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RESEARCH ARTICLE

ASTUDY OF CARTILAGEOLIGOMERICMATRIXPROTEIN (COMP) & TUMOR NECROSIS FACTOR – αINPOSTMENOPAUSALKNEE OSTEOARTHRITIC FEMALE PATIENT

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Abstract

Osteoarthritis is a type of arthritis that occurs when the flexible ends of tissues at the end of the bones wear down and it could be due to various causes affecting the daily life of the people. Women are the most important part of society and according to studies it was stated women are more affected than men. There are many biochemical markers involved in the diagnosis of osteoarthritis with other investigations like radiological, and clinical approaches. Here in this study the Cartilage oligomeric matrix protein (COMP) and Tumor necrosis factor –alpha (TNF-?) were determined in post-menopausal knee osteoarthritic female patients and normal healthy subjects taking into consideration of all the exclusion and inclusion criteria. The samples were collected and tests were performed by ELISA. The study suggested that raised levels of the serum COMP & TNF-? in the study group were age-related changes with inflammation and infection at the knee joint which were suggestive of knee osteoarthritis.

Introduction:-

The musculoskeletal system disorders are prevalent, amongst them most common is arthritis, affecting millions of the people worldwide. Osteoarthritis is more common than the rheumatoid arthritis. It is very common chronic disease that affects all the joint tissues, finally, the failure of the joint as an organ.[1]

Osteoarthritis of the knee is more common, affecting around 33.6% adults over the age of 65. Interestingly the women are more affected and burdened by OA of the knee than men.[2]

Osteoarthritis (OA), also known as osteoarthrosis or degenerative joint disease, is a disease of synovial joints. It is characterized by progressive deterioration and loss of articular cartilage with concomitant structural and functional changes in the entire joint, including the synovium, meniscus (in the knee), periarticular ligaments, and subchondral bone.[3] The knee is the largest synovial joint in humans, it is composed by osseous structures (distal femur, proximal tibia, and patella), cartilage (meniscus and hyaline cartilage), ligaments and a synovial membrane. The latter is in charge of the production of the synovial fluid, which provides lubrication and nutrients to the avascular cartilage. Unfortunately, given the high use and stress of this joint, it is a frequent site for painful conditions including OA.[4] The development of OA is dependent to interactions between several factors and so this process may be considered the product of an interplay between systemic and local factors. This progressive and disabling disease can be resulted from a combination of risk factors, including advancing age, genetics, trauma, knee malalignment,

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increased biomechanical loading of joints through obesity, augmented bone density and an imbalance in physiological processes.[5]

The potential biological marker of arthritis is COMP. Cartilage oligomer matrix protein (COMP) is also known as thrombospondin 5. Originally described in cartilage, COMP has also been identified in ligaments, meniscus, tendons, synovium, osteoblasts and vascular smooth muscle.[6] COMP is known to play a role in collagen secretion and fibrillogenesis, chondrocyte proliferation and mechanical strength of tendons.[7] It can be considered as diagnostic and prognostic indicator and as a marker of disease severity and effect of treatment. Inflammation is a necessary response of the immune system to different stimuli such as infection and injury, resulting in elevated production of cytokines and acute-phase proteins. However, chronic activation of these pathways is associated with serious detrimental effects. Increased serum concentrations of inflammatory markers, such as tumor necrosis factor-α (TNF-α), have been implicated in the pathophysiology of various disease. During osteoarthritis degradation of cartilage of knee joints causes inflammation may be due to release of TNF-α & IL-1 which are responsible for proteolytic digestion of cartilage in joints. The indirect action appears to decrease the level of cytokines and TNF-α in non-osteoarthritic patients, that promote osteoclastic activity. Thus estrogen depletion after menopause or ovariectomy may deviate the TNF-α and cytokines. These finding suggest that TNF-α could mediate the loss of bone in estrogen deficiency. [8]

The present study was aimed to find out the major role of COMP & TNF - α in the development and progression of knee OA disease in postmenopausal females.

Materials & Methods:-

The study protocol was evaluated by the Institutional Ethical Committee of UPUMS, Saifai, Etawah. Written informed consent from each subject was obtained. They were clinically and radiologically diagnosed osteoarthritis patients, attending OPD of orthopedic department UPUMS, Saifai, Etawah (U.P.) for regular checkup. 100 normal healthy female control subjects of same age group have also been included in our study for statistical comparison. 5 ml of blood was collected from all the subjects in fasting condition and the serum was separated and stored at -20° C until used. The COMP & TNF – α were estimated byELISA technique in Biochemistry department. The student independent 't' test was used for the statistical analysis of the data. The written consent was also taken from patients prior to study.

