J. Exp. Biomed. Sci. 2012, 18(4): 384~390
pISSN : 1738-3226

Original Article

Comparison of Stress and Physiological Variables between Diabetic and Nondiabetic Adults

Byung-Jo Han[1], Seok-Cheol Choi[1], Seong-Min Moon[1], Dae-Sik Kim[2] and Kyung-Yae Hyun[3,†]

[1]Department of Clinical Laboratory Science, College of Health Sciences, Catholic University of Pusan, Busan 609-757, Korea,
[2]Department of Clinical Laboratory Science, Dongnam Health College, Suwon 440-714, Korea,
[3]Department of Clinical Laboratory Science, College of Nursing & Healthcare Sciences, Dong-Eui University, Busan 614-714, Korea

Diabetes mellitus (DM) is considered to be a serious metabolic disease which may cause systemic complications. The present study was designed to clarify a difference on stress, physiological variables and their correlation between diabetic (DM group) and nondiabetic adults (control group). The levels of body weight, waist circumference, blood pressure, body mass index, body fat mass, total cholesterol (TcH), triglyceride (TG), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT), total bilirubin (TB), autonomic balance (AB), stress index (SI), fatigue index (FI), and heart rate (HR) were all significantly higher in the DM group than in the control group. However, the levels of autonomic activity (AA), stress resistance (SR), and electrocardiac stability (ES) were significantly lower in the DM group than in the control group. The percentages of persons with abnormal levels in the Tch, high density lipoprotein, low density lipoprotein, TG, AST, ALT and GGT were significantly greater in the DM group than in the control group. In the correlation of glucose and hemoglobin A1c (HBA1c) to stress indices, the DM group had a significant relationship with AB, SR, SI, FI, ES, and HR, whereas the control group had no significant relationship with these, excepting AB. These results suggest that DM was harmfully associated with body, biochemical and stress indices and that blood glucose and HBA1c levels must be exhaustively regulated.

Key Words: Diabetes, Body index, Biochemical index, Stress index

INTRODUCTION

Diabetes mellitus (DM) has threatened public health and is increasing around the world. WHO (World Health Organization 2010) has reported that DM may rise from 171 million to 366 million worldwide by 2030. This major increase in the morbidity and mortality of DM is due to the development of both micro and macrovascular complications, including failure of the wound healing process. DM, a serious metabolic disease, can lead to cardiovascular and cerebrovascular disease, nephropathy, retinopathy, and widespread disease of both the peripheral and central nervous system. DM has particularly adverse affects on the vascular endothelium, which is not simply an inert, single-cell lining covering the internal surfaces of blood vessels, but in fact plays a crucial role in regulating vascular tone and structure. A healthy endothelium inhibits platelet and leukocyte adhesion to vascular surface and maintains a balance of profibrinolytic and prothrombotic activity (Libby et al., 2002). Hyperglycemia is the major causal factor in the development of endothelial dysfunction in DM, by which DM-induced endothelium dysfunction can contribute

*Received: November 3, 2012 / Revised: December 3, 2012
Accepted: December 4, 2012
†Corresponding author: Kyung Yae Hyun. Department of Clinical Laboratory Science, College of Nursing & Healthcare Sciences, Dong-Eui University, Busan 614-714, Korea.
Tel: +82-51-890-2680, Fax: +82-51-890-2622
e-mail: kyhyun@deu.ac.kr

to the above mentioned systemic complications. However most studies have focused on the general systemic complications rather than the cause.

DM is a chronic disease for which we must consider both early diagnosis and continuous management. Chronic diseases, including DM, may lead to emotional, mental and/or psychological stresses as well as systemic complications. A number of studies have demonstrated stress-induced physiological disturbances which can contribute to airway reactivity, inflammation, acute asthma exacerbation (Joachim et al., 2003), cellular immune dysfunction (Naliboff et al., 1991), thrombogenesis, fibrinolytic activity and cardiovascular disease (von Känel et al., 2001).

