DOI: https://doi.org/10.54393/pjhs.v6i2.2646

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 6, Issue 02 (February 2025)

Original Article

OPEN ACCESS

Association of Different Formulation with Oral Contraceptive Agents in Lipid and Carbohydrates Metabolism in Women

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ARTICLE INFO

Keywords:
Oral Contraceptives, Ethinylestradiol-Levonorgestrel, Lipid, Carbohydrate Metabolism

How to Cite:
Hussain, S. M., Khan, S. A., Noor, S., Fida, N., Bukhari, S. M. S. A., & Zeb, J. (2025). Association of Different Formulation with Oral Contraceptive Agents in Lipid and Carbohydrates Metabolism in Women: Oral Contraceptive Agents in Lipid and Carbohydrates Metabolism in Women. Pakistan Journal of Health Sciences, 6(2), 67-74. https://doi.org/10.54393/pjhs.v6i2.2646

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Received date:11th December, 2024
Acceptance date: 16th February, 2025
Published date: 28th February, 2025

ABSTRACT

Oral contraceptives impact lipid and carbohydrate metabolism differently based on formulation. **Objectives:** To assess the association between Ethinylestradiol-Levonorgestrel, Ethinylestradiol-Norgestimate, and Progestin-Only contraceptives and key metabolic markers, including lipid profile and carbohydrate metabolism, in women using these formulations. **Methods:** A cross-sectional study recruited women aged 18–45 using one of these contraceptives for at least 6 months. Exclusion criteria included metabolic disorders, cardiovascular disease, and recent medication use affecting metabolism. Demographic and health data (BMI, blood pressure, waist-to-hip ratio) were collected. Metabolic markers—including cholesterol, LDL, HDL, triglycerides, Apolipoproteins A1/B, fasting glucose, fasting insulin, HOMA-IR, OGTT, and HbA1c were measured. Statistical tests included One-Way ANOVA, Kruskal-Wallis, and Tukey's post-hoc ($p<0.05$). **Results:** Significant metabolic differences were observed. Ethinylestradiol-Levonorgestrel users had higher total cholesterol ($p=0.002$) and increased insulin resistance (HOMA-IR, $p=0.019$), suggesting a potential long-term cardiovascular risk. Ethinylestradiol-Norgestimate users exhibited higher Apo-lipoprotein A1 levels ($p=0.005$), indicating a possible cardio-protective effect in reducing atherosclerosis risk. HOMA-IR was also higher in Progestin-Only users compared to Ethinylestradiol-Norgestimate ($p=0.006$). No significant differences were found in fasting glucose or HbA1c. **Conclusions:** It was concluded that Ethinylestradiol-Norgestimate may have a more favourable metabolic profile, with lower cholesterol and insulin resistance.Tailored contraceptive selection could reduce metabolic risks, particularly in women with cardiovascular concerns. Further research is needed to assess long-term effects. However, the exclusion of women with pre-existing metabolic disorders limits the generalizability of these findings. Future studies should include these subgroups to provide a broader understanding of metabolic responses to oral contraceptives.

INTRODUCTION

Oral contraceptives are extensively used worldwide, both for effective birth control and for the management of hormonal and reproductive health issues [1]. Combinations of ethinylestradiol with progestins like levonorgestrel or norgestimate are frequently prescribed, as they replicate natural hormonal cycles, aiding in contraception and providing additional benefits like cycle regulation, reduction in menstrual pain, and lowered ovarian cyst. Progestin-only formulations, which omit estrogen, offer an alternative for women who cannot use estrogen, providing similar contraceptive efficacy through progestin's influence on ovulation risk [2]. However, these oral contraceptives are known to change certain metabolic activities, most notably lipid and carbohydrate metabolism, which is important for cardiovascular and metabolic health. Long-term oral contraceptives, especially among women already predisposed to metabolic problems, may promote the development of cardiovascular

