



Effect Of Pearl Millet (*Pennisetum Glaucum*) On Some Sex Hormones In Streptozocin Induced Rat Models Of Type-2 Diabetes Mellitus

L. O. Mallasiy, Fayza. M. EL-Ezaly

¹Muhayil Asir, Applied College, King Khalid University, Abha 61913, Saudi Arabia,

²Department of Home Economics, Faculty of Specific
Education, Mansoura University, Egypt

Abstract

This study used 30 adult albino male Sprague-Dawley strain rats to determine the therapeutic effect of Pearl Millet on certain sex hormones in a type-2 diabetes mellitus male rat model. The rats were divided into five groups of six rats each. The first, third, fourth, and fifth group rats were induced with streptozocin STZ (40 mg/kg, IP) and classed into control positive (+ve) group (fed on basal diet only), group treated with (30% pearl millet from b.w), and group treated with streptozocin STZ (40 mg/kg, IP) alone. , group treated with (60 %pearl millet from b.w) and group treated with (100 %pearl millet from b.w) .The outcomes showed that insulin glutathione reduced (GSH), catalase (CAT), and glutathione peroxidase (GPX) levels significantly decreased in the control (+ve) group. superoxide dismutase (SOD), High density lipoprotein (HDL), Dehydroepiandrosterone (DHEA), Estradiol, Progesterone, Testosterone, Prolactin (PRL), Despite a considerable rise in blood glucose, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) , Low density lipoprotein (LDL), triglyceride (TG), cholesterol (CH), and very Low density lipoprotein (VLDL) compare with control (- ve) group. While showed in (30, 60, 100% of pearl millet) significant decrease in blood glucose, LDL, TG, CH and VLDL but found significant increase in insulin GSH, CAT, GPX , SOD, HDL, DHEA, Estradiol, Progesterone, Testosterone, PRL, LH and FSH compared with control (+ ve).

Key words: Pearl millet , Streptozocin , Sex hormones, Type-2 Diabetes mellitus.

Received: 07 June 2024

Revised: 21 July2024

Accepted: 27 July 2024

1. Introduction

Diabetes mellitus has developed into a problematic and pervasive case. Improvements in dietary and lifestyle management are largely responsible for treatment techniques for diabetes prevention in both high-risk and affected persons. As a result, it's crucial to comprehend the nutritional elements that will be utilised in dietary intervention. Daily consumption of meals made from millet is linked to a lower risk of developing diabetes. Although it is only consumed by lower-class members of society, When compared to other major grains, regarding calories, protein, vitamins, and minerals, pearl millet is more nutritious. Pearl millet contains phenolic compounds with anti-diabetic properties.. (Pei et al., 2022)

Hyperglycemia, also referred to as persistently increased blood sugar levels (hyperglycemia), is a symptom of a group of metabolic diseases collectively referred to as diabetes. (Mechchate et al., 2021). It is generally known that after eating, a diabetic patient's blood glucose level increases rapidly over normal range. It is also true that whenever the body tries to store the additional glucose for later use, the level of blood glucose rapidly drops. Diabetes can be categorized into types 1 and 2. Due to the patient's pancreas' inability to make insulin, Type 1 diabetes also goes by the labels juvenile diabetes and insulin-dependent diabetes.. (Zou et al., 2018) However, the body starts to resist insulin or is unable to produce enough insulin, type 2 diabetes (T2D) typically develops in adults. (Nolan and Prentki, 2019) 90% of

people with diabetes globally have type 2 diabetes. It may be caused mostly by physical inactivity and obesity. T2D has an additional difficulty in that fewer symptoms than type 1 diabetes are reported, and it is frequently detected after side effects have already shown. **(Shen et al., 2018)**

For patients with type-2 diabetes, dietary therapies are a quick and affordable option to improve their quality of life and provide preventive advantages (Asif, 2014). Therefore, The current recommendations for type-2 diabetes advocate for adopting healthy, nutrient-rich diets, especially those with low-GI (glycaemic index) starchy carbs and high quantities of dietary fibre that can help minimise post-prandial hyperglycemia and reduce body weight. A low glycemic carbohydrate/high fibre diet has successfully improved blood glucose balance and decreased plasma cholesterol in people with type 2 diabetes.. **(Willett et al., 2002)**.

Endogenous sex hormones can signal problems with glucose control. Lower levels of sex hormone binding globulin in both men and women increase risk of metabolic syndrome and diabetes, according to cross-sectional studies, but higher levels of testosterone in men and lower levels in women increase risk of both diseases.

We describe known longitudinal research that point to comparable findings in a comprehensive review. However, these studies frequently only include one sex steroid measurement.. It is also unclear whether these correlations are primarily a measure of obesity and if there are any differences between older hypogonadal adults and younger eugonadal adults. The outcomes of exogenous sex steroid medication could not fully reflect the relationships between sex hormones and inadequate glucose control that exist without it. so, studying the relationship between endogenous sex steroid and obesity trajectories among individuals should help us better understand how sex steroids affect glucose regulation. **(Kim and Halter, 2014)**. the connection between glucose and T:E2. Similarly, as sex hormone binding globulin (SHBG) binds to estradiol (E2) more strongly than estrogen, Lower SHBG levels imply a more androgenic setting. Therefore, rather than being due to any inherent characteristics of SHBG, relationships between SHBG and hyperglycemia have been proposed to represent this steroid balance. **(Torrens et al., 2009)**. One of the main coarse grain crops and a staple diet for the underprivileged is pearl millet. In the comparatively arid parts of the country, it quickly feeds the impoverished with staple foods. Among cereals and millets, it is the crop that can withstand droughts the best. Pearl millet has a stronger capacity to tolerate adverse environmental conditions and still produce significantly. **(Raju and Gudla, 2021)**

Millets are a major source of protein and nutrition for millions of people living in tropical areas of the world. When compared to other cereals like rice and wheat, millets have significant nutritious content and a climate resistance trait. Millets could be a promising ingredient for the functional food market because to their exceptional nutrient profile and hypoglycemic ability **(Ben-Nun, 2022)**. Diabetes is less common in millet-eating cultures, according to epidemiological studies. **(Kangama, 2021)**

Consuming pearl millet lowers the risk of type 2 diabetes, constipation, and anemia and has significant therapeutic value. Pearl millets are a high-energy diet since they are a fantastic source of protein, fiber, and carbs. It is a superior food option for infants starting at six months old since it is abundant in nutrients and simple to digest. The most popular millet variety worldwide is pearl millet. **(Abubakar et al., 2021)** One of the few meals, pearl millet has every important amino acid. Unfortunately, because they are hypo-allergic, food preparation renders many of these amino acids useless. It is easier to consume these amino acids in a low-cooked form in order to consume as many of them as possible. **(Krishnan et al., 2022)** Due to the abundance of proteins and minerals in pearl millet, it provides several nutritional advantages. along with vital minerals like magnesium, phosphorus, zinc, and others, it is high in protein. Additionally, it supplies essential vitamins and amino acids that enhance a number of human treatments. **(Krishnan and Meera, 2018)**

2.1. Materials

Pearl millet (*Pennisetum glaucum* L.) grain samples were obtained from the Field Crop Research Institute, Agriculture Research Center, Giza, Egypt., and processed via a professional grinder (SANYO-Made in Japan) into a fine powder. The MP whole grain (MPG) flour powder was kept in a tidy, dry location for later usage.

To cause diabetes, streptozocin was acquired from Sigma-Aldrich in St. Louis, Missouri, USA.

Experimental animals: Thirty wholesome mature male Sprague-Dawley rats that are albino underwent this study. At the start of the experiment, male rats had an average weight of 200 ± 10 g. The livestock was bought from the Giza Agricultural Research Center in Egypt. Rats were kept under observation for seven days prior to the commencement of the studies to allow for adaptation. They were provided a basal diet, and they had unlimited access to water during the four-week experiment. According to NRC (1992), the chemical components of the basic diet are displayed in table (1).

