Original Article

Association of heat shock 70 protein 1B gene polymorphisms and the susceptibility to asthma in pediatric patients

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Abstract: Background: Childhood asthma and wheezing are very common, especially in those born preterm. Genetic and environmental factors are associated with developing asthma and wheezing. Epidemiological data show that obesity could increase the risk of asthma, and insulin resistance, or metabolic syndrome are an important risk factor for obesity asthma. Some studies identified some sites within the heat shock protein (HSP)-B gene region 1267 polymorphism was associated insulin resistance or metabolic disorders, while this site was closely related to asthma. But no research was performed to evaluate the influence of HSPA1B 1276A/G polymorphism on metabolic syndrome in pediatric asthma patients. Methods: Here, we recruited 246 pediatric asthma patients, who were separated into pediatric asthma patients with MetS or without MetS groups and 224 matched healthy controls from Tianjin Province to evaluate the influence of HSPA1B 1276A/G polymorphism on metabolic syndrome in pediatric asthma patients. Single nucleotide polymorphism of HSPA1B 1276 locus was genotyped using PCR-RFLP. Some biochemical variables were also determined. Results: Our results showed that the genotypic and allelic frequency of rs1061581 did not show significant difference between pediatric asthma patients and normal controls. However, the frequency of G allele was significantly higher in asthma group with MetS (21.36%) than in controls (14.71%) (P = 0.022; OR = 0.667; 95% CI = 0.407-0.916). After analyzing the relationship between biochemical features of patients and genotype of HSPA1B 1276A/G, we found levels of LDL cholesterol, fasting insulin, and HOMA-IR were significantly higher in the asthmatic patients carrying the GA and GG genotypes than in the carriers of AA genotype (P = 0.031, P = 0.021, P = 0.041, respectively). Conclusion: Thus, Our data suggested that HSPA1B 1276A/G variation was related to metabolic phenotype in pediatric asthma patients. Furthermore, we first identified HSPA1B 1276G allele was the risk factor for pediatric asthma patients with MetS in Tianjin population, China.

Keywords: Pediatric asthma patients, metabolic syndrome, insulin resistance, HSPA1B gene, polymorphism

Introduction

Asthma is a chronic allergic disorder of the airways that is characterized by inflammatory infiltrates in the bronchial walls, airway hyper-responsiveness (AHR) and reversible airway obstruction [1, 2]. Currently, the global prevalence of asthma is 1%-18%, with the number of pediatric asthma patients around 300 million, and the incidence of this disease is on the rise. The overall prevalence of asthma in China is 1%, but in children is up to 3%, with both increasing. It is believed to be a multifactorial disease whereby genetic factors contribute to its etiology and/or clinical severity [3, 4]. While, the genes involved in asthma are still unknown and are likely to be numerous. To date, numerous risk genes have been reported to be associated with asthma susceptibility in various populations. One of the candidate susceptible genes that have been intensely investigated is heat shock 70 protein (HSP-70) [5-23].

Heat shock proteins, which function mostly as molecular chaperones, participate in the folding and assembly of newly synthesized proteins in cells, facilitate protein transport to subcellular compartments, and are involved in the refolding of damaged proteins. HSP-70 family is one of the most conserved families. In humans,
HSPA1B gene and pediatric asthma patients

There are 13 different genes encoding HSPA proteins including HSPA1A, HSPA1B, HSPA1L, HSPA2, HSPA4, HSPA4L, HSPA5, HSPA6, HSPA7, HSPA8, HSPA9, HSPA12A and HSPA14. The HSPA1A and HSPA1B genes were shown to encode an identical product which is the major heat inducible HSPA protein [24]. Several polymorphisms in the region of HSPA1B have been associated with different HSPA1B expression levels. Of these, the HSPA1B 1267A>G (also referred to as rs1061581) is the best studied. It involves the substitution of a guanine (G) by an adenine (A) and is associated with an increase in HSPA1B expression levels [25-28]. Up to now, a lot of studies of genetic epidemiology have assessed the association of HSPA1B gene polymorphisms and risk of asthma in different populations, but conflicting results were obtained due to the heterogeneity of the genetic background among populations. Furthermore, this support the need for replication studies among all ethnic groups.

