The importance of blood lipids in the association between BMI and blood pressure among Chinese overweight and obese children

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Abstract

We aimed to examine the contribution of blood lipids to the association between BMI and blood pressure (BP) in children with overweight and obesity. Data were collected in elementary and high schools of Chaoyang District, Beijing, China in 2012. Participants' weight, height, BP and fasting plasma lipid profile were measured by standard protocols. Mediation analysis was used to examine the mediation role of blood lipids on the relation between BMI and BP, with age included as a covariate. We found that in boys 826·0% (mediation effect = 0·016, P = 0·012) of the association between BMI and systolic BP was mediated through TAG. TAG mediated 125·3% (mediation effect = 0·032, P = 0·018) and LDL-cholesterol mediated 7·75% (mediation effect = 0·057, P = 0·046) of the association between BMI and diastolic BP was mediated by TAG and LDL-cholesterol, respectively. However, blood lipids did not show the mediation effect in girls. Our findings suggested that there was a sex difference in the contribution of blood lipids to the association between BMI and BP. Controlling TAG or LDL-cholesterol may be beneficial for reducing the risk of the BMI-related high BP in overweight boys; however, this outcome is not the case when controlling TAG or LDL-cholesterol in girls. This study may provide clues to explore the underlying mechanism of the association between obesity and hypertension.

Key words: Blood lipids; BMI; Blood pressure; Mediation analyses; Children

The strong association between blood pressure (BP) and BMI has been well documented in various populations including adults and children1–5. It was reported that an increase of 1 SD in BMI was associated with a 26·3–3·70 mmHg increment of systolic blood pressure (SBP) in children4. Nowadays, along with the increasing trend of obesity worldwide6, there is no surprise to see the rising prevalence of hypertension in adults and high BP in paediatric populations7,8. This situation is particularly marked in children of the biggest developing country, China. The prevalence of obesity of 7–18-year-old children increased thirty-eight times from 1985 to 20109. Mirroring the obesity epidemic, the BP level among Chinese children has also increased substantially in recent years10.

Previous studies have explored potential mechanisms linking adiposity and high BP, including sympathetic nervous system activation, activation of the renin-angiotensin system, inflammatory responses and insulin resistance11. However, few studies explored the influence of an unfavourable blood lipid profile. Obese adolescents with moderate and high SFA intake presented higher plasminogen activator inhibitor-1, an independent predictor of BP12, and reduction in SFA intake improves cardiovascular risks (mean BP and LDL-cholesterol decreased)13. Genetic studies have shown a clear association between dyslipidaemia and hypertension14, and the Physicians’ Health Study, a prospective study with a mean follow-up of 14·1 years, showed that men with the highest quintile of total cholesterol (TC), TC:HDL-cholesterol ratio and non-HDL-cholesterol had significantly increased risks of developing hypertension of 23, 54 and 39%, respectively, and men with the highest quintile of HDL-cholesterol had a 32% decreased risk of developing hypertension, which implies that dyslipidaemia may contribute to the subsequent development of hypertension15. Another prospective study in China aimed to investigate the risks of hypertension development in relation to the level of lipid variables among populations who had normal BP at baseline16. The study showed that dyslipidaemia might occur before hypertension, and hypertension was associated with HDL-cholesterol, TC:HDL-cholesterol and TAG16. Dyslipidaemia was reported as a cause of endothelial damage17,18, and the loss of physiological vasomotor activity that

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure; TC, total cholesterol.

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results from endothelial damage may manifest as increased BP\(^{[15]}\). Consequently, an unfavourable blood lipid profile may mediate the association between obesity and BP.

However, this mediating effect of blood lipids has not been reported yet. In this study, we hypothesised that the association between obesity and BP but also the mediating role of blood lipids in the association between BMI and BP. These results were presented by sex, when potential covariates were controlled.

**Methods**

**Participants**

Participants aged 7–18 years were recruited from ten primary schools (grade two to five), junior schools (grade seven and eight) and senior schools (grade eleven and twelve) in Chaoyang District, Beijing, China in 2012. On the basis of students’ medical history, children who reported a previous diagnosis of overt heart, renal, lung and liver diseases, asthma or physical/mental deformities were excluded\(^{[19]}\). As Asian populations and other populations, including blacks and Hispanics, may have different growth patterns and fat accumulations\(^{[20]}\), the BMI references for screening Chinese children with overweight and obesity were used in children in this study (online Supplementary Table S1)\(^{[21]}\).

