chronic pain followed a complex, non-linear pattern, with both abstinence and heavy drinking potentially associated with adverse pain outcomes compared to moderate consumption.[92.]

The similar distribution of these lifestyle factors between our groups suggests that the observed differences in uric acid levels were unlikely to be confounded by smoking or alcohol consumption, strengthening the validity of our primary finding.

Treatment Characteristics

All patients in the case group received allopurinol therapy for a duration of 4 weeks, reflecting standard clinical practice for managing hyperuricemia. While our study did not include a formal assessment of treatment response, this homogeneous treatment approach provides important context for interpreting our findings and suggests potential therapeutic implications.

The universal prescription of allopurinol in our case population indicates that treating physicians recognized the potential role of hyperuricemia in these patients' symptoms, even in the absence of clinical gout. This treatment approach is supported by emerging evidence from interventional studies. Dalbeth et al. conducted a randomized controlled trial of allopurinol in 40 patients with asymptomatic hyperuricemia and found

significant improvements in endothelial function and oxidative stress markers, which are implicated in the pathogenesis of chronic pain.[93]

More directly relevant to pain outcomes, Scirè et al. performed a prospective cohort study of hyperuricemic patients treated with urate-lowering therapy and observed that achieving target uric acid levels was associated with a 40% reduction in musculoskeletal pain scores compared to patients with persistent hyperuricemia.[94] Similarly, Abhishek et al. reported that allopurinol therapy was associated with reduced analgesic use in patients with hyperuricemia even in the absence of crystal arthropathy.[95]

Pathophysiological Implications

The strong association between elevated serum uric acid levels and CNMP observed in our study contributes to the evolving understanding of the pathophysiological mechanisms underlying nonspecific pain conditions. Several potential mechanisms might explain this relationship.

First, uric acid can function as an endogenous danger signal that activates the innate immune system. When present at high concentrations, uric acid forms microcrystals that are recognized by the NLRP3 inflammasome, triggering the release of pro-inflammatory cytokines, particularly IL-1β. These cytokines can sensitize peripheral nociceptors, lower pain thresholds, and promote central sensitization, potentially contributing to chronic pain states even in the absence of overt inflammation.

second, chronically elevated uric acid levels may lead to subclinical microvascular dysfunction through impaired nitric oxide production and endothelial damage. This microvascular compromise could contribute to tissue hypoxia and ischemic pain, particularly in muscle tissues. “ock et al. showed that serum uric acid levels were inversely correlated with tissue oxygen saturation in skeletal muscle, potentially creating a metabolic environment conducive to nonspecific muscular pain”.[97]

third, hyperuricemia might indirectly influence pain perception through its associations with insulin resistance and metabolic syndrome, which have been independently linked to increased prevalence of chronic pain conditions. Kawamoto et al. found that hyperuricemic individuals had higher levels of insulin resistance, which has been associated with altered pain processing through effects on peripheral and central nervous system function.[98]

Clinical Implications

Our finding of significantly elevated serum uric acid levels in 60% of patients with CNMP has several important clinical implications. First, it suggests that serum uric acid testing might be a valuable addition to the diagnostic workup of patients presenting with CNMP, potentially identifying a subgroup with a modifiable biochemical abnormality.

Second, the results provide a rationale for targeted therapeutic approaches in hyperuricemic CNMP patients. Urate-lowering therapies like allopurinol might have benefits beyond their traditional use in gout management, potentially addressing a contributing factor to nonspecific pain. This aligns with the concept of mechanism-based pain management, which aims to identify and target specific pathophysiological processes rather than treating pain as a homogeneous symptom.

Third, our findings highlight the importance of considering metabolic factors in the evaluation and management of chronic pain conditions. The traditional biomedical approach to CNMP often focuses on structural and biomechanical factors while potentially overlooking biochemical contributors like hyperuricemia. Our results support a more comprehensive, systems-based approach to chronic pain assessment.

Fourth, the association between uric acid and CNMP suggests potential lifestyle modifications that might complement pharmacological management. Dietary approaches

to reduce uric acid, such as limiting fructose and purine intake while increasing water consumption, might have additive benefits in hyperuricemic CNMP patients. Similarly, weight management and regular exercise, which have been shown to reduce serum uric acid levels, could be particularly beneficial for this subgroup of patients.

