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ORIGINAL ARTICLE

TO STUDY THE ACCEPTABILITY AND EFFICACY OF COMBINED CONTRACEPTIVE VAGINAL RING AMIDST INDIAN WOMEN

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ABSTRACT: OBJECTIVES: To study the efficacy, and acceptability and reasons for discontinuity of CCVRs in Indian women along with cycle control, safety aspects, local and systemic adverse effects, chances of spontaneous expulsion and partner compliance. **METHODS:** This interventional longitudinal study included 45 married women aged between 18-45 years seeking reversible means of contraception but with no history of usage of any form of hormonal contraceptives in the previous 6 months. The outcome variables were measured in terms of contraceptive efficacy, cycle regularity, systemic effects on blood pressure, liver function, body weight, lipid parameters and blood sugar along with local effect on cervix and vagina. Patient compliance, acceptability and spouse compliance was also measured by questionnaires**. RESULTS:** In this study there were no unwanted pregnancies in women amongst 117 exposed cycles. The incidence of intended bleeding pattern was 95%, the effect of CCVR on liver function, blood pressure, etc. was not clinically relevant. It was not associated with an increased risk of cervical or vaginal abnormalities, 96% women were satisfied with the ring usage and 97% would recommend it to others, 70% of women and 82% of their partners never/ rarely felt the ring during intercourse. **CONCLUSION:** From the present study, it can be concluded that CCVR is an effective contraceptive with good cycle control, minimal systemic or local adverse effects along with low incidence of spontaneous expulsion and higher level of user and partner acceptability.

KEYWORDS: COCs (Combined oral Contraceptives), CCVR (Combined contraceptive vaginal ring).

INTRODUCTION: Voluntary control of infertility is one of the most important issues in modern society in order to meet the social and individual needs. The term 'contraceptive' includes all temporary and permanent methods designed to prevent pregnancy due to coital act. Since the introduction of hormonal contraceptive methods in early 1960s, combined oral contraceptives (COCs) have become the method of choice for many women worldwide.

Ongoing research has concentrated on lowering the doses of oestrogen and progestogen and developing progestogens that are more selective i.e., with higher progestogenic activity and little affinity for androgen receptors.[1-5] But these oral contraceptives have some unavoidable disadvantages like first-pass metabolism, large fluctuations in serum hormone levels and poor compliance in some users[6-8] for which non–oral hormonal methods have been tried with their own drawbacks.[9,10]

One of the advances in the contraceptive field has been the development of combined contraceptive vaginal rings (CCVRs).[11-13] The acceptability of a new method of contraception is an important consideration as it may affect overall uptake and compliance. The anatomy, histology and physiology of vagina make it an ideal route for administering contraceptive hormones.[14] The large surface area of non-keratinized squamous epithelium, it's rich blood supply and insensitivity of its

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upper part makes it ideally suited for the uptake of drugs. With vaginal route, there is no first–pass metabolism, steady serum levels, thus the same contraceptive effect is obtained with lower doses of hormones. Again, compliance is improved with once monthly dosing.[15]

CCVR (Nuvaring) is a flexible, transparent ring made from ethylene-vinyl acetate (EVA), with an outer ring diameter of 54mm and a cross-sectional diameter of 4mm. Each CCVR contains 2.7mg ethinyl estradiol (EE) and 11.7mg etonogestrol (ENG) uniformly dispersed within the EVA core. A surrounding EVA membrane controls hormone release from the ring. CCVR releases 15microgram EE and 120microgram ENG per day. Each CCVR is intended for 1 cycle of use (3weeks of ring use followed by 1 week ring-free period). It can be easily inserted and removed by the woman herself. Like COCs, contraceptive effects of CCVR are a result of ovulation inhibition and the increased viscosity of the cervical mucus. Moreover after removal of the ring there is a rapid return to normal cycle, the median time to ovulation after ring removal is 19 days.[16] Based on pharmacokinetic data, the co-administration of vaginal spermicides or antimycotics are unlikely to affect the contraceptive efficacy and safety of CCVR.[17]

The study is targeted towards the study of efficacy, and acceptability and reasons for discontinuity of CCVRs in Indian women along with cycle control, safety aspects, local and systemic adverse effects, chances of spontaneous expulsion and partner compliance.

