Original Article

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Childhood Obesity as Interactions of Environmental and Genetic Factors: A Community – Based Study on Primary School Children of Hanoi, Vietnam

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Abstract:

Objective: Obesity is a complex disease that involves interactions between environmental and genetic factors in its pathogenesis. The aims of this present study were to analyse the overall effects of some nutritional, physical and genetic factors with childhood obesity, and to build predictive models of childhood obesity.

Material and Methods: A case–control study was conducted on 559 Hanoi primary school children (278 obese cases and 281 normal controls). Genetic analysis was performed to evaluate genotype on the rs6265 gene *BDNF*, rs6548238 gene *TMEM18*, rs6499640 gene *FTO*, and rs17782313 gene *MC4R*. Univariate and multivariate regression analysis were conducted to compare the two groups of children, so as to draw conclusions regarding influencing factors and to establish predictive models of obesity for Hanoi primary school children.

Results: Factors increasing the risk of obesity found included: urban living areas (odds ratio (OR)=1.5), caesarean section (OR=2.1), high birth weight (OR=1.9–3.1), parental overweight and obesity (OR=2.1–5.1), short night sleeping times (OR=2.6), characteristics of child feeding; including early weaning (OR=2.1), gluttony (OR=19.1), no snacking (OR=2.4), controlled eating (OR=2.4) fat food hobbies (OR=2.7), and CC rs6548238–*TMEM18* genotype (OR=1.8). A predictive model of childhood obesity for Hanoi primary school children was built, based on the BMI of parents, gluttonous characteristics, unrestricted eating with ROC=0.871.

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Conclusion: Childhood obesity develops as a result of interaction between eating habits, lifestyle characteristics of the child and genetic characteristics inherited from over nutritious parents. Encouraging parents to manage both their own weight and their children's eating habits such as allowing children to consume food without undue restriction and reducing gluttony can serve as effective interventions to diminish the prevalence of childhood obesity within the community.

Keywords: childhood obesity, genotype, parent's BMI, primary school children, predictive model

Introduction

The incidence of childhood obesity in Vietnam is increasing rapidly, especially in urban areas. Additionally, it is estimated that up to 1.9 million children worldwide will be obese by 2030[1]. Vietnam is a developing country in the Southeast-Asia region, which is facing a health burden of overweight of children. In 2020, it was estimated that up to 38.4 million children, 5–19 years of age, within this region suffer from being overweight (7.4%)[2]. This is a health concern, as overweight and obesity not only affect the health and psychology of children, but over 50% of obese children will sustain this condition in adulthood, combined with many other related diseases[3]. Therefore, prevention of obesity at an early stage can reduce the incidence of obesity and related adult disease; thereby, reducing the burden on health care for the population.

Obesity is a multi-factorial disease, due to its interaction between genetic and environmental factors[4]. Family characteristics, eating habits, sedentary lifestyles, and total night sleeping times were reported as the factors related to childhood obesity in primary school children in our previous reports[5,6]. Also, in primary school children in Hanoi, it was discovered that the effects of the rs6265 in *BDNF* (Brain derived neurotrophic factor)[6], the rs6548238 in Transmembrane protein 18 (*TMEM18)* on childhood obesity[7] as well as effect of the rs6499640 in *FTO* (Fat mass and obesity associated)[8], and rs17782313 in *MC4R* (Melanocortin 4 receptor) attributed to some anthropometric features of children[9].

The effects of obesity genes in different populations are variable, due to the diversity of ethnic characteristics, eating habits, physical activity, and socioeconomic factors[10,11]. Therefore, there is a requirement to conduct studies on the interaction between genetic and environmental factors on obesity within different populations. However, there are limited published studies on the interaction between lifestyle, genetic factors and obesity in Vietnamese children. Hence, this study aimed to determine the association of defining characteristics; such as: familial, neonatal, lifestyle and some single nucleotide polymorphism (SNPs) on genes *FTO, MC4R, TMEM18* and childhood obesity in primary school children of Hanoi, in addition to establishing a predictive model of obesity for primary school children to effectively prevent obesity at an early stage of life.

