

Research Article**Paleo diet and its relationship with Testosterone levels*****¹ Hariharan V, ² Hempragadish. J.G**¹ Associate Professor, Department of Biochemistry, Karpagam Faculty of Medical Sciences and Research, Pollachi Main Road, Othakkalmandapam, Coimbatore² MBBS student, Department of Biochemistry, Karpagam Faculty of Medical Sciences and Research, Pollachi Main Road, Othakkalmandapam, Coimbatore**(Received: 20-07-2024****Revised: 23-09-2024****Accepted: 13-10-2024)**Corresponding Author: **Hariharan V** Email: drhariharanv@gmail.com**ABSTRACT**

Introduction: Adult-onset hypogonadism (AOH) is a disorder due to low serum testosterone levels and is seen in 50% of obese and diabetic males. In Obesity, excess adipose tissue converts Testosterone to estrogen thereby effectively lowering levels of testosterone in men. Obesity causes a reduction in levels of sex hormone binding globulin, which leads to a reduction of available testosterone. Metabolic syndrome (Insulin resistance syndrome) is a major driver of obesity and in various ways, it reduces serum testosterone levels.

Aim: This study aims to find out whether a Low carbohydrate diet like paleo diet improves metabolic syndrome components like diabetes and obesity thereby elevating serum testosterone levels in males.

Materials and methods: 44 adult males with lower testosterone levels were selected as the study population and their weights, and HbA1c were measured. A paleo diet was advised for a period of 3-6 months. After 3 months Serum testosterone, weight, and HbA1c were measured and analyzed. Student 't' test was used to compare the means before and after intervention and $p < 0.05$ was taken as statistically significant.

Results: Almost all of the participants showed significant elevation in their serum testosterone levels ($p < 0.0001$). The mean testosterone levels before dietary intervention was 218ng/dL and post diet was 366ng/dL. There is also a reduction in average weight ($p < 0.0001$) and HbA1c ($p < 0.00001$) levels.

Conclusion: Our study showed that a short-term Paleo diet improves serum testosterone levels, reduces weight and improves diabetes in adult males.

Keywords: Paleo diet, testosterone, adult onset hypogonadism, Metabolic syndrome, low carbohydrate, Insulin resistance

INTRODUCTION

The male sex organs and masculine characteristics are a product of Testosterone, a hormone produced in the Testes. The androgen-sensitive tissues like testes, Prostate gland, hair follicles, and muscle convert Testosterone into its more active androgenic form called Dihydrotestosterone (DHT), an important component in the development of external genitalia in males. As testosterone decreases, males develop features such as an abnormal decrease in sexual desire and erectile dysfunction. It also affects mood and decreases intellectual activity and spatial orientation, leading to fatigue, depression, and anger, a

decrease in lean body mass associated with a reduction in muscle volume and strength, a decrease in body hair and skin alterations, and decreased bone mineral density resulting in osteoporosis. The causes of low testosterone levels are Klinefelter syndrome, Lutuenizing hormone and Follicle stimulating hormone receptor gene mutations, androgen synthesis defects, varicocele, cryptorchidism, Kallmann syndrome, Prader-Willi syndrome, hyperprolactinemia, and chronic systemic illnesses; Acquired hypogonadism may be due to trauma, testicular torsion, drugs like alkylating agents, ketoconazole and some others [1].

But one of the most common causes of low testosterone levels is Adult-onset hypogonadism (AOH) disorder. Androgen deficiency symptoms and low testosterone levels characterize this disorder. One previous study shows that the prevalence of AOH is between 2.1% to 38.7 % in age groups of middle-aged and older men, whereas it was around 50% among diabetic and obese subjects [2]. Adipose tissue can be considered as a link between obesity and Diabetes versus low testosterone.

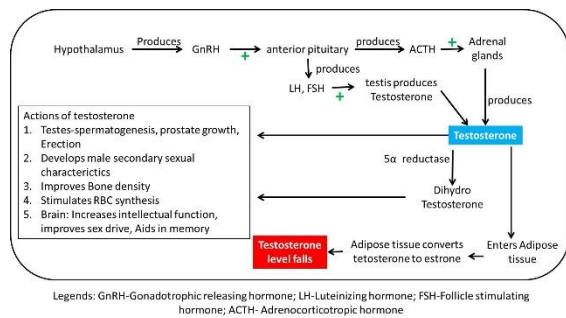


Fig. 1. Connection between adipose tissue and testosterone synthesis.

