The Determinants for Adolescent Glycolipid Metabolism Disorder from Prenatal Period through Adolescence: a Cohort Study

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Abstract

To explore the prevalence of and risk factors for glycolipid metabolism disorder (GLMD) from the prenatal period through childhood and adolescence. A bidirectional cohort study which was established in 2014 and followed between March 1 and July 20, 2019 were designed to evaluate the risk factors for GLMD. Two stage stratified cluster sampling was used to include participants from four communities in two counties in Chongqing. 2808 healthy children aged between 6 and 9 years in 2014 entered the cohort in 2014, and followed in 2019 with a follow-up rate of 70%. 2,136 samples (aged 11·68 ± 0·60 years) were included. The prevalence of insulin resistance (IR), prediabetes/diabetes and dyslipidemia was 21·02%, 7·19% and 21·61%, respectively. Subjects with an urban residence, no pubertal development, dyslipidemia in 2014, higher family income, higher parental education, low quality of life (QoL), and unstable neurotic and psychotic personalities had significantly elevated fasting insulin (FI) or homeostasis model assessment insulin resistance (HOMA-IR) levels; subjects with female sex, no pubertal development, dyslipidemia in 2014, obesity, gestational hypertension, maternal weight gain above Institute of Medicine guidelines, single parents, low QoL, introverted and unstable personality had increased triglyceride or triglyceride/high-density lipoprotein (HDL). Adolescent with rural residence and living convenience had higher HbA1c level. We observed that low QoL status, unstable and psychotic personality traits were associated with increased GLMD risk independent of obesity, suggesting that the community intervention to improve the QoL and psychological health of children is essential.

Introduction

The increased prevalence of glycolipid metabolism disorders (GLMD) in childhood and adolescents has a well-established association with adult type 2 diabetes and cardiovascular diseases (CVDs) [1]. GLMD in adolescents includes insulin resistance (IR), dyslipidemia and hyperglycemia. The prevalence of IR and dyslipidemia in children and adolescents ranged from 25·3% to 44·3% among children and adolescents according different region and different diagnosed criteria [2,3]. Dyslipidemia in childhood tracks into adulthood and predicts the severity of atherosclerosis in adults [1]. The triglyceride/high-density lipoprotein cholesterol (HDL-C) ratio was used as an IR marker for overweight and obese children [4] and was also an index of GLMD. The prevalence of hyperglycemia ranged from 5·7% to 11·13% among children with obesity [5]. Despite having a lower prevalence than IR and dyslipidemia, hyperglycemia during childhood is a predictor of type 2 diabetes in adulthood [6]. Because childhood metabolic disorders can predict CVDs in adulthood [4,6], determinants of GLMD need to be evaluated during this period. Therefore, it is important to increase our understanding of the prevalence and risk factors for GLMD during the perinatal, younger childhood and adolescence periods.

Obesity is the main cause of GLMD, and our previous study revealed that obesity is positively associated with low-density lipoprotein cholesterol (LDL-C) and TGs, but negatively correlated with HDL-C [7]. Moreover, previous studies have shown an increased prevalence of GLMD in individuals with a sedentary lifestyle, unhealthy dietary habits, genetic factors, exposure to higher maternal fasting blood glucose (FBG) levels in utero [8] and gestational diabetes [9]. A study found that extraverted personality is positively correlated with triglycerides, FBG and metabolic syndrome (MS) score in adults [10]. However, to our knowledge, there are no studies exploring the correlation between quality of life (QoL) and GLMD or between personality traits and GLMD in children aged 10~14 years in a rural-urban cohort study. This cohort study included measures of perinatal variables, social economic status (SES), anthropometric variables and biochemical indexes in 2014 and 2019 along with QoL scores and personality characteristics in adolescents, providing an excellent opportunity to fully examine the risk factors for GLMD. Moreover, it is not clear to what extent these variables account for the variance in GLMD in the transition period from childhood to adolescence.

Methods

Patient and Public Involvement

The children and their guardians or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Subjects

Two stage stratified cluster sampling was used to include participants from two counties in Chongqing that represent urban and rural areas; then, two regions per county were randomly selected, and finally, all children living in the selected region were informed and included if they satisfied the inclusion criteria. In addition, a birth-cohort in which retrospective and prospective variables were analysed to evaluate the development of glycolipid metabolism risk factors from the perinatal period through adolescence, and the perinatal variables were retrospectively collected, with physical examination conducted prospectively in 2014 and in 2019. Participants who met all the following criteria were recruited: (1) aged between six and nine years in 2014, (2) resided in the target region for more than six months, (3) did not have serious diseases (e.g., nephropathy, cardiovascular disease or cancer), and (4) obtained consent from the parents and children for participation. At baseline, all participants completed SES and family health history questionnaires and were recruited mainly from grade one and grade two from primary public-schools screening of children whose families were interested in health research. The questionnaires were administered and collected by the teachers, and the physical measures results were disseminated also by the teachers. Two thousand one hundred and thirty-six subjects (with a follow-up rate of 70%) were ultimately included (Fig. 1) and the difference between children with follow-up and withdraw was compared in Supplementary Table S1. All work in this study was conducted in accordance with the ethical guidelines of 1964 Declaration of Helsinki and its later amendments[11]. The Institutional Review Board at the Children's Hospital of Chongqing Medical University gave its approval for the study (File No.: 2019-86). Informed consent was provided by all subjects and parents/guardians.

Demographic variables

Demographic information, SES (parents' occupation and education level, family income and single-parent status) were collected. Parental education level was measured on a four-point scale (≤9 years (compulsory education in China), 9~12, 12~15 and >15 years), and we combined bachelor and master's degrees as there were few parents with master's degrees. Prenatal variables included maternal preconception obesity, increased body mass index of mother during pregnancy, birth with cesarean section, premature delivery (<37 weeks), birth-weight, breastfeeding, gestational hypertension (GH) and gestational diabetes. Family history of obesity and CVD was investigated. The degree of pubertal development was surveyed both by the visit of paediatrician and children or parents filling the questionnaires, which included the date of the first menstruation and first nocturnal emission, then the age was calculated.

The validity and reliability of the questionnaire were checked, and were described in detail in a previous publication [12]. The questionnaire was completed by the parents or guardians of the children after standard training by the research group.

Physical examination

Anthropometric measurements were conducted by well-trained pediatric nurses, and the protocol for these measurements was described in a previous publication [12]. Waist circumference or waist-height ratio (WHtR=waist circumference/height) was used as an alternative measure of central adiposity. Hip circumference was measured twice horizontally at the level of the pubic symphysis in the front and the gluteus maximus in the back, with the participant standing upright and with their legs together and placing their arms naturally at their sides; the mean value was used.

Blood pressure (BP) and heart rate were measured on three separate occasions with an OMRON arm-type electronic sphygmomanometer (HEM7051) using an appropriately sized BP cuff placed on the subject's right arm, with the subject in a seated position, which was described in a previous publication [12].

Biochemical indexes

Venous blood (three ml) was drawn from each subject in the morning after at least 12 hours of fasting and 24 hours of abstaining from high-fat and spicy foods. The biochemical markers and glycosylated hemoglobin were measured within two hours after venous blood was drawn and the protocol was introduced in detail in our previous publication [12]. Moreover, the ratio of TG/HDL-C was used as a parameter to assess lipid metabolism [4]. Siemens Centaur XP was used to measure fasting insulin (FI), and HbA1c was measured by an automatic hemoglobin analyzer (ARKRAY, Japan).

Measurement of QoL and Eysenck's Personality Questionnaire (EPQ)

The QoL questionnaire for adolescents consists of 49 items, including four factors (psychosocial function, physical and mental health, living environment and QoL satisfaction) and 13 dimensions, such as self-satisfaction, relationship of teacher and pupil, physical feeling, companionship, parenthood, physical activity ability, learning ability and attitude, self-esteem, negative emotion, attitude towards doing homework, opportunity for activity, living convenience and others (picky-eating and surroundings). The order of presentation of the 49 items was randomized. Children rated the statements on a four-point scale, and the direction of response (positive or negative) varied item by item to limit response bias. Individual item values were recoded prior to analysis so that the direction was consistent. Responses were summed and normalized according to the age-, sex- and region-specific norms of Chinese into a score ranging from 0 to 100, normalized with a mean of 50 and SD of 10, with higher scores suggesting a better QoL [40].

