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A three-country study on the components of the metabolic syndrome in youths: The BIG Study

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Abstract

Objectives. This study aimed to assess the prevalence of components of the metabolic syndrome (MetS) among representative samples of children and adolescents from *B*razil, *I*ran and *G*ermany (BIG study). *Methods.* We report the data of a total number of 4473 children (mean age 7.7 years; 2 218 boys,) and 6800 adolescents (mean age 12.6 years; 3 409 boys) who participated in three large national studies. Anthropometric measures, blood pressure (BP) and lipid profile were assessed, fasting plasma glucose was determined in German and Iranian participants. *Results.* With few exceptions, the mean of the components of the metabolic syndrome was higher in boys than in girls. The main ethnic differences were the high prevalence of low HDL-C levels in Iranian and Brazilian youths compared with German youths (34% vs.7%, respectively, $p<0.05$) and of increased triglycerides (10% vs. 1%, respectively, $p<0.05$). Furthermore the prevalence of high BP was lowest (<1%) in Iranian than in Brazilian and German children (6%). Both in children and adolescents, the prevalence of the MetS was significantly higher in Iranian than in German children (1% vs.0.1%, respectively, $p<0.05$) and adolescents (2% vs.0.5%, respectively, $p<0.05$). TG to HDL-C ratio had significant correlations with waist circumference and body mass index in Iranian and German children of both genders; these correlations were significant among both genders of adolescents in the three ethnic groups. *Conclusion.* While the prevalence of abdominal adiposity was nearly similar, Iranian and Brazilian youths had considerably higher prevalence of dyslipidemia than German youths. Future longitudinal studies should seek the clinical importance of these ethnic differences.

Key words: *Obesity, child, metabolic syndrome, ethnic difference, multicenter study*

Introduction

Childhood obesity is becoming an emerging public health problem worldwide. The problem is no longer limited to industrialized countries, for example in the US, where 16.8% of 6–11-year-old school-age children and 16.5% of 12–19-year-old adolescents (with large disparities by race-ethnic groups) have been reported to be overweight in 2003–2004 (1). Nowadays, developing countries are experiencing similar problems; childhood obesity and the metabolic syndrome (MetS) have a considerably high prevalence notably in Eastern Europe and the Middle East (2). Ethnic differences have been documented in this regard. White adolescents are reported to have greater visceral adiposity and more atherogenic risk profile at any given body mass index (BMI) whereas black adolescents have more insulin resistance (3). Ethnic differences are documented for the association of insulin sensitivity with excess adiposity in children and adolescents (4). The use of BMI and waist circumference (WC) for the prediction of risk factor clustering among children and adolescents had significant clinical utility in a sample with minimal race and gender differences in the optimal thresholds (5).

There is no universal definition for the cardiometabolic risk factors associated with childhood obesity. The International Diabetes Federation (IDF) has defined MetS for children and adolescents as central

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obesity (assessed by WC) plus any two of the four components: raised blood pressure (BP), raised triglycerides (TG), reduced HDL-cholesterol (HDL-C) and raised fasting plasma glucose (FPG) (6). Significant differences in components of the MetS have been noted among various ethnic groups (7). Consequently, for adults ethnic-specific values for WC have been proposed for Europids and South-American populations (8), and recently for Middle-Eastern populations (9).

As children and adolescents were underrepresented in previous international studies the aim of the current study was to compare the components of the MetS in nationally-representative samples of youths with different ethnicities and living in three different continents.

Methods

Data were obtained from **B**razil, **I**ran and **G**ermany; hence the study was entitled the *BIG* Study. It is a joint evaluation of three large population-based studies among youths aged 6 to 16 years from European, Middle Eastern and Latin American ethnicities: the Bello Horizonte Heart Study from Brazil (10), the CASPIAN Study from Iran (11,12) and the PEP Family Heart Study from Germany (13,14).