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disease through long-term dysregulation of lipid and carbohydrate metabolism. Other studies suggest that combined contraceptives containing ethinylestradiol can increase triglyceride and low-density lipoprotein (LDL) levels with a concomitant decrease in high-density lipoprotein (HDL), thus raising the risk for cardiovascular diseases. More importantly, progestin-only formulations appear to have this neutral or varying impact on lipid metabolism, as several different progestins could be used. Furthermore, another component of metabolic syndrome, insulin resistance, has been associated with the chronic use of androgenic progestins such as levonorgestrel. These effects are important for determining the women who need special care while using hormonal contraceptives [3]. In most contraceptives, formulations that have ethinylestradiol along with either levonorgestrel or norgestimate and also progestin-only contraceptives affect lipid markers like total cholesterol, LDL, HDL, Apo-lipoprotein A1 and B, and triglycerides. Ethinylestradiol-based formulations are likely to increase the total cholesterol and triglyceride levels as well as the LDL, and HDL levels, thus increasing cardiovascular risks [4]. The combination methods, the progestin-only choice may have unique metabolic effects because of the lack of estrogen. The metabolic impacts caused by progestin-only contraceptives are different from those of combined formulations because ethinylestradiol, which has a proestrus effect, is absent in those formulations. The progestin-only methods of contraception are lipid a sedentary form of energy storage arthritis through androgenic receptors. There is net deposition of LDL cholesterol reduced HDL cholesterol and altered triglyceride levels due to the different types of progestin used, and also diabetic partial inhibition of lipid metabolism. In addition, increased doses of various progestins may enhance the insulin effects and activity of pancreatic β-cells which aid in insulin resistance. Some studies suggest that certain progestins which have a reputation for higher insulin-resistance setting androgenic activity, such as levonorgestrel, seem to worsen insulin resistance which results in higher homeostasis model assessment-estimated insulin resistance (HOMA-IR) levels. Others with lower androgenic activity, like desogestrel, may have a neutral effect in disposition tissues and free fatty acids. These considerations all suggest a need for more in vivo studies. There seems to be limited understanding regarding its long-term effects on subjects using progestin-only contraceptives [5]. Oral contraceptives (OCP) alter the metabolism of carbohydrates as well. The variables, 'fasting insulin, HOMA-IR (a measure of insulin resistance), fasting blood glucose, and OGTT (oral glucose tolerance test)' results are relevant in determining glucose metabolism within the body with different formulations. In addition, the impact of OCP use on blood glucose control over time can be estimated from HbA1c, an indicator of average blood glucose levels over some time. This information is crucial as it highlights shifts in lipid and carbohydrate metabolism that occur after extensive periods and tends to predispose one to cardiovascular and other metabolic abnormalities. Because women respond to various forms of contraception differently within the metabolism, behavioural contraceptive management is important. Underlying metabolic disorders or conditions that predispose an individual towards increased insulin resistance may benefit from low androgenic weight Ethinylestradiol-Norgestimate which, as proposed, has more favourable effects on lipid and carbohydrate metabolism. On the other hand, people who have a lower metabolic should be exposed to a wider variety of contraceptive options. Metabolic screening, including lipid levels, glucose level after fasting, and insulin resistance (HOMA-IR), assists clinicians in choosing the most appropriate contraceptive method for the patient. This may reduce the burden of long-term metabolic risks that arise from using hormonal contraception.

This study aims to assess the association between Ethinylestradiol-Levonorgestrel, Ethinylestradiol-Norgestimate, and Progestin-Only contraceptives and key metabolic markers, including lipid profile (total cholesterol, LDL, HDL, triglycerides, Apo-lipoprotein A1/B) and carbohydrate metabolism (fasting glucose, insulin resistance, HbA1c, and HOMA-IR), in women using these formulations. By evaluating changes in 'cholesterol, triglycerides, apolipoproteins, insulin levels, glucose tolerance, and HbA1c', this research seeks to provide a broad view of how different hormonal combinations in contraceptives influence metabolic health, helping to guide informed contraceptive choices for women. Despite widespread use of oral contraceptives, limited comparative research in Pakistani women has evaluated how different contraceptive formulations distinctly influence lipid and carbohydrate metabolism, particularly regarding cardiovascular and metabolic risk markers. Previous studies often focused on general hormonal effects without directly comparing Ethinylestradiol-Levonorgestrel, Ethinylestradiol-Norgestimate, and Progestin-Only users in local populations. Therefore, this study aimed to assess and compare the metabolic effects of these commonly used oral contraceptive formulations on lipid profiles, insulin resistance, and carbohydrate metabolism to guide safer, individualized contraceptive choices.