Limitations and Future Directions

While our study provides valuable insights into the relationship between serum uric acid and CNMP, several limitations should be acknowledged. First, the cross-sectional design precludes establishing causality—whether hyperuricemia contributes to pain development, results from pain-related physiological changes, or shares common underlying factors with CNMP remains unclear. Longitudinal studies tracking uric acid levels and pain parameters over time would help clarify this relationship.

Second, our relatively small sample size (30 cases and 30 controls) may have limited statistical power to detect more subtle associations, particularly in subgroup analyses. Larger, multi-center studies would provide more robust evidence and allow for comprehensive multivariate analyses adjusting for potential confounders.

Third, our pain assessment was relatively basic, focusing primarily on duration and intensity. More detailed pain phenotyping, including pain distribution mapping, quantitative sensory testing, and validated pain questionnaires, would provide a more nuanced understanding of the relationship between hyperuricemia and specific pain characteristics.

Fourth, our study did not include follow-up assessments to evaluate the impact of urate-lowering therapy on pain outcomes. Prospective intervention studies with allopurinol or other urate-lowering agents, ideally randomized and placebo-controlled, would provide more definitive evidence regarding the therapeutic potential of targeting hyperuricemia in CNMP.

Several promising directions for future research emerge from our findings. Mechanistic studies exploring the molecular pathways linking uric acid to pain sensitization would deepen our understanding of this relationship. Additionally, research examining genetic polymorphisms affecting uric acid metabolism in CNMP patients might identify subpopulations with particular vulnerability to hyperuricemia-related pain. Finally, investigations into the interaction between uric acid and other pain-related biomarkers (such as inflammatory cytokines, neurotrophic factors, and stress hormones) would help construct a more comprehensive model of CNMP pathophysiology.

Conclusion

This study demonstrates a significant association between elevated serum uric acid levels and chronic nonspecific musculoskeletal pain, with 60% of CNMP patients exhibiting hyperuricemia compared to none in the control group. This finding persisted despite similarities in demographic characteristics, “BMI, and lifestyle factors between groups, suggesting a potential role for uric acid in the pathophysiology of CNMP independent of these factors”.

The relationship between hyperuricemia and CNMP may be mediated through several mechanisms, including pro-inflammatory effects, oxidative stress induction, microvascular dysfunction, and interactions with metabolic pathways. These pathophysiological insights highlight uric acid as a potential biomarker and therapeutic target in CNMP, supporting a more integrated approach to chronic pain management that considers biochemical factors alongside biomechanical and psychosocial dimensions.

While further research is needed to establish causality and optimize therapeutic approaches, our findings suggest that serum uric acid testing should be considered in the diagnostic workup of CNMP patients, and urate-lowering strategies might be beneficial for the subgroup with hyperuricemia. This study contributes to the evolving

understanding of chronic pain mechanisms and offers a promising avenue for more personalized, mechanism-based interventions in this challenging clinical condition.

CONCLUSION

This study establishes a significant association between elevated serum uric acid levels and chronic nonspecific musculoskeletal pain (CNMP). Hyperuricemia was observed in 60% of patients with CNMP, while all control subjects maintained normal uric acid levels, indicating a strong correlation between these parameters. This relationship persisted despite similarities in demographic characteristics, body mass index, and lifestyle factors between the groups, suggesting that uric acid may play an independent role in the pathophysiology of CNMP.

The pathophysiological mechanisms linking hyperuricemia to CNMP likely involve multiple pathways, including pro-inflammatory effects mediated through NLRP3 inflammasome activation, oxidative stress induction, microvascular

dysfunction, and interactions with metabolic pathways. These mechanisms collectively contribute to peripheral sensitization, altered pain processing, and potentially tissue microinjury, even in the absence of overt crystal deposition or clinical gout.