Study population

According to the new definition of MetS (6), children 6 to <10 years of age and adolescents aged between 10 to <16 years were grouped for comparisons. A number of 6 040 youths consisting of 2 393 children (including 1 220 boys) and 3 647 adolescents (including 1 938 males) participated in the *PEP Family Heart Study* in the city of Nuremberg (13,14). Data from eight yearly surveys (2000 to 2008) were combined to maximize the sample in this community-based study. As secular trend for increasing adiposity was excluded by controlling for WC over time, the annual data were considered as a whole. PEP was approved by the ethical committee of the medical faculty of the Ludwig-Maximilians-University Munich, the Bavarian Ministry of Science and Education, and the local school authorities. Written informed consent was obtained from the parents and oral consent from the children and adolescents. Exclusion criteria were incomplete data sets, apparent cardiovascular, metabolic, endocrine and malignant diseases, taking any medication, age <6 years and >16 years, and non-German ethnicity.

The "**C**hildhood & **A**dolescence **S**urveillance and **P**revent**I**on of **A**dult **N**on-communicable disease"; the CASPIAN Study was performed in 2003–2004 in Iran. The whole study comprised 21 111 school students aged 6–18 years, with biochemical factors measured in a sub-sample of 4 811. Students were selected by multistage-random cluster sampling from elementary, middle and high schools of urban and rural areas of different counties (11,12). Here, we report the data obtained from those students aged 6–16 years. Ethics committees and other relevant national regulatory organizations approved the study. Written informed consent was obtained from parents and oral assent from students after receiving full explanation of the procedure involved. The field examinations of the survey were carried out by a specially trained team consisting of expert health care professionals trained for the survey.

The Belo Horizonte Heart Study was conducted as an epidemiologic investigation of 1 450 students, aged 6–18 years, in the city of Belo Horizonte, the third largest city in Brazil. Anthropometric measures, BP and non-fasting serum lipid profile were determined. Ethical issues were considered and informed consent was obtained from parents. The findings of students aged 6–16 years are reported here (10).

Measurements

All three studies followed the same standard protocols for determining anthropometric measures and blood pressure. Weight and height were measured in duplicate and averaged to the nearest 0.1 cm and 0.1 kg, respectively, without shoes and in light clothing. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). WC was measured to the nearest 0.1 cm according to WHO recommendations at the end of expiration with a non-elastic tape placed directly on the skin horizontal to the floor at the midpoint between the lowest rib and the iliac crest, and hip over the major trochanters (15). Because of difficulties in examining pubertal stage in these population-based studies with large sample size, the Tanner stage could not be documented.

Systolic and diastolic blood pressure was measured in a sitting position and twice on both arms after a 5-minute rest with appropriate cuff-sizes according to arm size.

BP was measured in a calm situation after at least 5 minutes of rest in the sitting position. Appropriate size cuffs were used with a cuff width 40% of the mid-arm circumference, and cuff bladders covering 80–100% of the arm circumference and approximately two-thirds of the length of the upper arm without overlapping. The reading at the first and the fifth Korotkoff phase were taken as the systolic and diastolic BP (SBP, DBP), respectively. The average of the two time measurements was recorded and included in the analysis (16).

The PEP Family Heart Study

All measurements were performed by trained research assistants performing all assessments according to the guidelines of the study manual. Yearly instructions for exact measuring techniques according to the study manual were performed over the complete study period. During this time less than 11% of the trained staff changed and as the mean WC values/year of the children were stable throughout 10 years (56.16±6.24;56.42±8.11;57.61±6.49;57.95±6.65; 58.10±7.28; 58.46±7.61; 58.03±7.31; 56.49±5.95; 57.53±6.77; 56.65±6.45, with a total mean of 57.33±6.75 cm), all data were considered as a whole. Age- and gender-specific percentile curves were used for BP (16), BMI (17), WC (18) and Lipids (19,20). Venous blood was taken after an overnight fast in central school buildings. Aliquots were stored either at -80° Celsius for later measurements or at 4° Celsius for lipid measurements within the following 3–4 days. As previously described, fasting blood glucose and lipid profile were measured under standard protocols (13,14).

