

Original Article

INSULIN RESISTANCE AND BETA-CELL FUNCTION IN ADOLESCENT HYPERTENSIVE PATIENTS

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Objective: To find out the role of insulin resistance and beta cell function in developing hypertension in adolescent hypertensive patients.

Methods: Study included 50 students of Shalamar Medical and Dental College, age range 17-19 years with family history of hypertension. 50 age matched subjects with no history of any disease were taken as controls. Duration of study was Dec 2016 to June 2017. Demographics of patients were entered in Proforma. Level of blood glucose was estimated by glucose oxidase method. Level of serum insulin was estimated by ELISA. Values of insulin resistance and function of beta cell were calculated using formula.

Results: Mean age of both subjects and control was 19 years with increased BMI and sedentary life style belonging to middle and high socioeconomic status. Both systolic and diastolic blood pressure in subjects with positive family history was non-significantly high in comparison with controls. Fasting blood sugar and insulin resistance was increased in tested subjects, but significant difference was only observed in case of insulin resistance in comparison with controls. Beta cell function was significantly decreased in subject with family history of hypertension in comparison with controls.

Conclusions: It is concluded that adolescent with positive family history of hypertension may have sustained hypertension which may be due to increased oxidative stress of pancreas followed by insulin resistance and β -cell dysfunction.

Keywords: family history of hypertension, insulin resistance and beta cell function.

Introduction

Family history is a significant risk factor for hypertension and its prevalence is about 30% may be characteristic to genetic factors.¹ Worldwide the prevalence rate of hypertension in adolescent varies 5 - 20 % with an increased BMI.² A link of blood pressure between children and parents is demonstrated by studies.^{3,4} It is proposed that an association between family history of hypertension and hypertension may be due to increased reabsorption of sodium via renal proximal tubule,⁵ enhanced counter transport of lithium-sodium, enhanced level of serum uric acid, increased level of serum insulin, BMI, oxidative stress and heavy exposure of metal ions.^{6,7} It is proved that primary functional changes in cardiac tissue modified vascular capacity and response to presser stimuli in normotensive people with a family history of hypertension.⁸ Hypertension in most cases associated with Insulin resistance may be due to increased response of angiotensin receptor.⁹ Signaling of angiotensin II increases the formation of ROS or reactive oxygen species in heart tissue, tissue of pancreas and adipose tissue.^{10,11} Furthermore, angiotensin II decreases the secretion of insulin in response to blood glucose

and also decreases the flow of blood to islet cells of pancreas.¹² It is therefore demonstrated that oxidative stress due to signaling of angiotensin II is the contributing factor linked to hypertension.¹³ Sustained or borderline hypertension leads to abnormal morphology of pancreatic islet and causes the secretion of insulin in response to increased level of glucose and enhances oxidative stress in the tissue of pancreas. Additionally close association between oxidative stress in tissue of pancreas and blood pressure is also observed. It is therefore suggested that sustained or borderline hypertension enhances oxidative stress or formation of ROS and thereby modifying function and structure of β cells.^{14,15} Studying positive family history of high blood pressure and finding the risk factors in healthy people offers a chance to discover factors leading to increased blood pressure, before ruling out hypertension.¹⁶ Our study is therefore designed to find out the role of insulin resistance and function of beta cell in developing hypertension in adolescent hypertensive patients

Methods

Study included 50 adolescents age range 17-19 years With family history of hypertension. 50 age matched

subjects with no history of any disease were taken as controls. Adolescents were the students of Shalamar Medical and Dental College, Lahore. Demographics of patients were entered in Proforma. Level of blood glucose was estimated by glucose oxidase method. Level of serum insulin was estimated by ELISA in the Laboratory of Sheikh Zayed Medical Institute, Lahore. HOMA- β or beta cell function of Pancreas and HOMA of insulin resistance or HOMA-IR were calculated using the online calculator.¹⁷

$$\text{HOMA-IR} = (\text{Fasting insulin (uU/ml)} \times \text{Fasting blood glucose (nmol/l)}) / 22.5.$$

$$\text{HOMA-}\beta = (20 \times \text{fasting insulin (uU/ml)}) / (\text{Fasting blood glucose (mmol/L)} - 3.5)$$

The blood pressure of subjects was recorded in a sitting position with sphygmomanometer after a rest of 5-min, following the guidelines of WHO, hypertension was described as blood pressure 160/95 mmHg. Obesity was described as a BMI > 25 or above of 25 kg/ m². The family history was described as positive when a person having a first-degree relative (a parent or grandparent). Study was approved by Local Committee of Sheikh Zayed Medical Institute, Lahore. Letter of consent was taken from each subject and control. Data was entered and analyzed by SPSS 20. Student's t-test was applied to calculate the significant difference among subjects and controls. P < 0.05 was taken as significant.