MATERIALS AND METHODS: The study was carried out in the out-patient department of Obstetrics and Gynaecology, Eden Hospital, Medical College and Hospital, Kolkata between 1st June, 2011 to 31st May, 2012. It was an interventional longitudinal study. 45 women were recruited for the study.

All married women aged between 18-45 years seeking reversible means of contraception but who have not used any form of hormonal contraceptives in the last 6months were included in the study. Women with medical disorders, severe pelvic inflammatory disease, sexually transmitted disease, known or suspected malignancy of genital organs or breast, undiagnosed vaginal bleeding or irregular cycle were excluded from this study.

Initially 45 women fulfilling inclusion and exclusion criteria were selected for the study. Informed written consent was taken and all the participants. They were informed about the procedure, purpose and possible consequences of the study. Participants were verbally instructed about the procedure of insertion and removal of the ring and given written information sheet about general instruction. 1st insertion of the CCVR was done under supervision. After every insertion of the ring it was maintained for 3 weeks. After the 3rd week, ring was removed. Subsequent rings were inserted by the patient with a gap of 1 week. After use of 3 rings, participants were reviewed and reassessment for the outcome variables was done.

The outcome variables were measured in terms of contraceptive efficacy, cycle regularity, systemic effects on blood pressure, liver function, body weight, lipid parameters and blood sugar along with local effect on cervix and vagina. Patient compliance, acceptability and spouse compliance was also measured.

Menstrual history was obtained and speculum examination of the cervix and vagina was done. Routine blood tests (Haemogram, fasting, postprandial blood sugar, liver function tests and lipid profile) and weight was recorded. In case of amenorrhea, urine pregnancy test was done. Opinion of patient and her husband was taken by means of questionnaires which were in the following domain—clarity of instruction, sexual comfort, satisfaction domain, cycle-related characteristics and reason for discontinuation of the ring.

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RESULTS: The demographic characteristics of age and parity of women are shown in Fig. 1 & 2. Among the 39 women, who completed our study, 5 were in 15-20 and 31-35 yrs age groups respectively. Maximum were in 21-25 yrs age group, amounting to 19. Another 10 women were in 26-30 yrs age group. The average age was 24 yrs. Majority of women (24) had one child, 14 had two children and 1 had three children.

