



PSYCHOLOGICAL STRESS AND TYPE2 DIABETES MELLITUS

Premshanker Singh^{1*}, Granth Kumar², Achutya Pandey³, Manoj Kumar⁴ and Vidyasagar⁵

¹FMR Prof, Head Medicine and Dean, UP University of Medical Sciences(UPUMS), India.

²Granth Kumar, Assoc Prof Medicine, UPUMS, India.

³Fmr Assoc Prof, Psychiatry, UPUMS, India

⁴Professor Medicine, UPUMS, India.

⁵Assoc Prof Medicine, UPUMS, India.

*Corresponding Author: Premshanker Singh

FMR Prof, Head Medicine and Dean, UP University of Medical Sciences(UPUMS), India.

Article Received on 02/02/2022

Article Revised on 23/02/2022

Article Accepted on 21/03/2022

ABSTRACT

This study aims to analyze and compare psychological stress levels with long-term risk of type 2DM among productive The high incidence rate of Diabetes Mellitus (DM) among Asian productive age population significantly affects the quality of the human capital in this country. Thus, it is highly necessary to manage and to prevent the onset of DM by identifying its risk factors, both direct and indirect ones. One of these factors is psychological stress, which triggers increased level of the body's fight-or-flight hormone making the body release extra energy in the form of glucose and fat into cells. The long term psychological stress prevents the insulin from enabling the extra energy to be absorbed into the cells thereby leading the glucose to build up in the blood. Therefore, it is important to identify the psychological stress in the attempt to avoid the future incidence of DM. To determine the association between psychological stress and risk of type 2 DM among male and female,a prospective cohort study was conducted in 85 participants (aged 26-45 years) from rural population of north India. A single centric study was conducted at tertiary care hospital under UP University of Medical Sciences,India The Spearman rho was used to analyze the inferential statistic. Result of the study showed there was a strong relationship between psychological stress and the risk of type 2 DM at baseline (RR = 0.46 , p<.05) and the coefficient of determinant showed 22%. Same as on 2nd and 3rd measurements were found that the p- values are < .05, while the determinant coefficient were 33% and 19%, respectively. The evidence reflected that a long term stress or uncontrolled psychological stress for a sufficiently long period might disturb insuline regulation in the body, which in turn increases the risk of developing type 2 DM.

KEYWORDS: Psychological Stress; Risk of Type 2 Diabetes Mellitus; Glucose intolerance

INTRODUCTION

There were two types of DM risk factors,modifiable risk factors including diet, resting patterns, activity patterns, and stress management and non-modifiable factors such as age, gender, history of DM in the family.^[1,2,3,4,5] American Diabetic Association (ADA)stated that psychological stress as one of modifiable risk factor of DM should be a great concern to prevent the occurrence of type 2 DM in the future (ADA, 2017).^[6,7,8,9,10] It is almost impossible to avoid psychological stress in the daily life due to every daily activity that may lead stress with different extent such as marriage, work, health, or financial problems. Ideally, human body can tolerate with physical, emotional, or mental stress for a limited length of time,so the experiances of psychological stress in long period contributes the occurrence of certain disease, including type 2 DM.^[11,12,13,14,15] Many studies in

past have found that people with high level of psychological stress was 33% more likely to experience metabolic disorders including type 2 DM rather than those with low level of psychological stress. Psychological stress triggers increased levels of the body's fight-or-flight hormone which causes the body to release extra energy in the form of glucose and fat for cell.^[16,17,18,19,20] These cells are then provoked to help the body avoid harm. However, this fight-or-flight response among people who are at risk for type 2 DM may not work properly.^[21,22,23,24,25] The constant psychological stress will hinder the insulin to allow the extra energy to be absorbed into the cells thereby leading the glucose to build up in the blood.

METHOD

This study was conducted at UP University of medical sciences India amongst rural population of North India wef Apr 2008 to Apr 2017(09) years. The sample size was calculated by using a cohort sample calculation formula to test the hypothesis against the relative risk. The sample was obtained as many as 95 people. Stratified random sampling technique was performed for selecting the participant of rural population. The instrument that has been used in this study including 1) DASS (Depression, Anxiety, Stress Scale). This tool consisted of 42 items to assess and determine the level of psychological stress, and 2) FRS (Framingham Offspring Type 2 Diabetes Risk Score) which consisted of six indicators to assess long-term risk of type 2 DM in this study. Data were collected for three times, on April 2008 as the base line, then on June and September as the follow up data. Descriptive statistics were used to analyze and describe demographic characteristics of the

participants. Spearman rho was performed to detect any significant relationship between the variables.