Material and Methods

Recruitment of subjects

A case-control study was conducted, consisting of a total of 559 subjects (278 obese cases and 281 normal controls), recruited from a cross-sectional population-based study. The sample selection method was cluster sampling (multi-stage sampling), for this cross-sectional study. It recruited 7,750 children: aged 6-11 years, from 31 primary schools in both 5 urban and 3 suburban districts of Hanoi. These children were measured for anthropometric indices and were then classified into 4 groups: underweight-, normal weight-, overweight-, and obese; using the criteria of World Health Organization (WHO) 2007, and the International

Obesity Task Force (IOTF) 2000. For this case-control study, the sample size was calculated by QUANTO software with prevalence of obesity in children 6 - 11 years old and was an estimated at 4.0%[12]. Type I error (α) was set as 0.01 with adjusted, two-tailed hypothesis testing' sample being 0.85. The ratio of alleles of interest was 0.15-0.3, with the additive genetic model and proportion of objects, with interactive environmental factors, ranging from 0.2-0.3. The main influence on genetics was 1.25 - main impact on the environment was 1.25; effect of gene and environment interaction was: 3.0-6.0, and the case/control ratio was 1:1. All of the above identified a sample size of 260 children for each group. Inclusion criteria consisted of: obese children that were not related to underlying diseases or adverse effects of therapy, with written participating consent signed by family members or guardians. Exclusion criteria consisted of: children having obesity, due to medication, or diseases or without participating agreement of family or guardians. Data collection was performed from September 2015 to September 2017. For genetic analysis, 2 ml of venous blood was collected from 321 normal children and 366 obese children. Parents of these children were asked for the agreement of the statement written by the National Institute of Nutrition, which clearly stated that blood samples would be used for scientific research purposes; including genetic studies. Next, the information of children's lifestyles; including: age, ethnicity, delivery method, living areas, nutritional behaviours; as exclusive breast feeding or acquired formula in the first 4 months, infant periods of feeding characteristics, eating characteristics; as greedily (consume food quickly and voraciously) or lazily (lack of interest in eating, eats little), with or without snacks, unrestricted eating, sweets/fats/fruits and vegetables, duration of night-time sleep, time of sport activites, time for watching television (TV) and playing games/day and also rarely changed indicators as to the parents' weight and height were answered by their parents through a structured questionnaire. Out of the 687 recruited children, only 559 subjects with completely fulfilled questionnaire were used for analysis. The Ethics Committee of the National Institute of Nutrition approved this study. Written consent to participate in the study was given by the parents of all subjects.

Measurements

Anthropometric indices including: weight, height, waist circumference (WC), and hip circumference (HC), were measured twice for each individual. This was performed by uniformly trained medical staff, and the mean was used for the purpose of analysis. Body weight and height were measured with subjects wearing light clothing and without shoes. Electronic scales were used to measure weight (accuracy 0.1 kg), and vertical height rulers were used to measure height (accuracy 0.1 cm), body mass index (BMI) was calculated as the weight per square of the height (kg/m^2). WC was measured midway between the lower rib margin and the iliac crest, while HC was measured at the broadest circumference below the waist. Waist-hip ratio (WHR) was calculated as the WC (cm) divided by the HC (cm).

Obese children and normal weight children were classified using the criteria of age- and sex-specific (biological sex) BMI cut-off points as proposed by the IOTF, 2000. Children who were identified as underweight, stunting and wasting by the criteria of WHO, 2007 were excluded from the study. In addition, children who were obese due to medical reasons were also excluded.

Genotypic method

Genomic DNA was extracted from peripheral blood leukocytes, via the Wizard® Genomic DNA Purification Kit (Promega Corporation, USA). Genotyping of the studied SNPs (rs6499640 in *FTO*, rs17782313 in *MC4R*, and

rs6548238 in *TMEM18*) were carried out by using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method; as presented in the recent publication[8].

