Original Article

# Correlation Of Smoking And The Level Of Icam-1 AndVcam-1 Serum As A Criterion Of Buerger's Disease

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## Abstract

**Background and Aim:** Obliterative thromboangitis (TAO) or Buerger's disease is an inflammatory obstructivedisorder that affects the vascular organs of young smokers. The immune system appears to play a major role in theetiology of TAO. However, information on aspects related to the evolution of vascular inflammation and the diseaseis still limited.

**Objective:** This study was performed to evaluate the concentration of (ICAM-1, VCAM-1) in smokers and non- smokers.

**Methods**: 108 samples of this study consisted of two groups of smokers and non-smokers. Blood samples of non- smokers were collected from non-smokers who donated blood in Mashhad Blood Transfusion Center and blood samples of smokers were collected from Mashhad University of Medical Sciences, Imam Reza Hospital. Through a comprehensive questionnaire, we extracted information about each individual completed by the individual. In this study, 108 people, 57 smokers and 51 non-smokers, were studied. The mean age of smokers and non-smokers was
49.67 ± 8.91 and 48.08 ± 7 7.7 respectively. The number and mean age of participants in this study in two groups ofsmokers and non-smokers, the concentration of ICAM-1 and VCAM-1 measured were by ELISA kit method to determine the levels of these markers in two groups. The results of this study were analyzed using SPSS 26 statistical software and using Chi-square ($2\chi$), t-test and Mann-Whitney test (for abnormal data) with a significance level of P
<0.05.

**Results:** The smokers participating in this study are 45 people with an average of 0.13± 0.17. Also, 45 non-smokers with an average of 0.16 ± 0.12 form the control group. As the results show (Z = 2.15, P = 0.031), the amount of ICAM-1in the non-smoking group is higher than the smoking group. The smokers participating in this study were 45 with a mean of 0.81± 0.36. Also, 45 non-smokers with an average of 0.74± 0.26 constitute the control group. As the resultsshow (Z = 0.024, P = 0.981), there is no significant difference between the mean of VCAM-1 in the non-smoking andsmoking groups.

**Conclusion:** ICAM-1 as a potential target for diagnosing the immune response against tobacco and its association with vascular diseases such as Burger disease.

**Keywords:** Smokers, Tobacco, Immune system, ICAM-1, VCAM-1, Burger disease

## Introduction

TAO is a vascular disease that was introduced and published in an official article by Leo Buerger in 1908. For this reason, it is also called Buerger's disease. Burger's disease is a vascular disorder of the lower extremities and around the body that is characterized by features such as thrombotic and inflammatory(1). It should be noted that this disease is non-atherosclerotic and should not be confused with atherosclerosis(2). The main cause of this complication is not yet known, but the factors involved in its occurrence have been introduced to some extent, and smoking undoubtedly plays a major role in the progression of this disease(3). There are also reports that the disease has an autoimmune root and is stimulated and becomes clinical following the use of tobacco and the presence of nicotine and other components in them(4). Following inflammation, blood vessels become swollen, narrowing the blood flow path and weakening blood flow to the lower extremities. In progressive and acute cases, this swelling leads to blockage of the arteries. As a result, blood and oxygen do not reach the relevant organs, resulting in serious tissue damage, bruising and tissue breakdown, and eventually tissue death and amputation. Vascular blockages are regional, and we may see healthy and diseased parts in the same vein in a patient at the same time(5). According to the relevant authorities, it is the most prevalent in the Middle East and the Far East. In the next rank, we can mention North America and Western Europe (6). In general, the prevalence of burgers has decreased in the last 5 years, which is due to the reduction of smoking and the achievement of more accurate diagnostic criteria(7). ICAM-1 is a transmembrane glycoprotein from members of the immunoglobulin family. Families that are made up of proteins that contain antibodies and T-cell receptors(8). ICAM-1 is commonly expressed on the surface of endothelial cells and immune system cells and plays an important role in intercellular communication. Interestingly, this protein has recently been introduced as a site for human rhinovirus to enter(9). Activation of ICAM-1 triggers proinflammatory effects. This protein is mainly expressed on the surface of endothelial cells and leukocytes, thus facilitating the binding of leukocytes to the vascular endothelium to enter the arteries in the processes of vasodilation or inflammatory responses(8). VCAM-1 is a vascular cell adhesion protein that acts like ICAM-1 as a cell adhesion molecule. This molecule is expressed on the surface of large and small vessels only when endothelial cells are stimulated by cytokines. VCAM-1 mediates the binding of lymphocytes, monocytes, and eosinophils and basophils to the vascular endothelium and plays an important role in the development of atherosclerosis and rheumatoid arthritis(10). On the other hand, there are hypotheses that the immune system may be involved in the development of this disease. In general, most autoimmune diseases are closely related to abnormalities in the regulation of cytokines, increased levels of lymphocyte apoptosis, and the continued presence of immune complexes in the bloodstream and body fluids. All of this has focused our attention on the production of cytokines and other circulatory factors in TAO patients. There is currently little evidence of immune regulation abnormalities in TAO patients that affect humoral and cellular immunity. In the meantime, there have been reports of changes in the level of secretion and functional pattern of some immune system factors, which confirms the hypotheses(11). Immunological studies have shown that the adhesive molecules of endothelial cells in this disease are stimulated and their expression pattern is altered. Thus, in this study, we decided to assess the serum levels of VCAM-1, ICAM-1 factors in smokers and non-smokers. It is hoped that the results of these evaluations will provide useful information on the efficacy and role of smoking in burger disease as well as immune system changes(9). The aim of this study isevaluation the correlation of smoking and the level of ICAM-1 and VCAM-1 serum as a criterion of Buerger’s disease.