RESULT

The demographic data of the participants were shown in Table.1. Result of the study showed psychological stress in high category is more prevalent in women than men in the average age of 39.39 years old. In addition, the stress (low, moderate or high) is more prevalent in the group of respondents who are not married than those married. Meanwhile, seen from the educational level, the incidence of stress is more prevalent in the group of senior high school graduates than those of the college. Finally, seen from the category of occupational position and employment length, the respondents with structural positions have been in high category of psychological stress than functional positions. The average of respondents' working experience for high category is 9 years.

Table 1: Characteristics and Levels of Psychological Stress at Baseline Apr 2008 (N=95)

	Level of Psychological Stress							
	normal (n=58)		low (n=26)		moderate (n=8)		high (n=3)	
	f	%	f	%	f	%	f	%
Age, mean (SD)	M=39.62	SD=5.58	M=39.39	SD =4.39	M=40.13	SD =4.22	M =39	SD =4.94
Sex								
Male	20	58.6%	11	31.4%	1	4.3%	2	5.7%
Female	38	63.3%	14	24.2%	6	10.8%	1	1.7%
Marriage Status								
Marriage	7	82.4%	2	17.6%	0	0	0	0
Unmarriage	51	59.5	24	27.7%	8	9.2%	3	3.5%
Level of Education								
Higher Education	24	62.7%	10	26.7%	4	9.3%	2	4.3%
Primary Education	35	60.9%	15	27%	4	7.8%	2	4.3%
Job Position								
Structural	48	68.3%	19	26.8%	3	4.2%	1	0.7%
Fungsional	10	41.7%	6	27.1%	5	20.8%	2	10.4%
Working experience	M=17.71	SD=8.27	M=17.53	SD =7.15	M=15.95	SD =6.24	M =17.67	SD =6.86

Then, the comparison of psychological stress levels with component risk factors of Type 2 DM were shown in Table 2. Result of study showed that the average of fasting glucose is 95.91 in normal situation (not stress) and 157.17 in high level category. Similarly, the different trends was also found in the respondents' average BMI depending on their level of psychological stress (normal, low, moderate or high), in which the heavier the stress

the higher the BMI. Furthermore, related to HDL levels, the table shows that the heavier the stress, the higher the HDL value. Triglyceride levels showed that the higher the stress level, the higher the triglyceride level. Furthermore, regarding systole and diastole level, the table indicates that the higher the stress level, the higher the systole and diastolic values.

Table 2: Comparison of Psychological stress levels with component risk factors of Type 2 DM based on FRS at baseline February 2020 (N = 95)

Level of Psychological Stress	FRS													
	Fasting Glucose		BMI		HDL-C Level		Parental history of DM		Triglycerida Level		BP (Sistole)		BP(Diastole)	
	Mean	SD	Mean	SD	Mean	SD	Yes	No	Mean	SD	Mean	SD	Mean	SD
Normal	95.91	11.59	27.95	1.45	55.34	8.66	77 (65.8%)	37 (31.6)	131.50	20.56	129.97	13.60	83.39	4.96
Low	112.43	32.45	28.17	1.48	56.84	8.25	35 (68.6)	16(31.4)	125.27	18.13	125.24	16.11	81.63	5.30
Moderate	109.75	12.11	27.63	1.36	58.75	5.36	11(68.8)	5 (31.3)	122.19	17.23	127.19	6.92	82.63	3.98
High	157.17	87.3	28.18	1.72	60.17	2.71	1(16.7%)	5 (83.3)	135.97	17.84	133.17	8.91	84.67	3.20

Furthermore, the relationship between psychological stress and the risk of type 2 DM (table 3) showed that there is a relationship between psychological stress and the risk of developing type 2 diabetes mellitus in which the first measurement obtained p-value = 0.000, RR = 0.464 and coefficient of determinant = 22%. Thus, there

is a significant relationship of psychological stress and the risk of type 2 diabetes mellitus. Likewise, on the 2nd and 3rd measurements, the obtained p value = 0.000, RR = 0.576, the determinant coefficient of 33% for 2nd test and the obtained p value is also 0.000 with RR = 0.434, the determinant coefficient of 19% for the 3rd test.