Table (1): Chemical components of the basic diet:

ingredients	g/kg Basal diet	% Basal diet
Casein	200	20
Corn starch	497	49.7
Sugar (Sucrose)	100	10
Cellulose	30	3
Corn oil	50	5
mineral admixtures	100	10
Vitamin admixtures	20	2
DL-methionine	3	0.3

2.2 Methods:

2.2.1 Induction of Diabetes mellitus by streptozocin:

In specified cages, rats fasted the previous night. Streptozocin was dissolved in a buffer solution of Na citrate (pH=4,5) the following day. Once diabetes has been induced, streptozocin is administered intraperitoneally at a single dose of 40 mg/kg. (**Satyam *et al.*, 2013**) . to avoid the drug's initial hypoglycemic mortality, the rats were fed 5% glucose solution for the first 48 hours rather than water. Blood was taken from the retro-orbital plexus of the rat that fasted all night on the third day following the injection and used to estimate measure of blood sugar in order to determine the rats' hyperglycaemic condition. rats having fasting blood sugar levels more than 250 mg/dl were classified as diabetic.

A glycemic analysis was performed on a random sample of groups of rats after infection with STZ to confirm induction and the result was as follows: (413 , 386 , 257, 347, 396 , 297 , 315 , 298 , 281 , 441 , 361 , 326 , 301 , 374 , 403 , 418mg/dl)

2.2.2 Experimental Animals Protocol:

The experiments contained on (30) healthy Sprague-Dawley male adult albino rats of 5 groups, each group contain 6 rats and classified into;a control group that was orally administered normal saline during the experimental period,the other groups were diabetic and divided as follows , diabetes group rats administered streptozocin STZ; 40mg/kg, IP , treated groups for pearl millet 30% ,60% and 100% respectively from basil diet, The body's own mass and food consumption of the rats were measured on a every week basis during the trial.

2.2.3 Biochemical Analysis

following the experimentation time, di-ethyl ether was used to anesthetize the animals in all groups. using heparinized capillary tubes, blood samples were taken from the inner canthus of the rat's eye. The serum was then recovered by centrifugation at 3000 rpm for 10 minutes. Before being employed for various biochemical analyses, samples were kept in a deep freezer at -20 C.

2.2.3.1 Serum samples were used for the determination of: Glucose was determined according to (Trinder, 1969), Insulin (Product Code: 2425-300)

2.2.3.2 Lipid pattern fractionation:

Lipid pattern fractionations were evaluation through utilization the kits of spin react enzyme as the Serum of cholesterol (CHO) was calculated accordance (Young, 2001), Serum of triglyceride (TG) was calculated d by enzymatic method accordance to (Bucolo and David 1973), (HDLc) was calculated accordance to (Grodon and Amer, 1977), Serum Total Lipids was calculated accordance to (Tietz 1976), Low density lipoprotein cholesterol (LDLc) and very low density lipoprotein cholesterol (VLDLc) were measured accordance to (Lee and Nieman, 1996) as following: $VLDL = TG / 5$, $LDL-c = TC - (TG / 5 + HDL-c)$.

2.2.4 Measurement of some antioxidant enzymes level

2.2.4.1 GLUTATHIONE PEROXIDASE (GPx): Anticoagulants like heparin, citrate, or EDTA should be used to collect blood. 2. Plasma should be taken off after the red cells are gathered using centrifuged (for instance, at 4°C for 10 minutes at 4000 rpm). 3. Wash the cells with 4 volumes of cold saline three times, or 10 volumes of cold saline, once. 4. To the predicted volume of red cell pellets, add 4 volumes of cold deionized water to lyse them. 5. Centrifuging the red cell stroma (for example, at 4°C for 10 minutes at 4000 rpm) will remove it. 6. Gather the supernatant that has been cleared to be used in the test. If the sample will be used right away, freeze it at -70°C, or if it will be tested the same day, store it on ice. depending on (Paglia and Valentine 1967)

2.2.4.2 GLUTATHIONE REDUCED (GSH): Whole blood and erythrocyte lysate are two types of blood that can be used for testing. An anticoagulant such heparin, citrate, or EDTA should be used to take blood. A 4x solution of ice-cold, clean water should be used to lyse red blood cells. 4. Centrifuge erythrocyte lysate (supernatant) for testing purposes at 4,000 rpm for 15 minutes at 4 °C. If possible, freeze at -80°C on the same day. For at least a month, the sample will remain stable.. according to (Beutler et al., 1963).

2.2.4.3 SUPEROXIDE DISMUTASE (SOD) Use whole blood samples that have been EDTA or heparinized. Erythrocytes are advised to be cleaned with 0.9% NaCl solution four times. 2. Aspirate off the plasma after centrifuging 0.5 ml of whole blood for 10 minutes at 4000 rpm. 3. After that, centrifuge erythrocytes four times for ten minutes each time with 3 ml of a 0.9% NaCl solution.. 4. Following a 2.0 ml make-up with cold, redistilled water, the washed, centrifuged erythrocytes should be combined and allowed to stand at +4 °C for 15 minutes. if not analyzed right away, maintain -70. The lysate is diluted with water to achieve a range of 30% to 60% inhibition. 5. Lysate dilutions of 25 fold (final dilution factor = 100) for human samples and 50 fold (final dilution factor = 200) for bovine samples are advised.)according to (Nishikimi et al., 1972).

2.2.4.4 CATALASE ASSAY (CAT) IN Plasma : Use an anticoagulant to collect blood, such as heparin, citrate, or EDTA. 15 minutes of centrifuging at 4,000 rpm and 4 °C. Gather the plasma for analysis and keep it chilled. If possible, freeze at -80°C on the same day. For at least a month, the sample will remain stable. according (Aebi ,1984).

2.2.5 Hormone Analysis

Dehydroepiandrosterone (DHEA) (Product Code: 7425-300), Serum estradiol (E2) (Product Code: 4925-300), Progesterone (Product Code: 4825-300), Testosterone (Product Code: 3725-300),

(FSH) (Product Code: 425-300), (LH) (Product Code: 525-300), and (PRL) (Product code: 725-300), were assessed using Accu Bind ELISA microwells made by Monobind Inc. in Lake Forest, California (USA), 92630. Microplate reader, Model: STAT FAX 303/PLUS, Serial Number 303-6668, produced by Awareness Technology Inc., Palm City, FL 34990, was used to read the tests.

2.2.6 Statistical data analysis:

The least significant difference (LSD) statistic test was used to compare the group means in the statistical analysis, which was conducted using one-way analysis of variance (ANOVA). Means and standard deviations (means S.D.) were used to present the acquired data. The statistical analysis programme was used to run each test on a computer. (SPSS, version 24, 2016)., according to (Artmitage and Berry 1987).

All biological experimentation was conducted in accordance with internationally accepted standards for the treatment and use of laboratory animals. Additionally, approval for the experiment was received from the Mansoura University Faculty of Specific Education's Research Ethics Committee..