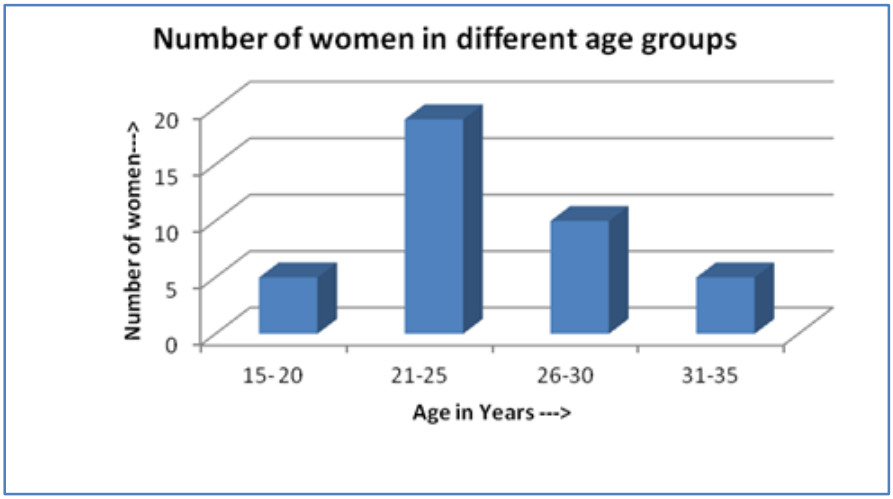

Fig. 1

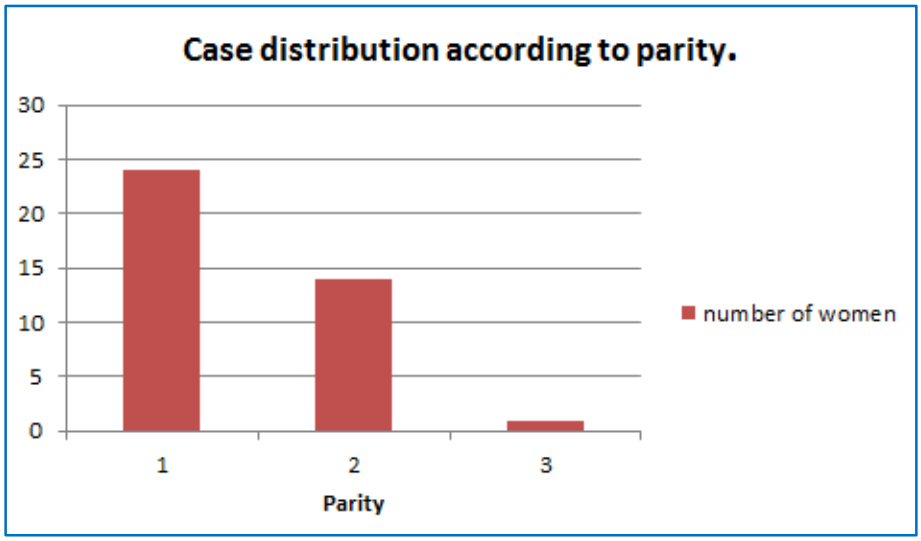

Fig. 2

No unwanted Pregnancies were noted amidst 117 exposed cycles, eliciting higher contraceptive efficacy of CCVR.

The occurrences of withdrawal bleeding and with duration are summarized in Fig. 3. Incidence of withdrawal bleeding occurred in 100% of cycles observed with mean duration being 4.2 days. Early and late withdrawal bleeding was noted in 1.2% and 13.7% of cycles.

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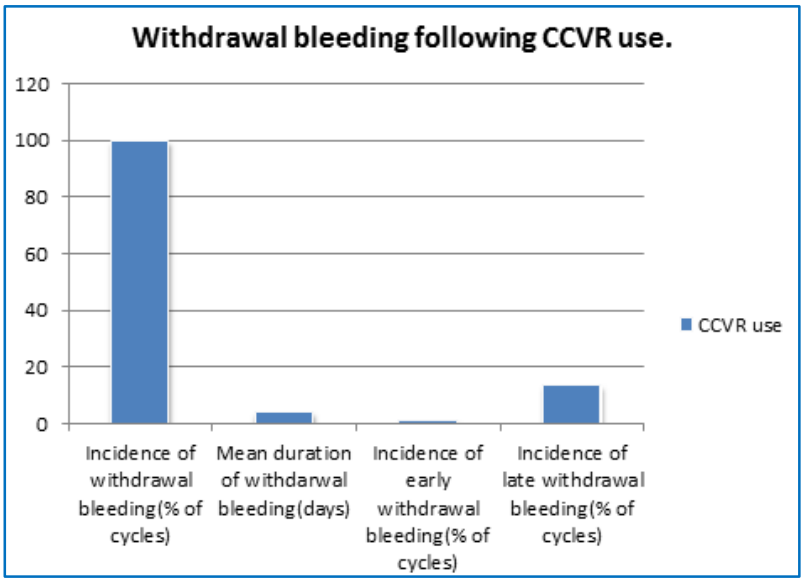

Fig. 3

In our study, incidence of irregular bleeding and intended bleeding pattern during CCVR use was 3.6% and 95%.

