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(RESEARCH ARTICLE)

Evaluation of fibrinogen level among Sudanese women who use contraceptive implant in Khartoum state

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Abstract

Background: Fibrinogen, a key protein in coagulation, plays a crucial role in hemostasis and thrombotic disorders. Contraceptive implant use is associated with increased fibrinogen levels, potentially contributing to a hypercoagulable state and elevated thrombotic risk. Objectives: This study is aimed to evaluate and compare fibrinogen levels among women using contraceptives implant and non-users.

Materials and Methods: Descriptive, Case Control study was conducted at Khartoum state between October and December 2024 with 100 participants divided equally into cases (contraceptive users) and controls (non-users). Fibrinogen levels were measured by Clauss method and analyzed using SPSS.

Results: The mean fibrinogen level was significantly higher in the case group (462 ± 31.3 mg/dL) compared to the control group (281 ± 39.2 mg/dL), with a p-value <0.001, indicating a statistically significant difference. When analyzed by age, the mean fibrinogen levels were (438.2 ± 12.2 mg/dL) for participants aged 22–30 years and (471.4 ± 10.1 mg/dL) for those aged 31–40 years, indicating that increase in age it associated with increase in fibrinogen levels this difference was statistically significant (p = 0.04). The duration of contraceptive implants use had a marked Impact on fibrinogen levels. Women who had used contraceptive implants for 1–2 years had a mean fibrinogen level of (429.8 ± 16.8 mg/dL), whereas those with a usage duration exceeding two years had a significantly higher mean fibrinogen level of (459.3 ± 17.5 mg/dL) (p = 0.03), suggesting that prolonged contraceptive implants use is associated with an increase in fibrinogen levels.

Conclusion: Contraceptive implants use, is associated with increase fibrinogen levels, also contraceptive implants use is association with increase fibrinogen levels depending on increase age and duration, indicating a higher thrombotic risk.

Keywords: Fibrinogen level; Women fibrinogen level; Contraceptive implant; Women implant; Contraceptive use

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1. Introduction

Fibrinogen, a glycoprotein synthesized by the liver, is a critical component in the blood coagulation cascade [1]. It serves as the precursor to fibrin, which forms the structural framework of blood clots. Fibrinogen levels in the blood are tightly regulated, as imbalances can lead to either hemorrhagic disorders or thrombotic complications [2]. Elevated fibrinogen levels are particularly concerning as they contribute to an increased risk of cardiovascular diseases, including stroke, myocardial infarction, and deep vein thrombosis (DVT) [3].

some types of hormonal contraception is known as a risk of venous thromboembolism (VTE) and this is an important issue when health care providers (HCPs) counsel patients about contraceptive options [4]. The risk of venous thrombosis was more pronounce and increased among injectable depot–medroxyprogesterone acetate contraceptive users, while there was no risk associated with levonorgestrel intrauterine device use. Therefore, the latter seems to be the safest option regarding the risk of venous thrombosis [5].

It is essential understand natural hormone mechanisms since these hormones are still present in circulation while hormonal contraceptives, which have been shown to indeed negatively affect fibrin clot features and lysability are used [6]. This relationship is influenced by various factors, including the type and dose of hormones, individual genetic predispositions and pre-existing health conditions [7].

Contraceptive, family planning or birth control prevents pregnancy by barrier methods that physically prevent sperm and egg from engagement, hormonal methods that prevent ovulation, and behavioral such as abstinence around the time of ovulation. It used to limit family members and space births [8].Hormonal contraceptive can include a combination of estrogen and progestin, or progestin alone. It can be administered orally, injection, intravaginally, implant, or intrauterine device. Progestin inhibit ovulation by suppressing luteinizing hormone (LH), thickening of cervical mucus hampering the transport of sperm. Oral contraceptives block ovarian stimulation by prevent release of follicular stimulation hormone from anterior pituitary gland and prevent ovulation (9).The progestin causes the cervical mucus to thicken and become viscid and scant. These actions inhibit sperm penetration into the uterus. Also progestin impairs the motility of the uterus and oviducts and therefore decrease transport of both ova and sperm to the normal site of fertilization in the distal fallopian tube. Progestin also produce changes in the endometrium that are not conducive for implantation of the embryo (10).Estrogen increase the thickness of the endometrium by increasing the number and size of the endometrial cells. It also stimulates the formation of progesterone receptors on endometrial cells and increase blood flow to the endometrium. Estrogen is change the cervix and cervical mucus and prevents the sperm from entering the uterine (11).

