

The Effect of Inflammatory Markers in Patients with Diabetes Mellitus

Rusul Ali Al-Masaoodi*

College of Applied Medical Sciences, University of Kerbala, Kerbala, Iraq

The purposes of this research are to identify the significance of inflammatory substances in individuals with type 2 diabetes mellitus and investigate the relationship involving inflammatory responses and illness duration. The fifty specimens used in the present investigation were split between thirty specimens of individuals who had diabetes with type 2 and twenty specimens about the unaffected population. In this investigation, the body mass index (BMI), HbA1C, as well as levels of C-reactive proteins among individuals having diabetes type 2 and the unaffected population were calculated. also shows the relationship between HbA1C, CRP, and a body mass index HbA1C, CRRACTIVE PROTINE, and a body mass index all increased significantly ($p < 0.05$) throughout the present study. Additionally, in individuals with diabetes with type 2, there was a substantial ($p < 0.05$) positive association among the Creative Protein and body mass index (B and a significant ($p < 0.05$) beneficial relationship among the C Reactive protein and HbA1C. According according to the research's findings, those suffering from type 2 diabetes had higher levels of inflammation-related markers, and their HbA1C readings increased in tandem alongside the progression of the illness, suggesting an advantageous correlation across the two variables.

Keyword: Diabetes, CRP, HbA1C, Inflammation

Introduction

According to Petersmann et al. (2018), elevated blood sugar levels are a key indicator of the presence of diabetes, a dangerous multifaceted condition. According to Dahlstrom and Sandholm (2017), a higher glucose in the blood concentration can't cause feelings alone its own, but it might eventually cause micro- and macro-vascular problems such as kidney failure, heart failure multiple medical conditions, amputees, and blindness.

The autoimmune condition identified as type one diabetes (type 1 diabetes is typified primarily the death of cells in the pancreas, which results in total insulin insufficiency.

Approximately ninety percent of all instances of metabolic syndrome are caused by type 2 diabetes, which is distinguished with diabetes-related insulin resistance and dysfunction of β -cells that develops progressively (IDF Diabetes Atlas, 2019). According to America Diabetes (2020), type two diabetes is currently more common in young people and adolescents than in older individuals, however among those aged between the ages of twenty and forty, there is additionally a significant amount of variability underlying the condition (Niroomand et al., 2017).

The small pouches of cells known as Langerhans make up approximately two percent of the whole pancreas under normal circumstances. It has cells called α and β that release both glucagon and insulin, correspondingly (Da Silva Xavier, 2018). When blood glucose levels are greater, the β cells release glucose. But when the blood sugar levels drop, the α cells release insulin (Vanhorebeek et al., 2007). In order to prevent hyperglycemia or hypoglycemia, both glucagon and insulin are crucial enzymes (Van den Berghe, 2004).

Following a meal, the breakdown of starchy carbohydrates into glycogen and a raise in blood sugar concentrations trigger the pancreatic β islet cell population to begin producing insulin into the circulatory system. The production of insulin then improves the absorption of carbohydrates through the circulatory system through cells and including muscle in the skeleton, fatty tissues, including hepatocytes (Vanhorebeek et al., 2007). The T2D risk variables The main risk variables for developing type-2 diabetes are being overweight or obese, a lack of exercise, and a family history of GDM and diabetes (Wu et al., 2014). According to Alva et al. (2017), those over 45 had a 2-4 times increased chance of developing type 2 diabetes.

According to the kind of blood vessel concerned, complications associated with diabetes are typically classified as either macrovascular or vascular. Cerebrovascular illnesses, peripheral arterial disease (PAD), and cardiovascular illness (CVD) are examples of macrovascular problems; retinal degeneration, nephropathy, and neuropathy are examples of complications of microvascular disease. Atherosclerosis cardiovascular disease, or macrovascular consequences, is the primary cause of death and disability (Fowler, 2008).

The progression of diabetes consequences appears to have been significantly influenced by elevated reactive oxygen species and inflammatory. In addition to increasing the levels of inflammation and oxidative stress, the hyperglycemia milieu also lowers defenses against these conditions by activating many mechanisms. The previously fibrinolytic pathway along with additional variables controlling the contraction and dilation of vessels may also have an impact on blood vessel function (Lotfy et al., 2017).