Statistical analysis

Binary logistic regression analysis was used to test several models for the associations of obesity to the risk alleles and other variables (nutritional characteristics, physical activity traits, birth weight, living regions, and parent's BMI). The variables included in the analyses were checked for multicollinearity to ensure the stability of the parameter estimates. Herein, data were presented as odds ratios (OR), with 95% confidence intervals (CI). The Akaike information criterion (AIC) was used to assess model fit for a given set of data: lower values indicated improved model fit. In order to assess the model performance, a receiver operating characteristic (ROC) curve was built to plot probabilities resulting from the multivariate logistic regression analysis, and the area under ROC curve (AUC) was used to measure the power to predict individuals with obesity. The above statistical procedures were performed using statistical package for the social sciences (SPSS) version 16.0 (SPSS, Chicago, USA). Bayesian model averaging was used to cross-validate the final model using Bayesian Model Averaging Software, with the R Statistical Environment version 3.1.3. The value of p-value≤0.05 on two sides was considered as statistically significant.

Results

Effects of nutritional factors, physical activity and SNPs on child obesity

Table 1 shows the relationship of nutritional characteristics, physical activity, three studied SNPs, and characteristics of family and living regions to the risk of obesity in primary school children in Hanoi, Vietnam; before and after adjustment by age and gender.

The results showed that, after adjustment for age and gender there was a correlation between nutritional characteristics and the obesity of children; including: the age of children when ceasing breastfeeding, difficulty in feeding children in early life, how the children felt about their food, with or without snacking, unrestricted eating, fat food hobbies. In the physical activity factors, there was only the effect of lesser night sleeping times on obesity in Hanoi children.

Table 1 also indicated that urban living areas, caesarean sections, high birth weight, and high parental BMI were factors that increased the risk of obesity, when making both before and after adjustments by age and gender.

In multivariate logistic regression analysis, the AIC was used to evaluate the significance of the predictive model (simple and sufficient). The optimal model is the model with the lowest AIC value. As shown in Table 1, the over dominant genetic model was selected for the analysis of the effect of rs6499640 in *FTO*, a recessive genetic model selected for the analysis of the effect of rs17782313 in *MC4R* and rs6548238 in *TMEM18*. All 555 children were identified as to the genotypes of all three SNPs; only one child did not have any of the risk alleles (this child had a normal nutritional status); additionally, only one child had all five risk alleles (this child belonged to the obese group). On average, the number of risk alleles in each child was higher in the obese group than in the normal group (2.45 vs. 1.12, respectively). Furthermore, the number of children with more than 2 risk alleles was higher in the obese group than in the control group (71.1% vs. 65.5%, respectively, p-value=0.041). Analysis of the association of the number of risk alleles and obesity among primary school children in Hanoi, by univariate logistic regression analysis and age and gender adjusted analysis, showed that children with 2-3 risk alleles (of studied SNPs) had increased the risk of obesity by nearly 1.5 times, compared to those with less than 2 risk alleles (p-value=0.041) (Table 2).

Table 1 Association of some nutritional, physical activity factors, SNPs and obesity in Hanoi primary school children

