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# Association between the duration of oral contraceptive use and the prevalence of type 2 diabetes mellitus: Korea National Health and Nutrition Examination Survey (KNHANES) 2007–2021

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**Objectives:** Previous studies have explored the link between oral contraceptive (OC) use and type 2 diabetes mellitus (T2DM), but few have specifically focused on the duration of OCs or used recent data. We investigated the association between OC use, its duration, and T2DM. **Methods:** Data of the Korea National Health and Nutrition Examination Survey (KNAHANES) from 2007 to 2021 were analyzed, focusing on 52,434 subjects over 20 years old. Multiple logistic regression determined the odds ratios (ORs) and 95% confidence intervals (CIs) for T2DM risk based on OC use duration. **Results:** Participants using OCs had a 1.33 times higher risk of developing T2DM than non-users (p=.006). Those who used OCs for more than a year but less than two years, and for two years or more, had a significantly higher risk of developing T2DM compared to those using them for less than three months (OR=1.477, 95% CI=1.000–2.179, p=.050; OR=1.468, 95% CI=1.023–2.107, p=.037, respectively). The increased risk among long-term users remained consistent. **Conclusion:** Women with long-term use of oral contraceptives (OCs) have a higher prevalence of T2DM. This study contributes to public health by emphasizing the importance of monitoring metabolic health in women who use OCs and provides foundational data for developing policies that promote women's health through a better understanding of OC-related risks.

**Key words:** insulin resistance, oral contraceptives, database research, observational study, diabetes complications, population study

## Ⅰ. Introduction

Diabetes is one of the major public health problems affecting approximately 537 million adults (20-79 years) worldwide as of 2021, the number of which is predicted to reach 643 million by 2030 and 783 million by 2045 (International Diabetes Federation [IDF], 2021). Additionally, the Centers for Disease Control and Prevention in the United States estimated that around 34.1 million adults (18 years or older) in the country had diabetes and 90-95% of them had type 2 diabetes mellitus (T2DM) as of 2018 (Centers for Disease Control and Prevention [CDC], 2020). The prevalence of T2DM in Korea has been steadily increasing over the past few decades and it is estimated that approximately 6.05 million adults (30 years or older) had diabetes mellitus in 2020 (Bae et al., 2022).

T2DM is a chronic metabolic disorder characterized by elevated blood glucose levels due to insulin resistance and/or inadequate insulin secretion (American Diabetes Association, 2014). T2DM is a complex disease with multiple factors that contribute to its pathogenesis. In addition to genetic factors, the primary reasons behind the worldwide increase in T2DM are the growing rates of obesity, inactive lifestyle, high-calorie diets, and aging populations (Zheng, Ley, & Hu, 2018). However, recent studies

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have suggested that the use of oral contraceptives (OCs) may also contribute to the development of T2DM (Kim et al., 2016; Rosenthal et al., 2004).

Of the 1.9 billion women of reproductive age (15-49 years) worldwide in 2019, 922 million are contraceptive users, which include 842 million using modern methods and 80 million using traditional methods, and over 20% of women of reproductive age in 27 countries use OCs (United Nations, 2019). OCs are a combination of two female hormones—estrogen and progestin—and suppress ovulation by synergizing the two synthetic hormones (Lee, Yoo, Jung, & Park, 2014). Studies have reported different findings on the impact of OCs on glucose metabolism and insulin homeostasis whether insulin resistance may be induced by progesterone or estrogen, but impaired insulin sensitivity and glucose tolerance, as shown by increased glucose and insulin levels, are commonly observed with the use of OCs (Coussa, Hasan, & Barber, 2020).

To date, studies have investigated the association between OC use and T2DM, but the results have been inconsistent and controversial (Gourdy, 2013). According to the population-based case-control study conducted by Rosenthal et al. (Rosenthal et al., 2004), although there was no general association between OC use and the risk of diabetes, a duration of more than one year and recent use of OCs significantly raised the risk of developing diabetes. Kim et al. (Kim et al., 2016) examined the long-term effects of OC use at childbearing age and found that past use of OCs for more than 6 months, as well as the duration of OC use, had a significantly higher prevalence of diabetes in post-menopausal women compared to those who did not use OCs, by increasing insulin resistance post-menopause.

On the other hand, other previous studies have reported no significant association between the use of OC and T2DM (Dawson et al., 2003; Godsland, Crook, & Wynn, 1990; Gourdy, 2013). Godsland et al. (1990) found that, despite consistent evidence of diabetic and impaired glucose tolerance test profiles in OC users, the use of OC did not increase prevalence of obvious symptoms of diabetes mellitus. Dawson et al. (Dawson et al., 2003) concluded that while some OC combinations may cause minor changes in insulin sensitivity, it does not have any significant clinical relevance in terms of diabetes incidence.