Observations & Results:-

Table-1:- Showing the status of serum COMP & TNF - α in Postmenopausal knee osteoarthritic female patients and normal healthy postmenopausal female subjects.

Study Group		COMP (pg/mL)	TNF – α (ng/mL)
Normal healthy Postmenopausal Female subjects (n=100)	**Min**	75	11.45
	Range		
	Max.	621.4	35.9
	Mean ± SD	169.07 ± 91.77	17.95 ± 2.65
	SE	9.17	0.26
Postmenopausal Knee osteoarthritic female patients (n=100)	**Min**	342.7	40.12
	Range		
	Max.	4387.6	210.12
	Mean ± SD	1431.04 ± 1027.16***	110.23 ± 18.98***
	SE	102.71	1.89

Values expressed as Mean ± SD, ***P<0.0001, NS = Non- significant

Table 2:- Correlation of serum COMP & TNF - α in Postmenopausal Knee osteoarthritic female patients of age group II.

VARIABLE	COMP	TNF - α
AGE	0.73***	0.59**
COMP	-	0.48*

Pearson correlation
Values expressed as correlation coefficient (r), **moderately correlated, *low correlation, ***highly correlated

Results:-

The above mentioned table were formed after analyzing the serum COMP & TNF- alpha by ELISA method and it was observed that serum COMP levels were raised in the postmenopausal knee osteoarthritic female patients (table-1) and when the correlation was studied it was evident that with age it had highly positive correlation (0.73). similarly, it was seen that the serum TNF – alpha levels were also raised significantly (table - 1) and with age it had moderately positive correlation (0.59) whereas when COMP and TNF – alpha were correlated it was seen that they are slightly significant (0.48).

Discussion:-

Knee osteoarthritis (KOA), also known as degenerative joint disease, is typically the result of wear and tear and progressive loss of articular cartilage. It is most common in the elderly.[11]**Serum COMP**, the biochemical marker which is an extracellular matrix (ECM) protein primarily present in cartilage and was studied and found to be significantly ($p<0.0001$) raised among the postmenopausal female patients (1431.04 ± 1027.16) compared to the normal healthy female subjects (169.07 ± 91.77). COMP is considered a marker of cartilage breakdown. So the serum COMP levels may be used as a diagnostic OA marker along with prognostic value in determining the patients at risk of rapidly progressing this debilitating joint disease. As the values of this study were corresponded to the several studies out of which one of them done by Priyanka Verma et.al. The study resulted in the median (range) serum COMP levels were observed to be 1117.21 ng/ml (125.03–4209.75 ng/ml) in OA patients and 338.62 ng/ml (118–589 ng/ml) in control subjects with $p < 0.001$.[9] Another study which was done in 1999 by Clark et.al in which it was found that Serum COMP levels were significantly elevated (P = 0.0001) in the age > or = 65 group (mean +/- SD 1,302.1 +/- 496.7 ng/ml) versus the age 45-54 and age 55-64 groups (1,058.1 +/- 432.4 and 1,038.6 +/- 313.3, respectively).[10]

Serum TNF – α, is an adipokine and a cytokine which is raised in the (110.23 ± 18.98) in the postmenopausal knee osteoarthritis female patients than the (17.95 ± 2.65) normal healthy postmenopausal female subjects. This is consistent with Kenan Ozler et.al in which they found the raised values of the serum TNF – **α** in the patients suffering from osteoarthritis. [11]G Gundogdu et.al also stated that the there was a significant decrease in adropin level and an increase in TNF-α level parallel to the increase in the KL grade.[8]Similarly it was concluded from the study done by Dr. Pradeep Sharma et. al that in postmenopausal stage (40-60 years) females the production of TNF-α is due to lack of estrogen. TNF-α could be taken as suggestive marker for assessment of onset of osteoarthritis. [12]

Conclusion: -

Consequently, it was evident that as the age increases the serum levels of COMP & TNF – α increases in the patients which proves compromised bone health. Thus with increase in COMP levels suggested that increase in the bone and cartilage degeneration with increase inflammation. Therefore, same goes with the TNF- alpha as it is cytokine which is released at site of inflammation and infection.

Conflict of Interest
The authors declare there is no conflict of interest regarding thesubmission and publication of the manuscript and its potential implications.

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Ethical Assurance:
After being evaluation of my project by the ethical committee of the institution i.e. UPUMS, the study was done. It is totally in compliance with the ethical standards.

Informed written consents weretaken from the study groups prior collecting the samples.

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