Majority of women (29) had no change in body weight, whereas 6 women gained weight and 4 women lost weight i. e 0.2% increase and 0.18% decrease of body weight during CCVR use. (Fig. 4).

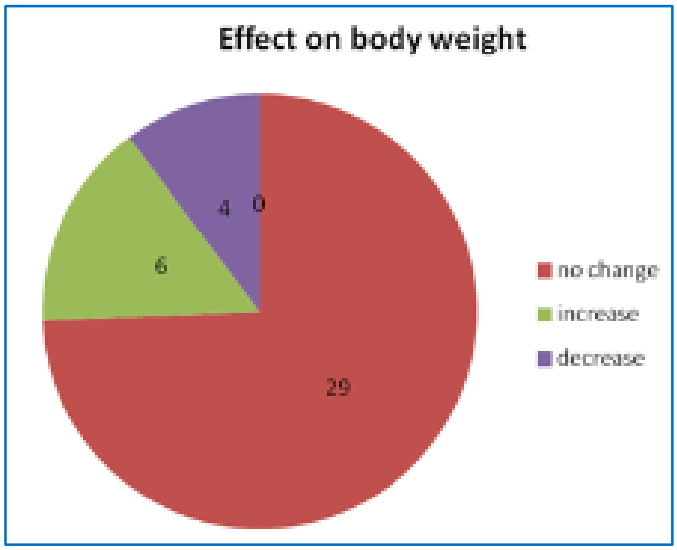

Fig. 4

Mean change of blood pressure from baseline value was clinically insignificant. Systolic blood pressure change was ± 9.8mmHg and diastolic was ±8.4mmHg. Effect on blood sugar during CCVR use was also very negligible. In our study, as per changes in lipid variables, median percentage change from baseline values was total cholesterol- 0.9%, HDL- cholesterol – 1.3%. LDL- cholesterol – 0.2% and triglycerides – 20.1%. (Fig. 5).

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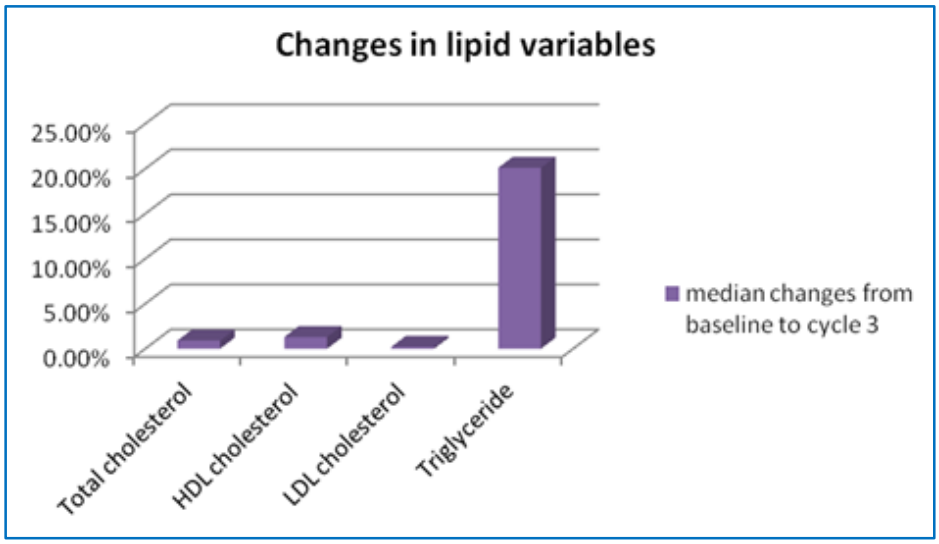

Fig. 5

During CCVR use, mean percentage change of liver function from baseline value was total bilirubin-0.23%, SGPT-0.18% and SGOT-0.35%.

Regarding cervical cytology, 37 women had no change. Shifting from class I to IIb and class IIa to I was only 1 each. (Fig. 6).