The Chinese version of Eysenck's personality questionnaire of China [41] consisted of 88 items scored on a two-point scale (for positive items NO=0 and YES=1), including four domains: extraversion (E) (25 items), neuroticism (N) (23 items), psychoticism (P) (18 items), and lie scales (L) (22 items). High scorers on the E scale indicate sociable, exciting, pleasurable, carefree, and aggressive characteristics. A higher score on the N scale is more likely to be a worried and moody person who tends to suffer from emotional and psychosomatic disorders. The P scale was designed to measure behaviour patterns that might be considered schizoid or psychopathic in extreme cases. The L scale assesses response bias. Items in the E, N, P and L domains are summed and normalized to the age- and sex-specific norm of China into a score ranging from 0 to 100, normalized with a mean of 50 and SD of 10. People are defined as middle type, tendency type and typical type if the T score (E and N) ranges from 43·3~56·7, 38·5~43·3 or 56·7~61·5, <38·5 or >61·5. People were considered psychotic personality if T score of the P domain >56·7, and response bias was indicated when the T score of the L domain was >70.

Diagnostic criteria

Children were considered to have prediabetes/diabetes if they met at least one of the following criteria: FBG ≥5·6 mmol/L or HbA1c level ≥5·7% [13], and high lipids were defined if adolescents met one of the following criteria [14]: total cholesterol (TC)≥200 mg/dL; TG≥130 mg/dL; LDL-C ≥130 mg/dL; or HDL-C≤40 mg/dL. Moreover, IR was indicated by HOMA-IR>3·0 based on the criteria from China [2]; HOMA-IR was calculated as (FI mU/L) × (FBG mmol/L) /22·5. Overweight was indicated by a body mass index [15] at or above the 85th percentile and below the 95th percentile, and obesity was defined as a BMI at or above the 95th percentile according to the sex-specific Centers for Disease Control BMI-for-age growth charts [15]. The definitions of size for gestational age used the global reference for fetal-weight and birthweight percentiles [16]: birth weight at or above the 90th percentile indicated large for gestational age (LGA), and birth weight less than the 10th percentile indicated small for gestational age (SGA), using the parameters of mean birthweight at 40·5 weeks of 3,332·93 g and a variation coefficient of 14·36%. Maternal overweight and obesity was indicated by a BMI of 24~27·9 kg/m^2 and a BMI ≥ 28 kg/m^2, respectively; BMI < 18·5 kg/m^2 was defined as a low BMI [17]. According to guidelines of the Institute of Medicine (IOM) for maternal pregnancy weight gain [18], the recommendation is for underweight, normal weight, overweight, and obese women to gain 12·5~18·0 kg, 11·5~16·0Kg, 7·0~11·5 kg, and 5·0~9·0 kg, respectively; if weight gain exceeded that range, weight gain was defined as "above IOM guidelines", and if weight gain was below that range, was defined as "below the IOM guidelines".

Statistical analyses

Differences in glycolipid metabolism indexes between two groups were assessed using Student's t-test, ANOVA was used to compare more than two groups, and post-hoc comparison was perfoemed using Student-Newman-Keuls test. Continuous variables (insulin, HOMA-IR, TG and TG/HDL) that did not satisfy a normal distribution were subjected to natural logarithmic transformation before analyses. The χ^2 test was used to test the difference in prevalence rates of GLMD. A generalized linear model (GLM) was used to analyze the risk factors that may impact glycolipid metabolism. To reduce the collinearity of variables, model 1 mainly included the variables measured prenatally and in 2014, and model 2 mainly included the variables measured in 2019. Finally, model 3 included all the variables that may impact GLMD. Moreover, multivariable logistic regression was performed using diagnosed GLMD as the dependent variables with the impact factors from perinatal to adolescent, as independent variables. Adjusted R^2 was calculated to locate the variance of dependent variables can be explained by independent variables. Participants with the missing responding variables were not included in the analyses. And the participants finish the follow were compared with the dropouts.

The data analysis was conducted using SAS 9.4 software (Copyright © 2020 SAS Institute Inc. Cary, NC, USA). A significant difference was defined by an α level of 0.05.

Results

General characteristics

The general characteristics of the subjects are presented in Table 1. A total of 2,136 samples were included, with a follow up rate of 70·0%. And the difference of characteristics of childhood between participants with follow-up and withdraw were described in Supplementary Table S1. The mean age was 11·68 ±0·60 years, and 52·25% (1,116/2,136) were males. Biochemical indexes; anthropometric, perinatal, and SES variables; QoL; and personality characteristics are shown in Table 1.

Table 1. General Characteristics of Glycolipid Metabolism Study in Adolescents.

Variables	Participants included in 2019
Sample size	2136
Region	
Urban, No. (%)	1594(74·63%)
Rural, No. (%)	542(25·37%)
Anthropometric measures	
Male sex, No. (%)	1116(52·25%)
Age, mean, y	11·68(0·60)
BMI, mean, kg/m^2	19·10(3·77)
Height, mean, cm	151·78(7·99)
Weight, mean, kg	44·39(11·05)
Waist circumference, mean, cm	66·02(10·14)
WHtR, mean	0·43(0·06)
Hip circumference, mean, cm	81·80(8·30)
SBP, mean, mmHg	105·71(9·56)
DBP, mean, mmHg	62·81(6·76)
Puberty, No. (%)	586(31·32%)
Serum biochemical indexes	
FBG, mean, mmol/L	4·45(0·43)
TC, mean, mmol/L	3·52(0·61)
tg, mean, mmol/L	1·06(0·50)
TG, mean†	-0·03(0·39)
hdl-C, mean, mmol/L	1·44(0·31)
ldl-C, mean, mmol/L	1·84(0·44)
TG/ HDL-C, mean	0·80(0·50)
Insulin, mean, pmol/L	83·54(74·85)
Insulin, mean†	4·15(0·73)
HbA1c, mean, %	5·37(0·19)
Insulin resistance index (IR), mean	2·40(2·38)
IR, mean†	0·57(0·74)
Uric acid, mean, μmol/L	319·64(76·98)
Perinatal measures	
Maternal prepregnancy obesity, No. (%)	
Low weight	352(21·13%)
Normal weight	1158(69·51%)
Overweight/Obesity	156(9·36%)
Increased BMI during pregnancy, mean, kg/m^2	5·40(2·62)
Maternal weight gain, No. (%)	
Weight gain below IOM guidelines	519(31·36%)
Within IOM guidelines	637(38·49%)
Weight gain above IOM guidelines	499(30·15%)
Gestational age of mother, mean, y	27·26(4·98)
Gestational age of father, mean, y	30·23(5·31)
Gestational weeks of child, mean, weeks	38·86(2·16)
Birth weight, mean, g	3271·09(493·62)
Fatal weight of pregnancy week, No. (%)*	
SGA	133(7·68%)
Appropriate for gestational age	1180(68·13%)
LGA	419(24·19)
Gestational hypertension, No. (%)*	
No	1967(97·18%)
Yes	57(2·82%)
Gestational diabetes, No. (%)*	
No	2001(98·52%)
Yes	30(1·48%)
Smoke during pregnancy, No. (%)*	
No	1642(87·67%)
Yes	231(12·33%)
Birth with Caesarean operation, No. (%)*	
No	700(36·76%)
Yes	1204(63·24%)

