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Original

# Serum ICAM-1 level and ICAM-1 gene 1462A>G (K469E) polimorphism on microalbuminuria in nondiabetic, nonhypertensive and normolipidemic obese patients: Genetical background of microalbuminuria in obesity

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ABSTRACT

*Background:* A growing body of evidence suggest that obese individuals are under risk of renal parenchymal disorders when compared to nonobese counterparts. Microalbuminuria is the early marker of renal involvement. Although most of obese patients carries multiple risk factors for microalbuminuria, some obese individuals without risk factor may progress to microalbuminuria. The present study was performed to examine the role of ICAM-1 gene 1462A>G (K469E) polymorphism on microalbuminuria in obese subjects without diabetes mellitus, hypertension, hiperlipidemia and older age.

*Methods:* Ninety eight obese and 96 nonobese individuals without a comorbidity enrolled into the study. Serum ICAM-1 level was measured by enzyme linked immunoabsorbent assay (ELISA) method. ICAM-1 gene 1462A>G (K469E) polymorphism was examined by restriction fragment length polymorphism-polymerase chain reaction (RFLP-PCR). Nepholometric method was used to examine urinary albumin loss, and microalbuminuria was measured by albumin to creatinine ratio.

*Results:* Obese individuals had significantly higher microalbuminuria and proteinuria level compared to nonobese subjects ($p$: 0.043 and $p$: 0.011; respectively). GG genotype of ICAM-1 carriers have significantly higher microalbuminuria compared to individuals with AA or AG genotype carriers ($p$: 0.042). Serum ICAM-1 level was significantly correlated with creatinine

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and microalbuminuria (*p*: 0.002 and *p*: 0.03; respectively). Logistic regression analysis indicated a 7.39 fold increased risk of microalbuminuria in individuals with GG genotype of ICAM-1 gene 1462A>G (K469E) polymorphism.

*Conclusions:* GG genotype of ICAM-1 gene K469E polymorphism is associated with increased microalbuminuria in obese individuals without another metabolic risk factor.



## Polimorfismo 1462A>G (K469E) del gen *ICAM-1* y nivel sérico de ICAM-1 en la oligoalbuminuria de pacientes obesos no diabéticos, no hipertensos y normolipidémicos: acervo genético de la oligoalbuminuria en la obesidad

*Palabras clave:*
Obesidad
Oligoalbuminuria
Molécula de adhesión
Gen *ICAM-1*
Polimorfismo

RESUMEN

*Introducción:* Un conjunto de datos en aumento indica que los individuos obesos corren más riesgo de sufrir trastornos del parénquima renal si se los compara con sus homólogos no obesos. La oligoalbuminuria es un primer rasgo de afectación renal. Aunque la mayoría de los pacientes obesos presentan múltiples factores de riesgo de oligoalbuminuria, esta puede manifestarse en algunos individuos obesos sin factores de riesgo. El presente estudio se realizó para analizar el papel del polimorfismo 1462A>G (K469E) del gen *ICAM-1* en la oligoalbuminuria de individuos obesos sin diabetes mellitus, hipertensión, hiperlipidemia ni vejez.

*Métodos:* Para el estudio fueron reclutados 98 individuos obesos y 96 individuos no obesos sin comorbilidad. Se midió el nivel sérico de ICAM-1 mediante el ensayo de inmunoabsorción enzimática (ELISA). Se analizó el polimorfismo 1462A>G (K469E) del gen *ICAM-1* por reacción en cadena de la polimerasay polimorfismo de longitud de los fragmentos de restricción (RFLP-PCR). El método nefolométrico se utilizó para analizar la pérdida urinaria de albúmina, y la oligoalbuminuria se midió con la tasa de albúmina/creatinina.

*Resultados:* Los individuos obesos presentaron unos niveles de oligoalbuminuria y proteinuria considerablemente más elevados que los individuos no obesos (p: 0,043 y p: 0,011, respectivamente). La oligoalbuminuria en los portadores del genotipo GG de *ICAM-1* fue bastante mayor que la de los portadores del genotipo AA o AG (p: 0,042). El nivel sérico de ICAM-1 se correlacionó notablemente con la creatinina y la oligoalbuminuria (p: 0,002 y p: 0,03, respectivamente). El análisis de regresión logística mostró un riesgo 7,39 veces mayor de oligoalbuminuria en los individuos con el genotipo GG del polimorfismo 1462A>G (K469E) del gen *ICAM-1*.

*Conclusiones:* El genotipo GG del polimorfismo 1462A>G (K469E) del gen *ICAM-1* se asocia con un aumento de la oligoalbuminuria en personas obesas sin otro factor de riesgo metabólico.



## Introduction

Obesity is becoming worldwide epidemic which accounts a risk factor for metabolic and hormonal disorders.[1] Because insulin resistance is frequently seen, obese individuals are considered as candidates of diabetes mellitus (DM) and associated microvascular complications.[2] Additionally, increased adipose tissue is also a source of subclinic inflammation which is closely related to endothelial damage.

Microalbuminuria (MA) is initial stage of diabetic nephropathy which is strongly correlated with endothelial injury.[3] MA comprise an independent risk factor for coronary artery disease in both diabetic and nondiabetic population.[4] Obese individuals even without overt DM and hypertension may exhibit microalbuminuria.[5,6] Enhanced blood flow and glomerular filtration rate (GFR) are resulted with MA. An increasing number of evidence indicates low-grade inflammation as a cause of MA.[7] Also obesity is a well-known risk factor for focal segmental glomerulosclerosis.[8]

One of the suggested mechanisms in the pathogenesis of microalbuminuria is overexpression of adhesion molecules including ICAM-1 which closely associated with severe inflammatory processes that usually resulted with tissue injury.[9] Patients with obesity and diabetic nephropathy exhibit overexpression of ICAM-1.[10,11] Experimental studies showed that hyperglycemia is associated with overexpression of ICAM-1 in renal glomerular tissue and renal endothelial injury.[12] However, varying degree of renal injury among patients with normal ICAM-1 level or disassociation of ICAM-1 level with microalbuminuria may suggest the role of genetic mutations in ICAM-1 gene. As a marker of cell integrity and complexity,