Metabolic Level and Hypothalamic-Pituitary-Gonadal Axis (HPGA) Function in Prepubertal Male Children with Simple Obesity and Sexual Retardation

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Abstract

With the increasing morbidity of obesity in children and adolescents in worldwide,more and more diseases are recognized by people. Our aim was to study the effects of obesity on metabolic level and hypothalamic-pituitary-gonadal axis function in prepubertal males.Ninety-two patients participated in our study and then were divided into two groups according to whether the peak value of LH was less than 4.8 mIU/ml in Gonadotropin-releasing hormone(GnRH) stimulation test. All of them were underwent a comprehensive physical examination,laboratory tests and imaging examinations.The obesity with sexual retardation group in bone age, BMISDS, blood pressure, testicular volume and penile length, IGF-1SDS, HOMA-IR, AST, ALT, HDL-C, LDL-C and triglyceride were significantly different from control group ($P < 0.01$).There were significant differences in age, BMISDS, diastolic blood pressure, penile length and HDL-C between normal HPGA group and hypogonadotropic hypogonadism(HH) group ($P < 0.01$).FSH and INB had statistical differences before and after human chorionic gonadotropin (HCG) stimulation test between the two groups($P < 0.05$), while T and DHT had statistical differences after the test ($P < 0.01$). Conclusion Prepubertal obesity can cause metabolic disorders and increase the risk of metabolic syndrome, and lead to sexual retardation.

Background

Obesity has become one of the most common chronic diseases among children and adolescents since the 1980s, which seriously affects their growth and development.[1]. According to statistics, the overweight rate of children over the age of 7 has increased from 2.1% to 12.2%, while the obesity rate has increased from 0.5% to 7.3%the corresponding number of overweight and obesity has increased from 6.15 million to 34.96 million in the past 30 years in China[2]. Simple obesity is a state of excessive accumulation of adipose tissue in the whole body caused by many factors, such as excessive energy intake, metabolic disorder and insufficient energy consumption and so on. The incidence of obesity-related diseases in children is also increasing, such as hyperinsulinemia, type 2 diabetes mellitus, obesity sleep apnea syndrome, non-alcoholic fatty liver disease (NAFLD) and so on. Studies have shown that obesity can also lead to abnormal sexual development in male children [4], with the clinical manifestations of small penis, small testicles, gynecomastia and so on. The purpose of this article is to study the metabolic levels of prepubertal obese boys with sexual retardation, and to analyze the effect of obesity on HPGA function, so as to guide the clinical treatment.

Methods

Studied subjects

The objectives were recruited from the Department of Pediatrics of Shandong Provincial Hospital between July 2016 to November 2018. The inclusion criteria included1) age between 7 and 11 years; 2) body mass index (BMI) exceeded the 95th percentile for age and sex[5]; 3) with micropenis (length less than 2.5 standard deviation of the average value of the same age population) [6], or small testicle

(volume did not increase with age, texture was soft and scrotal development was poor) [7,8]. Finally，92 male patients were selected as the experimental group, and 93 healthy children of the same age were selected as the control group. According to whether the peak value of LH in GnRH stimulation test was less than 4.8 mIU/ml [9], the experimental group were divided into normal HPGA group (65 cases) and HH group (27 cases). Our exclusion criteria included：1) children with secondary obesity caused by inherited metabolic diseases or neuroendocrine factors; 2) children with sexual dysplasia caused by 5a-reductase deficiency, androgen receptor gene mutation and disease of HPGA itself; 3) children with infections， hepatic and renal diseases and systemic diseases.

Anthropometry

Systolic and diastolic blood pressures were measured in sitting position after having a five-minute rest in each paticipant, and we chose the average of three measurements for each of them. All of participants should be weighed with minimal clothing，and record their weitht to the nearest 0.1kg. Height measurement was concentrated in the morning, and then calculating height standard deviation scores (Ht SDS) [10] based on growth and development data of Chinese children. Although BMI is a common index for assessing obesity, it is susceptible to age and sex, so we also calculate BMISDS based on physical development data of children in China[5,11].The length of penis (the straight distance between the root of penis and the urethral orifice of penis head) was measured by vernier caliper, and the diameter of penis was measured under the coronal sulcus.

