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Comparison of Ovarian Hyperstimulation Risk and Stimulation Duration Between Natural and OCP-Pretreated IVF Cycles: A Randomized Clinical Trial

Atemie Gordon[1*], Augustine Osayande[2], John Ekweani[2], Okafor C. Nwachukwu[2], Collins E. Iyelobu[2], Amadi-Oyioma M Chigesilem[1], Michael J. Ofem[2], Porbeni-Fumudoh B. Offiong[1], Amiete E. Fetepigi[2]

[1]Department of Obstetrics and Gynaecology, Federal Medical Centre, Yenagoa, Bayelsa State, Nigeria.

[2]Department of Obstetrics and Gynaecology, Federal Medical Centre, Jabi, Abuja, Nigeria.

ABSTRACT

Background: Controlled ovarian stimulation (COS) is integral to in-vitro fertilization (IVF) but carries a risk of ovarian hyperstimulation syndrome (OHSS). Oral contraceptive pill (OCP) pretreatment is commonly used for cycle programming; however, its influence on OHSS risk and stimulation duration remains controversial, particularly in low- and middle-income settings.

Objective: To compare the incidence of severe to critical OHSS and the duration of ovarian stimulation between natural cycle initiation and OCP-pretreated IVF cycles.

Methods: This single-centre, open-label randomized clinical trial included 86 women undergoing IVF at a Nigerian tertiary centre. Participants were randomized in a 1:1 ratio to either natural cycle initiation (n = 43) or OCP pretreatment prior to COS (n = 43). Both groups underwent COS using a short GnRH agonist protocol. The primary outcome was the incidence of severe to critical OHSS, while the secondary outcome was the duration of ovarian stimulation. Data were analyzed using an intention-to-treat approach, with a significance level set at $p < 0.05$.

Results: The mean age was comparable between the OCP and natural cycle groups (33.05 ± 3.65 vs. 33.05 ± 3.96 years). Severe to critical OHSS occurred in one participant (2.3%) in the OCP group and none in the natural cycle group, with no statistically significant difference ($p = 0.314$). The duration of ovarian stimulation was significantly shorter in the OCP-pretreated group compared with the natural cycle group (11.09 ± 2.86 vs. 11.51 ± 1.62 days; $p = 0.016$).

Conclusion: OCP pretreatment did not increase the risk of severe OHSS and was associated with a shorter duration of ovarian stimulation compared with natural cycle initiation. These findings support the safe and efficient use of OCPs for IVF cycle scheduling, although larger multicentre trials are required to confirm these results.

ARTICLE DETAILS

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KEYWORDS: In-vitro fertilization; ovarian hyperstimulation syndrome; oral contraceptive pills; controlled ovarian stimulation.

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INTRODUCTION

In vitro fertilization (IVF) has become an established and effective treatment for infertility, with controlled ovarian stimulation (COS) forming a central component of most treatment protocols. The primary aim of COS is to promote the development of multiple follicles, thereby increasing the number of oocytes available for fertilization and enhancing the chances of successful pregnancy. Despite its benefits, COS is associated with ovarian hyperstimulation syndrome (OHSS), a potentially serious iatrogenic complication that remains one of the most significant safety concerns in assisted reproductive technology.

Ovarian hyperstimulation syndrome encompasses a spectrum of clinical severity, ranging from mild, self-limiting symptoms to severe and critical forms characterized by massive ovarian enlargement, ascites, thromboembolic events, respiratory compromise, and, rarely, mortality. Although advances in stimulation protocols and monitoring

have reduced its incidence, severe to critical OHSS continues to contribute to treatment-related morbidity, unplanned hospital admissions, and increased healthcare costs. Identifying stimulation strategies that minimize OHSS risk without compromising treatment efficiency is therefore a key objective in contemporary IVF practice.