Results

Mean age of both subjects and control was 19 years. BMI of subjects was non significantly high in

Table-1: Clinical characteristics of adolescents with and without family history (control) of hypertension.

No of cases in parenthesis Variables	Variables are expressed as mean \pm SD Subjects (50) Controls (50)	
Age (Years)	18.58 \pm 7.9	19.78 \pm 8.9
BMI (Kg/m ²)	26.18 \pm 4.31	23.60 \pm 1.94
Life style	Active=15 Sedentary =35	Active=30 Sedentary=30
Socioeconomic status	Upper Class=15 Middle Class=35	Upper Class=16 Middle Class=34
Systolic blood pressure (mmHg)	114.78 \pm 6.71	112.58 \pm 5.8
Diastolic blood pressure (mmHg)	76.21 \pm 8.01	70.21 \pm 8.5
Fasting blood sugar	88.76 \pm 6.56	80.0 \pm 8.5
Insulin Resistance	1.7 \pm 0.23*	1.0 \pm 0.15
Beta cell function	104 \pm 0.38*	1.9 \pm 0.43

*P<0.05 = Significant difference.

comparison with control subjects. Life style of

most of the subjects (35) with positive family history of hypertension was sedentary life style in comparison with controls. Both controls and subjects have middle to high socioeconomic status. Both systolic and diastolic blood pressure in subjects with positive family history was non significantly high in comparison with controls. Fasting blood sugar and insulin resistance was increased in tested subjects, but significant difference (P<0.05) was only observed in case of insulin resistance in comparison with controls. Beta cell function was significantly decreased (P<0.05) in subject with family history of hypertension in comparison with controls.

Discussion

The benefits of family history in finding the risk factors for hypertension over the genomic study included its low cost, cooperation of researchers and subjects, and consideration of both environmental and genetic factors.¹⁸ Moreover, positive family history and hypertension indicated a rating link i.e. as the occurrence of disease increased, the number of affected generation is also increased.¹⁹

In our study mean age of both subjects and control was 19 years with increased BMI and sedentary life style. It is reported that the occurrence of hypertension in adolescents is increasing not only due to positive family history but also due to increased rate of obesity.²⁰ Another study demonstrated that due to high-calorie diets and sedentary life style there is an increased prevalence of non-communicable diseases like hypertension.²¹

Both controls and subjects have middle to high socioeconomic status. However, a study reported that chances of developing hypertension declined with enhanced urbanization, education and adequate income of parents.²²

Both systolic and diastolic blood pressure in subjects with positive family history was insignificantly high in comparison with controls. It is evident that hypertension comparatively appear late, however the rate of occurrence of hypertension is high in adolescent with positive family history.²³ Moreover, increased level of 8-Hydroxy-29-deoxyguanosine (a product of oxidized DNA) and advanced Glycosylated End product are directly related with systolic blood pressure.¹⁵

We found that fasting blood sugar and insulin resistance was also increased in adolescents, but significant difference was only observed in case of insulin resistance in comparison with controls. It is demonstrated that angiotensin II causes insulin resistance by disturbing signaling of insulin and alters

insulin sensitivity by decreasing the synthesis of adiponectin.^{10,24} A study suggested that insulin resistance gives a shared pathway for the development of obesity, diabetes and hypertension.²⁵ Beta cell function was significantly decreased in subject with family history of hypertension in comparison with controls. Results of a study shows that an imbalance between antioxidant capacity of pancreas and generation of reactive oxygen species is the reason of impaired function of islet cells of pancreas.¹⁵ It is suggested that expression of hypertension is a complex trait and it may be due to an interaction between genes, life style and environment.^{26,27}

Conclusion

It is concluded that adolescents with positive family history of hypertension may have sustained hypertension which may be due to increased oxidative stress of pancreas followed by insulin resistance and β -cell dysfunction. Besides, sedentary life style may have a role in developing hypertension in first degree relatives of hypertension.

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