Laboratory and Imaging examinations

blood lipid, Liver function, blood glucose, insulin, insulin-like growth factor-1 (IGF-1), thyroid function，sex hormone level and chromosomes were taken on an empty stomach in the morning. The LMS method was used to calculate the standard deviation scores of IGF-1 (IGF-1 SDS)=$[(IGF\text{-}1/M)^{L}\text{-}1]/(L\ S)$ [12].Homeostasis model assessment-insulin resistance(HOMA-IR)= fasting insulin (uIU/ml) x fasting blood glucose (mmol/L)/22.5 [13], and it is an index used to evaluate insulin resistance in obese population. GnRH stimulation experiment was performed by subcutaneous injection of triproline (2.5ug/Kg, maximum dose of 100ug)，and venous blood samples were collected from 0min, 30min, 60min and 90 min for detection of FSH and LH by chemiluminescence method. HCG experiment was performed by intramuscular injection of chorionic gonadotropin (7-10 years, 1000 u/d; 10-11 years, 1500 u/d) for 5 days，venous blood samples were drawn before and after the experiment for detection of sex hormones, inhinbin B (INB) and dihydrotestosterone(DHT).The imaging examinations included abdominal and gonadal color doppler ultrasound, X-ray of left hand ,pituitary and olfactory bulb MRI.

Definition of abnormal metabolic indicators

Impaired fasting blood glucose means that fasting blood glucose (FPG) > 5.6 mmol/L. Systolic blood pressure (SBP)≥120mmHg and diastolic blood pressure (DBP)≥80mmHg can be used as warning values for hypertension in children aged 6 to 9 years，SBP≥130mmHg and DBP≥85mmHg were defined as hypertension in children aged 10 to 16 years. The standard of low high-density lipoprotein

cholesterol(HDL-C) in China is less than 1.04mmol/L. The criteria for high triglyceride lipase(TG) according to age were more than 1.13 mmol/L (0-9 years) and more than 1.47 mmol/L (older than 10 years). Abdominal obesity is a basic and necessary condition for Metabolic syndrome(MS) in children and adolescents，at the same time, it should possess at least two of the following items: hyperglycemia， hypertension，Low HDL-C and high triglyceride lipase.

Statistical method

Statistical analysis was carried out by using SPSS 23.0. Data were expressed by means ± standard deviation (SD) when normally distributed, or by median if skewed. The comparison between the two groups using two independent samples t-test or non-parametric test. Pearson analysis was used for correlation analysis, $P < 0.05$ was considered statistically significant.

Results

We assessed the metabolic levels of 92 cases patients and found a high proportion of hyperinsulinemia and fatty liver, suggesting that obesity may increase the risk of type 2 diabetes and NAFLD in this age group (Table 1).

The obesity with sexual retardation group had higher levels of bone age, BMISDS, SBP,DBP, and lower levels of testicular volume and penile length than the control group ($P < 0.01$). This shows that obesity in pre-puberty can lead to bone age advanced, but the height is not affected for the time being. Obesity can also increase the preload of the heart, causing high blood pressure, and lead to shorter penis and lagged testicular volume, which in turn affect the process of sexual development (Table 2).

There was no significant difference in free triiodothyronine(FT3), free thyroid hormone(FT4), thyroid stimulating hormone(TSH), total cholesterol, lipoprotein and free fatty acid(FFA) between the two groups ($P > 0.05$). The obesity with sexual retardation group had higher HOMA-IR, AST, ALT, LDL-C, glycerin levels, and lower IGF-1 SDS and HDL-C levels ($P < 0.01$). This suggests that obesity can affect the expression of IGF-1, increase insulin resistance, cause liver damage and dyslipidemia (hypertriglyceridemia, low HDL-C). The levels of progesterone and testosterone in obesity group were significantly lower than in control group ($P < 0.01$), which indicated that obesity could reduce the level of testosterone and lead to the backwardness of sexual characteristics (Table 3).

GnRH stimulation test is an experimental method to evaluate reserve function of pituitary gonadotropin. Based on the peak value of LH, we divided the obesity with sexual retardation group into two groups again. As shown in Table 4, the BMISDS, DBP and HDL-C in HH group were significantly higher than normal HPGA group ($P < 0.01$), while age and penile length were lower. The remaining indicators were meaningless between them. The results may indicate that the earlier weight gain and the higher BMI index, the more serious the effect on HPGA(Table 4).