Metabolic syndrome (MetS) which was firstly described by Reaven as syndrome X, is a major public challenge worldwide [29, 30]. The main components of the syndrome are obesity, insulin resistance (IR), hypertension, and dyslipidemia. There is agreement that MetS causes pro-inflammatory and thrombogenic state, leading to late-onset diabetes mellitus and cardiovascular diseases with increased mortality and morbidity. Recently, a great deal of epidemiological data show that obesity and insulin resistance can increase the risk of asthma [31-34]. Its mechanism is unclear. Several studies have confirmed that HSPA1B 1276A/G polymorphisms are associated with insulin resistance or metabolic disorders.

Taken together the association of HSPA1B gene polymorphisms and asthma, the aim of the present study was to investigate whether SNP in HSPA1B 1276A/G, rs1061581 is associated with metabolic syndrome in pediatric asthma patients and further explore the pathogenesis of asthma complicated by metabolic syndrome.

Subjects and methods

Ethics statement

The Medical Ethics Committee of the Tianjin People’s Hospital approved this study. Written informed consents conforming to the tenets of the Declaration of Helsinki were obtained from each participant prior to the study.

Participants

A total of 246 patients with pediatric asthma patients (Age from 0-9 years old), defined according to the criteria of the Global Initiative for Asthma (GINA), and 224 matched healthy controls were enrolled in this study from the Tianjin People’s Hospital pulmonology outpatient clinic. All subjects are Han Chinese. Respiratory symptoms and medications were assessed in detail and pulmonary function tests were performed in a standard fashion using electronic spirometer (MIR), for every subject. The inclusion criteria for controls were as follows: no symptoms or history of asthma or other pulmonary diseases; no symptoms or history of atopy; negative skin prick test results with a battery of common aeroallergens; and absence of first-degree relatives with a history of asthma or atopy; without autoimmune or inflammatory disease.

All the subjects’ height and weight were measured by the same person using the same equipment. Body mass index was calculated by dividing body weight to height square (kg/m²). Biochemical features, including total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL) were collected for further study.

Diagnosis of metabolic syndrome

For the diagnosis of metabolic syndrome, modified Chinese Diabetes Society (CDS) diagnostic criteria were used. The CDS definition for MetS required impaired glucose tolerance plus two of the following three disorders: obesity (waist-to-hip ratio ≥0.9 cm in men or ≥0.85 cm in women), dyslipidemia (triglyceride level ≥1.7 mmol/L and/or HDL cholesterol level ≤1.03 mmol/L in men or ≤1.29 mmol/L in women), and high blood pressure (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg). Glucose concentration was determined using the glucose oxidase method, and insulin concentration was determined using a radioimmunoassay (Diagnostic Products Corp, Los Angeles, CA). To assess insulin resistance, homeostasis model assessment of insu-
HSPA1B gene and pediatric asthma patients

Table 1. Anthropometric and biochemical data of patients and healthy controls

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Asthma</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mets [n (%)]</td>
<td>150 (61.29)</td>
<td>50 (22.81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension [n (%)]</td>
<td>96 (38.71)</td>
<td>37 (16.23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.25±1.98</td>
<td>22.34±1.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting insulin (μU/mL)</td>
<td>14.8±8.2</td>
<td>8.1±7.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting glycemia (mmol/L)</td>
<td>6.14±1.24</td>
<td>4.21±0.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>3.9±2.3</td>
<td>1.6±1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.34±0.87</td>
<td>5.52±1.08</td>
<td>0.574</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.81±0.76</td>
<td>1.79±0.36</td>
<td>0.637</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.03±0.48</td>
<td>1.29±0.45</td>
<td>0.067</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>3.02±1.41</td>
<td>2.65±1.26</td>
<td>0.059</td>
</tr>
<tr>
<td>HSPA1B (pg/ml)</td>
<td>53.21±3.84</td>
<td>27.93±6.50</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Mets, Metabolic syndrome; BMI, Indicates body mass index; HDL, High-density lipoprotein; LDL, Low-density lipoprotein.

