

*Research Article***Osteopontine in knee osteoarthritis**

**Walaa F. Mohammed \***, **Faten Ismail Mohamed\***, **Gehan M. Ahmd \***,  
**Rasha A. Abdelmagied\***, **Aliaa M. Mounir\*\*** and **Mustafa Abdel- Kader\*\*\***

\* Department of Rheumatology and Rehabilitation,

\*\* Department of clinical pathology, Faculty of Medicine, El-Minia University, Egypt.

\*\*\*Department of Radiology\*\*\*, Faculty of Medicine, El-Minia University, Egypt.

**Abstract**

**Background:** Osteoarthritis is a painful chronic joint disease characterized by structural changes to the whole joint, including loss of articular cartilage, development of osteophytes, synovial inflammation, subchondral bone changes, meniscal damage, muscle weakness, and ligamentous laxity. **Aim of the work:** To detect osteopontine (OPN) in knee osteoarthritis. **Methods:** 60 patients diagnosed as primary knee OA fulfilling Arthritis Rheum 1986 OA classification criteria, And 60 healthy control were included. All patients subjected to through history taking and full examination, body mass index, plain x ray knees PA view to assess severity according to Kellgren and Laurence grading, plasma and synovial fluid OPN levels, and plasma OPN for control. Assessment of pain for OA patients by patient pain visual analogue scale (VAS) and for functional status by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), ESR,CRP were done. **Results:** there was significant difference between both groups regarding plasma osteopontine ( $p < 0.0001$ ), OPN levels in OA patients in plasma and synovial fluid was correlated with each other ( $p < 0.0001$ ), patient pain VAS, WOMAC score, K-L grading were correlated with plasma OPN levels with p value (0.001,  $< 0.001$ ,  $< 0.001$ ), and with synovial fluid OPN levels in primary OA patients with p value (0.008,  $< 0.001$ ,  $< 0.001$ ) respectively. ESR positively correlated with plasma OPN  $p = 0.004$ . **Conclusion:** OPN is higher in OA patients more than control, and it is higher in synovial fluid than plasma in knee OA patients, OPN correlated with markers of systemic inflammation and has impact on functional status so it can be used as a diagnostic and prognostic factor in knee osteoarthritis.

**Keywords:** Osteoarthritis – OPN.

**Introduction**

Osteoarthritis is a painful chronic joint disease characterised by structural changes to the whole joint including: loss of articular cartilage, development of osteophytes, synovial inflammation, subchondral bone changes, meniscal damage, muscle weakness, and ligamentous laxity. It results from a complex interplay of genetic, metabolic, biomechanical, and biochemical factors. At the knee, osteoarthritis most commonly affects the medial tibiofemoral and patellofemoral joint compartments. (Zhang et al., 2010).

Biochemical markers can be used to detect the disease and determine its severity. Therefore the extracellular matrix proteins were crucial to the occurrence and

development of osteoarthritis. some extracellular matrix proteins such as osteopontin (OPN) was found to play important roles in promoting the inflammatory occurrence of cartilage cells in knee osteoarthritis, As an important extracellular matrix protein, OPN can mediate cellular growth, survival, adhesion and migration in osteoarthritis (Hasegawa et al., 2011 and Qin et al., 2013).

**Aim of the work**

To detect osteopontine (OPN) in knee osteoarthritis.

**Patients and methods**

The study conducted in Minia university hospital, included 60 patients with primary knee osteoarthritis (group I) and 60

apparently healthy controls (group II), patients in group I was complaining of knee effusion candidate for aspiration for detection of synovial fluid OPN level, both groups also were tested for plasma OPN level. All patients fulfilled criteria for diagnosis of primary knee osteoarthritis (Altman et al., 1986) were included as (group I). Sixty apparently healthy volunteers were served as a control group (group II). Patients with other rheumatological diseases as rheumatoid arthritis, systemic lupus, gouty arthritis, Other forms of arthritis, cancer or other chronic inflammatory diseases, Secondary knee osteoarthritis, Diabetes mellitus were excluded from the study. The nature of the study was explained to all patients. plain x ray knees PA view to assess severity according to Kellgren and Laurence grading (Kellgren, and Lawrence, 1957), were ordered in all the patients, functional assessment of OA patients using WOMAC score (Bellamy et al, 1986) and pain assessed by patient pain VAS (Price et al., 1983)., plasma OPN level were done for all patients and control while synovial fluid done for patients with knee OA ESR and

CRP also done. A consent was obtained from all patients.