Table 3: The Relationship between Psychological Stress and the Risk of Type 2 DM

Level of Psychological Stress:	Risk of Type 2 Diabetes Melitus			P value	RR	CD
	Low	Moderate	High			
1st Measurement I (n=95)						
Normal	22 (54.3%)	18(45.7%)	0 (0%)	0.000	0.464	22%
Low	2 (12,1%)	14 (84,8%)	1 (3.0%)			
Moderate	1 (8.3%)	5 (83.3%)	1 (8.3%)			
High	0 (0%)	2 (80%)	1 (20%)			
2nd Measurement (n=92)						
Normal	27 (58,1%)	19 (40,9%)	1 (1,1%)	0.000	0.576	33%
Low	1 (4.0%)	11 (92.0%)	1 (4.0%)			
Moderate	1 (1.6%)	30 (96.8%)	1 (1.6%)			
High	0 (0%)	1 (66.7%)	1 (33.3%)			
3rd Measurement III (n=182)						
Normal	85 (91.4%)	8 (8.6%)	0 (0%)	0.000	0.434	19%
Low	19 (86.4%)	2 (9.1%)	1 (4.5%)			
Moderate	28 (52.8%)	19 (35.8%)	6 (11.3%)			
High	1 (7.1%)	6 (42.9%)	7 (50.0%)			

DISCUSSION

Study showed that there is a contradicts between theories and the result about HDL-c levels. Result of study showed that the heavier the stress, the higher the HDL value. Then, this is also applying to tryglyceride levels that the higher the stress level, the higher the triglyceride level.^[26,27,28]

HDL or High Density Lipoprotein is a lipoprotein that contains more protein and less fat, which functions as a cholesterol carrier from the tissues to the liver for metabolic processes. HDL is also referred to as good fat. Several studies have linked individuals' stress response with HDL, LDL, and triglyceride level. The study by many investigators state that the increased cortisol levels due to stress can increase serum levels of total cholesterol, LDL' triglycerides but decrease HDL serum levels.^[27,28,29,30] As for triglyceride level, the table showed that the higher the stress level, the higher the triglyceride level. This is relevant with many studies explain that the relationship of psychological stress and increased lipid metabolism.^[31,32,33,34,35] Number of studies in recent past state that the increase in basal cortisol concentrations and variability of circadian cortisol among respondents with stress causes dyslipidemia. The increased cortisol levels increases serum levels of total cholesterol, LDL, triglycerides, and decreases HDL level. Furthermore, regarding systole and diastole level, the table indicates that the higher the stress level, the higher the systole and diastolic values.^[36,37,38,39,40]

Chronic stress triggers changes in the immune system. Activation of the immune system provokes neuroendocrine and neurotransmitter changes. Stress causes an overproduction of cortisol, a hormone that counteracts the effects of insulin and causes high blood sugar level. If a person experiences severe stress for a long time, the cortisol will increase significantly, and it will reduce the body's sensitivity to insulin. Stress is a factor with an important effect on diabetes due to an increase in stress hormones increasing blood sugar levels. The research reveals that stress is a strong risk factor for the occurrence of type 2 DM in the future. The pathophysiological mechanisms to explain the relationship of psychological stress and diabetes mellitus risk are direct neuroendocrine effect (the fact that stress hormones such as cortisol and adrenaline are against insulin regulation) and indirect effect (e.g. stress can reduce mood to do exercise, maintain diet and practice healthy lifestyle).. The work stress can increase the risk of type 2 diabetes in women but not in men is proven only in the subgroup analysis. This study also explains that in the future the occurrence of type 2 diabetes will involve multiple factors instead of one factor only. Another study suggests that the relationship between psychosocial factors and type 2 diabetes may be complex. Long-term stress triggers the body to produce the hormone epinephrine, also known as adrenaline. The hormone epinephrine is usually produced by the body as a physiological response to danger, being attacked, and trying to survive. This condition is called fight-or-flight response. Epinephrine raises blood sugar by increasing

the release of glucose from glycogen. After that, epinephrine increases the formation of glucose from amino acids or fats in the body. When the amount of blood sugar increases dramatically, the pancreas will automatically produce insulin to control blood sugar.