In resistance (HOMA-IR) index was calculated as follows: [fasting insulin (μU/mL) × [fasting glucose (mmol/L)]/22.5. The HOMA-IR index is a mathematical model designed by Matthews et al. [35].

Genotyping of SNP in HSPA1B 1276A/G, rs1061581

Genome DNA from whole blood cells of each sample was extracted by using Blood Genomic DNA Miniprep Kit (Axygen, USA) according to the manufacturer’s instructions. Genotyping for the HSPA1B1276A/G polymorphisms in genomic DNA was performed using the PCR and restriction fragment length polymorphism (RFLP). The genomic region encompassing the 1276A/G polymorphism was amplified using the following primers: forward 5’-ACAGGCCCCAGATTCAGC-3’ and reverse 5’-TCCCTGCTCCGATTCCG-3’. Polymerase chain reaction products were generated in a 10 μL reaction volume containing 50 ng of genomic DNA, 1 × PCR buffer, 2 mmol/L MgCl₂, 0.2 mmol/L of each dNTP, 1 μmol/L of each primer, and 0.25 U of Taq DNA polymerase (Invitrogen Corporation, Carlsbad, CA). Cycling conditions consisted of an initial denaturation step at 94°C for 5 minutes, followed by 35 cycles of denaturation at 94°C for 30 seconds, annealing at 60°C for 30 seconds, and extension at 72°C for 30 seconds and a final elongation step at 72°C for 1 minute. Polymerase chain reaction products were digested with 2 U of NcoI restriction enzyme at 37°C, according to the manufacturer’s instructions (New England BioLabs, Ipswich, MA). The -308G allele contains an NcoI restriction site not present in the -308A allele; thus, in the presence of the -308G allele, the PCR product (107 bp) is cut into 2 fragments of 80 and 27 bp in length [36].

Assay of serum HSPA1B levels

The serum level of HSPA1B was determined by ELISA Quantikine Human HSPA1B immunoassay kit (Biosource, USA). The lower limit of detection ranged from 4 to 6 pg/mL. Assay was carried out according to the manufacturers’ instructions.

Statistical analysis

Data were statistically described in terms of mean ± standard deviation (SD), or frequencies (number of cases) and percentages as required depending on their distribution. The Hardy-Weinberg equilibrium (HWE) was assessed for each variation to identify the deviation. The differences of the genotypes and alleles of HSPA1B 1276A/G between patients and normal controls were evaluated by using Pearson Chi-square test. Exact test was used instead when the expected frequency is less than 5. The odds ratio (OR) and 95% confidence intervals (95% CI) were calculated. Unpaired Student’s t test or Mann-Whitney tests were used for two-group comparisons. Because of skewed distributions, log-transformed values for HDL cholesterol, LDL cholesterol, insulin, HOMA-IR, and HSPA1B were used in analyses and back-transformed for data presentation. Statistical analysis of data was performed using the SPSS software package 16.0 (SPSS Inc. USA). P-value less than 0.05 was considered statistically significant.

Results

In this study, 246 asthmatic (106 males and 140 females) and 224 controls (110 males and 114 females) were screened for rs1061581 polymorphisms using PCR-RFLP methods. The mean age of asthmatic patients was 6.48 years, and mean age of matched controls was 6.71 years. There were no significant differences between two groups with regard to gender and age distribution. Table 1 showed the
The incidence of MetS in pediatric asthma group was about triple that of control (61.30% vs 22.80%). Ninety-six (38.70%) patients in asthma group and 37 (16.21%) patients in control group had Hypertension. Body mass index, glucose and insulin blood levels, HOMA-IR and serum HSPA1B levels were significantly higher in pediatric asthma patients ($P < 0.001$ for both parameter). There were no differences in lipid panels between groups including total cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol.