2. Materials and Methods

2.1. Subjects

Individuals suffering from diabetes participated in this investigation. Serum samples were obtained among the control group and individuals experiencing diabetes who were diagnosed with type 2. The fifty specimens that were analyzed were split into two groups: twenty

specimens representing the control group and 30 samples from patients with type Two diabetes.

2.2. Blood samples collection

Five milliliters of sterile syringes have been utilized to extract the blood specimens through the venous. This specimen has been put in two separate tubes with labels; the initial assortment diabetic tube includes EDTA, a drugs that prevents blood coagulation and is used to determine the HbA1C. The additional set of containers, which were gel tubes no anticoagulant, was utilized to prepare plasma during subsequent biochemical examination using plasma. After centrifuging blood of ten minutes at a speed of 6000 rpm to allow it to form a coagulate, the blood product had been separated then frozen at -80 oC until the laboratory testing for the purpose of the research could be completed.

2.3. Body Mass Index (BMI)

A accurately calibrated the internet weighing and height scale measuring instrument served to assess the individuals a weight as well as lengths while they were dressed comfortably indoors. The BMI, or body mass index, was calculated by splitting the weight in kilograms by the corresponding square for the person's height in meters, as shown using the formula: a body mass index = weight (kilograms) / height (meters)².

2.4. Estimation of HbA1C level

Principle of Assay:

The Basis of Response During the initial response, the level of hemoglobin is determined at a set wavelengths of absorption while this protease process simultaneously generates fructosyl dipeptides that derived from the the N-terminal amino groupings of the beta-chain of blood sugar levels. In the next step, Ten (carboxymethyl-aminocarbonyl)-3,7-bis(dimethylamino) a compound called sodium salt develops a color in a concentration of peroxide due to its interaction of fructosyl peptide oxidase (FPOX) using fructosyl dipeptides, which produces hydrogen peroxide. To determine the HbA1c, an alteration in absorption is assessed. The apparatus computes and displays HbA1c(%) based around the combination hba and HbA1c test findings.

2.5. Estimation of C-Reactive protein

Reaction Principle

The concentrated activity of C Reactive Protin is determined by photometrically measuring the immune complex among the antibodies that are capable of CRP with the CRP found in the biopsy specimen. The absorbance increase is directly related to the total amount of CRP. Anti-human CRP antibody + CRP Immunocomplex → (Agglutination).

2.6. Statistical Analysis

The statistical software SPSS was used for statistically analyzing the information (SPSS, Version 23). The t-test was used to compare the means and standard deviations of the individuals and unaffected groups. The correlation coefficient was computed to determine the correlation amongst indicators and variables, and Pearson correlation and one-way ANOVA by LSD were used to compare the dividing categories according to the parameters that were determined. The Microsoft Office 2016 Excel application was used to create the figures. A substantial $P < 0.05$ was used for statistical analysis of each of them.

3. Results

Figure 1 illustrates the present moment the research's findings, which showed people with Type 2 diabetes mellitus had a significantly higher BMI ($p < 0.05$) than the unaffected categories. These findings were in contrast to the research of Alzamil (2020), where revealed that the majority of patients with diabetes during the present research had BMIs above thirty and that their resistance to insulin was significantly positively correlated between it and increased TNF- α levels. the impact of body mass index on the time it takes to diagnose diabetes mellitus and its consequences in people older than sixty-five

Underlying both men and women, we discovered that obesity and being overweight are significant risk factors for type 2 diabetes and its consequences. The probability of getting diabetes mellitus was thirty percent greater for males and ten percent greater for women in the overweight category ($25 < \text{BMI} \leq 29.99$). Both men and women were one hundred percent more likely to develop diabetes mellitus at $30 < \text{BMI} \leq 39.99$ than those with a normal BMI. The possibility of acquiring diabetes mellitus are raised significantly up to 150% for women and 180% for men if their body mass index (BMI) is ≥ 40 (Grey et al., 2015).

