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RESEARCH ARTICLE

ASSOCIATION BETWEEN SERUM URIC ACID LEVEL AND NODAL OSTEOARTHRITIS IN A SAMPLE OF MIDDLE AGED IRAQI FEMALES.

Dr. Juman Ali Nasir¹, Dr. Waseem Kamil Kaith² and Dr. Mohammed Hadi Alosami³.

1. M.B.Ch.B. Baghdad Teaching Hospital.
2. M.B.Ch.B., Diploma in (Rheum & Rehab.) Rheumatology specialist at Al-Yarmouk Teaching Hospital.
3. C.A.B.M., F.I.B.M.S. (Rheum. & Rehab.) Assistant professor, Consultant Rheumatologist, College of Medicine/Baghdad University.

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Key words:-

Nodal osteoarthritis, Uric acid,
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Abstract

Background: Nodal osteoarthritis (NOA) a subset of OA, is characterized by polyarticular interphalangeal and thumb base OA, Heberden's nodes are a classic sign of hand osteoarthritis, which is presented in the distal interphalangeal joint. The epidemiologic relationship between hyperuricemia and OA raises the question of whether data support a biologic relation of the two entities.

Patients and methods: A case-control study. A total of 100 patients (50 cases with nodal osteoarthritis and 50 healthy control) aged from (40 to 70) years old were included in the study.

Results: There was no significant association between serum uric acid and nodal osteoarthritis. Age, and high body mass index was positively correlated to nodal osteoarthritis. There was positive relationship between serum uric acid and radiological osteoarthritic changes of hand which has been assessed by using Kellgren-Lawrence scale (P-value < 0.001).

Conclusion: Serum uric acid can be used as a mean to give us an idea about radiological osteoarthritic changes of hand assessed by using Kellgren-Lawrence scale.

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Introduction:-

Osteoarthritis (OA) is the leading cause of arthritis in the world affecting 10-15% of adults, with a lifetime risk as high as 50% ⁽¹⁾. Nodal osteoarthritis (NOA) is a subset of OA, Heberden's nodes are a classic sign of hand osteoarthritis, and Bouchard's nodes is predominant in women and has a clear genetic predisposition ⁽²⁾. The incidence of hand osteoarthritis in people over 55 years of age was 13.4% for men and 26.2% for women, and these levels are increased with age ⁽³⁾. OA affects 302 million worldwide ⁽⁴⁾.

Being obese female aged more than 40 years, at menopause, has history of OA, high bone density, and joint laxity all are considered as risk factors for NOA ⁽⁵⁾. It is presented clinically by the following classical symptoms: joint pain, morning stiffness (of < ½ hour in duration), and loss of motor function ⁽⁶⁾.

Corresponding Author:-Dr. Juman Ali Nasir.
Address:-M.B.Ch.B. Baghdad Teaching Hospital.

On examination; crepitus, joint effusion and Heberden's and Bouchard's nodes were found. Osteoarthritis, although considered as a degenerative consequence of aging, is a disease with an increasingly well-characterized molecular pathophysiology. Biomechanical factors, obesity, and malignant, result in chemical alterations within the joint that promote cartilage degradation ⁽⁷⁾.

Uric acid (UA) in human is the main final product of purine metabolism ⁽⁸⁾. Hyperuricemia was recently defined as above 7.7 mg/dl in men and above 6.6mg/dl in women ⁽⁹⁾, or above 7.0 mg/dl in men and above 5.7 ⁽¹⁰⁾ or 6 mg/dl in women ⁽¹¹⁾.

The epidemiologic relationship between hyperuricemia and OA raises the question of whether data support a biologic relation of the two entities. Four possibilities deserve consideration: presence of shared risk factors (e.g., obesity), rather than any direct relationship; osteoarthritis in a joint might promote urate crystallization locally; monosodium urate (MSU) crystal deposition on/in cartilage may create local mechanical and/or inflammatory damage promoting OA development; urate may function intrinsically in the process of OA development and/or progression ⁽¹²⁾.

Aim of study:

This study was conducted to assess the relationship between level of serum uric acid and hand osteoarthritis in middle aged Iraqi females.

Patients and method:-

Study Design:

A case-control study conducted at Baghdad Teaching Hospital, Unit of Rheumatology during the period from October 2018 through April 2019, after approval of the study protocol by University of Baghdad, College of Medicine, Department of Medicine, Rheumatology and Medical Rehabilitation Unit.

Sample selection:

A total of 100 patients (50 cases and 50 healthy control) aged from (40 to 70) years old were enrolled in this study, cases were met the Criteria designed for classification of hand osteoarthritis which published by American College of Rheumatology in 1990 (6). Participants were excluded if they were: 1- having history of hypertension, diabetes mellitus, renal or heart disease. 2- history of gout, psoriasis or psoriatic arthritis, rheumatoid arthritis. 3- drugs that affect level of serum uric acid like: Anti-TB medications (ethambutol, pyrazinamide), thiazide diuretics, cyclosporine, aspirin. 4- malignancy and use of chemotherapy.