Risk factor	n (%)		Univariate analysis		Adjusted for age, sex	
	Normal Group (n=278)	Obese group (n=281)	OR	p-value	OR*	p-value*
Nutritional characteristics						
No breast feeding	8 (2.9)	15 (5.5)	2.0	0.133	1.9	0.151
Acquired formula in first 4 months	151 (54.7)	143 (52.6)	0.9	0.616	0.9	0.582
Cease of breastfeeding before 12 months	27 (10.0)	42 (15.9)	1.7	0.042	1.7	0.045
Feeding without difficulty under 2 years old	136 (49.1)	209 (76.3)	3.3	<0.001	3.3	<0.001
Gluttonous eating	12 (4.3)	150 (54.5)	19.2	<0.001	19.1	<0.001
Lazily eating	84 (30.0)	5 (1.8)	0.1	<0.001	0.1	<0.001
No snack	55 (19.9)	100 (36.4)	2.3	<0.001	2.4	<0.001
Unrestricted eating	92 (33.9)	148 (54.4)	2.3	<0.001	2.4	<0.001
Sweet liking	208 (76.2)	201 (75.0)	0.9	0.747	0.9	0.604
Fat food hobbies	130 (48.9)	194 (72.7)	2.8	<0.001	2.7	<0.001
Fruits and vegetable liking	226 (82.8)	220 (79.4)	1.3	0.315	1.3	0.258
Physical activity traits						
Night sleeping duration <8 hours/day	29 (10.6)	65 (23.6)	2.6	<0.001	2.7	<0.001
Taken to school (compared to walking or biking)	186 (66.7)	202 (73.7)	1.4	0.07	1.4	0.091
Playing sports	203 (75.2)	210 (76.6)	1.1	0.691	1.1	0.574
Time spent watching TV and playing games >2 hours/day	174 (59.2)	175 (59.5)	1.2	0.629	1.1	0.524
Genetic traits						
FTO-rs6499640: AG	28 (10.0)	35 (12.6)	1.3	0.320	1.3	0.373
MC4R-rs17782313: additive alleles C	47 (8.4)	41 (7.4)	0.9	0.585	0.9	0.621
TMEM18-rs6548238: CC	248 (88.6)	258 (93.1)	1.8	0.061	1.8	0.05
Other traits						
Urban area living	147 (53.2)	172 (61.9)	1.5	0.023	1.5	0.019
Caesarean section	66 (23.7)	108 (39.3)	2.1	<0.001	2.1	<0.001
Birth weight <2.500 g	15 (5.5)	6 (2.3)	0.5	0.127	0.5	0.145
Birth weight >3.500 g and <4.000 g	35 (12.9)	55 (20.8)	1.9	0.010	1.9	0.009
Birth weight ≥4.000 g	9 (3.3)	24 (9.1)	3.1	0.005	3.2	0.004
Father or mother with BMI ≥23 kg/m^2	91 (34.1)	119 (44.1)	2.1	<0.001	2.1	<0.001
Both parents with BMI ≥23 kg/m^2	16 (6.0)	51 (18.9)	5.1	<0.001	5.3	<0.001

BMI=body mass index, p-value by logistic regression analysis, SNPs=single nucleotide polymorphism, OR=odds ratio, TV=television

Table 2 Association of the number of risk allele with obesity in Hanoi primary school children

Number of risk allele	Univariate analysis		Adjusted for age, sex	
	OR (95% CI)	p-value	OR* (95% CI)	p-value*
0 – 1	1		1	
2 – 3	1.4 (1.1 – 1.6)	0.035	1.4 (1.1 – 1.7)	0.041
4 – 5	1.5 (0.8 – 3.2)	0.235	1.6 (0.7 – 3.5)	0.325

OR=odds ratio, CI=confidence interval

Probability of each risk factor included in the predictive model for obesity in Hanoi primary school children

For the concurrent analysis of all risk factors presented in Table 1, the Bayesian Model Averaging (BMA) method was used to determine the probability of each risk factor that was included in the predictive models for obesity among Hanoi primary school children. The probability of the risk factors greater than 0% is shown in Figure 1.

Figure 1 showed the probability that the: "high parental BMI" and "children eating greedily," were the factors included in the predicting models of obesity (100%). There was 0.5% that had the: "rs6548238 variant in *TMEM18*".

Optimal predictive model of obesity among Hanoi primary school children

BMA analysis to identify predicting models of obesity in primary school children in Hanoi consisted of 10 predictive models, which were shown in the results (Figure 2). Next, in order to select the predictive models that can be applied in practice; according to three criteria: "simple", "effective" and "realistic", each model was analyzed. As a result, model 3 was selected as the optimal model for community use (nutritional clinics, families, and schools)/ This model requires the following information: (1) parental BMI, (2) gluttonous eating and (3) unrestricted eating. This model had good predictability, as the area under the ROC curve was greater than 0.8 (ROC=0.871).

The formula of prediction obesity in Hanoi primary school children

Table 3 shows the influent coefficients of risk factors in the predictive model.

From the coefficient β of the effect factors shown in Table 3, the calculating formula for obesity in primary school children in Hanoi was constructed, as follows: P=ey/(1+ey). In the formula: P is the probability of the child to become obese; *e* is the base of the natural logarithm, with a value of approximately 2.718; The y value is: $y=\beta_{\text{Parental BMI}}+\beta_{\text{Eating trait}}+\beta_{\text{Unrestricted eating}}-1.36$.

