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Année : **2019**

Titre communication : **PCSK9 synonymous variant gln342=, insulin and adiponectin levels in type 2 diabetes mellitus patients**

In : Nom ou Auteur moral du colloque : **Université d'Abomey-Calavi, Conseil Scientifique**

N° du colloque : **VII^{ème} Colloques des sciences, cultures et technologies**

Lieu du colloque : **Campus universitaire d'Abomey-Calavi-Bénin**

Date du colloque : **16 au 21 Septembre**

Titre du colloque : ***La valorisation des résultats de recherche et de l'innovation technologique, un facteur de développement des nations***

Lieu d'édition : **Abomey-Calavi- Bénin**

Éditeur : **Conseil scientifique de l'Université d'Abomey-Calavi**

Pagination : **54**

Notes : https://colloque.uac.bj

ABSTRACT

Background: Proprotein convertase subtilisin/kexin 9 (PCSK9) is a negative regulator of low-density lipoprotein cholesterol (LDL-c) via LDL-receptor (LDLR) expression reduction. PCSK9 inhibitors (PCSK9i) emerged as the most effective LDL-c-lowering drugs. But whether the long-term use of PCSK9i is associated with diabetes mellitus (DM) in humans is not clear. The enhanced expression of LDLR promoted by PCSK9 knock-out in mice triggers the apoptotic death of pancreatic β-cells subsequent to cholesterol overcharge. This in turn reduces insulin secretion and impairs glucose metabolism. Adiponectin, a key player in diabetes, also promotes PCSK9 expression/production. The aim of this study was to assess glucose metabolism related parameters in type 2 diabetes mellitus (T2DM) patients carrying PCSK9 variant Gln342=. ***Material and methods****:* Socio-demographic, anthropometric data and blood samples were collected. Serum glucose was measured by Glucose Oxidase and Peroxidase method (ELITech Group, Puteaux, France). Insulin, total and high molecular weight (HMW) adiponectin was determined by sandwich ELISA (ALPCO, Salem NH, USA). PCSK9 gene Exon7 was sequenced by Sanger method. ***Results:*** 132 T2DM patients aged of 57±11 years were included in the study. Female were predominant with a sex ratio of 1.59. The Gln342= variant (c.1026A>G, where A is the normal allele) was detected in 98.48% of patients (61% female; 39% male) among whom 17.69% were heterozygous and 82.31% homozygous carriers. The fasting glycemia, insulin, total and HMW adiponectin levels were 163.44±113.72 mg/dL, 7.14±6.87 µIU/mL, 3.60±2.17µg/mL and 1.30±1.38µg/mL respectively. Both total and HMW adiponectin showed negative correlation with insulin (respectively r=-0,47; p<0.05 and r=-0.39; p<0.05) in Gln342= homozygous but not in heterozygous. Insulin was higher in heterozygous than homozygous carriers (p<0.05), who showed high frequencies of insulin resistance and hypertension. ***Conclusion:*** These results suggest that homozygosity of Gln342= PCSK9 variant is associated with insulin resistance and hypertension in T2DM.

Mots clés : Diabetes mellitus, PCSK9, insulin, adiponectin, Hypertension, Benin