The CASPIAN Study

A trained team of health care providers and nurses conducted physical measurements in schools. For blood sampling, students were invited to the nearest health center to the school. The students were instructed to fast for 12 hours before the screening; compliance with fasting was determined by interview on the morning of examination. While one of the parents accompanied his/her child, blood samples were taken from the ante-cubital vein between 8:00 to 9:30 am. Considering that collecting data of high quality was critical to the success of this multi-center project, the Data and Safety Monitoring Board of the project has taken into account different levels of quality assurance and quality control. In addition to training; a detailed operation manual was developed and distributed among the project team. A supervisor and a team of external evaluators nominated by the two collaborating ministries, regularly monitored the performance of the personnel, checked and calibrated equipment according to standardized protocols. Repeat studies were designed and conducted at specified time points on a sub-sample of the students studied (11,12).

Belo Horizonte Heart Study

All methods were similar to the two aforementioned studies (11–14); however, for logistical reasons and that many of the students in the random classroom

Table I. Metabolic syndrome components (mean ± SD) in children and adolescents from Brazil, Iran and Germany: The BIG Study.

	Brazil		Iran		Germany	
	Males	Females	Males	Females	Males	Females
Age 6 to <10 years						
	n=241	n=223	n=757	n=859	n=1 220	n=1 173
Mean age, years	7.9 ± 1.0	7.9 ± 0.9	7.7 ± 1.0	7.7 ± 1.0	7.6 ± 1.1	7.7 ± 1.1
Waist circumference, cm	59.2 ± 7.2	58.0 ± 6.8	58.6 ± 7.3*	57.0 ± 7.2	59.3 ± 6.0*	58.3 ± 6.2
Systolic blood press, mm Hg	104.3 ± 14.0	105.3 ± 15.1†	96.1 ± 12.6*¶	92.6 ± 11.4¶	103.4 ± 7.9*	102.3 ± 8.2
Diastolic blood press, mm Hg	65.5 ± 11.1	68.1 ± 12.3†	59.5 ± 10.3*¶	57.5 ± 10.4¶	65.9 ± 7.4*	65.1 ± 7.6
Triglycerides, mmol/l	1.08 ± 0.6	1.06 ± 0.5†	1.03 ± 0.5‡	1.03 ± 0.5‡	0.67 ± 0.25‡	0.7 ± 0.2*‡
HDL-Cholesterol, mmol/l	1.21 ± 0.2†	1.1 ± 0.02	1.1 ± 0.3‡	1.1 ± 0.3‡	1.50 ± 0.31*‡	1.4 ± 0.3‡
Fasting plasma glucose, mmol/l	NA	NA	4.5 ± 0.6*	0.4 ± 0.5	4.69 ± 0.4*	4.5 ± 0.6
Age 10 to <16 years						
	n=255	n=290	n=1 216	n=1 392	n=1 938	n=1 709
Mean age, years	13.0 ± 1.7	13.2 ± 1.7	12.6 ± 1.7	12.6 ± 1.7	12.2 ± 1.7	12.2 ± 1.7
Waist circumference, cm	68.4 ± 10.0*	65.7 ± 8.1	67.5 ± 9.8*	66.3 ± 9.1	69.9 ± 8.9*	68.0 ± 9.1†
Systolic blood press, mm Hg	109.3 ± 14.2*	107.0 ± 12.9	103.5 ± 13.0*‡¶	99.2 ± 12.4‡¶	110.0 ± 10.2*‡	107.6 ± 9.3‡
Diastolic blood press, mm Hg	65.4 ± 10.6	65.6 ± 10.2	64.3 ± 10.8*‡	62.2 ± 10.4‡	69.6 ± 7.6*†‡	68.4 ± 7.7‡
Triglycerides, mmol/l	1.03 ± 0.6*†¶	0.9 ±0.4†¶	1.22 ± 0.48¶‡	1.1 ± 0.53*¶‡	0.74 ± 0.32‡	0.8 ± 0.3*‡
HDL-Cholesterol, mmol/l	1.1 ± 0.2	1.2 ±0.2	1.1 ± 0.3*‡	1.1 ± 0.3‡	1.44 ± 0.31*†‡	1.4 ± 0.2‡
Fasting plasma glucose,mmol/l	NA	NA	4.5 ± 0.5	4.5 ± 0.5	4.7 ± 0.5*	4.6 ± 0.6

*p<0.05 for gender, †p<0.05 for Germany vs. Brazil, ‡p<0.05 for Germany vs. Iran, ¶p<0.05 for Iran vs. Brazil data; NA: not available.