Cycle programming with combined oral contraceptive pills (OCPs) prior to COS is widely used to facilitate scheduling, synchronize follicular recruitment, and prevent functional ovarian cyst formation. However, OCP pretreatment suppresses endogenous gonadotropin secretion and may alter early follicular dynamics, potentially influencing ovarian responsiveness. This suppression has been postulated to affect both the duration of ovarian stimulation and the risk of exaggerated ovarian response, including OHSS. While some studies suggest that OCP pretreatment may prolong stimulation and increase gonadotropin requirements, others report no significant impact on stimulation characteristics or OHSS incidence, resulting in inconsistent and sometimes conflicting evidence.

The duration of ovarian stimulation is an important clinical parameter that reflects ovarian response and has practical implications for patient burden, treatment cost, and cumulative gonadotropin exposure. Prolonged stimulation may increase physical, emotional, and financial stress, whereas shortened stimulation may signal hyper-responsiveness and heightened OHSS risk. Understanding how different cycle initiation strategies influence stimulation length and safety outcomes is therefore essential for optimizing individualized IVF care.

Evidence comparing ovarian hyperstimulation risk and stimulation duration between natural cycle and OCP-pretreated IVF cycles remains limited, particularly in low- and middle-income countries where population characteristics, resource availability, and monitoring practices may differ from those in high-income settings. This randomized clinical trial was designed to compare the incidence of severe to critical ovarian hyperstimulation syndrome and the duration of ovarian stimulation between women undergoing IVF cycles initiated in a natural menstrual cycle and those pretreated with combined oral contraceptive pills, with the aim of providing evidence-based guidance for safer and more efficient IVF practice.

In vitro fertilization (IVF) is an established and effective treatment for infertility, with controlled ovarian stimulation (COS) constituting a core component of most treatment protocols. The principal objective of COS is to induce the development of multiple follicles in order to increase the number of oocytes available for fertilization and thereby improve the probability of achieving pregnancy[1]. Despite its benefits, COS is associated with ovarian hyperstimulation syndrome (OHSS), a potentially serious iatrogenic complication that remains a major safety concern in assisted reproductive technology[2].

Ovarian hyperstimulation syndrome represents a spectrum of clinical severity, ranging from mild, self-limiting symptoms to severe and critical forms characterized by marked ovarian enlargement, ascites, hemoconcentration, thromboembolic events, respiratory compromise, and, in rare cases, death[3]. Although refinements in stimulation protocols, improved monitoring, and the use of preventive strategies have reduced its incidence, severe to critical OHSS continues to contribute significantly to treatment-related morbidity, unplanned hospital admissions, and increased healthcare costs[4]. Consequently, minimizing OHSS risk while maintaining treatment efficiency remains a key goal in modern IVF practice[5].

Cycle programming using combined oral contraceptive pills (OCPs) prior to COS is widely practiced to improve scheduling flexibility, synchronize follicular development, and reduce the occurrence of functional ovarian cysts[6]. However, OCP pretreatment suppresses endogenous gonadotropin secretion and alters early follicular dynamics, which may influence ovarian responsiveness during subsequent stimulation[7]. This suppression has raised concerns that OCP pretreatment could affect both the duration of ovarian stimulation and the risk of an exaggerated ovarian response, including OHSS[8]. While some studies have reported longer stimulation periods and higher gonadotropin requirements following OCP pretreatment[9], others have found no clinically significant impact on stimulation characteristics or OHSS risk[10], resulting in conflicting evidence.

The duration of ovarian stimulation is an important clinical parameter, as prolonged stimulation may increase patient burden, treatment cost, and cumulative gonadotropin exposure, whereas excessively short stimulation may indicate hyper-responsiveness and heightened OHSS risk[11]. Understanding how different cycle initiation strategies influence stimulation length is therefore essential for optimizing both the safety and efficiency of IVF cycles.

Comparative data on ovarian hyperstimulation risk and stimulation duration between natural cycle and OCP-pretreated IVF cycles remain limited, particularly in low- and middle-income countries, where patient characteristics, resource availability, and monitoring practices may differ from those in high-income settings[12]. This randomized clinical trial was therefore designed to compare the incidence of severe to critical ovarian hyperstimulation syndrome and the duration of ovarian stimulation between women undergoing IVF cycles initiated in a natural menstrual cycle and those pretreated with combined oral contraceptive pills, with the aim of providing context-specific evidence to guide safer and more efficient IVF practice.