METHODS

A cross-sectional study recruited 84 women aged 18–45 who had been using one of these contraceptives for at least

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six months at Sheikh Khalifa Bin Zayed Al Nahyan Hospital/ Azad Kashmir (AK) Combined Military Hospital (CMH) Rawalakot, from January 2023 to July 2023. The study focused on three commonly used contraceptive formulations: 1. Ethinylestradiol-Levonorgestrel, 2. Ethinylestradiol-Norgestimate, and 3. Progestin-Only. The ethical approval was obtained from the 'institutional review board (IRB)' of Sheikh Khalifa Bin Zayed Al Nahyan Hospital/ AK CMH Rawalakot (375-A/SKBZ/CMH/RKT) before the start of the study. The sample size analysis was conducted with a significance level of 0.05 and a power of 80% to detect significant differences among groups. Based on estimated effect sizes from previous studies [6], a minimum sample size of 80 participants was required. To account for potential data inconsistencies and dropouts, a total of 84 participants were recruited. While purposive sampling ensured the inclusion of participants actively using the contraceptive formulations under study. The study population may not fully represent different age groups, ethnicities, or metabolic backgrounds. 'Participants were fully informed of the study's purpose, procedures, risks, and benefits'. Written informed consent was obtained from each participant, and they were assured of confidentiality and their right to withdraw from the study at any time without any negative consequences. The inclusion criteria were age: 18 to 45 years, Consistent use of Ethinylestradiol-Levonorgestrel, Ethinylestradiol-Norgestimate, or Progestin-Only for at least six months, Willingness to complete a 12-hour fasting period before sample collection and agreement to participate, indicated by providing written informed consent after a full explanation of study details. The exclusion criteria history of diabetes, polycystic ovary syndrome (PCOS), any lipid disorder, known cardiovascular conditions that could independently affect lipid or carbohydrate metabolism, Recent use of medications impacting metabolic profiles, antidiabetic drugs, lipid-lowering agents, or corticosteroids, Current pregnancy or breastfeeding and switches in contraceptive type or formulation within the past six months, to maintain stable exposure. Additionally, potential confounders such as diet, physical activity, and family history were not explicitly controlled, participants with a history of metabolic syndrome or recent major dietary interventions (extreme diets, weight loss programs) were excluded to reduce variability. Data Collection and Biochemical Assessment, data were gathered through structured interviews and clinical assessments, focusing on demographic and health information relevant to the study's aims. Upon enrolment, participants were interviewed to collect baseline 'demographic data, including age, body mass index (BMI)', duration of contraceptive use, systolic and diastolic blood pressure, and waist-to-hip ratio. BMI was calculated from measured height and weight, and waist-to-hip ratio was determined to assess body fat distribution. Blood pressure measurements were conducted using an Omron HEM-7121 which has been calibrated. To enhance reliability, every reading was documented two times and a mean was taken. To mitigate bias from self-reported contraceptive use, participants were asked to provide medical records or prescriptions detailing the contraceptive type and duration of use. Self-reported data were checked against other structured interviews. Only women on the same contraceptive formulation for at least six months were included, assuring they had the same hormonal context and less variability. To assess the biochemical parameters of lipid and carbohydrate metabolism, blood samples were obtained from participants after an overnight fasting 12 hours. This was performed to ensure accurate ground-level metabolic measures are taken without the inflating impact of food intake. Samples were taken by qualified phlebotomists through venepuncture to maintain the quality of the samples. The samples, post-collection, were separated into plasma and serum, the samples were then stored under strictly controlled temperatures until they were analyzed for any deviations. For the analysis of lipid profiles, a Roche Cobas 6000 Analyzer equipped with enzymatic colourimetric assays was used to determine total cholesterol, LDL, HDL, and triglycerides. These methods ensured precise quantification due to the enzyme reactions that are unique to each lipid parameter. An immune-turbidimetric assay on the Roche Cobas 6000 was used to measure Apolipoprotein A1 and Apolipoprotein B by utilizing antibodies to measure the concentration of each Apo-lipoprotein in serum. These measurements help analyse the profile of cardiovascular risks associated with various contraceptive formulations, which is the reason these specific lipid measurements were significant.