Previous studies have explored the association between OC use and diabetes mellitus; however, limited research has focused specifically on T2DM or employed up-to-date data. In addition, while previous studies have utilized data from the Korea National Health and Nutrition Examination Survey (KNHANES), which has monitored the health and nutritional status of the Korean population since 1998 (Kweon et al., 2014), they have neither analyzed the most recent data nor have they incorporated all female participants to establish the association between OC use and T2DM (Kim et al., 2016). Given that T2DM accounts for over 90% of diabetes cases worldwide and poses a substantial public health issue (IDF, 2021), the association of T2DM with its risk factors, such as the use of OCs, by analyzing the more recent data must be elucidated. Therefore, we investigated the association between OC use and T2DM by analyzing the KNHANES data from 2007 to 2021.

Identifying the association between OCs use and T2DM is essential for providing accurate information to women in health education programs and developing personalized health promotion strategies that minimize risk factors (Gourdy, 2013).

Additionally, raising awareness about the metabolic changes associated with OCs use and supporting women in making informed decisions about their health choices is crucial (Lee et al., 2014). Health education can enhance awareness of these risk factors and offer individualized health management strategies through education on alternative contraceptive methods. This approach can have a positive impact not only on the prevention of T2DM but also on the overall promotion of women's health.

Therefore, this study aims to make a significant contribution to women's health management by analyzing the association between OCs use and the incidence of T2DM, providing essential scientific evidence for improving metabolic health in women through health education and promotion programs (Kim et al., 2016; Rosenthal et al., 2004). By utilizing the latest data, this study offers more specific and clear evidence on the long-term effects of OCs use, thereby contributing to the development and implementation of public health policies (Bae et al., 2022).

# Ⅱ. Methods

## 1. Study population

This study used data from the Korea National Health and Nutrition Examination Survey (KNHANES, 2007–2021). KNHANES began its first phase in 1995 and was conducted every three years until it was restructured into an annual survey system starting from the fourth phase (2007-2009), and it has been conducted annually since then (Kweon et al., 2014; Oh et al., 2021). This nationwide survey comprises three main components: a health interview, a nutrition survey, and a health examination. Its primary aim is to produce nationally representative and reliable data on the health status, health-related behaviors, and dietary and nutritional intake of the Korean population. The data serve as a foundational resource for the development of national health policies (Kweon et al., 2014; Oh et al., 2021).

The primary sample units (PSUs) were selected from a sampling frame of all census blocks or addresses of resident registration, with each PSU consisting of approximately 50–60 households. The KNHANES employs a complex, multistage probability sample design that represents the entire noninstitutionalized civilian population of Korea. After selecting the PSU, 20 households were chosen for screening through a field survey, and all family members who are one year of age or older were eligible to participate in the final round of selection. Each year, 192 PSUs survey a total of about 10,000 individuals.

The primary objective of this study is to explore the association between the use of OCs and the incidence of T2DM among adult women in Korea. Cross-sectional studies collect data at a specific point in time, which limits the ability to infer causality. However, this approach is useful for identifying characteristics and trends within a population and for suggesting potential associations (Levin, 2006).

In this study, KNAHANES data from 2007 to 2021 was used to examine 52,434 women out of 93,092 individuals who were over 20 years of age. Of the total sample, 52,434 were female and 9,764 had a history of T2DM. Of the 9,764 women, only those with complete information on OC duration, T2DM prevalence, and health checkup outcomes were included. Of the eligible women selected, 7,325 reported using OCs more than once.

## 2. Measurements

### 1) Dependent variable: T2DM

T2DM was defined in accordance with the Screening for Prediabetes and Type 2 Diabetes US Preventive Services Task Force Recommendation Statement as having a fasting plasma glucose level of 126 mg/dL or higher (6.99 mmol/L), an HbA1c level of 6.5% or higher, or a 2-hour post-load glucose level of 200 mg/dL (11.1 mmol/L) or higher (US Preventive Services Task Force, 2021).

The 2021 Clinical Practice Guidelines for Diabetes in Korea provide alternative criteria for the diagnosis of T2DM. According to these guidelines, an HbA1c level of ≥6.5%, a fasting plasma glucose level of ≥126 mg/dL for >8 hours, or a 2-hour of plasma glucose level of ≥200 mg/dL during 75-gram oral glucose tolerance test or the classic symptoms of hyperglycemia (polyuria, polydipsia, and unexplained weight loss) with a random plasma glucose of ≥200 mg/dL (Hur et al., 2021).

