DNA DAMAGE AND LIPID PARAMETERS AMONG HEALTHY SMOKERS AND NON-SMOKERS IN DUHOK, KURDISTAN REGION OF IRAQ

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ABSTRACT

Background: Oxidative DNA damage has been linked to smoking habit in several populations. This study investigated the level of oxidative DNA damage among healthy smokers and non-smokers.

Methods: The present study investigated 8-hydroxy-2-deoxiguanosine (8-OHdG), malondialdehyde (MDA), and lipid profile in a sample of men subjects attended out -Patient Department (OPD) of Internal Medicine at Azadi Teaching Hospital in Duhok city, Kurdistan Region, Iraq, as attendant of patients. The study included a total of 410 men volunteers, of which 170 were smokers and 240 were non-smokers.

Results: In those with smoking habit, significantly higher 8-OHdG (4.3+2.2 vs. 7.2+5.4 p<0.001) and MDA levels (1.4+0.32 vs. 1.7+0.34 p=0.025) was found compared to the non-smokers. A similar pattern was observed when comparing total cholesterol (TC) (183+49 vs. 204+38 p=0.017) and Low density lipoprotein-cholesterol (LDL-C) (115+44 vs.134+36 p<0.001). In the smoker group, a positive correlation was observed between 8-OHdG with TC (r=0.36, p=0.010) and a negative correlation with high density lipoprotein-cholesterol (HDL-C) (r=-0.230, p=0.020), with both patterns being statistically significant.

Conclusion: The results of this study showed elevated levels of 8-OHdG and MDA in conjunction with abnormal lipid profile in those with smoking habit which may be a strong indicator of oxidative DNA damage in the studied population.

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Keywords: DNA damage, smoking habit, lipid profile, healthy men

Epidemiological data support a link between cigarette smoking and oxidative stress[1]. Smokers are at greater risk than no-smokers of having intracellular oxidizing agents, particularly reactive oxygen species (ROS)[2,3,4]. The high production of these oxidants associated with smoking may exceeding the capacity of the oxidative defense system resulting in oxidative damage to certain proteins, lipids and DNA[3]. The association between cigarette smoking and high levels of serum cholesterol is a hallmark of increasing risk for coronary artery disease, atherosclerosis and peripheral vascular disorders[5]. However; little is known about the association between DNA damage and lipid parameters in the Kurdish population, especially among those with smoking habit. It is important to investigate the level of oxidative DNA damage among healthy smokers and non-smokers, as this association might provide insight into the nature of the disease in our population. Therefore, this study measured serum 8-OHdG an oxidative DNA damage marker and analyzed its relation to MDA a pro -oxidant by-product and lipid parameters in apparently healthy smokers, as well as a group of healthy non-smokers.

MATERIALS AND METHODS

A cross-sectional sample was obtained using a random sampling procedure for subjects with smoking habit and non-smoking who were attended Out -Patient Department (OPD) of Internal Medicine at Azadi Teaching Hospital in Duhok city, Kurdistan Region of Iraq, as attendants of

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patients, between September 2022 and March 2023. The study was approved by the scientific Committee of College of Medicine, University of Duhok as well as by Ethics Committee of Generate Directorate of Duhok health with reference number 618/5.11.2022. Informed written consent was obtained from the respondents after explaining the objective of the study. A total of 410 volunteers were registered for the study over the course of seven consecutive months. Of these,170 smokers who used to smoke at least 20 sticks per day and excluded mild or casual smokers to leave a better zone of comparison. The Inclusion criteria were: apparently healthy men, ages 30-60 years, with fasting glucose <100 mg/dl, HbA1c < 5.7%, CRP < 6.mg/dl, without history or presence of cardiovascular diseases, endocrine, or metabolic disorders, acute inflammatory diseases and malignancy, as well as, those not taking drugs such as lipid lowering drugs, antihypertensive drugs and anti-inflammatory drugs. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared[6]. After an overnight fast, 5 mL of blood was drawn from each subject by vein puncture. The blood was then divided into two parts. The first part (3 mL) was collected in a gel separated tube with no anti-coagulant. Samples were allowed to clot for 30 minutes and then centrifuged at 3000 rpm for 10 minutes. The serum sample for each subject was divided into aliquots and was placed in an empty tube. The Cobas 6000 Roche (open, automated, discrete and random access) clinical chemistry analyzer was used to determine the serum TC, LDL-C, HDL-C, Triglycerides (TG), glucose and C-reactive protein (CRP) concentrations. The portions of liquid sera were held at -80 C, until it was used for the 8-OHdG and MDA analysis. Measurement of 8-OHdG was done using ELISA technique (Elabsciencecata/log number E-El-0028, USA). Reference ranges for lipid parameters were according to National Cholesterol Education Program Adult panel III guidelines as follow: Total cholesterol less than 200 mg/dl, HDL-C above 40 mg/dl, TG less than 150 mg/dl and LDL-C less than 100 mg/dl[7]. Standard colorimetric analysis was done to estimate MDA at 532nm. The second part of blood (2 mL) was placed in a test tube containing EDTA for HbA1c testing.

