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ORIGINAL ARTICLE

IMPACT OF PHYSICAL FITNESS SCORES AND ITS ASSOCIATION WITH INDUCIBLE NITRIC OXIDE SYNTHASE (INOS) IN HEALTHY INDIVIDUALS AND PATIENTS WITH TYPE 2 DIABETES MELLITUS

Syed Shahid Habib[1], Thamir Al-khlaiwi[1], Syed Hamid Habib[2], Syed Mohammad Habib[3], Syed Abubakar Habib[3], Huthayfah Al-khliwi[1]

[1]Department of Physiology, College of Medicine, King Saud University, Riyadh, Saudi Arabia. [2]Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Pakistan. [3]Sulaiman Alrajhi University Bukayria, Saudi Arabia.

ABSTRACT

Background: Whether physical fitness score has a correlation with any endothelial dysfunction players needs to be evaluated. This study aimed to assess and compare Fitness Scores of Type 2 Diabetes Mellitus (T2DM) patients with healthy individuals and their relationship to Inducible Nitric Oxide Synthase.

Materials & Methods: A cross sectional study conducted at department of Physiology in 198 subjects. Subjects were grouped into Group1: control (n=88), Group 2: T2DM (n=110). Physical fitness score parameters and serum iNOS was compared between different groups.

Results: Waist to hip ratio (WHR) is significantly different between control group (0.92±0.15) and DM group (1.0±0.08) with a p value= 0.00. BMI is also significantly different between the two groups (control: 27.8±5.0, DM: 29.4±4.9 p= 0.02). In addition, fat mass is significantly different between the two group (control: 23.4±8.9, DM: 26.4±10.1, p=0.02) and % fat (control: 29.3±7.7, DM: 32.5±10.8, p=0.01). eNOS is also significantly different between the two groups (control: 112.9±47.5, DM: 86.4±47.3, p=0.00) while iNOS is not significantly different (Control: 25.5±15.4, DM: 27.2±24.1, p=0.55). There is no significant difference in fitness score between control group (69.1±9.9) and DM group (68.2±7.7) with p=0.49. Linear regression analysis is performed to evaluate the association of iNOS as the dependent variable with fitness score as predictors. Linear regression analysis showed a significant negative association of iNOS with fitness score (r=-0.386, p<.001) for all cases, (r=-0.427, p<.001) for control group, and (r=-0.365, p<.001) for diabetes mellitus group.

Conclusions & recommendations: Our findings address the negative correlation between iNOS and fitness score in healthy and DM patients. It reveals the decrease of iNOS as fitness score increases. Fitness score can be used as a predictor of cardiovascular prognosis in diabetic patients. Further and extensive studies are needed in this area to confirm the findings.

KEY WORDS: Type 2 Diabetes Mellitus; Fitness score; iNOS.

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Corresponding Author:

Dr. Syed Shahid Habib
Professor & Consultant
Department of Physiology, College of Medicine
King Saud University, Riyadh 11461
Kingdom of Saudi Arabia
E-mail: shahidhabib44@hotmail.com

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INTRODUCTION

Controlling Type 2 Diabetes mellitus (T2DM) and its complications would be one of the main achievements of health authorities in this century. It is not a secret to mention that T2DM is one of the harmful consequences of sedentary life. In 2021, around 7 million deaths were due to DM and its complications.[1,2] With strict dietary interventions , exercises and medications, the impact of diabetes can be minimized.

The effect of endothelial dysfunction, which comprises of endothelial cells injury and oxidative stress induced inflammation are considered as part of the pathways that lead to different metabolic disorders including T2DM.[3,4] Among others, inducible Nitric Oxide Synthase (iNOS) is one of the main factors involved in endothelial dysfunction.[5] Elevated levels of serum iNOS has been reported in T2DM leading to endothelial dysfunction.[6] It therefore can be assumed that by controlling the iNOS serum level, the impact of endothelial dysfunction can be minimized.

