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02 (69) 2025 : 001-003 • RESEARCH ARTICLE

Impact of oral contraceptive pills on the activity of rheumatoid arthritis in women

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SUMMARY

AUTHORS' CONTRIBUTION: (A) Study Design · **(B)** Data Collection. **(C)** Statistical Analysis · **(D)** Data Interpretation · **(E)** Manuscript Preparation · **(F)** Literature Search · **(G)** Funds Collection

Background: Rheumatoid Arthritis (RA) is an inflammation of the joints that is more common in women, particularly in those between 30 and 50 years old than in men.

Aim: Role of Oral Contraceptive Pills (OCPs) on reduces the severity of RA.

Method: 200 women suffering from rheumatoid arthritis. The study population was separated into two groups (case and control), with 100 women in each category. The case group was constituted of women who stated a willingness to utilize OCPs and did not have any contraindications to hormonal therapy. In contrast, the control group selected non-hormonal means of contraception. Consequently, the control group was forbidden from getting a placebo in place of OCPs, due to the potential danger of pregnancy. Women in both study groups had rheumatologist assessment for disease activity using the DAS-28 measure prior to the administration of any therapies.

Results: The data showed there were no significant differences between the two groups in terms of baseline characteristics, including age, BMI, disease duration and treatment duration. No significant pre-intervention differences in DAS28 parameters and total scores ($p>0.05$) were observed between the groups. Subsequent to the intervention, the OCP group exhibited substantial enhancements in swollen joint scores, joint tenderness, general health ($p \leq 0.05$), and DAS28 total score ($p=0.05$), yet no variations in ESR values were observed. The control group showed no discernible difference (3.58±1.07 vs. 3.79±1.22). The groups' pre-intervention DA severity was comparable. Following the intervention, 58% of women in the control group had moderately severe DA, compared to 52% of women in the OCPs group ($p=0.04$).

Conclusion: Oral contraceptives do more than prohibit you from getting pregnant; they also diminish the activity of Rheumatoid Arthritis (RA), which was already known to be the case.

Keywords: CRP; Estrogen; Progesterone; HRT; Inflammatory; Bleeding

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Word count: 1632 **Tables:** 02 **Figures:** 01 **References:** 18

Received: 06.03.2025, Manuscript No. gpmp-25-163272; **Editor assigned:** 07.03.2025, PreQC No. P-163272; **Reviewed:** 28.03.2025, QC No. Q-163272; **Revised:** 04.04.2025, Manuscript No. R-163272; **Published:** 30.06.2025

INTRODUCTION

Rheumatoid Arthritis (RA) is a frequent inflammatory condition that damages connective tissue, with a higher frequency in women, particularly between the ages of 30 and 50, compared to men. The prevalence of RA ranges from 0.8% to 1%, with a reported 0.34% of Asian countries and lower than in Western ones [1]. Pregnancy in women with disabilities is a significant problem, as they receive less healthcare and family planning services. Furthermore, childbearing is rendered more complex due to the limitations associated with rheumatoid arthritis, thus rendering contraception a critical issue. Research has indicated that the use of Oral Contraceptive Pills (OCPs) can positively impact rheumatoid arthritis disease activity [2,3].

All methods of family planning, including intrauterine devices, are judged suitable for patients diagnosed with Rheumatoid Arthritis (RA) who are not undergoing immunosuppressive medication. However, oral contraceptive pills are considered the most beneficial alternative, as they may positively affect the advancement of RA. The potential of hormonal contraceptives to lower disease activity and severity is particularly relevant considering the autoimmune nature of rheumatoid arthritis [4].

The present study focuses on the evaluation of the possible benefits of Oral Contraceptive Pills (OCPs) in the decrease of Rheumatoid Arthritis (RA) activity and severity. By focusing on Iraqi women of reproductive age, the study intends to remedy the vacuum in data regarding specific demographics. The fundamental aims of the study are twofold: firstly, to examine the association between duration of OCP consumption and RA activity levels; and secondly, to establish whether hormonal effects play a part in alleviating symptoms. The findings could provide useful insights into customized treatment techniques and inspire future investigation in varied demographic groups.