HCG stimulation test was used to evaluate testicular function. Before the experiment, FSH, LH and INB in normal HPGA function group had statistical differences compared with HH group ($P < 0.05$), while E2, P, T, PRL and DHT had no statistical difference ($P > 0.05$). After the test,we found there was also significant differences in T and DHT between them ($P < 0.01$), but there was no significant differences in LH, E2, P and PRL. These results suggest that obesity can lead to the decrease of T level by inhibiting the release of pituitary gonadotropin, thus affecting testicular function, but whether this effect is reversible needs to be further explored. INB is superior to DHT as a sensitive index for early evaluation of testicular function.

Pearson correlation analysis was used to evaluate the relationship between penile length and metabolic parameters. The results showed that penis length was positively correlated with IGF-1SDS ($P < 0.001$, $r = 0.310$), HDL-C ($P < 0.001$, $r = 0.240$), negatively correlated with BMISDS ($P < 0.001$, $r=-0.834$), SBP（$P < 0.001$，$r=-0.430$）DBP ($P < 0.001$, $r=-0.475$), HOMA-IR ($P < 0.001$, $r=0.470$), AST ($P < 0.001$, $r=0.266$), ALT ($P < 0.001$, $r=0.330$), GGT ($P<0.001$, $r=-0.388$), LDL-C ($P<0.05$, $r=-0.188$) and TG ($P<0.001$, $r=-0.311$),and was no correlation with CHOL and FFA (Table 6).

Discussion

Simple obesity not only affects the 24-hour serum concentration of growth hormone(GH), but also reduces its secretion peak [14]. BMI is inversely proportional to GH peak [15]. GH plays its physiological role through IGF-1. At present, there is no unified conclusion about the statistical correlation between BMI and IGF-1 [16,17]. For these obese pre-adolescent patients, we found that their BMI is negatively correlated with IGF-1. Obese children usually show accelerated linear growth and advanced bone age, but lifelong height will not be impaired [18]. This may be related to the increased binding rate of GH to its receptor due to insulin resistance induced by obesity [19]. Our results also show that obese patients have advanced bone age, but there is no significant acceleration of growth at present. Previous view suggested that thyroid dysfunction could lead to obesity, clinical studies [20-21] also found that TSH levels were increasing in obese children and adolescents. However, after treatment with thyroid hormone, the body condition of them did not change [22]. On the contrary, thyroid function returned to normal after weight loss[23]. Therefore, it is speculated that thyroid dysfunction is the result of obesity rather than the cause. There is no difference in thyroid function between obese patients and control group according our study , and it may be related to small sample capacity, so further research is needed.

Obesity is considered to be the strongest risk factor for hypertension in children and adolescents. Excessive secretion of inflammatory cytokines from adipose tissue, increased vascular resistance and atherosclerosis can lead to systolic and diastolic dysfunction of the heart [24]. We found that the systolic and diastolic blood pressures of obese pre-adolescent boys were higher than healthy children, so for the former, although there may be no clinical symptom, the cardiovascular disease has already happened.

Obesity can reduce the number of insulin receptors on the peritoneum of target cells, thus leading to hyperinsulinemia and insulin resistance [25]. Free fatty acids (FFA) and lipid intermediates activate

insulin receptors and protein kinase C and phosphoserine residues on their substrates, thereby impairing tyrosine phosphorylation and increaseing insulin resistance step by step.

Liver can counteract the increase of FFA by enhancing synthesis of cholesterol and resynthesis of TG, producing very low density lipoprotein and so on, which leads to the deterioration of blood lipid circulation [26]. This disorder eventually leads to the occurrence of MS. Its significant features include impaired glucose tolerance, insulin resistance, hypertension, obesity and dyslipidemia (low HDL-C, high triglyceride) [27]. We also confirmed that HDL-C in obese patients was significantly lower, LDL-C, triglyceride and HOMA-IR levels were higher than control group. Because the physiological characteristics of children under 10 years old change rapidly, it is not easy to diagnose MS [28]. There were 59 obese patients over 10 years old in our study, 11 of whom were MS (18.6%).

NAFLD is regarded as a manifestation of MS in the liver [29]. It is closely related to the decrease of insulin sensitivity, the increase of gluconeogenesis, the impaired insulin response to inhibiting gluconeogenesis and the impaired fatty acid oxidation [30,31]. It includes a series of histological spectra from simple steatosis to nonalcoholic steatohepatitis, advanced liver fibrosis and cirrhosis[32]. It is reported that the incidence of NAFLD in Chinese children is 3.4%[33], while in overweight and obese children, the incidence is as high as 50-80%[34]. Long-term development is bound to affect their liver metabolic function.