According to our findings, losing obesity can help overweight people having pre-diabetes avoid becoming Type 2 diabetes by delaying the onset of the disease. Additionally, because a body mass index (BMI) of even a little bit above twenty-five increases the relative risk of a problem, managing one's weight is crucial for preventing consequences associated to diabetes mellitus. Numerous current weight-loss initiatives, such as nutritional, psychological, and lifestyle modifications, are effective in reducing body weight over the course of time and significantly lowering the risk of diabetic. (Appel *et al.*, 2011)

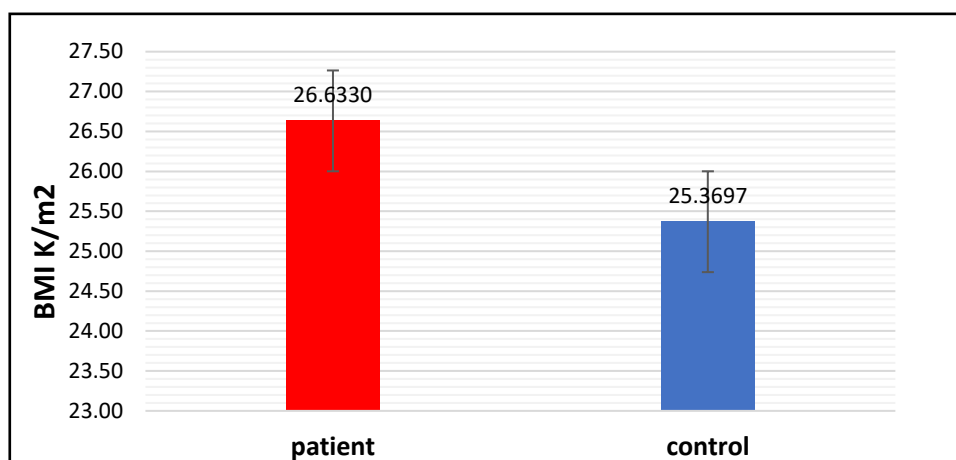


Figure 1: Comparison of BMI level between patients with Type 2 diabetes mellitus and control group

As seen in Figure 2, the present research's findings showed that individuals with diabetes type 2 mellitus had a significantly higher HbA1C ($p < 0.05$) than those in the control categories. They were in agreement with the findings of another study by Al-Attaby and Al-Lami (2019), which showed that the HbA1c was significantly higher in the second and third levels based on illness durations (61-120 and 121-180 months) than in the initial group (1-60 months).

According to Chakraborty et al. (2016), the problems were substantially correlated with both the HbA1c level and the length of diabetic. Chronic high blood sugar levels and a number of the metabolic syndrome components are determined by the possibility of microvascular consequences among those with type 2 diabetes. In diabetes individuals, HbA1c indicates an increased likelihood of complications of diabetes after serving primarily a measure for the mean blood glucose level.

In contrast, individuals with diabetes may have a lower risk of cardiovascular diseases if their control of glucose is improved. The measurement of the amount of beta-N-1-deoxy fructosyl component of haemoglobin in the circulatory system is known as HbA1C, or the percentage of hemoglobin that has been glycosylated A1c. The hemoglobin protein stays glycosylated throughout the rest of its lifespan (120 days) after a molecule of sugar attaches itself to it within the red blood cells (Piccini et al., 2016). Accordingly, HbA1C can be used for diagnostic purposes and serves as a measurement of the permanent (about three months) state of glycemia (Bowman et al., 2012).

The human blood's HbA1c concentration is influenced by both red blood cell lifespan and the level of glucose in the blood (David et al., 2012). Consequently, the duration of the disease influences the significant increase that occurs in the HbA1c blood sugar levels of the

type 2 diabetic participants in the present investigation, a conclusion similar to a previous study (Ito et al., 2017). This finding could be related to accompanying health care professionals' growth, which happens when changes in therapy can occur after years of uncontrolled HbA1c levels (Hayashino et al., 2017).

