

## The Physiological Significance of Thyroid Stimulating Hormone and Thyroid Hormones with Hemoglobin A1C level

Ezmat Jalil<sup>1</sup>, PawanVishwakarma<sup>2</sup>, Rajmangal Choudhary<sup>3</sup>

<sup>1</sup>Assistant Professor, Dept. of Physiology, Govt. Medical College Azamgarh U. P. (India)

<sup>2</sup>Associate Professor, Dept. of Medicine, Govt. Medical College Azamgarh U. P. (India)

<sup>3</sup>Assistant Professor, Dept, of Biochemistry, Govt. Medical College Azamgarh U.P. (India)

Received: 11-01-2022 / Revised: 25-02-2022 / Accepted: 23-03-2022

Corresponding author: Dr. EzmatJalil

Conflict of interest: Nil

### Abstract

**Introduction:** Hypothyroidism causes many metabolic abnormalities as well as multiple clinical symptoms. Some studies suggest that blood sugar may be affected in hypothyroidism and levels may increase. Indeed, it has been noted that patients with diabetes who also have hypothyroidism may have higher levels of Hemoglobin A1C (HbA1C). The HbA1c test reveals the average level of blood sugar over past 2-3 months. It is also called as glycosylated hemoglobin test and glycohemoglobin.

**Aims and Objectives:** To find out the correlation of the serum level of Hemoglobin A1C (HbA1c) with that of thyroid hormones and TSH.

**Materials and Methods:** The study design is cross sectional which has included 215 healthy participants. The blood sample was taken from each participant. 5 ml of blood was drawn HbA1c was determined by modified ELISA. Auto analyzer was employed for analysing Fasting Blood Sugar or FBS. Serum level of TSH, T4 and T3 were determined by using centrifugation at 5500 rpm for 5 minutes.

**Results:** The study found that there is a significant negative correlation between glycosylated hemoglobin with T3 (P=0.004) and glycosylated hemoglobin with T4 (<0.001). But the level of TSH has statistically positive variation with HbA1c.

**Conclusion:** The study concluded that T3 and T4 has negative correlation with the serum level of HbA1c while TSH has positive correlation with HbA1c. Hence the patients of hypothyroidism may show increased level of glycosylated hemoglobin.

**Keywords:** hemoglobin, glycosylated haemoglobin, t3, t4, tsh, thyroid hormones

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

### Introduction

Hypothyroidism causes many metabolic abnormalities as well as multiple clinical symptoms. Some studies suggest that blood sugar may be affected in hypothyroidism and levels may increase. Indeed, it has been noted that patients with diabetes who also have hypothyroidism may have higher levels of Hemoglobin A1C (HbA1C).

Thyroid disease can affect insulin levels. Because hyperthyroidism increases metabolism, insulin is eliminated faster, causing blood sugar levels to rise. This can increase the risk of diabetes or make diabetes harder to control. Hypothyroidism can lead to low blood sugar.

The HbA1c test reveals the average level of blood sugar over past 2-3 months. It is also called as glycated hemoglobin test and glycohemoglobin. This can also be used to diagnose diabetes. For a better understanding of this term we need to understand various components of words that make up this term – ‘hemoglobin’ is a protein found in red blood cells it gives blood the red color to the blood and it is the oxygen carrier of our body. The sugar on the other hand in our body is called glucose and when this glucose builds up in the body it gets bind to the hemoglobin of the red blood cells the test hba1c measures how much glucose is found in the body as red blood cells live for about three months hence the test depicts an average level of sugar glucose in the blood for the past three months. During this time frame the glucose level in the body was high the hemoglobin hba1c test will be higher [1].

For normal people without diabetes the normal range of this test is between 4% - 5.6%. level between 5.7- 6.4% indicate the condition called pre-diabetes, such people are at higher risk of getting diabetes. Level more than 6.5% indicate presence of diabetes

There are some conditions although where the HbA1c test can give misleading results these conditions include anemia, supplements specially vitamin c and vitamin E, high cholesterol levels in blood, kidney and liver diseases. People of the age under 45 years and having risk factors like obesity, hypertension, history of heart diseases, and sedentary way of lifestyle, should be considered to undergo testing for HbA1c. If not these but people having following symptoms should also opt to go for this test the symptoms include feeling thirsty frequently, increased urination, blurring of vision and feeling of fatigue [2].

