

# Comparative study of serum 8-hydroxydeoxy-guanosine levels among healthy offspring of diabetic and non-diabetic parents

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## ABSTRACT

**Objective:** Parental diabetic status might inherit the likelihood of disease susceptibility. The risk of Type 2 diabetes mellitus is increased among individuals with diabetic parents. Moreover, oxidative stress is thought to be a risk factor in the onset and progression of diabetes. 8-hydroxydeoxy-guanosine (8-OHdG) is widely analyzed biomarker to assess the oxidative DNA damage. We aimed to investigate that serum 8-OHdG level among offspring of diabetic and non-diabetic parents.

**Materials and Methods:** A total of 84 volunteers participated in the study. Questionnaires were applied to record information including demographics, physical activity, smoking, and family history. Blood samples were collected, and laboratory investigations 8-OHdG levels, lipid, and glucose were analyzed using the standard technique. Finally, 24 samples were considered for further analysis. Student's *t*-test was applied for statistical analysis.

**Results:** Serum 8-OHdG levels were significantly ( $P < 0.05$ ) high among healthy offspring of diabetic in comparison of healthy offspring of non-diabetic parents. While nonsignificant differences were found in their body mass index, glucose, and lipid level between the groups.

**Conclusion:** There is possibility of a mild degree of oxidative DNA damage among offspring of diabetic due to family history. Such understanding is essential to avoid other modifiable risk factors related to lifestyle and dietary habit which could possibly control further oxidative stress, to delay the onset of diabetic especially among offspring of diabetic parents.

**Keywords:** Diabetes, diabetic offspring, oxidative DNA damage, Saudi, serum 8-hydroxydeoxy-guanosine

## Introduction

Diabetes mellitus (DM), an exponentially increasing problem worldwide, is one of the major health problems in Saudi Arabia.<sup>1,2</sup> Environmental factors and genetic components have a significant impact for progression of diabetes.<sup>3</sup> Few studies reported the existence of an association between diabetes and family history of disease.<sup>4</sup> The risk to have diabetes increases 2-4 folds when one or both parents have diabetes. Approximately, 15-25% of the first-degree relatives of patients with diabetes develop either impaired glucose tolerance or diabetes.<sup>5,6</sup> Moreover, a number of identified genes have been associated with the metabolic syndrome and its components such as hypertension, hypercholesterolemia, Type 2 DM (T2DM), and obesity.<sup>7-9</sup>

Over the recent decades, Saudi Arabia shifted toward the westernized pattern of lifestyle that leads to increase the

prevalence of diabetes.<sup>10-12</sup> Moreover, the prevalence of metabolic syndrome among Saudis is reported as 39.3%.<sup>13</sup> In addition, various factors contribute to the progression of metabolic diseases starting from intrauterine environment of an infant in mothers with gestational diabetes.<sup>14,15</sup> Furthermore, environmental factors have its impact to minimize the Saudi outdoor activities. These factors include excessive hot/cold weather, high intake of high calorific diet, fast food, sleep restriction,<sup>16,17</sup> consanguine marriages,<sup>18</sup> and unregulated eating pattern after marriage.<sup>19</sup>

We hypothesized that the existence of aforesaid multiple risk factors along with coexistence of family history of diabetes may lead the genetically predispose individuals to be at more probable and earliest liable for onset of diabetes. The research question raised was that whether some relative degree of increased reactive oxygen species (ROS) production or degree

of oxidative stress exist among the offspring even then if they are healthy, due to the genetically makeup of diabetic descents. Is this warranted in such individuals to take preventive measure at some level from the beginning relatively than those of non-diabetic offspring? This study was designed to estimate the serum 8-hydroxydeoxy-guanosine (8-OHdG) levels, the marker of oxidative damage among the lean and normal offspring's of Saudis diabetic parents to speculate the genetically involvement of diabetes. No study has been conducted in this area, and still, there is scarce of study on offspring.

## Materials and Methods

### Study design and subject

In this case, control study 84 apparently healthy volunteers of age group between 15 and 30 years participated, most of them were a college student, and few were from general populations in Al-Qassim region, Kingdom of Saudi Arabia. Institutional ethical approval was done, and informed consent was obtained from individual. Demographics were recorded on a pre-piloted questionnaire included age, gender, weight, height, physical exercise, smoking, and family history of diabetic of parent was taken; moreover nonsmokers, nonobese, non-diabetic/non-pre-diabetic, normotensive. Without any recent or chronic illness, no medication, no strenuous physical exercise Saudi individual were included. Individuals with plasma glucose value more than 140 mg/dl, serum cholesterol value more than 200 mg/dl, serum triglyceride more than 150 mg/dl, body mass index (BMI) more than 25 and <18, and smokers were excluded from the study (Table 1).