Contraceptive implant is a small plastic rod, that a doctor or nurse puts under the skin of women's arm. The primary action of all subdermal implants is to prevent ovulation. Secondary modes of action include prevention of sperm penetration of the cervical mucus and prevention of implantation by thinning the endometrium. Contraceptive implants are a highly cost-effective form of long-acting reversible contraception. They are the most effective reversible contraceptives and are of a similar effectiveness to sterilization. There are very few contraindications to use of implants, and they have an excellent safety profile. Both acceptability and continuation with the method are high (12).Bleeding problems are one of the more likely reasons for early discontinuation of the method (12). Other side effects of implants are similar to those observed with hormonal pills- headache, weight changes, mood swings and abdominal bloating (13).

2. Materials and Methods

This case-control study was conducted in Khartoum State to evaluate and compare fibrinogen levels among women using contraceptives implant and non-users, during the period of OctoberstoDecember2024.A total of (50) samples were collected from women on contraceptive implants and (50) samples were collected from healthy women not use contraceptive implants as control group. The study was conducted in Khartoum state, Sudan, and included healthy women who use contraceptive implants between 22 – 40 years.

Under a septic precautions 5ml venous blood was drawn by using one venipuncture and transferred into test tubes containing 3.2% trisodium citrate, after the blood added to the anticoagulants should gently mix. The sample was then centrifuged at 1000-2000 rpm for 15 minutes to separate plasma.

By using Clauss method Diagen Fibrinogen Determination Kit the excess of thrombin converted the fibrinogen to fibrin in diluted plasma. The clotting time of a dilution of plasma with a standard concentration of thrombin is inversely related

to the fibrinogen concentration. At low level of fibrinogen and high thrombin concentration, the rate of reaction is a function of fibrinogen concentration. 100 µL of plasma was diluted with 900 µL of buffer as specified in the instructions, and prepared the thrombin reagent and calibration standards, then 200 µL of the diluted plasma was pipetted into a test tube or cuvette, and followed by addition 100 µL of thrombin reagent at the specified concentration. The time was started immediately after adding thrombin and the clotting time was recorded as the fibrin clot was formed. Then the measured clotting time was compared to the standard calibration curve provided in the kit. Quality control samples with known fibrinogen levels was included to verify accuracy, and reported the results within the recommended reference range. The normal range of fibrinogen is 170-400 mg/dl.

2.1. Statistical analysis

The data was analyzed using SPSS-22 and included the descriptive measures of frequency, percentages, mean and standard deviation. Two tailed t-test was applied for testing the significance of difference of two independent sample means of the quantitative data. P value < 0.05 was considered significant.

3. Results

This Case control study was conducted in Khartoum state to evaluate fibrinogen level among women who use contraceptive implant.

The study population was equally distributed between cases (women using contraceptives) and controls (non-users), with each group comprising 50% participants, representing 50% of the total sample (Figure.1). Within the case group, 56.0% were aged between 22–30 years, while 44.0% were aged between 31–40 years (Figure.2). The majority of contraceptive users 72.0% had used them for 1–2 years, while 28.0% had used them for more than two years (Figure.3). Additionally, 68.0% of the case group reported 1–3 pregnancies, whereas 32.0% had more than three pregnancies before using the contraceptive implant (Figure .4).

The mean fibrinogen level was significantly higher in the case group (462 ± 31.3 mg/dL) compared to the control group (281 ± 39.2 mg/dL), with a (p-value < 0.001), indicating a statistically significant difference (Table .1).