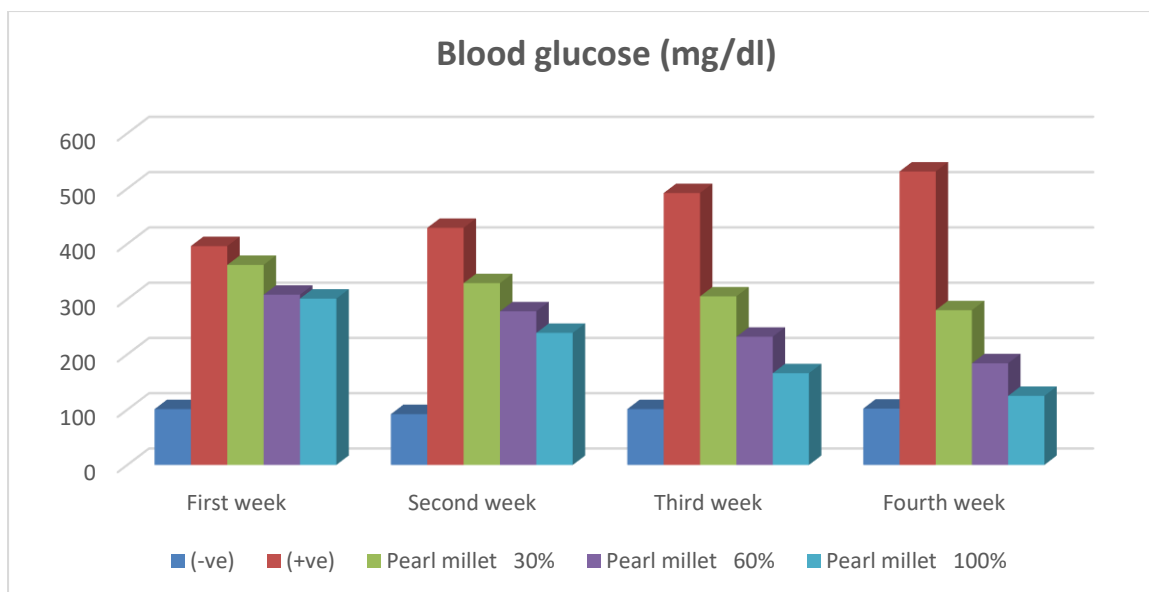
3 Results

The result of blood glucose reduction potentials of streptozocin induced diabetic rats fed on the pearl millet samples are shown in **Table (2)** shows obvious decrease in Blood glucose in first week of 30% > 60% > 100% of pearl millet with values of 362.75, 308.75 and 301.75 mg/dl respectively, while the second week of 30% > 60% > 100% of pearl millet with values of 329.75, 287.5 and 239.25 mg/dl respectively, however the third week of 30% > 60% > 100% of pearl millet with values of 305.5, 232.5 and 166.5 mg/dl respectively, while we find of 30% > 60% > 100% of pearl millet with values of 280.5, 184.75 and 125.75 mg/dl in fourth week of experiment respectively.

Table (2) Effect of pearl millet on Blood glucose in control and streptozocin diabetic rat groups.

Blood glucose (mg/dl)					
Groups	Control(-ve)	Control(+ve)	Pearl millet 30%	Pearl millet 60%	Pearl millet 100%
First week	101 ^c ±11.817	396 ^a ± 26.29	362.75 ^{ab} ±61.17	308.75 ^{ab} ±41.17	301 ^{ab} ±38.01
Second week	92.75 ^c ±17.17	429.5 ^a ±38.63	329.75 ^{ab} ±61.92	278.5 ^b ±45.61	239.25 ^{bc} ±63.88
Third week	101.5 ^d ±10.67	492 ^a ±46.62	305.5 ^b ±57.65	232.5 ^{bc} ±28.72	166.5 ^c ±41.41
Fourth week	102.75 ^d ±14.22	531 ^a ±47.42	280.5 ^b ±44.39	184.75 ^c ±22.01	125.75 ^{cd} ±29.12

Mean and standard deviation values, letters with different superscripts are statistically different at ($P \leq 0.05$) or are very significant at ($P \leq 0.001$), while letters with the same superscripts are no significant.



Diabetic effects on body weight was presented in Table (3). In this study, the diabetic group (STZ) experienced a considerable ($P < 0.05$) weight decrease. It was observed that rat's body weight between control, Pearl millet 30%, 60% and 100% treatments have no significant differences .

Table(3) Effect of pearl millet on Body weight in control and streptozocin diabetic rat groups.

Body weight (mg)					
Groups	Control(-ve)	Control(+ve)	Pearl millet 30%	Pearl millet 60%	Pearl millet 100%
Initial weight	197.5 ±10.78	198.5 ±8.74	195.7 ±7.8	202 ±7.48	196.7 ±11.35
First week weight	209.75 ^a ±11.32	190.2 ^b ±9.15	203.5 ^a ±6.95	208.5 ^a ±7.16	200.7 ^a ±11.55
Second week weight	227.5 ^a ±12.82	173.2 ^c ±6.88	209 ^b ±6.97	210 ^b ±7.43	199.25 ^b ±10.21
Third week weight	239 ^a ±10.72	158.5 ^c ±4.26	211.25 ^b ±7.36	209.75 ^b ±8.65	197.5 ^b ±11.1
Fourth week weight	247.5 ^a ±9.79	143.2 ^c ±3.17	211.25 ^b ±6.60	208.5 ^b ±8.22	195 ^b ±10.23

Mean and standard deviation values, letters with different superscripts are statistically different at ($P \leq 0.05$) or are very significant at ($P \leq 0.001$), while letters with the same superscripts are non significant.

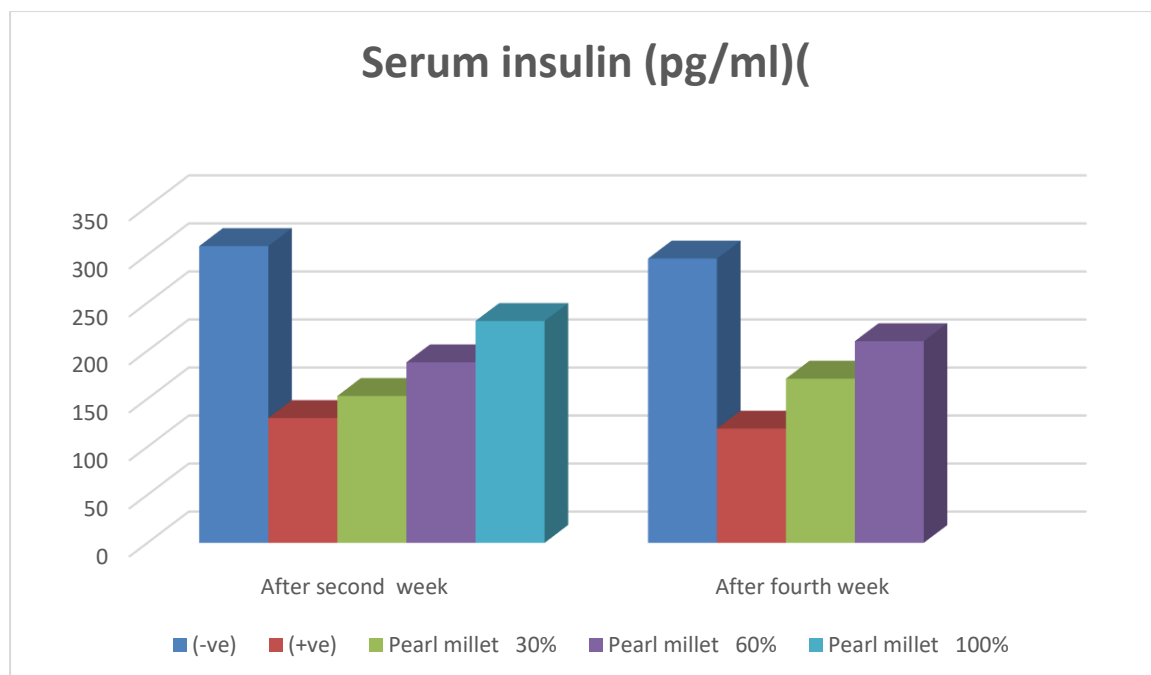


The findings reveal that on day 28, diabetic rats had a gradually significant ($P \leq 0.001$) decline in insulin levels compare with control values, as indicated in **Table (4)**.while found Gradual significant increase in insulin after second week of 30% < 60% < 100% of pearl millet with values of 153.33, 188.66 and 321.33 pg/ml respectively, also found after fourth week gradual significant increase in insulin of 30% < 60% < 100% of pearl millet with values of 171.66, 210 and 232 pg/ml respectively.

Table (4) Effect of pearl millet on insulin in control and STZ diabetic rat groups.

