DISCUSSION

Osteoarthritis (OA) is the most common chronic joint disorder. It usually results in pain and deformity, ultimately leading to chronic disability. Hence, it is rapidly becoming a significant medical and financial burden in a world whose population is ageing.(182)

OA is a complex, active degradative and repair process of cartilage and subchondral bone with a synovial inflammation. Several factors are involved in this process such as mechanical stress, biochemical and genetic factors. Chondrocytes respond to injuries by producing degradative enzymes and by developing inappropriate repair responses. A lot of pro-degradative agents such as proteinases and proinflammatory cytokines have been extensively studied and might compromise macromolecular synthesis resulting in the development of cartilage breakdown.(183)

Osteoarthritis is commonly described as a non inflammatory disease which distinguishes from inflammatory arthritis, such as rheumatoid arthritis (RA) or seronegative spondyloarthropathies.(184) Despite this, inflammation is increasingly recognized as contributing to the symptoms and progression of OA. .(185,186)

The initiation of the osteoarthritic process therefore appears to involve abnormalities in biomechanical forces and/or cartilage, Once begun, the pathway leading to osteoarthritis involves numerous other factors. These include mechano-transduction, the interplay between proteases, protease inhibitors and cytokines on cartilage degradation and mechanisms cartilage repair and the contributions from multiple risk factors (such as obesity, aging, mineral deposition, systemic hormones, and abnormalities in neurogenic control)..(187)

An abnormality associated with osteoarthritis extends beyond the cartilage often involving the subchondral bone, juxtaarticular bone marrow and the synovial membrane.(188)

It is believed that cytokines and growth factors play an important role in pathophysiology of OA. They are closely associated with functional alterations in synovium, cartilage and subchondral bone. Cytokines activate the chondrocytes, which in turn could produce catabolic factors such as proteases and proinflamatory cytokines. (189)

The present study was conducted on 50 patients with knee osteoarthritis (group **I**) fulfilling the ACR criteria for diagnosis of the disease and 20 age- sex matched healthy individual control (group **II**)

ESR and CRP were measured as inflammation markers ,our results suggested that inflammatory process in the joint micro-environment may lead to synovial inflammation in osteoarthritis.

In the current work there was statistically significant difference between group **1** and group **11** as regards to ESR (P = 0.001). In group **1**, the median ESR was 18 mm/h ranged from 10 to 26 mm/h, while the median ESR of group II was 11mm/h ranged from 6 to 16 mm/h.

Also there was statistically significant difference between group **1** and group **11** as regards to CRP (P = 0.001). In group **1**, the median CRP was 3.5 ranged from 1 to 7, while the median CRP of group **11** was 1 ranged from 0 to 2 u.

In a study done by Sermin et al 2010 [(190)], they examined the relation between oxidant stress and inflammation in plasma of RA and primary OA patients.Their study included 20 RA patients and 20 OA patients. they measured (protein carbonyl content, thiol level, plasma protein fraction) as the oxidation marker, and ESR –CRP as inflammation markers. they found that the ESR and CRP levels were higher in both the patient groups than the normal group ($p<0.001$). These results suggested that alterations in the oxidant stress markers could be the cause of inflammation in these diseases.[(190)]

Wolfe et al 1997 [(191)] reported that The C-reactive protein but not erythrocyte sedimentation rate is associated with clinical severity in patients with osteoarthritis of the knee or hip. Their study was carried on a total of 655 consecutive patients with OA of the knee or hip. they underwent a rheumatic disease examination, completed a clinical health assessment questionnaire (CLINHAQ), and had laboratory tests performed, including hemoglobin, CRP, and ESR.