There has been continuous research to find out quantitative and reliable noninvasive indices of the human body that can be used for the assessment of body well-being as well as the prognosis of diseases.[7-9] Several indices have been discovered as valid and reliable methods to assess body composition such as body mass index (BMI) and waist circumference (WC).[8-10] However, each index has its limitation specially to detect cardiovascular and metabolic abnormalities. For example, an elevated levels of fat-free mass (FFM) increases BMI even though it does not indicate increase cardiovascular risk. Recently, we observed several indices that can predict cardiovascular complications in diabetes mellitus patients such as Arm Circumference (AC), Arm Muscle circumference (AMC), Adiponectin-Resistin (AR) ratio, and Insulin Resistance Adiponectin-Resistin (IRAR) ratio.[11-13] Similarly, physical fitness score, as one of body composition indices, has been mentioned in the literature to be negatively correlated with serum total leptin and free leptin index in T2DM.[14] Thus, it might be used as a predictor for cardiovascular risk outcomes. Whether physical fitness score has a correlation with any endothelial dysfunction players needs to be evaluated. This study aimed to assess and compare Fitness Scores of Type 2 Diabetes Mellitus (T2DM) patients with healthy individuals and their relationship to Inducible Nitric Oxide Synthase.

MATERIALS AND METHODS

A cross-sectional study was conducted at the Physiology department, College of Medicine and King Khalid University Hospital, King Saud University. A total of 88 healthy adult subjects and 104 T2DM patients were recruited. All participants underwent body composition analysis. BIA, assessed body composition of the participants with a commercially available body analyzer (InBody 3.0, Biospace, Seoul, Korea). Measurements included body weight, BMI, protein mass, fat mass, % body fat and fitness scoring based on the target values for ideal body fitness. The participant stood on the device while it measured body weight, and age, height and gender were entered on the touch screen. Serum iNOS, was compared between control and diabetes groups. Patients were recruited from the outpatient diabetic clinic of the King Khalid University Hospital. Informed consent was obtained from all subjects. Ethical approval of the study was obtained from the institutional review board of King Saud University Medical City (KSUMC). Inducible Nitric Oxide Synthase (iNOS) kits were obtained from USCN Life China (Catalog Number: E0837h).

SPSS version 25 was used to analyze data. Descriptive characteristics were calculated as Mean ± Standard Deviation (SD) for continuous variables, and as frequencies and percentages for categorical variables. Independent sample t test was used to assess significant differences. We assessed a linear regression models with iNOS as dependent variable and fitness score as predictors in all cases combined, and separately in control and diabetes mellitus group keeping an alpha error of 5%. *P* value of <0.05 was considered as significant.

RESULTS

The data was collected from total 198 subjects with 88 healthy and 110 T2DM subjects. Table 1 shows the anthropometric characteristics and blood parameters of both groups. In the anthropometric parameters Waist to hip ratio (WHR), weight, BMI, fat mass, and percent fat is significantly high in diabetic group compared to control. Furthermore, HbA1c, FBS, TGs and HOMA-IR was significantly raised in the diabetic group compared to control (Table 1). In contrast, the eNOS levels were significantly high in control group compared to diabetic, however, no significant difference was observed in iNOS levels between the groups.

eNOS level were different between control group (0.92±0.15) and DM group (1.0±0.08) with a p value= 0.00. BMI is also significantly different between the two groups (control: 27.8±5.0, DM: 29.4±4.9 p= 0.02). In addition, fat mass is significantly different between the two group (control: 23.4±8.9, DM: 26.4±10.1, p=0.02) and % fat (control: 29.3±7.7, DM: 32.5±10.8, p=0.01). eNOS is also significantly different between the two groups (control: 112.9±47.5, DM: 86.4±47.3, p=0.00) while iNOS is not significantly different (Control: 25.5±15.4, DM: 27.2±24.1, p=0.55). There is no significant difference in fitness score between control group (69.1±9.9) and DM group (68.2±7.7) with p=0.49.

Linear regression analysis was performed to evaluate the association of iNOS as the dependent variable with fitness score as predictor. Linear regression analysis showed a significant negative association of iNOS with fitness score (r=-0.386, p<.001) for all cases (figure 1).Furthermore, negative association was observed for control group (r=-0.427, p<.001), and T2DM group (r=-0.365, p<.001) as shown in Figure 2, and 3 respectively.