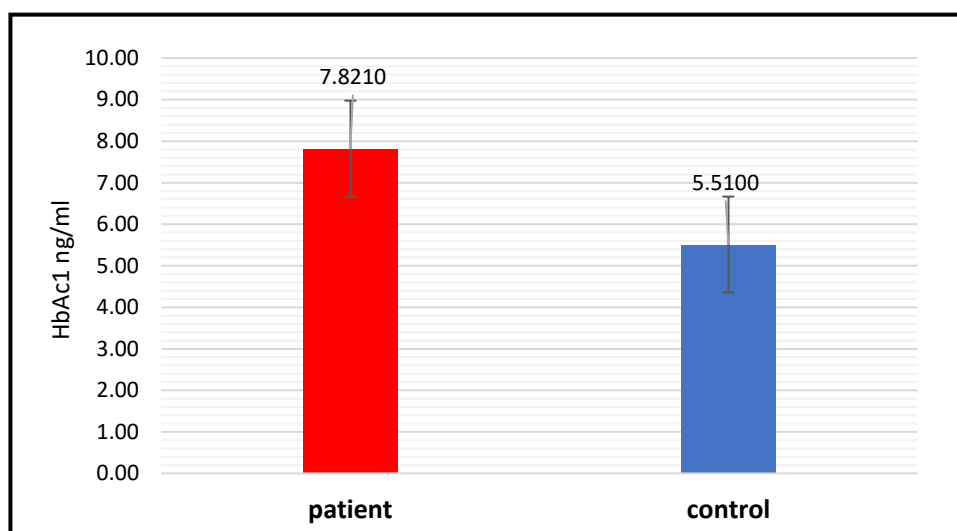


Figure 2: Comparison of HbA1 concentration between patients with Type 2 diabetes mellitus and control group

According to the research's findings, individuals who had Type 2 diabetes mellitus had significantly higher CRP concentrations ($p < 0.05$) than the comparison category, as seen in Figure (3). Agho et al. (2021) discovered that people with diabetes had higher salivary concentrations of CRP, IL-6, as well as TNF- α compared to normal controls. This finding supports the idea that subclinical in nature ongoing inflammation plays a role in the development and progression of diabetes type 2 diabetes mellitus (Badawi et al., 2010).

The following is additionally consistent with research that found diabetics have greater salivary concentrations of CRP than healthy subjects (Dezayee et al., 2016). They discovered that the rise in the incidence of type 2 diabetes, insulin resistance, and cholesterol was substantially correlated with raised blood CRP levels (Jeong et al., 2019).

Those with serious autoimmune disorders and conditions like type 2 diabetes and cardiovascular disease have higher levels of CRP, an important inflammatory indicator. CRP has been demonstrated to be greater in individuals with T2DM compared to healthy individuals in a Chinese population survey (Wen et al., 2010), indicating that CRP is a standalone indicator of incidence T2DM. Greater CRP levels are additionally linked to a greater probability of type 2 diabetes, according to some previous research (Liu et al., 2007).