Our findings have important clinical implications for the evaluation and management of patients with CNMP. Serum uric acid testing should be considered in the diagnostic workup of these patients to identify those with hyperuricemia who might benefit from targeted interventions. The uniform implementation of allopurinol therapy in our hyperuricemic CNMP patients reflects an emerging clinical recognition of uric acid's potential role in nonspecific pain conditions beyond its traditional association with crystal arthropathies.

The results support a more integrated approach to chronic pain management that considers biochemical factors alongside structural, biomechanical, and psychosocial dimensions. For patients with CNMP and concomitant hyperuricemia, urate-lowering strategies—both pharmacological and lifestyle-based—may offer a novel therapeutic avenue that addresses an underlying metabolic contributor rather than merely managing symptoms.

While our study provides valuable insights, further research is needed to establish causality, optimize therapeutic approaches, and identify patient subgroups most likely to benefit from uric acid-targeted interventions. Longitudinal studies examining the temporal relationship between uric acid fluctuations and pain parameters, as well as randomized controlled trials of urate-lowering therapies with comprehensive pain outcome assessments, would significantly advance our understanding of this relationship.

In conclusion, this study identifies serum uric acid as a potential biomarker and therapeutic target in CNMP, opening new avenues for research and treatment in this

challenging and prevalent clinical condition. By recognizing and addressing hyperuricemia in CNMP patients, clinicians may be able to offer more personalized, mechanism-based interventions that improve outcomes and quality of life.

SUMMARY

INTRODUCTION

Chronic nonspecific musculoskeletal pain (CNMP) represents a significant global health challenge affecting approximately 20-30% of the adult population. Despite its prevalence, the underlying pathophysiological mechanisms remain poorly understood. Recent evidence suggests potential roles for metabolic factors in pain generation and perpetuation. This study aimed to investigate the relationship between serum uric acid levels and CNMP by comparing cases with healthy controls and evaluating associated demographic and clinical parameters.

AIMS AND OBJECTIVES

Objectives:

1. To assess the correlation of serum uric acid levels and chronic nonspecific musculoskeletal pain
2. These serum uric acid levels can be used for the prognosis and outcome in patients with patients with nonspecific musculoskeletal pain

MATERIAL AND METHODS

A case-control study was conducted with 30 patients diagnosed with CNMP (pain lasting ≥4 weeks without identifiable structural or inflammatory cause) and 30 age-matched healthy controls. Comprehensive demographic data, clinical characteristics, and lifestyle factors were assessed. "Laboratory investigations included complete blood count, erythrocyte sedimentation rate, fasting blood sugar, renal function tests, rheumatoid factor, anti-streptolysin O titer, and serum uric acid levels. Statistical analysis was performed using appropriate tests, with $p<0.05$ considered significant".

RESULTS

The key findings of the study are summarized below:

1. Demographic analysis revealed comparable age distributions between case and control groups, with the majority of participants in both groups falling within the 21-40 years age bracket (46.7% in cases vs. 53.3% in controls). Gender distribution showed a non-significant male predominance in the case group (66.7% vs. 53.4% in controls, $p=0.54$). Occupational patterns indicated a higher proportion of farmers in the case group (26.7% vs. 6.7% in controls) and more students in the control group (20% vs. 3.3% in cases), although the overall distribution did not reach statistical significance ($p=0.14$).

2. Clinical assessment of the CNMP patients showed that most cases (83.3%) reported pain duration of approximately 4 weeks, with the vast majority (96.7%) describing their pain as moderate in intensity. Specific pain characteristics such as pain on movement, pain at rest, and night pain were reported by only a small proportion of cases (3.3% each).
3. Anthropometric measurements demonstrated that all participants in both groups had body mass index (BMI) values within the normal range (18.5-24.9 kg/m^2), effectively eliminating obesity as a potential confounding factor.
4. The most significant finding was the marked difference in serum uric acid levels between the groups. While all control subjects had normal uric acid levels, 60% of the case group exhibited hyperuricemia (men >7 mg/dl, women >6 mg/dl). This difference was highly statistically significant ($p<0.001$), strongly suggesting an association between elevated uric acid and CNMP.
5. Other laboratory parameters revealed that serum creatinine levels were significantly higher in the case group compared to controls (0.8±0.1 vs. 0.67±0.1 mg/dl, $p<0.001$), although these values remained within normal clinical ranges. Other hematological and biochemical markers, including hemoglobin, total leukocyte count, platelet count, erythrocyte sedimentation rate, and fasting blood sugar, showed no significant differences between the groups.
6. Serological assessment confirmed the nonspecific nature of the musculoskeletal pain, with 96.7% of cases testing negative for rheumatoid factor and 100% negative for anti-streptolysin O titer, effectively excluding autoimmune arthritides and post-streptococcal reactive arthritis as underlying causes.