## Material and methods

### Samples collection

The samples of this study consist of two groups of smokers and non-smokers. Blood samples were collected from who donated blood in Mashhad blood transfusion center and blood samples of smokers were collected from Imam

Reza Hospital. Through a comprehensive questionnaire, we extracted information about each individual completed by the individual. In this study, 108 people, 57 smokers and 51 non-smokers, were studied. The mean age in smoker and non-smoker groups was 49.67 ±8 8.91 and 48.08 ±7 7.7, respectively. The number and mean age of participants in this study in both smokers and non-smokers can be seen in Table (1).

| **Specifications** | **Smokers** | **Non-smokers** |
|---|---|---|
| Numbers of samples | 51 | 57 |
| Mean of age | 49.67 ±8 8.91 | 48.08 ±7 7.7 |

Table (1): number and mean age of participants in this study

**Elisa evaluation of ICAM-1 and VCAM-1**

The serum levels of ICAM-1 and VCAM-1 of smokers and non-smokers were evaluated by human intracellular adhesion molecule-1 kit (Zell Bio, cat. No: ZB10212-10212C-H9648, GmBH Germany.

**Data analysis**

The results of this study were analyzed using SPSS 26 statistical software and using Chi-square ($2\chi$), t-test and Mann- Whitney test (for abnormal data) with a significance level of $P < 0.05$.

## Results

**Results of descriptive statistics**

Graphs showing a significant difference in mean are indicated by the symbol **.

**3-2- Age distribution**

The smokers participating in this study are 57 people with a mean age of 49.67 8 8.91 years. Also, 51 non-smokers with a mean age of 48.08± 7 7.7 constitute the control group. As the results show (t = 0.98, df = 106, P = 0.327) there is no significant difference between the mean age of the non-smoking and smoking groups. Figure (1)

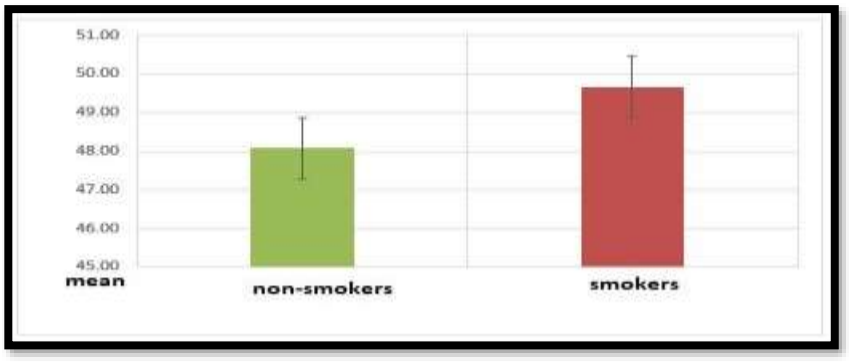


Figure (1): Age distribution

**Weight distribution**

The smokers participating in this study are 57 people with an average of 70.26 12 12.28. Also, 51 non-smokers with an mean of 75.2 13± 13.56 constitute the control group. As the results show (t = 1.98, df = 106, P = 0.048) the