Table 3 Influent coefficient of factors in predictive model of obesity in Hanoi primary school children

Risk factor	β±SE	p-value
Parental BMI (kg/m^2)		
Both parents with BMI <23	0.00	
Father or mother with BMI ≥23	0.64±0.25	0.001
Both parent with BMI ≥23	1.46±0.38	<0.001
Eating traits		
Normal	0.00	
Gluttonous eating	3.00±0.35	<0.001
Lazily eating	−2.13±0.45	<0.001
Eating follow liking		
Unrestricted eating	0.00	
Controlled eating	1.11±0.24	<0.001
Constant	−1.36±0.22	<0.001

β=beta coefficient, SE=standard error, BMI=body mass index, kg=kilogram, m=meter
p-value obtained from multivariate logistic regression analysis

Discussion

The results of this study showed that there are multifactorial effects on childhood obesity; including neonatal and nutritional factors (as cesarean section, high birth weight, early ceasing of breastfeeding, eating greedily, no additional meals, controlled eating, and fat food hobbies), one lifestyle factor (as short night sleeping times) and genotype (as CC-SNP rs6548238-*TMEM18* genotype), familial factors (as high parental BMI, urban living areas) also increased the risk of childhood obesity. From a comprehensive analysis of all risk factors, the predictive models of childhood obesity were constructed.

The relationship of birth delivery (normal or caesarean) to child obesity has been reported[13]. In this study, primary school children in Hanoi born via caesarean section had a higher risk for obesity than children born via normal delivery (OR=2.1), p-value<0.001), which can be explained by the relation of caesarean section with high birth weight neonates, low gestational age, high maternal age, and high maternal BMI[14,15]: these factors are all related to increased risk of childhood obesity.

Both, low birth weight and high birth weight have been reported in relation to the risk of obesity in many studies[16-18]. This study showed a link between high birth weight (greater than 3.500 g) and obesity risk in primary school children in Hanoi. Excessive fetal exposure (such as; maternal deficiency or over-nutrition) in the uterine environment can lead to epigenetic changes in the fetal genome, altering gene expression associated with anatomy, physiology and metabolism of various organs; therefore, the fetus can adapt to these conditions. These adaptations may be beneficial for short-term survival of the fetus; however, they may have negative consequences after birth and in later life; such as an increased risk of obesity[16].

According to WHO recommendations, infants should be breastfed immediately after birth and this should last for up to 24 months. Breastfeeding duration (the age of the child when having ceased breastfeeding) has been reported in relation to BMI and to the growth of children[19]. This study showed that weaning before 12 months increased the risk of childhood obesity by 1.7 times. This can be explained by the fact that children ceasing breastfeeding early are often fed instead with formula or solid foods. Although, this may provide more energy for children, as a result the risk of weight gain and obesity is increased; as per the research of Papoutsou et al[20].

Characteristics of feeding children during the first few years of life and a good appetite in children in this analysis has shown a strong influence on the risk of childhood obesity (OR=3.3 and 19.1 respectively). This can be explained by the fact that children with good appetites and being easy-to be fed usually eat more than hard-to be fed children in the quantity and variety of their food. Hence, they are more likely to gain weight with a fast temp, and therefore they are at a higher risk of becoming overweight or obese. The relationship between infant feeding and the risk of childhood obesity in this study has been clarified beyond the remaining open questions; as in the study of Lumeng et al[21].

Additional meals have been reported to be associated with BMI in both directions of weight gain and weight loss[22,23]. In this study, most children attend school with a semi-boarding regime (with school lunch), and children are usually given a meal after school in the afternoon or an extra meal before bed. In our interviews, we found that overweight and obese children often did not receive these supplemental meals, because their parents were afraid of them gaining weight; therefore, these children were often very hungry at the time of their main meal, and thus they tried to eat more. This explains the result that children without additional meals have an increased risk of obesity of two times. This is similar to the results of Grigorakis et al. on Greek children and Guo et al in Chinese children[23,24].