They found that the median value of CRP was 5.9 micrograms/ml. CRP was significantly associated with functional disability, joint tenderness, pain, fatigue, global severity, and depression. In addition, correlations were noted for body mass index (BMI) and sex. ESR, by contrast, was unassociated with clinical signs or symptoms except for a weak association with functional disability. They concluded that CRP is elevated in OA compared to healthy individuals, and is correlated with rheumatic disease signs and symptoms, including HAQ disability, joint count, and pain. The associations, not seen with ESR, appear to be real, but are not strong. An inflammatory component associated with OA can be detected in the serum. [(191)]

Early stages of OA are difficult to diagnose.joint structure and function are typically altered substantially before symptoms cause patients to seek medical care, that is, the osteoarthritic process begins long before OA presents as a clinical disease. The insidious onset an silent progression of OA not only obscure an early diagnosis, but also delay treatment that may help prevent further cartilage destruction and joint failure. Hence, diagnostic tests that can detect and monitor molecular events early in the pathogenesis of OA would be potentially very useful. [(192)]

The ability to use bio-markers of joint remodelling to predict disease progression and identify patients most likely to progress is atop priority in the future management of primary and secondary OA. [(193)]

Type II collagen is possibly the ideal marker of cartilage degradation. First, it is relatively specifi c to articular cartilage. Second, type II collagen is the most abundant protein in cartilage, representing 15–25% of the wet weight, 50% of the dry weight, and 90–95% of the total collagen content. Third, type II collagen turnover is normally very slow in adult cartilage, thus pathological turnover is readily detected above background metabolism. [194]

To the best of our knowledge, all the researchs for CTX-II in human osteoarthritis were in the urine samples, so the current work is a novel one in detecting the serum level of CTX-II among patients with osteoarthritis.

In the present study the readings of serum CTX-II among the cases of knee osteoarthritis ranged from 120- 600 pg/ml with a mean 249.8 pg/ml and standard deviation 125.5 and a median 200 pg/ml.

While among the control group the readings of serum CTX-II ranged from 110 -200 pg/ml with a mean 150.5 and standard deviation 38.8 and a median 130 pg/ml.

The readings of serum CTX-II among cases of knee osteoarthritis were higher in comparison to that of control group and this difference was of high statistical significance (p=0.001).

Kalai E et al, [195] studied the level of urinary CTX-II among Tunisian patients with knee osteoarthritis and to assess the relation between CTX-II and radiological signs of osteoarthritis .Their study included 125 female patients aged 53.6 ± 7.6 years with disease duration of 3.6± 3.8 years and 57 female age-matched controls underwent X-ray examination of both knees. They had applied Kellgren/Lawrence scale for assessment severity of osteoarthritis.The urinary concentration of CTX-II was measured by a competitive ELISA. Their results showed that urinary CTX-II levels were significantly higher in knee osteoarthritis patients compared with controls (323.98 vs 218.04 microg/mol creatinine)

Tanishi et al [196] , conducted a study to assess the usefulness of the urinary crosslinked C-telopeptide of type II collagen (uCTX-II) or crosslinked N-telopeptide of type I collagen (uNTX-I) for evaluating radiological knee osteoarthritis (OA), a cross-sectional study was conducted in the cohorts of the Matsudai knee osteoarthritis survey performed in Niigata, Japan. Urine specimens and standing knee AP X-rays were obtained from 1040 subjects who provided informed consent. The relationship between these markers and gender, age (patients aged 40-59 or 60-79 years), use of bisphosphonates, and OA grades (K-L classification) were analyzed. The diagnostic ability of uCTX-II to detect radiological knee OA was confirmed in the over 60-year-old subjects using a ROC curve.

They found that, the over 60-year-old men with OA grade 3,4 group had significantly higher uCTX-II levels than the other OA grade groups. In the over 60-year-old women, the uCTX-II levels significantly increased according to the progression of the

knee OA grade.and concluded that the uCTX-II level is strongly correlated with the knee OA grade .

In the present study there was positive correlation of high statistical significance between serum CTX-II and radiological grading of osteoarthritis (r =+0.348, p =0.013). In grade 1: readings of CTX-II ranged from 120-220 pg/ml with a median of 190 pg/ml In grade 2 : readings of CTX-II ranged from 140 to 500 pg/ml with a median 200,while in grade 3 the readings ranged from 130 to 500 pg/ml with a median 200. In grade 4 the readings ranged from 150 to 600 pg/ ml with a median 320. This is in agreement with Jordan KM et al [197] who reported that urinary CTX-II was found to be higher in patients with severe radiologic osteoarthritis (Kellgren and Lawrence score 2, 3, or 4) than in patients with less severe radiologic osteoarthritis (Kellgren and Lawrence score 1) or no radiologic signs of OA.