Firstly, the frequency of genotypes and alleles of HSPA1B gene SNP rs1061581 was detected in pediatric asthmatic patients and controls. HWE of rs1061581 in patients and controls were listed in Table 2, and the results showed allelic distribution of rs1061581 was not deviated from HWE in both case and control populations. The genotypic and allelic frequency of rs1061581 did not show significant difference between asthmatic patients and normal controls.

<table>
<thead>
<tr>
<th>Genotype/Allele</th>
<th>Patients (n = 246)</th>
<th>Controls (n = 224)</th>
<th>P-value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HWE $P = 0.24$</td>
<td>HWE $P = 0.27$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>163</td>
<td>185</td>
<td>0.611</td>
<td>0.905 (0.611-1.331)</td>
</tr>
<tr>
<td>GA</td>
<td>76</td>
<td>37</td>
<td>0.073</td>
<td>0.822 (0.682-1.481)</td>
</tr>
<tr>
<td>GG</td>
<td>7</td>
<td>2</td>
<td>0.126</td>
<td>4.560 (0.551-37.422)</td>
</tr>
<tr>
<td>A</td>
<td>406</td>
<td>411</td>
<td>0.318</td>
<td>0.841 (0.594-1.181)</td>
</tr>
<tr>
<td>G</td>
<td>90</td>
<td>41</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Chi-square test for deviation from the Hardy-Weinberg equilibrium (a value of $P<0.001$ was regarded as a deviation from the HWE).

In the patients with pediatric asthma, anthropometric and biochemical parameters were analyzed according to the genotypes of rs1061581 between pediatric asthmatic patients and normal controls did not show significant difference.

On the basis of MetS criteria, the asthmatic patients were further subgrouped as pediatric asthma with MetS and pediatric asthma without MetS. As shown in Table 4, among the pediatric asthmatic patients with MetS, the GG genotype of the rs1061581 was found in 59.20% (88/150) of the cases, whereas the GA and AA were present in 36.85% (56/150) and 3.95% (6/150) of the asthmatic patients with MetS, respectively. In the pediatric asthmatic patients without MetS, the GG, GA and AA genotypes were found in 78.12% (75/96), 20.81% (20/96) and 1.05% (1/96) of the cases, respectively. The frequency of G allele was significantly higher in asthma group with MetS (22.37%) than in controls (15.70%) ($P = 0.022$; OR = 0.645; 95% CI = 0.441-0.937). While asthmatic patients without MetS failed to show any such difference ($P = 0.16$; OR = 1.445; 95% CI = 0.863-2.467).

In the patients with pediatric asthma, anthropometric and biochemical parameters were analyzed according to the genotypes of rs106-
HSPA1B gene and pediatric asthma patients

Table 4. The comparison of genotype and allele frequency of HSPA1B site in pediatric asthmatic subgroups and the control group

<table>
<thead>
<tr>
<th>Groups (N)</th>
<th>Genotype (%)</th>
<th>Allele (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AA</td>
<td>GA</td>
</tr>
<tr>
<td>Pediatric with MetS (150)</td>
<td>88 (59.21)</td>
<td>56 (36.84)</td>
</tr>
<tr>
<td>Pediatric without MetS (96)</td>
<td>75 (78.13)</td>
<td>20 (20.83)</td>
</tr>
<tr>
<td>Controls (224)</td>
<td>187 (69.03)</td>
<td>37 (30.53)</td>
</tr>
<tr>
<td>Control with Mets (52)</td>
<td>42 (80.77)</td>
<td>8 (15.38)</td>
</tr>
<tr>
<td>Control without Mets (172)</td>
<td>145 (83.33)</td>
<td>27 (16.67)</td>
</tr>
</tbody>
</table>

Table 5. Anthropometric and biochemical parameters in patients with asthma according to HSPA1B genotypes for 1276A/G polymorphisms