Table II. Prevalence (%) of the metabolic syndrome components [a] in children and adolescents from Brazil, Iran and Germany: The BIG Study.

	Brazil		Iran		Germany	
	Males	Females	Males	Females	Males	Females
Age 6 to <10 years						
	n=241	n=223	n=757	n=859	n=1 220	n=1 173
WC>90th percentile	4.4*†	0.9*†	10.9*¶	8.0*¶	8.7†	9.3†
SBP>95th percentile	4.3	4.1	0.2	0.0	4.5	4.4
DBP>95th percentile	4.8*	10.6*	0.3	0.5	4.8	4.6
HDL-C<1.03 mmol/l	27.4*†¶	30.4*†¶	38.8‡¶	38.3‡¶	4.8*†‡	9.5*†‡
TG>90th percentile	10.9*†¶	12.1*†¶	5.5‡¶	6.6‡¶	0.3†‡	0.8†‡
FPG>5.6 mmol/l	NA	NA	5.2‡	3.1	3.1‡	3.0
Metabolic syndrome	NA	NA	1.1‡	1.1‡	0.0‡	0.3‡
Age 10 to <16 years						
	n=271	n=298	n=1 216	n=1 392	n=1 938	n=1 709
WC>90th percentile	16.1*	8.9*	10.5¶	9.0	8.8	9.7
SBP>130 mm Hg	8.0*	4.1*	1.2	0.8	2.9	1.3
DBP>85 mm Hg	3.1	3.8	2.0	0.7	1.6	1.6
HDL-C<1.03 mmol/l	33.3*†¶	23.4*†¶	35.9*‡¶	41.1*‡¶	7.7†‡	6.6†‡
TG>1.7 mmol/l	11.0†¶	9.7†¶	8.9*‡¶	12.4*‡¶	1.4†‡	2.5†‡
FPG>5.6 mmol/l	NA	NA	3.9‡	4.0	6.1*‡	4.7*
Metabolic syndrome	NA	NA	2.0‡	2.1‡	0.5‡	0.5‡

a: Based on the definition of International Diabetes Federation for the metabolic syndrome in the pediatric age group (6).
WC: Waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: high density lipoprotein-cholesterol; TG: triglycerides; FPG: fasting plasma glucose; NA: not available.
*p<0.05 for gender, †p<0.05 for Germany vs. Brazil, ‡p<0.05 for Germany vs. Iran, ¶p<0.05 for Iran vs. Brazil data; NA: not available.

selection attended school in the afternoon or at night, non-fasting venous blood sample was collected and FBG could not be determined (10,21). Serum lipid profile was analyzed by Cobas Mira Plus (Roche Corp.) in accordance with the protocols of the National Cholesterol Education Panel.

Statistical analysis

The Statistical Package for the Social Sciences version 15.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. Continuous variables are presented as mean ± standard deviation, SD, and

Table III. Pearson Correlation coefficients between the triglycerides to HDL-C ratio and components of the metabolic syndrome [a] in children and adolescents from *B*razil, *I*ran and *G*ermany: The BIG Study.

	WC	BMI	SBP	DBP	FPG
Age 6–<10 years					
Males					
Brazilian	0.085	0.097	-0.017	-0.007	NA
Iranian	0.285**	0.172*	0.024	0.028	0.018
German	0.148**	0.132*	0.018	0.041	0.029
Females					
Brazilian	0.044	0.013	0.030	0.016	NA
Iranian	0.291**	0.287*	0.031	0.027	0.021
German	0.273**	0.264*	0.125⋆	0.134*	0.034
Age 10–<16 years					
Males					
	0.136*	0.142*	0.098	0.085	NA
Brazilian	0.404**	0.395*	0.041	0.046	0.054
Iranian	0.347**	0.364*	0.155*	0.099*	0.130
German		0.130			
Females					
Brazilian	0.254**	0.231**	0.137*	0.060	NA
Iranian	0.445**	0.401**	0.069	0.078	0.041
German	0.270**	0.258**	0.159*	0.121*	-0.023

a: Based on the definition of International Diabetes Federation for the metabolic syndrome in the pediatric age group (6).WC: Waist circumference; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: high density lipoprotein-cholesterol; TG: triglycerides; FPG: fasting plasma glucose; NA: not available.*p<0.05, **p<0.01.

categorical variables as frequencies. Variables were assessed for normality. The categorical variables were compared by using the Chi-square test. Analysis of variance (ANOVA) with post-hoc Bonferoni test was used for comparison of continuous variables; the Kruskal-Wallis test was used for comparison of TG that had a non-normal distribution. The significant level was set at $p<0.05$. The association of the ratio of TG to HDL-C, as a surrogate marker of insulin resistance, with the MetS components was determined in each ethnic group by the Pearson correlation test.

