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Changes in the Hematological Parameters among Women Using Oral Contraceptives in Dhamar City, Yemen

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Abstract

Background: Oral contraceptives (OCs) are widely used, yet their hematological effects in resource-limited settings like Yemen, where anemia is highly prevalent, are poorly characterized. This study investigated the impact of OCs on hematological and coagulation parameters in women from Dhamar City, Yemen.

Methods:A comparative cross-sectional study included 76 women (42 OC users, 34 non-users) recruited from healthcare facilities and community settings. Complete blood count parameters (hemoglobin, hematocrit, red cell indices, white cell differential) and coagulation markers (platelet count, prothrombin time, activated partial thromboplastin time [APTT], international normalized ratio) were measured. Statistical analyses included t-tests, Mann-Whitney U, chi-square, Spearman's correlation, and multivariate logistic regression.

Results:OC users showed significantly higher platelet counts than non-users (309.76 vs. 271.56 $\times 10^3/\mu$L, p=0.024) and prolonged APTT (26.52 vs. 23.06 seconds, p=0.005), though all values remained within normal ranges. APTT correlated negatively with OC duration (r_s=-0.452, p=0.004), decreasing from 28.9 seconds (1–2 years) to 25.3 seconds (>4 years). Microcytosis (MCV<80 fL) was more prevalent among OC users (42.9% vs. 20.6%, p=0.041, OR=2.89), despite similar hemoglobin levels. Younger users (<30 years) had higher platelet counts than older users (342.8 vs. 284.2 $\times 10^3/\mu$L, p=0.004). Multivariate regression confirmed APTT (OR=1.202) and platelet count (OR=1.009) as independent correlates of OC use.

Conclusion:OC use in Yemeni women is associated with elevated platelets, duration-dependent APTT changes, and increased microcytosis. These findings underscore the need for comprehensive hematological monitoring particularly platelet and coagulation profiles for OC users in anemia-endemic, resource-limited settings.

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Oral contraceptives, hematological parameters, coagulation, APTT, Yemen, family planning.

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Introduction

Oral contraceptives (OCs) are among the most widely used methods of fertility regulation worldwide. However, their influence extends beyond reproductive health to systemic physiological processes, including significant alterations in hematological profiles [1, 2]. Hematological parameters, such as hemoglobin (Hb) levels, erythrocyte and platelet counts, and coagulation markers, such as prothrombin time (PT) and activated partial thromboplastin time (APTT), serve as critical indicators of overall health, reflecting both adaptive physiological changes and potential pathological risks [1–3].

Synthetic hormones in OCs, particularly estrogen and progestin, modulate hematopoiesis and hemostasis.

Existing literature documents that OC use can lead to elevated hemoglobin and erythrocyte counts, often attributed to reduced menstrual blood loss and enhanced iron absorption, which may be particularly beneficial for women with pre-existing anemia [4–6]. However, OCs can induce a prothrombotic state characterized by thrombocytosis, shortened coagulation times, and increased levels of factors such as fibrinogen, thereby elevating the risk of venous thromboembolism (VTE) [7, 8]. This risk is further influenced by the specific OC formulation, with third-generation pills being associated with a higher VTE incidence [9] The hematological impact of OCs is not uniform and appears to be moderated by regional variations in the genetic background, nutritional status, and healthcare practices. Studies from Ethiopia, Nigeria, and Egypt, for instance, have reported divergent findings, highlighting higher platelet counts in some populations and improved iron stores in others, underscoring the necessity for context-specific research [10–12].

In Yemen, a nation grappling with a severe humanitarian crisis, understanding these effects is particularly urgent. Approximately 30% of women of reproductive age rely on hormonal contraception, yet the country suffers from one of the highest rates of anemia globally, affecting about 44% of women, driven by malnutrition, frequent pregnancies, and limited healthcare access [13, 14]. This creates a complex public health dilemma: while the anti-hemorrhagic effect of OCs could potentially mitigate anemia, the pro-thrombotic effects could pose a significant threat in a population where monitoring and managing thrombotic events is challenging. Despite the high reliance on OCs in cities such as Dhamar, a densely populated urban center, there is a critical lack of localized data on their hematological effects. This gap impedes the development of evidence-based clinical guidelines and safe contraceptive practices, leaving a vulnerable population at risk. Therefore, this study aimed to address this knowledge gap by comprehensively evaluating the changes in hematological and coagulation parameters in women using oral contraceptives in Dhamar City, Yemen.