At present, serum ALT and AST levels are still important indicators for screening NAFLD in overweight or obese children [35]. Fatty acid infiltration and inflammatory stimulation can lead to liver injury, which results in the increase of these enzymes. We found that the levels of ALT and AST in obese patients are significantly higher than in control group, which also confirms the above viewpoint. Recent studies have found that serum levels of these enzymes are positively correlated with multiple components of MS, such as the increase of ALT was positively correlated with the increases of TG, glucose, DBP and the decrease of HDL-C[36]. GGT is also a marker of liver function,which is associated with obesity, hypertension, hyperinsulinemia, dyslipidemia, inflammation and oxidative stress [37,38,39]. This indicates that there may be a pathogenic relationship between fatty liver disease and vascular endothelial function.

Obesity can decrease the levels of GnRH secreted by hypothalamus or FSH and LH secreted by pituitary, which can affect the reproductive function of men,but the specific mechanism is still unclear. The serum level of testosterone is directly related to the degree of male sexual development. At present, there are different opinions on the effects of obesity on the sexual development of boys. Denzer et al. found that there was no difference in the age of pubarche and gonadarche between obese boys and normal children through a study of 1232 obese patients (582 males) aged between 6 and 18 years, so they did not support the viewpoint that weight gain would affect testicular volume. They also found that T level was decreased between 8 and 10 years [40]. However,some studies have suggested that obesity can reduce the levels of testosterone and dehydroepiandrosterone sulfate (DHEAS) [41], which leads to the sexual retardation of adolescent males, and BMI is negatively correlated with T level. Our results show that T level of obese patients in pre-puberty is significantly lower than that of normal children of the same age, which may delay the development of penis and testis, but the consequences of this effect in adolescence

or adulthood need to be further studied. The low concentration of T in obese patients may be related to the transformation of testosterone to estrogen promoted by aromatase in peripheral adipose tissue[42,43], but we found that there was no significant difference in estrogen levels between obese patients and normal children of the same age. This may be associated with the reduction of androgen production by testicular Leydig cells because of insulin resistance, but the mechanism is not clear [44].

Studies have found that insulin sensitivity, LH, FSH and sex hormone binding globulin (SHBG) increased significantly in obese children during weight loss[45]. It is speculated that HH in males may be the result of insulin resistance acting on the level of GnRH neurons [46,47]. Animal studies have shown that selective deletion of insulin receptors in mouse neurons could lead to HH [48]. In order to understand the effect of obesity on HPGA function, GnRH stimulation test was conducted in all obese patients. According to whether the peak value of LH was less than 4.8 IUL, 27 cases of HH were found. Through their comparative analysis, we hypothesized that the earlier the weight gain, the greater the BMI, and the more severe inhibition of secretion function of HPGA. Although there was no significant difference in basic T level between the two groups, the penile length of the HH group was smaller. Of course, this did not exclude the age factor. Leydig cells secrete testosterone, which is converted into DHT by 5a-reductase. Both of them can bind to receptors of penile target cells, thus promoting penile growth and development. INB is a kind of diglycopeptide hormone produced by testis Sertoli cells under the action of FSH. It is a functional marker of Sertoli cells. The decrease of its serum level is related to the abnormal production of spermatozoa [49]. HCG test is usually used to evaluate testicular function. Through our data analysis, we found that the levels of T and DHT in HH group were still low after the test, which indicated that obesity not only affected the hypothalamic-pituitary secretion function, but also directly reduced testicular function. There was significant difference in INB between the two groups before and after HCG test, which suggests that INB can be used as a marker for early assessment of testicular function to guide our clinical treatment.

Conclusions

Overweight and obesity in childhood not only affect the function of various organs and systems, but also lead to diseases such as type 2 diabetes mellitus, myocardial infarction, liver fibrosis and even cirrhosis in the long term [50]. So we should pay more attention to this part of the population. According to our data, although there are no obvious abnormal clinical symptoms in prepubertal obese children, the risk of MS has been exposed. If not given timely treatment, it will affect the quality of life in adolescence and even adulthood. At present, we have confirmed that obesity can affect the pituitary and testicular function of obese children in pre-puberty, but the changes of their external genitalia and sex hormone levels in adolescence need further observation and research.