Table 1: Anthrpometric, blood parameter, eNOS and iNOS levels among T2DM and Control group.

Variable	All, n=198	Control, n=88	T2DM, n=110	*P value*
Age (year)	50.5±10.7	49.3±10.8	51.8±10.6	0.09
TBW (Liters)	40.7±12.4	40.3±6.8	41.1±5.6	0.34
WHR	0.96±0.1	0.92±0.15	1.0±0.08	0.00*
Height (cm)	165.9±11.6	167.5±8.2	164.4±15.1	0.67
Weight (Kg)	81±17.9	78.1±14.9	83.9±20.9	0.02*
BMI (Kg/m2)	28.6±4.9	27.8±5.0	29.4±4.9	0.02*
Fat mass (Kg)	24.9±9.5	23.4±8.9	26.4±10.1	0.02*
% FAT	30.9±9.2	29.3±7.7	32.5±10.8	0.01*
Protein mass (Kg)	10.9±1.6	10.9±1.8	11.0±1.5	0.65
eNOS (U/ml)	49.8±47.4	112.9±47.5	86.4±47.3	0.00*
iNOS (U/ml)	26.3±19.7	25.5±15.4	27.2±24.1	0.55
Fitness score	68.6±8.8	69.1±9.9	68.2±7.7	0.49
FBS (mmol/dl)	6.9±1.8	5.0±0.5	8.8±3.1	0.00*
Insulin (microliter/ml)	24.3±10.9	24.4±13.2	24.4±8.6	0.98
HOMA-IR	7.5±4.0	5.5±3.2	9.6±4.9	0.00*
HbA1c (%)	6.3±1.0	5.0±0.5	7.7±1.5	0.00*
TG (mmol/L)	1.6±1.1	1.2±0.6	2.1±1.6	0.00*
TC (mmol/L)	4.5±1.0	4.7±1.0	4.3±1.1	0.15
HDL (mmol/L)	1.0±0.1	1.1±0.2	1.0±0.3	0.22
LDL (mmol/L)	2.7±0.9	2.9±0.9	2.6±0.9	0.29

Data are represented as mean ± standard deviation, * significant. BMI: body mass index; WHR: waist/hip ratio, FBS: fasting blood sugar; TC: total cholesterol; TG: triglycerides; LDL: low-density lipoprotein; HDL: high-density lipoprotein, HOMA-IR: Homeostatic Model Assessment for Insulin, HbA1c: Glycosylated Hemoglobin, TBW: Total body water.

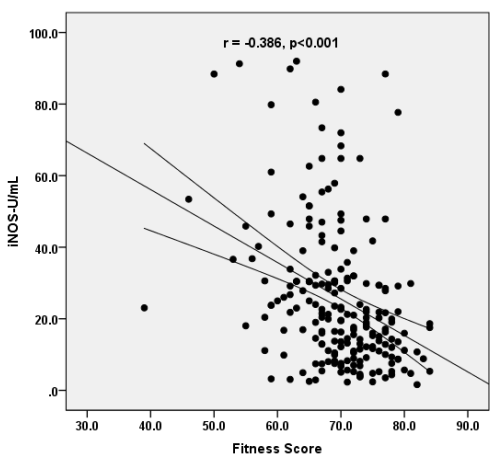

Figure 1. Linear regression analysis between serum iNOS and fitness score in all cases. (N=198).

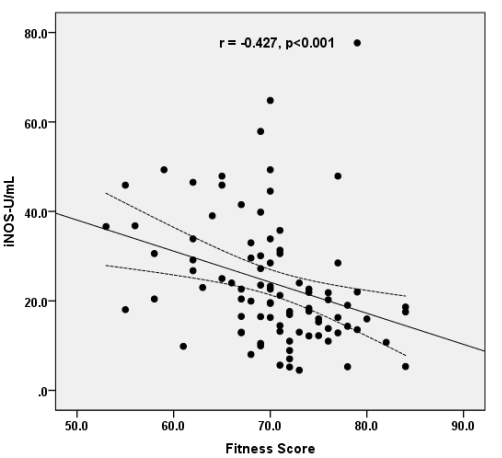

Figure 2. Linear regression analysis between serum iNOS and fitness score in control group.