Methods and Materials

Study Design and Setting

A comparative cross-sectional study was conducted in Dhamar City, Yemen, from December 2024 to May 2025. Participants were recruited from multiple sites, including Al-Hilal Red Crescent Hospital, the Fever Center, community neighborhoods, and the university campus, to enhance sample diversity.

Study Participants

The study comprised 76 women divided into two groups: 42 current oral contraceptive (OC) users (cases) and 34 non-users (controls). The OC user group included women who had been using combined oral contraceptives (e.g., Novyneete, Indynette, Regulon) for a minimum of six months. The control group comprised women who had never used hormonal contraception.

Inclusion Criteria

Eligible participants were women aged 18–45 years old. The OC user group included women who had been using combined oral contraceptive pills continuously for at least six months. The non-user group comprised women with no history of hormonal contraceptive use. All participants were required to have no known chronic medical conditions, hematological disorders, or current use of medications that could significantly affect their hematological or coagulation parameters.

Exclusion Criteria

Women were excluded from the study if they had a known history of any hematological disorder, were current smokers, or were using any medication that could alter blood composition or coagulation. Additionally, women using non-oral hormonal contraceptive methods (e.g., implants, injectables, or intrauterine devices) were excluded.

Sample Size

The sample size was convenient, comprising all eligible women who consented to participate during the six-month study period. This pragmatic approach was necessitated by the time and resource constraints of this study.

Data and Sample Collection

After obtaining written informed consent, demographic information, clinical history, and details on OC use (type and duration) were collected using a structured questionnaire. Venous blood samples (approximately 10 mL) were drawn from each participant under aseptic conditions using standard venipuncture techniques. Blood was distributed into two vacuum tubes: a K2-EDTA tube for complete blood count (CBC) analysis and a 3.2% sodium citrate tube for coagulation studies.

Data Collection and Laboratory Measurements

Venous blood samples were collected from all participants under standardized conditions.

Hematological parameters, including white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and platelet count, were analyzed using a Sysmex XN-550 fully automated hematology analyzer.

Citrated blood samples were centrifuged at 2500 RPM for 5 min at room temperature to obtain platelet-poor

plasma. Coagulation tests were performed immediately after.

Prothrombin Time (PT) and International Normalized Ratio (INR): Measured using a semi-automated coagulation analyzer. The test was performed by incubating 0.1 mL of plasma at 37℃, followed by the addition of 0.2 mL of a pre-warmed mixture of thromboplastin and 0.025 M calcium chloride. The time to clot formation was recorded in seconds.

Activated Partial Thromboplastin Time (APTT): 0.1 mL of plasma was mixed with 0.1 mL of APTT reagent and incubated for 5 min at 37℃. Then, 0.1 mL of pre-warmed 0.025 M calcium chloride was added, and the clotting time was measured using a stopwatch.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 26. The Shapiro-Wilk test was used to assess the normality of data distribution. Normally distributed data were presented as mean ± standard deviation (SD) and compared between groups using the independent samples t-test. Non-normally distributed data were presented as median with interquartile range (IQR) and compared using the Mann-Whitney U test. Categorical variables were presented as frequencies (n) and percentages (%) and compared using the Chi-square test. Odds ratios (OR) with 95% confidence intervals (CI) were calculated for significant associations. Correlations between duration of OC use and hematological parameters were assessed using Spearman's rank correlation coefficient due to the non-normal distribution of duration data. Multivariate analysis was performed using binary logistic regression (enter method) to identify factors independently associated with OC use. Variables were entered simultaneously, and adjusted odds ratios with 95% confidence intervals were calculated. Effect sizes were calculated as Cohen's d for t-tests (interpreted as: small = 0.2, medium = 0.5, large = 0.8) and as r = $Z/\sqrt{N}$ for Mann-Whitney U tests (interpreted as: small = 0.1, medium = 0.3, large = 0.5). A p-value < 0.05 was considered statistically significant for all analyses.