In Korea, morbidity and mortality from DM have been rapidly increasing with industrialization and western eating. We have also carried out many studies to investigate DM-induced systemic complications. However, prospective data have been limited.

We designed this study to clarify a difference on stress, physiological variables and the correlation of diabetic markers to such variables between diabetic and nondiabetic adults.

MATERIALS AND METHODS

Study population

100 diabetic (DM group) and 100 nondiabetic adults (Control group) were voluntarily subjected to this study. The exceptive criteria that prevented participation in this study were severe DM, cancers, cerebral and cardiovascular diseases, immune disorder, heart and renal failure, inflammatory diseases, colds, liver cirrhosis, and other irregular health conditions. This study was accepted from *IRB (Institutional Review Board)* of Catholic University of Pusan.

Body indices

For the two groups, height, body weight (BWt), waist circumference, body mass index (BMI), body fat mass (BFM), and body fat rate (BFR) were measured by FA-94H (Fanics Co., Korea) and GENIVS-220 (Jawon-Medical Co., Korea) instruments.

Blood pressure

Systolic and diastolic blood pressure (SBP and DBP, respectively) were determined by Autoanalyzer (Green-Cross Co., Korea).

Biochemical indices

In fasting condition, 3 mL of blood were collected from all subjects and infused into vacuum tubes. The blood samples were separated into serum. Diabetic markers [glucose, hemoglobin A1c (HBA1c)], lipid metabolic markers [total cholesterol (T-ch), triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL)], liver function markers [aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT), total bilirubin (TB)], and renal markers [creatinine, blood urea nitrogen (BUN), uric acid] in the serum were analyzed by Autohumalyzer 9500 (Human Lab., Germany).

Stress indices

Autonomic activity (AA), autonomic balance (AB), stress resistance (SR), stress index (SI), fatigue index (FI), electrocardiac stability (ES), and heart rate (HR) were measured by TM2655 (A&D Co. Japan), BMF 5000P (Medicore Co. Korea), and X-SCAN plus I, II (Jawon medical Co., Korea).

Statistical analysis

Data were presented as mean ± SD (standard deviation). For comparison between the two groups in all variables, unpaired *t*-test and F-test were applied, and for correlation of diabetic markers to stress indices, Pearson's correlation method was used. Statistical significance was accepted with $P \leq 0.05$.

RESULTS

Body indices

The levels of body weight (Bwt), waist, BMI, BFM, SBP and DBP in the DM group were significantly higher than those of the control group ($P<0.000$) (Table 1). The other indices were not different between the two groups ($P>0.05$).

Table 1. Demographic characteristics of the normal and diabetes mellitus (DM) groups

Variable \ Group	Control	DM	Reference value
Total number (n)	100	100	
Gender (M : F)	57 : 43	60 : 40	
Age (years)	57.16 ± 9.12	56.94 ± 8.40	
Body weight (kg)	60.52 ± 9.89	66.09 ± 10.50†	
Height (cm)	162.64 ± 8.58	163.04 ± 8.13	
Wast (cm)	78.41 ± 7.93	84.46 ± 8.43†	M<90, F<85
SBP (mmHg)	114.95 ± 10.25	130.93 ± 10.03†	<120
DBP (mmHg)	72.93 ± 7.62	78.01 ± 9.18†	<80
BMI (kg/m^2)	23.50 ± 2.80	24.80 ± 3.45†	18.5~23
BFM (kg)	15.48 ± 4.49	17.70 ± 5.77†	
BFR (%)	25.59 ± 6.25	26.51 ± 6.62	

†, $P<0.000$ (compared with the control group).
Abbreviation: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; BFM, body fat mass; BFR, body fat rate.