SHBG (Sex hormone binding globulin) is a protein synthesized in the liver, with a higher affinity to bind to DHT and testosterone and a lower affinity to bind to estradiol thus regulating protein-bound and free forms of these hormones. Only 1% of Testosterone is free or unbound which is active and the remaining is either bound to albumin or SHBG. When this free testosterone enters cells, almost the same amount of the hormone is released from these proteins keeping its level in equilibrium. In spermatogenesis, DHT is responsible for the maturation of sperm. Increased Adipose tissue and low SHBG levels are the major causes in decrease in testosterone production.

Metabolic diseases like obesity and those associated increased visceral fat, are correlated with decreased testosterone levels in males and SHBG levels in both males and females. Insulin resistance seen in moderate obesity is also accompanied by a decrease in SHBG levels; which in turn showed a decline in total testosterone levels ; whereas in severe obesity where adipose tissues are usually inflamed, in the insulin resistant state, increasingly expresses aromatase enzyme that converts testosterone to Estradiol leading to suppression of HPT axis,

further leading to reduced testosterone production (Fig 1).

Adult-onset hypogonadism is usually not due to a defect in the Hypothalamo-pituitary-testes (HPT) axis, instead, most of them show low SHBG levels [3]. Low SHBG levels are also seen in type 2 diabetes, dyslipidemia, and Nonalcoholic fatty liver disease (NAFLD) [4-6]. One study showed that low SHBG levels and reduced levels of testosterone are seen in patients with Hyperinsulinemia [7]. Strong associations between markers of insulin sensitivity like HDL, LDL, TG, and SHBG are seen, indicating the role of SHBG in metabolic syndrome which is a proven risk factor for obesity and diabetes. A hypothesis on elevated production of cortisol in abdominal obesity contributing to hyperinsulinemia further reducing SHBG production was also postulated [7].

Obesity, metabolic syndrome, insulin resistance, and other metabolic abnormalities alter the HPT axis by interaction with adipose tissue. Increased Adipose tissue mass and the resulting increase in cytokines like IL-1b, IL-6 (IL- Interleukins), and TNF-α (Tumor necrosis factor alpha), along with increased levels of estradiol synthesized in the adipose tissue from testosterone, using aromatase enzyme suppresses the higher centres in hypothalamus and pituitary, decreasing testosterone levels (Fig 2).

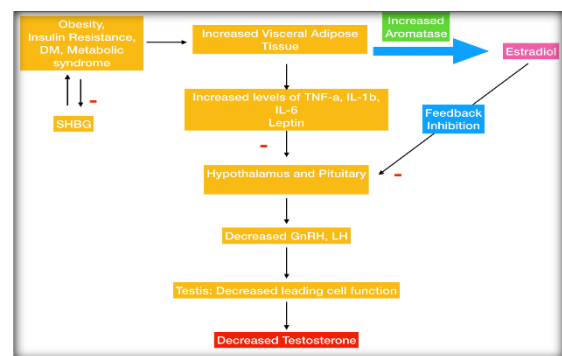


Fig. 2. Association between metabolic abnormalities and testosterone levels
Legend: DM- Diabetes mellitus; SHBG-steroid hormone binding globulin; GnRH- Gonadotrophin releasing hormone; LH- Luteinizing hormone; TNF- Tumor necrosis factor; IL- Interleukin.

Low carbohydrate diets reduce blood glucose levels and reduce weight. LCHF (low carbohydrate high fat), Paleolithic diet, Ketogenic diet, and Atkins diet are types of Low carbohydrate diets. A Very low carbohydrate ketogenic diet, has previously been shown to decrease fat mass in obese or overweight individuals. In addition, this diet strategy showed an increase in testosterone values while simultaneously increasing insulin sensitivity [8]. The possible mechanisms for higher weight loss may be controlled hunger due to the higher satiety effect of proteins, direct appetite suppressant action of ketone bodies, and changes in circulating the level of several hormones such as ghrelin and leptin which control the appetite. Other mechanisms proposed are reduced lipogenesis, increased lipolysis, reduction in resting respiratory quotient, increased metabolic costs of gluconeogenesis, and the thermic effect of proteins. A long-term Ketogenic diet (12 months or more) resulted in decreased body weight, triglycerides, and diastolic blood pressure whereas, it caused an increased HDL (High density lipoprotein) Cholesterol when compared to that of a low-fat diet. Ketone bodies can alleviate certain inflammatory processes by blocking specific cytokines [10]. Since all these metabolic and immunological processes modulate testosterone levels detrimentally, by carbohydrate restriction (paleo diet) and weight loss, it may be possible to increase testosterone levels. This study aims to find whether an Indian version of the Paleo diet improves Testosterone in adult males via the above possible mechanisms.