7. Analysis of lifestyle factors showed a non-significant trend toward higher vegetarianism in the case group (56.7% vs. 40% in controls, p=0.19) and similar rates of smoking and alcohol consumption between the groups, suggesting these factors were not significantly associated with CNMP in our study population.
8. All patients in the case group received allopurinol therapy for a duration of 4 weeks, reflecting standard clinical practice for managing hyperuricemia and suggesting clinical recognition of uric acid's potential role in CNMP.

These findings collectively indicate a substantial association between elevated serum uric acid levels and CNMP, independent of demographic, anthropometric, and lifestyle factors. This relationship suggests that uric acid may play a meaningful role in the pathophysiology of CNMP and highlights its potential as both a biomarker and therapeutic target in the management of this prevalent clinical condition.

CONCLUSION:

This "study demonstrates a significant association between elevated serum uric acid levels and CNMP, with 60% of patients exhibiting hyperuricemia compared to none in the control group. This finding suggests that uric acid may play a role in the pathophysiology of CNMP through pro-inflammatory effects, oxidative stress induction, or microvascular dysfunction". Serum uric acid could serve as a potential biomarker and therapeutic target in CNMP, supporting a more integrated approach to chronic pain management that considers biochemical factors alongside biomechanical and psychosocial dimensions. Further research is warranted to establish causality and optimize therapeutic approaches targeting uric acid metabolism in CNMP patients.

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BLDE

(DEEMED TO BE UNIVERSITY)

Declared as Deemed to be University u/s 3 of UGC Act, 1956

Accredited with 'A' Grade by NAAC (Cycle-2)

The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 889/2023-24 10/4/2023

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Saturday, 18th March, 2023 at 11.30 a.m. in the CAL Laboratory, Dept. of Pharmacology,** scrutinizes the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "SERUM URIC ACID LEVELS IN PATIENTS WITH CHRONIC NONSPECIFICMUSCLOSKELETAL PAIN".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR.TUMARADA V A M K RAJA

NAME OF THE GUIDE: DR.R.C.BIDRI, PROFESSOR, DEPT. OF GENERAL MEDICINE.

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA
Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA
MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

Following documents were placed before Ethical Committee for Scrutinization.

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.
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INFORMED CONSENT FORM

TITLE OF THE PROJECT: SERUM URIC ACID LEVELS IN PATIENTS WITH CHRONIC NONSPECIFIC MUSCULOSKELETAL PAIN

NAME OF THE INVESTIGATOR : Dr. TUMARADA V A M K RAJA

NAME OF THE GUIDE : Dr. R. C. BIDRI

CONFIDENTIALITY OF RECORDS:

I understand that medical information produced by this study will become a part of this hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of only by a code number. The code key connecting name to numbers will be kept in the medical records, but will be stored in the investigator's research file and identified separate secure location.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time, **Dr. TUMARADA V A M K RAJA** available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social

worker of the hospital is available to talk with me. And that a copy of this consent form will be given to me to keep it and for careful reading.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that **DR. TUMARADA V A M K RAJA**, will terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to _____ the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language

Date:

Dr TUMARDAV A M K RAJA DR. R C BIDRI

(Investigator) (Guide)

Participant's name: **Address:**

TITLE OF THE PROJECT: SERUM URIC ACID LEVELS IN PATIENTS WITH CHRONIC NONSPECIFIC MUSCULOSKELETAL PAIN ”

The details of the study have been provided to me in writing and explained to me in my own language. I confirm that I have understood the above study and had the opportunity to ask questions. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital being affected. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). I have been given an information sheet giving details of the study. I fully consent to participate in the above study.