Ethical Considerations

The study protocol was reviewed and approved by the Ethical Committee of the University of [Approval No: GUFMHS-LM-25002]. Written informed consent was obtained from all participants prior to enrollment. Confidentiality was maintained, and the participants were informed of their right to withdraw from the study at any time without penalty.

Results

As presented in Table (1), there were no significant differences in age between OC users and non-users (p=0.284). Among red blood cell parameters, no statistically significant differences were observed, although MCV showed a trend toward being lower in OC users (82.85 ± 4.73 vs. 84.74 ± 4.14 fL, p=0.067) with a small-to-medium effect size (d=0.43), while white blood cell parameters were similar between groups (all p>0.05). However, significant differences were observed in platelet and coagulation parameters; OC users had significantly higher platelet counts than non-users (309.76 ± 84.70 vs. 271.56 ± 56.00 $\times 10^3/\mu$L, p=0.024) with a medium effect size (d=0.53), although all platelet values remained within the normal clinical reference range (150-450 $\times 10^3/\mu$L). OC users demonstrated significantly prolonged APTT compared to non-users (26.52 ± 4.88 vs. 23.06 ± 5.56 seconds, p=0.005) with a medium-to-large effect size (d=0.66), while no significant differences were observed in PT or INR (p>0.05).

As shown in Table (2), microcytosis (MCV < 80 fL) was significantly more prevalent among OC users than non-users (42.9% vs. 20.6%, p=0.041), with OC users having nearly three times higher odds of microcytosis (OR = 2.89, 95% CI: 1.04-8.02). Although hypochromia (MCH < 27 pg) was observed more frequently in OC users (16.7% vs. 8.8%), this difference was not statistically significant (p=0.312). The prevalence of anemia (hemoglobin < 12 g/dL) was similar between the two groups (9.5% vs. 8.8%, p=0.915), indicating that despite evidence of iron deficiency (microcytosis), hemoglobin levels were maintained in OC users

As shown in Table (3), a statistically significant moderate negative correlation was observed between the duration of OC use and APTT (r_s = -0.452, p = 0.004), with APTT decreasing progressively from 28.9 ± 4.6 seconds in users of 1-2 years to 26.1 ± 4.8 seconds in users of 3-4 years and 25.3 ± 4.7 seconds in users of >4 years, indicating a progressive shortening of APTT (coagulation activation) with a longer duration of OC use. No other hematological parameters showed significant correlations with duration of use; platelet count showed a slight but non-significant increase (306.2 ± 82.4 to 324.8 ± 86.2 $\times 10^3/\mu$L, r_s = 0.089, p = 0.578), red blood cell parameters including MCV and MCH exhibited non-significant decreasing trends (r_s = -0.184, p = 0.243 and r_s = -0.156, p = 0.324, respectively), and white blood cell parameters remained stable across all duration categories (all p > 0.05).

As presented in Table (4), younger OC users (<30 years, n=24) had significantly higher platelet counts than older users ($\geq$30 years, n=18), with mean values of 342.8 ± 68.4 $\times 10^3/\mu$L versus 284.2 ± 54.6 $\times 10^3/\mu$L (t=3.02, p=0.004), representing a mean difference of 58.6 $\times 10^3/\mu$L (95% CI: 19.8 to 97.4). This finding indicates that age modifies the effect of OC use on platelet count, with younger users showing a more pronounced platelet elevation, although all platelet values remained within the normal clinical reference range (150-450 $\times 10^3/\mu$L).

As shown in Table (5), multivariate logistic regression analysis revealed that after adjusting for all variables in

Table[1]: Association between hematological and coagulation parameters changes in oral contraceptive pill users and non users (n=76)

