# Effect of Gender on Cholesterol Levels in Type 2 Diabetes Mellitus Patients

*Rahayu* Anggraini[1*], *Firdaus*[2], *Devyana* Dyah Wulandari[1], *Naufal* Iman Yulian Pratama[1], *Moch.* Sahri[3]

[1]Medicinal Laboratory Technology, Faculty of Health, University Nahdlatul Ulama Surabaya, Indonesia
[2]Nursing Laboratory, Faculty of Nursing and Midwifery, Universitas Nahdlatul Ulama Surabaya, Indonesia
[3]Occupational Health and Safety Laboratory, Faculty of Health, Universitas Nahdlatul Ulama Surabaya, Indonesia

**Abstract.** In women aged 17-50 years, a decrease in Follicle-stimulating hormone (FSH) levels will increase the hormone estrogen which requires cholesterol, so that cholesterol becomes low through inhibition of liver cholesterol biosynthesis. The purpose of this study was to determine differences in cholesterol levels between women and men with Type 2 Diabetes Mellitus. The study design was a cross-sectional analytic observational and purposive sampling technique with inclusion criteria of HbA1c > 6.5%. As a result, the average age of the male respondents was 44 years (SD±18.4), HbA1c 8.5% (SD±2.4), and cholesterol 212 mg/dL (SD±40), the average age of females was 58 years old (SD ± 7.7, HbA1c 10.6% (SD ± 3.4), and cholesterol 181 mg/dL (SD ± 37.6). The results of the Mann- Whitney test with p = 0.038 (p <0.05) mean that there is a significant difference in cholesterol levels between men and women, which means there are differences in how the brain works between men and premenopausal women who suffer from type 2 Diabetes Mellitus Suggestions for future researchers, it is necessary to conduct research on High-sensitivity C-reactive protein (hs-CRP) and low-density lipoprotein (LDL) cholesterol in premenopausal women regarding the role of estrogen and FSH in regulating cholesterol.

## 1 Introduction

The traditional perspective, which holds that a deficiency in estrogen is the cause of dyslipidemia, states that gender has an impact on total cholesterol levels. During menopause, follicle-stimulating hormone (FSH) levels rise in addition to a decrease in estrogen. This study discovered that by inhibiting the hepatic cholesterol manufacture, blocking FSH decreased blood cholesterol. Serum FSH levels and serum total cholesterol levels are found to favorably correlate. Additionally, compared to pre-menopausal women, post-menopausal

* Corresponding author: anggrek@unusa.ac.id

women have a much higher prevalence of hypercholesterolemia. According to the findings of studies conducted in rat models, normal levels of estrogen (E2) were maintained with exogenous supplementation, and FSH was increased by injecting exogenous FSH intraperitoneally in ovariectomized rats (OVX). Consistently, these results demonstrate that FSH is independent of estrogen.

In the mouse model, serum cholesterol levels rise. Furthermore, it is possible to successfully avoid hypercholesterolemia brought on by FSH injections or the consumption of a high-cholesterol diet by suppressing the FSH receptor gene (FSHR) or by blocking FSH signaling with anti-FSHβ antibodies. Mechanistically, FSH binds to the hepatic FSHR, which activates the Gi2α/β-arrestin-2/Akt pathway. This, in turn, blocks FoxO1 from binding to the SREBP-2 promoter and reducing the transcription of the SREBP-2 gene. As a result, SREBP-2 is upregulated, which raises cholesterol levels by stimulating HMGCR transcription and de novo cholesterol production [1].

Type 2 diabetes mellitus (DM) is on the rise worldwide. Cardiovascular disease (CVD) is the primary cause of death in people with type 2 diabetes (DM), and the death rate can rise to four times higher than in non-diabetics. Dyslipidaemia is one of the risk factors for CHD. Assessing the link between total cholesterol, LDL, HDL, and TG levels with age as well as the lipid profile based on age and sex [2].

By measuring LDL cholesterol, atherogenic dyslipidemia has been linked to an increased risk of cardiovascular morbidity and mortality, particularly in people with type 2 diabetes. For HDL cholesterol alone, the gender interaction was significant ($p = 0.0009$). For women's HDL cholesterol and men's triglycerides, the correlation with death was stronger. Conclusion: Lower HDL cholesterol, higher TG: HDL and higher triglycerides were found to be independently linked to an increased risk of all-cause death in patients with type 2 diabetes [3]. This time, we'll look at type 2 Diabetes Mellitus patients to see if there are any gender differences in the effects of total cholesterol.

## 2 Materials and Methods

The material used is an HbA1c kit using the Fluorescent Immune Assay (FIA) method with the Bio time tool, while the total cholesterol test uses the "CHOD-PAP" method, which is an enzymatic photometric test with the principle of cholesterol hydrolysis and enzymatic oxidation. [Daisy's Diagnostic Systems GmbH, 2016]. The colorimetric indicator is a quinonimine that is produced from 4-aminoantipyrine and phenol by hydrogen peroxide under the catalytic action of peroxidase or based on (Trinder reaction).