When analyzed by age, the results showed increase in fibrinogen level according to increase in age. the mean fibrinogen levels were (438.2 ± 12.2 mg/dL) for participants aged 22–30 years and (471.4 ± 10.1 mg/dL) for those aged 31– 40 years, and these indicating statistically significant difference between the age and fibrinogen level (p-value = 0.04) (Table .2).

The duration of contraceptive implant use had marked Impact on fibrinogen level. Women who had used contraceptive implants for 1–2 years had a mean fibrinogen level of (429.8 ± 16.8 mg/dL), whereas those with a usage duration exceeding two years had a significantly higher mean fibrinogen level of (459.3 ± 17.5 mg/dL) (p-value = 0.03), suggesting that prolonged contraceptive use is associated with an increase in fibrinogen level (Table .3).

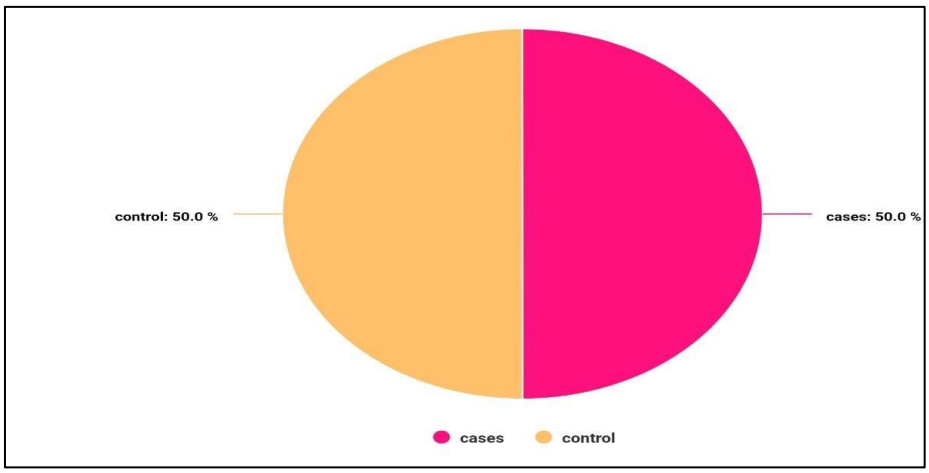

Figure 1 Distribution of Study group

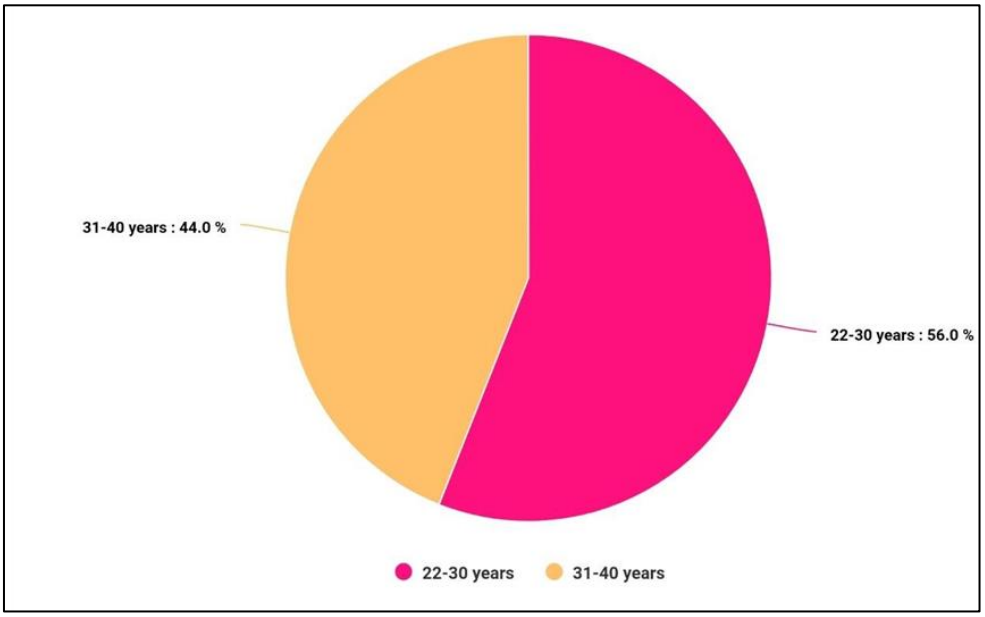

Figure 2 Distribution of the case group according to the age

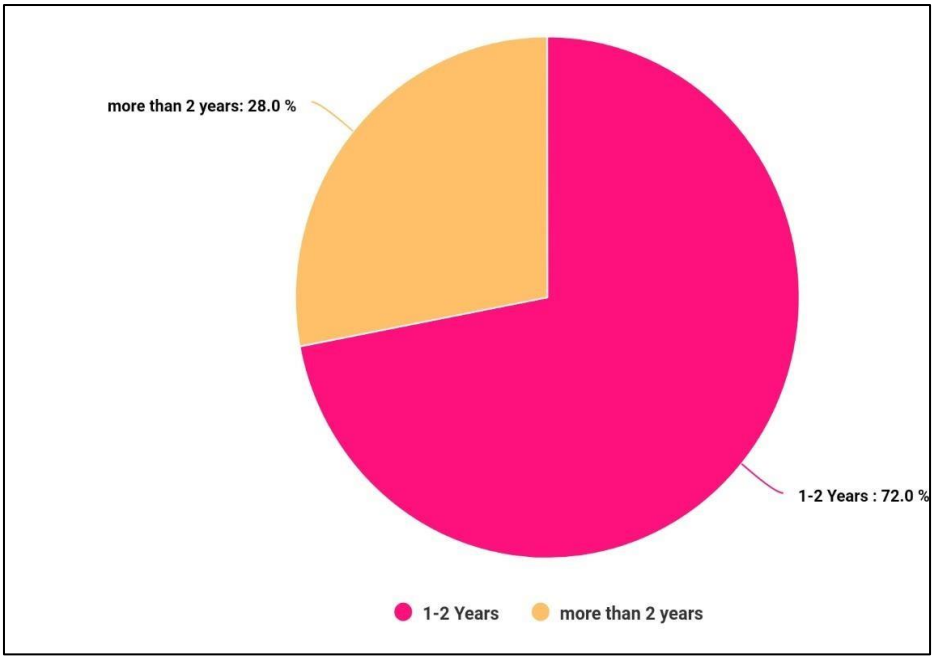

Figure 3 Distribution of the case group according to duration of use

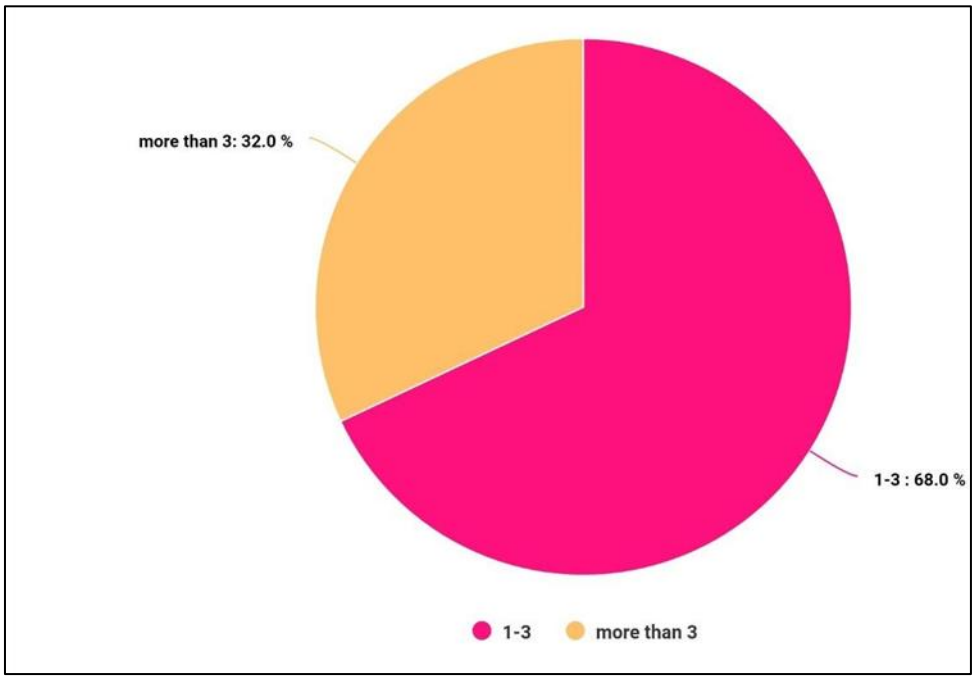

Figure 4 Distribution of the case group according to number of pregnancies

Table 1 Mean of fibrinogen level among the study population

Fibrinogen(mg/dl)	Mean	Std diviation	P.vlue
Case group	462	31.3	< 0.001
Control group	281	39.2	

Table 2 Mean of fibrinogen level according to age

Age	Fibrinogen mg/dl
Years 22–30	438.2 ± 12.2
Years 31–40	471.4 ± 10.1
P-value	0.04