(n=88).

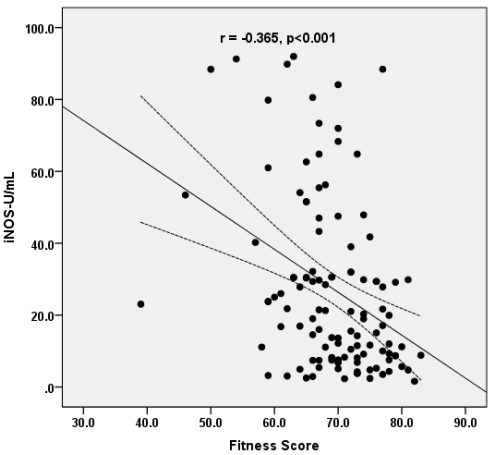

Figure 3. Linear regression analysis between serum iNOS and fitness score in diabetes mellitus group. (n=110).

Table 2: linear regression analysis for iNOS as dependent variable for all cases. (N=198):

Predictor	Unstandardized Beta Coefficients	Standardized Beta Coefficients	t.	Sig.	95% confidence interval Lower-upper	
Age	.331	.133	2.488	.015	.066	.596
BMI(Kg/m2)	.128	.435	.394	.770	-.738	.993
%FAT	-.248	.329	-.752	.454	-.903	.407
HbA1c	.580	.020	.190	.850	-5.496	6.656
HOMA-IR	-.148	-.034	-.331	.741	-1.034	.739
Fitness score	-.902	-.416	-3.190	.000	-1.465	-.340

Table 3: Linear regression analysis for iNOS as dependent variable for control group. (n=88).

Predictor	Unstandardized Beta Coefficients	Standardized Beta Coefficients	t.	Sig.	95% confidence interval Lower-upper	
Age	-.313	-.131	-1.422	.158	-.751	.124
BMI(Kg/m2)	-.555	-.113	-.979	.330	-1.680	.569
%FAT	-.367	-.164	-1.295	.198	-.928	.195
HbA1c	1900	.108	1.121	.265	-1.461	5.262
HOMA-IR	.007	.001	.013	.989	-.985	.998
Fitness score	-1.552	-.466	-4.151	.000	-2.294	-.811

Table 4: Linear regression analysis for iNOS as dependent variable for diabetes mellitus group. (n=110).

Predictor	Unstandardized Beta Coefficients	Standardized Beta Coefficients	t.	Sig.	95% confidence interval Lower-upper	
Age	.016	.008	.121	.904	-.244	.276
BMI(Kg/m2)	-.130	-.032	-.360	.719	-.842	.582
%FAT	-.354	-.168	-1.686	.094	-.769	.060
HbA1c	1.483	.123	1.556	.121	-.397	3.363
HOMA-IR	-.019	-.004	-.056	.956	-.707	.668
Fitness score	-1.278	-.436	-5.179	.000	-1.765	-.792

DISCUSSION

One of the main pathophysiological changes that accompany diabetes mellitus is endothelial dysfunction that leads to inflammatory process and hence increase production inducible nitric oxide synthase (iNOS).[15] This eventually leads to cardiovascular and other serious complications of diabetes mellitus.[16] Therefore, minimizing the production of iNOS would decrease the cardiovascular complications and its consequences.[6] One of the approaches that has been evaluated to decrease iNOS level is to improve physical activities.[17,18]

The World Health Organization (WHO) declared that in Saudi Arabia, there are 2.8 to 4.3 million T2DM patients between the ages of 27 to 60 years in 2022.[19] One reason that led to this astonishing rise in the burden of T2DM is the result of change in the life style in the last few decades. It has been observed that Saudi Arabia has high obesity prevalence with low physical fitness score[20] which has very strong association with the prevalence of Diabetes mellitus in Saudi Arabia.