This in agreement with Jordan et al [197] ,who investigated the association between biochemical markers of bone, cartilage, and synovial turnover with the presence and severity of knee osteoarthritis (OA) in men. their study included 176 men aged 59–70 years. Weightbearing anteroposterior and lateral semiflexed radiographs were taken of both knees. A lifestyle questionnaire including basic demographic details and a questionnaire detailing knee pain was completed. This random sample was stratified based on the Kellgren and Lawrence (K&L) score, and the following biochemical markers were analysed: serum osteocalcin, urinary C-terminal crosslinked telopeptide of type II collagen (CTX-II),andurinaryglucosylgalactosyl- pyridinoline(Glc-Gal-Pyd).

Their results showed a strong significant association between the presence of knee OA and urinary CTX-II and urinary Glc-Gal-Pyd (p = 0.0001 and p = 0.009), which persisted after adjustment for age and BMI. A significant positive association was also found between urinary CTX-II and urinary Glc-Gal-Pyd and the severity of K&L grade. They concluded that urinary CTX-II and Glc-Gal-Pyd, are strongly associated with disease severity and the presence of OA at the tibiofemoral and patellofemoral joints .

Garnero et al [198] , performed study aimed at assessing the clinical performance of the levels of U-CTX-II and U-Glc-Gal-PYD and of a panel of existing biochemical markers of connective tissue metabolism in patients with knee OA . The following biochemical markers were measured in a group of 67 patients with knee OA (mean age 64 years, median disease duration eight years) and in 67 healthy controls: serum osteocalcin, urinary C-telopeptide CTX-II, serum cartilage oligomeric matrix protein (COMP), urinary Glc- Gal-PYD, serum type III collagen, serum hyaluronic acid (HA); and serum Creactive protein. Biochemical markers were correlated with pain and physical function (WOMAC index) and with quantitative radiographic evaluation of the joint space using the posteroanterior view of the knees flexed at 30°.

Among their results U-CTX-II and S-COMP were significantly increased in patients compared with controls . U-CTX-II (ng/mmol Cr) 431 (154) in patients, 345 (140) in control .And S-COMP (ng/ml) 1677 (360) in patients , 1449 (190) in control group. It may be concluded that Knee OA appears to be characterized by increased cartilage and synovial tissue turnover. CTX-II may be useful marker of disease severity in patients with knee OA.

In the current work there was non –significnt correlation between serum CTX-II and BMI in group **I (**r= 0.217, p = 0.130). This agrees with Karsdal *et al* [199] who investigated correlations between bone and cartilage degradation in patients with OA as a function of sex, Kellgren-Lawrence (KL) score, Body Mass Index (BMI), oral salmon calcitonin (sCT) treatment and diurnal variation. They concluded that CTX-II showed a weak and non-significant positive correlation with BMI, r = 0.25 (*p* = 0.12)

Duclos ME et al [200] studied the significance of the serum CTX-II level in an osteoarthritis animal model: a 5-month longitudinal study. The aim of their study was to investigate the clinical value of serum measurement of C-telopeptide of type II collagen (CTX-II). In correlation with late stages of osteoarthritis (OA) evaluated with histological assessment, the evolution of serum CTX-II concentration was followed during a 20-week longitudinal study in rabbit anterior cruciate ligament transection (ACLT) OA model in adult and growing animals.

OA was induced in five adult and nine growing rabbits. Four adult and four young rabbits were unoperated. Serum sampling was made at week 0, 1, 2, 3, 4, 6, 8, 10, 12, 14, 16 and 20 after the surgery in all rabbits. Animals were euthanized 20 weeks after the surgery. Serum CTX-II levels were analyzed with a recently available enzyme-linked immunosorbent assay (ELISA) kit, the protocol of which has been modified to increase the sensitivity of the test.