Statistical analysis

Statistical Package for Social Science (SPSS 25, IBM: USA) was used to analyze all the data. The laboratory parameter values are displayed as a mean and standard deviation (SD). The chi-square test was used to compare variables, and Student's independent t-test to compare variables between groups. A statistically significant cutoff point was set at P- value ≤0.05.

RESULTS

Table1 shows the baseline characteristics of the participants. Significant differences in serum 8-OHdG level ($p<0.001$) and MDA level ($p=0.025$) between smoker and non-smoker groups. The TC and LDL-C was observed to be significantly higher in the smokers compared to non-smokers. No significant differences was found with respect to age, body mass index, TG, HDL-C.

Table 1. Baseline characteristics of studied subjects

Characteristics	non-smokers n=240	Smokers n=170	*P*-value
Age(years)	44.5±7.3	45.9±8.1	0.170
BMI(kg/m^2)	27.0±3.4	27.3±3.7	0.650
8-OHdG(ng/mL)	4.3±2.2	7.2±5.4	<0.001
MDA (nmo/L)	1.4±0.32	1.7±0.34	0.025
Total cholesterol(mg/dL)	183±49	204±38	0.017
HDL-c(mg/dL)	39.1±9.0	40.2±9.9	0.320
LDL-c(mg/dL)	115±44	134±36	0.001
Triglycerides(mg/dL)	154.5±66.1	156.8±63.2	0.150

Data are presented as mean+ standard deviation
n=number, SD=standard deviation, BMI=body mass index, 8-OHdG=8-hydroxy-2-deoxiguanosine, MDA=malondialdehyde, HDL-C= high density lipoprotein-cholesterol, LDL-C= low density lipoprotein-cholesterol

Table2 shows the relationship between 8-OHdG and both MDA and lipid parameters in smokers and non-smokers. As shown, in the smoker group, 8-OHdG correlated positively with cholesterol and LDL-Ch (p=0.010 and P<0.01 respectively) and correlated negatively with HDL-Ch (P=0.020). In the non-smoker group, no significant correlations were found between 8-OHdG and lipid parameters.

Table 2 Pearson Correlation Coefficients (r) between 8-OHdG and studied parameters in healthy smokers and non-smokers.

Variable	Non-Smokers n=240		Smokers n=170	
	r	*P*	r	*P*
Age(years)	0.04	0.590	0.09	0.299
BMI(kg/m^2)	0.18	0.090	0.04	0.541
MDA (nmo/L)	0.08	0.723	0.19	0.080
Total cholesterol(mg/dL)	0.03	0.690	0.36	0.010
HDL-C(mg/dL)	-0.09	0.340	-0.230	0.020
LDL-C(mg/dL)	0.14	0.990	0.42	<0.01
Triglycerides(mg/dL)	0.02	0.770	0.04	0.640

n=number, BMI=body mass index, 8-OHdG=8-hydroxy-2-deoxiguanosine, MDA=malondialdehyde, HDL-C= high density lipoprotein-cholesterol, LDL-C= low density lipoprotein-cholesterol

DISCUSSION

This prospective investigation was the first studying the association between oxidative DNA damage biomarker (8-OHdG) and lipid profile in healthy smokers and non-smokers population in Duhok City, Iraq. The results of this study showed a significant difference in the 8-OHdG between study groups, and a similar pattern were observed for cholesterol. These results confirmed an association between DNA damage and smoking habit, as the mean 8-OHdG level observed in smokers was about 2 times higher than that in non-smokers. These results agreed with those of previous studies[8,9]. Moreover a significant relationship was reported between 8-OHdG with cholesterol and LDL-Ch levels in smokers. Regarding association of DNA damage and lipid parameters, a significant positive correlation was found between 8-OHdG and cholesterol and LDL-Ch levels in smokers. Cholesterol has consistently shown a positive association with markers of DNA damage in many prospective studies[10-12]. However, in non-smoker

group; 8-OHdG did not significantly correlated with cholesterol levels. Furthermore, we did not observe a significant correlation of triglycerides with 8-OHdG either in smoker or in non-smoker groups. However, recent evidence supports a wide array of atherogenic effects by oxidative stress, including smoking effects[5,13,14]. It is important to note that about (41.4%) of the studied subjects were heavy smokers, indicating that smoking can influence higher risk of oxidative damage in our population. Other evidence has also demonstrated that smoking play a significant role in modulating serum lipids levels as well as risk of oxidative DNA damage[10]. Since it reported that smoking habit can disturb lipid metabolism. In the present study, we measured lipid peroxidation by-product (MDA) and showed a higher levels in smokers compared to non-smokers, which is similar to results of other studies[10,11].