### Statistical analysis

Analysis of data was done by personal computer using SPSS (Statistical program for social science) version 16. The data of all software patients and controls were fed into an IBM personal computer. Data were expressed as mean  $\pm$  SD for parametric variables and as number and percent for non-parametric variable. Comparison between groups for parametric data was done by independent samples t-test (unpaired t-test). The difference was considered significant if  $P < 0.05$ . The Bivariate Correlations procedure computes Pearson's correlation coefficient with its significance levels. Pearson's correlation coefficient is a measure of linear association for parametric variables and Spearman-rho correlation coefficient for nonparametric variables.

### Results

Characters of OA patients; demographic data, laboratory investigation, functional status and radiological KL grading in table (1).

**Table (1): characters of OA patients**

Parameters mean $\pm$ SD and/or n(%)		OA patient n.= 60
Age (y)		46-72(56.3 $\pm$ 7.95)
DD (y)		2-10 (5.8 $\pm$ 2.33)
BMI	Over weight	4 (6.7%)
	Obese I	16 (26.7%)
	Obese II	24 (40%)
	Obese III	16 (26.7%)
VAS		5-10 (7.53 $\pm$ 1.22)
WOMAC total score		45-96 (74.26 $\pm$ 14.07)
KL grading	I	5 %
	II	35 %
	III	38.33 %
	IV	21.67 %
Plasma OPN		92-222 (136.67 $\pm$ 35.1)
Synovial fluid OPN		162-298 ( 218.4 $\pm$ 37.7)
ESR mm/ 1 <sup>st</sup> hour		8-36 (23.97 $\pm$ 7.4)
CRP		53 (88.3%)

**Functional status and severity in group I (OA patients):** Table 2 shows that patient pain VAS, WOMAC score, K-L grading were correlated with plasma OPN levels with p value (0.001, <0.001, <0.001), and

with synovial fluid OPN levels in primary OA patients with p value (0.008, <0.001, <0.001) respectively. ESR positively correlated with plasma OPN p= 0.004.

**Table 2: Correlation between plasma & synovial osteopontine with demographic data, disease functional and severity indices in OA patients:**

Parameters r (p)	Plasma OPN	Synovial fluid OPN
Age	0.032 (0.730)	0.800 (<0.0001)
DD	0.155 (0.236)	0.390 (0.002)
BMI	0.629 (<0.0001)	0.074 (0.574)
Patient pain VAS	0.431(0.001)	0.338 (0.008)
WOMAC totoal score	0.342 (<0.001)	0.358 (<0.001)
KL grading	0.358 (<0.001)	0.680 (<0.001)
ESR	0.362 (0.004)	0.087 (0.510)
CRP	0.017 (0.895)	0.689 (0.455)

## Discussion

Osteoarthritis (OA) is a low-grade inflammatory disease of synovial joints and the most common form of arthritis (Berenbaum, 2013). It is a leading cause of chronic pain and physical disability in older individuals. OA is one of the most costly and disabling forms of joint disease, being far more common than rheumatoid arthritis (RA) and other forms of joint disease (Cross et al., 2014).

Osteopontin is a critical intrinsic regulator that plays an important role in OA progression (Gao et al., 2010). The increased expression of OPN has been observed in the joints of patients that were reported to be correlated with the severity of joint lesion and inflammatory status in the OA patients (Honsawek et al., 2009 and Matsui et al., 2009).

In our study patient pain VAS, WOMAC score, KL grading was positively correlated with plasma and synovial OPN levels.

In agreement with our study Lee et al., (2013) studied thirty four patients with knee OA included eight men and 26 women, with a mean age of  $65.5 \pm 7.9$  years and mean disease duration of  $38.2 \pm 48.9$  months. Also in the study of Kim et al., (2016) VAS of knee pain was  $5.68 \pm 0.42$ ,

Total WOMAC was  $89.9 \pm 7.5$ , WOMAC pain was  $17.4 \pm 1.3$ , WOMAC stiffness was  $7.3 \pm 0.9$ , and WOMAC function was  $63.8 \pm 6$ .

Plasma osteopontine show statistically significant difference between both groups (p<0.001), and synovial fluid OPN was significantly higher than paired plasma level in primary OA patients.