Their results showed Significant differences for the CTX-II levels at W3, W6, W8, W10, W12, W14, W16 and W20 were observed between the adult ACLT and the control groups. A negative correlation between CTX-II levels and cartilage thickness of the medial compartment of the knee at W8, W10, W12 and a positive correlation between the CTX-II levels and the histomorphological score of the medial compartment of the knee at W3, W6, W8, W10, W12 were noted in adult animals. In young animals, operated or not, they observed high CTX-II levels at the beginning of the study, which decreased until the end.

They concluded that the results suggest the interest of the serum CTX-II monitoring for the OA progression and the relevance of the multiple time point analysis of this biomarker. [200]

Synovial fluid CTX-II levels directly represent articular cartilage status in OA. Our present study showed that Synovial fluid samples were collected from 15 patients (30%). the level of synovial CTX- II ranged from 200-400 pg/ml with a mean of 238.67 and standard deviation 70. Similar results were obtained by Yuanhui et al [201] they found that synovial CTX- II were significantly higher in OA patients than those in control subjects SF CTX-II (ng/ml) 32.80 ± 14.46 in control group and 66.00 ± 65.11 in OA.

Oestergaard et al [202] , conducted a study to assess the utility of measuring C-terminal telopeptides of collagen type II (CTX-II) in serum and synovial fluid samples for estimation of articular cartilage status in experimental models of destructive joint diseases. They induced arthritis in rats using either bovine collagen type II or mono-iodoacetate.

CTX-II levels were measured in the serum and synovial fluid of the affected femoro-tibial joint and correlated with microscopic severity of joint lesions as determined by validated scoring systems .

In the collagen-induced arthritis (CIA) model, the assay indicated markedly increased levels of CTX-II in both the synovial fluid and the serum. Furthermore, CTX-II levels in both the synovial fluid (r ¼ 0.76; P < 0.0001) and the serum (r ¼ 0.85; P < 0.0001) showed strong correlations with the microscopic severity scores of joint lesions . Concluding that Preclinical CTX-II assay could provide a useful supplement to currently available methods for the non-invasive assessment of cartilage status.

Standard plain radiography is the primary imaging modality used to evaluate osteoarthritis traditionally; plain radiography demonstrates osteoarthritic bony abnormalities and show indirect signs of articular cartilage lesion. However this technique is limited by its inability to directly visualize articular cartilage, synovial recesses, menisci and other soft tissues involved in the pathophysiology of osteoarthritis.

Newer imaging modalities such as high frequency muscloskeletal ultasonograghy (US) offer an overall assessment of the osteoarthritic joint. High frequency muscloskeletal US effectively depicts superficial periarticular and intra articular structures involved in rheumatic disesases. This technique has demonstrated accuracy and reliability in the identification of knee effusion, synovitis and Baker's cyst as well as higher sensitivity than physical examination for the detection of these pathological findings. [(203)]

In the current study 30 patients (60%) had effusion detected by ultrasonographic examination and this in agreement with Naredo et al[(204)] , their study was conducted on 50 patients with primary knee osteoarthritis and found that 28 patients (56%) had ultrasonographic effusion. our results disagree with Miguel M et al[(205)] who enrolled 81 patients with knee osteoarthritis in their study and found that 64 patients (79%) had ultrasonographic effusion.

Our results agree with those of Mendieta *et al* [(205)] , who compared 81 patients having symptomatic knee OA with 20 patients having asymptomatic knee OA. They found that the frequent ultrasonographic findings in the knees of patients with symptomatic OA were suprapatellar effusions (79%), meniscal lesions (45%), Baker's cysts (37%), and anserine bursitis (0.6%) .

In the current work patients who had ultrasonographic findings of effusion , Baker`s cysts and synovitis had higher VAS levels than patients without ultrasound findings. In cases with effusion mean VAS was 46.33 mm and in cases without effusion mean VAS was 38.75mm , in patients with synovitis mean VAS was 49.6 mm while in patients without synovitis it was 42.2 mm.