### Measurement of BMI

Body weight and height was recorded for each participant. Weight was measured using calibrated electronic weighing scales (Proton Digital Scale, Model PHC 309 MD) and height was measured using a portable height scale (Mentone Educational, Model PE087, Australia). BMI was calculated as weight (in kg) divided by height (in m) squared.

### Blood pressure measurement

We just asked the subjects whether they had anytime diagnosed as hypertensive or using any medicine for high blood pressure.

### Blood sample collection

After informed verbal consent from each participant, random blood samples in gray top vacutainer and 5 ml red top vacutainer were collected under aseptic condition. Samples were centrifuged at 4000 rpm speed, aliquoted and stored at -80°C until analysis.

### Laboratory analysis

Estimation of plasma glucose by glucose oxidase-peroxidase method. Serum cholesterol by cholesterol oxidase-phenol-

aminophenazone method and serum triglyceride by glycerol phosphate oxidase-phenol-aminophenazone were performed. Kits were supplied Human Diagnostics (Germany). 8-OHdG was measured using enzyme-linked immunosorbent assay method kit supplied from EIAab Wuhan EIAAB Sciences Co. Ltd China.

### Statistical analysis

The results were analyzed using Microsoft Excel 2013 to calculate mean, standard deviation. Student's "t"-test was used to compare between the two groups.  $P < 0.05$  was taken as the level of significance.

## Results

There was no significance difference between the groups in BMI and biochemical parameters. However, there was a significant difference in serum 8-OHdG levels, the marker of oxidative DNA damage. The study results are shown in Table 2 and Figures 1 and 2.

## Discussion

Physio-biochemical phenomenon generates free radical which are ROS and reactive nitrogen species (RNS) are highly reactive molecules.<sup>20</sup> In our system, there are mechanisms to counterbalance the free radical, to combat the damage. When

**Table 1:** Sample rejected at different stages before laboratory analysis of serum 8-OHdG levels

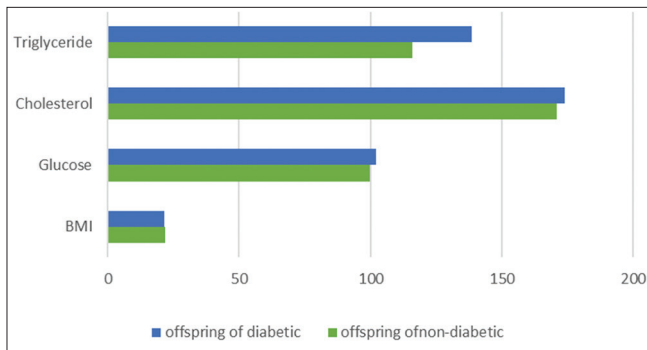
N=84 (male=73, female=11)
BMI>25 (N=17) excluded
BMI<18 (N=4) excluded
Dyslipidemia (N=21) excluded
Glucose levels>140 mg/dl (N=18)
Finally, we consider control group (N=12, offspring of non-diabetics) and case group (N=12 offspring of diabetics)
↓
Serum 8-hydroxydeoxy-guanosine estimation

8-OHdG: 8-hydroxydeoxy-guanosine, BMI: Body mass index

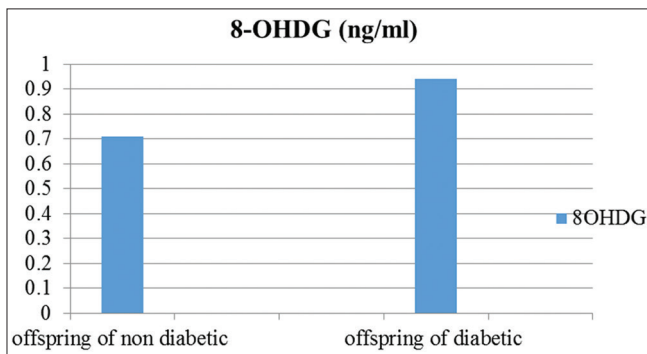
**Table 2:** Characteristics of the study participants, control group (offspring of non-diabetic) and case group (offspring of diabetic)

Characteristics	Control group	Case group	P value
Number of subjects	12	12	
Gender (male/female)	10/2	12/0	
Age (years)	23±3.65	23.9±1.6	0.64
BMI (kg/m <sup>2</sup> )	22.1±1.79	21.56±2.16	0.170
Glucose (mg/dl)	94.55±15.44	94.6±14.4	0.925
Cholesterol (mg/dl)	171.6±14.59	174±13.8	0.70
8-OHdG (ng/ml)	0.71±0.25	0.94±0.23	0.038*

Value expressed in mean±SD. \* $P < 0.05$  was considered as significant, BMI: Body mass index, 8-OHdG: 8-hydroxydeoxy-guanosine