The carbohydrate metabolism assessment, including 'fasting blood glucose, HbA1c, fasting insulin, HOMA-IR, and OGTT' results, were also analysed. 'Fasting blood glucose was measured with the glucose oxidase method on the Roche Cobas 6000', known for precise glucose quantification in serum. HbA1c levels, reflecting average blood glucose over the past 3 months, were analysed using high-performance liquid chromatography (HPLC) on the Tosoh G8 HPLC Analyser. The levels of fasting insulin were measured using an immunoassay on the (Abbott Architect i2000SR) analyser, antibodies identify insulin concentrations, providing insights into pancreatic function and insulin sensitivity. HOMA-IR was measured based on fasting insulin and glucose values, offering an estimate of insulin resistance, an important factor in evaluating the metabolic effects of the contraceptives.

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Additionally, participants underwent an Oral Glucose Tolerance Test (OGTT), where they consumed a standard glucose solution followed by blood glucose measurements at intervals using the Roche Cobas 6000. OGTT results highlight glucose handling over time, allowing assessment of glucose tolerance potentially influenced by the contraceptive formulations. Statistical analysis was performed with SPSS version 22.0, to examine the effects of different oral contraceptive formulations on metabolic and demographic variables, data were initially assessed for normality using the Shapiro-Wilk test. Potential confounding factors, diet, physical activity, and genetic predisposition to metabolic disorders, were not explicitly controlled in this study. However, to minimize bias, participants with pre-existing metabolic disorders and recent medication use affecting lipid and carbohydrate metabolism were excluded. While this approach reduced some variability, future studies should incorporate more detailed assessments of lifestyle factors to refine these associations Variables that were normally distributed ($p>0.05$) were summarized using mean and standard deviation, while non-normally distributed data were summarized with median and interquartile ranges (IQR). For demographic variables, normally distributed variables (Age, BMI, Duration of Contraceptive Use, Systolic Blood Pressure, Diastolic Blood Pressure, Waist-to-Hip Ratio) were compared across the three contraceptive groups (Ethinylestradiol-Levonorgestrel, Ethinylestradiol-Norgestimate, and Progestin-Only) using One-Way ANOVA. In analysing lipid metabolism variables, One-Way ANOVA was used for between-group comparisons, followed by Tukey's post-hoc test when significant differences were detected. For carbohydrate metabolism variables, normally distributed data were analyzed using One-Way ANOVA with Tukey's post-hoc test for pairwise comparisons. Non-normally distributed data (e.g., Fasting Blood Glucose and HbA1c) were evaluated with the non-parametric Kruskal-Wallis test to identify 'any significant differences between groups'. 'All statistical tests were two-sided, and a p-value of <0.05 was considered statistically significant'.

RESULTS

The normality of each variable was assessed using the Shapiro-Wilk test. Variables with p-values greater than 0.05 in all groups were considered normally distributed and analyzed with parametric tests (One-Way ANOVA). These normally distributed variables included Age, BMI, Duration of Contraceptive Use, Systolic Blood Pressure, Diastolic Blood Pressure, Waist-to-Hip Ratio, Total Cholesterol, LDL, HDL, Triglycerides, Apo-lipoprotein A1, Apo-lipoprotein B, Fasting Insulin, HOMA-IR, and OGTT Result. For these variables, group comparisons were conducted using One-Way ANOVA. Moreover, Fasting Blood Glucose and HbA1c had p-values below 0.05 in at least one group, indicating non-normal distribution. As a result, these variables were analyzed using the non-parametric Kruskal-Wallis test. The One-Way ANOVA test revealed significant differences in BMI ($p=0.050$), Duration of Contraceptive Use ($p=0.001$), Systolic Blood Pressure ($p=0.030$), and Waist-to-Hip Ratio ($p=0.003$) across contraceptive groups. Specifically, Ethinylestradiol-Norgestimate users had a longer duration of contraceptive use compared to other groups, and Ethinylestradiol-Levonorgestrel users exhibited a higher waist-to-hip ratio. No significant differences were observed in age or diastolic blood pressure between groups. Demographic variables are shown in Table 1.