Table 3 Mean of fibrinogen level according to duration of contraceptive use

Duration of use	Fibrinogen mg/dl
1-2 year	429.8 ± 16.8
More than 2years	459.3 ± 17.5
P-value	0.03

4. Discussion

The results of the current study align with findings from previous research, highlighting the significant impact of contraceptive implant use on fibrinogen levels and the associated thrombotic risks.

A study conducted in Nigeria by Abubakar *et al*, in November 2018, to assess the serum fibrinogen and D-dimer levels in hormonal contraceptives users. They found that the significant increase in the procoagulant protein-fibrinogen (536±62.5mg/dl), and increase in fibrinolytic activity as demonstrated by elevated D-dimer level reflect a balance between fibrin formation and degradation hence minimizing the venous thromboembolism (VTE) risk [14], and these findings were in agreement with our findings.

A study conducted in Brazil by Brito *et al*, in September 2012, to investigate the etonogestrel (ENG)-releasing contraceptive implant inserted immediately postpartum on maternal hemostasis markers during the first six weeks of delivery. They found that a reductions in factors II, VII, X, and fibrinogen were greater in the control than in the implant group [15], and these findings were similar with our findings.

In a study conducted in North Carolina by Dorflinger *et al*, in February 2002, to investigate the metabolic effects currently available contraceptive implant products that release the progestin levonorgestrel, etonogestrel, nomegestrol acetate and nestorone. Data on liver, kidney and renal function, carbohydrates and insulin release, hemostasis, blood pressure and lipids are considerate. They found that a slight increase in median fibrinogen levels of contraceptive implant [16], and these findings were similar with our findings.

A study conducted Singapore by Viegas *et al*, in October 1996, to investigate the change in hemostasis parameters among prolong use of reformulated and the original 2-rod Norplant implant, and they reported that the fibrinogen levels were significantly elevated by 36 months of both implant use [17], and these findings were similar with our findings.

A study conducted in Japan by Koh *et al*, in May 2010, to evaluate the long-term effects of the new reformulated 2-rod Norplant implant on haemostasis in prospective group of subjects who have completed 5 years of use, and they reported that the fibrinogen and factor Ⅶ levels increased at 36 months and 42 months of use [18], and these findings were similar with our findings.

5. Conclusion

The current study demonstrated a significant elevation in fibrinogen levels among women using contraceptives implant compared to non-contraceptive users. Additionally, fibrinogen levels were significantly higher among age and long-term contraceptives implant users than short-term users.

Compliance with ethical standards

Acknowledgement

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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