### 2) Independent variables: Past use of OCs and duration of OC use

Past OC use was measured through a self-reported questionnaire as part of the KNHANES 2007-2021 project. The question was, "Have you ever taken oral contraceptives for at least one month?" Participants were asked a "yes" or "no" question about their use of OCs (Lee et al., 2014). The question about the total duration of use in years and months was recorded in the KNHANES 2007-2009, and 2010-2012 project. Based on the reported duration of use, participants were divided into four groups: group 1 (less than 3 months), group 2 (more than 3 months and less than 1 year), group 3 (more than 1 year and less than 2 years), and group 4 (2 years or more).

### 3) Confounding factors

Potential confounding variables were identified based on the results of statistical correlation analysis with OC use and previously reported associations with T2DM (Kim et al., 2016). Of them, a set of variables included the KNHANES data source were selected (Rubin, Glintborg, Nybo, Abrahamsen, & Andersen, 2017; US Preventive Services Task Force, 2021; Zheng et al., 2018). These variables included age, body mass index (BMI), education level (elementary school, middle school, high school, or more than university graduation), household income (low, middle-low, middle-high, or upper), smoking status (less than 5 packs, 5 packs or more, or non-smoker), alcohol consumption (non-drinker, less than once a month, once a month, 2 to 4 times a month, 2 to 3 times a week, or 4 times a week or more, for the past 1 year), and physical activities (yes or no). Laboratory data on systolic blood pressure (SBP, mmHg), diastolic blood pressure (DBP, mmHg), triglyceride (TG, mg/dL), cholesterol (Chol, mg/dL), high-density lipoprotein cholesterol (HDL-C, mg/dL), low-density lipoprotein cholesterol (LDL-C, mg/dL), aspartate aminotransferase (AST, IU/L), alanine aminotransferase (ALT, IU/L), and creatinine (CREA, mg/dL) were also included.

## 3. Statistical analysis

Mean (±standard deviation) were used to describe the numerical values of variables, while numbers (percentages) were used to describe the categorical values. The chi-square test was performed to compare the frequency values in each group (T2DM or non-T2DM and duration of OC use), and an independent t-test was conducted to examine the differences among clinical variables in each group. The binomial logistic regression was used to determine odds ratios (ORs) and 95% confidence intervals (CIs) to identify an association between duration of OC use and T2DM with the women participants. For p values, the significance level was less than .05. We utilized IBM SPSS Statistics 22.0 software (IBM Corp, Armonk, NY) for our analysis.

# Ⅲ. Results

All factors in 〈Table 1〉 were strongly correlated with the prevalence of T2DM. 16.1% of those without T2DM used OCs, compared to 23.1% of those with the disease, and this difference was statistically significant ($p<.001$) between the two groups. The proportion of long-term users with T2DM was significantly higher than that of non-users when OCs were divided into

〈Table 1〉 Results of an association analysis between the prevalence of T2DM, OC use and duration, income and education levels, smoking, drinking, and exercise habits

Unit: N(%)