MATERIALS AND METHODS

This study was conducted as a single-centre, open-label, randomized controlled trial designed to compare outcomes

between two treatment arms. Eligible participants were randomly allocated in a 1:1 ratio into two equal groups using a simple randomization method. The study population consisted of women diagnosed with either primary or secondary infertility who attended the In-Vitro Fertilization (IVF) clinic of the Federal Medical Centre, Abuja, a tertiary referral facility providing assisted reproductive services.

The study was carried out in accordance with the ethical principles outlined in the 2013 revision of the Declaration of Helsinki governing research involving human subjects. Ethical approval for the study protocol was obtained from the Research and Ethics Committee of the Federal Medical Centre, Abuja. Written informed consent was obtained from all participants prior to enrollment, and confidentiality of patient information was strictly maintained throughout the study period.

Women were excluded from the study if they had any contraindication to the use of combined oral contraceptive pills, including but not limited to thromboembolic disorders, hormone-dependent malignancies, or severe liver disease. Additional exclusion criteria included women aged 21–38 years with evidence of premature ovarian decline or ovarian failure, as indicated by clinical history or ovarian reserve testing, as well as those who declined or withdrew consent to participate in the study.

INTERVENTIONS

Eligible participants were randomized in a 1:1 ratio into two study arms using a sealed opaque envelope method. Each envelope contained a unique identification number linked to a pre-generated randomization sequence, allocating participants to either Group A (control) or Group B (intervention).

Group A – Natural Cycle (Control)

Participants in Group A underwent controlled ovarian stimulation (COS) using their natural menstrual cycle without prior hormonal pre-treatment. COS was initiated according to the short GnRH agonist protocol, irrespective of the cycle day. Buserelin acetate (Suprefact® 1 mg/mL; Sanofi, France) was administered subcutaneously at 0.5 mL daily from cycle day 2. Recombinant or urinary FSH (Humog®, Bharat Pharmaceuticals, India) was initiated on cycle day 2 or 3, with doses individualized based on age, body mass index (BMI), antral follicle count, and baseline serum FSH. FSH doses were adjusted according to BMI and ovarian response, including a 75 IU reduction for women with polycystic ovarian morphology and incremental increases of 75 IU per 5 kg/m² above standard dosing.

Group B – OCP-Programmed Cycle (Intervention)

Participants in Group B received combined oral contraceptive pills (OCPs) for menstrual cycle programming prior to COS. Microgynon® (150 µg levonorgestrel + 30 µg ethinyl estradiol; 28 tablets per pack, 21 active and 7 placebo) was administered orally, one active tablet daily at a fixed time, for at least two weeks. The OCP regimen commenced between day 10 and day 30 of the pre-IVF treatment month, ensuring that the last active dose coincided with the day before initiation of COS. Withdrawal bleeding was expected within the first week of the subsequent month. COS then commenced using the same short GnRH agonist protocol as Group A.

Ovarian Stimulation and Monitoring (Both Groups)

All participants underwent COS using a short GnRH agonist protocol. Buserelin acetate was administered at 0.5 mL subcutaneously daily from cycle day 2. FSH stimulation was initiated on cycle day 2 or 3 at individualized doses (Humog®), adjusted for BMI, age, and ovarian reserve. Subcutaneous injections were administered peri-umbilically. Dose modifications were made based on follicular response assessed by serial transvaginal ultrasound scans and serum hormone measurements. Monitoring occurred every 48 hours starting day 7 of stimulation until the leading follicular cohort reached 18–21 mm and endometrial thickness measured 8–15 mm.