People suffering from any kind of diabetes (1 or 2) and/or insulin resistance/ metabolic syndrome are more prone to acquire a thyroid disease; in the same way people

having thyroid malfunction have greater chances of developing type 2 diabetes the condition is aggravated if an individual is obese/overweight [3].

At the base of our neck is present a butterfly shaped gland called thyroid gland. It secretes two types of hormone T3 and T4, and these play a vital role in maintaining the synchrony of metabolic activities of our body. In a patient suffering from thyroid malfunction blood sugar gets accumulated instead of getting used as a source of energy, this makes such people easily prone to acquiring diabetes. Hyperglycemia (a condition characterized by high blood-sugar) -one of its main cause is the thyroid disease that frequently leads to metabolic syndrome. Which is an combination of following five conditions-‘high glucose, hypertension, high triglycerides, low HDL cholesterol’, and larger waist diameter (all these physical states makes a patient easily vulnerable to cardiac mishaps, diabetes, and stroke)[4].

### Materials and Methods

The study design is cross sectional which was performed from April 2021 to February 2022. This study is hospital based cross-sectional study of sample size 215 participants, among which 112 participants were males and 103 participants were females. These participants were randomly selected from the students, staffs, faculty of this hospital. The main characteristics of this cohort are they are all Indians and the age ranged between 18 years old to 52 years old.

### Inclusion and Exclusion Criteria

The inclusion and exclusion criteria were strictly followed. The patients, who had chronic conditions, acute diseases or any infection, were not included. The patients who cooperated with the complete procedure were only included.

The patients who had blood disorders, pregnancy or lactation, family history of

blood disorders or smoking history, were all excluded. The Ethical approval was obtained from the Ethical Committee of our institution.

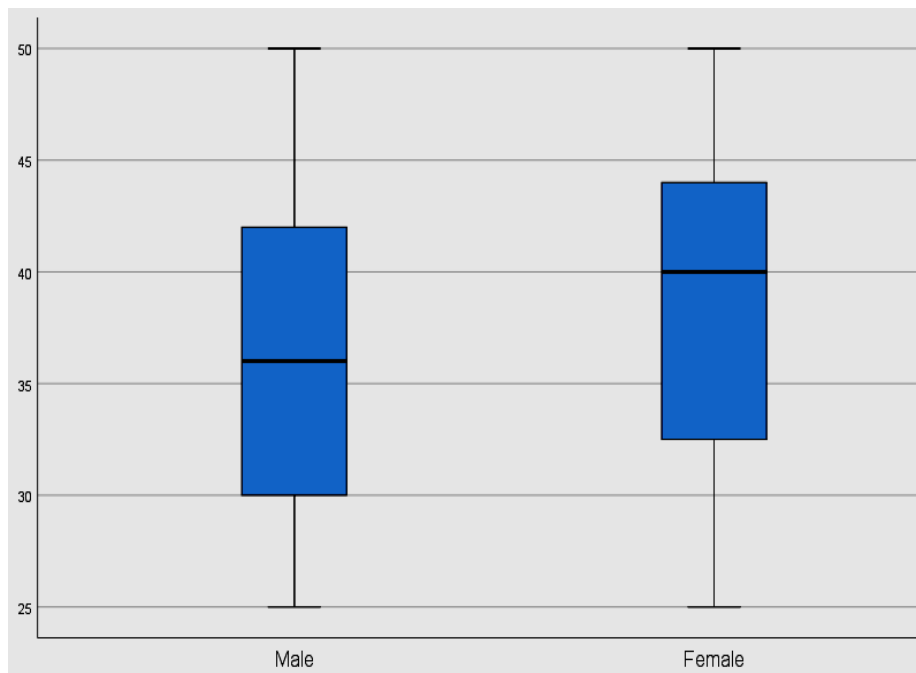
The study was conducted by filling a questionnaire about general health and their history. The blood sample was taken from each participant. 5 ml of blood was drawn HbA1c was determined by modified ELISA. Auto analyzer was employed for analysing Fasting Blood Sugar or FBS. Serum level of TSH, T4 and T3 were determined by using centrifugation at 5500 rpm for 5 minutes.

### Statistically Analysis

The study considered Mann-Whitney U-Test to statistically analyze the non-parametric continuous variables. The other data have been presented as mean±standard deviation. SPSS 25 software was used for statistical analysis.

### Results

The study found that the age of the males and females are  $36.53 \pm 7.31$  years old and  $38.44 \pm 7.52$  years old, respectively. Figure 1 shows the boxplot diagram depicting the demographic characteristics of the participants, including minimum and maximum value and mean value among the male participants and female participants.