| Items | | Total | | No (n=40,785) | | Yes (n=8,005) | | p-value |
|---|---|---|---|---|---|---|---|---|
| Past OC use | No | 36,161 | (83.2) | 32,687 | (83.9) | 3,474 | (76.9) | 〈.001 |
| | Yes | 7,325 | (16.8) | 6,280 | (16.1) | 1,045 | (23.1) | |
| Duration of OC use | Less than 3 months | 723 | (25.4) | 674 | (26.9) | 49 | (14.4) | 〈.001 |
| | 3 months - 1 year | 652 | (22.9) | 593 | (23.6) | 59 | (17.4) | |
| | 1 year - 2 years | 591 | (20.7) | 503 | (20.0) | 88 | (25.9) | |
| | 2 years or more | 883 | (31.0) | 739 | (29.5) | 144 | (42.4) | |
| Quartile of monthly household income (n, %) | Low | 10,930 | (24.3) | 9,567 | (23.8) | 1,363 | (28.8) | 〈.001 |
| | Middle-low | 11,271 | (25.1) | 10,014 | (24.9) | 1,257 | (26.5) | |
| | Middle-high | 11,405 | (25.4) | 10,305 | (25.6) | 1,100 | (23.2) | |
| | Upper | 11,335 | (25.2) | 10,315 | (25.7) | 1,020 | (21.5) | |
| Education level | Ele_school | 12,406 | (28.0) | 9,780 | (24.6) | 2,626 | (57.2) | 〈.001 |
| | Mid_school | 4,546 | (10.3) | 3,893 | ( 9.8) | 653 | (14.2) | |
| | Hig_school | 13,960 | (31.5) | 13,041 | (32.8) | 919 | (20.0) | |
| | ≥ University | 13,395 | (30.2) | 13,003 | (32.7) | 392 | ( 8.5) | |
| Alcohol consumption (year) | Non-drinker | 10,685 | (21.9) | 8,524 | (20.9) | 3,162 | (39.5) | 〈.001 |
| | Less than once a month | 15,125 | (31.0) | 12,643 | (31.0) | 2,402 | (30.0) | |
| | Once a month | 7,026 | (14.4) | 5,955 | (14.6) | 897 | (11.3) | |
| | 2 to 4 times a month | 10,587 | (21.7) | 9,095 | (22.3) | 1,017 | (12.7) | |
| | 2 to 3 times a week | 4,050 | ( 8.3) | 3,467 | ( 8.5) | 392 | ( 4.9) | |
| | 4 times a week or more | 1,317 | ( 2.7) | 1,101 | ( 2.7) | 136 | ( 1.7) | |
| Smoking status | Less than 5 packs (100 cigarettes) | 1,025 | ( 2.1) | 897 | ( 2.2) | 80 | ( 1.0) | .003 |
| | 5 packs (100 cigarettes) or more | 4,635 | ( 9.5) | 3,834 | ( 9.4) | 857 | (10.7) | |
| | Non-smoker | 43,130 | (88.4) | 36,054 | (88.4) | 7,068 | (88.3) | |
| Walking activity | No | 16,995 | (38.4) | 15,162 | (38.3) | 1,833 | (40.0) | .021 |
| | Yes | 27,220 | (61.6) | 24,471 | (61.7) | 2,749 | (60.0) | |
| Intensive physical activity | No | 21,519 | (83.5) | 18,880 | (82.5) | 2,639 | (91.9) | 〈.001 |
| | Yes | 4,241 | (16.5) | 4,009 | (17.5) | 232 | ( 8.1) | |
| Moderate physical activity | No | 18,032 | (71.3) | 15,658 | (69.9) | 2,374 | (82.3) | 〈.001 |
| | Yes | 7,248 | (28.7) | 6,736 | (30.1) | 512 | (17.7) | |

four categories: less than three months, more than three months and less than one year, more than one year and less than two years, and two years or more (p<.001). The ratio of low and middle-low was substantially larger in individuals without T2DM when the individual income level was divided into four quartiles: low, middle-low, middle-high, and upper (p<.001). When the level of education was categorized into four groups (elementary school graduates, middle school graduates, high school graduates, and university graduates), the proportion of T2DM patients who had completed high school or university was lower than that those of without T2DM (p<.001). In the case of drinking frequency for one year, all groups except those who answered that they did not drink at all showed a higher percentage of people without T2DM compared to those with T2DM (p<.001). The proportion of subjects who did not practice intense physical activity, moderate physical activity, or walking activity was significantly higher in subjects with T2DM (p<.001 for each).

〈Table 2〉 shows the results of an association analysis between the prevalence of T2DM, duration of OC use (in months), general characteristics, and blood test results. All variables in 〈Table 2〉, except for diastolic blood pressure, were found to have a statistically significant correlation with the prevalence of T2DM. When converted to a monthly basis, the average duration of OC use was 17.7 (±27.2) months in participants without T2DM and 26.8 (±34.5) months in those with T2DM, indicating a significant difference (p<.001). The average age of participants with T2DM was significantly higher than those without T2DM, with mean ages of 64.3 (±12.0) years and 49.3 (±16.0) years, respectively (p<.001). Patients without T2DM had a higher mean height, while those with T2DM had significantly higher mean weight and body mass index (p<.001 for each). Participants with T2DM had significantly higher systolic blood pressure compared to those without T2DM (p<.001). In comparison to