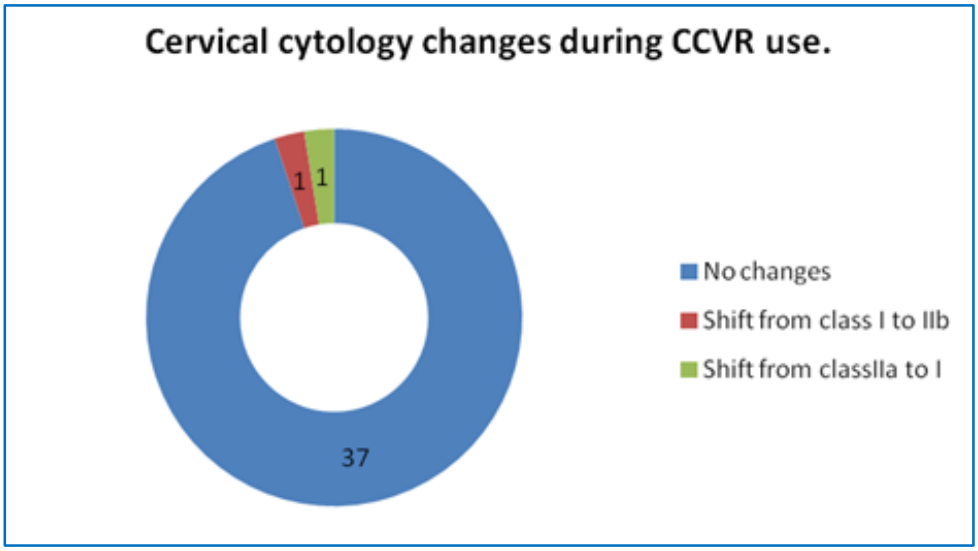

Fig. 6

Adverse events are one of the major concerns as CCVR are generally used by healthy women for prolonged periods of time. The most frequently observed adverse events noted in our study was Device- related events (8%) included foreign body sensation, coital problem and expulsion. Leucorrhoea (4%), headache (3.8%), nausea (2.8%) and vaginitis (2.5%) were the other adverse events observed during CCVR use. (Fig. 7). The pie chart below represent in percentage the incidences of various adverse effects.

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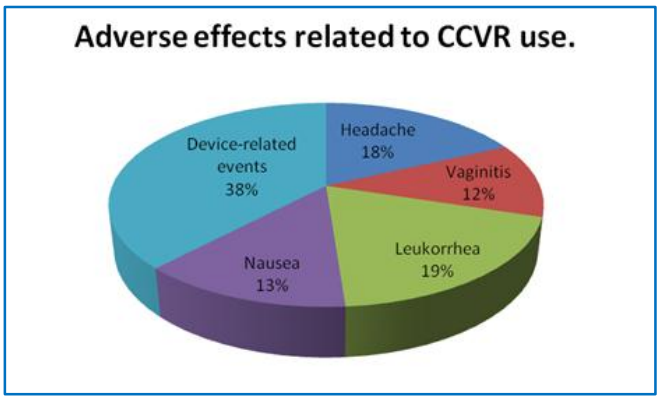

Fig. 7

Regarding acceptability, Fig. 8 shows the domain regarding response to clarity of instruction. 92 % women agreed that instructions on CCVR insertion and removal were easy to follow.

This pie chart graph below represents in % the incidents of various adverse effects.

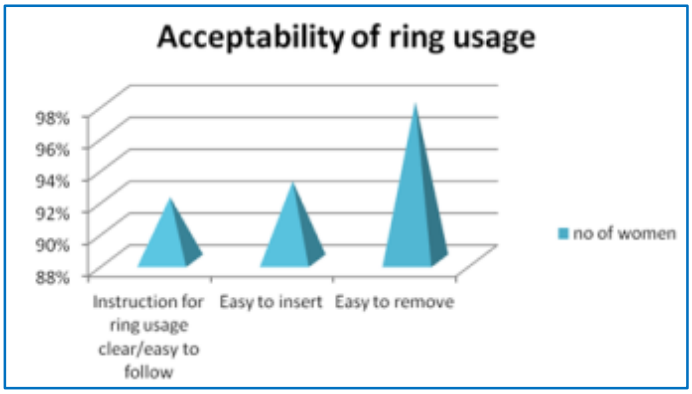

Fig. 8

30% women could feel the ring, 18% partners felt the ring during intercourse whereas in 21% cases partner minded that the women were using the ring. (Fig. 9).