**Figure 1: The boxplot diagram showing the demographic characteristics of the study sample**

Figure 2 shows the T3 serum level found among the participants, which ranged between 0.71 ng/ml and 1.61 ng/ml while

Figure 3 shows the distribution of T4 serum level among the participants that ranged between 4 ug/ml and 10.3 ug/ml.

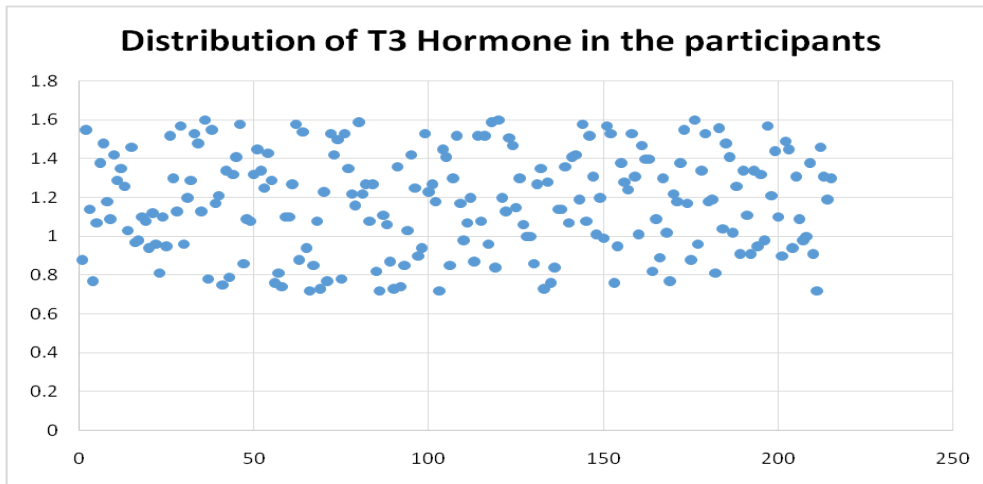


Figure 2: Distribution of T3 hormone among the participants

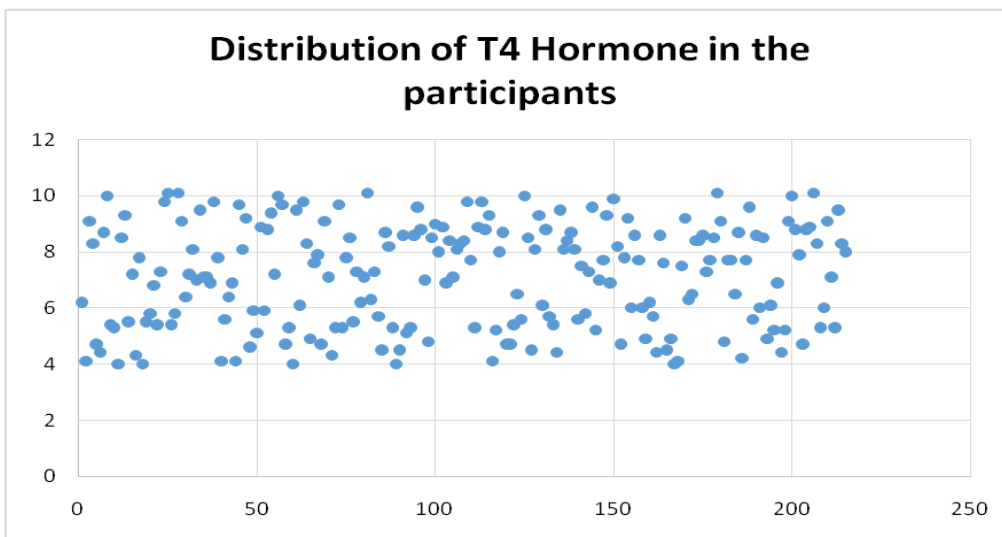


Figure 3: Distribution of T4 hormone among the participants

Figure 4 shows the distribution of TSH serum level among the participants that ranged between 0.46  $\mu$ IU/ml - 3.624  $\mu$ IU/ml.