Table 1: Demographic Variables between Groups

Variables	Ethinylestradiol-Levonorgestrel (Mean ± SD)	Ethinylestradiol-Norgestimate (Mean ± SD)	Progestin-Only (Mean ± SD)	p-value
Age (Years)	31.65 ± 4.3	31.60 ± 5.9	31.17 ± 6.1	0.920
BMI (kg/m^2)	26.67 ± 2.95	24.42 ± 4.27	25.98 ± 3.88	0.050
Duration of Contraceptive Use (months)	22.77 ± 6.90	29.58 ± 9.40	16.67 ± 5.98	0.001
Systolic Blood Pressure (mmHg)	119 ± 8.7	113 ± 11.7	117 ± 9.3	0.030
Diastolic Blood Pressure (mmHg)	119.95 ± 6.20	77.7 ± 8.66	78.31 ± 6.47	0.270
Waist-to-Hip Ratio	0.850 ± 0.47	0.816 ± 0.43	0.834 ± 0.24	0.003

In lipid metabolism variables, One-Way ANOVA indicated significant group differences for Total Cholesterol ($p=0.004$) and Apo-lipoprotein A1 ($p=0.007$). Tukey's post-hoc test showed that Total Cholesterol levels were significantly higher in the Ethinylestradiol-Levonorgestrel group compared to Ethinylestradiol-Norgestimate ($p=0.002$), and Apolipoprotein A1 was higher in Ethinylestradiol-Norgestimate compared to Progestin-Only ($p=0.005$). No significant differences were found in LDL, HDL, Triglycerides, or Apolipoprotein B. Lipid Metabolism Variables are shown in table 2.

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Table 2: Lipid Metabolism Variables between Group

Variables	Ethinylestradiol-Levonorgestrel (Mean ± SD)	Ethinylestradiol-Norgestimate (Mean ± SD)	Progestin-Only (Mean ± SD)	ANOVA p-value	Significant Group Differences
Total Cholesterol (mg/dL)	31.65 ± 4.3	31.60 ± 5.9	193.10 ± 25.94	0.92	Ethinylestradiol-Levonorgestrel vs. Ethinylestradiol-Norgestimate (p=0.002)
LDL (mg/dL)	118.75 ± 23.81	114.70 ± 17.62	111.82 ± 21.20	0.403	None
HDL (mg/dL)	50.60 ± 10.85	53.88 ± 8.03	54.26 ± 8.38	0.207	None
Triglycerides (mg/dL)	157.48 ± 33.79	142.00 ± 23.09	147.17 ± 41.92	0.174	None
'Apo-lipoprotein A1 (g/L)'	1.38 ± 0.18	1.46 ± 0.23	1.31 ± 0.15	0.007	Ethinylestradiol-Norgestimate vs. Progestin-Only (p=0.005)
'Apo-lipoprotein B (g/L)'	0.98 ± 0.17	0.97 ± 0.09	0.91 ± 0.14	0.109	None

For normally distributed carbohydrate metabolism variables, One-Way ANOVA revealed a significant difference in HOMA-IR (p=0.004). Tukey's post-hoc analysis showed that HOMA-IR levels were higher in both Ethinylestradiol-Levonorgestrel and Progestin-Only groups compared to Ethinylestradiol-Norgestimate (p value 0.019 and p value 0.006, accordingly). Fasting Insulin and OGTT Results showed no significant differences across groups (p value=0.378 and p value 0.247, respectively). For the non-normally distributed variables, Fasting Blood Glucose (p=0.566) and HbA1c (p=0.086), the Kruskal-Wallis test indicated no statistically significant differences among groups. Carbohydrate metabolism variables are shown in Table 3.