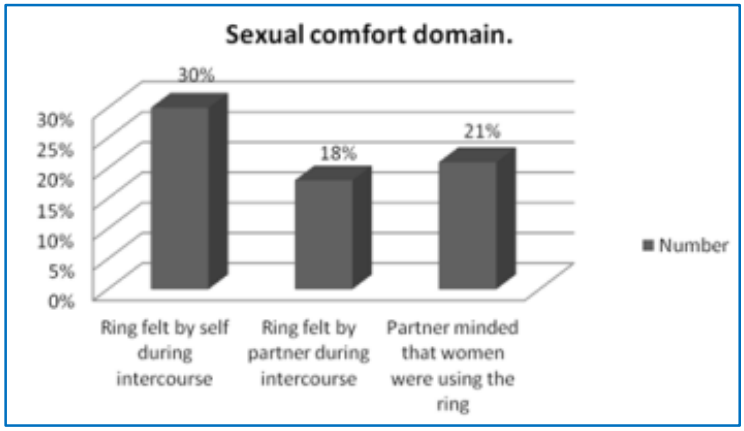

Fig. 9

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Responses to questions in satisfaction domain are seen in Fig. 10.

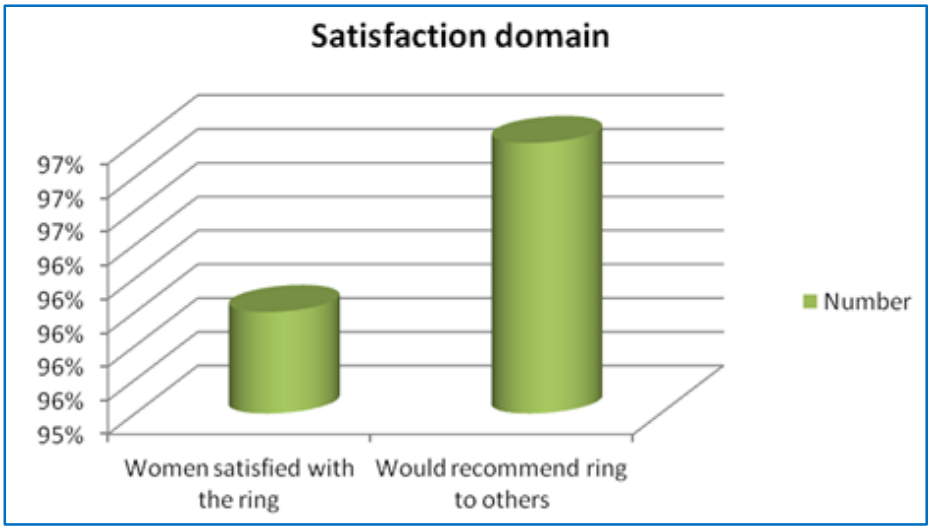

Fig. 10

Regarding cycle related characteristics, 98.6% women reported that the length of their period was either same or no change and 83.6% reported the severity of their menstrual pain did not change or was less. (Fig. 11).