Socioeconomic measures	
Income, Yuan/year, No. (%)*	
~50,000	645(31·96%)
~150,000	853(42·27%)
>150,000	520(25·77%)
Expenditure of Food, median(IQR), Yuan/ month/person	665·6(499·2,998·4)
Marriage status, No. (%)*	
Double parents	1763(91·82%)
Single parents	157(8·18%)
Mother's education, y, No. (%)*	
~9	694(33·27%)
~12	726(34·80%)
≥15	666(31·93%)
Father's education, y, No. (%)	
~9	587(28·15%)
~12	750(35·97%)
≥15	748(35·88%)
Mother's occupation, No. (%)*	
Manager	112(5·39%)
Worker	708(34·07%)
Technician/Researcher	65(3·13%)
Farmer	567(27·29%)
Other	626(30·13%)
Father's occupation, No. (%)*	
Manager	175(8·49%)
Worker	706(34·24%)
Technician/Researcher	177(8·58%)
Farmer	573(27·79%)
Other	431(20·90%)
13 domains of QoL, mean	
Self-satisfaction	50·05(11·34)
Relationship of teacher and pupil	53·52(10·08)
Physical feeling	49·90(10·73)
Companionship	53·70(10·52)
Parenthood	51·35(11·34)
Physical activity ability	50·11(10·67)
Learning ability and attitude	51·73(10·20)
Self-esteem	50·38(11·08)
Negative emotion	47·65(11·24)
Attitude towards doing homework	51·41(9·07)
Activity opportunity	54·63(9·58)
Living convenience	54·43(7·78)
Other	50·68(10·16)
Four factors of QoL, mean	
Psychosocial factor	64·79(10·31)
Physical and mental health factor	35·84(5·97)
Living environment factor	24·02(4·27)
Quality of life satisfaction factor	24·90(4·38)
Total score of QoL, mean	52·60(12·33)
Personality Characteristics, mean	
Extraversion (E)	50·32(13·03)
Neuroticism (N)	50·37(14·67)
Psychoticism (P)	39·90(9·03)
Lie bias (L)	54·12(9·45)

BMI, body mass index; WHtR, waist-height-ratio; SBP, systemic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; IOM, 2009 Institute of Medicine; SGA, small for gestational age; LGA, large for gestational age; QoL, quality of life.

† natural logarithmic transformation.

* the total sample size is unequal to 2136 in 2019 as there are missing data.

Glycolipid metabolism of children with different characteristics

Table 2 displays the glycolipid metabolism results in adolescents. Adolescents with the characteristics of urban residence, female sex, older age, no pubertal development, dyslipidemia, obesity, low QoL score and instable personality traits had higher FI or HOMA-IR, TGs or TG/HDL than their counterparts. Whereas, HbA1c was higher in rural children and those with pubertal development, obesity, or maternal prepregnancy obesity than in their counterparts. In addition, TGs and/or TG/HDL were elevated in children with mother who experienced weight gain above IOM guidelines (P<0·05), single-parents (P<0·05), maternal hypertension (GH) and introversive personality compared with their counterparts (P<0·05 and P=0·06). The levels of FI and HOMA-IR were higher in children with parents with higher education levels and family incomes than in their counterparts (P<0·01). Moreover, adolescents with psychotic personality had elevated FI and IR compared with the levels in their counterparts (all P<0·01).

Table 2. The Glycolipid Metabolism Levels and Prevalence of Adolescent According to Perinatal and Childhood Experiences.

Variables	Glycolipid indexes levels (median (IQR) or mean)					Prevalence of GLMD					
	Insulin, median(IQR)[#]	HOMA-IR, median(IQR)[#]	TG, median(IQR)[#]	TG/HDL, median(IQR)	HbA1c, mean%[¶]	HOMA-IR (>3)		Dyslipidaemia		Prediabete	
						Prevalence	*P*	Prevalence	*P*	Prevalence	
Sample size	2097	1979	2018	2018	932	416(21·02%)		436(21·61%)		67(7·19%)	
Region											
Urban	60·30(41·30,99·40)[**]	1·70(1·16,2·79)[**]	0·96(0·77,1·24)[**]	0·67(0·49,0·96)	5·34±0·19[**]	336(22·86%)	<0·01	309(20·7%)	0·09	28(6·91%)	0
Rural	55·65(35·90,86·50)	1·56(0·95,2·34)	0·90(0·68,1·22)	0·66(0·46,0·96)	5·40±0·18	80(15·72%)		127(24·19%)		39(7·40%)	
Anthropometric measures											
Sex											
Male	57·10(38·20,93·85)[**]	1·59(1·05,2·62)[*]	0·91(0·70,1·21)[**]	0·65(0·46,0·95)[**]	5·37±0·19	205(19·86%)	0·19	223(21·2%)	0·64	41(8·17%)	0
Female	62·00(42·30,97·60)	1·71(1·16,2·75)	0·98(0·79,1·26)	0·69(0·51,0·97)	5·37±0·18	211(22·28%)		213(22·05%)		26(6·05%)	
Age, y											
~10	53·50(35·30,80·00)[†**]	1·53(1·01,2·30)[†**]	0·91(0·75,1·17)	0·64(0·48,0·85)[†*]	5·39±0·20	44(15·17%)	<0·01	49(16·55%)	0·03	7(6·67%)	0
~11	57·70(39·90,91·70)[‡]	1·59(1·09,2·59)[‡]	0·94(0·74,1·25)	0·67(0·48,0·97)[†‡]	5·36±0·19	205(19·51%)		252(23·53%)		39(7·80%)	
≥12	67·50(43·10,112·40)[§]	1·87(1·19,3·13)[§]	0·97(0·76,1·26)	0·69(0·49,0·98)[‡]	5·38±0·18	167(26·18%)		135(20·74%)		21(6·42%)	
Pubertal development											
No	60·70(41·00,99·40)	1·71(1·14,2·83)[**]	0·96(0·76,1·26)[**]	0·68(0·49,0·98)[*]	5·36±0·20[*]	276(23·08%)	<0·01	262(21·56%)	0·96	34(7·80%)	0
Yes	59·50(39·30,89·40)	1·62(1·05,2·55)	0·89(0·69,1·17)	0·65(0·45,0·92)	5·39±0·18	96(17·55%)		120(21·47%)		29(7·09%)	
Dyslipidemia, in 2014											
No	55·4(37·4,89·9)[**]	1·59(1·03,2·58)[*]	0·91(0·73,1·16)[**]	0·62(0·46,0·82)[**]	5·37±0·20	138(18·42%)	0·06	114(15·64%)	<0·01	28(8·75%)	0
Yes	59·2(41·5,108·1)	1·64(1·15,2·99)	1·02(0·8,1·35)	0·78(0·56,1·16)	5·34±0·21	61(23·74%)		96(32·65%)		5(4·31%)	
Obesity, in 2014											
Normal	54·60(36·90,87·00)[†**]	1·52(1·00,2·43)[†**]	0·92(0·73,1·21)[†**]	0·64(0·46,0·90)[†**]	5·37±0·18	200(17·33%)	<0·01	242(20·46%)	<0·01	34(6·19%)	0
Overweight	77·30(51·20,124·70)[‡]	2·10(1·42,3·27)[‡]	1·02(0·84,1·26)[‡]	0·72(0·59,1·03)[‡]	5·37±0·17	56(29·63%)		44(22·92%)		6(6·19%)	
Obesity	89·35(52·80,141·90)[‡]	2·55(1·44,3·91)[‡]	1·05(0·80,1·42)[‡]	0·79(0·54,1·13)[‡]	5·41±0·20	73(38·42%)		60(31·41%)		16(11·85%)	
Obesity, in 2019											
Normal	53·70(37·20,82·80)[†**]	1·49(1·02,2·33)[†**]	0·90(0·72,1·17)[†**]	0·63(0·46,0·87)[†**]	5·36±0·18[†**]	245(16·21%)	<0·01	281(18·33%)	<0·01	41(6·35%)	0
Overweight	79·80(54·50,124·65)[‡]	2·22(1·51,3·39)[‡]	1·10(0·83,1·39)[‡]	0·86(0·61,1·15)[‡]	5·39±0·17[†‡]	89(32·36%)		86(30·71%)		6(5·94%)	
Obesity	96·80(63·65,150·40)[§]	2·74(1·78,4·17)[§]	1·14(0·91,1·48)[‡]	0·90(0·66,1·24)[‡]	5·42±0·20[‡]	81(44·75%)		64(34·78%)		18(10·47%)	
Abdominal obesity, in 2014											
Normal	55·90(37·80,90·20)[**]	1·58(1·03,2·56)[**]	0·92(0·73,1·20)[**]	0·65(0·47,0·90)[**]	5·37±0·18	243(19·57%)	<0·01	265(20·88%)	0·05	39(6·20%)	0
Abdominal obesity	87·50(52·40,140·50)	2·36(1·36,3·85)	1·03(0·81,1·39)	0·79(0·55,1·09)	5·40±0·19	64(32·99%)		53(26·9%)		15(11·90%)	
Abdominal obesity, in 2019											
Normal	55·60(38·20,86·60)[**]	1·55(1·05,2·47)[**]	0·91(0·73,1·18)[**]	0·64(0·47,0·89)[**]	5·36±0·18[**]	287(17·28%)	<0·01	321(19·04%)	<0·01	45(6·27%)	0
Abdominal obesity	90·40(58·00,144·70)	2·55(1·61,4·05)	1·17(0·91,1·50)	0·92(0·66,1·27)	5·40±0·20	127(41·91%)		108(35·06%)		20(9·95%)	
Perinatal measures											
Maternal prepregnancy obesity											
Low weight	62·20(41·70,98·90)	1·71(1·16,2·78)	0·95(0·75,1·21)	0·66(0·49,0·94)	5·36±0·20[†‡*]	241(22·25%)	0·12	221(20·16%)	0·06	36(7·33%)	0
Normal weight	56·00(39·00,92·50)	1·58(1·10,2·60)	0·96(0·75,1·29)	0·70(0·48,0·99)	5·34±0·17[†]	57(17·87%)		84(26·09%)		3(2·17%)	
Overweight/Obesity	61·30(42·10,109·30)	1·77(1·14,3·08)	1·01(0·75,1·23)	0·73(0·50,0·96)	5·41±0·16[‡]	37(25·52%)		35(23·33%)		9(11·69%)	
Maternal pregnancy weight gain											
Below IOM guidelines	62·40(41·10,100·30)	1·73(1·15,2·73)	0·92(0·73,1·17)[†*]	0·65(0·48,0·90)	5·37±0·18	105(22·01%)	0·98	96(19·92%)	0·45	16(7·21%)	0
Within IOM guidelines	59·65(39·30,97·80)	1·67(1·05,2·70)	0·97(0·77,1·28)[†‡]	0·70(0·49,0·99)	5·36±0·22	129(21·57%)		140(23·1%)		22(7·64%)	
Above IOM guidelines	61·20(43·00,96·80)	1·70(1·18,2·73)	0·99(0·75,1·24)[‡]	0·68(0·51,0·96)	5·36±0·16	100(21·65%)		102(21·75%)		10(5·15%)	
Premature delivery											
No	59·90(40·50,96·10)	1·65(1·13,2·69)	0·94(0·75,1·22)	0·67(0·48,0·95)	5·36±0·19	317(21·40%)	0·53	316(21%)	0·12	47(6·98%)	0
Yes	61·50(41·20,104·40)	1·73(1·12,2·83)	1·01(0·77,1·26)	0·71(0·49,1·02)	5·37±0·18	44(23·40%)		49(25·93%)		5(6·17%)	
Fatal weight of pregnancy week											
SGA	60·5(40·4,94·2)	1·67(1·13,2·61)	0·94(0·74,1·24)	0·68(0·48,0·96)	5·37±0·19	226(20·68%)	0·03	236(21·22%)	0·72	35(7·09%)	0
Appropriate for GA	55(39·3,85·1)	1·53(1·04,2·44)	0·89(0·73,1·14)	0·61(0·44,0·88)	5·36±0·14	20(15·75%)		24(18·75%)		4(5·88%)	
LGA	61·3(41·6,105·3)	1·71(1·15,3·04)	0·95(0·76,1·21)	0·67(0·49,0·95)	5·35±0·20	99(25·52%)		87(22·14%)		13(7·43%)	
Gestational hypertension											
No	59·90(40·40,96·60)	1·67(1·13,2·70)	0·94(0·75,1·24)	0·67(0·48,0·96)	5·37±0·19	384(21·03%)	0·83	399(21·45%)	0·48	61(7·30%)	0
Yes	59·70(40·50,88·55)	1·62(1·12,2·61)	0·99(0·76,1·32)	0·70(0·54,1·06)	5·35±0·20	12(22·22%)		14(25·45%)		2(8·33%)	
Gestational diabetes											
No	59·90(40·20,96·60)	1·66(1·12,2·70)	0·94(0·75,1·24)	0·67(0·48,0·96)	5·37±0·19	393(21·14%)	0·62	409(21·59%)	0·63	63(7·35%)	0
Yes	73·00(46·60,90·20)	1·92(1·21,3·00)	1·01(0·74,1·22)	0·70(0·55,0·97)	5·41±0·17	7(25·00%)		5(17·86%)		0(0·00%)	
Birth with Caesarean operation											
No	57·40(38·50,93·90)	1·60(1·08,2·61)	0·93(0·76,1·23)	0·67(0·49,0·96)	5·36±0·20	132(20·06%)	0·34	139(20·81%)	0·51	22(6·92%)	0
Yes	60·60(41·55,96·85)	1·69(1·15,2·74)	0·96(0·75,1·25)	0·68(0·48,0·96)	5·37±0·18	245(21·99%)		250(22·12%)		35(7·22%)	
Breast feeding											
No	65·20(40·50,106·00)	1·78(1·13,2·90)	0·95(0·8,1·24)	0·69(0·54,0·95)	5·38±0·18	43(23·24%)	0·55	46(24·6%)	0·40	5(5·32%)	0