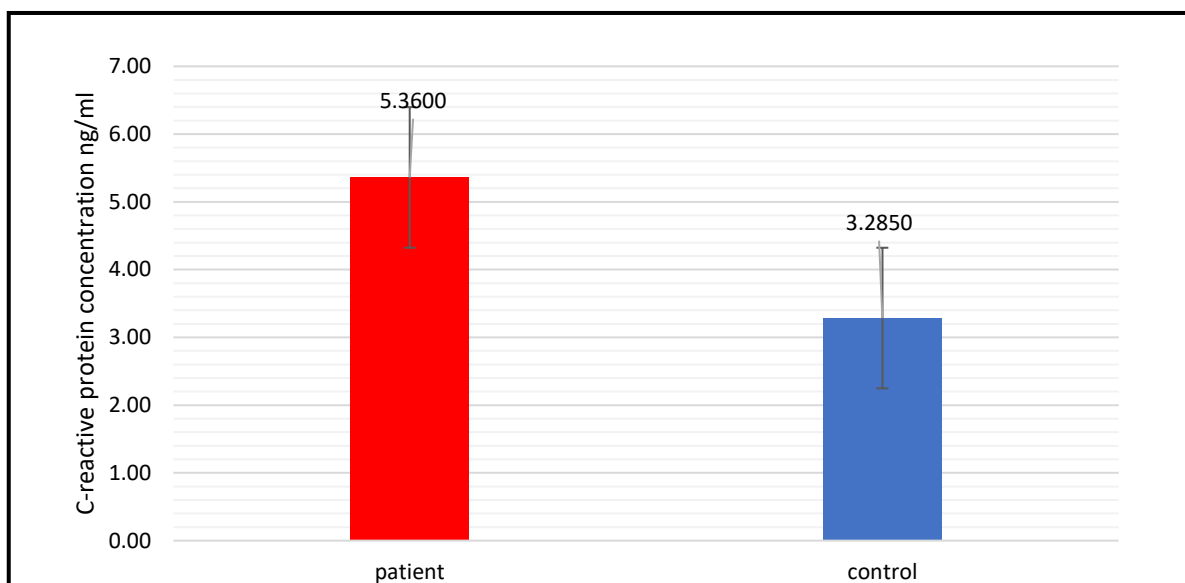


Figure 3: Comparison of C-reactive protein concentration between patients with Type 2 diabetes mellitus and control group

According to the current research's findings, people with type 2 diabetes mellitus had a significant positive correlation ($r=0.145$) between their HbA1c and levels of C-reactive protein (Figure 4). This outcome is consistent via Seo and Shin's (2021) investigation, which found The purpose of the present research aimed to ascertain how diabetic individuals' HbA1c with hs-CRP relate to one another. We discovered that when the percentile of high-sensitivity CRP rose, so did the correlation parameter value. Consequently, the HbA1c levels were impacted by the hs-CRP levels. Consistent with other research, these findings show a link among levels of blood sugar and inflammation in diabetes individuals (Son, 2019).

The determination drawn from this outcome Utilizing big data, the present investigation demonstrated the connection between glucose regulation, symbolized by HbA1c, and markers of inflammation, indicated by hs-CRP. The levels of HbA1c were impacted by hs-CRP concentrations. nevertheless controlling considering a number of associated factors, there was a substantial rise in HbA1c when hs-CRP rose. Therefore, the current study's findings can serve as a foundation to further research that will determine the connection between diabetes and other variables.