〈Table 2〉 Results of an association analysis between the prevalence of T2DM, duration of OC use (in months), general characteristics, and blood test results

| Items | No (n=40,785) | Yes (n=8,005) | p-value |
|---|---|---|---|
| | Mean±SD | Mean±SD | |
| Duration of OC use (month) | 17.7 ±27.2 | 26.8 ± 34.5 | <.001 |
| Age (year) | 49.3 ±16.0 | 64.3 ± 12.0 | <.001 |
| Height (cm) | 157.3 ± 6.5 | 153.9 ± 6.1 | <.001 |
| Weight (kg) | 57.5 ± 9.1 | 60.8 ± 10.7 | <.001 |
| Body mass index (kg/㎡) | 23.3 ± 3.4 | 25.6 ± 3.8 | <.001 |
| Waist circumference (cm) | 78.5 ± 9.6 | 87.3 ± 9.7 | <.001 |
| Systolic blood pressure (mmHg) | 115.9 ±17.5 | 127.9 ± 17.6 | <.001 |
| Diastolic blood pressure (mmHg) | 73.76± 9.78 | 74.02± 10.14 | .096 |
| Fasting glucose (mg/dL) | 92.9 ± 9.2 | 138.4 ± 42.8 | <.001 |
| TC (mg/dL) | 192.3 ±36.2 | 184.7 ± 43.1 | <.001 |
| HDL-C (mg/dL) | 53.8 ±12.3 | 47.3 ± 11.2 | <.001 |
| LDL-C (mg/dL) | 116.0 ±33.0 | 112.4 ± 38.6 | .004 |
| TG (mg/dL) | 110.6 ±74.9 | 154.9 ±102.5 | <.001 |
| AST (IU/L) | 21.0 ± 9.9 | 25.3 ± 16.3 | <.001 |
| ALT (IU/L) | 17.7 ±13.1 | 24.8 ± 19.3 | <.001 |
| Creatinine levels in blood (mg/dL) | 0.7 ± 0.2 | 0.8 ± 0.3 | <.001 |

**Notes.** SD=Standard Deviation

those without T2DM, participants with T2DM had significantly higher levels of fasting glucose, triglycerides, AST, ALT, and blood creatinine (p〈.001 for each). In participants without T2DM, HDL and cholesterol was considerably higher (p〈.001, p=.004, respectively).

Regression analysis was used to determine how using OCs affected the prevalence of T2DM. The results are shown in 〈Table 3〉. By simple regression analysis, it was determined that subjects using OCs had a statistically significant risk of T2DM prevalence of up to 1.566 odds ratio compared to those not using them (p〈.001). The model considered factors such as age, level of education, income, walking activity, body mass index, systolic blood pressure, total cholesterol, HDL cholesterol, triglyceride, GOT, GPT, and creatinine, among others. Results from multiple regression analyses showed that participants taking OCs had a 1.330 odds ratio higher risk of T2DM than those who did not take them, and the statistical significance was verified (p=.006).

〈Table 4〉 shows the effect of duration of OC use on the prevalence of T2DM. Regression analysis was conducted to determine the impact of the duration of the OC use on the prevalence of T2DM. Based on the findings of a simple regression analysis, subjects who used OCs for over a year but less than two years, as well as those who used them for two years or more, exhibited a significantly higher risk of developing T2DM compared to those who used them for a short

〈Table 3〉 Effects for past OC use by T2DM prevalence

| Items | | Unadjusted models | | | Adjusted models | | |
|---|---|---|---|---|---|---|---|
| | | OR¶ | 95% CI$^{\varphi}$ | p-value | OR¶ | 95% CI$^{\varphi}$ | p-value |
| Past OC$^{\theta}$ use | No (ref) | - | - | - | - | - | - |
| | Yes | 1.566 | 1.454-1.686 | 〈.001 | 1.330 | 1.089-1.653 | .006 |
| Age (year) | | - | - | - | 1.059 | 1.055-1.063 | 〈.001 |
| Education level | Ele_school (ref) | - | - | - | - | - | - |
| | Mid_school | - | - | - | 1.102 | 0.990-1.226 | .075 |
| | Hig_school | - | - | - | 0.953 | 0.858-1.060 | .378 |
| | ≥ University | - | - | - | 0.688 | 0.596-0.795 | 〈.001 |
| Quartile of monthly household income (n, %) | Low (ref) | - | - | - | - | - | - |
| | Middle-low | - | - | - | 0.893 | 0.813-0.980 | .017 |
| | Middle-high | - | - | - | 0.802 | 0.728-0.884 | 〈.001 |
| | Upper | - | - | - | 0.794 | 0.718-0.878 | 〈.001 |
| Walking activity | No (ref) | - | - | - | - | - | - |
| | Yes | - | - | - | 0.864 | 0.804-0.928 | 〈.001 |
| Body mass index (kg/㎡) | | | - | - | 1.118 | 1.107-1.129 | 〈.001 |
| Systolic blood pressure (mmHg) | | | - | - | 1.007 | 1.005-1.009 | 〈.001 |
| TC (mg/dL) | | | - | - | 1.012 | 1.011-1.013 | 〈.001 |
| HDL-C (mg/dL) | | | - | - | 0.995 | 0.991-0.998 | .004 |
| TG (mg/dL) | | | - | - | 1.004 | 1.003-1.004 | 〈.001 |
| AST (IU/L) | | | - | - | 0.977 | 0.972-0.983 | 〈.001 |
| ALT (IU/L) | | | - | - | 1.031 | 1.027-1.035 | 〈.001 |
| Creatinine levels in blood (mg/dL) | | | - | - | 1.409 | 1.239-1.603 | 〈.001 |