Yes	59·50(39·10,96·20)	1·62(1·07,2·72)	0·92(0·72,1·23)	0·65(0·46,0·96)	5·38±0·19	207(21·27%)	217(21·83%)	42(7·38%)
Socioeconomic measures								
Income, Yuan/year								
~50,000	56·20(38·35,90·00)†**	1·57(1·07,2·55)†**	0·96(0·75,1·26)	0·68(0·48,1·00)	5·38±0·20	114(18·84%) 0·02	146(23·78%) 0·21	27(8·39%) 0
~150,000	60·50(40·00,94·80)†	1·64(1·07,2·64)†	0·93(0·76,1·21)	0·66(0·48,0·93)	5·36±0·19	161(20·43%)	160(19·88%)	24(6·47%)
>150,000	63·85(42·60,106·45)‡	1·79(1·19,3·09)‡	0·94(0·73,1·22)	0·66(0·48,0·96)	5·38±0·17	122(25·42%)	105(21·47%)	12(6·09%)
Marriage status								
Double parents	59·90(40·40,96·20)	1·67(1·13,2·70)	0·94(0·75,1·24)*	0·67(0·48,0·96)	5·37±0·19	349(21·33%) 0·47	356(21·42%) 0·44	56(7·49%) 0
Single parents	61·90(40·10,91·20)	1·67(1·11,2·59)	1·06(0·80,1·30)	0·72(0·51,1·05)	5·35±0·22	28(18·79%)	36(24·16%)	3(4·17%)
Mother's education, y								
~9	56·10(36·90,93·50)†**	1·59(0·97,2·55)†**	0·94(0·73,1·25)	0·66(0·47,0·97)	5·37±0·18	125(19·20%) 0·05	153(22·97%) 0·41	24(6·02%) 0
~12	58·20(40·40,92·60)†‡	1·62(1·14,2·62)†‡	0·93(0·76,1·23)	0·66(0·49,0·96)	5·38±0·20	132(19·76%)	145(21·45%)	25(8·59%)
≥15	63·85(43·60,100·25)‡	1·76(1·22,2·90)‡	0·96(0·75,1·23)	0·68(0·49,0·95)	5·36±0·20	149(24·31%)	125(19·94%)	17(7·56%)
Father's education, y								
~9	54·85(36·90,90·60)†**	1·52(0·97,2·48)†**	0·93(0·74,1·22)	0·65(0·48,0·94)	5·38±0·19	102(18·44%) <0·01	128(22·78%) 0·44	23(6·69%) 0
~12	58·95(40·50,92·00)†	1·62(1·15,2·65)†	0·94(0·74,1·22)	0·66(0·47,0·96)	5·38±0·18	134(19·20%)	157(22·11%)	26(8·12%)
≥15	64·40(42·35,105·70)‡	1·80(1·17,3·00)‡	0·97(0·76,1·26)	0·69(0·50,0·97)	5·36±0·20	170(25·00%)	139(19·97%)	17(6·77%)
Mother's occupation								
Manager	71·90(43·10,127·80)	1·93(1·16,3·27)	1·00(0·75,1·31)	0·75(0·48,1·03)	5·39±0·22	29(27·36%) 0·61	32(29·91%) 0·09	6(11·32%) 0
Worker	60·50(39·80,92·60)	1·67(1·09,2·66)	0·95(0·74,1·26)	0·67(0·49,0·97)	5·38±0·18	135(20·58%)	133(19·79%)	21(6·58%)
Technician/Researcher	62·50(45·50,92·65)	1·73(1·38,2·72)	1·01(0·7,1·19)	0·68(0·46,0·84)	5·33±0·15	13(21·31%)	10(16·39%)	2(8·00%)
Farmer	57·60(39·70,96·70)	1·64(1·09,2·70)	0·93(0·75,1·26)	0·66(0·48,0·98)	5·36±0·19	110(20·87%)	126(23·55%)	20(7·49%)
Other	58·20(40·00,96·90)	1·61(1·13,2·65)	0·94(0·76,1·19)	0·67(0·47,0·92)	5·37±0·19	119(20·70%)	121(20·65%)	17(6·88%)
Father's occupation								
Manager	65·60(41·90,96·85)	1·81(1·17,2·78)	0·94(0·77,1·24)	0·68(0·50,0·91)	5·40±0·20	35(22·15%) 0·09	33(20·50%) 0·55	7(10·29%) 0
Worker	58·65(38·90,89·90)	1·62(1·05,2·55)	0·94(0·74,1·23)	0·66(0·49,0·97)	5·37±0·19	130(19·55%)	136(20·09%)	28(8·31%)
Technician/Researcher	61·10(39·50,116·30)	1·69(1·07,3·39)	0·96(0·73,1·26)	0·69(0·46,0·96)	5·34±0·23	47(29·19%)	32(19·39%)	5(8·62%)
Farmer	57·00(40·10,94·80)	1·62(1·14,2·67)	0·94(0·75,1·28)	0·67(0·48,0·98)	5·38±0·19	106(19·78%)	129(23·71%)	17(6·46%)
Other	60·05(40·70,99·50)	1·69(1·16,2·83)	0·94(0·76,1·17)	0·66(0·49,0·95)	5·37±0·16	84(21·37%)	89(22·19%)	9(5·03%)
Score of Quality of life								
~40	64·70(42·40,111·40)†*	1·85(1·15,3·08)	1·05(0·82,1·34)†**	0·71(0·53,1·07)†**	5·37±0·18	82(25·71%) 0·06	84(26·09%) 0·02	7(4·93%) 0
~70	58·25(40·00,93·65)‡	1·62(1·11,2·65)	0·93(0·74,1·22)‡	0·67(0·48,0·94)‡	5·37±0·19	293(20·10%)	314(21·2%)	52(7·60%)
≥70	55·60(38·20,84·70)‡	1·54(1·06,2·43)	0·85(0·71,1·22)‡	0·59(0·46,0·92)‡	5·4±0·18	26(18·44%)	22(15·07%)	4(6·06%)
Extraversion (E)								
Introversive type	60·10(40·25,104·90)	1·69(1·12,2·90)	0·97(0·78,1·27)	0·71(0·51,1·01)*	5·38±0·18	111(23·67%) 0·17	108(22·69%) 0·60	14(5·13%) 0
Middle type	60·10(40·40,96·10)	1·69(1·14,2·66)	0·95(0·74,1·24)	0·67(0·47,0·96)†‡	5·37±0·19	166(21·20%)	176(22·14%)	33(8·85%)
Extrovert type	58·70(39·60,90·10)	1·59(1·09,2·61)	0·93(0·74,1·23)	0·65(0·48,0·90)‡	5·37±0·19	121(19·03%)	132(20·37%)	17(7·05%)
Neuroticism (N)								
Emotionormal	56·8(39·00,89·90)†*	1·59(1·11,2·57)	0·92(0·73,1·23)*	0·65(0·47,0·92)†*	5·38±0·19	139(19·39%) 0·07	146(20·03%) 0·29	29(8·63%) 0
Middle type	59·7(39·80,95·00)†‡	1·62(1·10,2·65)	0·98(0·76,1·25)	0·70(0·50,0·97)‡	5·38±0·19	114(19·93%)	126(21·72%)	20(7·63%)
Instability	62·6(41·4,108·6)‡	1·78(1·14,2·92)	0·96(0·77,1·29)	0·68(0·48,1·01)†‡	5·36±0·17	145(24·21%)	144(23·61%)	15(5·19%)
Psychoticism (P)								
No	59·05(39·8,94·2) **	1·64(1·10,2·65) **	0·95(0·75,1·24)	0·67(0·48,0·96)	5·37±0·19	363(20·47%) 0·01	391(21·67%) 0·99	62(7·44%) 0
Yes	69·05(44·25,137)	1·91(1·25,3·91)	0·96(0·70,1·29)	0·65(0·47,1·00)	5·36±0·17	35(30·43%)	25(21·74%)	2(3·70%)