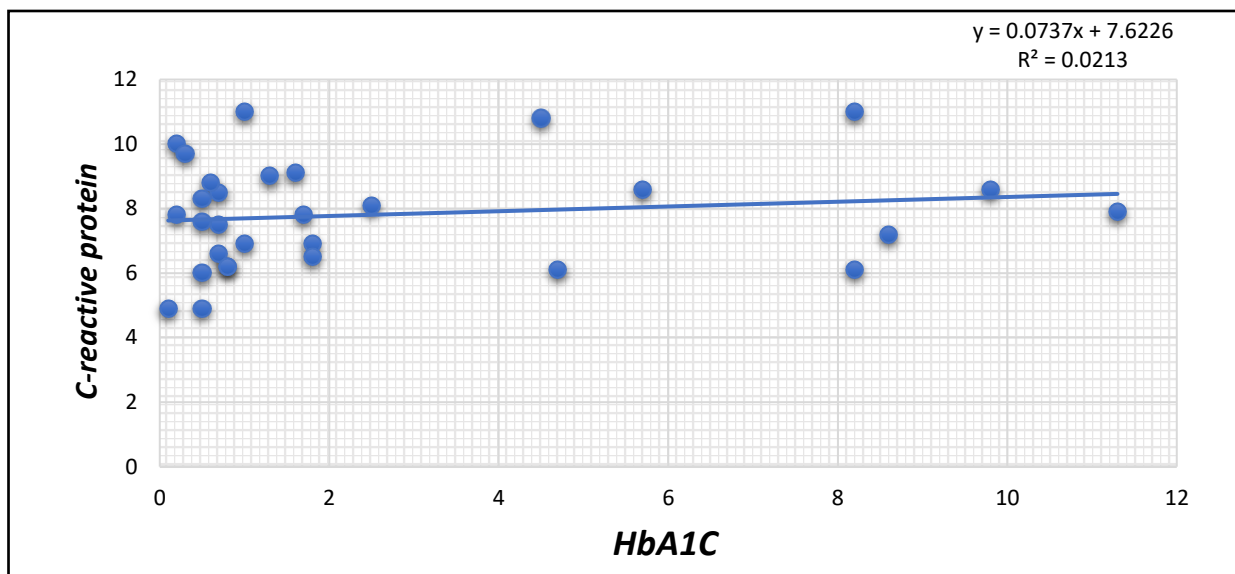


Figure (4): Correlation between the HbA1C and c-Reactive Protein

. The results of the present investigation revealed a noteworthy positive correlation ($r=0.$) among a body mass index and C-reactive protein levels in individuals with diabetic mellitus, as illustrated in figure (5). According to the research conducted by Seo1 and Shin (2021), among the additional risk variables affecting the development of metabolic syndrome, the hs-CRP is connected with BMI, blood pressure, cholesterol levels, triglycerides, HDL-cholesterol, fasting blood sugar, and uric acid. body mass index was previously described as being a particularly significant indication and found predominantly associated the hs-CRP. Therefore, in addition to age and gender, a body mass index has been added as a criterion.

Timpson et al. (2011) found a high correlation between blood CRP and a body mass index suggesting that reduced average plasma CRP levels in the Korean population may be caused by Asians having comparatively lower BMIs than those in Western nations. At the population level, plasma CRP levels and mean BMI are highly correlated throughout ethnic communities. fortunately the plasma concentrations of CRP cannot be fully explained by fat. The distribution of plasma CRP varies by ethnicity and sexual orientation (Saito, 2012).

The body mass index (BMI) and glucose tolerance levels of people with Type 2 diabetes are greater, and they are comparatively obese (Chatterjee et al., 2012). We investigated the connection among CRP and sudden development of type 2 diabetes in the context of being overweight and high blood pressure. It is believed that elevated CRP levels cause increased resistance to insulin through a variety of potential processes, such as the encouragement about thrombogenic agent development, stimulation of the cascade of complements, the improvement of cardiovascular attachment molecules expression, and

decreased endothelial nitric oxide synthase (eNOS) (Fukuchi et al., 2008). We discovered observed the relationship among CRP and incidence type 2 diabetes is influenced by both obesity and hypertension.

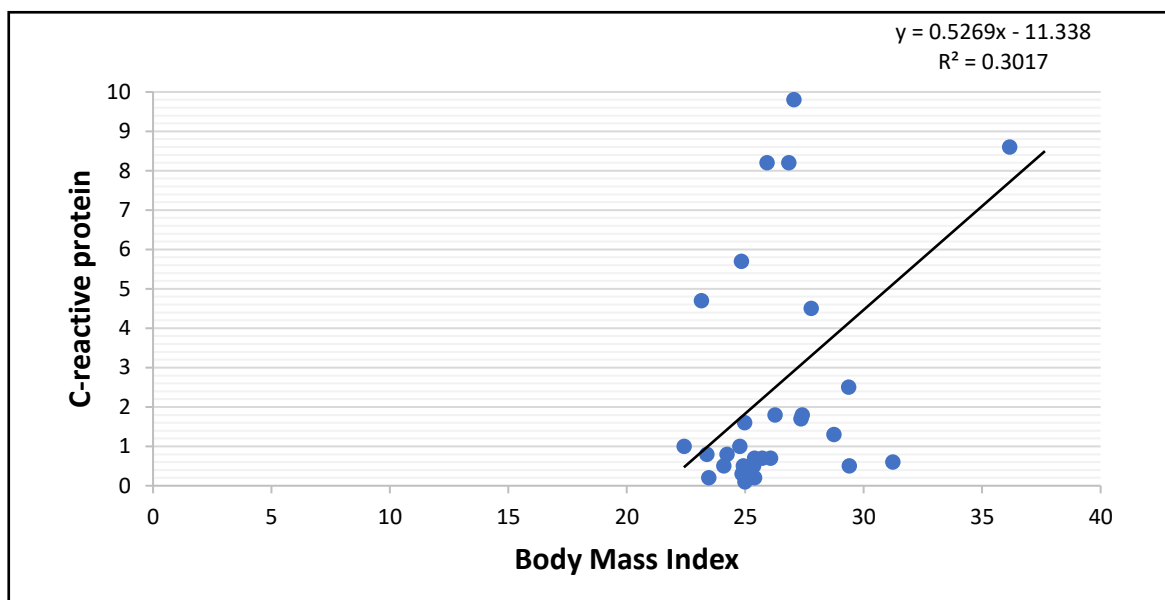


Figure 5: Correlation between the BMI and C-reactive Protein

4. Conclusion

According to the research's findings, those suffering from type two diabetes had higher levels of the inflammatory marker CRP, indicating that inflammatory is more common in diabetics. The metabolic syndrome, a condition which causes diabetes, was discussed after the most recent research also discovered variations in sufferers' BMIs and managed problems. The investigation also discovered a favorable association involving inflammation indicators and the advancement of the illnesses, as well as a correlation between the rise in HbA1C and the progression of the illness. Research suggestions involve looking into the relationship between diabetes and COVID-19 as well as its additional inflammation. indicators.