MATERIALS AND METHODS

This is a prospective Non-randomized interventional study, without controls done on adult males visiting the outpatient department for dietary consultations, including for weight loss at Karpagam Medical College Hospital. Among more than 1000 people, minors and senior age groups, people with a history of genital disorders, heart diseases, Chronic kidney failure were excluded from the study. All those included were tested for lipid profile, HbA1c, blood glucose

levels (fasting blood sugar-FBS), and testosterone levels.

60 people who showed low testosterone levels and satisfied the inclusion criteria were selected as the study population. A detailed history was obtained from the study participants followed by a thorough explanation of the course of the study and its implications, and advantages. An informed consent explaining the study characteristics, its many outcomes, and relatively minor downsides was obtained from the subjects, who were then enrolled in the study. The necessary anthropometric measurements were measured from the test subjects and the said results and the subject characteristics were integrated along with their biochemical laboratory parameters. They were advised to follow an Indianized version of the Paleo diet for 3 to 6 months.

A model Indian Paleo diet consists of 50-80 almonds with 30 grams of butter mixed in 200ml of milk or coffee or tea for breakfast; 4 whole eggs, 30 grams cheese with 200 grams of vegetables as lunch; Or 300 grams of vegetables with 50 grams of cheese and 50 grams of raw coconut for lunch; 150-300 grams of meat (chicken, mutton, fish, etc.) or 100-200 grams of paneer as dinner in a typical day. For the occasional snack, 100ml curd, one raw guava (100 grams), soups, lemon juice (1 or 2 lemons), and 100 grams of vegetables may be consumed. The subjects are advised to avoid all sugars, sweets, breads, biscuits, other fruits, juices, tuberous vegetables, grains, lentils, and Millets. From the above diet, the Non-vegetarian regimen yields 1640kcal/day which contains 64 grams of carbohydrates/day. The vegetarian regimen yields 1870kcal/day having 66 grams of carbohydrates /day. From the above regimen, the daily calorie requirements of participants were calculated using height and weight and quantities of each items are provided individually. They were regularly monitored via phone calls and after 3 months of diet, their weight and other measurements were done and blood tests repeated. Some followed diet for 90- days and others from 12 to 24 weeks. 16 people were excluded from the study due to poor compliance.

Weight, HbA1c and serum testosterone levels were compared before and after the dietary intervention. The data was analyzed using SPSS 20 software. Means and SD were calculated and the student's t-test was used to calculate the p-value. A 'p' value less than 0.05 was taken as statistically significant.

RESULTS

44 Adult males with testosterone levels below 250 ng/dl were our study participants. The minimum weight of participants was 58kg and maximum was 151kg. People ages ranged from 23yrs to 58 years. Only 9 had a BMI of less than 25 and others were either overweight or obese. Among 44 participants, 18 were diabetic. Many had testosterone levels between 215-235ng/dl. We not only included subjects who had testosterone lower than 250ng/dl but 6 people who had near-range testosterone levels but had a history or features of AOH (Adult onset Hypogonadism). The general characteristics and test results of subjects before dietary intervention are given in Table 1.

Table 1. General characteristics of test subjects

Total Participants	44
Mean age	42.2 ± 9 Years
Mean Diet duration	145 ± 40days
Mean Hba1c	6.69 ± 1.6 %
Weight Mean	102.1 ± 26kg
Mean Testosterone levels	218.1 ± 32ng/dl

The participants were asked to follow the diet for 3 months and asked to return for tests. Some finished the 90 day diet study and came for evaluation.