CONCLUSION

The result showed that from 3 measurements of the level of psychological stress and the risk of type 2 diabetes mellitus, it concluded stress has a relationship with the risk of a person suffering from type 2 diabetes mellitus in the next 09 years. Research suggests that a person who are unable to control his stress for a sufficiently long period of time may be at risk for developing type 2 diabetes mellitus. Type 2 diabetes is preceded by a period of marked changes in glucose regulation.

Conflict of Interests: None

Funding: None.

Ethical clearance: Taken from ethical committee.

REFERENCES

- Picard, M. & Turnbull, D. M. Linking the metabolic state and mitochondrial dna in chronic disease, health, and aging. *Diabetes*, 2013; 62: 672–678.
- McEwen, B. S. & Wingfield, J. C. The concept of allostasis in biology and biomedicine. *Horm. Behav*, 2003; 43: 2–15.
- Shpilberg, Y. et al. A rodent model of rapid-onset diabetes induced by glucocorticoids and high-fat feeding. *Dis. Model. Mech*, 2012; 5: 671–680.
- McEwen, B. S. & Stellar, E. Stress and the individual. Mechanisms leading to disease. *Arch. Intern. Med*, 1993; 153, 2093–2101.
- Chavez, M. et al. Adrenalectomy increases sensitivity to central insulin. *Physiol. Behav*, 1997; 62: 631–634.
- Loizzo, S. et al. Post-natal stress-induced endocrine and metabolic alterations in mice at adulthood involve different pro-opiomelanocortin-derived peptides. *Peptides*, 2010; 31: 2123–2129.
- Loizzo, A. et al. Overweight and metabolic and hormonal parameter disruption are induced in adult male mice by manipulations during lactation period. *Pediatr. Res*, 2006; 59: 111–115.
- Maniam, J., Antoniadis, C. P. & Morris, M. J. The effect of early-life stress and chronic high-sucrose diet on metabolic outcomes in female rats. *Stress*, 2015; 18: 524–537.
- Paternain, L. et al. Postnatal maternal separation modifies the response to an obesogenic diet in adulthood in rats. *Dis. Model. Mech*, 2012; 5: 691–697.
- Sadeghimahalli, F., Karbaschi, R., Zardooz, H., Khodagholi, F. & Rostamkhani, F. Effect of early life stress on pancreatic isolated islets' insulin secretion in young adult male rats subjected to chronic stress. *Endocrine*, 2015; 48: 493–503.
- Rosenblum, L. A. & Smiley, J. Therapeutic effects of an imposed foraging task in disturbed monkeys. *J. Child Psychol. Psychiatry*, 1984; 25: 485–497.
- Kaufman, D. et al. Early-life stress and the development of obesity and insulin resistance in juvenile bonnet macaques. *Diabetes*, 2007; 56: 1382–1386.
- McEwen, B. S. Protective and damaging effects of stress mediators: central role of the brain. *Dialogues Clin. Neurosci*, 2006; 8: 367–381.
- Di Dalmazi, G., Pagotto, U., Pasquali, R. & Vicennati, V. Glucocorticoids and type 2 diabetes: from physiology to pathology. *J. Nutr. Metab*, 2012; 2012; 1–9.
- Lacroix, A., Feelders, R. A., Stratakis, C. A. & Nieman, L. K. Cushing's syndrome. *Lancet*, 2015; 386: 913–927.
- Clore, J. & Thurby-Hay, L. Glucocorticoid-induced hyperglycemia. *Endocr. Pract*, 2009; 15: 469–474.
- Asfeldt, V. H. Hypophyseo-adrenocortical function in diabetes mellitus. *Acta Med. Scand*, 1972; 191: 349–354.
- Chiodini, I. et al. Association of subclinical hypercortisolism with type 2 diabetes mellitus: a case-control study in hospitalized patients. *Eur. J. Endocrinol*, 2005; 153: 837–844.
- Adam, E. K. & Kumari, M. Assessing salivary cortisol in large-scale, epidemiological research. *Psychoneuroendocrinology*, 2009; 34: 1423–1436.
- Fries, E., Dettenborn, L. & Kirschbaum, C. The cortisol awakening response (CAR): facts and future directions. *Int. J. Psychophysiol*, 2009; 72: 67–73.
- Hackett, R. A., Steptoe, A. & Kumari, M. Association of diurnal patterns in salivary cortisol with type 2 diabetes in the Whitehall II study. *J. Clin. Endocrinol. Metab*, 2014; 99: 4625–4631.
- Kumari, M., Shipley, M., Stafford, M. & Kivimäki, M. Association of diurnal patterns in salivary cortisol with all-cause and cardiovascular mortality: findings from the Whitehall II study. *J. Clin. Endocrinol. Metab*, 2011; 96: 1478–1485.
- Bruehl, H., Wolf, O. T. & Convit, A. A blunted cortisol awakening response and hippocampal atrophy in type 2 diabetes mellitus. *Psychoneuroendocrinology*, 2009; 34: 815–821.
- Champaneri, S. et al. Diurnal salivary cortisol and urinary catecholamines are associated with diabetes mellitus: the Multi-Ethnic Study of Atherosclerosis. *Metabolism*, 2012; 61: 986–995.
- Vreeburg, S. A. et al. Associations between sociodemographic, sampling and health factors and various salivary cortisol indicators in a large sample without psychopathology. *Psychoneuroendocrinology*, 2009; 34: 1109–1120.
- Hackett, R. A., Kivimäki, M., Kumari, M. & Steptoe, A. Diurnal cortisol patterns, future diabetes, and impaired glucose metabolism in the Whitehall II