In this study, 796 children (486 boys and 310 girls) identified as overweight or obese were recruited. We excluded fourteen participants with missing data on blood lipids (\(n = 8\)) and BP (\(n = 1\)), and five participants aged >18 years or <7 years. A total of 782 children aged 7–18 years with completed data were included in the final analysis.

The study was approved by the medical ethics committee of Peking University Health Science Center. Written informed consent was obtained from all children and their parents.

**Measurements**

Anthropometric measurements, including height, weight and BP, were taken according to standard protocols\(^{[19]}\). Weight was measured to the nearest 0.1 kg using a lever scale. Height was measured to the nearest 0.1 cm using a stadiometer. BMI was calculated as weight (kg) divided by height (m) squared (kg/m\(^2\)). BP was measured according to the recommendation of the National High Blood Pressure Education Program Working Group in Children and Adolescents\(^{[22]}\) using standard clinical sphygmomanometer. BP measurements were taken 5 min after resting. The first and fifth Korotkoff sounds were used for SBP and DBP measurements. If the measured difference was >10 mmHg, measurement was repeated until the final two measures differed ≤10 mmHg, and the mean of the final two measures was used in analyses.

Venous blood samples were collected after 12 h of fasting. Metabolic indicators such as TAG, TC, LDL-cholesterol and HDL-cholesterol were measured using the Automatic biochemical analyzer (Roche Modular P800 ISE900; Hoffmann-La Roche Ltd).

**Statistical analyses**

Data were analysed with SPSS 17.0. General characteristics were described as mean values and standard deviations. Differences of general characteristics between groups were analysed by \(t\) test. Mediation analyses were conducted to analyse the mediation effect of blood lipids on the association between BMI and BP, according to the mediation theory developed by Baron & Kenny\(^{[23]}\). The mediation analysis procedure is illustrated in Fig. 1. First, we used linear regression to analyse associations (total association, \(c\)) between independent variable and dependent variable. The associations (\(a\)) between independent variable and potential mediators were also assessed. Then, associations between potential mediators and dependent variables were examined (\(b\)) and controlled for independent variables (direct association, \(a \times b\)). Finally, if \(c\), \(a\), and \(b\) were all statistically significant, we included the term of multiplying \(a\) and \(b\) (indirect association, \(a \times b\)) as the mediation effect of potential mediator, and use Sobel test to examine its mediating effect on the association between independent variable and dependent variable\(^{[24]}\). SPSS procedures provided by Andrew Hayes were performed for the mediation analyses\(^{[25]}\).

**Results**

Table 1 showed the general characteristics of these children, and the mean age was 11–58 years. The concentrations of DBP (71–43 mmHg, SD 10–81), TC (3–82 mmol/l, SD 0–74), TAG (0–87 mmol/l, SD 0–43), HDL-cholesterol (1–26 mmol/l, SD 0–33) and LDL-cholesterol (1–94 mmol/l, SD 0–58) were similar in boys and girls. However, boys had significantly higher BMI and SBP compared with girls (\(P = 0.025\) and 0.012, respectively).

![Fig. 1. Model of mediation analysis. First, we used linear regression to analyse associations (total association, \(c\) coefficient) between independent variable \(X\) (e.g. BMI) and dependent variable \(Y\) (e.g. SBP, DBP). We thereafter used linear regression to analyse associations (\(a\) coefficient) between independent variable \(X\) (e.g. BMI) and potential mediators \(M\) (e.g. TC, TAG, HDL-cholesterol and LDL-cholesterol). Then, associations between potential mediators \(M\) (e.g. TC, TAG, HDL-cholesterol and LDL-cholesterol) and dependent variable \(Y\) (e.g. SBP, DBP) were examined (\(b\) coefficient) and controlled for the independent variable \(X\) (direct association, \(c\) coefficient). Finally, if \(c\), \(a\), and \(b\) coefficients were all statistically significant, then the mediation effect of potential mediator \(M\) on the association between independent variable \(X\) and dependent variable \(Y\) was examined by multiplying \(a\) and \(b\) (indirect association, \(a \times b\) coefficient).](https://www.cambridge.org/core/doi/10.1017/S0007114516001744)
Boys and girls, respectively (95% CI 0.59, 1.62; P < 0.001). Similarly, DBP was associated with BMI in both boys and girls, adjusted for age (Table 3). The corresponding total associations (a) for DBP were 0.74 (95% CI 0.49, 0.96; P < 0.001) and 0.88 for boys and girls, respectively (95% CI 0.59, 1.16; P < 0.001).