Respondents with Type 2 Diabetes Mellitus were screened using the HbA1c test, if the results were > 6.5% which was (abnormal) then they were used as research samples. The total sample size was 34 respondents, consisting of 17 women and 17 men with ages ranging from 21-73 years old. Venous blood was taken from both groups of respondents and collected in a tube without anticoagulant, after which it was centrifuged for 30 minutes at 3000 rpm. Furthermore, the serum was separated into a 1.5 ml Eppendorf tube for immediate cholesterol examination.

Numerical data on gender, HbA1c, and total cholesterol levels were analyzed by univariate test to obtain mean test scores between study groups. Then the data was tested for normality and homogeneity. Then a parametric different test is carried out with the independent t-test, and if it is not normal and homogeneous then the "Mann- Whitney" different test is carried out.

# 3 Results and Discussion

## 3.1 Characteristics of Respondents

Table 1. shows that the majority of males aged 21-29 years is 41.2% (7/17) and females aged 48-56 years is 47.1% (8/17). Respondent characteristics related to age ranged from 21-29 years for men as much as 41.2% (7/17) and for women aged between 48-56 years as many as 47.1% (8/17). The tendency of young men to develop type 2 Diabetes Mellitus is similar to the incidence in the United States where diabetes is more common in adolescents and young adults [2].

**Table 1.** Distribution of Respondents Diabetes Mellitus Type 2.

| Gender | Age | Total | Percentage (%) |
|---|---|---|---|
| Male | | | |
| | 21 – 29 years | 7 | 41.2 |
| | 30 – 38 years | 0 | 0 |
| | 39 – 47 years | 15 | 0.9 |
| | 48 – 56 years | 3 | 17.6 |
| | 57 – 65 years | 5 | 29.4 |
| | 66 – 74 years | 1 | 5.9 |
| Female | 21 – 29 years | 0 | 0 |
| | 30 – 38 years | 0 | 0 |
| | 39 – 47 years | 1 | 5.9 |
| | 48 – 56 years | 8 | 47.1 |
| | 57 – 65 years | 6 | 35.3 |
| | 66 – 74 years | 2 | 11.8 |

*Source: Primary data, 2023*

## 3.2 Research Finding

### *3.2.1 Identification of HbA1c in Diabetes Mellitus Type 2*

The results showed that HbA1c levels at 6.6 - 9.0% were found in men at 76.5% (13/17) and in women at 47.1% (17/8). The results of Ruben's study examined whether premature ovarian failure occurs through various mechanisms, in women without diabetes and in women with type 2 DM [3]. The results of this study were that there was no difference in the age of menopause between women without diabetes and women with type 2 diabetes [5].

**Table 2.** Distribution of HbA1c Levels in Diabetes Mellitus Type 2

| Gender | % HbA1c | Total | Percentage (%) |
|---|---|---|---|
| Male | 6,6 - 9,0 % | 13 | 76,5 |
| | 9,1 - 11,5 % | 1 | 5,9 |
| | 11,6 - 14,0 % | 3 | 17,6 |
| | 14,1 - 17,1 % | 0 | 0 |
| | | | |
| Female | 6,6 - 9,0 % | 8 | 47,1 |
| | 9,1 - 11,5 % | 3 | 17,6 |
| | 11,6 - 14,0 % | 2 | 11,8 |
| | 14,1 - 17,1 % | 4 | 23,5 |

*Source: Primary Data, 2023*

### *3.2.2 Identification of Cholesterol levels in Diabetes Mellitus patients*

The results showed that cholesterol levels in men (201-250 mg/dL) were found at 52.9% (9/17) and in women found at 151-200 mg/dL there were 52.9% (9/17). The pathways and locations where men and women store body fat, the ratio of hormones they release to fat, and the pathways their brains process signals related to body fat regulation are all different. The intra-abdominal adipose depot's accumulation of fat is linked to an increased risk of heart disease, type-2 diabetes, cancer, and other illnesses. Compared to pre-menopausal women, postmenopausal men and women collect more fat in the intra-abdominal depots, which puts them at higher risk for metabolic issues linked to obesity [6].

**Table 3**. Distribution of Cholesterol Levels in Diabetes Mellitus Type 2

| Gender | Cholesterol (mg/dL) | Total | Percentage (%) |
|---|---|---|---|
| Male | 100 – 150 | 0 | 0 |
| | 151 – 200 | 6 | 35,3 |
| | 201 – 250 | 9 | 52,9 |
| | 251 – 300 | 2 | 11,8 |
| | | | |
| Female | 100 – 150 | 2 | 11,8 |
| | 151 – 200 | 9 | 52,9 |
| | 201 – 250 | 6 | 35,3 |
| | 251 – 300 | 0 | 0 |