Table 2. Biochemical indices of the normal and diabetes mellitus (DM) groups

Variable \ Group	Control	DM	Reference value
Glucose (mg/dL)	91.93 ± 5.78	152.60 ± 24.21†	70~99
HBA1c (%)	5.48 ± 0.33	7.05 ± 0.36†	4~6
T-cholesterol (mg/dL)	200.00 ± 13.38	210.40 ± 17.70*	98~199
HDL (mg/dL)	53.60 ± 12.06	52.49 ± 12.43	40~99
LDL (mg/dL)	123.13 ± 32.28	123.74 ± 33.09	<129
Triglyceride (mg/dL)	118.56 ± 24.56	164.79 ± 25.89†	<149
AST (IU/L)	27.86 ± 12.08	32.89 ± 14.27*	0~33
ALT (IU/L)	24.16 ± 11.61	32.88 ± 21.57**	0~38
GGT (IU/L)	29.61 ± 16.74	72.46 ± 28.79†	M: 0~56, F: 0~38
T-bilirubin (mg/dL)	0.94 ± 0.36	1.14 ± 0.51**	0.3~1.7
BUN (mg/dL)	14.21 ± 3.86	15.54 ± 4.26*	6.2~23.3
Creatinine (mg/dL)	0.84 ± 0.17	0.84 ± 0.17	0.6~1.2
Uric acid (mg/dL)	5.20 ± 1.39	5.21 ± 1.29	2.1~7.7

*, $P<0.05$; **, $P<0.01$; †, $P<0.000$ (compared with the control group).
Abbreviation: HBA1c, hemoglobin A1c; T, total; HDL, high density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase, GGT, gamma-glutamyltransferase; BUN, blood urea nitrogen.

Biochemical indices

The levels of glucose, HBA1c, total cholesterol (T-ch), triglyceride (TG), AST, ALT, GGT and total bilirubin in the DM group were significantly higher than those of the control group ($P<0.05$, $P<0.01$ or $P<0.000$, respectively) (Table 2). The other indices were not different between the two groups ($P>0.05$).

Stress indices

The levels of autonomic activity (AA), stress resistance (SR) and electrocardiac stability (ES) were significantly lower, while the levels of autonomic balance (AB), stress index (SI), and fatigue and heart rate (HR) were significantly higher in the DM group than in the control group ($P<0.05$, $P<0.001$ or $P<0.000$, respectively) (Table 3).

Table 3. The levels of stress indices in the normal and diabetes mellitus (DM) groups

Variable \ Group	Control	DM	Reference value
Autonomic activity	93.05 ± 16.19	86.48 ± 13.61†	>91
Autonomic balance	53.21 ± 18.55	56.02 ± 28.92*	<50
Stress resistance	98.07 ± 14.20	90.10 ± 15.40†	>91
Stress index	94.39 ± 13.15	111.90 ± 116.35†	<110
Fatigue index	105.32 ± 17.41	112.68 ± 16.26†	<110
Electrocardiac stability	96.35 ± 18.53	90.19 ± 18.98***	>91
Heart rate (beat/min)	67.16 ± 10.70	72.21 ± 12.11†	60~100

*, $P<0.05$; ***, $P<0.001$; †, $P<0.000$ (compared with the control group).

Table 4. Numbers and percentages of person with abnormal levels of biochemical indices in the two groups

Variable \ Group	Control n (%)	DM n (%)
T-cholesterol (>199 mg/DL)	34 (34%)	53 (53%)**
HDL (<40 mg/dL)	9 (9%)	21 (21%)**
LDL (>129 mg/dL)	31 (31%)	48 (48%)*
Triglyceride (>149 mg/dL)	19 (19%)	41 (41%)**
AST (>33 IU/L)	3 (3%)	21 (21%)***
ALT (>38 IU/L)	5 (5%)	25 (25%)**
GGT (>56 IU/L)	4 (4%)	21 (21%)***
T-bilirubin (>1.7 mg/dL)	0	0
BUN (>23.3 mg/dL)	0	0
Creatinine (>1.2 mg/dL)	0	0
Uric acid (>7.7 mg/dL)	0	0

*, $P<0.05$; **, $P<0.01$; ***, $P<0.001$ (compared with the control group).
Abbreviation: HBA1c, hemoglobin A1c; T, total; HDL, high density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase, GGT, gamma-glutamyltransferase; BUN, blood urea nitrogen.