5. References

- [1] Petersmann, A. (2018). Definition, Classification and Diagnosis of Diabetes Mellitus. *Exp Clin Endocrinol Diabetes*, 126(7), 406-410.
- [2] Dahlström, E., & Sandholm, N. (2017). Progress in defining the genetic basis of diabetic complications. *Current diabetes reports*, 17(9), 1-13.
- [3] IDF Diabetes Atlas, Ninth edition, 2019. International diabetes federation.

- [4] American Diabetes Association. (2020). 2. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes—2020. *Diabetes care*, 43(Supplement_1), S14-S31.
- [5] Niroomand, M., Ghasemi, S. N., Karimi-Sari, H., & Khosravi, M. H. (2017). Knowledge, attitude, and practice of Iranian internists regarding diabetes: a cross sectional study. *Diabetes & metabolism journal*, 41(3), 179-186.
- [6] Da Silva Xavier, G. (2018). The cells of the islets of Langerhans. *Journal of clinical medicine*, 7(3), 54.
- [7] Vanhorebeek, I., Langouche, L., & Van den Berghe, G. (2007, February). Modulating the endocrine response in sepsis: insulin and blood glucose control. In *Novartis Foundation symposium* (Vol. 280, p. 204). Chichester; New York; John Wiley; 1999.
- [8] Van den Berghe, G. (2004). How does blood glucose control with insulin save lives in intensive care?. *The Journal of clinical investigation*, 114(9), 1187-1195.
- [9] Wu, Y., Ding, Y., Tanaka, Y., & Zhang, W. (2014). Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. *International journal of medical sciences*, 11(11), 1185.
- [10] Alva, M. L., Hoerger, T. J., Zhang, P., & Gregg, E. W. (2017). Identifying risk for type 2 diabetes in different age cohorts: does one size fit all?. *BMJ Open Diabetes Research and Care*, 5(1), e000447.
- [11] Fowler, M. J. (2008). Microvascular and macrovascular complications of diabetes. *Clinical diabetes*, 26(2), 77-82.
- [12] Lotfy, M., Adeghate, J., Kalasz, H., Singh, J., & Adeghate, E. (2017). Chronic complications of diabetes mellitus: a mini review. *Current diabetes reviews*, 13(1), 3-10.
- [13] Alzamil, H. (2020). Elevated serum TNF- α is related to obesity in type 2 diabetes mellitus and is associated with glycemic control and insulin resistance. *Journal of obesity*, 2020.
- [14] Gray, N., Picone, G., Sloan, F., & Yashkin, A. (2015). The relationship between BMI and onset of diabetes mellitus and its complications. *South Med J.*, 108(1), 29-36.
- [15] Appel, L. J., Clark, J. M., Yeh, H. C., Wang, N. Y., Coughlin, J. W., Daumit, G., ... & Brancati, F. L. (2011). Comparative effectiveness of weight-loss interventions in clinical practice. *England Journal of Medicine*, 365(21), 1959-1968.
- [16] Al-Attaby, A. K. T., & Al-Lami, M. Q. D. (2019). Effects of duration and complications of type 2 diabetes mellitus on diabetic related parameters, adipocytokines and calcium regulating hormones. *Iraqi Journal of Science*, 2335-2361.
- [17] Chakraborty, N. and Mandal, A. K. (2016). A study on complications of type 2 diabetes mellitus in a diabetes clinic of a tertiary care hospital, Kolkata, west Bengal. *IOSR JDMS*, 15(10):,29-33.
- [18] Piccini, B., Artuso, R., Lenzi, L., Guasti, M., Braccresi, G., Barni, F., ... & Toni, S. (2016). Clinical and molecular characterization of a novel INS mutation identified in