Ovulation Trigger and Oocyte Retrieval

COS was terminated when criteria for follicular maturation were met. Ovulation was triggered with human chorionic gonadotropin (HCG) (Hucog®, 5,000 IU IM; Bharat Pharmaceuticals, India) administered 35–36 hours prior to oocyte retrieval. Oocyte retrieval was performed under transvaginal ultrasound guidance with conscious sedation (IV pethidine 100 mg and midazolam 5 mg). Follicular fluid was aspirated and immediately transferred to a pre-warmed incubator at 37 °C for identification and counting by the clinical embryologist.

Fertilization, Embryo Culture, and Transfer

Oocytes underwent conventional insemination or intracytoplasmic sperm injection (ICSI) depending on semen parameters. Embryos were cultured using a closed, one-step media system in a standard CO_2 incubator (6% CO_2, ambient O_2). Fertilization was assessed 16–18 hours post-insemination, and cleavage-stage embryos were graded on day 2 based on cell number, symmetry, and fragmentation (Grades 1–4). Blastocyst assessment was performed on day 5.

Embryo transfer was performed under transabdominal ultrasound guidance using a Wallace® catheter, transferring up to three top-quality embryos 0.5–1 cm below the fundus. Participants received luteal phase support consisting of vaginal progesterone (Cyclogest® 400 mg twice daily), intramuscular progesterone (Gestone® 100 mg every 48 hours), oral estradiol valerate (Progynova® 4 mg three times daily), oral acetylsalicylic acid (Vasoprim® 75 mg daily), and oral prednisolone (Perilon® 5 mg twice daily).

Pregnancy Assessment and Follow-Up

Biochemical pregnancy was assessed 14 days post-transfer using serum β-HCG. Positive pregnancies were confirmed via transvaginal ultrasound for intrauterine fetal viability. Follow-up continued for six weeks post-confirmation, after which participants were referred to routine antenatal care. Participants with negative tests were counselled on subsequent treatment options, including repeat IVF cycles, alternative protocols, or donor gametes

PRIMARY OUTCOME MEASURES

The primary outcome was the incidence of severe to critical ovarian hyperstimulation syndrome (OHSS), defined according to standard clinical criteria, and compared between women undergoing IVF cycles initiated in a natural menstrual cycle versus those pretreated with combined oral contraceptive pills (OCPs).

SECONDARY OUTCOME MEASURES

The secondary outcome measure was the duration of ovarian stimulation, defined as the number of days from the start of gonadotropin administration to the day of ovulation trigger, and compared between the two groups

SAMPLE SIZE DETERMINATION

The sample size for this study was determined using a standard formula for comparative studies designed to detect a clinically meaningful difference between two independent groups. The calculation was based on the expected difference in mean outcomes between the groups, the estimated population variability, a two-sided significance level of 5% ($\alpha = 0.05$), and a study power of 80% to detect the specified difference. To account for potential loss to follow-up and incomplete data, an attrition rate of 20% was included. Based on these assumptions, a total sample size of 86 participants was required, with 43 participants allocated to each study group.

RECRUITMENT

Participants were sequentially enrolled from the eligible study population based on their appearance at the IVF clinic and willingness to participate. All women diagnosed with infertility and scheduled for ovarian stimulation for IVF were approached either by the principal investigator or a trained research assistant. Eligibility and exclusion criteria were confirmed through review of medical records and direct patient interview. Women with contraindications to oral contraceptive use, evidence of premature ovarian decline or failure, or who declined participation were excluded. Informed consent was obtained after the study objectives, procedures, potential benefits, and risks were explained in clear and simple language. Participants were assured of the confidentiality and safety of the procedures. Only women who demonstrated understanding of the study and expressed voluntary willingness were asked to provide written informed consent before enrollment.

RANDOMIZATION AND ALLOCATION CONCEALMENT MECHANISM

Allocation Sequence Generation

Randomization was conducted using WINPEPI software, generating a balanced allocation sequence assigning numbers 1 to 86 to either Group A (control) or Group B (intervention). Group A participants did not receive combined oral contraceptive pills (OCPs) prior to ovarian stimulation, whereas Group B participants received OCPs for cycle programming before commencing stimulation.