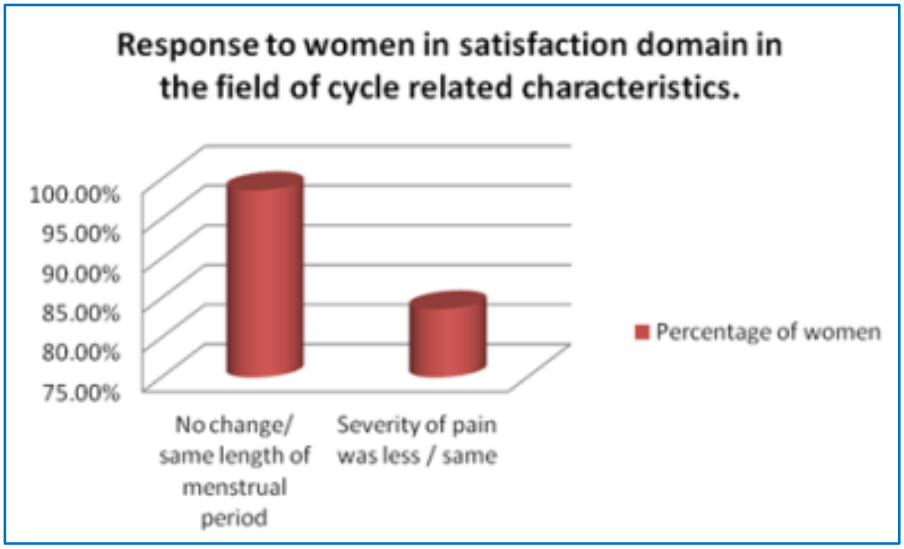

Fig. 11

Out of 45 women, 6 women discontinued from our study (13.3%). Among these women, bleeding irregularities noted in 2 cases, 2 withdrew due to coital problem, 1 due to spontaneous expulsion of the ring and 1 due to foreign body sensation. (Fig. 12).

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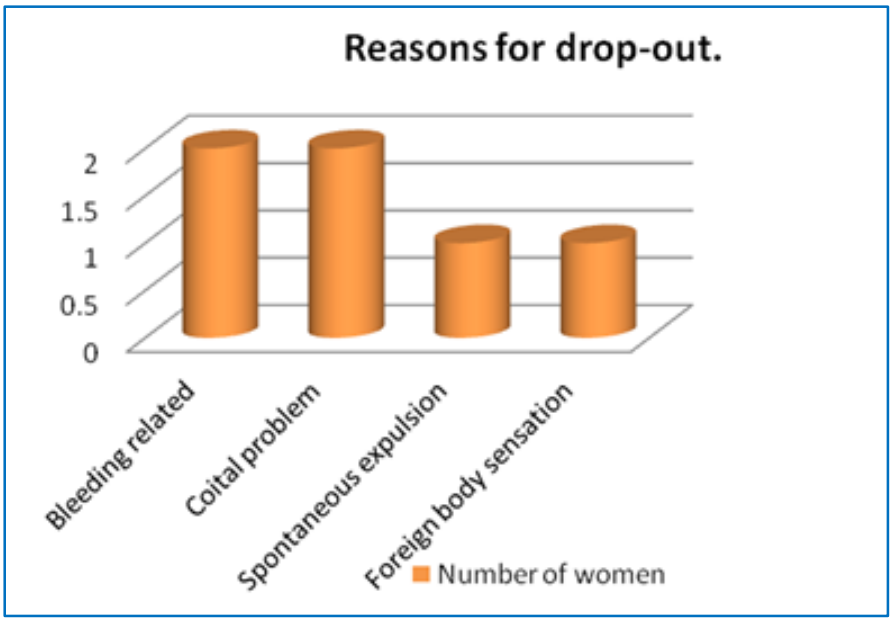

Fig. 12

DISCUSSION: The present study has been carried out in the department of Obstetrics and Gynaecology, Medical College and Hospital. Forty-five women were chosen and followed-up in a prospective manner. All the parameters mentioned above were studied, relevant data collected and analysed.

Of the women who completed the study, 5 were in the age group of 15-20years, 19 in 21-25years group, 10 in 26-30 years group and 5 in 31-35years age group. The average age was 24 years. Majority of the women, 24 had 1child, 14 had 2 children and 1 had 3 children.

