INTRODUCTION

Osteoarthritis, also called osteoarthrosis is the most common joint disorder and one of the leading causes of pain, functional disability and reduced health-related quality of life worldwide. The word ‘osteoarthritis’ derived from the Greek word “osteo”, meaning “of the bone”, “arthro”, meaning “joint” and “itis”, meaning inflammation (Arya et al., 2013). With increasing life expectancy and aging population, osteoarthritis is estimated to be the fourth leading cause of disability by the year 2020 (Woolf et al., 2003). In India, it is the second most common rheumatological problem and the most frequent joint disease with the prevalence of 22% to 39% (Chopra et al., 2001). Osteoarthritis generally occurs in women than men and it increases in prevalence, incidence, and severity after menopause (Kellgren et al., 1963; Felson, 1990). The American College of Rheumatology defined osteoarthritis as “a heterogeneous group of conditions that lead to joint symptoms and signs, which are associated with the defective integrity of articular cartilage, in addition to related changes in the underlying bone at the joint margins”(Altman et al., 1986). It is characterized by the slow progressive degeneration of articular cartilage, subchondral bone sclerosis, synovial inflammation and marked osteophyte formation, with the involvement of whole joint (i.e. joint failure) (Hunter et al., 2006).

The knee is the most commonly affected joint and osteoarthritis of the knee is a major cause of mobility impairment, particularly among females (Davis et al., 1988; Akinpelu et al., 2009). 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 (Solomon et al., 1975; Davis et al., 1988; Akinpelu et al., 2009). The etiology of knee osteoarthritis is idiopathic and multifactorial. Aging,
menopause, obesity and genetic variations are the major risk factors of knee osteoarthritis (Hochberg et al., 2004; Kerkhof et al., 2010; Valdes et al., 2010; Sridhar et al., 2012). However, recent advances in the knowledge of osteoarthritis have highlighted the involvement of other risk factors such as type 2 diabetes or dyslipidemia and defining a new phenotype of osteoarthritis called metabolic osteoarthritis (Bijlsma et al., 2011). Socioeconomic status, lifestyle factors such as physical activity and exercise have also been associated with knee osteoarthritis.

Diabetes mellitus is a group of metabolic diseases characterized by persistent hyperglycemia that has both acute and chronic biochemical and anatomical squeal, may cause irreversible damage to many organs and organ systems (Crispin et al., 2003). This disease affects connective tissues in many ways and causes different alterations in the periarticular & musculoskeletal system (Arkkila et al., 2003; Cagliero, 2003). Type 2 diabetes is frequently reported comorbidity in the elderly female population with knee osteoarthritis. Singh et al., 2002 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. The walking disabilities of knee osteoarthritis have been identified as a major risk factor for the death of elderly population with Type 2 Diabetes Mellitus and cardiovascular diseases (Nuesch et al., 2011). Although the exact pathophysiology behind the link between diabetes and osteoarthritis is not clear 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 (Verzijl et al., 2003; Berenbaum, 2011; Atayde et al., 2012; Mobasher, 2012).
For a long time, osteoarthritis was considered as a non-inflammatory condition. More recently, however, it became evident that synovial inflammation plays an important role in the pathophysiology of osteoarthritis (Benito et al., 2005; Loeuille et al., 2005; Felson, 2006; Pearle et al., 2007; Sellam et al., 2010). Synovitis is generally occurring in an early and advanced phase of osteoarthritis and has been associated with knee pain and progression of cartilage degeneration (Goldring et al., 2004; Benito et al., 2005; Ayral et al., 2005; Hill et al., 2007). Some in vivo diabetic models have shown that diabetes induces more synovial inflammation especially in type 2 diabetic than non-diabetic (Ribeiro et al., 2016). This is in line with the clinical observation of more synovitis in knee osteoarthritis in diabetic than in non-diabetic patients using ultrasound examination (Schett et al., 2013). The inflammatory changes occur in osteoarthritis synovium include synovial hypertrophy and hyperplasia with an increase in the number of the synovial lining cells (Pelletier et al., 2001). These changes are often accompanied by infiltration of the underlying tissue by various inflammatory cells such as synovial macrophages, activated B and T lymphocytes. Adhesion and infiltration of leukocytes from the vascular compartment into synovial fluid and synovial tissue occur in response to cytokines and cell adhesion molecules (Scanzello et al., 2012).

Adhesion molecules are cell surface molecules that are involved in either cell-cell or cell-matrix interactions. These molecules perform many cell functions including cell migration, cell signaling and binding of cells to their basement membrane. In inflammation, adhesion molecules are intricately involved in leukocyte extravasation. Soluble cell adhesion molecules (sCAMs) are class of adhesion molecules that can be derived from cell surface adhesion molecule following cell stimulation or activation.
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(Volin, 2005). These molecules can be detected in serum or plasma and are increased in many conditions with an inflammatory component (Gearing et al., 1993). Vascular cell adhesion molecule -1 (VCAM-1) is an inducible cell surface sialoglycoprotein that belongs to immunoglobulin gene superfamily (IgSF). In joints, VCAM-1 is expressed by microvascular endothelial cells, synovial fibroblasts and chondrocytes (Kriegsmann et al., 1995). It is not expressed on resting vascular endothelium but is quickly induced in response to inflammatory stimuli, such as the cytokines tumor necrosis factor-α, interleukin-1β (Carter et al., 2001). VCAM-1 serves as a surface ligand for α4β1 and α4β7 integrins on macrophages, monocytes, lymphocytes, basophils, and stromal cells and plays a main role in the adhesion of lymphocytes to endothelium in the site of inflammation (Albelda, 1991). When endothelial cells are activated by inflammatory cytokines, soluble VCAM-1 is generated via proteolytic cleavage at or near the site where the protein inserts into the endothelial cell membrane, although the mechanisms involved are unknown (Carter et al., 2001, Pigott et al., 1992). Soluble VCAM-1 possesses angiogenesis activity (Koch et al., 1995) and chemotactic activity for T lymphocytes (Kitani et al., 1998) and monocytes (Tokuhira et al., 2000). It is widely distributed in human tissues and organs, thus the role of VCAM-1 occurs in various diseases such as cardiac disease, inflammation in osteoarthritis and in the metastasis of cancers.

In osteoarthritis, chondrocytes produce or respond to a number of pro-inflammatory cytokines and chemokines such as tumor necrosis factor-α, interleukin-1β (Goldring et al., 2008; Martel-Pelletier et al., 2008). These proinflammatory mediators induce the generation of VCAM-1. VCAM-1 mediates the adhesion of lymphocytes, monocytes and macrophages to vascular endothelium and plays a role in the
development of inflammation (Muller, 2009). Thus in osteoarthritis, VCAM-1 mediates the interaction of chondrocytes with immune cells and could thus by itself contribute to immune mediate cartilage damage (Kienzle et al., 1998). Angiogenesis and inflammation are integrated processes in osteoarthritis and it appears to be strongly correlated with synovial hyperplasia occur in synovial inflammation (Mapp et al., 2012). Soluble VCAM-1 possesses angiogenic activity which increases the delivery of inflammatory cells at the site of inflammation and worsens the symptoms and outcomes of osteoarthritis.

Thus, the present study has been aimed to know the role of soluble VCAM-1 in knee osteoarthritis in diabetic postmenopausal women.