mean weight of the non-smoking group is higher than the smoking group. Figure (2)

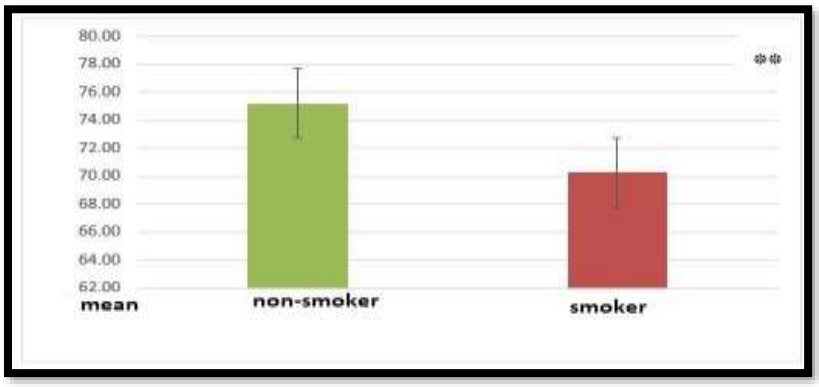


Figure (2) weight distribution

**BMI distribution**

The smokers participating in this study are 57 people with an average of 25.21 ±74 3.74 kg. Also, 51 non-smokers with an average of 26.45± 4.18 constitute the control group. As the results show (t = 1.62, df = 106, P = 0.108) there is no significant difference between the mean BMI of the non-smoking and smoking groups. Figure (3)

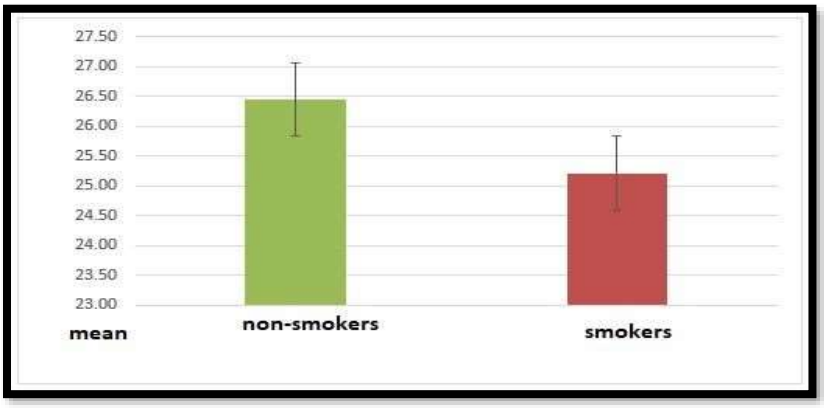


Figure (3) IBM distribution

**Obesity distribution**

Among the smokers participating in this study, 52 had obesity less than 30 and 5 had obesity more than 30. Also, 51 non-smokers are in the control group, of which 43 have obesity less than 30 and 8 have obesity more than 30. There was no significant difference between obesity of non-smokers and smokers (P = 0.27, $\chi$ ^ 2 = 1.21). figure (4)