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Genotype</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AA (n = 163)</td>
<td>GA + GG (n = 83)</td>
</tr>
<tr>
<td>Fasting insulin (μU/mL)</td>
<td>11.15±3.64</td>
<td>15.78±8.31</td>
</tr>
<tr>
<td>Fasting glycemia (mmol/L)</td>
<td>6.15±1.85</td>
<td>6.36±2.14</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.63±0.69</td>
<td>4.25±2.37</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.32±0.97</td>
<td>4.74±1.08</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.91±0.92</td>
<td>1.71±0.86</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.03±0.24</td>
<td>1.02±0.17</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>2.52±1.26</td>
<td>3.13±1.04</td>
</tr>
</tbody>
</table>

For statistical purposes, the carriers of the A allele in the heterozygous and homozygous states were treated together (Table 5). We observed that the levels of LDL cholesterol and insulin, and HOMA-IR were significantly higher in the asthmatic patients carrying the GA and GG genotypes than in the carriers of AA genotype of rs1061581 (P = 0.028, P = 0.021, P = 0.042, respectively). Furthermore, results revealed at among asthmatic patients, the rs1061581 GA and GG genotypes exhibited significantly higher serum HSPA1B levels than that of AA genotype (57.21±1.62 vs 52.43±1.42, P<0.001).

Discussion

Genetic predisposition has been considered as a crucial determinant in patients, and candidate genes have concentrated on leukotriene-related genes. However, conflicting results have been reported. Aron et al. suggested that HSP70 overexpression in asthma was independent on HSP gene polymorphisms, and Smith et al. reported that HSPA1A and HSPA1B do not share common patterns of polymorphisms. HSPA1B has important biological effects on airway inflammation and remodeling. Several studies have shown that high serum HSPA1B level is linked to hyperresponsiveness in asthma. Furthermore, the concentration of HSPA1B was found to be elevated in asthmatic airways and sputum. HSPA1B has many effects relevant to the pathogenesis of asthma, including neutrophil release, epithelial cell barrier permeability, macrophage activation, recruitment of inflammatory infiltrates, effectiveness of the local and systemic inflammatory response, and amplification of the effects of other proinflammatory cytokines. Because secretion of cytokine is genetically regulated at the level of transcription, and the linkage of HSPA1B polymorphisms with the genotype of asthma has been demonstrated in accumulating studies [37-41].

HSPA1B gene is located in the class III region of the human major histocompatibility complex (MHC) on chromosome 6p21 [42, 43]. Among the several single nucleotide polymorphisms (SNPs) identified in HSPA1B, HSPA1B rs1061581 is the most extensively studied. The A allele of this polymorphism can lead to high binding affinity of nuclear factors to the TNF promoter, resulting in a high level of transcription activity and secretion levels of HSPA1B. So, it was suggested to have a significant functional effect [44]. A number of studies have tried to determine whether the polymorphism of HSPA1B rs1061581 influences HSPA1B expression, susceptibility to asthma, but no accordant result was obtained due to the heterogeneity of the genetic background among populations [45-47]. Whether genetic variations of the HSPA1B rs1061581 conferred susceptibility to asthmatic patients in Chinese was puzzled.
In this study, we analyzed HSPA1B gene SNP rs1061581 in 246 asthmatic patients and 224 matched controls from Tianjin, China. In order to exclude the gender bias, the percentage of males was extremely similar in patients (43.54%, 108/246) and controls (49.56%, 112/224). No difference was found in genotypic and allelic frequency of rs1061581 between asthmatic patients and normal controls. This result was in contrast with other previous studies that the HSPA1B rs1061581 polymorphism was strongly associated with the risk of asthma. According to stratified analysis by ethnicity, Zhang et al. showed significant associations were showed in Asians, but not Caucasians. However, Silva et al. meta-analysis suggested the positive association was shown in West Asians and South Asians, but not in East Asians. It is possible that different genetic backgrounds and environmental exposure may account for these differences [48].