Limitation

The data obtained from male subjects, which may not represent both gender was the main limitation of this study. Furthermore, lack of using more than one marker of oxidative DNA damage was another important limitation of this study, despite these limitations subjects with smoking habit showed high levels of 8-OHdG and cholesterol compared with non-smokers which renders Kurdish population more susceptible to DNA damage.

CONCLUSION

This study showed that apparently healthy men with smoking habit had a higher level of 8-OHdG and cholesterol compared to the non-smokers. The results of present study also demonstrated a significant association between 8-OHdG and lipid parameters which may render smokers more susceptible to oxidative damage. Efforts to quit smoking in this group may help correct abnormal levels of 8-OHdG and reducing oxidative damage.

Conflict of interest:

The author declared that he have no conflict of interest.

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پوختە

زیانی DNA و پێوەری چەوری لە نێو جگەرەکێشانی تەندروست و جگەرەنەکێشاندا لە دهۆک , هەرێمی کوردستانی عێراق.

پێشەکی و ئارمانج: زیانی ئۆکسیدی DNA پەیوەندی بە جگەرەکێشانەوە هەیە لە چەندین دانیشتووانداد. ئەم توێژینەوەیە ئاستی زیانی ئۆکسیدی DNA لە نێو جگەرەکێشانی تەندروست و جگەرە نەکێشاندا لێکۆڵینەوەی کردووە.

شێوازەکان: ئەم دراسەدا توێژینەوە لەسەر (8-OHdG)، (MDA) و پرۆفایلی چەوری لە نمونەی کەسانی کورد کرد کە سەردانی بەشی نورینگەی دەرەوە بوون لە نەخۆشخانەی فێرکاری ئازادی لە شاری دهۆک لە هەرێمی کوردستانی عێراق. توێژینەوە 410 خۆبەخش لەخۆ دەگرێت کە 170 کەسیان جگەرە کێشبون و 240 کەسیان جگەرە نەکێشبون.

ئەنجام: لە کەسانی جگەرە کێشاندا ڕێژەی 8-OHdG و MDA بە بەراورد لەگەڵ ئەوانەی جگەرە ناکێشن بە شێوەیەکی بەرچاو بەرزتر بوو. هەمان شێواز لە بەراوردکردنی کۆلیسترۆلی گشتی (TC) و کۆلیسترۆلی کەم چڕی (LDL-C) بەدی کراوە. لە گروپی جگەرەکێشان، پەیوەندییەکی پۆزەتیڤ لە نێوان 8-OHdG لەگەڵ TC و پەیوەندییەکی نەرێنی لەگەڵ لیپۆپرۆتینی چڕی بەرز (HDL-C) بەدی کراوە.

دەرئەنجام: ئەنجامەکانی ئەم توێژینەوەیە بەرزبوونەوەی ڕێژەی 8-OHdG و MDA لەگەڵ نائاسایی چەوری لە کەسانی جگەرە کێشاندا دەردەخات کە لەوانەیە نیشانەیەکی بەهێز بێت بۆ زیانگەیاندنی ئۆکسیداتیڤی بە DNA لە دانیشتوانی کورددا.

الخلاصة

تلف الحمض النووي ومعلمات الدهون بين المدخنين الأصحاء وغير المدخنين في دهوك ، إقليم كردستان العراق

الخلفية والأهداف: تم ربط تلف الحمض النووي التأكسدي بعادة التدخين لدى العديد من السكان. بحثت هذه الدراسة مستوى تلف الحمض النووي التأكسدي بين المدخنين الأصحاء وغير المدخنين.

الطريقة: بحثت الدراسة الحالية (OHdG-8)، (MDA) ، وملف الدهون في عينة من الأفراد الأكراد الذين حضروا قسم العيادات الخارجية للمرضى في مستشفى آزادي التعليمي في مدينة دهوك ، إقليم كردستان ، العراق ، كمرافقين للمرضى. شملت الدراسة ما مجموعه 410 متطوعين ، منهم 170 مدخنا و 240 غير مدخنين.

النتائج: في مجموعة المدخنين، تم العثور على مستويات أعلى بكثير من OHdG-8 و MDA مقارنة بغير المدخنين. لوحظ نمط مماثل عند مقارنة الكوليسترول الكلي (TC) والبروتين الدهني منخفض الكثافة (LDL-C). في مجموعة المدخنين ، لوحظ وجود علاقة إيجابية بين OHdG-8 مع TC وعلاقة سلبية مع البروتين الدهني عالي الكثافة (HDL-C) ، مع كون كلا النمطين ذا دلالة إحصائية عالية.

الاستنتاج: أظهرت نتائج هذه الدراسة مستويات مرتفعة من OHdG-8 و MDA بالتزامن مع صورة دهنية غير طبيعية لدى أولئك الذين لديهم عادة التدخين والتي قد تكون مؤشرا قويا على تلف الحمض النووي التأكسدي لدى السكان الأكراد.