Serum insulin (pg/ml)(
Groups	Control(-ve)	Control(+ve)	Pearl millet 30%	Pearl millet 60%	Pearl millet 100%
After second week	309.66 ^a ±24.11	130 ^d ±17.43	153.335 ±17.78	188.66 ^{bc} ±23.18	231.33 ^b ±38.42
After fourth week	296 ^a ±23.64	119.33 ^d ±241	171.665 ±31.2	210 ^{bc} ±22.64	232 ^{ab} ±21.93

Mean and standard deviation values, letters with different superscripts are statistically different at ($P \leq 0.05$) or are very significant at ($P \leq 0.001$), while letters with the same superscripts are non significant.



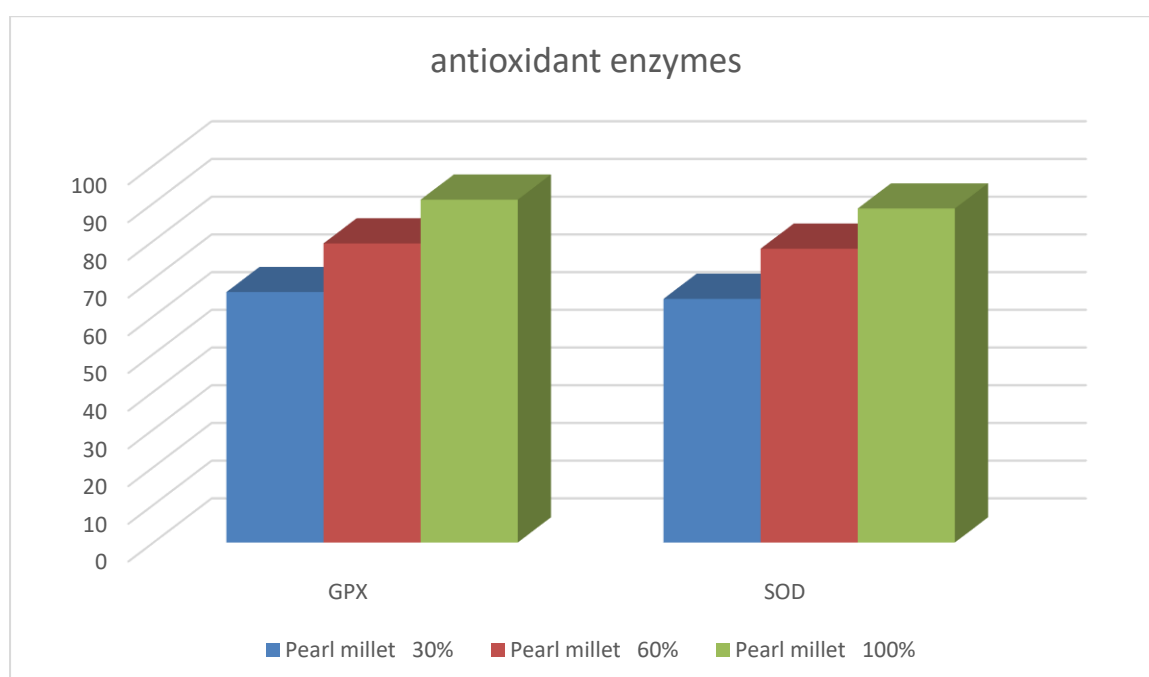
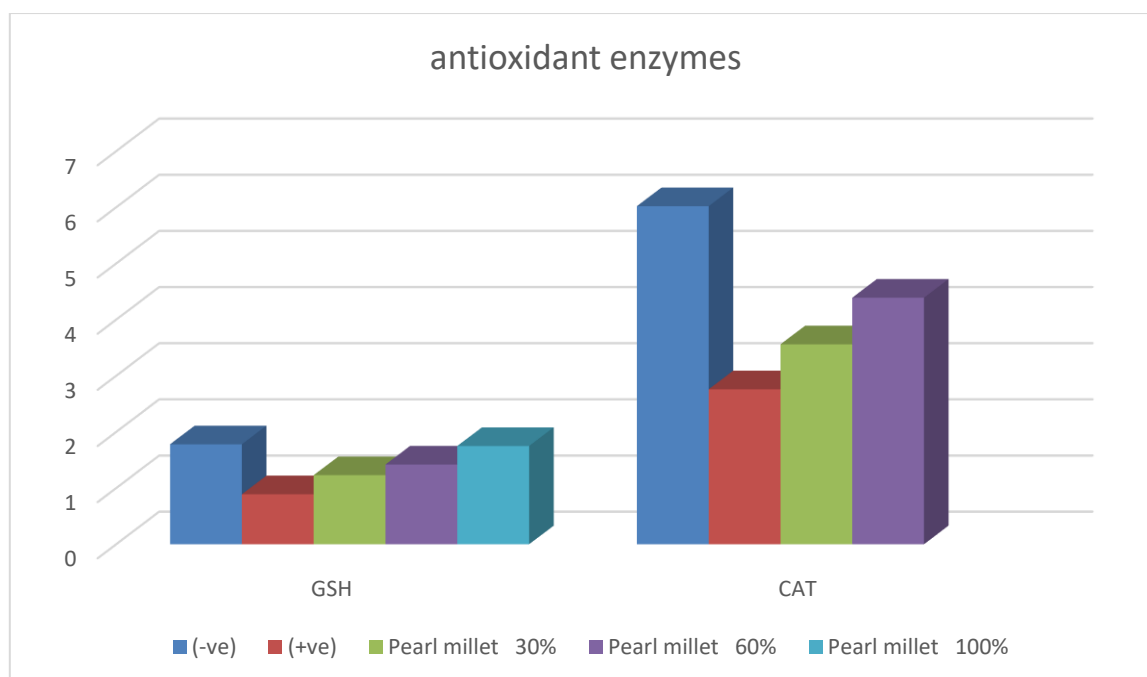
Data in **Table (5)** revealed significant reduced in GSH, CAT, GPx and SOD levels in diabetic rat compare with The untreated group, Pearl millet 30, 60, 100% treated groups appeared significant (($P \leq 0.01$) and $P \leq 0.001$) increased in GSH, CAT, GPx and SOD levels comparing with the affected group, however found slightly lowering in GSH, CAT, GPx and SOD levels in pearl millet 30% treated group compared with the untreated group, whereas find non-significant variation in GSH, GPx and SOD levels with pearl millet 100% treated group comparing with the untreated group.

Table (5) Effect of pearl millet on some antioxidant enzymes in control and streptozocin diabetic rat groups

Groups	GSH(mmol/L)	CAT(U/L)	GPX(mU/ml)	SOD (U/ml)
Control(-ve)	1.78 ^a ± 0.12	6.02 ^a ± 0.29	105.81 ^a ±7.16	91.66 ^a ± 5.41
Control(+ve)	0.89 ^c ±0.16	2.76 ^d ±0.38	53.66 ^d ±6.71	55.23 ^d ±5.71
Pearl millet 30%	1.23 ^b ±0.23	3.56 ^c ±0.32	66.43 ^c ± 9.33	64.6 ^c ±10.64
Pearl millet 60%	1.42 ^b ± 0.15	4.39 ^b ± 0.44	79.3 ^b ± 8.903	77.9 ^b ± 6.75
Pearl millet 100%	1.75 ^a ± 0.13	4.92 ^b ±0.29	90.93 ^a ± 14.32	88.56 ^a ± 8.46

Mean and standard deviation values, letters with different superscripts are statistically different at ($P \leq 0.05$) or are very significant at ($P \leq 0.001$), while letters with the same superscripts are non significant.