Table 2. Comparison of parameters before and after dietary intervention

	Before dietary intervention	After dietary intervention	p value
Weight in kg (mean)	102.1 ± 26	91.1 ± 22	<0.00001 (significant)
HbA1c % (Mean)	6.69 ± 1.6	5.56 ± 0.57	<0.00001 (significant)
Testosterone ng/dL(Mean)	218.1 ± 32	366.8 ± 111	<0.0001 (significant)

Others followed diet to extended periods of time and came for evaluation after that. The average duration of dietary intervention was 145 days. The Weight, HbA1c and serum testosterone showed excellent improvements..

A statistically significant mean weight loss of around 21kg, 1.1% mean reduction of HbA1c and 150ng/dL mean elevation of testosterone was observed as seen in Table 2.

The range of testosterone level before diet varied between 90-275ng/dL. After dietary intervention the levels ranged between 250-900ng/dL. The average increase in testosterone was 149ng/dl (p<0.0001) represented by Fig 3.

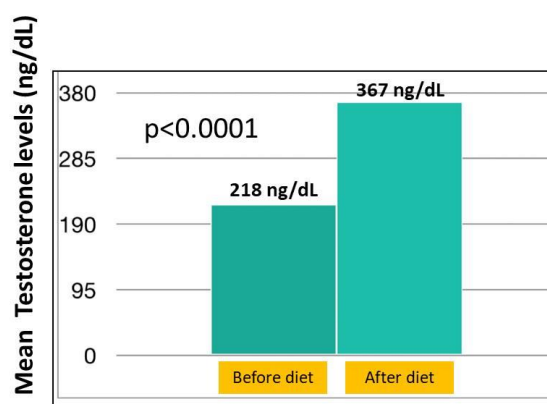


Fig 3. Mean Testosterone levels before and after Paleo diet

The increment in testosterone levels ranged from 231 ng/dl to 863ng/dl in one case and many cases show moderate increases (Fig 4). Many showed a slight increase but achieved normal ranges. Around 22 males achieved levels more than 300; 9 males had levels more than 400; and 4 males had levels more than 500. Testosterone was elevated across all age groups in the study, with most increases in patients aged 30 to 40 years.

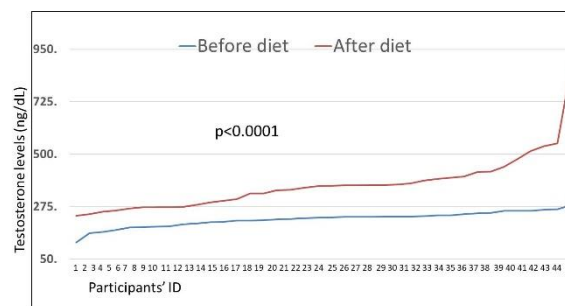


Fig 4. Testosterone levels of subjects before and after diet

Among those less than 35 years old, the increment was 196ng/dl; and between 35-45year

olds, it was 134ng/dl; and above 45 years, it was 141ng/dl. Our results show that the paleo diet for a period of 3-6 months increased testosterone levels in most study subjects.

An average of 11kg weight loss ($p < 0.00001$) among 44 men was observed in a time of 3-6 months. The minimal weight loss was 1kg and maximum was 21.5kg (Fig 5).

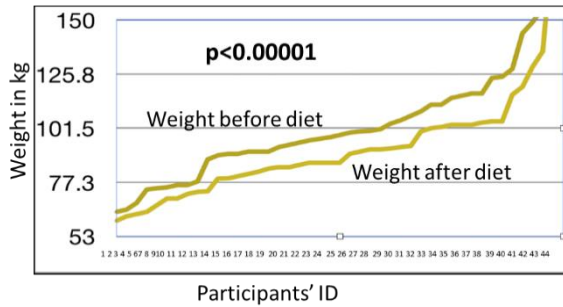


Fig 5. Weight of study subjects before and after diet

Many tapered and stopped their diabetic medicines and an average reduction of 1.3 in HbA1c level ($p < 0.00001$) was achieved (Table 2, Fig 6). The minimum HbA1c difference after and before the diet was -0.1 and maximum was 5 among all participants. The 18 diabetics enrolled in the study showed a massive reduction of mean HbA1c from 8.1 to 5.9.