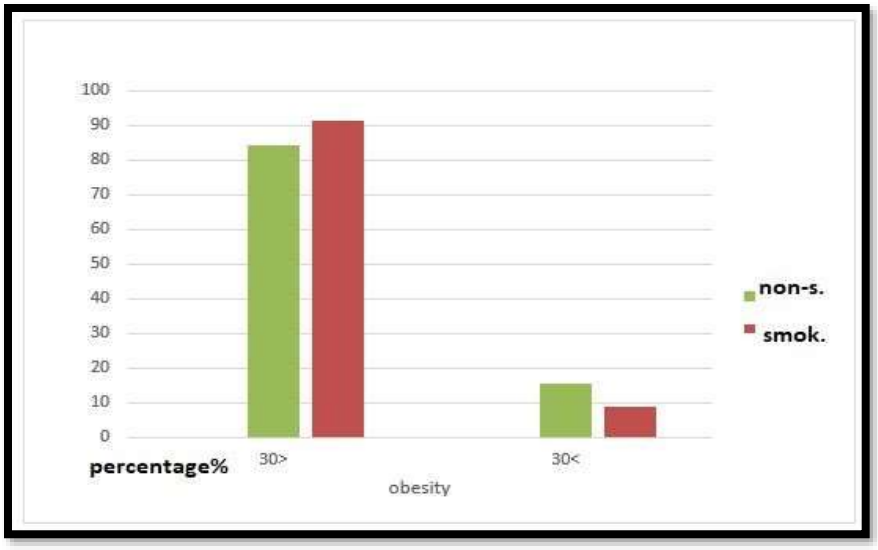


Figure (4): Obesity distribution

**Gender distribution**

Among the smokers participating in this study, 56 are male and 1 is female. Also, 51 non-smokers are in the control group, of which 48 are men and 3 are women. There was no significant difference between the sexes of the non-smokers and smokers (P = 0.257, $\chi$ ^ 2 = 1.29). figure (5)

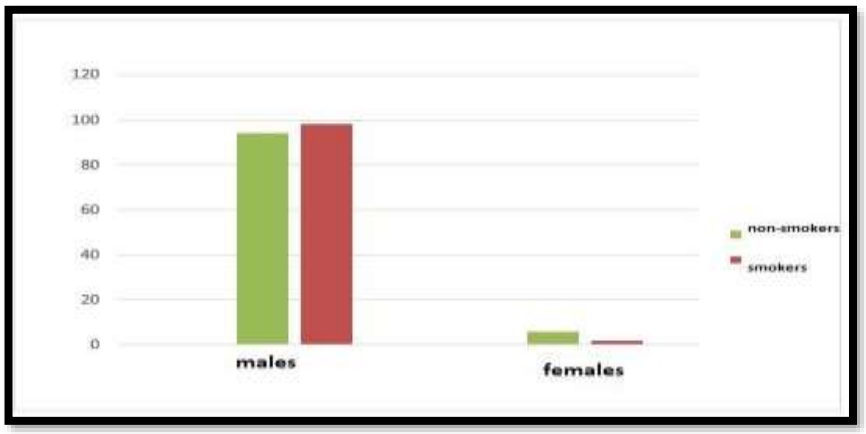


Figure (5): Gender distribution

**ICAM-1 distribution**

The smokers participating in this study are 45 people with an average of 0.13± 0.17. Also, 45 non-smokers with an average of 0.16 ± 0.12 form the control group. As the results show (Z = 2.15, P = 0.031) the amount of ICAM-1 in the non-smoking group is higher than the smoking group. Figure (6)