MATERIALS AND METHODS

Method: A randomized controlled clinical trial was conducted on 200 women suffering from rheumatoid arthritis. The study was conducted in rheumatology clinics in government hospitals and private clinics in Al-Najaf, Iraq. The study population was divided into two groups (case and control), with 100 women in each group. The groups were classified according to American Rheumatism Association criteria. Women who met the inclusion criteria were divided into two study groups using a randomized block of size two (100 women in each

group) *via* a sequential sampling technique. The study excluded pregnant women, women with mental and physical problems other than rheumatoid arthritis, and those using oral contraceptives with contraindications.

The case group was comprised of women who expressed a desire to utilize OCPs and did not have any contraindications to hormonal therapy. In contrast, the control group selected non-hormonal methods of contraception. Consequently, the control group was prevented from receiving a placebo in place of OCPs, due to the potential risk of pregnancy.

Women in both study groups underwent rheumatologist assessment for disease activity using the DAS-28 measure prior to the administration of any treatments (5). The DAS-28 instrument is comprised of three sections. Firstly, the clinical component enumerates painful and swollen joints. Secondly, the laboratory test component involves the erythrocyte sedimentation rate. The third section of the DAS-28 instrument is concerned with the general health component, in which the patient's global assessment of disease activity over the past seven days is measured using a visual scale of 0-100mm, with a score ranging from 0 to 100. Values below 3.2 are regarded as modest disease activity, those between 3.2 and 5.1 as moderate, and all values above 5.1 as severe [5,6].

Statistics

The data was analyzed using SPSS 26v, with the mean ± standard error being reported. For qualitative data, the chi-square test was employed. GraphPad v. 8.1 was utilized to set a significance level at $p<0.05$, and the graphs were generated.

RESULTS

Basic clinical characteristics

The present study comprised 200 women, with 100 women in each of the intervention and control groups. The data revealed no statistically significant differences between the two groups with respect to the basic characteristics. In the OCPs group, the participants' mean age was 28.48 ± 5.17 years; in the control group, it was 30.18 ± 4.19 years (p=0.34). The BMI of the OCPs group was 26.72 ± 6.37 kg/m² and 25.91 ± 5.33 kg/m² in the control group (p=0.34). The duration of rheumatoid arthritis in both groups was found to be 8.00 ± 4.34 and 7.42 ± 6.05 years, respectively, with a p-value of 0.29. Furthermore, treatment for rheumatoid arthritis was received for 6.42 ± 3.05 and 6.60 ± 3.58 years, respectively, with a p-value of 0.62. The characteristics of the participants are detailed in **Tab. 1.**

As demonstrated in **Tab. 2.**, the DAS28 parameters and total score prior to the intervention exhibited no significant changes ($p>0.05$) between the two study groups. Subsequent to the intervention, the OCP group exhibited substantial disparities in contrast to the control group with respect to swollen joint scores (p=0.01), joint tenderness ratings (p=0.01), general health assessments ($p<0.001$), and the DAS28 total score (p=0.01). However, no significant differences were identified between the two groups with regard to ESR values (see **Tab. 2.** and **Fig. 1.**).

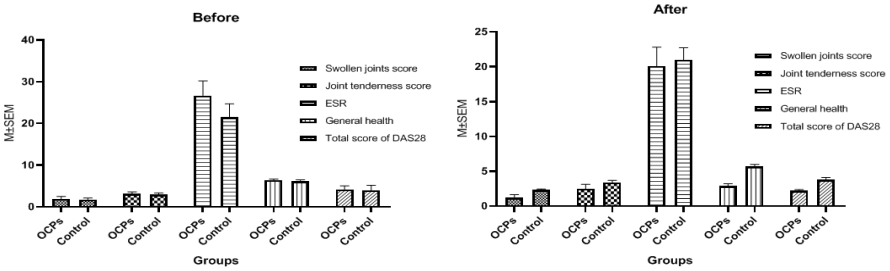
Tab. 1. Basic characteristics of the studied sample.