In this study, children were not allowed to eat following their likes/dislikes had an increased their risk of obesity; with OR=2.4 p-value<0.001. This finding may be explained by these obese children likely being restricted by

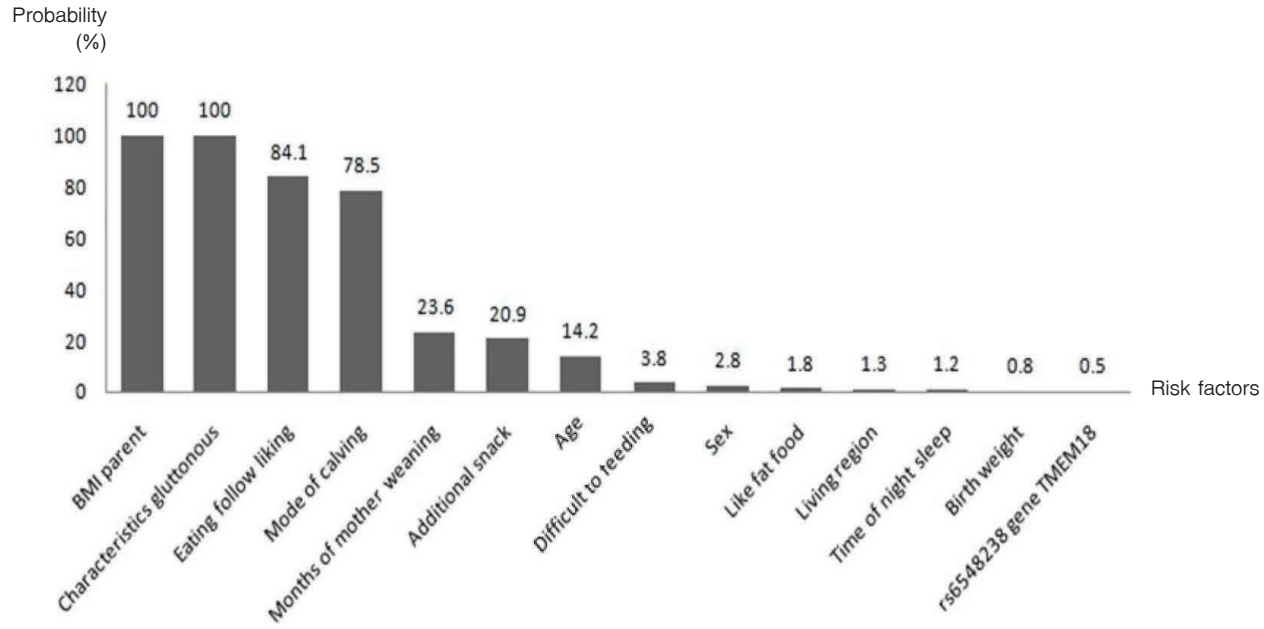

Figure 1 Probability of risk factors included in predictive models for obesity in Hanoi
(The probability of factors that contribute to obesity in Hanoi primary school children was assessed through Bayesian model averaging (BMA) analysis in prediction models)

their parents, and being not fed as often as they preferred, while children with normal or under being weight were usually encouraged to eat, and were allowed to eat as to their preference.

The relationship between preferences for each type of food and obesity has been reported extensively; particularly the preference for fatty foods[22]. Fatty foods often make for a good appetite, which often makes children feel like eating. Fatty foods are high-energy, so children that like to eat fat increase their risk of obesity by many times. This study also showed similar results with children who love fatty foods have the risk of obesity being increased by 2.7 times compared with the remaining children.

Four characteristics of physical activity were evaluated, and only found that lesser night sleeping times had an effect on obesity in children. At primary school age, children should sleep between 9 and 11 hours a day, because short sleep duration can lead to severe changes in cortisol and growth hormone (GH) levels[24,25]. This can also alter leptin and ghrelin–hormones, which play an important role in regulating feelings of hunger and fullness of the organism. Several cross-sectional studies have found an association between short nocturnal sleep duration and obesity[22,24], while other studies do not find this link[26]. In this study, children with nocturnal sleep duration of less than eight hours were likely to be obese by 2.7 times than those whom had night sleeping times of eight or more hours.

