Single Nucleotide Polymorphism in the MTHFR Gene and Its Relation to Hypertension in Obese Children

A Thesis

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Mohammed Saad

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List of Abbreviations

Abb.	Full term

AAP .....American Association of Pediatrics
ACEI .....Angiotensin Convertase Enzyme Inhibitor
ARBs .....Angiotensin II Receptor Blockers
ARC .....Arcuate Nucleus
AS .....Alstrom Syndrome
BBS .....Bardet-Biedl Syndrome
BMI .....BODY MASS Index
BP .....Blood Pressure
CCBs .....Calcium Channel Blockers
CCK .....Cholecystokinin
CHF .....Congestive Heart Failure
CKD .....Chronic Kidney Disease
CVD .....Cardiovascular Disease
DBP .....Diastolic Blood Pressure
DMH .....Dorsomedial Nucleus
EPO .....Erythropoietin
ESRD .....Ends Stage Renal Disease
FDA .....Food and Drug Administration
FVa .....Factor V
GH .....Growth Hormone
GLP-1.....Glucagon-Like Peptide
Hcy .....Homocysteine
HTN .....Hypertension
IGF-1.....Insulin Growth Factor 1
LHA .....Lateral Hypothalamic Area
LVH .....Left Ventricular Hypertrophy
LVMI .....Left Ventricular Mass Index
MAOIs .....Mono Amine Oxidase Inhibitors

List of Abbreviations (Cont...)

Abb.	Full term
MTHFR	*Methylenetetrahydrofolate Reductase*
NHBPEP	*National High Blood Pressure Education Program*
NSAIDs	*Non Steroidal Anti Inflammatory Drugs*
OB	*Obese*
OCP	*Oral Contraceptive Pills*
OW	*Overweight*
PVN	*Paraventricular Nucleus*
QOL	*Quality of Life*
SBP	*Systolic Blood Pressure*
SES	*Socioeconomic Status*
SNP	*Single Nucleotide Polymorphism*
UTI	*Urinary Tract Infection*
VLEDS	*Very Low Energy Diets*
VMH	*Ventromedial Hypothalamic Nucleus*

ABSTRACT

Our study revealed a highly statistically significant positive correlation between hypertension and MTHFR gene SNP.

Regarding the C667T polymorphism, a higher frequency was detected among obese hypertensive children (60%) than obese normotensive children (26.7%) with a highly significant difference between them (p =0.009).

Genotypic analysis of the cases regarding C667T MTHFR revealed that 25 patients (35.7%) had genotype (CC), While 45 patients (64.3%) had mutant type, and 42 of them (60%) were heterozygous genotype (CT) and 3 (4.3%) were homozygous genotype (TT).

Keywords: Bardet-Biedl Syndrome - Angiotensin II Receptor Blockers - Congestive Heart Failure

INTRODUCTION

In the past 2 decades there has been increased recognition of the importance of blood pressure (BP) measurement in the pediatric population particularly in relation to the rising prevalence of childhood obesity. However, the importance of high BP goes beyond its relation to obesity, because longitudinal studies reveal a relation between childhood BP and future cardiovascular risk factors in young adults, independent of body mass index (BMI) ***(LO et al., 2013)***.

The relationship between obesity and hypertension is well recognized. Overweight and obesity increase the risk of elevated blood pressure. The prevalence of hypertension was 2 to 6 fold higher in obesity than in normal weight crowd ***(Yin et al., 2012)***.

The prevalence of childhood obesity has increased markedly over the last 2 decades. This increase is associated with an increase in hypertension rates which could lead to atherosclerotic disease in adulthood. Primary hypertension in children has become increasingly common in association with other cardiovascular risk factors that include being overweight, insulin resistance, and dyslipidemia ***(Abolfotouh et al., 2011).***

Methylenetetrahydrofolatereductase (MTHFR) is one of the key enzymes in folate metabolism that is essential for numerous cellular functions. The C677T polymorphism in the

coding region of human MTHFR gene that changes an alanine to a valine residue is a common single nucleotide polymorphism (SNP). Its polymorphic distribution varies greatly in different populations. This gene variant encodes a thermolabile form of MTHFR, which decreases the enzyme activity by approximately 35% in heterozygote (CT) and 70% in mutant homozygote (TT). The homozygous C667T in the MTHFR gene is reported to be associated with the risk of certain human diseases, including some cardiovascular disorders, cancers and neural tube defects ***(Yang et al., 2007)***.

Aim of the Work

To assess the relationship between MTHFR gene polymorphisms and hypertension in obese children.

Chapter 1

HYPERTENSION

Hypertension is a major long-term health condition and is the leading cause of premature death among adults throughout the world, including both developed, developing, and lesser developed countries. Primary hypertension emerges from a complex inter-play of genetic, environmental, and behavioral factors. Owing to the hereditary component of hypertension, the disorder is considered to have its origins in the young. It is now established that hypertension is detectable in children and adolescents and is not uncommon ***(Falkner, 2010).***

Obesity and hypertension are both common health problems in children and adolescents and, in concert with the increasing prevalence of obesity in children; pediatric hypertension has undergone an epidemiological shift. Among all the demographic and clinical factors analyzed, body mass index (BMI) has been most strongly associated with hypertension. Several studies have reported positive associations between obesity and elevated blood pressure and childhood obesity is often associated with the future development of hypertension ***(Zhang, 2011).***

Definition:

Hypertension is defined as average systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) that is greater than or equal to the 95th percentile for sex, age, and