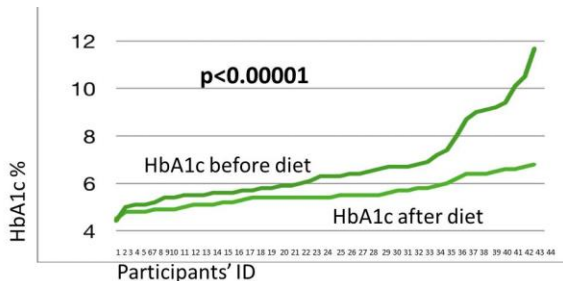


Fig 6. HbA1c before and after study

The weight loss seemed to have an opposite effect on testosterone levels. i.e. testosterone levels increased with weight loss. HbA1c reduction also showed similar effect as seen in Fig7.

Even though this study aimed to study only the link between a low carbohydrate diet versus testosterone in adult males, the results indicate that this dietary intervention has reduced weight and improved glycemic status of these individuals.

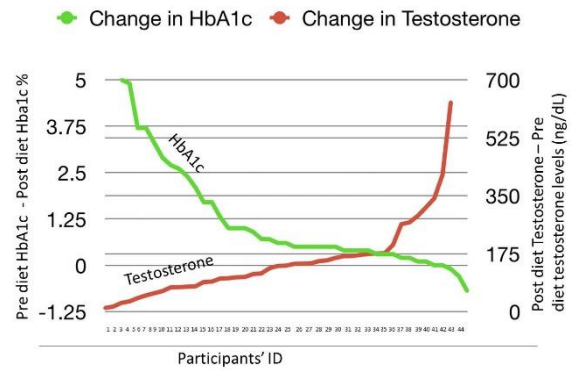


Fig 7. Change in HbA1c with respect to change in Testosterone levels

This has numerous implications. Many individuals with longterm uncontrolled diabetes also have Erectile dysfunction due to low testosterone levels. Also morbidly obese individuals tend to have a low testosterone level. From our results we can see that these two categories of men are excellent candidates to follow this dietary intervention.

DISCUSSION:

The above results show clearly that Testosterone levels were increased in most test subjects who underwent a paleo diet program for 3-6 months duration. The age group of 30-40 years of an Indian male is important in this context. Most cases of male infertility are documented in this age group and our diet delivers success where it is needed. The current diagnosis of Low testosterone levels is done mostly when couples are trying for pregnancy and fail to conceive. The cause for the decrease in testosterone levels is rarely evaluated and patients are usually advised to go for medical management. As said before, many males are afflicted with low testosterone levels and early screening for the same may benefit many because it is our understanding that low testosterone leading to symptoms of AOH takes a longer time to develop. This is from our observation that most of our test subjects showed no symptoms of AOH but had low testosterone levels. But these men will have problems in the case of fertility now and in the future. It can be understood that a paleo diet improves obesity, metabolic syndrome, and insulin resistance states and increases lipolysis; these may remove the interference with the HPT axis and raise

testosterone levels; another mechanism is that the decreased visceral adipose tissue leads to reduced conversion of available testosterone to estradiol and may have increased the testosterone levels (Fig 8). These mechanisms of increase in testosterone levels by reducing weight, improving glycemia, reducing insulin resistance is well documented [11]. During our search in this subject, we found only a few similar studies. Our findings is concurrent with a previous study done in 2023 [12], which showed an increase in testosterone levels using a low carbohydrate diet. But another study in 2022 did not found such elevation of testosterone in low carbohydrate diet [13].

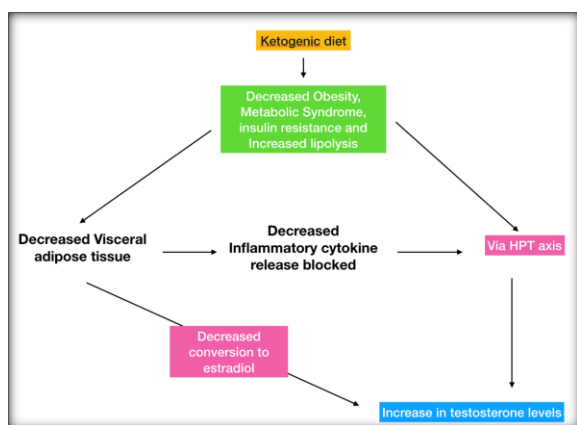


Fig 8. How Low carb diets may have improved testosterone levels

Many of our subjects lost weight. The weight loss induced by the Paleo diet may have increased SHBG and Testosterone levels, and a decrease in serum insulin and leptin levels. This is due to the modification of the HPT axis as shown in Fig 9. Weight loss also causes decreased visceral adipose tissue size and mass and this may increase the testosterone level by decreasing the conversion of testosterone to estradiol in adipose tissue. This reduction in estradiol levels may remove inhibition of the HPT axis leading to a surge in testosterone production.