Our results addressed the negative correlation between iNOS and fitness score in both healthy subjects and T2DM patients. It also reveals that decrease in the iNOS level shows increase in the fitness score. The decrease of iNOS is known to be a sign of reduction of inflammation and hence controlling the disease progression. In addition, fitness score can be used as a predictor of cardiovascular risk in subject with diabetes mellitus. The regression analysis reveals that fitness scores are negatively correlated with the iNOS level independently in both the healthy and diabetic subjects. This suggests that reduce physical activity may be the sole factor responsible for increase in the iNOS. This correlates with the sedentary lifestyle of Saudi population along with decline in the fitness score reported previously.[20] However, the eNOS levels were significantly high in control compared to T2DM subjects suggesting a deranged endothelial function. Indeed, there is a need for more extensive studies in this regard and in other population as well.

This is the first study to evaluate the relationship of physical fitness score and iNOS in Diabetes mellitus patients. In addition, we have collected good sample size. However, it is a cross sectional study and more elaboration is needed to confirm the association of fitness score with iNOS.

Conclusion and recommendations:

Our findings address the negative correlation between iNOS and fitness score in healthy and DM patients. It reveals the decrease of iNOS as fitness score increases. Fitness score can be used as a predictor of cardiovascular prognosis in diabetic patients. Further and extensive studies are needed in this area to confirm the findings.

REFERENCES

1. International Diabetes Federation (IDF). Diabetes Facts and Figures, Atlas, 10th edition. Available from: https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html.
2. Al-Khlaiwi T, Alsabih AO, Khan A, Habib SH, Sultan M, Habib SS. Reduced pulmonary functions and respiratory muscle strength in Type 2 diabetes mellitus and its association with glycemic control. Eur Rev Med Pharmacol Sci. 2021;25(23):7363-8. https://doi.org/10.26355/eurrev_202112_27430. PMID: 34919236.
3. Meo SA, Al-Khlaiwi T, Aqil M. Impact of the residential green space environment on the prevalence and mortality of Type 2 diabetes mellitus. Eur Rev Med Pharmacol Sci. 2022;26(10):3599-606. https://doi.org/10.26355/eurrev_202205_28856. PMID: 35647842.
4. Meo SA, Al-Khlaiwi T, Abukhalaf AA, Alomar AA, Alessa OM, Almutairi FJ, et al. The Nexus between Workplace Exposure for Wood, Welding, Motor Mechanic, and Oil Refinery Workers and the Prevalence of Prediabetes and Type 2 Diabetes Mellitus. Int J Environ Res Public Health. 2020;17(11):3992. https://doi.org/10.3390/ijerph17113992.
5. Dellamea BS, Leitão CB, Friedman R, Canani LH. Nitric oxide system and diabetic nephropathy. Diabetol Metab Syndr. 2014;6(1):17. https://doi.org/10.1186/1758-5996-6-17.
6. Habib SS, Al-Regaiey KA, Al-Khlaiwi T, Habib SM, Bashir S, Al-Hussain F, et al. Serum inducible and endothelial nitric oxide synthase in coronary artery disease patients with Type 2 Diabetes mellitus. Eur Rev Med Pharmacol Sci. 2022;26(10):3695-702. https://doi.org/10.26355/eurrev_202205_28865. PMID: 35647851.
7. Casadei K. Anthropometric measurement [Internet]. StatPearls [Internet]. U.S. National Library of Medicine; 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537315/.
8. Tabary M, Cheraghian B, Mohammadi Z, Rahimi Z, Naderian MR, Danehchin L, et al. Association of anthropometric indices with cardiovascular disease risk factors among adults: A study in Iran. Eur J Cardiovasc Nurs. [Epub ahead of print]. Available from: https://pubmed.ncbi.nlm.nih.gov/33620478/.
9. Mahdavi-Roshan M, Rezazadeh A, Joukar F, Naghipour M, Hassanipour S, Mansour-Ghanaei F. Comparison of anthropometric indices as predictors of the risk factors for cardiovascular disease in Iran: The Persian Guilan Cohort Study. Anatol J Cardiol. 2021;25(2):120-8. https://doi.org/10.14744/AnatolJCardiol.2020.73557. PMID: 33583819.
10. Vidal Martins M, Queiroz Ribeiro A, Martinho KO, Silva Franco F, Danésio de Souza J, Bacelar Duarte de Morais K, et al. Anthropometric indicators of obesity as predictors of cardiovascular risk in the elderly. Nutr Hosp. 2015;31(6):2583-9. https://doi.org/10.3305/nh.2015.31.6.8372.