Table 5. The correlation of diabetic markers to stress indices in the two groups

Variable \ Group	Control		DM	
	Glucose	HBA1c	Glucose	HBA1c
Autonomic activity (*r*)	ns	ns	Ns	ns
Autonomic balance (*r*)	-0.13*	-0.13*	-0.26†	-0.26†
Stress resistance (*r*)	ns	ns	-0.21***	-0.21***
Stress index (*r*)	ns	ns	0.22***	0.22***
Fatigue index (*r*)	ns	ns	0.25†	0.25†
Electrocardiac stability (*r*)	ns	ns	-0.21***	-0.21***
Heart rate (*r*)	ns	ns	0.25†	0.25†

*, $P<0.05$; ***, $P<0.001$; †, $P<0.000$ (compared with the control group).
r, correlation coefficient.

Number of persons with abnormal levels in the biochemical indices

The numbers of persons with abnormal levels in T-ch, HDL, LDL, TG, AST, ALT and GGT was significantly higher in the DM group than in the control group ($P<0.05$, $P<0.01$ or $P<0.001$, respectively) (Table 4). The other indices were within normal ranges.

Correlation of diabetic markers to stress indices

Glucose and HBA1c were negatively correlated with AB in both groups, but the correlation coefficient was higher in the DM group than in the control group.

Glucose and HBA1c were negatively correlated with SR and ES, while they were positively related with SI, Fatigue, and HR in the DM group ($P<0.05$, $P<0.01$ or $P<0.001$, respectively), but not signigicant in the control group (Table 5).

DISCUSSION

We have performed this study to investigate a difference on stress, physiological variables and the correlation of diabetic markers to such variables between diabetic and nondiabetic adults. The DM group had higher Bwt, waist, BMI and BFM compared with the control group, suggesting that such factors may be risk factors for the development of

hyperglycemia and diabetes.

Choi and Seok recently demonstrated that a high fat diet-induced increase of Bwt induces elevated glucose, AST, ALT and creatinine concentrations (Choi and Seok, 2011). These findings indicate the importance of controlling body indices in adults. In the biochemical indices, we observed that the DM group had abnormal concentrations of T-ch, TG and GGT and higher AST and ALT levels compared with the control group. Increased T-ch and TG concentrations are an important sign of lipid metabolic disorder, by which dyslipidemia may cause metabolic syndrome, including intraabdominal obesity, impaired insulin resistance, and hypertension. Higher SBP in the DM group agrees with previous studies.

As is commonly known, elevated T-ch, TG, GGT, AST and ALT levels may play a key role in the development of DM. AST, ALT and GGT are parameters conventionally used for diagnosing hepatobiliary disease and alcohol consumption (Whitfield, 2007), with incidents of cardiovascular disease (CVD) (Wannamethee et al., 1995), and major proatherogenic risk factors (Lee et al., 2003).

Akehi reported that increased levels of T-ch, TG and GGT are good clinical markers for predicting diabetic risk, even in young men with normal glucose tolerance, and of these, GGT was the most strongly related factor among subjects with relatively high BMI. Oda et al. demonstrated similar results, in which the prevalence of metabolic syndrome increases the elevation in GGT levels or ALT even through the normal range of GGT or ALT, in Japanese men and women.

Many others have also suggested that, in the general population of children and adults, high body weight and abdominal fat distribution were associated with increased GGT, leading to type 2 DM (Botton et al., 2007), that serum GGT levels may be an early predictor for the development of chronic renal disease (Ryu et al., 2007), that higher serum GGT levels are implicated in prehypertension, increased BP and the progression of hypertension (Stranges et al., 2005; Shankar et al., 2007), and that serum GGT levels are important risk factors of type 2 DM and CVD (Martins et al., 2010). Şen et al. showed an association between increased serum GGT activity and slow coronary blood flow. As concerns in body (BMI, wast, and BFM) and biochemical indices, our data indicate that DM group is at a dangerously high risk for liver dysfunction, metabolic syndrome, hypertension and/or CVD.