SGA, small for gestational age; GA, gestational age; LGA, large for gestational age.

Natural logarithmic transformation were used to calculate the P value.

¶ Nine hundred and thirty-two samples were included.

* P<0·05; ** P<0·01.

†, ‡, § Difference of post-hoc analyses among groups using "†", "‡", "§" labelled, different symbols mean the difference existed between two groups.

Prevalence of glycolipid metabolism disorder in adolescents

Table 2 displays the prevalence of childhood GLMD. Overall, the prevalence rates of IR, prediabetes/diabetes and dyslipidemia were 21·02%, 7·19% and 21·61%, respectively. The prevalence rates of IR and dyslipidemia were higher in children with the characteristics of older age, dyslipidemia in young childhood (6~9 years), obesity and lower QoL score than in their counterparts. Moreover, Children with urban residence, LGA status, higher family income and parental education, and unstable personality (P=0·07) also had an increased prevalence of IR. The prevalence of prediabetes/diabetes was higher in children with abdominal obesity in 2014 and maternal prepregnancy obesity than in their counterparts.

Relationship of QoL and personality traits with glycolipid indexes

The results in Table 3 showed the relationship of QoL and personality traits with glycolipid indexes after adjusting for age, sex, region and BMI. Elevated scores of self-satisfaction, relationship of teacher and pupil, physical feeling, physical activity ability, negative emotion, attitude toward doing homework, physical and mental health factor and QoL satisfaction factor were protective factors for FI, IR, TGs or TG/HDL (all P<0·05 or P<0·01), and the association of QoL satisfaction factor with TG/HDL was borderline significant (P=0·06). Moreover, the score of the relationship of teacher and pupil, and psychosocial factors were protective factors for TGs and TG/HDL. However, the score of living convenience was positively correlated with HbA1c. And a higher total QoL score was negatively correlated with FI, IR, TGs and TG/HDL (all P<0·01). High P and N personality scores among adolescents were positively correlated with FI and IR levels (all P<0·01). In addition, children with high E scores had decreased TG/HDL level (Table 3, all P<0·05).

Table 3. The Association of QoL and Personality Characteristics on Glycolipids Indexes Adjusting for Covariates.