11. Habib SS, Al-Khlaiwi T, Habib SM, Al-Khliwi H, AbaAlkhail MB, Albuhayjan NA, et al. Predictive value of arm circumference (AC) and arm muscle circumference (AMC) with cardiovascular risk in healthy and diabetic males. Eur Rev Med Pharmacol Sci. 2023;27(6):2477-84. https://doi.org/10.26355/eurrev_202303_31781.
12. Habib SS, Al-Khlaiwi T, Butt MA, Habib SM, Al-Khliwi H, Al-Regaiey K. Novel Adiponectin-Resistin Indices and Ratios Predict Increased Cardiovascular Risk in Patients with Type 2 Diabetes Mellitus. J Saudi Heart Assoc. 2023;35(1):59-65. https://doi.org/10.37616/2212-5043.1332.
13. Habib SS, Sultan M, Khan A, Al-Khlaiwi T, Bashir S. Circulating Adiponectin and Resistin Levels Are Associated with Adiposity Indices and Physical Fitness in Healthy Adult Males. Med Sci Monit Basic Res. 2021;27:e930322. https://doi.org/10.12659/MSMBR.930322.
14. Alzamil H, Aldokhi L, Habib SS. Physical Fitness and Its Relationship to Plasma Leptin, Leptin Soluble Receptor, and Free Leptin Index in a Saudi Population: A Comparison Between Diabetic and Non-Diabetic Individuals. Med Sci Monit Basic Res. 2018;24:113-9. https://doi.org/10.12659/MSMBR.910573.
15. Wilmes V, Scheiper S, Roehr W, Niess C, Kippenberger S, Steinhorst K, et al. Increased inducible nitric oxide synthase (iNOS) expression in human myocardial infarction. Int J Legal Med. 2020;134:575-81. https://doi.org/10.1007/s00414-019-02051-y.
16. Nagareddy P, Soliman H, Lin G, Rajput P, Kumar U, McNeill J, et al. Selective inhibition of protein kinase C beta (2) attenuates inducible nitric oxide synthase mediated cardiovascular abnormalities in streptozotocin-induced diabetic rats. Diabetes. 2009;58:2355-62. https://doi.org/10.2337/db09-0432.
17. Silva JF, Correa IC, Diniz TF, Lima PM, Santos RL, Cortes SF, et al. Obesity, Inflammation, and Exercise Training: Relative Contribution of iNOS and eNOS in the Modulation of Vascular Function in the Mouse Aorta. Front Physiol. 2016;7:386. https://doi.org/10.3389/fphys.2016.00386.
18. Al-Khlaiwi T, Habib SS, Al-Khliwi H, Alsomali A, Almushawah A, Alhumud M, et al. Relationship of serum inducible and endothelial nitric oxide synthase with exercise in healthy adult males and patients with type 2 diabetes mellitus. Eur Rev Med Pharmacol Sci. 2023;27(10):4619-25. https://doi.org/10.26355/eurrev_202305_32471
19. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. 2021. Available from: https://diabetesatlas.org/idfawp/resource-files/2021/07/IDF_Atlas_10th_Edition_2021.pdf.
20. Habib SS. Body composition analysis and estimation of physical fitness by scoring grades in Saudi adults. J Pak Med Assoc. 2013;63(10):1285-9. PMID: 24392562.

CONFLICT OF INTEREST
Authors declare no conflict of interest.
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None declared.

AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	SSH, TA, SHH
Acquisition, Analysis or Interpretation of Data:	SSH, TA, SHH, SMH, SAH, HA
Manuscript Writing & Approval:	SSH, TA, SHH, SMH, SAH, HA

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.