Chronic illnesses such as DM may induce emotional, mental and/or psychological stresses as well as systemic complications.

In the present study, indices associated with various stresses (Table 3) in the DM group were almost within abnormal ranges.

Several literature has showed that DM may induce distress, anxiety, autonomic imbalance and/or elevated fatigue (Balhara et al., 2011; Tovilla-Zárate et al., 2012; Boer-Martins et al., 2011; Fritschi et al., 2010), which can cause poor glycemic control and aggravate patients' conditions.

For persons with DM, associations between psychological factors and metabolic control are particularly significant as glycemia is critical in monitoring progression and controlling the disease. Diabetic patients are almost twice as likely to suffer from depression and anxiety as the general population (Trento et al., 2012), and both depression and diabetes are associated with deregulated and overactive hypothalamic-pituitary-adrenal (HPA) axis activity (Champaneri et al., 2010).

In addition depression as a chronic psychological stress is associated with subclinical hypercortism secondary to the activation of the HPA axis (Champaneri et al., 2010). Cortisol is a counterregulatory hormone, and its prolonged exposure leads to visceral adiposity, insulin resistance, dyslipidemia, and hypertension (all metabolic precursors to type 2 DM). This hormone stimulates the sympathetic nervous system, increases inflammatory and platelet aggregation responses, and decreases insulin sensitivity, resulting in CVD and DM (Champaneri et al., 2010; Vogelzangs et al., 2007; Danese et al., 2009).

Both our data and previous data suggest that DM-induced anxiety and distress can lead to physical consequences in the lives of patients, given that emotional problems may poorly influence lifestyle and treatment of patients. As a result, decreased quality of life, impaired self-care behavior, and poorer glycemic control may ensue and contribute to

elevating health care costs.

Our findings, in which the DM group had significantly negative or positive correlation of glucose and HBA1c concentrations to all of the stress indices, reveal that DM might induce increased stress and fatigue.

In conclusion, this study shows that DM might lead to higher dyslipidemia, liver dysfunction and severe stress.

REFERENCES

Akehi Y, Tsutsumi Y, Tatsumoto A, Yoshida R, Ohkubo K, Takenoshita H, Kudo T, Ashida K, Anzai K, Yamashita T, Kawashima H, Ono J, Yanase T. Serum γ-glutamyltransferase, triglyceride and total cholesterol are possible prediabetic risk markers in young Japanese men. Epub J. 2010. 11: 981-989.

Balhara YP, Sagar R. Correlates of anxiety and depression among patients with type 2 diabetes mellitus. Indian J Endocrinol Metab. 2011. 15: S50-S54.

Boer-Martins L, Figueiredo VN, Demacq C, Martins LC, Consolin-Colombo F, Figueiredo MJ, Cannavan FP, Moreno H Jr. Relationship of autonomic imbalance and circadian disruption with obesity and type 2 diabetes in resistant hypertensive patients. Cardiovasc Diabetol. 2011. 22: 10-24.

Botton J, Heude B, Andre P, Bresson JL, Ducimetiere P, Charles MA. Relationship between gamma-glutamyltransferase and fat mass in a general population of 8~17 years old children. The FLVS II study. Diabetes Metab. 2007. 5: 354-359.

Champaneri S, Wand GS, Malhotra SS, Casagrande SS, Golden SH. Biological basis of depression in adults with diabetes. Curr Diab Rep. 2010. 6: 396-405.

Choi SC, Seok SJ. An association between factor of metabolic syndrome and serum levels of gamma-glutamyl-transpeptidase at age 40 years. J Exp Biomed Sci. 2011. 1: 61-68.

Danese A, Moffitt TE, Harrington H, Milne BJ, Polanczyk G, Pariante CM, Poulton R, Caspi A. Adverse childhood experiences and adult risk factors for age-related disease: depression, inflammation, and clustering of metabolic risk markers. Arch Pediatr Adolesc Med. 2009. 12: 1135-1143.