Table 3: Carbohydrate Metabolism Variables between Groups

Variables	Ethinylestradiol-Levonorgestrel (Mean ± SD)	Ethinylestradiol-Norgestimate (Mean ± SD)	Progestin-Only (Mean ± SD)	ANOVA p-value	Significant Group Differences
Fasting Insulin (µIU/mL)	14.73 ± 4.58	14.25 ± 6.83	16.00 ± 4.02	0.378	None
HOMA-IR	3.14 ± 1.08	2.50 ± 0.95	3.23 ± 0.78	0.004	Ethinylestradiol-Levonorgestrel vs. Ethinylestradiol-Norgestimate (p=0.002)
OGTT Result (mg/dL)	135.58 ± 26.95	132.80 ± 18.11	141.63 ± 19.88	0.247	None
Fasting Blood Glucose (mg/dL)	87.29 [IQR 84.36–95.64]	90.05 [IQR 81.59–98.93]	90.06 [IQR 86.40–96.85]	0.566	None
HbA1c (%)	5.46 [IQR 5.26–5.83]	5.46 [IQR 5.08–5.65]	5.66 [IQR 5.25–5.88]	0.08	None

DISCUSSION

This study examined the metabolic effects of different oral contraceptive formulations on lipid and carbohydrate markers in women, specifically comparing Ethinylestradiol-Levonorgestrel, Ethinylestradiol-Norgestimate, and Progestin-Only contraceptives. Our findings reveal differences in lipid profiles and insulin resistance indicators among these formulations, offering insights into how various hormonal compositions can impact metabolic health, potentially influencing cardiovascular and metabolic risk factors. In lipid metabolism, significant differences were found in total cholesterol and Apo-lipoprotein A1 levels among the groups. The Ethinylestradiol-Levonorgestrel formulation showed a higher level of total cholesterol compared to the Ethinylestradiol-Norgestimate. This finding was consistent with prior research indicating that contraceptives containing levonorgestrel may increase lipid levels due to its relatively higher androgenic activity compared to other progestins, which can affect lipid synthesis and cholesterol levels [7, 8]. Such outcomes were consistent with other longitudinal studies that have shown an increase in total cholesterol levels with sustained use of Ethinylestradiol-Levonorgestrel contraceptive Dragoman et al., a meta-analysis was conducted, and it was revealed that the sustained use of Levonorgestrel-containing Oral Contraceptives for over 12 months led to an increase in LDL cholesterol levels with a mean difference of 10.2 mg/dL (95% CI: 6.2-14.2) [9]. This indicates that prolonged use of Levonorgestrel may have multi-faceted detrimental consequences on the lipid profile, increasing