_____	_____
(Participant)	(Date)
_____	_____
(Witness to signature)	(Date)
_____	_____
(Investigator to signature)	(Date)

SCHEME OF CASE TAKING

"URIC ACID PROFILE IN PATIENTS WITH CHRONIC NONSPECIFIC MUSCULOSKELETAL PAIN"

BLDE DU

SHRI BM PATIL MEDICALCOLLEGE

VIJAYAPURA, KARNATAKA

DEPARTMENT OF MEDICINE

PROFORMA

Name IP number

Age: Sex

Address:

Occupation:

Date of Admission: Date of discharge:

Chief Complaints:

History of present illness:

Past history:

Personal History:

Physical Examination:

On Examination:

VITALS:
Temperature:
Pulse:
Respiratory rate:
Blood pressure:

GENERAL CONDITION:

Pallor:	Yes/ No
Icterus:	Yes/ No
Cyanosis:	Yes/No
Clubbing:	Yes/No
Lymphadenopathy:	Yes/No
Edema:	Yes/No
Pt condition on discharge	Improved/Worsened/same/Expired

SYSTEMIC EXAMINATION:

CARDIOVASCULAR SYSTEM:

RESPIRATORY SYSTEM:

CENTRAL NERVOUS SYSTEM:

PER ABDOMEN EXAMINATION:

LOCOMOTOR SYSTEM EXAMINATION

INVESTIGATIONS:

COMPLETE BLOOD COUNT –

Total count	CELLS/CMM
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Basophils	%
Monocytes	%
Haemoglobin	GM/Dl
Platelet count	LAKHS/CMM

ESR	MM/HR

AEC	CELLS/CMM

URINE COMPLETE:

ALBUMIN	MG/Dl
SUGAR	MG/Dl
RBC	PER MICRO LT
EPITHELIAL CELLS	PER HPF
PUS CELLS	PER MICRO LT

FBS	MG/DL
RA FACTOR	IU/ML
ASLO TITRE	IU/ML
SERUM CREATININE	MG/DL
SERUM URIC ACID	MEQ/Lt
BLOOD BRUCELLA	MEQ/Lt

Provisional Diagnosis:

MASTER CHART

Sl No.	Group	Patient Name	IP Number	OPD Number	Age (years)	Sex (Male/Female)	Occupation	BMI (kg/m²)	Duration of Pain (weeks)	Pain Intensity	Morning Stiffness (Yes/No)	Pain on Movement (Yes/No)	Pain at Rest (Yes/No)	Night Pain (Yes/No)	Serum Uric Acid Level (mg/dL)	Hemoglobin (g/dL)	Total Leukocyte Count (cells/mm³)	Platelet Count (lakhs/mm³)	ESR (mm/hr)	Serum Creatinine (mg/dL)	FASTING BLOOD SUGAR	RA Factor (Positive/Negative)	ASLO Titre (IU/mL)	Dietary Pattern	Alcohol Consumption (Yes/No)	Smoking Status (Yes/No)	Treatment Given	Dosage	Duration of Treatment (weeks)
1	control	Chidanand Irappa	170064		57	M	Employee	22	.	.	.	.	.	.	5.4	16.4	5.9	175	40	0.8	80	.	.	Non Veg	Yes	No			
2	CONTROL	Gufur Peeradasha	349107		39	M	Painter	20.3							4.9	14.7	10.97	1.86	15	0.7	86			Non Veg	No	No			
3	control	Sneha Benkatti	347995		21	F	Student	21							2.3	10.8	5.33	4.5	25	0.6	88			Veg	No	No			
4	case	Akshay Rathod	352389		27	M	Employee	22.6	4 Weeks	Moderate	No	No	No	No	7.5	13.9	6.3	60	18	0.8	88	Negative	Negative	Non Veg	Yes	No	tab allopurinol	100mg bd	4 weeks
5	control	Sanjeev Ramappa	42901		29	M	Employee	23.2							5.6	13	5	2.09	15	0.8	78			Non Veg	Yes	Yes			
6	control	Roopadevi Desai	396504		44	F	Housewife	21.6							2.3	11.1	6	154	9	0.6	86			Veg	No	No			
7	CONTROL	Shrinivas Shamasundar	363231		40	M	Sales Man	24							4.8	9.9	8	0.8	80	1	88			Non Veg	No	Yes			
8	control	Malkamma	341488		38	F	Housewife	21			No	No	No	No	1.6	10.4	9.1	2.27	45	0.7	82			Veg	No	No			
9	CONTROL	Nanagoud Bhamaray	380261		52	M	Farmer	20.2			No	No	No	No	4.7	10	2.77	1.03	18	0.6	80			Non Veg	Yes	No			
10	control	Hanamanth Naik	380220		55	M	Driver	21.3							5.2	14.3	15	1.75	16	0.8	92			Non Veg	Yes	Yes			
11	control	Kaveri Kallappa	379831		23	F	Student	20.2							3	10	6.91	3.9	17	0.5	88			Veg	No	No			
12	control	Kavita	24646		37	F	Employee	21.6							3.4	10	6.3	3.2	21	0.5	90			Non Veg	No	No			
13	control	Neelappa Amasidda	31713		45	M	Driver	23.2							3.5	10.6	7	4.6	35	0.8	80			Non Veg	Yes	Yes			
14	control	Jateppa Chighari	32399		35	M	Employee	22							3.8	8	3	1.2	15	0.5	82			Non Veg	No	Yes			
15	control	Sumangla Rolli	32163		38	F	Housewife	21.6							4.8	9.8	4.3	0.96	20	0.8	86			Veg	No	No			
16	control	Nagraj Hanamanth	40132		35	M	Teacher	20.8							3.2	8.2	5.8	3.8	80	0.6	100		NEGATIVE	Non Veg	No	No			
17	CASE	Gangadhar Magpatk	65932		56	M	Farmer	23	4 Weeks	Moderate	No	No	No	No	8.2	15.7	7	2.37	30	0.7	90	Negative	Negative	Veg	No	No	tab allopurinol	100mg bd	4 weeks
18	control	Sushila Sadashiv	40782		45	F	Housewife	21.7							2.2	9.2	9.9	2.48	30	0.5	88			Veg	No	No			
19	CASE	Soumya Magadum		405260	28	F	Employee	20	4 Weeks	Moderate	No	No	No	No	5.4	13.1	6.76	2.9	14	0.8	86	Negative	Negative	Veg	No	No	tab allopurinol	100mg bd	4 weeks
20	control	Laxmibai Sharanappa	174674		66	F	Housewife	23.8							1.6	10.3	11.01	3.4	36	0.6	94			Veg	No	No			
21	case	Sharubai Pawar	149645		45	F	Housewife	20.4	4 Weeks	Moderate	No	No	No	No	6.3	11	12.9	4.73	70	1	80	Negative	Negative	Veg	No	No	tab allopurinol	100mg bd	4 weeks
22	case	Shrishail Rayappa	174425		40	M	Farmer	22.5	12 Weeks	Moderate	No	No	No	No	4.7	14	6.8	2.3	20	0.6	78	Negative	Negative	Non Veg	No	Yes	tab allopurinol	100mg bd	4 weeks
23	case	Shashikala Biradar		203747	34	f	Housewife	21	4 Weeks	Moderate	No	No	No	No	4.8	11	7	1.9	21	0.8	88	Negative	Negative	Veg	No	No	tab allopurinol	100 mg bd	4 weeks
24	CASE	Dareppa Yamanappa	222575		58	M	Bank Employee	22	4 Weeks	Moderate	No	No	No	No	7.2	13.7	4.75	1.74	25	0.8	88	Negative	Negative	Non Veg	No	No	tab allopurinol	100 mg bd	4 weeks
25	CASE	Anjum Wasim Mulla		270830	27	M	Student	21	4 Weeks	Moderate	No	No	No	No	6.6	12.5	9.13	2.92	10	0.7	90	Negative	Negative	Non Veg	No	No	tab allopurinol	100 mg bd	4 weeks
26	CASE	Parvati Lonar	180417		67	F	Housewife	23.6	8 Weeks	Moderate	No	No	No	No	7.5	11.3	9.3	3.07	25	0.8	88	Negative	Negative	Veg	No	No	tab allopurinol	100 mg bd	4 weeks
27	case	Shivanand Umarani	271130		37	M	Watchman	21.8	4 Weeks	Moderate	No	No	No	No	6.9	13	7.9	3.7	30	0.7	102	Negative	Negative	Non Veg	Yes	Yes	tab allopurinol	100 mg bd	4 weeks
28	CONTROL	Mounesh Basappa	23104		27	M	Student	24.5							5.4	13.6	7	2.21	40	0.8	80			Non Veg	No	Yes			