Previous conclusions on the relationship between US features and pain is knee OA are inconsistent. De Miguel *et al.* reported US effusion to increase the risk of knee pain by 6.5 times and Baker's cysts by 5.5 times but found no association between US features and pain severity. [(205)]Others have reported positive associations between US effusion with

higher pain VAS scores on motion and at rest. However, two recent cross-sectional studies reported no association between US features and either the presence of knee pain or pain severity. s

Moreover, our results agree with those obtained in the study by Naredo *et al* [(204)] . on patients with primary knee OA. They found that the more frequent ultrasonographic findings in symptomatic knees were effusion (47%), medial meniscus extrusion (61%), and Baker's cysts (22%). These patients were associated with a significantly higher pain score than those who had no findings at ultrasonography

In the current work 28 patients had synovitis detected by ultrasound .Kristoffersen *et al.* [(206)] demonstrated that primary OA is associated with synovial thickening in 61 of 71 patients, and hyperemia was detected in 51 of them. This confirms that there is a variable degree of inflammation among patients with knee OA. In the present work we investigated the relation between radiographic severity by using K/L grading and ultrasound features of knee osteoarthritis. We found that presence of effusion , synovitis and Baker`s cyst were associated higher K/L grade (grade 3, 4) with a p value (0.038 , 0.083 , 0.022) respectively.

Few studies have directly investigated the relationship between radiographic severity and US features in knee OA. D'agostino *et al.* [(207)]reported the presence of grey-scale US features was associated with higher radiological scores (K/L grade 3–4)[5], and MRI studies have also reported a significant relationship between synovial hypertrophy and radiographic severity.

OA is a multifactorial disease with both gentic and environmental determinants. Obesity Is most strongly linked to OA at the knee joint. there is a relationship between excess weight or obesity and knee OA. BMI is the anthropometric variable that clearly increases the risk of osteoarthritis.

Many population studies to date have found a cross sectional association between obesity and OA of the tibiofemoral joint of the knee.

The data demonstrate and lend support to what is a well-known observation : linear subjects have a smaller risk of radiographic knee OA compared with subjects with a high BMI.

In current work, The median BMI of group **I** was 29.5 kg/m^2 ranged from 26 to 31.5,while that of group **II** was 28.6 ranged from 23.5 to 30. BMI of patients was higher than BMI of the control but there was no statistically significant difference between the studied groups as regards their BMI with p value = 0.071.

This is in agreement with Cicuttini et al 2005 [(208)] who found that obesity was related with tibiofemoral OA and DIP joint OA. Some studies suggested that there was a weak association between obesity and DIP joint OA but a strong association between obesity, tibiofemoral OA and CMC joint involvement.

These findings agreed with Miguel Mendieta et al [205] who held up a cross sectional controlled study with primary knee OA based on ACR criteria with results showing that the increase in BMI is one of the factors associated with the appearance of OA and they concluded that higher BMI is more frequent and seen to be a risk factor of painful flare in knee OA with a p value less than 0.005.

Joints are usually tender during active motion testing and under pressure. Limited passive movement can be the first and only physical sign of symptomatic osteoarthritis. Bursitis,tendnitis, muscle spasm, and, especially for the knee, a torn meniscus, can cause the same pain syndrome and must be sought carefully during examination.

In our study 20 patients (40%) had clinical effusion, 16 had unilateral and 4 had bilateral clinical effusion,while 30 patients (60%) had no clinical effusion. This is in agreement with D`Agostino et al [207] who enrolled 600 patients with knee OA in their study and found that 204 patients (34%) had clinical effusion.

In the current work 27 patients (54%) had tenderness while 23 patients did not have tenderness; this agrees with D Agostino et al [207] who held a cross sectional,multi-centric, european study included 600 patients with primary knee osteoarthritis based on ACR criteria, out of 600 patients 52% of them had tender knees.

However our findings disagree with Naredo et al [204] who held a study of 50 patients with primary knee OA, 40 patients (80%) had tenderness.

Also these findings disagree with the study done by Ozcan et al[209] including 34 patients, 31 females and 3 males with primary knee OA, only 13 patients (38%) had tenderness disagreeing with our results. The difference in the findings related to tenderness may depend on the presence or absence of active inflammation.

Patellofemoral joint complaints are one of the most common muscloskeletal complaints in all age groups. Complaints vary from retropatellar crepitus to retropatellar knee pain. Slight crepitus may be observed in many normally functioning knees. Pain with crepitus may suggest patellofemoral degenerative arthritis.