Many subjects are diabetics and there seems a significant association between control of blood sugar levels versus improvement in testosterone levels. The average reduction of HbA1c is 2%. A few studies [14,15] show that an improved glycemic status of a diabetic patient may improve testosterone levels. Control of Diabetes by the

Paleo diet may improve hyperinsulinemia and thereby improve metabolic syndrome. Improvement in Metabolic syndrome may have led to improved testosterone levels. In the present study, improvement of glycemic control increased the testosterone level in a longer term of 3 months.

As said before, not everyone who had low testosterone levels had symptoms of hypogonadism. But people having low testosterone levels even without accompanying symptoms may have the advantages of improving testosterone levels like increased muscle mass and strength, decreased fat mass, improved bone mineral density, improved sexual function, mood, and a general sense of well-being. An increase in testosterone levels also improves metabolic syndrome which is a major risk factor for Diabetes, Hypertension, and heart disease [16].

The present management of low testosterone levels in males is usually oral, injectable, transdermal, and testosterone gel formulations. Testosterone replacement therapy regimen for a particular patient must be decided after a discussion between the physician, patient, and patient's caregiver by taking into consideration safety, efficacy, tolerability, availability, cost, and preference [17]. Potential benefits of testosterone replacement therapy include improved sexual desire and function, mood, energy, and quality of life, increased bone mineral density, changed body composition, improved muscle mass and strength, and cognitive functions. Potential risks include increased risk of prostate and breast cancers, worsening BPH (Benign prostatic hypertrophy), liver toxicity, gynecomastia, erythrocytosis, testicular atrophy, infertility, and skin diseases. These are the current lines of management of testosterone deficiency and dietary advice to increase testosterone levels naturally by managing causes like metabolic syndrome don't seem to exist [18]. Another advantage is that the cost of diet is far less than testosterone replacement therapy in many ways.

Sufficient evidence indicates that resistance exercises when combined with larger muscle

involvement (multi-joint movements), bigger exercise volume, sufficient intensity (moderate/high), and short resting intervals between training sets, may result in optimal acute increases in serum testosterone concentrations [19]. The immediate elevations of testosterone post-exercise and also long-term basal/resting elevations were documented [20]. But Sadly 55% Indian population does not exercise, so in such a case Paleo diet will be a boon for such people. Further long term studies in establishing the efficacy and safety of this diet.

LIMITATIONS OF THE STUDY

Our study has some limitations. First of all this is a short-term study to derive management decisions. Since we are not aiming to find out the incidence of AOH, we only used people as subjects who already had low testosterone levels and excluded normal people. We also didn't have controls such as people following a standard Indian diet or people who exercise or take testosterone replacement therapy or other such interventions. Also the long term efficacy or the safety of the diet was not determined in this study.

CONCLUSION

Dietary interventional studies are rare in India and this is one such study. This study has shed some light on the problem of decreased testosterone levels and dietary changes to prevent it. Low testosterone is fairly common and rarely diagnosed. The paleo diet effectively improves Testosterone levels as it attacks the root cause of development of the disease namely the carbohydrate intolerance in individuals. Testosterone replacement therapy which is costly, has more side effects, is only temporary, and is just a supplementation and one that does not treat the disease. Paleo diet can be an effective alternative for testosterone supplementation since it's cheap, and without major adverse events. Further studies should be done on levels of SHBG, cortisol, estradiol, free testosterone, and fatty liver in obese and diabetic individuals and their changes by following this diet compared with that of regular Indian diet, exercise, and pharmacological interventions.

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SOURCE OF FUNDS

Nil

CONFLICT OF INTEREST

The authors declare no conflict of interest

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