Analysis of the effects of each rs6499640, rs17782313, rs6548238 SNP on obesity in primary school children in Hanoi has been reported previously. It showed that variant in the SNP rs6499640 is related to the butt circumference in normal children[8]; SNP rs17782313 is also related to the Z-score of weight/age in normal children as well as waist-to-hip ratio in obese children[9] when SNP rs6548238 affects obesity in both recessive and cumulative genetic models[7]. This study indicated that children having

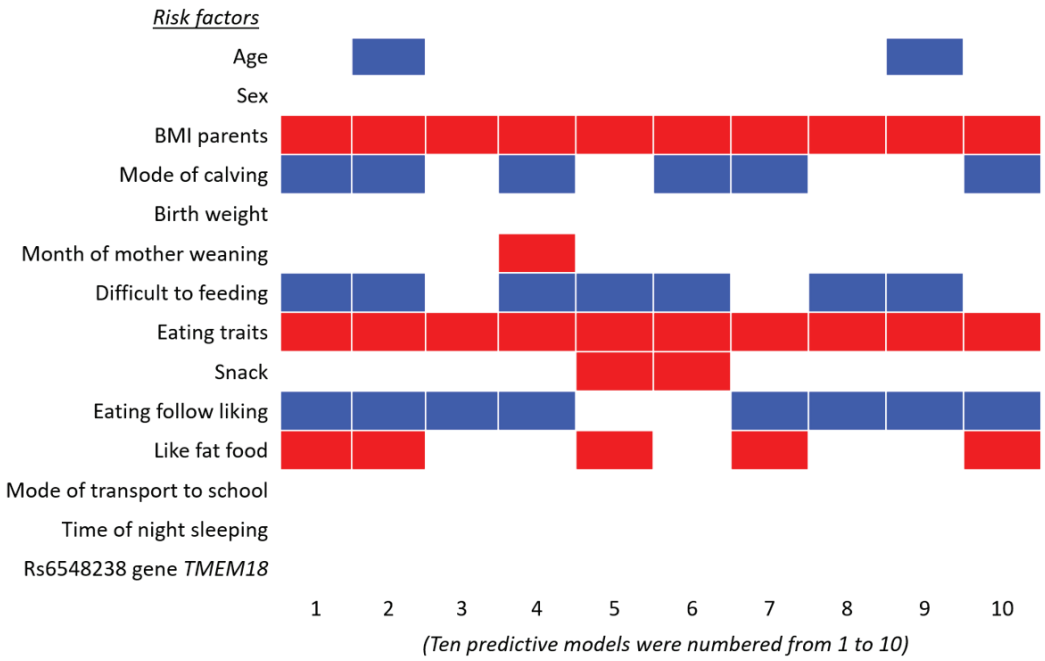

Figure 2 Predictive models of obesity in Hanoi primary school children

2-3 risk alleles (of the studied SNPs) has an increased the risk of obesity by nearly 1.5 times compared to those with less than 2 risk alleles (p-value=0.041). Genome-wide association studies[10], meta-analysis and a large number of SNP studies have shown that each risk allele contributes only to a small part of BMI changes[27,28]. However, the total number of risk alleles is positively correlated with the risk of obesity or a high BMI in humans. The study of Jääskeläinen et al. (2013) on 8 SNP: rs1421085 in *FTO*, rs17782313 in *MC4R*, rs6265 in *BDNF*, rs10938397 in *GNPDA2*, rs1424233 in *MAF*, rs6548238 in *TMEM18*, rs11084753 in *KCTD15* and rs2815752 in *NEGR1, in* more than 4,600 Finnish children showed that children with 8 risk alleles had a higher BMI of 0.9 kg/m^2 than children with less than 8 risk alleles[29]. Hong et al. (2013) on 23 SNPs in Han Chinese people aged 14-30 years, showed that people with a high risk of alleles had a higher risk of obesity and birth weight than the group with a total low number of alleles[28]. Also, in 2013, Ntalla et al also reported similar results when studying Greek children[30]. Research in Hanoi primary school children also showed similar results with the above reports: children with 2 to 3 risk alleles had an increased risk of 1.5 times for obesity compared to children with less than 2 risk alleles. However, due to the number of children with 4 or more alleles being relatively small, the relationship of the 4 – 5 group of alleles to obesity in Hanoi primary school has not been found.