Parameters	Mean ± SEM (Controls)	Mean ± SD (Cases)	P-value
Age	30.18 ± 4.19	28.48 ± 5.17	0.34
BMI (kg/m^2)	25.91 ± 5.33	26.72 ± 6.37	0.34
Duration of rheumatoid arthritis	7.42 ± 6.05	8.00 ± 4.34	0.29
Treatment for rheumatoid arthritis	6.60 ± 3.58	6.42 ± 3.05	0.62

Tab. 2. The frequency and percent of different types of tongue condition.

Parameter	Before			After		
	OCPs group (M ± SD)	Control group (M ± SD)	P value	OCPs group (M ± SD)	Control group (M ± SD)	P value
Swollen joints score	1.96 ± 0.56	1.71 ± 0.42	NS	1.2 ± 0.31	2.3 ± 0.11	S
Joint tenderness score	3.12 ± 0.49	2.98 ± 0.38	NS	2.5 ± 0.44	3.4 ± 0.21	S
ESR	26.7 ± 3.5	21.5 ± 3.19	NS	20.1 ± 1.91	21.08 ± 1.20	NS
General health	6.4 ± 0.31	6.1 ± 0.39	NS	2.92 ± 0.21	5.7 ± 0.21	S
Total score of DAS28	4.14 ± 0.93	3.98 ± 1.17	NS	2.25 ± 0.08	3.78 ± 0.23	S
NS: Non-Significant, S: Significant						

Fig. 1. A comparison of the DAS28 scores from before and after the intervention in the clinic and the laboratory.



A comparison of the Oral Contraceptive Pill (OCP) group before and after the trial revealed a substantial decrease in the severity of Disease Activity (DA), as evidenced by an examination of DA levels.

Conversely, no discernible change was observed in the control group, and no significant variations in DA severity were noted between the two groups prior to the intervention. However, post-intervention outcomes demonstrated a significant difference, with the majority of women in the OCPs group exhibiting mild DA severity and the majority of women in the control group displaying moderate DA severity.

DISCUSSION

The primary objective of this study was to investigate the impact of Oral Contraceptive Pills (OCPs) comprising both estrogen and progesterone on rheumatoid arthritis disease activity. The findings revealed that OCPs have the capacity to enhance and reduce the severity of Rheumatoid Arthritis (RA) activity in women of reproductive age who are also affected by RA, as indicated by the 28-joint DAS. This finding may be attributed to the hypothesis that sex hormones may contribute to rheumatoid arthritis (RA) activity due to their role in the immune system response, as estrogens can stimulate humoral system responses and androgens and progesterone can decrease the immune system [7,8].

Because of the different reactions people show to hormonal treatments, the association between Oral Contraceptives (OCPs) and Rheumatoid Arthritis (RA) is still unresolved and under debate [9]. While various research has studied the potential role of OCPs in the development of RA, definitive evidence about their ability to prevent or delay the beginning of the illness is missing. Recent study has not demonstrated a substantial link between Hormone Replacement Treatment (HRT) and RA [10,11]. OCP consumption might provide some preventive advantages against RA. Furthermore, androgen and steroid alternatives could influence the inflammatory status of joint tissues, underlining the crucial function of sex hormone balance in regulating immunological and inflammatory responses. Another study revealed that continued use of OCPs—exceeding five years—might lessen the incidence of mild RA in women, however it does not appear to appreciably influence the long-term prognosis of the disease [12-14].

It is generally accepted that RA tends to improve during pregnancy; consequently, oestrogen medication or the use of Oral Contraceptive Pills (OCPs) may be considered for young women with RA, as they may benefit from their non-contraceptive effects [15,16]. The hypothesis that oestrogen-mediated protective effects on the immune system may be responsible for the observed improvement in RA during pregnancy is one that merits further investigation. Furthermore, steroid and androgen hormones may be pivotal therapeutic modulators for rheumatoid arthritis [17]. The potential of OCPs to ameliorate RA even in the absence of symptoms has been suggested by Camacho et al., who hypothesize that their utilization prior to or concurrently with the onset of symptoms may yield enduring benefits [18].

CONCLUSION

Oral contraceptive medications have been demonstrated to be effective contraceptive approaches, and can also improve Rheumatoid Arthritis (RA) activity in affected women. The study results corroborate earlier findings on the favorable effects of OCPs on RA severity and activity.

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