Variables	Insulin		IR		TG		TG/HDL		HbA1c	
	β(95%CI)	*P*	*β*(95%CI)	*P*	*β*(95%CI)	*P*	*β*(95%CI)	*P*	*β*(95%CI)	*P*
13 domains of QoL										
Self-satisfaction	-0·003(-0·006,-0·001)	0·016	-0·003(-0·006,-0·001)	0·025	-0·002(-0·004,-0·001)	0·008	-0·002(-0·004,-0·001)	0·025	0·001(-0·001,0·002)	0·370
Relationship of teacher and pupil	-0·003(-0·006,0·000)	0·036	-0·003(-0·006,-0·001)	0·049	-0·002(-0·004,-0·001)	0·020	-0·003(-0·005,-0·001)	0·018	-0·001(-0·002,0·001)	0·390
Physical feeling	-0·005(-0·007,-0·002)	<0·001	-0·004(-0·007,-0·002)	0·002	-0·002(-0·003,-0·001)	0·025	-0·003(-0·005,-0·001)	0·006	0·001(0·001,0·002)	0·144
Companionship	-0·001(-0·004,0·002)	0·425	-0·002(-0·004,0·001)	0·292	-0·001(-0·003,0·001)	0·124	-0·001(-0·003,0·001)	0·304	0·001(-0·001,0·001)	0·710
Parenthood	-0·002(-0·005, 0·000)	0·071	-0·002(-0·005,0·001)	0·126	-0·001(-0·003,0·001)	0·091	-0·002(-0·004,0·001)	0·082	0·001(0·000,0·002)	0·266
Physical activity ability	-0·003(-0·006, 0·000)	0·023	-0·003(-0·006,-0·001)	0·043	-0·003(-0·004,-0·001)	0·002	-0·003(-0·005,-0·001)	0·010	0(-0·001,0·001)	0·846
Learning ability and attitude	-0·003(-0·006, 0·000)	0·044	-0·002(-0·005,0·001)	0·102	-0·001(-0·002,0·001)	0·368	-0·002(-0·004,0·000)	0·051	0·001(-0·001,0·002)	0·345
Self-esteem	-0·001(-0·003,0·002)	0·591	-0·001(-0·004,0·002)	0·588	-0·001(-0·002,0·001)	0·228	-0·001(-0·003,0·001)	0·197	0·000(-0·001,0·001)	0·616
Negative emotion	-0·004(-0·006,-0·001)	0·005	-0·003(-0·006,-0·001)	0·032	-0·002(-0·003,-0·001)	0·014	-0·002(-0·004,-0·001)	0·019	0·001(0·000,0·002)	0·094
Attitude towards doing homework	-0·006(-0·009,-0·003)	<0·001	-0·006(-0·009,-0·003)	0·001	-0·003(-0·005,-0·001)	0·003	-0·004(-0·006,-0·002)	0·001	-0·001(-0·002,0·001)	0·293
Activity opportunity	0·001 (-0·003,0·003)	0·896	0·001(-0·002,0·004)	0·673	0·001(-0·001,0·002)	0·724	0·001(-0·002,0·002)	0·950	0·001(0·000,0·002)	0·176
Living convenience	-0·002(-0·006,0·001)	0·215	-0·003(-0·007,0·001)	0·102	-0·001(-0·004,0·001)	0·196	-0·002(-0·005,0·001)	0·124	0·002(0·000,0·003)	0·017
Other	-0·003(-0·006,-0·001)	0·020	-0·003(-0·006,-0·001)	0·027	-0·001(-0·002,0·001)	0·805	-0·001(-0·002,0·002)	0·751	0·001(-0·001,0·002)	0·283
Four factors of QoL										
Psychosocial factor	-0·003(-0·005, 0·000)	0·063	-0·002(-0·005,0·001)	0·097	-0·002(-0·003,-0·001)	0·041	-0·002(-0·004,-0·001)	0·035	0·000(-0·001,0·001)	0·866
Physical and mental health factor	-0·010(-0·015,-0·005)	<0·001	-0·009(-0·014,-0·004)	0·001	-0·004(-0·007,-0·002)	0·003	-0·006(-0·010,-0·002)	0·001	0·001(-0·001,0·003)	0·236
Living environment factor	-0·006(-0·012,0·001)	0·116	-0·005(-0·013,0·002)	0·153	-0·004(-0·008,0·001)	0·066	-0·005(-0·010,0·001)	0·072	0·002(-0·001,0·005)	0·132
Quality of life satisfaction factor	-0·009(-0·015,-0·002)	0·009	-0·009(-0·016,-0·002)	0·014	-0·004(-0·008,-0·001)	0·024	-0·005(-0·01,0·001)	0·060	0·002(-0·001,0·004)	0·282
Total score of QoL	-0·004(-0·006,-0·001)	0·001	-0·004(-0·006,-0·001)	0·004	-0·002(-0·004,-0·001)	0·001	-0·003(-0·005,-0·001)	0·001	0·001(0·000,0·002)	0·295
Personality Characteristics										
Neuroticism (N)	0·003(0·001,0·005)	0·003	0·003(0·001,0·005)	0·014	0·001(0·001,0·002)	0·084	0·001(0·001,0·003)	0·098	-0·001(-0·001,0·001)	0·223
Psychoticism (P)	0·005(0·001,0·008)	0·004	0·005(0·001,0·008)	0·007	0·001(-0·001,0·003)	0·470	0·001(-0·002,0·003)	0·608	0·001(-0·001,0·002)	0·781
Extraversion (E)	-0·001(-0·003,0·001)	0·302	-0·002(-0·004,0·001)	0·211	-0·001(-0·002,0·001)	0·105	-0·002(-0·004,-0·001)	0·026	0·000(-0·001,0·001)	0·773

Adjusted age, sex, region and BMI in 2019.

Risk factors of glycolipid metabolism indexes using a GLM

In the GLM 1 (Table 4) (adjusted for sex, age and region), the results showed that female, living in urban areas and variables measured in 2014 (FBG, BMI, waist circumference [WC]) were risk factors for FI and HOMA-IR levels (all P<0·05), and older age was a risk factor of FI and IR(P<0·01); variables in 2014 (FBG, dyslipidemia, BMI) were the risk factors of TG and TG/HDL level (all P<0·01), and FBG and BMI in 2014 were risk factors for HbA1c level (Supplementary Table S2). Model 1 explained 12·43%, 11·92%, 6·79%, 10·32% and 7·06% of the variance in FI, HOMA-IR, TGs, TG/HDL and HbA1c levels, respectively

Table 4. The Risk Factors of Glycolipid Indexes Levels in Adolescents.

Variables	Insulin, pmol/L			HOMA-IR level			TG, mmol/L			TG/HDL		
	β	*P*	R^2	*β*	*P*	R^2	*β*	*P*	R^2	*β*	*P*	R^2
Model 1: Variables in 2014												
Sex, male *vs.* female	-0·136	0·004	12·43%	-0·110	0·029	11· 92%	-0·112	<0·001	6·79%	-0·102	<0·001	10·32%
Age, y	0·149	<0·001		0·123	0·005		0·026	0·21		0·041	0·12	
Region, Urban *vs.* Rural	0·213	0·005		0·285	<0·001		0·108	<0·001		0·074	0·12	
Prepregnancy weight gain, kg/m^2	-0·008	0·425		-0·011	0·299		..	..		..	..	
Birth weight, 50g	-0·001	0·644		-0·002	0·439		-0·002	0·19		-0·002	0·21	
FBG in 2014, mmol/L	0·14	0·005		0·142	0·006		0·080	<0·001		0·099	<0·001	
Dyslipidemia in 2014	0·064	0·238		0·044	0·450		0·099	<0·001		0·218	<0·001	
BMI in 2014, kg/m^2	0·031	0·018		0·041	0·003		0·019	<0·001		0·035	<0·001	
Waist in 2014, cm	0·018	<0·001		0·017	0·002		..	..		..	..	
Gestational hypertension	..	..		..	..		0·096	0·20		0·093	0·33	
Model 2: Variables in 2019												
Sex, male *vs.* female	-0·187	<0·001	26·10%	-0·168	<0·001	24·58%	-0·08	<0·001	16·00%	-0·091	<0·001	17·12%
Age, y	0·136	<0·001		0·124	<0·001		-0·011	0·51		0·001	0·98	
Region, Urban *vs.* Rural	0·147	0·001		0·214	<0·001		-0·04	0·15		-0·091	0·01	
Prepregnancy weight gain, kg/m^2	-0·012	0·071		-0·013	0·059		..	..		..	..	
Birth weight, 50g	-0·001	0·612		-0·001	0·618		0·001	0·89		0·001	0·80	
HOMA-IR level in 2019 †	..	..		..	..		0·144	<0·001		0·179	<0·001	
TG/HDL in 2019	0·293	<0·001		0·288	<0·001		..	..		..	..	
BMI in 2019, kg/m^2	0·033	<0·001		0·036	<0·001		..	..		..	..	
Waist in 2019, cm	0·014	<0·001		0·014	<0·001		..	..		..	..	
WHtR in 2019	..	..		..	..		1·150	<0·001		1·901	<0·001	
Gestational hypertension	..	..		..	..		0·139	0·02		0·157	0·04	
Prenatal weight gain												
Below IOM guidelines	..	..		..	..		0·074	<0·001		0·069	0·02	
Above IOM guidelines	..	..		..	..		0·037	0·13		0·033	0·29	
Puberty development	..	..		..	..		-0·083	<0·001		-0·072	0·03	
Father's Education, ref. ≤9y												
9~12	0·085	0·040		0·081	0·070		..	..		..	..	
≥15	0·183	<0·001		0·177	<0·001		..	..		..	..	
Physical activity ability	-0·001	0·461		-0·001	0·481		..	..		..	..	
Total score of QoL	..	..		..	..		-0·002	<0·001		-0·003	<0·001	
Psychoticism personality	0·003	0·089		0·003	0·093		-0·001	0·29		-0·001	0·37	
Model 3: Full model												
Gender, male *vs.* female	-0·178	<0·001	28·36%	-0·159	<0·001	26·33%	-0·107	<0·001	17·67%	-0·094	<0·001	19·39%
Age, y	0·135	<0·001		0·117	0·001		-0·013	0·58		-0·009	0·76	
Region, Urban *vs.* Rural	0·230	0·001		0·296	<0·001		0·010	0·85		-0·024	0·71	
Prepregnancy weight gain, kg/m^2	-0·019	0·020		-0·019	0·025		..	..		..	..	
Birth weight, 50g	-0·001	0·495		-0·002	0·459		-0·001	0·39		-0·002	0·40	
FBG in 2014, mmol/L	0·124	0·003		0·125	0·005		0·070	<0·001		0·098	<0·001	
Dyslipidemia in 2014	..	..		..	..		0·055	0·06		0·168	<0·001	
TG/HDL in 2019	0·271	<0·001		0·261	<0·001		..	..		..	..	
BMI in 2019, kg/m^2	0·045	<0·001		0·049	<0·001		..	..		..	..	
Waist in 2019, cm	0·012	0·009		0·011	0·023		..	..		..	..	
BMI in 2014, kg/m^2	..	..		..	..		-0·008	0·22		-0·001	0·93	
HOMA-IR level in 2019†	..	..		..	..		0·146	<0·001		0·17	<0·001	
WHtR in 2019	..	..		..	..		1·272	<0·001		1·687	<0·001	
Gestational hypertension	..	..		..	..		0·168	0·05		0·174	0·13	
Prenatal weight gain												
Below IOM guidelines	..	..		..	..		0·051	0·11		0·058	0·15	
Above IOM guidelines	..	..		..	..		0·059	0·08		0·078	0·07	
Puberty	..	..		..	..		-0·076	0·11		-0·081	0·18	
Education, ref. ≤9y												
9~12	0·081	0·123		0·08	0·145		..	..		..	..	
≥15	0·180	0·001		0·165	0·003		..	..		..	..	
Physical activity ability	-0·001	0·966		-0·001	0·989		..	..		..	..	
Psychoticism personality(P)	0·006	0·009		0·006	0·012		..	..		..	..	
Total score of QoL	..	..		..	..		0·001	0·79		-0·001	0·55	