In our study 37 patients (74%) had crepitus on clinical examination,while 13 patients (26%) had no crepitus. this is in agreement with Inaba et al [210] who enrolled 129 patients suffering from primary knee OA, 92 women and 37 men. 70% of them had crepitus on clinical examination.

In current study there was statistically significant difference between the patients and control group as regards their VAS ($P < 0.001$). Similar results were obtained by Barthel HR et al. Barthel correlations confirmed significant associations ($P < 0.001$) between VAS pain intensity and OA.[211]

WOMAC is a tested questionnaire to assess symptoms and physical functional disability in patients with OA of the knee and the hip.

In our study there was statistically significant difference between group **I** and group **II** as regards WOMAC ($p<0.001$).

In a study done by Salaffi F, Leardini G, et al, in 2003[212], they adapted the WOMAC for the Italian language and tested its metric properties in 304 patients with symptomatic OA of the knee and Found that the WOMAC discriminated better among subjects with varying severity of knee problems.They Concluded that WOMAC is a reliable and valid instrument for evaluating the severity of OA of the knee.

The lequsene index was assessed in group **1** and group **II**, the mean in patients was 11.4 (ranged from 8-17) and that of the control group was 0.5 ranged from (0- 2). there was significant difference between 2 groups as regard their index ($p < 0.001$)**.** this result is in agreement with Manicourt et al [213], who found that the median Lequsene Algo Functional Index (LAFI) scores were 14 (range 10–20) in the Patients with knee osteoarthritis.

Study Limitations

For proper interpretation of the results of the present study, we should take into consideration some limitations. The principal limitation of the present study is the relatively small study population putting into consideration that they were further divided into two groups. The cross-sectional nature of this study may have other limitations including ;the difficulty to evaluate a cause –effect relationship, as cross-sectional studies represent a snapshot in time which might limit our ability to determine the temporal sequence of the associations reported.

Our sample included subjects of Egyptian nationality only ; it might be uncertain whether our findings are applicable to other ethnic groups. Thus further multi-centric studies are required to assess serum CTX-II as a biomarker of knee osteoarthritis and to investigate its correlation with ultrasonographic, conventional imaging and clinical findings in knee OA.

Ultrasound imaging is limited by its inability to visualize the whole cartilage surface, by artefacts caused by position of the probe and finally by inter – and intra-observer variations. One notable drawback of sonography is operator –dependency in terms of imaging acquistion and interpretation. [214]

Other disadvantages include ; limited number and width of acoustic windows used to visualize joint structures, lack of standardization for definition and scoring system for osteoarthritis; thus, this imaging procedure needs standardization before use in daily clinical practice. [214]

Osteoarthritis (OA) is a group of chronic painful, disabling conditions affecting the synovial joints. It results from articular cartilage failure induced by a complex interplay of genetic, metabolic and biochemical factors with secondary components of inflammation. The process involves interactive degradation and repair processes of cartilage, bone and synovium. Osteoarthritis is the most common form of arthritis. [208]

In present study there was no statistically significant difference between group **I** and group **II** as regards the age (p=0.645) and the sex (p=0.617)

In group **I**, 20 were males and 30 were females while in group II, 7 were males and 13 were females in group A median age was 53ys ranged from 45ys to 65 ys while in group B median age was 55ys ranged from 40ys to 63ys.

In a study done by Lethbridge-Cejku M, Tobin JD, et al in1994 [209] to estimate the prevalence and pattern of radiographic changes of osteoarthritis (OA) of the knee by age and gender in Caucasian participants in the Baltimore Longitudinal Study of Aging. Bilateral standing weight-bearing radiographs of the knee in 547 male and 351 female subjects were read for changes of knee OA using Kellgren-Lawrence and individual features scales. Prevalence of definite (Kellgren-Lawrence grade > or = 2 changes) knee OA increased with advancing age in both sexes. Approximately 50 percent in both sexes showed bilateral involvement. They Concluded that age and gender influence both the prevalence and pattern of radiographic changes of knee OA.