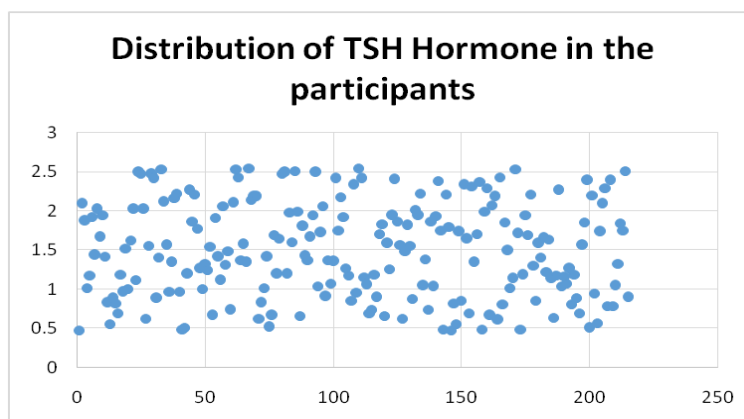


Figure 4: Distribution of TSH hormone among the participants

Table 1 shows the median level of HbA1c and the median value and ranges for T3 (ng/ml), T4 (ug/ml) and TSH ( $\mu$ IU/ml). It

reveals the finding of the statistical analysis, that is, the correlation of T3, TSH and T4 with the serum level of HbA1c.

**Table 1: The correlation between glycosylated hemoglobin and Thyroid Hormones**

Test Parameters	Mean	Range	P-value
Glycosylated hemoglobin (HbA1c)	4.9	4.1-5.7	<0.005
T3	1.3	0.71 - 1.61	.215
T4	7.2	4 - 10.3	>0.005
TSH	1.35	0.46 - 3.62	0.004

The study found that there is a significant negative correlation between glycosylated hemoglobin with T3 ( $P=0.216$ ) and glycosylated hemoglobin with T4 ( $>0.005$ ). But the study further found that there is positive correlation between glycosylated hemoglobin with TSH ( $P=0.004$ ).

Free T4 was found to be near the normal limit of the normal range and T3 level was also found to be near lower limit of the normal range.

### Discussion

The effect of thyroid hormone on insulin could be both good and bad. Hyperthyroidism and hypothyroidism are associated with insulin resistance. Studies have revealed that low and nearly low thyroid hormones promote the chances of diabetes [5]. Other studies have showcased that people having normal thyroid functioning may show chances of diabetes when the level of TSH rises up. Increased presence of FT4 in blood reduces the chances of diabetes both in abnormal and normal thyroid functioning conditions [6]. Diabetic patients persistently show lower level of thyroid hormones in comparison to subjects with normal glucose tolerance. In case of Pre-diabetic patients reports have shown that free T3 is negatively related with impaired glucose tolerance while free t4 is positively related to it [7]. Despite of

all what has been said above the effect of improved metabolic

indicators on functioning of thyroid gland is still not very clear [8, 9].

The amount of TSH has been directly found proportional to hypoglycemia and insulin resistance with patients otherwise having normal thyroid level reports. The possible reason attributed is that TSH can hamper metabolism of several compounds and initiate leptin secretion in fatty tissues. This alters glucose metabolism in liver and triggers hepatic production of glucose. High TSH level reduces release of insulin and increase insulin resistance. This leads to decreased peripheral tissue utilization of glucose contributing to glycation of hemoglobin[10].

Subclinical hypothyroidism (SCH), is the condition when TSH gets raised but free triiodothyronine (T3) and thyroxine (T4) remain in their normal range and this clinical condition has close connection with endothelial dysfunction [11]. The explanation to this is thyroid hormones have a direct impact on hematopoietic stem cells [12], that are able to transform into endothelial progenitor cells [13,14] which are responsible for thyroid follicle formation [15,16]. As endothelial progenitor cells have a vital role to play in endothelial repair [17] and thyroid hormones are produced by thyroid follicle

cells, proper secretion of thyroid hormones is closely related to be associated with endothelial repair capacity. The condition of hypoglycaemia, characterized by higher hemoglobinA1c (HbA1c) levels, is responsible for endothelial dysfunction [18]. Normal T3 and T4 level accelerates the progenitor cells of bone marrow to differentiate and mature into Erythrocytes. With level towards lower range, this effect is suppressed. One reason for HbA1c being elevated is due to reduced RBC turnover with raised TSH level [19,20].

There are some conditions although where the HbA1c test can give misleading results these conditions include anemia, supplements specially vitamin c and vitamin E, high cholesterol levels in blood, kidney and liver diseases. People of the age under 45 years and having risk factors mentioned below should get this test done that is factor: obesity, hypertension, history of heart diseases, and sedentary way of lifestyle. If not these but people having following symptoms should also opt to go for this test the symptoms include feeling thirsty frequently, increased urination, blurring of vision and feeling of fatigue [21].