Glutathione reduced (GSH) Catalase (CAT) , glutathione peroxidase (GPX) and Superoxide dismutase (SOD)



Data in **Table (6)** showed significant ($P \leq 0.001$) increase in LDL, TG, CH and VLDL, but significant reduced in HDL levels in infected rat comparison with the untreated group, pearl millet 30, 60, 100% treated groups appeared significant ($P \leq 0.01$) and $P \leq 0.05$) decreased in LDL, TG, CH and VLDL levels, however found significant ($P \leq 0.05$) raise in HDL comparing with positive group.

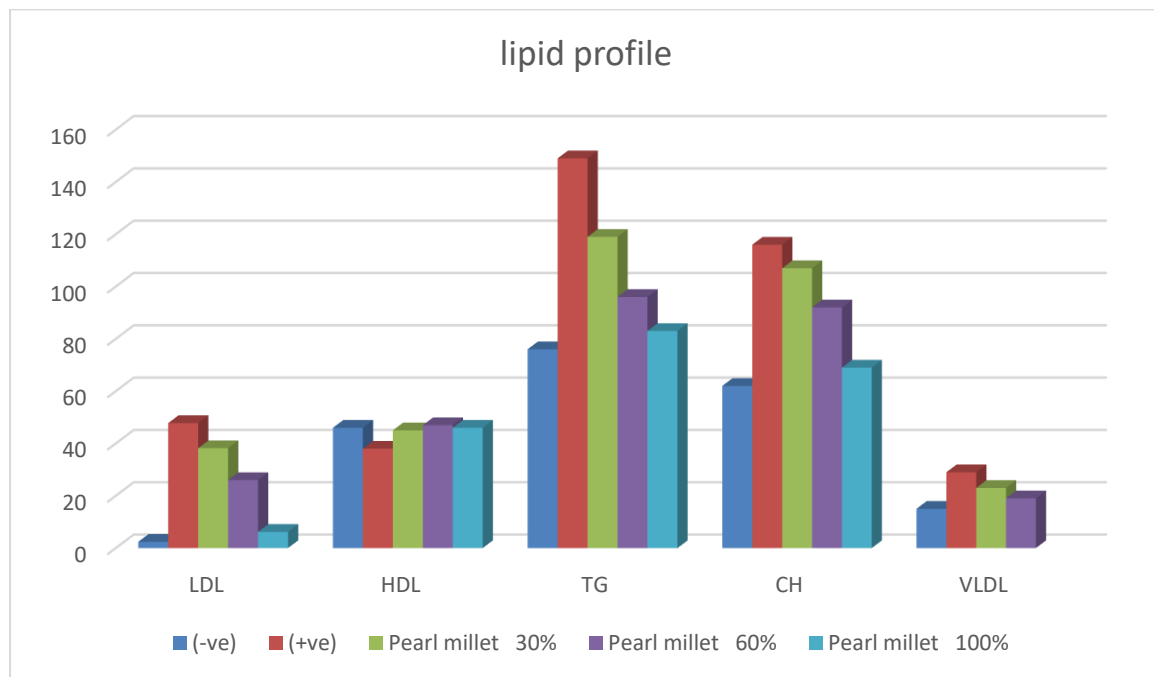
Table(6) Effect of pearl millet on lipid profile in control and streptozocin diabetic rat groups.

Groups	LDL (mg/dl)	HDL (mg/dl)	TG (mg/dl)	CH (mg/dl)	VLDL (mg/dl)
Control(-ve)	2.41 ^e ±1.96	46.12 ^a ±4.58	76.33 ^{cd} ±13.32	62 ^d ±9.84	15.26 ^e ±2.66

Control(+ve)	47.8^a ±2.16	38.33^b ±4.51	149.33^a ±13.05	116^a ±7.54	29.86^a ±2.61
Pearl millet 30%	38.2^b ±0.75	45.11^a ±6.11	119.01^b ±8.32	107^{ab} ±7.63	23.8^b ±1.66
Pearl millet 60%	26.13^c ±3.10	47.13^a ±3.60	96.02^{bc} ±17.08	92.33^b ±5.51	19.2^c ±3.41
Pearl millet 100%	6.266^d ±0.94	46.66^a ±7.51	83.66^c ±7.23	69.66^c ±8.62	16.73^d ±1.44

Mean and standard deviation values, letters with different superscripts are statistically different at ($P \leq 0.05$) or are very significant at ($P \leq 0.001$), while letters with the same superscripts are non significant.

High density lipoprotein(HDL), Low density lipoprotein (LDL), triglyceride (TG), cholesterol(CH) and very Low density lipoprotein (VLDL).



Data in **Table (7)** explain significant ($P \leq 0.001$) reduced in DHEA, Estradiol, Progesterone, Testosterone, PRL, LH and FSH levels in diabetic rat compared with the negative control group, pearl millet 30, 60, 100% treated groups appeared significant ($P \leq 0.01$) and $P \leq 0.05$) raise in DHEA, Estradiol, Progesterone, Testosterone, PRL, LH and FSH levels compared with untreated group. while showed significant slightly decrease in DHEA, Estradiol, Progesterone, Testosterone, PRL, LH and FSH levels with pearl millet 30 and 60% treated groups compared with normal group, however found non-significant deference in DHEA, Estradiol, Progesterone, Testosterone, PRL, LH and FSH levels with pearl millet 100 % treated group compared with normal group.

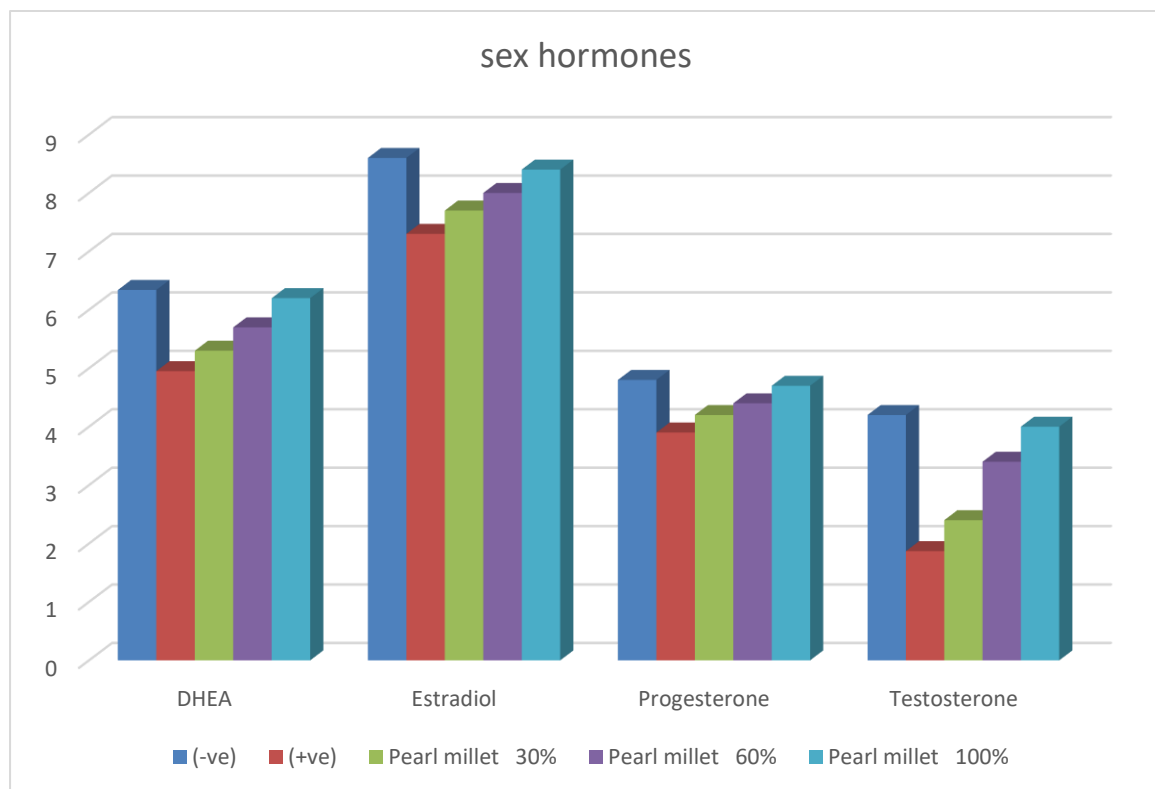
Table(7) Effect of pearl millet on some sex hormones in control and streptozocin diabetic rat groups.