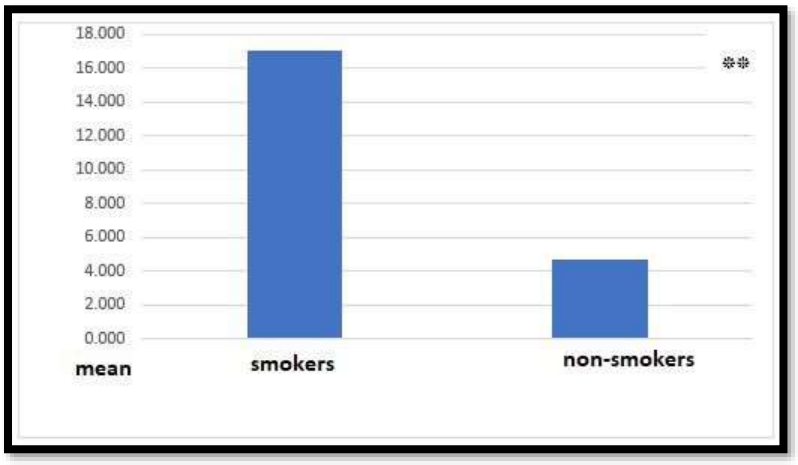


Figure (6) ICAM-1 distribution

Then, based on the standard curve below the concentration(ng/ml) of the sample, it was predicted that the amount of R ^ 2 of the fitted model is equal to 0.9975. The mean concentration of ICAM-1 in non-smokers participating in this study was 6.58 ±5.49 Also, the mean concentration of ICAM-1 in smokers participating in this study is 21.22± 28.35 As the results show (t = 2.87, df = 66, P = 0.005; Z = 2.59, P = 0.01) The concentration of ICAM-1 in the smoking group is higher than the non-smoking group. Figure (7)

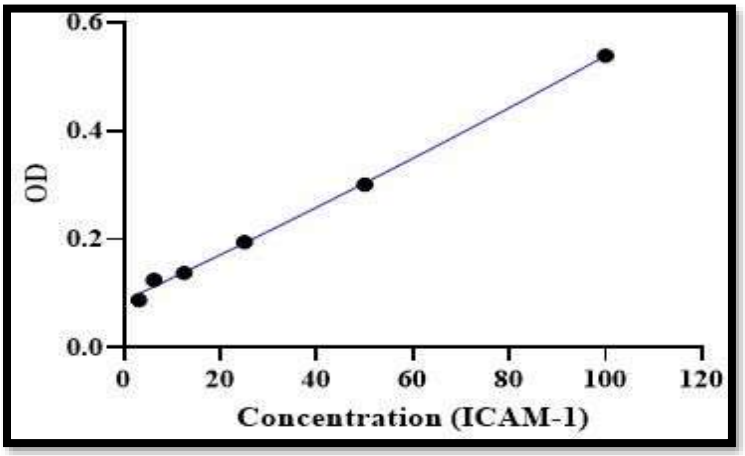


Figure (7): standard curve of ICAM-1 concentration (ng/ml)

**VCAM-1 distribution**

The smokers participating in this study were 45 with a mean of 0.81± 0.36. Also, 45 non-smokers with an average of 0.74± 0.26 constitute the control group. As the results show (Z = 0.024, P = 0.981), there is no significant difference between the mean of VCAM-1 in the non-smoking and smoking groups. Figure (8)

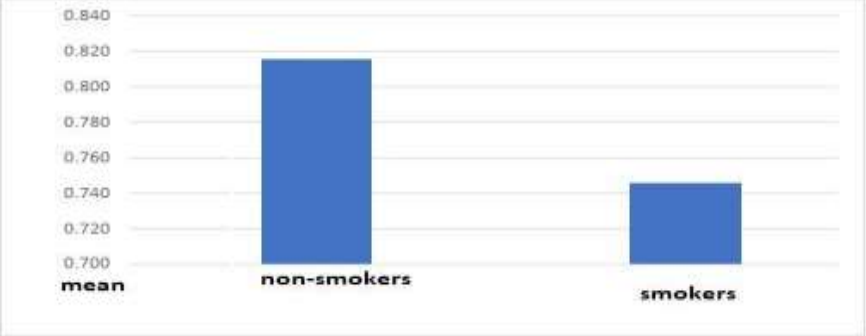


Figure (8): VCAM-1 distribution

Then, based on the standard curve below the concentration of the sample, it was predicted that the amount of R ^ 2 of the fitted model is equal to 0.9975. The mean concentration of VCAM-1 in smokers participating in this study was 4.25 ± 2.06 Also, the mean concentration of VCAM-1 in non-smokers participating in this study is 3.8± 1.5 As the results show (t = 1.18, df = 88, P = 0.243; Z = 0.2, P = 0.981) There was no significant difference between the mean concentrations of VCAM-1 in the non-smoking and smoking groups. Figure (9)