Abbreviations

HPGA,hypothalamic-pituitary-gonadal axis;GnRH, gonadotropin-releasing hormone; HCG,human chorionic gonadotropin; BMISDS,body mass index standard deviation scores; HtSDS, height standard

deviation scores;IGF-1,Insulin-like growth factor-1; HOMA-IR, homeostasis model assessment-insulin resistance; P,progesterone; E2,estrogen;FSH,follicle-stimulating hormone;LH,luteinizing hormone; T,testosterone;PRL,prolactin;INB, inhinbin;DHT, dihydrotestosterone; FPG,fasting blood glucose;SBP,systolic blood pressure;DBP, diastolic blood pressure;HDL-C,low high-density lipoprotein cholesterol;TG, triglyceride lipase; FT3,free triiodothyronine; FT4, free thyroid hormone;TSH,thyroid stimulating hormone;MS,metabolic syndrome; FFA,free fatty acid;LDL-C,low-density lipoprotein cholesterol;ALT,alanine aminotransferase;AST, valley grass transaminase.

Declarations

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Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

SG designed the project, collected and analyzed data, and finally drafted the initial manuscript.GL contributed substantially to the project design and revised the manuscript critically.PS contributed significantly to the data collection.QY,XS and YS contributed significantly to revision of the manuscript. All the authors endorsed the project and approved the final manuscript.

Ethics approval and consent to participate

The Ethics Committee Of the Shandong Provincial Hospital Affiliated to Shandong University approved the study protocol. All participants were informed of the purpose of the study, and all data were collected with the consent of their parents.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table1. Classification and proportion of abnormal metabolic levels in obese children with sexual retardation.

	case	proportion
Low HDL-C	17	18%
Hypertriglyceridemia	19	21%
Impaired fasting glucose tolerance	9	10%
Hyperinsulinemia	48	52%
Hepatic lesion	35	38%
Fatty liver	49	53%
Hepatic lesion and fatty liver	24	26%
Metabolic syndrome	11	18.6%
Hypertension	30	32.6%

Table2. Comparison of clinical characteristics of the subjects.

	obesity with sexual retardation group （n=92 cases）	control group （n=93 cases）	P value
Age(years)	9.81±1.20	9.47±1.22	0.058
Bone age(years)	10.94±2.11	9.41±1.40	<0.001*
HtSDS	0.86±1.16	0.87±0.79	0.939
BMI SDS	2.79±0.73	-0.036±0.25	<0.001*
SBP（mmHg）	118.71±9.03	107.05±9.57	<0.001*
DBP（mmHg）	78（59-109）	68（44-88）	<0.001*
Testicular volume（cm^3）	1.51±0.90	2.56±0.79	<0.001*
Penis length（cm）	2.48±0.64	4.34±0.47	<0.001*
Penis diameter（cm）	1.23±0.37	1.27±0.25	0.086

*P<0.05

Table3. Comparison of metabolic level and basic sex hormones in subjects

	Obesity with sexual retardation group （n=92 cases）	control group （n=93 cases）	P value
IGF-1 SDS	-0.27±1.14	0.74±1.19	<0.001*
HOMA-IR	4.84（0.49-18.52）	1.79（0.33-4.23）	<0.001*
FT3（pmol/L）	6.46±0.86	6.49±0.61	0.887
FT4（pmol/L）	17.15±2.56	17.53±2.62	0.513
TSH（μIU/ml）	2.72（1.10-9.83）	2.82（1.02-9.03）	0.303
AST（U/L）	36.41±21.88	26.02±6.53	<0.001*
ALT（U/L）	30（11-341）	14（8-39）	<0.001*
GGT（U/L）	31.09±23.81	14.80±4.53	<0.001*
TC（mmol/L）	4.44±1.04	4.34±0.78	0.459
HDL-C（mmol/L）	1.28±0.31	1.46±0.37	<0.001*
LDL-C（mmol/L）	2.44（1.02-5.42）	2.35（1.18-4.52）	0.009*
TG（mmol/L）	1.25±0.60	0.86±0.39	<0.001*
Lipoprotein（g/L）	0.09（0.01-0.96）	0.11（0.002-0.67）	0.219
FFA（mmol/L）	0.7（0.24-1.81）	0.57（0.05-1.72）	0.168
FSH（mIU/ml）	2.32±1.58	2.38±1.67	0.765
LH（mIU/ml）	0.46（0.02-4.39）	0.53（0.04-6.56）	0.071
E2（pg/ml）	5.0（0.01-53.15）	5.11（0.01-41.75）	0.544
P（ng/ml）	0.48±0.46	0.68±0.56	0.024*
T（ng/ml）	0.22±0.49	0.28±0.82	0.001*
PRL（ng/ml）	10.43（3.18-43.32）	11.92（2.75-34.02）	0.576