Allocation Concealment

To ensure allocation concealment, small opaque envelopes containing the sequentially numbered allocations (1–86) were prepared. Each envelope was stapled and placed in a secure plastic basket, preventing prior knowledge of group assignment.

Implementation

Eligible participants selected one envelope at random. The number inside the envelope was traced on the randomization chart to determine whether the participant was assigned to Group A or B. The randomization process was conducted by the principal investigator or trained research assistant who was not involved in subsequent oocyte retrieval or embryology procedures, maintaining separation of allocation from outcome assessment.

Data Collection

A purpose-designed proforma was used to collect participants' socio-demographic characteristics, reproductive and gynecologic history, BMI, and other relevant clinical information. All data were collected by trained research assistants and cross-checked for completeness and accuracy.

Data Management

Data from the paper proformas were entered into IBM SPSS Version 23. Double-entry verification was performed to minimize transcription errors, and all datasets were stored on a password-protected computer accessible only to the research team.

Data Monitoring

Trial monitoring was conducted in accordance with the standard operating procedures of the study center, ensuring adherence to the protocol, accurate data collection, and participant safety. Compliance with study procedures was verified at regular intervals by the principal investigator.

DATA ANALYSIS

An intention-to-treat (ITT) approach was employed for all analyses. Descriptive statistics were used to summarize participant characteristics: means and standard deviations for continuous variables and proportions or percentages for categorical variables. Comparisons between groups were conducted using the student's t-test for continuous variables and Pearson's chi-square test for categorical variables. Data were presented in tables and figures where appropriate. A

two-sided p-value < 0.05 was considered statistically significant.

RESULTS

A total of 86 participants were randomized equally into the OCP (n = 43) and natural cycle (n = 43) groups. The mean age was 32.10 ± 3.96 years in the natural cycle group and 33.05 ± 3.65 years in the OCP group, with a statistically significant difference (p = 0.001). Significant differences were also observed in occupation and marital status distributions (p < 0.05), while no significant differences were found in ethnicity (p = 0.418) or religion (p = 0.211). Most participants were married and identified as Christians.