**Associations between BMI and potential mediators (a)**

Associations between blood lipids and BMI were illustrated in Table 2. In boys, higher BMI was significantly associated with the increased levels of TC, TAG, and LDL-cholesterol (P < 0.005), whereas higher HDL-cholesterol was correlated with lower BMI (P < 0.001). However, in girls, only TAG and HDL-cholesterol were significantly positively associated with BMI (P < 0.0001).

**Mediation role of potential mediators (indirect association, a × b)**

On the basis of the mediation theory of Baron & Kenny (23), a subsequent mediation analysis was conducted to investigate the
mediation effect (indirect association, $axb$) of blood lipid indexes, such as TC, TAG and LDL-cholesterol, on the association between BMI and BP in boys (Table 4). The direct association between BMI and BP (c) was also presented. A weak, but significant, mediation effect of TAG on the relationship between BMI and SBP was detected (axb), with the mediation effect of 0.016 (95\% CI 0.004, 0.021, $P=0.002$) and the ratio of mediation effect in total association of 8.03\%. In addition, a slight mediation effect of TAG was also identified for the association between BMI and DBP (mediation effect 0.022, 95\% CI 0.009, 0.036, $P=0.002$), with the ratio of mediation effect in total association of 8.03\%.

In the association between BMI and DBP, about 7.75\% was mediated by LDL-cholesterol, with a mediation effect of 0.07 (95\% CI 0.002, 0.144, $P=0.002$).

In girls, as TC, TAG, HDL-cholesterol and LDL-cholesterol were no longer significantly associated with BP after BMI and age were adjusted, no significant mediation effect was detected (online Supplementary Table S2).

### Direct association of BMI on blood pressure (direct association, c)

As shown in Table 4, after potential mediator and age were adjusted for, the direct association between BMI and SBP was weak, but still significant. When TAG and age were adjusted for, the association between BMI and SBP changed from 1.277 to 1.171 ($P<0.001$) in boys, excluding the mediation effect of TAG; the direct association between BMI and SBP was as large as 91.7\% of the total association. The corresponding direct association between BMI and DBP was 0.647 ($P<0.001$), which explained 87.5\% of the total association. When the mediation effect of LDL-cholesterol and age was adjusted, the association between BMI and BP was mainly explained by the direct association (92.3\% of the total association).

### Discussion

Our study confirmed that high BMI was associated with elevated BP. When adjusting for BMI, TC, TAG and LDL-cholesterol were associated with SBP in boys, whereas no significant association was detected in girls. Similar results were also found for DBP. Furthermore, in boys with overweight and obesity, TAG partially mediated the relationship between BMI and BP, whereas TAG and LDL-cholesterol partially mediated the relationship between BMI and DBP. No mediation effect was identified in girls.

Our data suggested a strong crude linear association between BMI and BP measures, and an increase of one unit BMI was directly related to about 1-2 mmHg increment in SBP and a 0.7–0.9 mmHg increment in DBP. Ma et al.\(^\text{(2)}\) reported that SBP increased 3.70 and 2.63 mmHg in Chinese boys and girls, with a 1.60 increase in BMI (approximately 2–3 kg/m\(^2\) in 7–18-year-old girls and boys). Correa-Costa et al.\(^\text{(27)}\) showed that SBP increased with BMI by 3.2 and 2.6 mmHg/sq of BMI Z-score, in 4-year-old girls and boys, respectively. Consistent with these studies, our study confirmed the significant association between BMI and BP in children. Moreover, we further showed that the association between BMI and BP remains significant even after excluding the indirect association of lipid profile.