**Figure 1:** Biochemical parameters and body mass index levels were compared between groups



**Figure 2:** Serum 8-hydroxydeoxy-guanosine levels were compared between groups

there is cell's internal environment disturbance of aforesaid phenomenon due to any reason in conditions such as infections, inflammatory process, toxins or nutritional imbalance, mitochondria diverts electron flow away from itself, forming ROS and RNS. This "oxidative shielding" acts as a defense mechanism for either decreasing cellular uptake of toxic pathogens or chemicals from the environment, or to kill the cell by apoptosis and thus avoid the spreading to neighboring cells.<sup>21</sup> Therefore, ROS formation is a physiological response to stress. The term "oxidative stress" has been used to define a state in which ROS and RNS reach excessive levels, either by excess production or insufficient removal. Being highly reactive molecules, the pathological consequence of ROS and RNS excess is damage to proteins, lipids, and DNA.<sup>22</sup> Consistent with the primary role of ROS and RNS formation, this oxidative stress damage may lead to physiological dysfunction, cell death, pathologies such as diabetes and cancer, and aging of the organism.<sup>23</sup>

The origins of Type 2 diabetes are multifactorial. Obesity, age, ethnic origin, and familiar history of diabetes are among the factors that contribute to its development. Even though a strong genetic component has been recognized, genotype only establishes the conditions for the individual to be more or less prone to environmental effects and lifestyle factors.<sup>24</sup>

There are evidences from the several previous researchers about the genetic role of diseases and hereditary aspect of

various diseases in humankind since the Mendelian theory. Hereditary aspect of diabetic is very obvious. It is very well-known that oxidative stress is the hallmark of all diseases including diabetes, cardiovascular disease, cancer, and many more.<sup>25-30</sup>

Our results reflect that there is significantly high serum 8-OHdG level in lean non-diabetic offspring in comparison lean non-diabetic offspring of non-diabetic (Table 2 and Figure 2). The observed result is suggestive of possible increased oxidative DNA damage in lean non-diabetic offspring of T2DM. It was already revealed that serum 8-OHdG is an early oxidative marker in patients with pre-diabetes and diabetes. Previous studies have already established the fact increased oxidative DNA damage among pre-diabetics and diabetics.<sup>30,31</sup>

Recent studies in genetic research have also identified the genetic variants linked with T2DM.<sup>6,7</sup> Family history of diabetes is also used as a predictor of T2DM in population-based screening programs.<sup>9</sup> However, roughly half of the risk of T2DM can be attributed to lifestyle and a half to genetics. Lifestyle modification is particularly effective in the prevention, or delay of progression to diabetes among individuals with a family history of diabetes. However, the International Diabetes Federation recommends that diabetes control programs should simultaneously promote lifestyle modification among high-risk individuals, as well as the entire population. Intake of dietary energy in excess of expenditure simply results in weight gain and increases the risk of T2DM.<sup>2,32</sup>

Zengi *et al.*<sup>33</sup> had shown in their study about increased oxidative DNA damage in lean normoglycemic offspring of T2DM. To explain whether oxidative stress is present in genetically predisposed subjects and induces the insulin resistance. Our results confirm, the fact that a mild degree of oxidative stress is always there among the normal offspring of diabetic individuals. Oxidative stress occurs in a dose-dependent manner along with others risk factors lead to diabetic among so-called susceptible individuals of diabetic parents.

In Saudi Arabia, the prevalence of consanguinity is as high as 60%.<sup>18</sup> In a study of married couples from Saudi Arabia, there is a positive correlation between consanguine marriages and Type 2 diabetes, where 80% of all related marriages had a positive family history of Type 2 diabetes as compared to 20% in nonrelated marriages.<sup>34</sup> Family history has a major role in the cause of diabetes. First-degree relatives of diabetic patients have long been known to have an increased risk of developing T2DM.<sup>35</sup>

## Conclusion

An economic growth and simultaneous rapid urbanization have made the Saudi population to adopt lifestyles that include more modifiable risk factors of diabetes and that will leads to non-modifiable risk factors. The risk factors associated with T2DM

are modifiable and non-modifiable. Modifiable risk factors include diets rich in saturated fats and simple carbohydrates, impaired glucose tolerance, metabolic syndrome, high blood pressure ( $\geq 140/90$  mmHg), elevated plasma triglycerides ( $\geq 250$  mg/dl), and low levels of physical activity ( $< 3$  times a week). The non-modifiable risk factors are age (older than 45 years), family history of diabetes, ethnicity, and diabetes during pregnancy. Genetic risk factor has a major role to play for the onset and progression of diabetes among offspring's of diabetic. Offspring's are supposed to make endeavors on the modifiable factor to delay the onset of diabetes.

## Limitation and Further Scope

We could not include large number of sample size due to many reasons as follows: One, lack of willingness to participate in the study; second, we could not include more female volunteer in the study due to social bondages. We do not consider our study result toward generalization aspect due to less sample no for analysis of oxidative stress parameters; moreover, more parameters and large sample needed to authenticate the results.

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