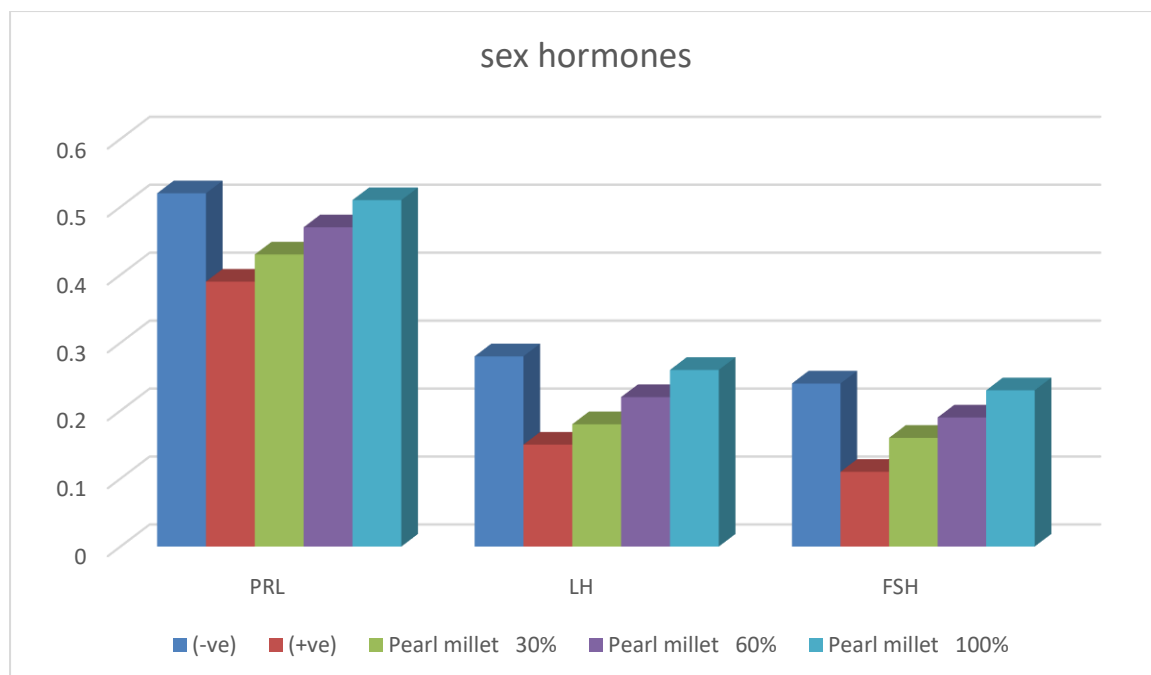
Gp.	DHEA)ng/ml	Estradio l	Progesteron e	Testosteron e	PRL)ng/ml	LH (mIU/ml)	FSH (mIU/ml
-----	----------------	---------------	------------------	------------------	---------------	--------------------	----------------

	()ng/ml()ng/ml()ng/ml(()
Control(-ve)	6.34^a ±0.14	8.67^a ±0.25	4.81^a ±0.12	4.21^a ±0.24	0.52^a ±0.03	0.28^a ±0.02	0.24^a ±0.01
Control(+ve)	4.95^d ±0.16	7.38^d 0.11	3.91^d ±0.13	1.87^d ±0.16	0.39^d ±0.01	0.15^e ±0.01	0.11^d ±0.02
Pearl millet 30%	5.34^c ±0.12	7.73^c ±0.11	4.20^c ±0.05	2.46^c ±0.28	0.43^c ±0.01	0.18^d ±0.01	0.16^c ±0.01
Pearl millet 60%	5.79^b ±0.15	8.05^b ±0.11	4.44^b ±0.12	3.45^b ±0.27	0.47^b ±0.011	0.22^c ±0.02	0.19^b ±0.01
Pearl millet 100%	6.21^a ±0.16	8.42^a ±0.27	4.73^a ±0.11	4.02^a ±0.14	0.51^a ±0.02	0.26^a ±0.01	0.23^a ±0.01

Mean and standard deviation values, letters with different superscripts are statistically different at ($P \leq 0.05$) or are very significant at ($P \leq 0.001$), while letters with the same superscripts are non significant.

Dehydroepiandrosterone (DHEA), Prolactin (PRL), luteinizing hormone (LH) and follicle-stimulating hormone (FSH)





Discussion

Chronic hyperglycemia brought on by an absolute or relative insulin insufficiency is known as diabetes mellitus. Glycaemic management and lipid metabolism can both be improved by millet. the aim of the study is to estimated how Pear Millet affected various hormones related to sex in the streptozocin model of type-2 diabetes mellitus..

In the current study, normal rats were intraperitoneally given STZ (40 mg/kg b.wt.) to cause diabetes mellitus. Diabetes is thought to be induced by STZ when serum insulin levels in rats drop after STZ induc. **Patel et al,2015**

This study showed that during the study periods, blood glucose levels decreased. These findings concur with the findings According to **Sukar et al., (2020)**, during the study periods, there was a significant increase in adiponectin along with a significant drop in blood glucose levels. These results suggest that a diet rich in pearl millet whole grains can contribute significantly to bringing back plasma levels of adiponectin to their normal levels. For an extended period of time, pearl millet (PM) helps diabetic people maintain stable blood sugar levels. Due to its low sugar index, it aids in containing and steadily releasing glucose at a slower rate than other foods.,which is beneficial for diabetic sufferers. **(Saini et al.,2021)**. Long periods of stable blood sugar levels will be aided by this.Pearl millet has a very high level of amylase activity—about ten times more than wheat. The main sugars in the flour are maltose and D-ribose, which are low in fructose and glucose. **(Dias-Martins et al., 2018)**. Because of its high fiber content, pearl millet is typically categorized as a reduced high sugar index (GI) food. The GI determines how much the amount of carbohydrates in food affects the rate and magnitude of change in post-prandial blood glucose levels. As a low-GI meal, pearl millet may help reduce the amount of blood glucose available for the formation of triacylglycerol. Additionally, millets reduce plasma levels of triacylglycerol by condensing VLDL cholesterol, which is a transporter of the fatty acid. PM showed low GIs and a high insulinemic index, whereas people with type 2 diabetes had high GIs and a low insulinemic index, suggesting that consuming millet grains may be helpful in decreasing blood lipid levels **(Salar et al., 2017)**. The insulin reserve in people with type 2 diabetes may not have been sufficient to mobilize insulin after consuming pearl millet, the investigators noted. Insulin separation caused by pearl millet in healthy individuals lowered the gastrointestinal tract. Due to the significant amount of polyphenols, which have antioxidant characteristics, found in pearl millet, it is well known for its beneficial health effects. **(Tomar et al.,2021)**. As a result, pearl millet is also particularly efficient at managing diabetes. Due to its high

fiber content, compared to other foods, it digests more slowly and releases glucose into the blood at a faster rate. This aids diabetic patients in long-term blood sugar stability maintenance.