Parameter	OC Users (n=42)	Non-Users (n=34)	Test Statistic	P-value	Effect Size
Demographics					
Age (years)[1]	27.50 (23.0–35.0)	25.00 (22.0–34.0)	U=612.5	0.284	r=0.12
Red Blood Cell Parameters					
RBC ($\times 10^6/\mu$L)[2]	4.84 ± 0.38	4.74 ± 0.33	t=1.28	0.204	d=0.29
Hemoglobin (g/dL)[2]	13.98 ± 1.24	13.91 ± 1.15	t=0.25	0.803	d=0.06
Hematocrit (%)[2]	40.58 ± 2.94	39.76 ± 3.06	t=1.20	0.235	d=0.27
MCV (fL)[2]	82.85 ± 4.73	84.74 ± 4.14	t=-1.86	0.067	d=0.43
MCH (pg)[2]	29.06 ± 2.48	29.72 ± 1.92	t=-1.30	0.198	d=0.30
MCHC (g/dL)[2]	34.84 ± 1.09	34.76 ± 0.91	t=0.34	0.732	d=0.08
RDW (%)[1]	**13.05 (12.0–14.0)**	**13.40 (13.0–14.0)**	U=678.5	**0.684**	r=0.05
White Blood Cell Parameters					
WBC ($\times 10^3/\mu$L)[2]	6.08 ± 2.12	5.68 ± 1.83	t=0.88	0.380	d=0.20
Neutrophil (%)[2]	49.59 ± 12.96	49.21 ± 10.81	t=0.14	0.890	d=0.03
Lymphocyte (%)[2]	38.89 ± 10.58	39.63 ± 9.88	t=-0.31	0.755	d=0.07
Monocyte (%)[2]	5.90 ± 2.27	5.64 ± 1.76	t=0.56	0.577	d=0.13
Eosinophil (%)[1]	**3.30 (2.1–6.4)**	**3.45 (2.8–5.9)**	U=712.5	**0.984**	r=0.002
Basophil (%)[1]	**0.20 (0.0–0.5)**	**0.30 (0.1–0.5)**	U=668.5	**0.586**	r=0.06
Platelet and Coagulation Parameters					
Platelet ($\times 10^3/\mu$L)[2]	309.76 ± 84.70	271.56 ± 56.00	t=2.31	**0.024**	d=0.53
APTT (seconds)[2]	26.52 ± 4.88	23.06 ± 5.56	t=2.89	**0.005**	d=0.66
PT (seconds)[1]	11.70 (11.0–13.0)	12.00 (11.0–13.0)	U=584.5	0.248	r=0.13
INR[1]	0.98 (0.91–1.09)	1.00 (0.91–1.09)	U=602.0	0.342	r=0.11

*Effect size interpretation: Cohen's d: small=0.2, medium=0.5, large=0.8; r: small=0.1, medium=0.3, large=0.5. *
Bold values indicate statistically significant differences ($p < 0.05$).
Data are presented as:
[1]Median (IQR) for non-normally distributed variables (Mann-Whitney U test)
[2]Mean ± SD for normally distributed variables (Independent t-test)
Abbreviations: SD, standard deviation; IQR, interquartile range; U, Mann-Whitney U statistic; t, t-test statistic; r, effect size for Mann-Whitney ($r = Z/\sqrt{N}$); d, Cohen's d for t-test; WBC = White Blood Cell; RBC = Red Blood Cell; HGB = Hemoglobin; HCT = Hematocrit; MCV = Mean Corpuscular Volume; MCH = Mean Corpuscular Hemoglobin; MCHC = Mean Corpuscular Hemoglobin Concentration; RDW = Red Cell Distribution Width; PT = Prothrombin Time; APTT = Activated Partial Thromboplastin Time; INR = International Normalized Ratio.

Table[2]: comparison of microcytosis, hypochromia, and anemia prevalence between oc users and non-users

Parameter	Threshold	OC Users (n=42)	Non-Users (n=34)	χ^2	P-value	OR (95% CI)
Microcytosis	MCV < 80 fL	18 (42.9%)	7 (20.6%)	4.18	**0.041**	2.89 (1.04–8.02)
Hypochromia	MCH < 27 pg	7 (16.7%)	3 (8.8%)	1.02	0.312	2.07 (0.49–8.68)
Anemia	Hb < 12 g/dL	4 (9.5%)	3 (8.8%)	0.01	0.915	1.09 (0.23–5.21)

Data are presented as n (%). The chi-square test was used for comparisons. OR = Odds Ratio; CI = Confidence Interval.

the model, two factors showed significant independent associations with OC use: APTT demonstrated the strongest association, with each 1-second increase associated with a 20.2% higher odds of being an OC user (OR = 1.202, 95% CI: 1.064-1.358, p = 0.003), while platelet count also showed a significant independent association, with each 1-unit increase ($\times 10^3/\mu$L) associated with a 0.9% higher odds of being an OC user (OR = 1.009, 95% CI: 1.001-1.017, p = 0.024), corresponding to a 9.3% increase in odds per 10-unit increase in platelet count. Age, MCV, MCH, and hemoglobin levels did not show significant independent associations with OC use in the multivariate model (all $p > 0.05$).

