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Original Research Article

Status of soluble vascular cell adhesion molecule-1 in knee osteoarthritis among type 2-diabetic postmenopausal women

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ABSTRACT

Background: Knee osteoarthritis is the most common form of joint disorder and a leading cause of pain and functional disability among elderly female population. Type 2-diabetes is frequently reported comorbidity in elderly female patients with knee osteoarthritis. VCAM-1 is emerging as a strong and independent predictor for severe osteoarthritis. VCAM-1 is an inducible cell surface sialo glycoprotein and mediates heterotypic cellular aggregation. Therefore, the aim of this study is to assess the role of soluble vascular cell adhesion molecule-1 at the onset of knee osteoarthritis among type 2 diabetic postmenopausal women.
Methods: The present study includes 100 type 2-diabetic female subjects of age above 50 years as cases and 100 normal healthy female age matched individuals as controls. Osteoarthritis of knee was ascertained using the American college of rheumatology classification criteria. Serum soluble VCAM-1 concentration was measured by ELISA method in all 200 subjects. Biochemical parameters-Fasting blood sugar and lipid profile were measured using Mind ray BS-400 and HbA1c was measured by turbidimetric immunoassay method. Statistical analysis was made by student independent sample t-test. Correlation was determined by using spearman's rank correlation coefficient.
Results: Serum level of soluble VCAM-1 was found statistically highly significant ($p<0.001$) in type 2 diabetic postmenopausal women having early stage of knee osteoarthritis as compared to control healthy subjects. The mean levels of fasting blood sugar, HbA1c, total cholesterol, TG, LDL-C and VLDL-C were also found significantly increased while HDL-C was found significantly decreased in cases as compared to controls.
Conclusions: The increased level of soluble VCAM-1 in type 2 diabetic subjects shows active inflammation or cartilage damage. Therefore, it can be used as an early biomarker for osteoarthritis among type 2 diabetic postmenopausal women.

Keywords: Knee osteoarthritis, Type 2 diabetes Mellitus, VCAM-1

INTRODUCTION

Knee pain is one of the most common musculoskeletal complaints that bring people to their physician and the most common cause of knee pain is osteoarthritis.[1] Especially in females, knee osteoarthritis is the major cause of mobility impairment.[2,3] Nearly, 45% of women over the age of 65 years have symptomatic findings of knee osteoarthritis while radiological evidence is found in 70% of those over 65 years.[2-4] In India, average menopausal age in women is 46.3 years as compared to 54 years in western countries.[5,6] This predisposes Indian women at higher risk of developing osteoarthritis in earlier age as compared to their western counterparts. It could be due to loss of estrogen especially close to menopausal years at this time.[7,8]

Diabetes mellitus is a multi-system disease characterized by persistent hyperglycemia that has both acute and chronic biochemical and anatomical squeal which may cause irreversible damage to many organs and organ systems.[9] This disease affects connective tissues in many ways and causes different alterations in periarticular and musculoskeletal system.[10] Type 2-diabetes is frequently reported co-occurring disease in elderly patient with knee osteoarthritis. Singh et al reported that there was around 55% of knee osteoarthritis patients of over 65 years old having hypertension and 13% of them showing Type 2 Diabetes Mellitus.[11] Many studies have reported a correlation of osteoarthritis with duration of diabetes mellitus and poor glycaemic control.[12-16] However, the link between diabetes mellitus and osteoarthritis is not well defined, but it may be due to deleterious role of excess of glucose through the accumulation of advanced glycation end products, oxidative stress and promotion of systemic inflammation.[16-19] So, there is a need of biomarker that identifies type 2 diabetic individuals who are at higher risk of developing osteoarthritis.