- cohort study. *J. Clin. Endocrinol. Metab*, 2016; 101: 619–625.
27. Donath, M. Y. & Shoelson, S. E. Type 2 diabetes as an inflammatory disease. *Nat. Rev. Immunol*, 2011; 11: 98–107.
 28. Galic, S., Oakhill, J. S. & Steinberg, G. R. Molecular and cellular endocrinology: adipose tissue as an endocrine organ. *Mol. Cell. Endocrinol*, 2010; 316: 129–139.
 29. Ehses, J. A., Ellingsgaard, H., Böni-Schnetzler, M. & Donath, M. Y. Pancreatic islet inflammation in type 2 diabetes: from α and β cell compensation to dysfunction. *Arch. Physiol. Biochem*, 2009; 115: 240–247.
 30. Tilg, H. & Moschen, A. Inflammatory mechanisms in the regulation of insulin resistance. *Mol. Med*, 2008; 14: 222–231.
 31. Grossmann, V. et al. Profile of the immune and inflammatory response in individuals with prediabetes and type 2 diabetes. *Diabetes Care*, 2015; 38: 1356–1364.
 32. Wang, X. et al. Inflammatory markers and risk of type 2 diabetes: a systematic review and meta-analysis. *Diabetes Care*, 2012; 36: 166–175.
 33. Davey Smith, G. & Hemani, G. Mendelian randomization: genetic anchors for causal inference in epidemiological studies. *Hum. Mol. Genet*, 2014; 23: R89–R98.
 34. Swerdlow, D. I. et al. The interleukin-6 receptor as a target for prevention of coronary heart disease: a mendelian randomisation analysis. *Lancet*, 2012; 379: 1214–1224.
 35. Swerdlow, D. I. Mendelian randomization and type 2 diabetes. *Cardiovasc. Drugs Ther*, 2016; 30: 51–57.
 36. International Diabetes Federation. *IDF Diabetes Atlas 7th edn.* (International Diabetes Federation, 2015).
 37. Emdin, C. A., Anderson, S. G., Woodward, M. & Rahimi, K. Usual blood pressure and risk of new-onset diabetes. *J. Am. Coll. Cardiol*, 66: 1552–1562.
 38. Knowles, J. W. & Reaven, G. Usual blood pressure and new-onset diabetes risk evidence from 4.1 million adults and a meta-analysis. *J. Am. Coll. Cardiol*, 2016; 67: 1656–1657.
 39. Aune, D., Ó Hartaigh, B. & Vatten, L. J. Resting heart rate and the risk of type 2 diabetes: a systematic review and dose–response meta-analysis of cohort studies. *Nutr. Metab. Cardiovasc. Dis*, 2015; 25: 526–534.
 40. Licht, C. M. M. et al. Increased sympathetic and decreased parasympathetic activity rather than changes in hypothalamic–pituitary–adrenal axis activity is associated with metabolic abnormalities. *J. Clin. Endocrinol. Metab*, 2010; 95: 2458–2466.