CCVR is an effective contraceptive as illustrated by its low Pearl index.[18]. Contraceptive efficacy of CCVR in this study was found to be high with no pregnancies noted amongst 117 exposed cycles. The Pearl Index could not be calculated due to the study being carried out on a small number of women for a short period. Roumen et al (2001),[18] and Dieben et al (2002),[19] have described an overall Pearl Index for CCVR as 0.65 and 1.18 respectively.

CCVR has excellent cycle control.[19,20] Cycle control during CCVR use was assessed by vaginal blood loss classified as either withdrawal bleeding (bleeding per vaginum during ring-free week) or irregular bleeding (unpredictable bleeding p/v during CCVR use period). Incidence of withdrawal bleeding occurs in 100% of cycle observed with mean duration of 4.2 days of which early withdrawal bleeding was 1.2% and late withdrawal bleeding was 13.7%. Study by Bjarnadottir et al 2002,[21] has also shown similar results. Incidence of irregular bleeding was 3.5%. The incidence of intended bleeding pattern was 95% which was comparable to studies conducted by Dieden et al (2002),[19] and Bjarnadottir et al (2002).[20]

In this study, a 7% increase or decrease in body weight was taken to be clinically significant. Our study showed an increase of 0.2% and decrease of 0.18% which was clinically non-significant. Studies by Dieden et al (2002),[19] have shown an increase of 0.14±3.1kg. Measurement of blood pressure and blood sugar both have shown no clinical relevant changes from baseline values.

In the study conducted by Tuppurainen et al (2004),[22] it was found that the total HDL and LDL cholesterol level remained unchanged while triglyceride level increased from baseline from

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CCVR use. In our study, median percentage change from baseline values was total cholesterol 0.9%, HDL cholesterol-1.3%, LDL cholesterol 0.2% and triglyceride 20.1%.

The effect of CCVR on liver function was not clinically relevant with mean percentage change from baseline value being total bilirubin -0.23%, SGPT-0.18% and SGOT-0.35%.

In our study, CCVR was not associated with an increased risk of cervical or vaginal abnormalities. Similar results were found by Roumen et al 1996.[23] Dieben et al 2002,[19] and Archer et al 2002.[24] In the present study treatment related adverse events with CCVR (nuvaring) were headache-3.8%, vaginitis-2.5%, leucorrea-4%, nausea-2.8% and device related events-8% which included coital problems, foreign body sensation and spontaneous expulsion.

The overall acceptability of a contraceptive is determined by several factors. These factors have a substantial influence on determining whether a woman continue to use a particular contraceptive method. In our study, 92% of the women agreed that the instruction on ring use were either clear or easy to follow, 98% found the ring easy to remove and 93% found it easy to insert. Regarding the sexual comfort domain, 30% women could feel the ring during intercourse with 18% partners felt it during intercourse, which means 70% of women & 82% of partners never felt the ring during intercourse.

96% women were satisfied with the ring usage and 97% would recommend it to others. Regarding the cycle-related characteristics, 98.6% women reported that the duration of their menstrual cycle were either same or shorter and 83.6% women reported that their menstrual pain remained unchanged or was even less.

In the study conducted by Novak et al 2003.[25] 96% agreed that the instructions for use were clear, 97% of women and 70% of their partners never/ rarely felt the ring during intercourse and 94% of partners never/rarely minded that the women were using the ring. Overall acceptance was high, 82% were satisfied with the ring and 97% would recommend the ring.

Of the 45 women who started the study, 6 prematurely discontinued participation in the study. Of these, 2 withdrew due to bleeding irregularities, 2 due to coital problems, 1 due to spontaneous expulsion of ring and 1 due to foreign body sensation.

CONCLUSION: From the present study, it can be concluded that CCVR is an effective contraceptive with good cycle control, minimal systemic or local adverse effects along with low incidence of spontaneous expulsion and higher level of user and partner acceptability and probably with a high contraceptive efficacy rate. Continuous long term studies are required for evaluating pearl index.

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