According to our findings, the body weight of diabetic rats has significantly decreased. This could be explained by the increased catabolic reactions brought on by the animal's inability to use carbohydrates as an energy source, which resulted in muscle waste. Additionally, the animal's hyperglycemia caused the animal to become catabolic, causing it to break down protein and fat reserves for energy because glucose is not available to the cell nutrition, which had prevented the actual healing process from taking place. **Kalaiarasi et al, 2009.** this might be as a result of a post-treatment rise in insulin levels that enhanced glycemic control and prevented weight loss. **Kumar et al, 2014.**

The biggest challenge for anyone trying to lose weight is controlling their calorie intake. Due to its high fiber content, pearl millet will aid in weight loss. Due to the grain's high fiber content, the journey from the stomach to the intestines takes longer. As a result, it helps to reduce overall food consumption because PM satiates appetite for a long time. **(Benton and Young, 2017).**

Dyslipidaemia is associated with type 2 DM, specifically, increased triglyceride levels, decreased (HDL) and high (LDL) **Lazarte and Hegele ,2020.** Because of their high levels of fiber, composition of fatty acids, and plant compounds, pearl millet grains have a variety of useful qualities. **Patel et al. 2015,** The knowledge we have learned on pearl millet's nutritional impacts is very important for nutritional programs. Obesity, inherited predispositions, and a high intake of high glucose in foods are the usual contributors to diabetes. The impact of pearl millet diet on the glucose metabolism in diabetic rats was evaluated by **Nani et al. 2015.** The authors suggested consuming food meals comprised of pearl millet might be advantageous in treating type 2 diabetes with induced hyperglycemia and decrease serious the condition as an alternate to protection. The typical complications of diabetes include hypercholesterolemia and hypertriglyceridemia, which can have catastrophic consequences including atherosclerosis. In this investigation, millet was fed to diabetic rats.

explained a significant ($P < 0.05$) increase in HDL and a significant ($P < 0.05$) decrease in LDL levels. When compared to a normal control, it is unknown how dietary PM impacts HDL and other lipid profile levels. The general consensus is that dietary proteins are a better option and high effect strategy to alter glycaemic reaction, lipid profile, adiponectin index, and insulin

This study demonstrated significant decrease in antioxidant levels in diabetic rat, while repaired increased in treatment groups by 30,60,100% dried pearl millet. **Silvestrin et al 2020** showed that Due to raise mitochondrial synthesis of the superoxide anion, non-enzymatic protein glycation, and glucose autoxidation, hyperglycemia results in oxidative stress. Since oxidative stress disrupts redox signaling as a result of either excessive ROS production or insufficient antioxidant defense systems, it is implicated in the etiology of many serious human diseases.

Clinical investigations have shown a strong sex-dimorphic relationship between testosterone and type-2 diabetes (T2DM), which is consistently seen across racial and ethnic groups. **Dwyer and, Quinton 2018 .**

Numerous population-based cross-sectional studies show that T2DM is associated with reduced levels of testosterone in men and greater levels of testosterone in women, whereas T2DM is also associated with lower levels of SHBG, especially in females. **Ding et al, 2006** Therefore, several prospective population-based studies suggest that endogenous testosterone may have a distinct impact on T2DM risk in males and women. In reality, lower testosterone levels (both total and free), as well as reduced SHBG levels, are linked to a higher risk of T2DM in males, whereas higher testosterone levels (both total and free), as well as higher SHBG levels, are linked to a raise risk of T2DM in women. **Gyawali et al. 2018.** It's interesting to note that male prospective studies have shown that the inverse connection between testosterone and the incidence of diabetes is primarily dependent on the phenotype of abdominal obesity. In reality, this association significantly weakens when accounting for waist circumference. **Grossmann , 2011.** In females, the risk of T2DM increases with the aggravation of hyperandrogenism **Fenske et al, 2015** and becomes particularly evident in hyperandrogenic disorders, such as polycystic ovary syndrome (PCOS).

This study referred to significant increase in six hormones for treated group from T2DM by 30, 60, 100 %dried pearl millet compared with positive control

Acknowledgments:

"The authors extend their appreciation to the Deanship of Research and Graduate Studies at King Khalid University for funding this work through Large Research Project under grant number RGP.2/409/45

REFERENCE

1. Abubakar, S. M.; Mohammed, S ; Lewu, F.B.; Danjuma, M. N.; Adetunji, A. T. and Kioko , J. I. (2021) Pearl Millet (*Pennisetum glaucum* [L. R. Rr.]) Varietal Loss and its Potential Impact on Smallholder Farmers in Northern Nigeria: A Review, *JOURNAL OF TECHNO SOCIAL* VOL. 12 NO. 2 1-11.
2. Aebi, H. (1984): Catalase in vitro, *Methods in Enzymology*, vol. 105, Academic Press, pp. 121-126.
3. Asif, M.(2014) The Prevention and Control the Type-2 Diabetes by Changing Lifestyle and Dietary Pattern. *J. Educ. Health Promot.* 3, 1.
4. Ben-Nun (2022) The impact of millet on human health , Book · January , B.N. Publication House. Israel
5. Benton, D.; Young, H.A. Reducing Calorie Intake May Not Help You Lose Body Weight. *Perspect. Psychol. Sci.* 2017, 12, 703–714. [CrossRef] [PubMed]
6. Beutler, E.; Duron, O. and Kelly, M.B. (1963): Improved method for the
7. Bucolo, G and David, H (1973): Quantitative determination of serum triglycerides by
8. determination of blood glutathione, *J. Lab Clin. Med.* 61:882-8.
9. Dias-Martins A.M., Pessanha K.L.F., Pacheco S., Rodrigues J.A.S., Carvalho C.W.P. Potential Use of Pearl Millet (*Pennisetum glaucum* (L.) R. Br. in Brazil: Food Security, Processing, Health Benefits and Nutritional Products. *Food Res. Int.* 2018;109:175–186. doi: 10.1016/j.foodres.2018.04.023. [PubMed] [CrossRef] [Google Scholar]
10. Ding EL, Song Y, Malik VS, Liu S. Sex differences of endogenous sex hormones and risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA* 2006. 295 1288–1299. (10.1001/jama.295.11.1288) [PubMed] [CrossRef] [Google Scholar]
11. Dwyer AA, Quinton R. The metabolic syndrome in central hypogonadotrophic hypogonadism. *Frontiers of Hormone Research* Home 2018. 49 156–169. (10.1159/000485998) [PubMed] [CrossRef] [Google Scholar]
12. Fenske B, Kische H, Gross S, Wallaschofski H, Völzke H, Dörr M, Nauck M, Keivil BG, Brabant G, Haring R. Endogenous androgens and sex hormone-binding globulin in women and risk of metabolic syndrome and type 2 diabetes. *Journal of Clinical Endocrinology and Metabolism* 2015. 100 4595–4603. (10.1210/jc.2015-2546) [PubMed] [CrossRef] [Google Scholar]
13. Grossmann M. Low testosterone in men with type 2 diabetes: significance and treatment. *Journal of Clinical Endocrinology and Metabolism* 2011. 96 2341–2353. (10.1210/jc.2011-0118) [PubMed] [CrossRef] [Google Scholar]
14. Gyawali P, Martin SA, Heilbronn LK, Vincent AD, Taylor AW, Adams RJT, O'Loughlin PD, Wittert GA. The role of sex hormone-binding globulin (SHBG), testosterone, and other sex steroids, on the development of type 2 diabetes in a cohort of community-dwelling middle-aged to elderly men. *Acta Diabetologica* 2018. 55 861–872. (10.1007/s00592-018-1163-6) [PubMed] [CrossRef] [Google Scholar]
15. Kalaiarasi P, Kaviarasan K, Pugalendi KV. Hypolipidemic activity of 18 β -glycyrrhetic acid on streptozotocin-induced diabetic rats. *Eur J Pharmacol.* 2009;612:93–97. doi: 10.1016/j.ejphar.2009.04.003. [PubMed] [CrossRef] [Google Scholar]
16. Kangama, C.O.(2021) Pearl millet (*Pennisetum glaucum*) perspectives in Africa. *Int. J. Sci. Res. Arch.* 2021, 2, 1–7.
17. Kim, C and Halter, J.B(2014) Endogenous Sex Hormones, Metabolic Syndrome, and Diabetes in Men and Women, *Curr Cardiol Rep.* Apr; 16(4): 467