- patients with MODY phenotype. *European journal of medical genetics*, 59(11), 590-595.
- [19] Bowman, P., Flanagan, S. E., Edghill, E. L., Damhuis, A., Shepherd, M. H., Paisey, R., ... & Ellard, S. (2012). Heterozygous ABCC8 mutations are a cause of MODY. *Diabetologia*, 55(1), 123-127.
- [20] Ito, H., Omoto, T., Abe, M., Matsumoto, S., Shinozaki, M., Nishio, S., ... & Togane, M. (2017). Relationships between the duration of illness and the current status of diabetes in elderly patients with type 2 diabetes mellitus. *Geriatrics & Gerontology International*, 17(1), 24-30.
- [21] Hayashino, Y., Izumi, K., Okamura, S., Nishimura, R., Origasa, H., Tajima, N., & JDCP Study Group. (2017). Duration of diabetes and types of diabetes therapy in Japanese patients with type 2 diabetes: The Japan Diabetes Complication and its Prevention prospective study 3 (JDCP study 3). *Journal of diabetes investigation*, 8(2), 243-249.
- [22] Agho, E. T., Owotade, F. J., Kolawole, B. A., Oyetola, E. O., & Adedeji, T. A. (2021). Salivary inflammatory biomarkers and glycated haemoglobin among patients with type 2 diabetic mellitus. *BMC Oral Health*, 21, 1-8.
- [23] Dezayee, Z. M. I., & Al-Nimer, M. S. M. (2016). Saliva C-reactive protein as a biomarker of metabolic syndrome in diabetic patients. *Indian Journal of Dental Research*, 27(4), 388.
- [24] Jeong, H., Eun, Y. H., Kim, I. Y., Park, E. J., Lee, J., Kim, H., & Jeon, C. H. (2019). C-reactive protein level as a marker for dyslipidemia, diabetes, and metabolic syndrome: results from the korean national health and nutrition examination survey. *annals of the rheumatic diseases*, 78, 2092-2092.
- [25] Wen, J., Liang, Y., Wang, F., Sun, L., Guo, Y., Duan, X., ... & Wang, N. (2010). C-reactive protein, gamma-glutamyltransferase and type 2 diabetes in a Chinese population. *Clinica Chimica Acta*, 411(3-4), 198-203.
- [26] Liu, S., Tinker, L., Song, Y., Rifai, N., Bonds, D. E., Cook, N. R., ... & Manson, J. E. (2007). A prospective study of inflammatory cytokines and diabetes mellitus in a multiethnic cohort of postmenopausal women. *Archives of internal medicine*, 167(15), 1676-1685.
- [27] Seo, Y. H., & Shin, H. Y. (2021). Relationship between hs-CRP and HbA1c in Diabetes Mellitus Patients: 2015–2017 Korean National Health and Nutrition Examination Survey. *Chonnam medical journal*, 57(1), 62.
- [28] Son, N. E. (2019). Influence of ferritin levels and inflammatory markers on HbA1c in the Type 2 Diabetes mellitus patients. *Pakistan journal of medical sciences*, 35(4), 1030.
- [29] Timpson, N. J., Nordestgaard, B. G., Harbord, R. M., Zacho, J., Frayling, T. M., Tybjaerg- Hansen, A., & Davey Smith, G. (2011). C-reactive protein levels and body mass index: elucidating direction of causation through reciprocal Mendelian randomization. *International journal of obesity*, 35(2), 300-308.

- [30] Saito, I. (2012). Epidemiological evidence of type 2 diabetes mellitus, metabolic syndrome, and cardiovascular disease in Japan. *Circulation Journal*.
- [31] Chatterjee, S., Khunti, K., & Davies, M. J. (2017). Type 2 diabetes. *The lancet*, 389(10085), 2239-2251.
- [32] Fukuchi, Y., Miura, Y., Nabeno, Y., Kato, Y., Osawa, T., & Naito, M. (2008). Immunohistochemical detection of oxidative stress biomarkers, dityrosine and N ϵ -(hexanoyl) lysine, and c-reactive protein in rabbit atherosclerotic lesions. *Journal of atherosclerosis and thrombosis*, 15(4), 185-192.