Several studies have demonstrated the link between BP and serum lipids in adults, but few studies were conducted in children. Our data suggested that there was a sexual difference in the association between blood lipids and BP. Previous studies showed that TAG was associated with BP/hypertension.\(^\text{28,29}\) Our study revealed that in boys, but not in girls, the significant associations of TC, TAG and LDL-cholesterol on SBP/DBP were detected after adjusting for BMI and age. This sexual dimorphism in the association between lipids and BP might be related to the different impacts...
Mediation effect of blood lipids on the association between BMI and blood pressure in boys

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>Outcome variables</th>
<th>Mediator (mmol/l)</th>
<th>Direct association (c')</th>
<th>Indirect association (ab)</th>
<th>% Mediation</th>
<th>% Direct association</th>
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<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>SBP (mmHg)</td>
<td>TC</td>
<td>1.244</td>
<td>0.013</td>
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<td></td>
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<td>TAG</td>
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<td>LDL-cholesterol</td>
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<td>0.016</td>
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<tr>
<td></td>
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<td>TAG</td>
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<td>0.012</td>
<td>&lt;0.0001</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>DBP (mmHg)</td>
<td>0.647</td>
<td>0.013</td>
<td>&lt;0.0001</td>
<td>0.003</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; c', direct association between the independent variable and the outcome variable was determined; ab, indirect association between the independent variable and the outcome variable through the proposed mediator; % mediation, percentage mediation of the potential mediator (a×b/c).

Mediators from BMI to blood pressure

It is revealed that blood lipids may mediate the relationship of BMI and BP, among children with overweight and obesity. In addition, the mediation of blood lipids may provide a more objective direct association between BMI and BP. However, because the BP records were based on two measurements in a single occasion, BP levels from multiple visits would be more desirable in future studies. In addition, abnormal blood lipids, high BP and high blood glucose or insulin resistance were all components of the metabolic syndrome. Insulin resistance was reported as a mechanism of obesity, high BP and high blood glucose or insulin resistance were also functions in the lipolysis of TAG-rich particles (30). Sex steroids could regulate the activities of hepatic lipase, which has an important role in the removal of hepatic triglycerides (17,18,34). The study of sex steroids on the regulation of serum lipoproteins has demonstrated that sex steroids could regulate the activities of hepatic lipase, which has an important role in the removal of hepatic triglycerides. These changes of blood vessels may result in the endothelial damage and loss of physiological function, which would lead to endothelial dysfunction. In addition, a dysfunctional endothelium cannot normally respond to the changes in intravascular conditions to contract and dilate, and the damage of physiological vasomotor activity may result in elevated BP levels.

For the mediation effects of blood lipids, we revealed that TAG mediated 49% of the relation between BMI and DBP in boys, whereas LDL-cholesterol mediated 6% and 12% of the relation between BMI and SBP, respectively (27). In terms of the association between BMI and BP, the mechanism between obesity and high BP was partly mediated by insulin resistance, which mediated 12% and 6% of the association between BMI and DBP in boys. A previous study had suggested that the association between BMI and DBP in boys, and 12.5% of the relation between BMI and DBP in boys. A previous study had suggested that the association between BMI and DBP in boys, and also functions in the lipolysis of TAG-rich particles (30). Sex steroids were also suggested to be important factors in the removal of hepatic triglycerides, which has an important role in the removal of hepatic triglycerides. These changes of blood vessels may result in the endothelial damage and loss of physiological function, which would lead to endothelial dysfunction. In addition, a dysfunctional endothelium cannot normally respond to the changes in intravascular conditions to contract and dilate, and the damage of physiological vasomotor activity may result in elevated BP levels.

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obesity-related hypertension; we cannot confirm the mediation role of insulin resistance on the association between adiposity and BP because of the lack of data on insulin resistance, which is a limitation. Furthermore, because only overweight and obese participants were included in the study, it is a limitation that we are not sure of the external generalisability of this study. Future study involving normal weight should be warranted to confirm the results.

Conclusions

In conclusion, our results first highlighted the sexual difference in the mediation role of blood lipids in the association between BMI and BP. In addition to the direct association between elevated BP and BMI, a mediation role of TAG and LDL-cholesterol was detected in the association between BMI and BP. Our findings suggest that both lipid profile and BMI should be considered when the intervention aimed to reduce the burden of hypertension is conducted in children.

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Y. D. Y., J. M. and Z. Y. Z. conceived and designed the study. S. W., X. H. L. and B. D. carried out the study. Y. D. Y. and Z. Y. Z. analysed data and drafted the manuscript. All authors were involved in reviewing the article and had final approval of the submitted and published versions.

The authors declare that there are no conflicts of interest.

Supplementary material

For supplementary material/s referred to in this article, please visit http://dx.doi.org/10.1017/S0007114516001744

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