Table4. Comparison of clinical characteristics and metabolic levels between normal HPGA group and HH group.

	Normal HPGA group (n=65 cases)	HH group (n=27cases)	P Value
Age(years)	9.99±1.20	9.37±1.08	0.008*
Ht SDS	0.86±1.14	0.85±1.12	0.984
BMI SDS	2.60±0.69	3.25±0.64	0.001*
Bone age(years)	10.90±2.12	11.06±2.14	0.816
SBP(mmHg)	117.54±8.79	121.48±9.14	0.067
DBP(mmHg)	77.58±8.20	82.92±9.06	0.010*
LH peak(mIU/ml)	10.13±5.60	1.44±0.64	0.001*
FSH peak(mIU/ml)	11.09±5.99	5.37±2.86	0.001*
Testicular volume(cm^3)	1.29(0.43-5.46)	1.08(0.49-3.69)	0.160
Penis length(cm)	2.60±0.64	2.19±0.54	0.008*
Penis diameter(cm)	1.24±0.36	1.20±0.40	0.521
IGF-1 SDS	-0.26±1.24	-0.29±0.88	0.672
HOMA-IR	5.13(0.49-18.52)	4.25(1.89-10.53)	0.186
ALT(U/L)	29(11-341)	30(13-128)	0.788
FT3(pmol/L)	6.46±0.90	6.45±0.78	0.986
FT4(pmol/L)	16.84±2.48	17.87±2.66	0.081
TSH(μIU/ml)	2.73(1.10-8.07)	2.69(1.29-9.83)	0.825
TC(mmol/L)	4.37±1.01	4.60±1.12	0.357
HDL-C(mmol/L)	1.25±0.34	1.34±0.24	0.030*
LDL-C(mmol/L)	2.59±0.64	2.61±0.78	0.890
TG(mmol/L)	1.26±0.58	1.24±0.66	0.693

Table 5. Changes of sex hormones and testicular function markers before and after HCG test

	Before HCG test			After HCG test		
	Normal HPGA group	**HH group**	P Value	Normal HPGA group	**HH group**	P Value
FSH (mIU/ml)	2.90±1.49	0.93±0.67	0.001*	1.02±0.98	0.54±0.37	0.039*
LH (mIU/ml)	0.66 (0.02-4.39)	0.12 (0.04-1.24)	0.001	0.1 (0.01-2.75)	0.21 (0.03-1.18)	0.346
E2 (pg/ml)	5.0 (0.01-53.15)	7.68 (0.01-32.8)	0.232	5.98 (2.48-45.6)	5.0 (0.01-73.29)	0.856
P(ng/ml)	0.49±0.50	0.46±0.34	0.982	0.40±0.20	0.34±0.24	0.268
T (ng/ml)	0.08 (0.01-3.41)	0.095 (0.01-0.8)	0.493	2.19±1.31	1.22±0.78	0.001*
PRL(ng/ml)	12.64±8.00	11.2±6.17	0.626	14.57±10.89	10.20±5.54	0.658
INB	78.81±39.26	49.38±26.35	0.014*	121.37±40.06	79.17±45.35	0.013*
DHT	29.48±15.44	24.30±10.68	0.413	97.38±58.21	48.30±25.23	0.004*

Table6.Correlation analysis between penile length and metabolic indexs

	P Value	rValue
BMI SDS	0.001*	-0.834
SBP	0.001*	-0.430
DBP	0.001*	-0.475
IGF-1SDS	0.001*	0.310
HOMA-IR	0.001*	-0.470
AST	0.001*	-0.266
ALT	0.001*	-0.330
GGT	0.001*	-0.388
CHOL	0.419	-0.061
HDL-C	0.001	0.240
LDL-C	0.013	-0.188
TG	0.001*	-0.311
FFA	0.433	-0.069