FBG, fasting blood glucose; BMI, body mass index; IR, insulin resistant; TG/HDL-C, The triglyceride/high-density lipoprotein cholesterol (HDL-C) ratio; WHtR, waist-height-ratio; IOM, 2009 Institute of Medicine; QoL, quality of life.

† Natural logarithm transformation.

The GLM (Table 4) revealed that female, older age, urban residence, and variables in 2019 (higher TG/HDL, BMI, WC, father's education ≥15 years) were risk factors for FI and HOMA-IR level, whereas increased BMI during pregnancy was a boundary protective factor for FI and HOMA-IR levels (P=0·07 and P=0·06); HOMA-IR and WHtR in 2019, GH and maternal weight gain below IOM guidelines were risk factors for TGs and TG/HDL levels (all P<0·05), whereas puberty and total QoL score were protective factors of TGs and TG/HDL levels (all P<0·05 or P<0·01); FI and living convenience in 2019 were risk factors of HbA1c, and maternal prepregnancy obesity was a borderline risk factor of HbA1c level in model 2 (P=0.07) (Supplementary Table S2). Model 2 explained 26·10%, 24·58%, 16·00%, 17·12% and 5·90% of the variance in FI, HOMA-IR, TGs, TG/HDL and HbA1c levels, respectively.

Finally, the results of the full model 3 were shown in Table 4. Older age, urban area, FBG in 2014, variables in 2019 (higher TG/HDL, BMI, WC, father's education ≥15 years) and high P scores were significantly correlated with elevated FI and IR levels (all P<0·05), while maternal prepregnancy weight gain were protective factor of FI and IR levels (all P<0·05). Variables in 2014 (FBG and dyslipidemia) and variables in 2019 (HOMA-IR and WHtR) were risk factors for TGs and TG/HDL (all P<0·05). FBG in 2014 and BMI in 2019 were risk factors for HbA1c level (Supplementary Table S2). The full model explained 28·36%, 26·33%, 17·67%, 19·39% and 12·33% of the variance of FI, HOMA-IR, TGs, TG/HDL and HbA1c levels, respectively.

Risk factors for IR, dyslipidemia and prediabetes/diabetes based on logistic regression

The risk factors for IR, dyslipidemia and prediabetes/diabetes were analyzed by logistic regression model (Supplementary Table S3). In the IR model, older age, urban residence, FBG in 2014, BMI in 2019, father's education ≥15 years and a higher P score had a significant impact on IR prevalence (*P*<0·05), explaining 20·09% of the variance in IR. The dyslipidemia model showed single-parents, dyslipidemia and high FBG in 2014, and BMI in 2019 were risk factors for dyslipidemia, explaining 12·07% of the variance in dyslipidemia. The prediabetes/diabetes model revealed WHtR in 2014 was a risk factor for prediabetes/diabetes, explaining 10·29% of the variance in prediabetes/diabetes.

Discussion

This study is the first prospective cohort study that involves QoL and personality traits, in addition to perinatal, SES and physical measurements over an average 12-year follow-up from birth to adolescence in urban-rural areas, to ascertain the prevalence of GLMD and its' potential influencing factors.

The prevalence of GLMD varies by region and age, and some variance is also attributed to different diagnostic criteria and methods. The current literature describes at least one lipid adverse level prevalence as 19%-25% in US children and adolescents [8,19], and the prevalence of prediabetes/diabetes in other study [5], was comparable with our study. An elevated prevalence of GLMD has been observed in children with obesity in cross-section study [20]. In this study, we found that childhood obesity is the strongest predictor of adolescent GLMD, even adjusted other risk factors. Moreover, the prevalence of HOMA-IR exceeded 44% in children who had obesity comparable with the result from Yin J et al. [2], and the prevalence of dyslipidaemia reached 28·57% in children with abdominal obesity, suggesting that health care programmes should be conducted for children who are obesity or abdominal obesity combined with other risk factors.

In addition, a cross-sectional study revealed that elevated TG level was associated with increased HOMA-IR [21], and our cohort study first found dyslipidemia and elevated fasting glucose at 6 ~ 9 years old were independent risk factors of HOMA-IR and dyslipidemia in adolescents (10 ~ 14 years old). And adolescents with menarche or spermarche had decreased IR and lipid levels, which indicated the prepubertal stage will impact GLMD among adolescents. Whereas, the transient IR phenomenon emerging during pubertal maturation is accepted as a physiological condition [2], which may be caused by an inadequate β-cell response to the decrease in insulin sensitivity [22]. In addition, glycolipid indexes (except HbA1c) were higher in females than in males, which coincided with the results of *Interator H.* et al [23], and the mechanism may be dependent on the difference in the age of prepubertal stages between males and females.

Maternal adverse perinatal experiences will impact GLMD in the offspring [24,25]. We found maternal prepregnancy obesity was a risk factor for irregular HbA1c level. An animal study found maternal obesity permanently alters the hypothalamic response to leptin and subsequently regulates appetite and pancreatic beta-cell physiology [24], which causes maternal and off-spring changes in glycolipid levels. Moreover, our study found both maternal pregnancy weight gain above IOM guidelines and GH were risk factors for elevated off spring TGs, which coincided with the results from young adulthood [26]. This phenomenon can be explained by shared genes or lifestyle. However, the conclusion was controversial, as a study with a small sample size found no association between GH and lipid levels in adolescent [27], this founding needs to be verified by a large cohort study. In addition, SGA and LGA correlated with elevated HOMA-IR prevalence, which coincided with other findings [28]. Birth-weight was correlated with nutritional status in utero, which may cause IR later in life; moreover, LGA is correlated with adolescent obesity, which is essential to IR.