**Notes.** $^{\theta}$ Oral Contraceptives, ¶ Odds Ratio, $^{\varphi}$ Confidence Interval

〈Table 4〉 The effect of duration of OC use on the prevalence of T2DM

| Items | | Unadjusted models | | | Adjusted models | | |
|---|---|---|---|---|---|---|---|
| | | OR[¶] | 95% CI[φ] | p-value | OR[¶] | 95% CI[φ] | p-value |
| Duration of OC[θ] use | Less than 3months | - | - | - | - | - | - |
| | 3 months - 1 year | 1.369 | 0.922-2.031 | .119 | 1.147 | 0.758-1.735 | .518 |
| | 1 year - 2 years | 2.406 | 1.666-3.477 | <.001 | 1.477 | 1.000-2.179 | .050 |
| | 2 years or more | 2.680 | 1.907-3.768 | <.001 | 1.468 | 1.023-2.107 | .037 |
| Age (year) | | - | - | - | 1.046 | 1.030-1.062 | <.001 |
| Education level | Ele_school (ref) | - | - | - | - | - | - |
| | Mid_school | - | - | - | 0.919 | 0.624-1.353 | .670 |
| | Hig_school | - | - | - | 0.565 | 0.361-0.884 | .012 |
| | ≥ University | - | - | - | 0.397 | 0.177-0.887 | .024 |
| Quartile of monthly household income (n, %) | Low (ref) | - | - | - | - | - | - |
| | Middle-low | - | - | - | 1.272 | 0.900-1.799 | .173 |
| | Middle-high | - | - | - | 1.177 | 0.818-1.695 | .380 |
| | Upper | - | - | - | 0.912 | 0.616-1.350 | .645 |
| Walking activity | No (ref) | - | - | - | - | - | - |
| | Yes | - | - | | 0.946 | 0.729-1.227 | .675 |
| Body mass index (kg/㎡) | | | - | - | 1.122 | 1.079-1.168 | <.001 |
| Systolic blood pressure (mmHg) | | | - | - | 1.011 | 1.004-1.019 | .004 |
| TC (mg/dL) | | | - | - | 1.011 | 1.008-1.015 | <.001 |
| HDL-C (mg/dL) | | | - | - | 1.005 | 0.992-1.019 | .456 |
| TG (mg/dL) | | | - | - | 1.004 | 1.003-1.006 | <.001 |
| AST (IU/L) | | | - | - | 0.981 | 0.960-1.002 | .070 |
| ALT (IU/L) | | | - | - | 1.026 | 1.012-1.040 | <.001 |
| Creatinine levels in blood (mg/dL) | | | - | - | 9.645 | 4.227-22.005 | <.001 |

**Notes.** θ Oral Contraceptives, ¶ Odds Ratio, φ Confidence Interval

duration of less than three months (OR=2.406, 95% Confidence Interval (CI)=1.666-3.477, p<.001; OR=2.680, 95% CI=1.907-3.768, p<.001, respectively). Furthermore, there was a tendency for the odds ratio of developing T2DM to increase as the duration of OC use extended.

By adjusting for various factors such as age, income level, education level, walking activity, body mass index, systolic blood pressure, total cholesterol, HDL cholesterol, triglycerides, AST, ALT, and creatinine, multiple regression analysis was performed. The results of our multiple regression analysis revealed that subjects who used OCs for more than a year but less than two years, as well as those who used them for two years or more, were both found to have a significantly higher risk of developing T2DM when compared to those who used them for less than three months (OR=1.477, 95% CI=1.000-2.179, p=.050; OR=1.468, 95% CI=1.023-2.107, p=.037, respectively). Although the odds ratio decreased compared to the simple regression analysis, the trend of a higher risk of T2DM among long-term users remained consistent.