*Source: Primary Data, 2023*

### *3.2.3 Normality and homogeneity test of research data*

**Table 4.** Shapiro-Wilk test on age, gender, HbA1c, and Cholesterol levels.

| Gender | Variables | Statistic | df | Shapiro-Wilk (p) |
|---|---|---|---|---|
| Male | Age | 0.889 | 17 | 0.045 |
| | HbA1c | 0.840 | 17 | 0.007 |
| | Cholesterol | 0.766 | 17 | 0.001 |
| | | | | |
| Female | Age | 0,961 | 17 | 0,654 |
| | HbA1c | 0,966 | 17 | 0,749 |
| | Cholesterol | 0,901 | 17 | 0,070 |

### *3.2.4 Lilliefors Significance Correction*

The results of the analysis of the normality test of Shapiro-Wilk in Table IV show the age of men and women with p=0.045 and 0.654, and HbA1c levels in men of 0.007 and women of 0.749. Cholesterol levels in men of 0.001 and in women 0.070, so it can be concluded that the normality test results are not normally distributed on HbA1c and cholesterol in men with $p<0.05$.

**Table 5.** Mann Whitney analysis in 34 Diabetes Mellitus patients.

| Variables | Z | Mann Whitney U<br>Asymp.Sig (2-tailed) |
|---|---|---|
| Gender with Cholesterol | - 2.075 | 0.038 |

Nonparametric analysis of Mann- Whitney U in Table V shows the results for gender and cholesterol levels with p=0.038 ($p<0.05$), meaning that there is a difference in type 2 Diabetes Mellitus patients. In this study, it was found that cholesterol levels in perimenopause women with type 2 DM did not increase compared to type 2 DM in men. This agrees with Zhang's study exploring sexual dimorphism in adipose tissue accrual and deposition [7]. Explaining the mechanism by which sex hormones can modulate the modes of fat accumulation and storage due to obesity and metabolic syndrome, and the rapid increase in the predisposition to these diseases after menopause. The results of research on the relationship between estrogen levels and the incidence of cardiovascular disease autonomic neuropathy (CAN) in menopause women with type-2 diabetes mellitus (DMT2), obtained the results of multifactor logistic regression analysis showing HbA1c (OR=3980.95% CI=1268~ 10319) and estradiol (OR=3.075, 95%CI=1.167~7.366) is an independent risk factor for CAN, so CAN morbidity will increase in menopause female patients with type 2 DM [7].

## Conclusions

There are significant differences in how the brain works between perimenopause women and men who suffer from type 2 Diabetes Mellitus. Signal responses regulate body fat (cholesterol). Whereas high cholesterol levels (> 200 mg / dL) can cause a heart attack (stroke). Suggestions for future researchers, it is necessary to do research on hs-CRP and LDL cholesterol in perimenopause women regarding the role of estrogen and FSH in regulating cholesterol in women.

Thank you to Firdaus, Devyana Dyah Wulandari, Naufal Iman Yulian Pratama, Moch. SahriNaufal for taking care of ethics, so that the process of sampling, laboratory examination, and data analysis ran smoothly.

### References

1. Y. Guo, M. Zhao, T. Bo, S. Ma, Z. Yuan, W. Chen, Z. He, X. Hou, J. Liu, Z. Zhang, Q. Zhu, Q. Wang, X. Lin, Z. Yang, M. Cui, L. Liu, Y. Li, C. Yu, X. Qi, J. Zhao, Blocking FSH inhibits hepatic cholesterol biosynthesis and reduces serum cholesterol. Cell Research, **29**, 2 (2019). https://doi.org/10.1038/s41422-018-0123-6
2. S. Josten, M. Mutmainnah, H. Hardjoeno, Profil Lipid Penderita Diabetes Mellitus Tipe 2 P. Indonesian Journal of Clinical Pathology and Medical Laboratory, **13,** 1 (2018). https://doi.org/10.24293/ijcpml.v13i1.894
3. R.-J. Koopman, A.-G. Mainous, V.-A. Diaz, M.-E. Geesey, Changes in age at diagnosis or type 2 diabetes mellitus in the United States, 1988 to 2000. Annals of Family Medicine, **3**, 1 (2005). https://doi.org/10.1370/afm.214
4. Orsi, E. Penno, G. Solini, A.. Bonora, E. Fondelli, C. Trevisan, R. Vedovato, M. Cavalot, F. Morano, S. Baroni, M. G. Nicolucci, A., Pugliese, G. Laviola, L. Independent association of atherogenic dyslipidaemia with all-cause mortality in individuals with type 2 diabetes and modifying effect of gender: a prospective cohort study. Cardiovascular Diabetology, **20**, (2021) https://doi.org/10.1186/s12933-021-01224-7
5. R. López-López, R. Huerta, J.-M. Malacara, Age at menopause in women with type 2 diabetes mellitus. Menopause, **6**, 2 (1999). https://doi.org/10.1097/00042192-199906020-00016
6. H. Shi, D.-J. Clegg, Sex differences in the regulation of body weight. Physiology and Behavior, **97**, 2 (2009).
7. G. Zhang, W. Wei, B. Tan, J. Liu, Correlations between hormone levels and cardiovascular autonomic neuropathy in menopausal patients with diabetes mellitus. Pakistan Journal of Medical Sciences, **36**, 6 (2020) https://doi.org/10.12669/pjms.36.6.2088