Discussion

This comparative cross-sectional study examined the association between oral contraceptive use and hematological parameters in women in Dhamar City, Yemen. The findings revealed significant differences in platelet counts and coagulation profiles between OC users and non-users, as well as important associations with duration of use and age.

The present study found that OC users had significantly higher platelet counts than non-users (309.76 ± 84.70 vs. 271.56 ± 56.00 $\times 10^3/\mu$L, p=0.024), with a medium effect size (d=0.53). This finding is consistent with a recent narrative review by Tekle et al. (2022), which reported that most oral contraceptive users had higher platelet counts than non-users [15]. Similarly, a study from Nigeria by Babatunde et al. (2004) demonstrated significantly increased platelet counts after three months of contraceptive use (p=0.0000) [16]. However, it is important to emphasize that all platelet values in the current study

Table[3]: Association between duration of oral contraceptive use and changes in hematological and coagulation parameters among users (n=42)

Parameter	Duration of OC Use			Correlation
	1–2 years (n=18)	**3–4 years (n=15)**	**>4 years (n=9)**	r_s **(P-value)**
Demographics				
Age (years)[1]	26.0 (22.0–34.0)	30.0 (25.0–35.0)	35.0 (30.0–40.0)	0.184 (0.243)
Red Blood Cell Parameters				
RBC ($\times 10^6/\mu$L)[2]	4.82 ± 0.36	4.79 ± 0.41	4.76 ± 0.38	-0.124 (0.432)
Hemoglobin (g/dL)[2]	14.2 ± 1.3	13.9 ± 1.2	13.8 ± 1.2	-0.089 (0.576)
Hematocrit (%)[2]	41.2 ± 2.8	40.4 ± 3.0	39.8 ± 2.9	-0.098 (0.534)
MCV (fL)[2]	84.2 ± 4.6	82.6 ± 4.8	81.4 ± 4.7	-0.184 (0.243)
MCH (pg)[2]	29.4 ± 2.4	28.9 ± 2.5	28.2 ± 2.4	-0.156 (0.324)
MCHC (g/dL)[2]	34.8 ± 1.1	34.9 ± 1.1	34.8 ± 1.0	0.042 (0.792)
RDW (%)[1]	13.0 (12.0–14.0)	13.1 (12.5–14.0)	13.5 (13.0–14.5)	0.112 (0.482)
White Blood Cell Parameters				
WBC ($\times 10^3/\mu$L)[2]	5.96 ± 2.08	6.08 ± 2.15	6.12 ± 2.20	0.067 (0.672)
Neutrophil (%)[2]	48.5 ± 12.8	50.2 ± 13.1	51.0 ± 12.9	0.089 (0.576)
Lymphocyte (%)[2]	39.8 ± 10.5	38.6 ± 10.6	37.8 ± 10.4	-0.078 (0.623)
Monocyte (%)[2]	6.0 ± 2.3	5.9 ± 2.2	5.8 ± 2.3	-0.045 (0.577)
Eosinophil (%)[1]	3.3 (2.1–6.5)	3.4 (2.2–6.2)	3.2 (1.9–6.4)	-0.034 (0.832)
Basophil (%)[1]	0.2 (0.0–0.5)	0.2 (0.0–0.5)	0.3 (0.1–0.5)	0.023 (0.886)
Platelet and Coagulation Parameters				
Platelet ($\times 10^3/\mu$L)[2]	306.2 ± 82.4	310.5 ± 85.6	324.8 ± 86.2	0.089 (0.578)
APTT (seconds)[2]	**28.9 ± 4.6**	**26.1 ± 4.8**	**25.3 ± 4.7**	**-0.452 (0.004)**
PT (seconds)[1]	11.6 (11.0–12.5)	11.8 (11.0–13.0)	11.7 (11.0–13.0)	-0.112 (0.482)
INR[1]	0.96 (0.91–1.00)	0.98 (0.91–1.09)	0.98 (0.91–1.09)	-0.098 (0.534)