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the chances of cardiovascular risks in certain populations. In the future, more focus should be placed on long-term cohort studies to see if these metabolic changes level off, worsen, or improve over time. There are studies which argue that Levonorgestrel's androgenic activity could affect total cholesterol levels and cardiovascular health [10, 11]. But Ethinylestradiol-Norgestimate, which is known to be less androgenic, had lower cholesterol levels which makes influencing cardiovascular health more favourable to women who desire to maintain a healthy lipid profile. Levels of Apo-lipoprotein A1 were greater in the Ethinylestradiol-Norgestimate group than the Progestin-Only group, suggesting a possible cardio-protective effect of this formulation. Apo-lipoprotein A1 is an HDL molecule involved in the cardiovascular protective processes. The increase of Apo-lipoprotein A1 in the Ethinylestradiol-Norgestimate group is consistent with data that show non-androgenic contraceptives tend to have a better influence on HDL and chances of Apo-lipoproteins [12]. On the other hand, Progestin-Only formulations have much less favourable effects on lipid markers because there is no estrogen which is important in preserving HDL [13]. The variability in lipid metabolism observed among Progestin-Only contraceptive users may be influenced by individual genetic factors and baseline health conditions. Polymorphisms associated with lipid metabolism, such as perilipin 1 (PLIN1) and lipoprotein lipase (LPL), have been found to affect body composition and lipid profiles. Andrade-Mayorga *et al.*, reported that some polymorphisms of the PLIN1 gene were associated with greater decreases in fat mass after 12 weeks of the intervention, indicating that certain genes did predispose one to factors affecting lipid metabolism [14]. Further, baseline health conditions such as insulin resistance, obesity, and pre-existing dyslipidemia may also help explain the observed inter-individual differences. Our study did not analyse these genetic and metabolic factors, highlighting the necessity for future studies to include genetic testing along with detailed health assessments to understand the altered responses to Progestin-Only contraceptive pills. When analysing carbohydrate metabolism, "there was a marked difference in HOMA-IR between the groups, whereby the Ethinylestradiol-Levonorgestrel and Progestin-Only formulations had higher HOMA-IR compared with Ethinylestradiol-Norgestimate." This aligns with previous research showing that certain contraceptives, particularly those with more androgenic progestins, can reduce insulin sensitivity, increasing the risk of insulin resistance over time [15]. Studies have shown that androgenic progestins, levonorgestrel can exacerbate insulin resistance in some women, which may contribute to metabolic risks, particularly with long-term use [16, 17]. In contrast, Ethinylestradiol-Norgestimate, which has a milder androgenic profile, may be less likely to disrupt glucose and insulin regulation, thus presenting a more favourable option in terms of glycemic control [18]. Fasting blood glucose and HbA1c did not show statistically significant differences among groups, suggesting that short- to medium-term use of these contraceptives may not significantly impact overall glycemic control in healthy women without pre-existing metabolic disorders. Although our study did not find significant differences in fasting blood glucose and HbA1c among the contraceptive groups, it is important to consider that specific subgroups, such as women with a family history of diabetes or metabolic syndrome, may exhibit different metabolic responses. Maria-Elina *et al.*, found that former long-term use of combined hormonal contraceptives was associated with an increased risk of prediabetes in perimenopausal women [19].This suggests that individuals with a predisposition to glucose metabolism disorders might experience more pronounced effects when using certain hormonal contraceptives. Future studies should consider stratifying participants based on metabolic risk factors to better understand these individualized responses 'However, it is worth noting that other studies have shown mixed results regarding the effect of hormonal contraceptives on glucose metabolism', with some findings indicating a potential increase in fasting glucose and HbA1c with prolonged use, particularly in formulations containing higher estrogen doses [20, 21]. Present results support the hypothesis that these formulations, especially when used at lower doses and for limited periods, may not have substantial adverse effects on glucose levels in otherwise healthy women.Nevertheless, 'further research is needed to clarify the long-term impact of these contraceptive types on glucose metabolism'. In conclusion, this study highlights that different oral contraceptive formulations may have distinct effects on lipid and carbohydrate metabolism, with Ethinylestradiol-Norgestimate appearing to offer a more favourable metabolic profile in terms of cholesterol, Apo lipoprotein A1, and insulin sensitivity. These findings indicate hormonal contraceptive choices might be customised to align with individual metabolic profiles, especially for women who prioritise women with metabolic and cardiovascular health concerns.

The study was limited by its cross-sectional design, small sample size, purposive sampling, and exclusion of women with pre-existing metabolic disorders, which restricts causal interpretation and broader generalizability. Potential confounding factors such as diet, physical activity, and genetic predisposition were not fully controlled. Future research should involve larger multicenter longitudinal studies, include metabolically

DOI: https://doi.org/10.54393/pjhs.v6i2.2646

diverse populations, and incorporate detailed lifestyle and genetic assessments to better understand long-term metabolic consequences of contraceptive use.

CONCLUSIONS

It was concluded that this study highlights the diverse metabolic impacts of different oral contraceptive formulations. Ethinylestradiol-Norgestimate demonstrated the most favourable effects on cholesterol and insulin sensitivity, whereas Ethinylestradiol-Levonorgestrel and Progestin-Only formulations exhibited varying influences on lipid markers. These findings underscore the importance of personalised contraceptive choices based on metabolic risk assessments. Long-term studies are needed to evaluate the sustained metabolic effects over extended durations, particularly in women with pre-existing cardiovascular or metabolic risks. Implementing metabolic screening tools in clinical practice could enhance safer contraceptive prescribing and improve long-term metabolic health outcomes.

Authors' Contribution

Conceptualization: SMH
Methodology: SMH, SMSAB, JZ
Formal analysis: SN, NF
Writing and Drafting: SAK, SN, JZ
Review and Editing: SAK, SN, JZ, SMSAB

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

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