Which could be explained by both genetic factors and lifestyle factors (nutrition, and physical activity) in the family. Overweight and obese individuals often have more risk alleles for obesity, which may be inherited in later generations, so if a child who was born from a parent with a high BMI they may have a higher risk of obesity. On the other hand, families with overweight parents are more likely to have high energy diets and sedentary lifestyles, which in turn will have a greater impact on the lifestyle of

children. As a result these children are at a higher risk of obesity[16,31]. In this study, urban living areas were a factor that increased the risk of obesity in children. This is similar to the results of Buitrago-Lopez's study in 2015[32]. This can be explained that in comparison with suburbs, the families of urban areas often have higher income levels, and a higher population density, so the inner city children are often cared for as too their eating habits, but are provided less space for physical activity. This could be aa reason for the higher risks of obesity of children in inner-city Hanoi when compared with children living in the suburbs.

Obesity is a multi-factorial disease, due to environmental factors (nutrition, physical activity, living environments, and lifestyles), genetic factors and epigenetic regulation[11]. According to BMA analyzing, the effects of parental BMI on child obesity may be due to genetic and/or lifestyle causes, so in BMA analysis, risk factors for: "high parental BMI" were always used in predictive models (with 100% probability). This is to prove that this factor is an important factor in an optimal predictive model.

The subjects of this research were children at primary school age, when children begin a new phase of their life that is important for physical and mental development. Nowadays, children are seen by their families and societies in a different way; as if they are more mature, and require more independence, especially in their eating habits. On the other hand, at this age children are not very conscious in regulating their food as recommended by sciences, or to fit the appearance of children, so children often eat according to their own needs. For this reason, the: "gluttonous or greasy" determines the amount of food that a child eats routinely. More education on this subject for children would serve as a component of multidisciplinary nutritional-based programs to prevent childhood obesity[33].

The probability that the SNPs (rs6499640, rs17782313, rs6548238) are included in the predicted models is not high (0.5% for SNP rs6548238, 0% for SNP rs6499640, rs17782313), this is also similar with GWA studies and studies on large numbers of genes, where each variant of the risk alleles has minor affects on obesity[10].

Some of the strengths of this study are: firstly, to the best of our knowledge, this study was one of the first researches analyzing the effects of the rs6499640 in *FTO*, rs17782313 in *MC4R*, rs6548238 in *TMEM18* on obesity in primary school children in Vietnam. Secondly, this study analyzed the effects of a number of environmental and genetic factors on obesity in primary school children in Hanoi. This identified the important role of risk factors, and therefore a predictive models for obesity of children was built and as a result an optimal predictive model for obesity in primary school children in Hanoi was developed. However, the limitation of the study was that the diet and the level of physical activity were not determined. Therefore, it is important to expand the study on a wide range of subjects, in different age groups, and geographic areas as well as to analyze more SNPs on more genes. Additionally, to analyze the effects of diet and physical activity to obesity in the future.

Conclusion

The prevalence of obesity is increasing in Vietnamese children, with long-term consequences that require effective intervention strategies. This study found affecting factors to obesity in Hanoi primary school children; including history of being overweight at birth, cesarean sections, lifestyle factors such as short night-time sleeps, feeding characteristics of children as well as the role of CC-genotype of polymorphism the rs6548238 in *TMEM18* and the overweight/obesity characteristics of parents. The model to predict a child's obesity probability was built from only 3 factors; including parents' BMI and two child eating characteristics, with a high ability of classification; in that the ROC index was greater than 0.8. This allows for wide application in the community, and could be used for intervention strategies to reduce obesity in children.

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Conflict of interest

The authors declare no conflict of interests.

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