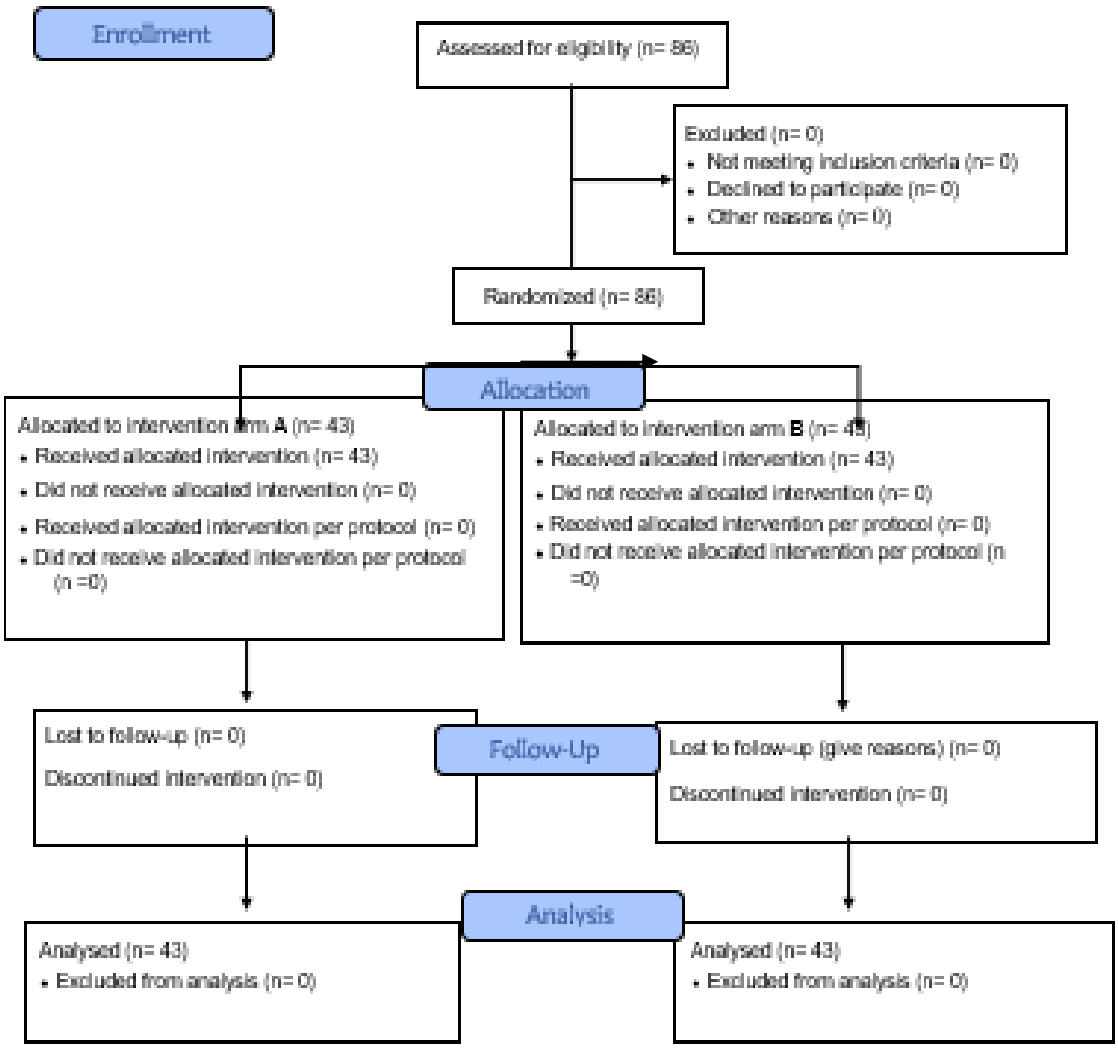

Figure 1: Study Flow Diagram

Table 1: Socio-demographic characteristics of study population

Parameters	**OCP Group (n=43)**	**Natural cycle Group (n=43)**	***Chi square value***
	Mean ±*SD*/n (%)	Mean ±*SD*/n (%)	
Mean age (year)	±SD 33.05±3.65	33.05±3.96	
Age groupig (years)			

1- 25	1(50%)	1(50%)	
26 -30	**10(41.7%)**	**14(58.3%)**	
31 -35	**20(64.5%)**	**11(35.5%)**	**0.247**
36 -40	**12(41.4%)**	**17(58.6%)**	
Ethnicity			
Hausa	**5(31.3%)**	**11(68.8%)**	
Yoruba	**9(52.9%)**	**8(47.1%)**	**0.418**
Igbo	**16(53.3%)**	**14(46.7%)**	
Others	**13(56.5%)**	**10(43.5%)**	
Occupation			
Employed	**31(64.6%)**	**17(35.4%)**	**0.006**
Unemployed	**9(35.3%)**	**23(64.7%)**	
Student	**3(50.0%)**	**3(50.0%)**	
Marital Status			
Married	**38(63.3%)**	**22(36.7%)**	
Single	**2(10.5%)**	**17(89.5%)**	**0.001**
Divorced	**3(42.9%)**	**4(57.1%)**	
Widow	**0(0%)**	**0(0%)**	
Religion			
Christianity	**35(55.6%)**	**28(44.4%)**	
Islam	**7(33.3%)**	**14(66.7%)**	**0.211**
Others	**1(50%)**	**1(50%)**	

The OCP and natural cycle groups were similar in mean age (33.05 ± 3.65 vs. 33.05 ± 3.96 years), ethnicity, and religion ($p > 0.05$). Significant differences were observed in occupation and marital status, with more employed and married participants in the OCP group ($p = 0.006$ and $p = 0.001$, respectively). Age group distribution did not differ significantly between groups ($p = 0.247$).

Table 2 Comparison between incidences of severe to critical (OHSS) between the two groups.