Foods that can be eaten in case of higher HbA1c level which will bring down it eventually comprise of flax seeds, more number of fruits and vegetables, healthy nuts like walnuts almond etc. Lentils and other member of leguminous family, whole grains, and avoiding foods like bread pizza etc. Body symptoms like: frequently feeling thirsty; frequency of urination; feeling hungry more often, despite of high intake of food; the condition of fatigue; vision impairment also require an early and immediate checkup for HbA1c levels [22]. Few simple methods to bring down the HbA1c levels are eating foods with high glycemic index, eating small portions, controlling sugar cravings, timely intake of medicines and multivitamins, regularly exercising and weight loss to attend an ideal

weight, not totally avoiding the carbohydrates but measuring the portion sizes and limiting it, reducing the body weight if required [23,24].

### Conclusion

The present study shows thyroid hormones within normal range but TSH is raised early indicating thyroid in hypoactive. Our study shows raised TSH level is positively correlated with high glycosylated hemoglobin (HbA1c) while T3 & T4 hormones shows no correlation. In prehypothyroids high level of TSH causes insulin resistance which hinders peripheral conversion of FT4 to T3 hormones. Through it predisposes to hypoglycemia but less utilization of glucose contribute to glycation of haemoglobin. Hence high HbA1c value should be interpreted carefully in prediabetics even as it can be caused by increased TSH level caused by low erythrocyte turnover.

Our study suggests that underactive thyroid may cause HbA1c value elevated in subclinical hypothyroidism (high TSH & normal level of T3 and T4 levels) despite having fair glycemic control.

### References

1. Jonsdottir B, Larsson C, Carlsson A, et al. Thyroid and islet autoantibodies predict autoimmune thyroid disease at type 1 diabetes diagnosis. *J ClinEndocrinolMetab.* 2017 Apr 1;102(4):1277-1285. doi: 10.1210/jc.2016-2335.
2. Răcățăianu N, Leach N, Bondor CI, et al. Thyroid disorders in obese patients. Does insulin resistance make a difference? *Arch EndocrinolMetab.* 2017 Dec;61(6):575-583. doi:10.1590/2359-3997000000306.
3. Wang C. The relationship between type 2 diabetes mellitus and related thyroid diseases. *J Diabetes Res.* 2013;2013:390534. doi:10.1155/2013/390534