Additionally, our results revealed asthmatic subjects with genotypes carrying at least one G allele (GG and GA genotypes) exhibited significantly higher HSPA1B serum levels than that of AA genotype. It has been shown previously that individuals carrying the GG genotype have higher amounts of HSPA1B mRNA, and serum protein levels, than individuals with the AA genotype. Similarly, Louis et al. reported that cells stimulated with lipopolysaccharide, from individuals with the rs1061581 A allele, expressed more HSPA1B than did the cells from individuals that were homozygous for the G allele.

HSPA1B rs1061581 polymorphism was suggested to have a significant functional effect, with the G allele being associated with higher constitutive and inducible levels of transcription for HSPA1B than the A allele [49]. The G allele of this polymorphism has been reported to be correlated with an increase in transcription activity and secretion levels of HSPA1B [25, 50]. The HSPA1B rs1061581 G allele leads to high binding affinity of nuclear factors to the HSP70 promoter and gives a high level of gene transcription. Several studies have shown that high serum HSPA1B level is linked to hyper responsiveness in asthma. In addition, HSPA1B was found in increased concentration in asthmatic airways, in lavage fluid from asthmatic lungs and induced sputum from subjects with severe pediatric asthma [22, 51-53].

In the patients with pediatric asthma, anthropometric and biochemical parameters were analyzed under the genotypes of rs1061581. We observed the levels of LDL cholesterol and insulin, and HOMA-IR content of GG + GA carriers were higher than that of the AA carriers. This finding is in contrast with a study conducted by Chang et al., who reported an association between the pediatric pediatric asthma patients and an insulin resistance state in relation with the GG + GA genotypes of the rs1061581 polymorphism. HSPA1B suppresses insulin induced tyrosine phosphorylation of insulin receptor and its substrates which may affect insulin sensitivity. LDL cholesterol is sometimes referred to as bad cholesterol because they can transport their content of fat molecules into artery walls, attract macrophages, and thus drive atherosclerosis. LDL cholesterol pose a risk for cardiovascular disease when they invade the endothelium and become oxidized, since the oxidized forms are more easily retained by the proteoglycans [54-56]. A complex set of biochemical reactions regulates the oxidation of LDL particles, chiefly stimulated by presence of necrotic cell debris and free radicals in the endothelium [57-59]. To our knowledge, this is the first time to identify that SNP rs1061581 in the HSPA1B conferred to IR and TBIL value in China pediatric asthmatic patients. All these results indicated that though the rs1061581 was not genetic susceptible factor for asthmatic patients, it associated with clinical features such as serum LDL cholesterol and insulin [60-63].

When the pediatric asthmatic patients were further subgrouped as asthma with MetS and asthma without MetS according to diagnosis of MetS criteria, significant association was observed between this polymorphism and asthmatic patients with MetS susceptibility. While asthmatic patients without MetS failed to show any such difference. Due to the limited sample size in this study, we suggested more MetS patients with pediatric asthma should be collected for further verification. To our knowledge, it is the first time to verify SNP rs1061581 polymorphism could impact on pediatric asthmatic patients with MetS in Chinese, and this result was partially consistent with high expression of HSPA1B mRNA and HSPA1B-stimulated genes in MetS patients [64-68].
Therefore, Carrier of HSPA1B 1267A/G locus, high level of LDL-C and decrement in lung function lead to insulin resistance. Thus, it results in an increased incidence of metabolic syndrome in asthmatic patients. So, people with asthma carrying rs1061581 G allele should be early intervention, such as reducing inflammation, weight control, improve insulin resistance, and improve lung function. These measurements can effectively reduce the metabolic syndrome and atherosclerosis occurs, thereby reducing asthma, heart and cerebrovascular disease incidence and mortality.

Conclusions

In summary, though no any relationship between genotypes and alleles in rs1061581 and asthma susceptibility was revealed, rs1061581 G allele increases insulin resistance and LDL cholesterol in pediatric asthmatic patients. Furthermore, we identified rs1061581 was the risk factor for pediatric asthmatic patients with MetS in Tianjin population.

Acknowledgements

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Disclosure of conflict of interest

None.

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