Fritschi C, Quinn L. Fatigue in patients with diabetes: a review. J Psychosom Res. 2010. 1: 33-41.

Joachim RA, Quarcoo D, Arck PC, Herz U, Renz H, Klapp BF. Stress enhances airway reactivity and airway inflammation in an animal model of allergic bronchial asthma. Psychosom Med. 2003. 5: 811-815.

Lee DH, Jacobs Kr Jt. Gross M. Gamma-glutamyltransferase is a predictor of incident diabetes and hypertension: the Coronary Artery Risk Development in Young Adults (CARDI) Study. Clin Chem. 2003. 49: 1358-1366.

Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. Circulation. 2002. 9: 1135-1143.

Martins MC, Faleiro LL, Afonso B, Fonseca A. Association of gamma glutamyltransferase, metabolic syndrome and cardio-vascular risk. Acta Med Port. 2010. 4: 579-588.

Naliboff BD, Benton D, Solomon GF, Morley JE, Fahey JL, Bloom ET, Makinodan T, Gilmore SL. Immunological changes in young and old adults during brief laboratory stress. Psychosom Med. 1991. 2: 121-132.

Oda E, Kawai R, Watanabe K, Sukumaran V. Prevalence of metabolic syndrome increases with the increase in blood levels of gamma glutamyltransferase and alanine amino-transferase in Japanese men and women. Intern Med. 2009. 16: 1343-1350.

Ryu S, Chang Y, Kim DI, Kim WS, Suh BS. gamma-Glutamyltransferase as a predictor of chronic kidney disease in nonhypertensive and nondiabetic Korean men. Clin Chem. 2007. 1: 71-77.

Sen N, Ozlü MF, Başar N, Ozcan F, Güngör O, Turak O, Malçok O, Cağli K, Maden O, Erbay AR, Demir AD. Relationship between elevated serum gamma-glutamyltransferase activity and slow coronary flow. Turk Kardiyol Dern Ars. 2009. 3: 168-173.

Shankar A, Li J. Association between serum gamma-glutamyltransferase level and prehypertension among US adults. Circ J. 2007. 10: 1567-1572.

Stranges S, Trevisan M, Dorn JM, Dmocbowski J, Donahue RP. Body fat distribution, liver enzymes, and risk of hypertension: Evidence from the Western New York Study. Hypertension. 2005. 46: 1186-1193.

Tovilla-Zárate C, Juárez-Rojop I, Peralta Jimenez Y, Jiménez MA, Vázquez S, Bermúdez-Ocaña D, Ramón-Frías T, Genis Mendoza AD, García SP, Narváez LL. Prevalence of anxiety and depression among outpatients with type 2 diabetes in the Mexican population. PLoS One. 2012. 5: 368-387.

Trento M, Raballo M, Trevisan M, Sicuro J, Passera P, Cirio L, Charrier L, Cavallo F, Porta M. A cross-sectional survey of depression, anxiety, and cognitive function in patients with type 2 diabetes. Acta Diabetol. 2011. 3: 199-203.

Vogelzangs N, Suthers K, Ferrucci L, Simonsick EM, Ble A, Schrager M, Bandinelli S, Lauretani F, Giannelli SV, Penninx

BW. Hypercortisolemic depression is associated with the metabolic syndrome in late-life. Psychoneuroendocrinology. 2007. 2: 151-159.

von Känel R, Mills PJ, Fainman C, Dimsdale JE. Effects of psychological stress and psychiatric disorders on blood coagulation and fibrinolysis: a biobehavioral pathway to coronary artery disease? Psychosom Med. 2001. 4: 531-544.

Wannamethee G, Ebrahim S, Shaper AG. Gamma-glutamyl transferase: determinants and association with mortality from ischmic heart disease and all causes. Am J Epidemiol. 1995. 142: 699-708.

Whitfield JB. Serum gamma-glutamyltransferase and risk of disease. Clin Chem. 2007. 1: 1-2.

World Health Organization, 2010. http://www.who.int/diabetes/facts/worldfigures/en/.