## Ⅳ. Discussion

This study aimed to investigate the association between the use of OCs and T2DM in Korean women by analyzing the KNHANES data from 2007 to 2021. Although KNHANES regarding the OC use had been conducted from 2007 to 2021, previous studies have primarily analyzed the data from 2007 to 2012 (Kim et al., 2016). By integrating the latest data, this study expected to provide more definitive evidence of the association between the OC use and the prevalence of T2DM.

In this study, we analyzed the KNHANES data from 2007 to 2021 and included all female participants aged 20 years or older. Additionally, we controlled for potential confounding factors, such as age, body mass index (BMI), level of education, income, physical activities, systolic blood pressure, total cholesterol, HDL cholesterol, triglyceride, AST, ALT, and creatinine, among other variables.

The outcome variable in this study is the prevalence of diabetes, not the incidence; therefore, caution is needed when interpreting the findings. Prevalence reflects the proportion of individuals with diabetes at a given time, rather than the rate of new cases, which limits the ability to establish a causal relationship between OC use and T2DM onset. This consideration is important when interpreting the results and their implications.

The findings in our study suggest that the use of OCs is associated with an increased risk of developing T2DM among women. The analysis revealed a statistically significant correlation between various factors and the prevalence of T2DM. Specifically, the rate of OC use was significantly higher in subjects with T2DM, particularly among long-term users (more than 1 year and less than 2 years and 2 years or more) as compared to non-users and short-term users (less than 3 months). Furthermore, our findings also demonstrated that the risk of T2DM prevalence in long-term OC users (more than 1 year and less than 2 years and 2 years or more) was considerably higher than in short-term users (less than 3 months).

Consequently, this study produced two findings: firstly, women who reported ever using OCs had a substantially higher prevalence of T2DM compared to non-users; and secondly, the longer the duration of OC use, the higher the risk of T2DM prevalence. These findings are consistent with previous studies that have reported a positive association between OC use and T2DM, particularly with longer durations of use (Kim et al., 2016; Rosenthal et al., 2004).

Rosenthal et al. (Rosenthal et al., 2004) identified that OC use for more than 1 year and recent use within the past 5 years significantly increased diabetes risk in women. Kim et al. (Kim et al., 2016) similarly reported a significant association between past use of OCs for more than 6 months and diabetes risk, suggesting that prolonged OC use during reproductive age could be a crucial risk factor for diabetes development in post-menopausal women. However, some prior studies reported no significant association between OC use and T2DM (Dawson et al., 2003; Godsland et al., 1990; Gourdy, 2013), which may be attributed to differences in study design, population characteristics, and analysis methods.

Dawson et al. conducted a cohort study on reproductive risk factors, including OC use, and their association with diabetes mellitus (Dawson et al., 2003). Their study did not find a significant association between OC use and T2DM. However, key differences in study design and methodology may account for the discrepancy in findings. Dawson et al. employed a cohort design, following women over time, which is advantageous for observing temporal associations. In contrast, our cross-sectional study limits the ability to infer causality. Nonetheless, by utilizing a large, nationally representative dataset (KNHANES), our study captures a broader population, enhancing the generalizability of our findings to the Korean population. The cohort study by Dawson et al. focused on a population from the UK, which differs demographically and genetically from our Korean participants. Differences in lifestyle, diet, and healthcare access between the two populations may contribute to the divergent findings. Furthermore, Dawson's study did not stratify participants based on the duration of OC use, whereas our study specifically analyzed the effects of varying OC usage durations on T2DM prevalence.

Godsland et al. examined the metabolic effects of low-dose OCs and their impact on carbohydrate metabolism (Godsland et al., 1990). Their study found no significant link between OC use and diabetes. However, important differences exist between their research and ours. Godsland et al.'s study focused on the metabolic effects of low-dose OCs over a short period, whereas our study investigates long-term OC use by incorporating subjects' responses regarding the total duration of contraceptive use into the outcome variable, despite not being a longitudinal study. Godsland et al.'s study involved a smaller sample of women, primarily of European descent. In contrast, our study included a much larger, ethnically homogeneous population of Korean women, allowing for more statistically robust conclusions. The genetic and environmental differences between European and Korean women may also account for the differing results. Furthermore, we stratified participants by OC use duration, facilitating a more nuanced understanding of the relationship between OC use and T2DM risk.