SES is negatively correlated with cardiovascular disease. Our current cohort study provided further support for this concept in the adolescent population. A previous study [29] revealed that the marital status of parents was the strongest socioeconomic predictor of young adult arterial stiffness, and we found the TG level was higher in single-parent adolescents. In addition, the relationship between parental education and the cardiovascular risk of adolescent is controversial, and our results showed a positive relationship between parental education or family income and FI or IR. Studies have revealed a positive correlation between parental education and childhood obesity [30], and obesity was the strongest predictor of insulin sensitivity. Moreover, we observed that rural residents have lower FI, IR and TG levels, but higher HbA1c levels, which could be induced by different dietary habits, as rural children consume less fat but more carbohydrates.

Our study revealed QoL scores were mainly negatively correlated with GLMD in adolescents. Research on the relationship between QoL and GLMD is limited. According to a previous cross-sectional study that included 74 diabetic adolescents [31], no significant relationship between QoL and HbA1c levels was

observed. However, a cross-sectional study found QoL scores were correlated with an increase in the components of MS, and the physical health domain of QoL had the most significant association [32]. In our study, we found 6 domains, four factors and the total QoL score were significantly negatively correlated with glycolipids indexes, and the effect was independent of obesity. Moreover, only the living convenience domain of QoL was positively correlated with HbA1c, as the child has greater chance of consuming high-sugar snacks. To our knowledge, this is the first cohort study with a large sample size to explore the relationship of QoL with GLMD in adolescents.

Personality traits may be associated with GLMD, but the conclusion remains controversial, and few studies have been conducted in adult populations; no related cohort study has explored this relationship in adolescents. The results from Japanese adult [10] showed the E score was positively correlated with TGs, FBG and MS components, and the P score was positively correlated with FBG. However, we found the E score in adolescents was negatively correlated with TGs and TG/HDL, suggesting the E score may be age dependent and have a different impact on lipid metabolism between adults and adolescents. And study from Evans, B. E. [33] reported that extraverted adolescents have less cortisol activity, which is associated with FBG and FI [34]. Therefore, E personality may regulate glycolipid indexes through the hypothalamic–pituitary–adrenal axis pathway [33], which may impact GLMD by regulating the reactivity of the sympathetic nervous system (SNS) [35], and the SNS will have potent effects on insulin secretion and sensitivity [36] and on lipid metabolism [37]. Higher N scores in adolescents would be more prone to responding more strongly to a stressor and anxiety, which could explain our results that the N score was positively correlated with FI and IR after adjusting for covariates, and N also correlated with lipid metabolism, which coincided with the results of study in adults [38]. Moreover, we found the P score was positively correlated with FI and IR, as P scores may be linked to the SNS, which may regulate insulin sensitivity [39].

Our study has some limitations that should be considered when interpreting the results. First, as this was an ambispective cohort study, recall bias may exist for the prenatal variables. We checked the birth certificates to verify the birth weight, stature and gestational age. Second, data on GH and diabetes were collected using a questionnaire, and recall bias existed. However, the perinatal information both were collected both in 2014 and in 2019 independently. Finally, we were collected QoL and personality traits variables in a cross-sectional manner, which makes it difficult to draw conclusions regarding causality relationships of QoL and personality traits with GLMD.

In conclusion, the prevalence of GLMD and high glycolipid levels was elevated in adolescents with the features of obesity, maternal prepregnancy obesity, GH, SGA, LGA, single-parents status, low QoL score, and unstable or psychotic personality. SES was positively correlated with HOMA-IR. To our knowledge, this is the first study to explore the relationship of QoL and personality characteristics with glycolipid indexes in a large-sample-size cohort study of adolescents, and the correlation was significant after adjusting for covariates. Our study emphasizes the importance of reducing or controlling adiposity of pre-pregnancy mother and children, increasing QoL, developing good personality traits, emphasizing the importance of providing support for single-parent children and reducing or preventing GH.

Declarations

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. Data are available from Xiao-Hua Liang (Clinical Epidemiology and Biostatistics Department, Children's Hospital of Chongqing Medical University, No.136 2nd Zhongshan Road, Yuzhong District, Chongqing, China, 400016; Email: xiaohualiang@hospital.cqmu.edu.cn or liangxiaohua666@sina.com).

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Author contributions

L.X.H conceived and designed the study; C.J.Y, Q.P and T.X participated in the acquisition and management of the data; L.X.H analysed the data; L.X.H wrote the paper and all authors revised the manuscript; and all authors critically reviewed and approved the final paper.

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Competing interest

The authors declare no competing interests.

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Figures

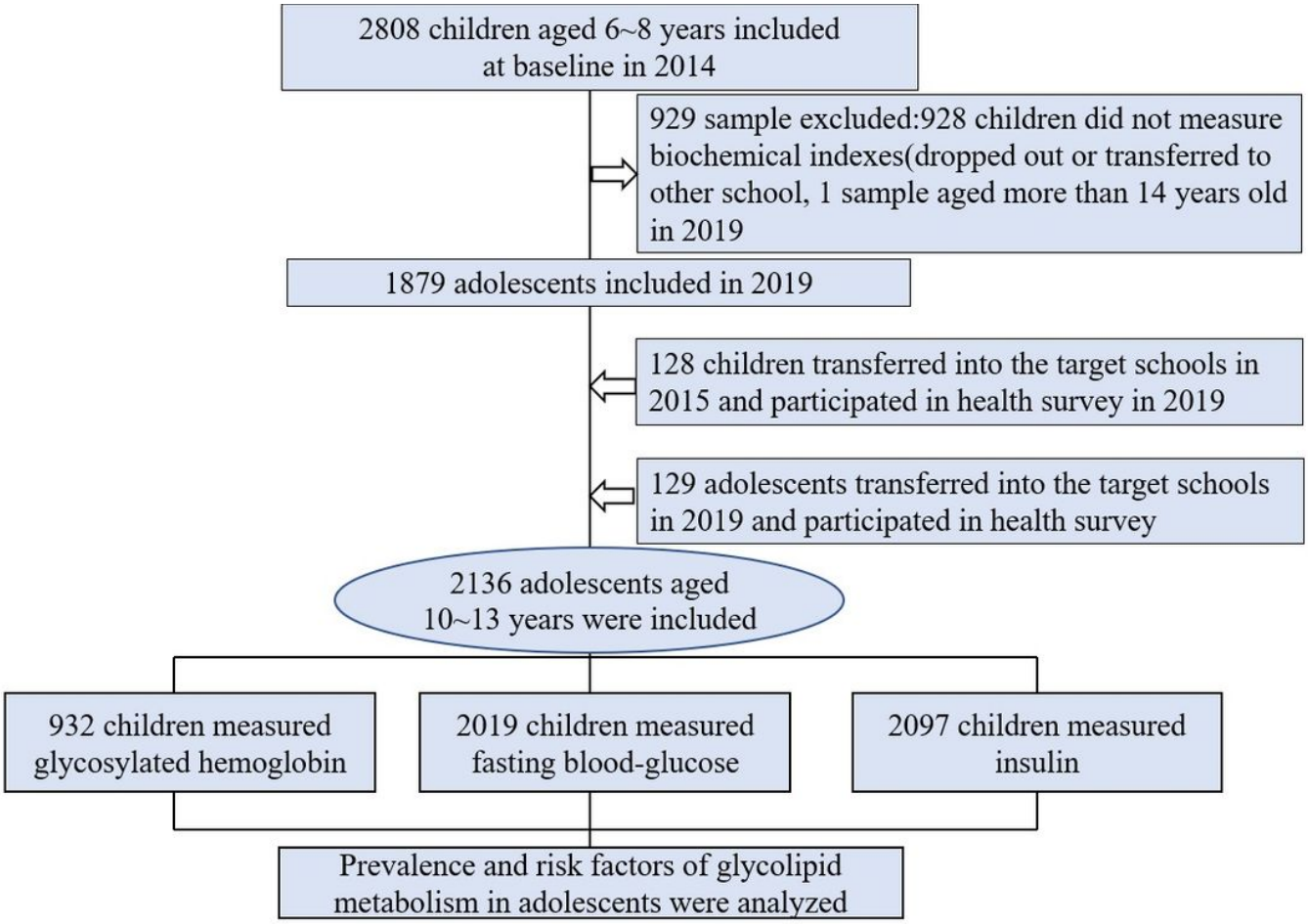

Figure 1

Subjects inclusion process

Supplementary Files

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- SupplementaryTableS1S3.pdf