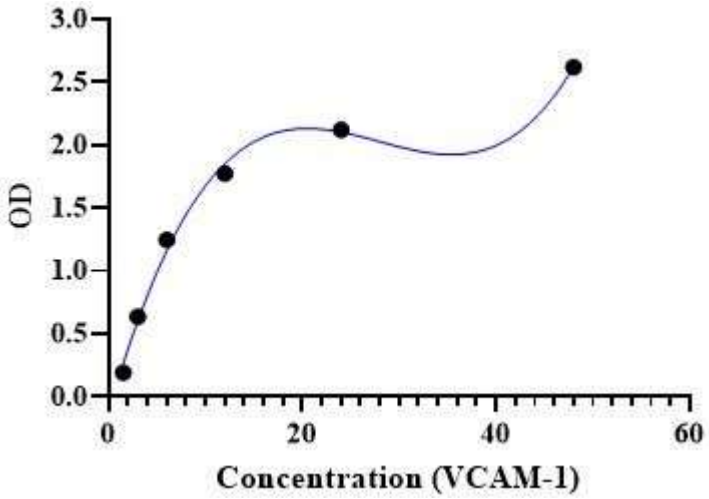

Figure (9): Standard curve of VCAM-1 concentration (ng/ml)

## Discussion

We also examined the expression in adhesion molecules from 2 adhesion molecules, ICAM-1, VCAM-1-. By ELISA kits, the concentration of these molecules showed that there is a relationship between smokingand secretion of these molecules. In smokers was associated with increased expression ICAM-1, VCAM-1in contrast in non-smokers. Therefore, it can be concluded that the expression of adhesion endothelial molecules is higher in smokers than non-smokers. The function of vascular endothelial cells in TAO patients is severely impaired, including the expression of intercellular adhesion molecule-1 (ICAM-1) andvascular cell-1 adhesion molecule (VCAM-1) in thickened vascular endothelial cells and someinflammatory cells(12). Finds, seriously damages life and health. The results of an ELISA study showed thatthe expression levels of ICAM-1 and VCAM-1 in the TAO group were significantly increased compared to the control group(8). Trombonists obliterans (TAO) is a disease whose cause and mechanism are unknown and mainly affects the arteries and small arteries of the upper and lower limbs. TAO seriously endangers people's lives, so effective treatment of TAO has been investigated to elucidate its molecular mechanism. , Which can reduce the level of soluble adhesion molecules (such as ICAM-1 and VCAM-1) inplasma in vascular patients, thereby delaying the development of vascular disease(7,13,14). In addition, ICAM-1 is highly expressed in TAO, which is closely associated with increased TAO-induced inflammatoryexpression, such as IL-1β, IL-6 and TNF-α. In addition, VCAM-1 is expressed in vascular endothelial cells, which mediates adhesion between lymphocytes, monocytes, and endothelial cells and is involved in many important pathophysiological processes and may be an important indicator of vascular dysfunction or progression of vascular disease. Be. The incidence of TAO has been reported to be closely related to ICAM- 1 and VCAM-1 (15). Leukocyte adhesion molecules are also heavily involved in a number of stages of theimmune and inflammatory responses. They are involved in the presentation of antigens in the cascade ofevents leading to additional vessels and in the interactions between agents and target cells. VCAM-1 is aninduction molecule that mediates endothelial adhesion of monocytes and T lymphocytes (16). A recent study of 20 showed that ICAM-1, VACM-1 and E-selectin increased endothelium and inflammatory cells inthe intima of TAO patients. In our study, VCAM-1 was expressed in endothelial cells as one of the markers of cell activation (4).

## Conclusion

In the present study, which is one of the comprehensive studies on samples of patients with burgers, 108healthy individuals in terms of clinical findings and findings related to hemorrhagic immunity and some cellular findings including flow cytometric view of cells in Circulation was. In this study, 51 smokers and 57 non-smokers were examined for their plasma secretion concentrations of ICAM-1, VACM-1. The resultsshowed that in the smoking group there were significant changes in the serum levels of ICAM-1, VACM-1compared to non-smokers. Despite significant differences in these parameters, it is the only serum level of ICAM-1 that becomes too standard in the smoking group. Given the significant association of immune system components with some clinical signs and their abnormal function in smokers to be similar to those with burger disease, they can be used as a criterion for determining the course of burger disease or basedon They identified a treatment strategy.

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