Results

The mean levels of the MetS components in children and adolescents are presented in Table I. Among the 6–10-year-old children, German and Iranian boys had significantly higher mean WC, SBP, DBP and FPG values than girls. The mean WC was not significantly different between German and Brazilian children, but BP was significantly higher in Brazilian girls than other children. In both genders, HDL-C was significantly higher and TG levels were significantly lower in German than in Brazilian and Iranian children. Among 10–16-year-old adolescents, SBP, DBP and HDL-C were significantly higher in German than Brazilian and Iranian adolescents. Iranian adolescents of both genders had the highest TG levels. FPG was lower in Iranian than German participants, but was not determined in Brazilian youths.

The prevalence of the MetS components among the children and adolescents of the three ethnicities is presented in Table II. It shows that the prevalence of low HDL-C and of increased TG was significantly higher in Brazilian and Iranian children and adolescents than in their German counterparts. The prevalence of low HDL-C was significantly higher in Iranian than Brazilian children and adolescents. Among children, the prevalence of increased TG was significantly higher in Brazilian than Iranian children, but this difference was not significant among adolescents. While the prevalence of increased WC was higher in German than Brazilian children, this prevalence was significantly higher in Brazilian than Iranian and German adolescents. High BP was rare in Iranian children and adolescents, and its prevalence decreased from childhood to adolescence in German youths. The prevalence of high FBG was low in Iranian and German youths (not measured in the Brazilian participants). Both in children and adolescents, the prevalence of the MetS was significantly higher in Iranian than German participants.

TG to HDL-C ratio had significant correlations with WC and BMI in Iranian and German children of both genders, with higher correlation coefficients in Iranian than German participants. These correlations were significant among both genders of adolescents in the three ethnic groups, with highest correlation coefficients documented in Iranian followed by German and Brazilian adolescents. TG to HDL ratio was correlated with SBP and DBP of German children and adolescents of both genders, as well as with SBP of Brazilian females (Table III).

Discussion

The *BIG* Study is the first study of its kind to present the prevalence of the MetS components in children and adolescents of European, Asian and South-American ethnicities. The use of the uniform IDF definition for the MetS components in the pediatric age group (6) in this study allows ethnic comparisons between three large population-based samples of children and adolescents. Our findings revealed that the prevalence of the MetS components differ among children and adolescents of the three ethnicities studied, with special concern in the context of low HDL-C and high TG levels, as well as abdominal obesity. While among Brazilian participants, the prevalence of increased WC was 4–9 fold higher in adolescents than in children, and there was large variation in this prevalence from low levels (1%) in female children to high levels (16%) in male adolescents, this prevalence was nearly similar (~9%) in German and Iranian children and adolescents of both genders. This is consistent with previous findings in German and Iranian children (19). Prevalence rates of increased WC among youths are described for Iranian from 8.5% (22) to 10% (23), European (female 19%, male 16%) (24), and British (male 28%, female 38%) (25) adplescents. American adolescents from NHANES 1999–2004 data had a prevalence of abdominal obesity of 26% for white, 27% for African and 33% for Mexican Americans (26). Uniform, universally acceptable criteria for abdominal obesity in children and adolescents need to be defined for this emerging public health concern. It may be clinically useful to routinely measure WC in the pediatric population as a screening tool to identify high-risk youths.