Methods and Data collection:

data were collected by a questionnaire designed for the purpose of the study. It collected data about:

Socio-demographic data:

which include: Age, gender, weight (in kilogram), height (in meter), body mass index (BMI), education level, and smoking status, alcohol consumption, marital status . Body mass index (BMI) was calculated.

Laboratory data:

Blood samples were obtained from all participants for measuring serum uric acid, complete blood count (CBC), erythrocyte sedimentation ratio (ESR), rheumatoid factor (RF), blood urea (B. Urea), serum creatinine (S.Cr), blood sugar, all of them except serum uric acid were obtained to exclude other diseases.

the reference range of SUA is typically 3.4-7.2 mg/dL (200-430 μ mol/L) for males, and 2.4-6.1 mg/dL (140-360 μ mol/L) for females ⁽¹¹⁾.

Radiological data:

Bilateral hand plain x-ray posteroanterior view (PA) were obtained for all participants and the severity of hand osteoarthritis was assessed by using Kellgren-Lawrence (KL) grading system. The Kellgren-Lawrence uses four radiographic features: joint space narrowing, osteophytes, subchondral sclerosis, and deformity. The severity of radiographic changes increases from grade 0 to 4 with grade 0 meaning no radiographic features of osteoarthritis while grade 4 means large osteophytes marked joint space narrowing, severe sclerosis, and definite bony deformity ⁽¹³⁾.

Statistical Analysis:

Statistical Package for the Social Sciences (SPSS) Software V 23 was used to perform statistical analysis. Data were presented as numbers, percentages, and mean. Chi-square test and its correction Fisher exact test, Student's t-test were used to measure the significance. Correlations were assessed using Pearson's correlation coefficient. P value of <0.05 was considered statistically significant.

Ethical issue:

Informed consent was obtained from each participant included in this study according to the declaration of Helsinki. Data and information of the participants were kept confidentially. This study was approved by the ethical committee of Baghdad University, College of Medicine-Medical Department.

Results:-

The study group (cases) composed of 50 patients with nodal osteoarthritis, and control group composed of 50 apparently healthy controls. Age of participants ranged from 40 years to 70 years, with a mean of (53.4 ± 7.2) . BMI of the study participants ranged from $(19.1) \text{ Kg/m}^2$ to $(46.7) \text{ Kg/m}^2$ with a mean of $(32.03 \pm 6.51) \text{ Kg/m}^2$ and a median of $(31.13) \text{ Kg/m}^2$. Table-1 compares the BMI status of the two study groups. There was a statistically significant difference in BMI between the two study groups = 2.95 ($P = 0.004$).

Table 1:-Body mass index of the study groups.

	Study group			Student's t- test
BMI	Cases (n=50)	Control (n=50)	Total (n=100)	
Range	19.10 – 46.14	22.58 – 46.68	19.10 - 46.68	0.004
Mean \pm SD	30.18 ± 6.90	33.88 ± 5.58	32.03 ± 6.51	

BMI: Body mass index, SD: Standard deviation

Table 2 represented the Comparison of BMI classes between the two study groups it again showed statistically significant difference, by chi-square test 14.5 ($P = 0.006$).

Table 2:-Body mass index classes of the study groups

BMI Classification	Study sample			P-value
	Case (n=50)	Control (n=50)	Total (n=100)	
Normal (18.5 – 24.9)	13 (26.0%)	2 (4.0%)	15 (15.0%)	0.006
Overweight (25 – 29.9)	13 (26.0%)	12 (24.0%)	25 (25.0%)	
Obese Class I (30 – 34.9)	14 (28.0%)	15 (13.0%)	29 (29.0%)	
Obese Class II (35 – 39.9)	3 (6.0%)	13 (26.0%)	16 (16.0%)	
Obese Class III (>39.9)	7 (14.0%)	8 (16.0%)	15 (15.0%)	

There was no statistically significant difference in uric acid level between cases and controls, Student's t-test = 0.13 ($P = 0.900$). Table-3 summarize the findings.