Gourdy's review on diabetes and oral contraception found no consistent evidence linking OC use to the development of diabetes (Gourdy, 2013). However, there are key distinctions between Gourdy's review and our study. Gourdy's study was a review article that summarized findings from various observational and clinical studies. While reviews provide an important synthesis of existing evidence, they often lack the ability to conduct original statistical analysis. In contrast, our study conducted original empirical analysis on KNHANES data, enabling us to apply advanced statistical methods, including multiple logistic regression, to examine the association between OC use and T2DM. Much of the data summarized in Gourdy's review originated from studies on Western populations, whereas our research focuses on the Korean population. This distinction is important due to the genetic and environmental differences that may influence metabolic responses to OC use. Furthermore, our study utilizes a more recent dataset and addresses potential biases identified in prior studies by controlling for a wide range of sociodemographic and health-related factors. Additionally, our analysis was stratified by OC duration, offering a more detailed examination of how extended OC use may affect diabetes risk—a level of specificity not commonly addressed in Gourdy's review.

It is worth noting that our study has several limitations that should be considered when interpreting the results. First, the cross-sectional design of the study limits our ability to establish a causal relationship between OC use and T2DM risk. Second, the self-reported data including OC use and duration may have led to recall bias and misclassification of exposure status. Third, we lacked information on the specific type and dose of OC formulations used by the participants, which may have influenced the magnitude of the association between OC use and T2DM risk. And fourth, although OC use was assessed in all five periods of the KNHANES data

(4th period: 2007–2009, 5th period: 2010–2012, 6th period: 2013–2015, 7th period: 2016–2018, and 8th period: 2019–2021), the duration of use was only documented in the fourth and fifth periods. This limited our analysis of the total duration of OC use and potentially have impacted our ability to identify any association between long-term OC use and T2DM.

Future studies should employ longitudinal research designs, such as cohort studies, to analyze the effects of OC use over time. Additionally, it is essential to utilize objective data, such as medical records, instead of relying on self-reported data. Finally, further analysis is needed to explore the metabolic effects of different types, dosages, and hormone compositions of OCs. These follow-up studies will provide a clearer understanding of the long-term metabolic impact of OC use and contribute significantly to the development of personalized health management strategies aimed at improving women's health.

The findings of this study suggest that the use of OCs was significantly associated with the risk of T2DM, which has important implications for women's health management and education. The onset of T2DM can substantially impact the overall quality of life in women, and the potential role of OC use as a risk factor necessitates heightened attention (Kim et al., 2016; Rosenthal et al., 2004). According to the study results, women who used OCs for an extended period had a higher risk of developing T2DM compared to those who did not use OCs. This underscores the importance of recognizing the metabolic side effects associated with OC use and establishing appropriate preventive strategies (Coussa et al., 2020).

The study's findings, which indicate that OC use was significantly associated with the risk of T2DM, support the need for comprehensive information on OC use in health education programs. Specifically, it is crucial to enhance education on blood glucose management for women using OCs, enabling them to regularly monitor their health status (Gourdy, 2013). This approach helps women considering OC use make informed decisions and may contribute to the long-term prevention of T2DM (Lee et al., 2014).

Furthermore, the results of this study suggest the need for a multifaceted approach to mitigate the metabolic risks associated with OC use. Individuals who require oral contraceptive (OC) use should be advised to regularly monitor their blood glucose levels and insulin resistance (Kim et al., 2016). Additionally, ongoing health monitoring and management, including blood glucose control and guidance from healthcare professionals, are essential during OC use. Such approaches can provide personalized health management strategies to protect the metabolic health of women (Dawson et al., 2003).

From a public health policy perspective, this study clarifies the health risks associated with OC use, providing foundational data for developing policies aimed at promoting health across the female life course. This includes supporting women in thoroughly considering their health status and potential risks when choosing contraceptive methods. Moreover, the findings of this study can be utilized in public health campaigns to raise awareness about the metabolic risks associated with OC use.

Finally, this study highlights the importance of managing women's metabolic health by investigating the association between OC use and T2DM incidence. Future research should further explore the relationship between different types of OC use and T2DM across diverse populations, contributing to the development of more comprehensive health education programs.

## Ⅴ. Conclusion

In conclusion, this study provides evidence of the association between the use of OCs and an increased risk of developing T2DM in women, using the most recent KNHANES data. Nonetheless, future studies are needed to further explore the underlying mechanisms behind this association and to investigate the impact of different types and dosages, as well as the duration of OC use, on the risk of T2DM. Furthermore, additional research could also investigate potential strategies for reducing the risk of T2DM among women who use OCs, which could ultimately contribute to improving the health outcomes for this population.

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