18. Krishnan, V.; Verma, P.; Saha, S.; Singh, S.; Vinutha, T.; Kumar, R.R.; Kulshreshta, A.; Singh, S.P.; Sathyavathi, T.; Sachdev, A.; et al, (2022) Polyphenol-enriched extract from pearl millet (*Pennisetum glaucum*) inhibits key enzymes involved in post prandial hyper glycemia (α -amylase, α -glucosidase) and regulates hepatic glucose uptake. *Biocatal. Agric. Biotechnol*, in press.
19. Krishnan, R.; Meera, M.S. (2018) Pearl Millet Minerals: Effect of Processing on Bioaccessibility. *J. Food Sci. Technol*, 55, 3362–3372.
20. Kumar GS, Kulkarni A, Khurana A, Kaur J, Tikoo K. Selenium nanoparticles involve HSP-70 and SIRT1 in preventing the progression of type 1 diabetic nephropathy. *Chem Biol Interact*. 2014;223:125–133. doi: 10.1016/j.cbi.2014.09.017. [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
21. Lazarte J, Hegele RA. Dyslipidemia management in adults with diabetes. *Can J Diabetes*. 2020; 44(1): 53-60. PubMed Web of Science@ Google Scholar
22. Lee, R and Nieman, D (1996) Nutritional Assessment. 2nd Ed. Mosby, Missouri, USA
23. Mechchate, H.; Es-safi, I.; Louba, A.; Alqahtani, A.S.; Nasr, F.A.; Noman, O.M.; Farooq, M.; Alharbi, M.S.; Alqahtani, A.; Bari, A.; et al (2021) In Vitro Alpha-Amylase and Alpha-Glucosidase Inhibitory Activity and In Vivo Antidiabetic Activity of *Withania frutescens* L. Foliar Extract. *Molecules* Jan, 26(2), 293.
24. Muniyappa, R.; Chen, H.; Muzumdar, R.H.; Einstein, F.H.; Yan, X. and Yue, L. Q. (2009) Comparison between surrogate indexes of insulin sensitivity/ resistance and hyperinsulinemic-euglycemic clamp estimates in rats. *The American Journal of Physiology: Endocrinology and Metabolism*, 297: 1023-9.
25. Nani, A.; Belarbi, M.; Ksouri-Megdiche, W.; Abdoul-Azize, S.; Benammar, C.; Ghiringhelli, F.; Hichami, A.; Khan, N.A. Effects of Polyphenols and Lipids from *Pennisetum glaucum* Grains–133. [[CrossRef](#)]
26. Nishikimi, M.; Roa, N.A. and Yogi, K. (1972) *Biochem. Bioph. Res. Common.*, 46, 849– 854.
27. Nolan, C.J.; Prentki, M. (2019) Insulin Resistance and Insulin Hypersecretion in the Metabolic Syndrome and Type 2 Diabetes: Time for a Conceptual Framework Shift. *Diabetes Vasc. Dis. Res*, 16, 118–127..
28. NRC National Research Council (1992): (Recognition and Alleviation of Pain and Distress in Laboratory Animals, Washington DC, National Academy Press.
29. Paglia, D. E. and Valentine, W. N. (1967) Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxidase. *J. Lab. Clin. Med*. 70:158-169
30. Patel SB, Santani D, Patel V, Shah M. Anti-diabetic effects of ethanol extract of *Bryonia laciniosa* seeds and its saponins rich fraction in neonatally streptozotocin-induced diabetic rats. *Pharmacognosy Res*. 2015;7:92–99. doi: 10.4103/0974-8490.147217. [[PMC free article](#)] [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
31. Pei, J.; Umapathy, V.R.; Vengadassalpathy, S.; Hussain, S.F.J.; Rajagopal, P.; Jayaraman, S.; Veeraraghavan, V.P.; Palanisamy, C.P. and Gopinath, K., A (2022) Review of the Potential Consequences of Pearl Millet (*Pennisetum glaucum*) for Diabetes Mellitus and Other Biomedical Applications, *Nutrients*, 14, 2932
32. Raju, K. A. and Gudla, V. (2021) Pearl Millet – a Minor Millet with Many Benefits, *AgriCos e-Newsletter*, 2582-7049.
33. Saini S., Saxena S., Samtiya M., Puniya M., Dhewa T. Potential of Underutilized Millets as Nutri-Cereal: An Overview. *J. Food Sci. Technol*. 2021;58:4465–4477. doi: 10.1007/s13197-021-04985-x. [[PMC free article](#)] [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
34. Salar R.K., Purewal S.S. Phenolic Content, Antioxidant Potential and DNA Damage Protection of Pearl Millet (*Pennisetum glaucum*) Cultivars of North Indian Region. *J. Food Meas. Charact*. 2017;11:126–133. doi: 10.1007/s11694-016-9379-z. [[CrossRef](#)] [[Google Scholar](#)]
35. Salar, R.K.; Purewal, S.S. Phenolic Content, Antioxidant Potential and DNA Damage Protection of Pearl Millet (*Pennisetum glaucum*) Cultivars of North Indian Region. *J. Food Meas. Charact*. 2017,

- 11, 126 Patel, S. Cereal Bran Fortified-Functional Foods for Obesity and Diabetes Management: Triumphs, Hurdles and Possibilities. *J. Funct. Foods* 2015, 14, 255–269. [CrossRef] 62.
36. Satyam, S.M.; Bairy, K. and Pirasanthan, R. (2013) Influence of Grape seed extract and Zincovit tablets (Nutritional food supplement) on glucose level in normal and streptozocin induced diabetic rats. *Int J Pharm Sci*, 2013. 5(3): p. 413- 416.
37. Shen, H.; Zhao, J.; Liu, Y.; Sun, G.(2018) Interactions between and Shared Molecular Mechanisms of Diabetic Peripheral Neuropathy and Obstructive Sleep Apnea in Type 2 Diabetes Patients. *J. Diabetes Res*, 1–15.
38. Silvestrini A, Mordente A, Martino G, Bruno C, Vergani E, Meucci E, Mancini A. The role of selenium in oxidative stress and in nonthyroidal illness syndrome (NTIS): an overview. *Curr Med Chem*. 2020;27:423–449. doi: 10.2174/0929867325666180201111159. [PubMed] [CrossRef] [Google Scholar]
39. the use of enzymes, *Clin Chem*. May; 19(5):476-82.
40. Tietz, N. W (1976) *Fundamentals of clinical chemistry*
41. Tomar M., Bhardwaj R., Kumar M., Singh S.P., Krishnan V., Kansal R., Verma R., Yadav V.K., Dahuja A., Ahlawat S.P., et al. Nutritional composition patterns and application of multivariate analysis to evaluate indigenous Pearl millet (*Pennisetum glaucum* (L.) R. Br.) germplasm. *J. Food Compos. Anal.* 2021;103:104086. doi: 10.1016/j.jfca.2021.104086. [CrossRef] [Google Scholar]
42. Torrens, J.; Sutton-Tyrrell, K.; Zhao, X.; Matthews, K.; Brockwell, S and Sowers, M. et al (2009) Relative androgen excess during the menopausal transition predicts incident metabolic syndrome in midlife women: Study of Women's Health Across the Nation. *Menopause*;16(2):257–64.
43. Trinder, P (1969): Determination of Glucose in Blood Using Glucose Oxidase with an Alternative Oxygen Acceptor, *Annals of Clinical Biochemistry*,6:24
44. Willett, W.; Manson, J.; Liu, S.(2002) Glycemic Index, Glycemic Load, and Risk of Type 2 Diabetes. *Am. J. Clin. Nutr*, 76, 274S–280S.
45. Young, D. S (2001): *Effect of disease on clinical lap.test*,4th AACC press
46. Zou, Q.; Qu, K.; Luo, Y.; Yin, D.; Ju, Y.; Tang, H, (2018) Predicting Diabetes Mellitus with Machine Learning Techniques. *Front. Genet*, 9, 515.