Parameter	**Took OCPs (n=43)**	**Natural cycle (n=43)**	***value***	***Chi square***
Incidence of severe to critical OHSS				
Yes	1(2.3%)	0(0%)	1.012	0.314
No	42(97.7%)	43(100%)		

There was no statistically significant difference in severe to critical OHSS between the two groups (participant that underwent OCPs and natural cycle).

Table 3 Comparing duration for simulation between the two groups

Parameters	***Mean ±SD/n (%)***	***T***	***Sig***
Took OCP (n=46)	11.09 ±2.86	-0.835	
Natural cycle (n=46)	11.51 ±1.62		0.016

There was statistically significant difference in duration for stimulation between OCPs participants (M=11.09, SD=2.86) and participants with natural cycle (M=11.51, SD =1.62); $t(84)$= -0.835, p=0.016. So those participants who had OCPs had shorter duration of ovarian stimulation.

DISCUSSION

This study examined the effect of combined oral contraceptive pill (OCP) pretreatment on the occurrence of severe ovarian hyperstimulation syndrome (OHSS) and on the length of ovarian stimulation in women undergoing in vitro fertilization (IVF). In terms of safety outcomes, there

was no statistically significant difference in the incidence of severe OHSS between women who received OCP pretreatment and those who commenced stimulation in a natural cycle, as shown by chi-square analysis ($p = 0.314$). OHSS occurred in only 2.3% of participants in the OCP group, indicating a generally low frequency of this complication in the study population. These findings suggest that, within contemporary IVF stimulation protocols and with appropriate clinical monitoring, OCP pretreatment does not substantially increase the risk of severe OHSS.

The low rate of OHSS observed aligns with current developments in assisted reproductive technology, where improved patient risk assessment, individualized gonadotropin dosing, and the use of safer ovulation trigger methods have contributed to a decline in OHSS incidence. Engmann et al [13] reported that the use of a gonadotropin-releasing hormone (GnRH) agonist trigger in patients at high risk of OHSS was highly effective in preventing the condition without compromising implantation or pregnancy outcomes. Although the ovulation trigger strategy was not the primary focus of the present study, this evidence emphasizes the importance of tailored stimulation protocols and adjunctive measures in reducing OHSS risk, irrespective of whether OCPs are used for cycle programming.

Similarly, Brauer et al [14] demonstrated that a dual suppression approach incorporating OCP pretreatment with a GnRH antagonist protocol in women with polycystic ovary syndrome (PCOS) was associated with a higher oocyte yield, shorter stimulation duration, reduced need for coasting, and a lower incidence of OHSS. These findings highlight the potential advantages of OCP pretreatment in selected patient groups, particularly when combined with antagonist protocols that enhance safety and flexibility. The absence of a significant increase in severe OHSS in the current study further supports the notion that OCP pretreatment does not inherently predispose patients to an exaggerated ovarian response when modern stimulation strategies are applied.

In contrast, assessment of stimulation parameters revealed a statistically significant difference in the duration of ovarian stimulation between the two groups. Women who received OCP pretreatment required fewer days of stimulation than those who initiated treatment in a natural cycle ($p = 0.016$). This observation suggests that OCP pretreatment may promote more uniform follicular recruitment, leading to more efficient follicular development and earlier fulfillment of criteria for ovulation triggering. Clinically, a shorter stimulation period may reduce patient discomfort, decrease cumulative exposure to gonadotropins, and lower overall treatment costs.

The finding of reduced stimulation duration in the OCP group is supported by Kim et al [15], who showed that a GnRH antagonist multiple-dose protocol with OCP pretreatment was at least as effective as a GnRH agonist low-dose long protocol in low responders, while requiring fewer days of stimulation and lower total gonadotropin doses to achieve adequate follicular maturation. This suggests that OCP pretreatment may improve stimulation efficiency in certain subgroups of patients.