The findings also agree with Avery L,Buchholz et al [211] who enrolled 21 patients, 13 females and 8 males with BMI ranging from 23.1 to 45.4 kg/m (mean 33.79 and 7.1 standard deviation) all suffering from knee osteoarthritis. from the findings of the current study and other previous mentioned studies, obesity seems to be an important modifiable risk factor for both development and progression of OA. This has been most strongly demonstrated in OAof the joint.

Crepitus, an audible or palbable sensation of crunching or crackling, is commonly felt on passive or active mobilization of osteoarthritis joints. This sensation is due to the irregularity of the opposing cartilage surfaces or intra-articular debris.

SUMMARY

Osteoarthritis is the most common form of arthritis causing a huge burden of morbidity and disability particularly in the elderly. Traditionally OA has been considered a disease of articular cartilage, but the disease is manifest in all joint structures; cartilage, subchondral bone,synovium, capsule and ligaments.

OA has been always classified as non-inflammatory arthritis; yet there is increasing evidence for inflammation occurring with cytokine and metalloproteinase release into the joint. Therefore the term degenerative joint disease is no longer appropriate when referring to OA.

OA was recognized as a non inflammatory arthropathy. However, recent studies have demonstrated that an inflammatory process plays a role in the pathogenesis of OA. Pro-inflammatory cytokines are implicated as potential mediators in the disease. Recently, the involvement of genetic factors has been extensively documented as well.

Osteoarthritis may be classified as primary or secondary according to its cause or major predisposing factor. Primary osteoarthritis is the most common type and has no identifiable etiology. Major factors that affect the degree of risk for developing osteoarthritis include age, gender, joint location, obesity, genetic predisposition, joint malalignment and trauma. Typical clinical symptoms are pain and stiffness, particularly after prolonged activity.

Molecular markers are molecules, or fragments of connective tissue matrices which are released into biological fluids during tissue biosynthesis and turnover and which can be measured by immunoassays. The type II collagen molecule has been investigated as a potential source of biomarkers in osteoarthritis. This is because type II collagen is the most abundant protein component of cartilage and it is relatively specific for hyaline cartilage. Furthermore, damage to the type II collagen meshwork is a critical event in the pathology-of-osteoarthritis.

The CTX-II epitope is a part of the non-helical carboxyterminal crosslinked telopeptide and consists of six amino-acids attached to a cross-link (X). It is released during the degradation of type II collagen. It is mainly concentrated in calcified articular cartilage at the junction with sub-chondral bone.

Musculoskeletal ultrasound (MSK US) has become an established imaging technique for diagnosis and follow up of patients with rheumatic diseases. It has considerable advantages over other imaging modalities including non –invasiveness, quick to perform, relatively low cost, ability to scan multiple joints, lack of ionizing radiation, repeatability and high patient acceptability.It can also be used for guidance of aspiration, biopsy and injection of treatment.

The aim of this work was to evaluate CTX-II as a marker of OA and correlate its level with ultrasound, conventional imaging and clinical findings.

The present study was conducted on 50 patients with knee OA and 20 healthy persons of matched age and sex as a control group.All were subjected to detailed history taking and through physical examination including joint examination, laboratory investigations, serum CTX-II level and in some cases synovial CTX-II level, x-ray both knees and musculoskeletal ultrasound (MSK US) of both knees). Data was collected and analyzed using computer based program.

The following results were obtained:

- There was statistically significant increase in serum CTX-II level in OA patients than the control group.
- Serum CTX-II was significantly positive correlated with ESR, CRP, OA grade and lequesne index.
- No correlation was found between CTX-II and VAS, WOMAC and cartilage thickness.
- ESR and CRP were significantly increased in patients with knee OA.

CONCLUSIONS

The following conclusions can be drawn from the current study:

1. CTX-II is highly expressed in the serum of osteoarthritis patients, so we can conclude that CTX-II may be a useful biomarker for osteoarthritis either in early diagnosis or in assessment of the severity of the disease.
2. CTX-II is highly correlated with ESR, CRP, Lequsene index and OA grading.
3. Analysis of CTX-II in serum samples provided a sensitive method to detect increased degradation of collagen type II in patients with knee osteoarthritis.
4. Ultrasound assessment of knee joint is better in detecting effusion, Baker cyst and synovitis than clinical examination.