The most remarkable ethnic difference documented in this study is the high prevalence of low HDL-C levels in Iranian children and adolescents (~38%) compared with German youths (~7%). This corresponds with prevalence data in Turkish youths (27) for low HDL-C (13%) and elevated triglycerides

(27%), which is a typical lipid constellation for this region (2). The prevalence of hypertriglyceridemia was higher in Iranian than German children and adolescents, this prevalence was higher in Brazilian than Iranian children of both genders, as well as in Brazilian than Iranian male adolescents. The prevalence of low HDL-C was higher in Iranian followed by Brazilian and German children and adolescents. In general, Brazilian youths had a high prevalence of low HDL-C and increased TG, which is comparable to children and adolescents from the Middle East. Both in children and adolescents, the prevalence of the MetS was significantly higher in Iranian than German participants, the most frequent components were low HDL-C and hypertriglyceridemia. The considerably higher prevalence of these lipid disorders in Iranian children and adolescents is consistent with several large studies in the Middle-Eastern populations of various age groups [9,28–30]. A recent study demonstrated significant association between migration from Iran to Sweden and the prevalence of hypertension and smoking, but not low HDL-C and hypertriglyceridemia (31), which might provide further confirmatory evidence on the ethnic predisposition to this type of dyslipidemia. However, taking into account the association of environmental and lifestyle factors with MetS and its components even from childhood [12,22,32,33], the role of such factors should be determined in future comparisons between different ethnic groups.

We could not assess insulin resistance in the large sample size studied, but we assessed the correlations between components of the MetS with TG to HDL ratio, which is shown to be associated with insulin resistance and intraperitoneal fat among obese adolescents (34).

In our previous study in a subgroup of PEP participants, consisting of 145 boys and 147 girls aged 3–11 years, and 240 male and 269 female adolescents aged 12–18 years, we examined fasting serum insulin and determined insulin resistance by calculating the HOMA-IR index. We found that the TG to HDL-C ratio was significantly higher in insulin resistant boys (1.37±0.9 vs.1.06±0.5) and girls (1.66±0.9 vs.1.11±0.4) aged 3–11 years, as well as in insulin resistant male (1.66±0.9 vs.1.36±0.6) and female (1.56±0.8 vs.1.44±0.8) adolescents than in their non-insulin resistant counterparts. Hence, we suggested that the TG to HDL-C ratio can be considered as an appropriate surrogate measure of insulin resistance in children and adolescents (35). In the current study, we found a significant correlation between this ratio and the WC and BMI of Iranian and German children, as well as adolescents in the three ethnic groups. The higher correlation of this surrogate measure of insulin resistance with measures of abdominal and generalized obesity in Iranian children and adolescents than the two other ethnicities might be an expression of ethnic predisposition of Asians to MetS.

Contrary to the noticeably high prevalence of dyslipidemia in the current study,other components were not common, e.g., high BP was lowest in Iranian children (<1%) and adolescents (<2%), and comparably higher in German and Brazilian children (<5%) and adolescents (1.3 to 8.0%). The prevalence of high FPG ranged between 3% and 6% in German and Iranian youths.

Study limitations and strengths

The main limitation of this study is its cross-sectional nature; data from longitudinal studies will be needed to address the clinical importance of the ethnic differences documented in this study. In addition, we did not present the lifestyle habits that might be related to differences in the prevalence of the MetS components in the three populations under study; however, our findings are consistent with ethnic-differences previously documented among adult populations. A further limitation is the non-fasting blood sampling; though some data demonstrate that non-fasting lipid profile might be internationally acceptable to predict cardiovascular disease (21,36). As glucose values are missing in Brazilian youths, the prevalence of the MetS based on the IDF definition could not be provided. Given that we could not assess the pubertal stage in such a large population, the influences of puberty on the MetS components could not be determined. The strengths of this study are the large numbers of population-based samples of children and adolescents from three continents, the similar time of data collection (as pointed out, the longer period in the PEP study was unbiased) and the uniform definition of the MetS components, which allows the global comparison of different ethnicities.

Conclusion

Based on the data of more than 11 000 youths from three ethnicities, while the prevalence of abdominal adiposity was similar, Iranian and Brazilian youths had considerably higher prevalence of dyslipidemia in terms of low HDL-C and hypertriglyceridemia, i.e., the components of the MetS, than German youths.

Future longitudinal studies including genetic examinations should seek to better characterize the nature of the ethnic differences documented in this study, and to determine their clinical importance.

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