In agreement with Sittisak et al., 2009 who found in a similar study on Plasma OPN (in patients and control) and in synovial fluid OPN (in patients) levels in knee OA patients, that patients had higher plasma OPN concentrations compared to healthy controls (P <0.0001). Also OPN levels in synovial fluid were significantly higher with respect to paired plasma samples (p <0.001).

In another study done by Qin et al., 2013, who examined the synovial fluid from 42 patients with knee OA and 40 cases of the normal control group had effusion due to traumatic causes as meniscus injury or lower extremity fracture surgery in the hospital at the same period for OPN level and demonstrated that the expression levels of OPN in OA group was significantly higher than those in the control (post traumatic) group, (P<0. 05)

In agreement with Haider et al., 2014 who found In their study about OPN in knee OA patients and control, that plasma OPN level significantly correlated with synovial OPN in OA patients ( $r = 0.806$ ,  $P < 0.001$ ), a significant difference between patients and controls as regards the plasma OPN levels ( $t = 8.534$ ,  $P < 0.001$ ), OPN in synovial fluid was higher with respect to paired plasma. Also, OPN level in both plasma and synovial fluid was significantly correlated with severity of knee pain ( $r = 0.878$ ,  $r = 0.795$ ,  $p < 0.001$ ).

### In conclusion

This study suggests that OPN is an inflammatory marker that can be used as a diagnostic and prognostic marker in knee OA.

### Acknowledgment:

Many deep thanks and gratitude go to my supervisors, my colleagues, patients and every person who had helped me by any means throughout this work.

**Conflict of interest:** The authors declare that there is no conflict of interest.

### References

- Altman, R., Alarcon, G., Appelrouth, D., Bloch, D., Borenstein, D., Brandt, K., Brown, C., Cooke, T. D., Daniel, W., Feldman, D., & Greenwald, R. (1991). The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. *Arthritis & Rheumatology*; 34 (5): 505-514.
- Berenbaum, F. (2013). Osteoarthritis as an inflammatory disease (osteoarthritis is not osteoarthrosis!). *Osteoarthritis and Cartilage*; 21 (1): 16-21.
- Cross, M., Smith, E., Hoy, D., Nolte, S., Ackerman, I., Fransen, M., & Laslett, L. L. (2014). The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. *Annals of the rheumatic diseases*; 73 (4): 2047-2063.
- Haider, H. M., Amin, I. R., & Ahmad, K. A. (2015). Plasma and synovial osteopontin levels, are they associated with disease severity of primary knee osteoarthritis in Egyptian patients?. *The Egyptian rheumatologist*, 37(1), 29-34.
- Honsawek, S., Tanavalee, A., Sakdinakiattikoon, M., Chayanupatkul, M., & Yuktanandana, P. (2009). Correlation of plasma and synovial fluid osteopontin with disease severity in knee osteoarthritis. *Clinical biochemistry*, 42(9), 808-12. doi:10.1016/j.clinbio.2009.07.014
- Qin, L. F., Wang, W. C., Fang, H., Mao, X. Z., Huang, G. L., Chen, Y., ... & Peng, D. (2013). Expression of NF- $\kappa$ B and osteopontin of synovial fluid of patients with knee osteoarthritis. *Asian Pacific journal of tropical medicine*, 6(5), 379-382.
- Tanamas, S. K., Wluka, A. E., Pelletier, J. P., Martel-Pelletier, J., Abram, F., Wang, Y., & Cicuttini, F. M. (2010). The association between subchondral bone cysts and tibial cartilage volume and risk of joint replacement in people with knee osteoarthritis: a longitudinal study. *Arthritis research & therapy*; 12(2): 58.
- Yamaga, M., Tsuji, K., Miyatake, K., Yamada, J., Abula, K., Ju, Y. J., ... & Muneta, T. (2012). Osteopontin level in synovial fluid is associated with the severity of joint pain and cartilage degradation after anterior cruciate ligament rupture. *PloS*
- Yamaga, M., Tsuji, K., Miyatake, K., Yamada, J., Abula, K., Ju, Y. J., ... & Muneta, T. (2012). Osteopontin level in synovial fluid is associated with the severity of joint pain and cartilage degradation after anterior cruciate ligament rupture. *PloS one*, 7(11), e49014.
- Zhang, W., Moskowitz, R. W., Nuki, G., Abramson, S., Altman, R. D., Arden, N., Bierma-Zeinstra, S., Brandt, K. D., Croft, P., Doherty, M., & Dougados, M. (2008). OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis and cartilage*; 16 (2): 137-162.