[1]Data presented as median (IQR) for non-normally distributed variables.
[2]Data are presented as mean ± SD for normally distributed variables.
*Spearman's rank correlation was used for all correlations due to the non-normal distribution of OC use duration. Bold indicates a statistically significant correlation ($p < 0.05$). *

Table[4]: Comparison of platelet counts between younger and older oc users

Age Group	n	Platelet Count ($\times 10^3/\mu$L)	Comparison	Test Statistic	P-value
<30 years	24	342.8 ± 68.4			
≥30 years	18	284.2 ± 54.6	<30 vs. ≥30	t=3.02	**0.004**

Data presented as Mean ± SD. Independent t-test used for comparison.

Table[5]: Multivariate logistic regression analysis of factors associated with oral contraceptive use

Predictor	B Coefficient	SE	Wald χ^2	Odds Ratio (OR)	95% CI for OR	P-value
APTT (seconds)	0.184	0.062	8.81	1.202	1.064–1.358	**0.003**
Platelet count ($\times 10^3/\mu$L)	0.009	0.004	5.06	1.009	1.001–1.017	**0.024**
Age (years)	-0.041	0.038	1.16	0.960	0.891–1.034	0.282
MCV (fL)	-0.089	0.062	2.06	0.915	0.810–1.033	0.151
MCH (pg)	-0.112	0.118	0.90	0.894	0.709–1.127	0.343
Hemoglobin (g/dL)	0.156	0.241	0.42	1.169	0.729–1.875	0.517
Constant	-2.847	5.894	0.23	0.058	–	0.629

Binary logistic regression analysis with OC use (0 = non-user, 1 = user) as the dependent variable. All predictors were entered simultaneously using the Enter method. B = unstandardized regression coefficient; SE = standard error; Wald χ^2 = Wald chi-square statistic; OR = odds ratio; 95% CI = 95% confidence interval for odds ratio. **Bold** values indicate statistically significant predictors ($p < 0.05$).

remained within the normal clinical reference range (150-450 ×$10^3/\mu$L), consistent with the observations of Aldrighi et al. (2006), who reported that platelet count increases with OC use but typically remains within normal limits [17].

The biological mechanism underlying this elevation may be related to the effect of estrogen on hematopoietic stem cells. Elsayid et al. (2016) demonstrated that estrogen increases hematopoietic stem cell self-renewal, potentially explaining the increased platelet production observed in OC users [18].

An unexpected finding of this study was the significantly prolonged APTT in OC users compared to non-users (26.52 ± 4.88 vs. 23.06 ± 5.56 seconds, p=0.005). This finding contrasts with several studies that have reported a shortened APTT in OC users. Sirhindi et al. (2004) found that PT, APTT, and TT were shortened in subjects using combined oral contraceptives compared to normal

controls [19]. Similarly, Aldrighi et al. (2006) reported a significant decrease in APTT during COC use [17]. However, Babatunde et al. (2004) found no significant difference in APTT values before and after oral contraceptive use (p=0.17) , suggesting that the APTT response to OCs may be variable [16]. The prolonged APTT observed in our study may reflect early transient effects on coagulation factors or could be influenced by other factors, such as nutritional status, which may differ in the Yemeni population.

The observation of a significant moderate negative correlation between duration of OC use and APTT (r_s = -0.452, p = 0.004), with APTT decreasing progressively from 28.9 seconds in 1-2 year users to 25.3 s in >4 year users, is consistent with several longitudinal studies that have examined hemostatic changes over time. Prasad et al., in a two-year prospective study of combined oral contraceptive users, reported that shortened APTT was apparent within three months and persisted throughout 12 months of use, with the most pronounced changes occurring in the first year [20]. Similarly, Aldrighi et al. observed significant APTT shortening after six months of COC use compared to pretreatment values, suggesting that coagulation activation occurs relatively early during OC exposure [17]. However, these studies did not extend follow-up beyond two years to examine whether APTT continues to shorten progressively or reaches a plateau with long-term use.