Vascular cell adhesion molecule-1 emerged as a strong and independent predictor for severe osteoarthritis.[20] Previous studies have reported that hyperglycemia, hyperinsulinemia or insulin resistance are responsible for elevation of this adhesion molecule.[21,22] VCAM-1 is an inducible cell surface sialo glycoprotein expressed on chondrocytes and synovial fibroblasts. VCAM-1 mediates the adhesion of lymphocytes, monocytes, eosinophils, and basophils to vascular endothelium and plays a role in the development of inflammation.[23] VCAM-1 mediates the interaction of chondrocytes with immune cells and could thus by itself contribute to immune-mediated cartilage damage.[24] Therefore, the present study is aimed to assess the serum level of sVCAM-1 in type 2-diabetic postmenopausal women having early stage of knee osteoarthritis.

METHODS

The present study has been carried out in the Department of Biochemistry and Department of Orthopaedics, G.R Medical College and J.A. Group of Hospitals, Gwalior. Total 200 human subjects were taken in the study. Out of which 100 type 2-diabetic postmenopausal women of age 50 years or above having clinical symptoms of knee osteoarthritis were considered as cases and 100 normal healthy individuals of same age as control.

Inclusion criteria

Postmenopausal women suffering from type 2 diabetes mellitus with complain of knee pain lasting longer than 1 month in addition to at least 3 of the following 6 criteria according to ACR guideline: age>50 years, morning stiffness more than 30 minutes, crepitus, bony enlargement, bony tenderness and absence of palpable warmth.

Exclusion criteria

Patients taking any hormone replacement therapy (HRT), non-steroidal anti-inflammatory drugs (NSAIDs), having metabolic bone disease, rheumatoid arthritis, serious systemic diseases, history of knee trauma or knee injury, cardiac heart diseases. Before starting analysis, the written consent was taken from all subjects. The study has been approved by institutional ethical committee and was carried out by keeping all norms in mind. The clinical manifestations of disease, personal history of patients was recorded in study proforma.

8ml of fasting blood sample was taken from all subjects under all aseptic precautions and dispensed into three tubes i.e. fluoride, EDTA and plain tubes. Serum and plasma from plain and fluoride tubes were separated after centrifugation for 5-10 minutes at 3000 rpm and analysed for routine biochemical parameters and serum was stored at -20° C in aliquots for ELISA analysis of sVCAM-1. Levels of Fasting blood sugar, total cholesterol, triglycerides, HDL-C were measured by standard biochemical kits (Erba) using BS 400 fully automated analyser (Mindray). EDTA tube was used for estimation of HbA1c (estimated by turbidimetric immunoassay). LDL and VLDL were calculated by using Friedewald formula. Serum levels of sVCAM-1was measured by enzyme-linked immunosorbent assay kit (Diaclone Elisa Kit).

Statistical analysis

The results were expressed as Mean ± Standard Deviation. The statistical differences between cases and control were determined by student independent t-test. Data analyses were performed with the Statistical Package for the Social Sciences, version 21.0 (SPSS, Chicago, Illinois, USA). In order to determine correlation, statistical analysis was carried out by using spearman's rank correlation coefficient. The p value less than 0.05 were considered as significant.

RESULTS

The descriptive statistics of glycemic status, lipid profile and sVCAM-1 are shown in (Table 1). The mean value of FBS, HbA1c and lipid profile such as TG, TC, LDL-C and VLDL-C were highly significantly increased while HDL-C was significantly decreased ($p<0.001$) in cases as compared to control. The serum level of sVCAM-1 was highly found statistically highly significantly increased ($p<0.001$) in Type 2-diabetic subject suffering from knee osteoarthritis as compared to control. Correlation analysis among the investigated serum parameters revealed a significant positive correlation of VCAM-1 with FBS, HbA1c, Total Cholesterol, and a significant negative correlation of VCAM-1 with HDL-C (Table 2).

Table 1: The changes of blood sugar, lipid profile and sVCAM-1 in control group and diabetic postmenopausal women cases.