Table 3:-Uric acid level of the study groups

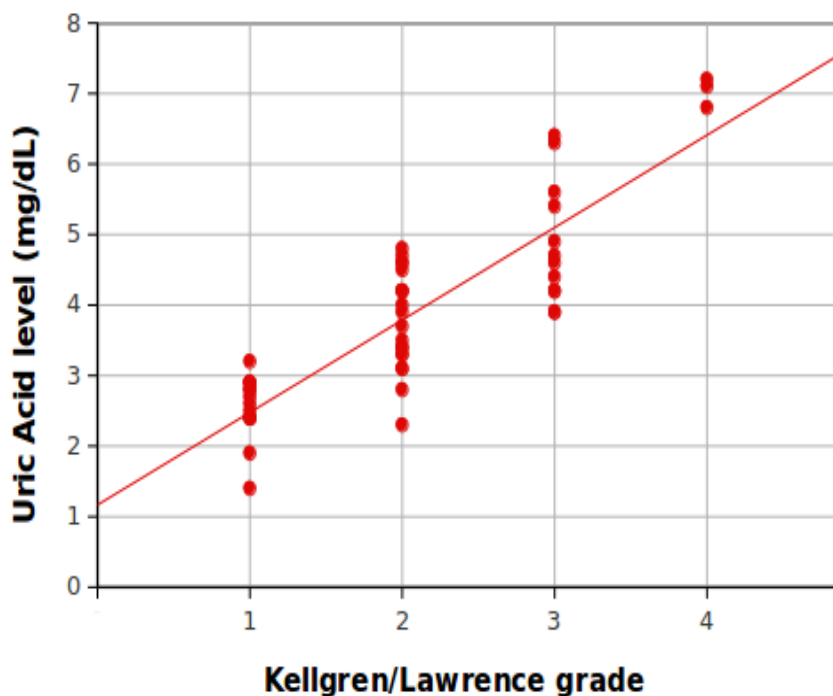
Study Group	Uric Acid Level		P-value
	Range	Mean \pm SD	
Case (n=50)	1.40 – 7.20	3.87 ± 1.35	0.900
Control (n=50)	1.20 – 6.10	3.90 ± 1.02	
Total (n=100)	1.20 – 7.20	3.88 ± 1.19	

Kellgren/Lawrence grades distribution among cases was described in details in (Table 5). Grade II showed the highest rate 20(40%) of cases while grade IV was the lowest rate of occurrence 3(6%). Uric acid was the highest 7.03 ± 0.21 in grade IV. Analysis of Variance (ANOVA) was utilized to calculate the statistical significance of the difference in uric acid level among the four grades; there was a strongly significant difference in uric acid level, with P-value < 0.001 .

Table 4:-Uric acid level in each Kellgren/Lawrence grade

Kellgren/Lawrence Grade	Frequency (%)	Uric Acid Level (Mean \pm SD)	P-value
Grade I	15 (30%)	2.55 \pm 0.45	< 0.001
Grade II	20 (40%)	3.78 \pm 0.70	
Grade III	12 (24%)	4.87 \pm 0.87	
Grade IV	3 (6%)	7.03 \pm 0.21	

Spearman's Rank-order correlation coefficient was calculated to further assess the correlation between Kellgren/Lawrence grade and the level of uric acid. There was a statistically significant positive correlation of high strength between the two variables, with correlation coefficient (R) = 0.844, P-value < 0.001. A scatter plot diagram in Figure-1 illustrates the finding.

**Fig 1:-**Correlation between uric acid level (mg/dL) and Kellgren/Lawrence grade.

Discussion:-

We found there was no significant relationship between serum uric acid and nodal osteoarthritis (P-value = 0.900), this finding was in agreement with the previous studies ^(14,15,16), however, there are controversial epidemiological data from both cross-sectional and cohort studies regarding the relationship between uric acid and OA ^(17,18).

Although prior experiments have shown that MSU crystals, or uric acid, have a catabolic effect on cartilage and synovial inflammation, still there is controversial epidemiologic evidence regarding the association between uric acid and OA. Some earlier investigators showed interest in a causal link between uric acid and the nodal changes in hand OA ^(19,20). They proposed that uric acid-induced inflammation contributed to an inflammatory response that led to nodal OA, rather than directly causing OA to develop.

Increased levels of SUA also increases morbidity and mortality in these patients (Suliman *et al.*, 2006). It is recommended that SUA should be routinely measured in all obese and overweight patients in order to prevent or at least delay complications due to raised SUA ⁽²¹⁾.

In our study there is significant correlation between serum uric acid and increased age (P-value = 0.012) which also has been found in other studies^(11,22). The serum level of uric acid is affected by aging and genetic and environmental factors. Obesity and alcohol consumption are well established as determinants of SUA levels^(22,23).

In this study there was positive relationship between serum uric acid and radiological osteoarthritic changes of hand which has been assessed by using Kellgren-Lawrence scale (P-value < 0.001), this finding was in agreement with the previous studies^(17, 18, 24) which mean serum uric acid level tend to raise with patients having osteoarthritic K/L stage \geq II, in this way it gives us an idea about the radiological progression. This also goes with the previous study published by Srivastava, et al. which found that the level of serum UA was found to be in increasing order, parallel to the grades of the disease. A probable mechanism of such UA related OA may be that the higher level of UA might lead to the formation of microcrystals in the joint space which is responsible for the commencement of inflammatory chain reaction leading to OA. Thus, it may be concluded that higher plasma UA levels have strong association with generalized OA/ KOA⁽²⁵⁾.

Limitations of this study:

1. Small sample size due to short time.
2. The study focused only on the association of serum uric acid and nodal osteoarthritis and not on the risk of OA development.
3. We had limited information about OA involvement in each patient, including the affected joint, its severity, treatment modalities and family history of hand OA.

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