Nevertheless, published evidence on this topic remains inconsistent. In contrast to the present findings, Griesinger et al [8], in a systematic review and meta-analysis of GnRH antagonist IVF cycles, reported that OCP pretreatment was associated with a longer duration of gonadotropin stimulation and increased gonadotropin consumption. Such divergent results may reflect differences in study design, patient characteristics, ovarian reserve profiles, duration and formulation of OCP pretreatment, and stimulation regimens. The heterogeneity inherent in meta-analyses may also limit the ability to detect effects that are more apparent in single-centre randomized trials.

Overall, the findings of this study indicates that OCP pretreatment does not significantly increase the risk of severe OHSS and may be associated with a shorter duration of ovarian stimulation compared with initiation in a natural cycle. These findings support the continued use of OCPs for IVF cycle programming, particularly where scheduling efficiency and treatment optimization are priorities. However, given the variability in existing evidence, further large, well-designed multicentre randomized trials are needed to more clearly define the influence of OCP pretreatment on stimulation characteristics and OHSS risk across diverse patient populations and clinical settings.

STRENGTHS AND LIMITATIONS

This randomized clinical trial is strengthened by its robust study design, clearly defined outcomes, and standardized stimulation protocols, which enhance the validity and reliability of the findings in a real-world, resource-limited IVF setting. However, its single-centre nature, modest sample size, baseline group differences, lack of blinding, and omission of long-term outcomes such as live birth rates may limit generalizability and warrant further investigation in larger multicentre studies.

CONCLUSION

Oral contraceptive pills pretreatment did not increase the risk of severe OHSS compared with natural cycle initiation and was associated with a shorter duration of ovarian stimulation. These findings support the safe and efficient use of OCPs for IVF cycle scheduling, although larger multicentre studies are needed to confirm their effects across diverse populations.

RECOMMENDATIONS

The results of this study support the use of combined oral contraceptive pill (OCP) pretreatment as a safe option for IVF cycle scheduling, as it was not associated with an increased risk of severe ovarian hyperstimulation syndrome when employed within modern stimulation protocols and under

careful clinical supervision. OCP pretreatment may therefore be considered in routine practice to facilitate cycle planning and potentially improve stimulation efficiency.

Clinical decision-making should remain individualized, taking into account patient-specific factors such as ovarian reserve, baseline risk of OHSS, and the most appropriate stimulation and ovulation trigger strategies. Continued emphasis on personalized gonadotropin dosing and the use of risk-reducing adjuncts is recommended to optimize safety.

Further large-scale, multicentre randomized studies are recommended to better define the impact of OCP pretreatment on stimulation characteristics, medication requirements, and long-term reproductive outcomes, including live birth rates, across different patient subgroups and clinical settings.

AUTHOR CONTRIBUTIONS

Idea/Concept: Atemie Gordon, Augustine Osayande, John Ekweani, Okafor C. Nwachukwu; Design: Atemie Gordon, Augustine Osayande, John Ekweani, Okafor C. Nwachukwu, Collins E. Iyelobu, Michael J. Ofem; Control/Supervision: Augustine Osayande, John Ekweani, Collins E. Iyelobu, Michael J. Ofem, Amiete E. Fetepigi, Okafor C. Nwachukwu; Data Collection and/or Processing: Austin Osayande, Collins E. Iyelobu, Michael J. Ofem, Amiete E. Fetepigi; Analysis and/or Interpretation: Atemie Gordon, Porbeni-Fumudoh B. Offiong, Amadi-Oyioma M Chigesilem; Literature Review: Atemie Gordon, Augustine Osayande, Porbeni-Fumudoh B. Offiong, Amadi-Oyioma M Chigesilem; Writing the Article: Atemie Gordon, Austin Osayande, Okafor C. Nwachukwu; Critical Review: Atemie Gordon, Augustine Osayande, John Ekweani, Okafor C. Nwachukwu, Collins E. Iyelobu, Michael J. Ofem, Porbeni-Fumudoh B. Offiong, Amadi-Oyioma M Chigesilem, Amiete E. Fetepigi.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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ETHICAL APPROVAL

Ethical approval was obtained from the ethical committee of the Federal Medical Centre, Abuja.

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