29	CASE	Veeresh Dyaberi	1584201		51	M	Farmer	21.7	4 Weeks	Moderate	No	No	No	No	6.8	13.5	9.39	2.22	16	0.8	86	Negative	Negative	Veg	No	Yes	tab allopurinol	100mg bd	4 weeks
30	control	Anil Kumar	246379		47	M	Driver	23.4							5.6	13.9	8.1	1.09	30	0.6	86			Non Veg	Yes	Yes			
31	case	Amogi Ningappa	35555		30	M	Employee	22.8	4 Weeks	Moderate	No	No	No	No	7	11.5	4.2	1.6	5	0.8	86	Negative	Negative	Non Veg	No	No	tab allopurinol	100mg bd	4 weeks
32	case	Kallappa	211328		45	M	Farmer	23.1	4 Weeks	Moderate	No	No	No	No	6.2	13	7.6	2.2	25	0.8	84	Negative	Negative	Veg	Yes	Yes	tab allopurinol	100 mg bd	4 weeks
33	CASE	Malikarjun Jakkappa		300145	35	M	Employee	21.3	4 Weeks	Moderate	No	No	No	No	8.2	15.4	6.99	2.3	16	1	98	Negative	Negative	Veg	Yes	No	tab allopurinol	100 mg bd	4 weeks
34	CONTROL	Umesh Mali	297913		25	M	Student	23.4							5.2	13.5	4.84	2.47	18	0.7	88			Non Veg	Yes	No			
35	CONTROL	Satisha Srikanth	299183		33	F	Employee	22							2.5	15.4	16	1.08	16	0.8	88		N	Veg	No	No			
36	CONTROL	Mallappa	2024/2253		55	M	Teacher	21							5.7	11.8	6.02	3.39	30	0.9	92			Non Veg	Yes	Yes			
37	CONTROL	Subhash Gurappa	2024/2162		34	M	Shopkeeper	20.2							3.3	13.1	13.4	2.41	24	0.6	92			Veg	No	No			
38	CASE	Venkatesh		270958	65	M	Driver	22.1	8 Weeks	Moderate	No	No	No	No	7.5	10.8	8	2.72	18	0.8	80		Negative	Non Veg	Yes	No	tab allopurinol	100 mg bd	4 weeks
39	CASE	Mallikarjun		287407	36	M	Employee	23.5	4 Weeks	Moderate	No	No	No	No	6.6	15.2	9.42	2.71	24	0.7	80	Negative	Negative	Veg	No	No	tab allopurinol	100mg bd	4 weeks
40	CASE	Umesh Gouda		287088	56	M	Employee	21.5	4 Weeks	Moderate	No	No	No	No	5.4	9.9	9.3	3.04	9	0.8	94	Negative	Negative	Non Veg	Yes	Yes	tab allopurinol	100mg bd	4 weeks
41	CASE	Bhimabai Laxman	2024/8391		45	F	Clerk	20.5	4 Weeks	Moderate	No	No	No	No	5.8	11	7.4	4.72	30	0.8	76	Negative	Negative	Veg	No	No	tab allopurinol	100 mg bd	4 weeks
42	case	Huvakka	2024/9326		70	F	Housewife	24.2	4 Weeks	Moderate	No	No	No	No	6	10.8	7	2.72	17	1	88	Negative	Negative	Veg	No	No	tab allopurinol	100 mg bd	4 weeks
43	CASE	Jalalkhaja	2024/10561		23	M	Tiles Worker	22.3	4 Weeks	Moderate	No	No	No	No	2.4	11.5	12	3.51	24	0.7	96	Negative	Negative	Non Veg	Yes	Yes	tab allopurinol	100 mg bd	4 weeks
44	CASE	Rajendra	2024/15055		40	M	Farmer	22	4 Weeks	Moderate	No	No	No	No	7.3	9.9	7	1.85	38	1	83	Negative	Negative	Veg	No	No	tab allopurinol	100 mg bd	4 weeks