4. Mitrou P, Raptis SA, Dimitriadis G. Insulin action in hyperthyroidism: a focus on muscle and adipose tissue. *Endocr Rev.* 2010;31(5):663-79. doi:10.1210/er.2009-0046
5. Chaker L, Ligthart S, Korevaar TI, Hofman A, Franco OH, Peeters RP, Dehghan A. Thyroid function and risk of type 2 diabetes: a population-based prospective cohort study. *BMC Med.* 2016 Sep 30;14[1]:150. DOI: 10.1186/s12916-016-0693-4.
6. Islam S, Yesmine S, Khan SA, Alam NH, Islam S. A comparative study of thyroid hormone levels in diabetic and non-diabetic patients. *Southeast Asian J Trop Med Public Health.* 2008 Sep; 39 [5]:913-6. PMID: 19058589.
7. Jing S, Xiaoying D, Ying X, Rui L, Mingyu G, Yuting C, Yanhua Y, Yufan W, Haiyan S, Yongde P. Different levels of thyroid hormones between impaired fasting glucose and impaired glucose tolerance: free T3 affects the prevalence of impaired fasting glucose and impaired glucose tolerance in opposite ways. *ClinEndocrinol [Oxf].* 2014 Jun;80[6]:890-8. DOI: 10.1111/cen.12384.
8. Gu L, Yang J, Gong Y, Ma Y, Yan S, Huang Y, Wang Y, Peng Y. Lower free thyroid hormone levels are associated with high blood glucose and insulin resistance; these normalize with metabolic improvement of type 2 diabetes. *J Diabetes.* 2021 Apr; 13 [4]: 318-329. DOI: 10.1111/1753-0407.13118.
9. Alexandraki KI, Boutzios G, Antonopoulou I, Papaioannoutg, Bartsioka LI, Moschouris P, et al. Thyroid autoimmunity has no negative impact on insulin dynamics in prediabetic patients with normal thyroid function. *Archives of the Balkan Medical Union* 2020; 55[2]: 215-223. DOI:10.31688/ABMU.2020.55.2.02.
10. Mehran L, Amouzegar A, Tohidi M, Moayedi M, Azizi F. Serum free thyroxine concentration is associated with metabolic syndrome in euthyroid subjects. *Thyroid.* 2014 Nov;24[11]:1566-74. DOI: 10.1089/thy.2014.0103.
11. Lu, M.; Yang, C.-B.; Gao, L.; Zhao, J.-J. Mechanism of subclinical hypothyroidism accelerating endothelial dysfunction (Review). *Exp. Ther. Med.* 2015, 9, 3–10.
12. Vacek, A.; Rotkowská, D.; Bartoničková, A.; Pospíšil, M. Effect of hyperthyroidism on haemopoietic stem cell kinetics in mice. *Cell Prolif.* 1978, 11, 487–496.
13. Daub, K.; Langer, H.; Seizer, P.; Stellos, K.; May, A.E.; Goyal, P.; Bigalke, B.; Schönberger, T.; Geisler, T.; Siegel-Axel, D.; et al. Platelets induce differentiation of human CD34+ progenitor cells into foam cells and endothelial cells. *FASEB J.* 2006, 20, 2559–2561.
14. Stellos, K.; Langer, H.; Daub, K.; Schoenberger, T.; Gauss, A.; Geisler, T.; Bigalke, B.; Mueller, I.; Schumm, M.; Schaefer, I.; et al. Platelet-derived stromal cell-derived factor-1 regulates adhesion and promotes differentiation of human CD34+ cells to endothelial progenitor cells. *Circulation* 2008, 117, 206–215.
15. Villacorte, M.; Delmarcelle, A.-S.; Lernoux, M.; Bouquet, M.; Lemoine, P.; Bolsée, J.; Umans, L.; Lopes, S.C.D.S.; van der Smissen, P.; Sasaki, T.; et al. Thyroid follicle development requires Smad1/5- and endothelial cell-dependent basement membrane assembly. *Development* 2016, 143, 1958–1970.
16. Degosserie, J.; Heymans, C.; Spourquet, C.; Halbout, M.; D'Auria, L.; van der Smissen, P.; Vertommen, D.; Courtoy, P.J.; Tyteca, D.; Pierreux, C.E. Extracellular vesicles from endothelial progenitor cells promote thyroid follicle formation. *J. Extracell. Vesicles* 2018, 7, 1487250.

17. Shimizu, Y.; Yamanashi, H.; Noguchi, Y.; Koyamatsu, J.; Nagayoshi, M.; Kiyoura, K.; Fukui, S.; Tamai, M.; Kawashiri, S.-Y.; Kondo, H.; et al. Association between chronic kidney disease and carotid intima-media thickness in relation to circulating CD34-positive cell count among community-dwelling elderly Japanese men. *Atherosclerosis* 2019, 283, 85–91.
18. Sheppard, T. . (2022). Pressure Injury Prevention: Patient Education for Spinal cord Injury Patients- The Importance of Teaching Nurses to Teach. *Journal of Medical Research and Health Sciences*, 5(2), 1791–1795. <https://doi.org/10.52845/JMRHS/2022-5-2-5>
19. Meza, C.A.; La Favor, J.D.; Kim, D.-H.; Hickner, R.C. Endothelial dysfunction: Is there a hyperglycemia-induced imbalance of NOX and NOS? *Int. J. Mol. Sci.* 2019, 20, 3775.
20. Endemann, D.H.; Schiffrin, E.L. Endothelial dysfunction. *J. Am. Soc. Nephrol.* 2004, 15, 1983–1992.
21. Kang, S.H.; Jung, D.J.; Choi, E.W.; Cho, K.H.; Park, J.W.; Do, J.Y. HbA1c levels are associated with chronic kidney disease in a non-diabetic adult population: A nationwide survey (KNHANES 2011–2013). *PLoS ONE* 2015, 10, e0145827.
22. Ooba N, Tanaka S, Yasukawa Y, et al. Effect of high-potency statins on HbA1c in patients with or without diabetes mellitus. *J Pharm Health Care Sci.* 2016;2:8. Published 2016 Mar 18. doi:10.1186/s40780-016-0040-0.
23. Ghazanfari Z, Haghdoost AA, Alizadeh SM, Atapour J, Zolala F. A Comparison of HbA1c and Fasting Blood Sugar Tests in General Population. *Int J Prev Med.* 2010;1(3):187-194.
24. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. *Biomark Insights.* 2016;11:95-104. Published 2016 Jul 3. doi:10.4137/BMI.S38440.