The significantly higher prevalence of microcytosis (MCV < 80 fL) among OC users (42.9% vs. 20.6%, p=0.041, OR=2.89) indicates a substantial burden of subclinical iron deficiency in this population. Notably, the prevalence of anemia did not differ between the groups, suggesting that iron deficiency in OC users may be masked by maintained hemoglobin levels. This dissociation between microcytosis and anemia has important clinical implications, as routine hemoglobin screening alone fails to detect iron deficiency in these women.

The association between OC use and micronutrient depletion is well documented. A recent review by Quest Health (2024) highlighted that oral contraceptives can negatively impact nutrient levels, including magnesium, phosphorus, selenium, vitamin B6, vitamin B9 (folate), vitamin E, and zinc [21]. Earlier work by Vijayalakshmi and Kochurani (1984) also demonstrated that oral contraceptive use decreased blood protein and zinc levels and mobilized body stores of copper, iron, manganese, and hemoglobin [22]. The high prevalence of microcytosis in our study population may reflect these nutrient-depleting effects, compounded by the high background prevalence of anemia in this region.

Younger (<30 years) OC users had significantly higher platelet counts than older users (342.8 ± 68.4 vs. 284.2 ± 54.6 $\times 10^3/\mu$L, p=0.004). This finding is consistent with a recent Nigerian study by Bukar et al. (2025), which reported that contraceptive users had significantly higher platelet counts than non-users, with the highest levels seen in the younger age group (18-25 years) [23]. An early epidemiological study by Meade et al. (1976) also noted that for the majority of variables studied, the differences between those using and not using oral contraceptives were greater in younger women than in older women [24]. These consistent findings across different populations and time periods suggest that age is an important modifier of hematological response to oral contraceptives.

The hematological parameters identified as significant in the multivariate model align with, and in some cases diverge from, previous findings in the literature. The significant association between OC use and APTT observed in the present analysis (OR = 1.202, p = 0.003) is consistent with the work of Getu et al. (2025), who reported a significantly shortened APTT in combined oral contraceptive (COC) users compared to non-users [25], indicative of a hypercoagulable state. However, this finding contrasts with an earlier study by Babatunde et al. (2004), which found no significant difference in APTT following three months of OC use in a Nigerian cohort [16]. This discrepancy may be attributed to differences in study design, duration of OC exposure, or the specific hormonal composition of the contraceptives used. In contrast, the significant association between platelet count and OC use (OR = 1.009, p = 0.024) is strongly supported by a broad consensus in the literature. Multiple studies, including those by Getu et al. (2025), Tekle et al. (2022), and Babatunde et al. (2004), have consistently reported elevated platelet counts among OC users, reinforcing the robustness of this association [15, 16, 25]. Regarding prothrombin time (PT), the multivariate analysis did not retain it as a significant independent predictor. This finding is contextualized by the highly mixed evidence base, where studies have reported PT to be shortened (Getu et al., 2025; Babatunde et al., 2004) [16, 25], prolonged (Obazelu et al., 2024), or unchanged with OC use [26]. The lack of a consistent direction in the literature suggests that PT may be a less reliable marker of OC-induced hemostatic changes compared to APTT and platelet count, which aligns with its non-significance in the final model after adjusting for other covariates.

Limitations

Several limitations should be considered when interpreting the findings of this study. The cross-sectional design precludes the determination of causality, and the relatively small sample size may limit the statistical power of some analyses. We were unable to measure specific coagulation factors, vitamin levels, or inflammatory markers, which might have provided additional mechanistic insights.

Conclusion

This study found that oral contraceptive (OC) use is associated with higher platelet counts and progressive shortening of coagulation time (APTT) with longer duration of use, while hemoglobin levels remain normal despite biochemical evidence of iron deficiency, such as microcytosis and hypochromia. These findings highlight that in resource-limited settings with a high prevalence of anemia, monitoring hematological parameters may be beneficial for women using OCs. Routine hematological screening and iron supplementation could help address underlying deficiencies and support safer family planning.

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