Variable	Control (100)	Cases (100)
FBS (mg/dl)	95.8±10.86	167.41±40.94**
HbA1c	4.92±0.38	7.5±1.44**
Triglyceride (mg/dl)	134.58±24.36	172.64±39.63**
Total cholesterol	190.30±15.02	257.21±36.39**
HDL-C (mg/dl)	45.41±4.43	32.76±7.42**
LDL-C (mg/dl)	117.61±16.93	190.68±38.88**
VLDL-C (mg/dl)	26.92±4.87	34.52±7.92**
sVCAM-1 (ng/ml)	464.31±28.54	784.47±115.97**

**Significant at p<0.001.

Table 2: Showing correlations between sVCAM-1 and biochemical parameters in diabetic postmenopausal women.

Variables	VCAM-1
FBS	0.297**
HbA1c	0.244**
TC	0.283**
TG	0.013NS
HDL-C	-0.207*
VLDL-C	0.013NS
LDL-C	0.186NS

Results are presented in r value. *Significant at p<0.05. **Significant at p<0.01. NS Non-Significant.

DISCUSSION

Knee osteoarthritis is a major public health problem especially in postmenopausal women. Type 2 diabetic postmenopausal women are at higher risk of incidence, severity and earlier onset of knee osteoarthritis than nondiabetic postmenopausal women. In diabetes hyperglycemia plays a role for joint degradation and may be induces osteoarthritis.[25] In this study, we found highly significant increased levels of HbA1c and FBS (p<0.001) in diabetic postmenopausal women with knee osteoarthritis compared to controls. Which is same as Cimmino et al who reported that mean fasting plasma glucose was significantly higher in women with osteoarthritis as compared to controls and out of which 5.5 percent women had type 2 diabetes.[26] Rouen et al reported that in postmenopausal women having type 2 diabetes glucose control is associated with the severity of those symptoms commonly attributed to menopause such as joint pain.[27] Hart et al also reported that in women of age 45-64 years blood glucose was associated with unilateral and bilateral knee osteoarthritis.[28] The possible explanation of link between hyperglycemia and osteoarthritis that hyperglycemia can induce an inflammatory state, and that an inflammatory state might predispose cartilage to damage that leads to osteoarthritis. [25] The level of TG, TC, LDL-C, VLDL-C were also found significantly increased while HDL-C was found significantly decreased in diabetic postmenopausal women with knee osteoarthritis as compared to controls. The alteration of lipid profile i.e. dyslipidemia, observed in our study may be due to deposition of lipids, particularly in chondrocytes, which aggravates lipid metabolism disorders in degenerative articular cells and promotes the development of osteoarthritis which is consistent with the study of Hart et al.[28] Some epidemiological studies have also shown that raised serum cholesterol and reduced HDL level to be risk factor for osteoarthritis development and progression.[29,30]

Along with raised FBS and dyslipidemia, in this study the serum level of sVCAM-1 was found statistically highly significantly increased (p<0.001) in diabetic postmenopausal having clinical symptoms of knee osteoarthritis as compared to controls. Hoeven et al also reported the increased level of VCAM-1 in elderly women having knee osteoarthritis than those without knee osteoarthritis. The increased levels of sVCAM-1 in our study shows inflammation or active cartilage damage. In this study, a positive correlation of hyperglycemia with VCAM-1 is present which is consistent with the hypothesis that high intracellular glucose concentration in diabetes promotes the formation of advanced glycation end products. AGE compounds interact with membrane receptors called RAGE present on chondrocytes and give rise to a cascade of events that promote release of pro-inflammatory factors such as TNF-α, and activate transcription factors such as Nf-kB, which in turn induces VCAM-1 and promotes inflammation and cartilage degradation.[25,32,33] Therefore, in our study hyperglycemia, dyslipidemia with VCAM-1 increase is suggestive of onset of inflammation or cartilage damage in knees.

CONCLUSION

This study concluded that hyperglycemia, dyslipidemia with VCAM-1 increase in diabetic postmenopausal women is suggestive of onset of osteoarthritis.

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