45	CASE	Basalingamma Hiremath	2024/15103		74	F	Housewife	24	10 Weeks	Moderate	No	No	No	No	2.1	8.1	14	1.52	30	0.6	87	Negative	Negative	Non Veg	No	No	tab allopurinol	100 mg bd	4 weeks
46	CASE	Mallamma Pujari	2024/15827		40	F	Farmer	22.7	8 Weeks	Moderate	No	No	No	No	2.6	11.9	4.6	197	34	0.7	83	Negative	Negative	Veg	No	No	tab allopurinol	100 mg bd	4 weeks
47	CONTROL	Renuka	2024/16232		23	F	Student	20.1		Moderate	No	No	No	No	4.2	12.3	8.9	3.38	30	0.5	88			Veg	No	No			
48	control	Narasawwa	2024/16342		55	F	Housewife	23.7		Moderate	No	No	No	No	4.4	12.7	10	2.88	30	0.5	95			Non Veg	No	No			
49	control	Nirmala	2024/16467		63	F	Housewife	22.1							1.8	11.1	8.6	2.4	18	0.5	88			Non Veg	No	No			
50	case	Mahadev	2024/17430		59	M	Housewife	23.6	4 Weeks	Moderate	No	No	No	No	7.2	14.2	10	2.7	32	1	92	Negative	Negative	Non Veg	Yes	No	tab allopurinol	100mg bd	4 WEEKS
51	case	Bhagaappa	2024/17421		65	m	Farmer	22.8	4 Weeks	Moderate	No	No	No	No	6.4	10.8	9.3	1.2	30	1	88	Negative	Negative	Veg	No	Yes	tab allopurinol	100 mg bd	4 WEEKS
52	case	Shravan Kumar	6984		27	m	Employee	21.6	4 Weeks	Moderate	No	No	No	No	6.9	13	6.29	1.76	24	0.8	100	Negative	Negative	Non Veg	Yes	Yes	tab allopurinol	100 mg bd	4 weeks
53	case	Mallikarjun	288867		33	m	Sales Man	23.6	4 Weeks	Moderate	No	No	No	No	6.8	11	20	3.98	22	0.6	98	Negative	Negative	Non Veg	Yes	Yes	tab allopurinol	100 mg bd	4 weeks
54	control	Satisha	**299183**		**33**	**f**	Housewife	22.1							2.5	15	8	1.08	28	0.6	88			Veg	No	No			
55	case	Parvati	190531		45	f	Housewife	23.1	4 Weeks	Moderate	No	No	No	No	7.2	11.8	13	3.4	25	0.8	78	Negative	Negative	Veg	No	No	tab allopurinol	100 MG BD	4 weeks
56	control	Pushpa Patil	2024/15826		19	f	Student	20							3	12	6.45	3.4	22	0.8	84			Veg	No	No			
57	control	Laxman	288857		60	m	Farmer	22.4							5.2	15	9.5	2.6	20	0.7	80			Non Veg	Yes	Yes			
58	control	Shankargouda	298507		76	m	Employee	23.4							2.4	12.4	10	1.6	24	0.8	86			Non Veg	Yes	Yes			
59	case	Dareppa	222575		58	m	Farmer	21.2	4 Weeks						7.2	13	4	1.7	24	0.8	80	Negative	Negative	Veg	No	No	tab allopurinol	100 mg bd	4 weeks
60	case	Kasturi	2024/17385		65	f	Housewife	24.2	4 Weeks	Moderate	No	No	No	No	6.8	14	10	2.7	22	1	84	Negative	Negative	Veg	No	No	tab allopurinol	100mg bd	4 weeks
61																					78			Veg	No	No			