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Acknowledgments

Acknowledgments should only be made to funding institutions and organizations and, if to persons, only to those who have made substantial contributions to the study.

References

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2- Books:

(a) Personal author: Speroff L, Glass RH, Kase NO. clinical gynecologic endocrinology and infertility. 4th edition, Baltimore, Williams & Wilkins; 1988: 105

(b) Chapter in book; Wilhelmsson L, Norstrom A, Tjugum 1, Hamberger L. Interaction between prostaglan dins and catecholamines on cervical collagen. In: Toppozada M., Bygdeman '. M., Hafez ESE, Eds. Prostaglandins and fertility regulation. Advances in reproductive health care. Lancaster, England, MTP Press Ltd., 1985 : 75 - 80.

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Contents :

Letter from the Editor:

Dear esteemed colleagues,

Warm greetings

We welcome your comments as well as the scientific activity to be incorporated in the upcoming issues. Very important subjects are included in this issue. Letrozole didn't show a significant improvement in the efficacy of misoprostol in induction of first trimester abortion. Immediately pre-incisional oxytocin infusion was superior to post-placental delivery oxytocin infusion as regard additional use of ecbolics in elective cesarean sections. Uterine rupture in an unscarred uterus is associated with more bleeding, hematoma formation and more risk for blood transfusion than scarred uterus group. Surgical repair is possible in most cases. Reducing the rate of CS, optimizing care for women with previous CS and careful management of labour can help to reduce the incidence of uterine rupture. Laparoscopic cystectomy of endometrioma has an adverse effect on ovarian reserve reflected by Anti-mul¬lerian hormone that decreases significantly af¬ter Laparoscopic ovarian cystectomy and FSH level that increases significantly after Laparo¬scopic ovarian cystectomy. Ultrasound diagnosis at 11–13th week gestational age is possible for some severe anomalies. An 11–13th week scan as first part of the routine anomaly screening in pregnancy is recommended. Seminal total antioxidant capacity is a major contributor to idiopathic repeated pregnancy loss. At cutoff point > 1.46; it had sensitivity 70% and specificity 64% in prediction of cases of RPL. Vitamin D and L-carnitine may play a role in intracytoplasmic sperm injection success rates in PCOS pa¬tients. Tranexamic Acid is effective in prevention of postpartum hemorrhage in high risk women fo under¬going cesarean section. Early feeding following an uncomplicated caesarean delivery was associated with a lower frequency of ileus symptoms, a shorter mean time to the first bowel movement, and greater mother satisfaction. This, together with the absence of gastrointestinal issues, indicates that ear¬ly oral feeding is preferable to late oral feeding.

Best regards.

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EFFECT OF LETROZOLE PRETREATMENT WITH MISOPROSTOL FOR INDUCTION OF MEDICAL ABORTION (RCT)

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Abstract

Background: The most widely used regimen for induction of medical abortion involves the use of oral or vaginal misoprostol. Indeed, the use of mifepristone (antiprogesterone drug) combined with prostaglandins has resulted in increased success in induction of abortion. The next logical step would be to explore the use of anti-estrogenic agents combined with misoprostol.

Aim: This trial was performed to evaluate the effect of letrozole combined with misoprostol on induction of abortion compared with usage of misoprostol alone.

Methods: The subject population was randomly divided into 2 groups: Group A: 99 women (underwent induction of abortion by letrozole 7.5 mg (Femara) once daily for 3 days, followed by misoprostol 400 mcg vaginally every 4h up to a maximum of five doses per day) Group B: 99 women (underwent induction of abortion by misoprostol 400 (Misotac) mcg vaginally every 4h up to five doses per day).

Results: The results of the study demonstrated no clinical significant difference between complete abortion rate of 78% within 24h in women diagnosed as missed abortion less than 13 weeks gestational age with the sequential regimen of letrozole and misoprostol, compared to 74% complete abortions using misoprostol alone. There was no significant difference in the induction to abortion interval (M: 8.2h & 9.4h respectively), also there was no difference concerning the side effects.

Conclusions: These results indicate that letrozole didn't show a significant improvement in the efficacy of misoprostol in induction of first trimester abortion.

Keywords: Letrozole pretreatment; Misoprostol; Medical abortion.

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INTRODUCTION

Medical abortion is the induction of abortion by using special drugs and a successful abortion is achieved when there is no need for any surgical intervention. Medical

management has become an effective and safe alternative to surgical management with better patient satisfaction. (1)

The most popular drugs used for medical abortion are Prostaglandins and their analogs. Owing to its simple and easy administration and less side effects; Misoprostol gained popularity over other prostaglandins. Misoprostol successes rate in inducing abortion successfully has been reported to range from 37% to 86% in many studies and depending on the route of administration, the regimen and dosage used. The combination of misoprostol with other drugs to augment its effect is confirmed to have higher effectivity [2].

It is well known that pregnancy estrogen and progesterone hormones are important hormones in maintaining healthy pregnancy. Indeed, the use of anti-progestogenic agents like mifepristone combined with prostaglandins has resulted in improved success in termination of early pregnancy. The next logical step would be to explore the use of anti-estrogenic agents. (3)

Letrozole is a third-generation aromatase inhibitor which causes suppression of estrogen production. When combined with misoprostol, there is an improvement in rate of abortion and decreased induction-of abortion time .(4)

In this study, we used letrozole (a third-generation selective aromatase inhibitor) as an effective adjunct to misoprostol for termination of first trimester missed abortion; its action is suppressing estrogen production by the corpus luteum which may assist in induction of abortion.

Research question and aim of study

The study involved women with first trimester missed abortion; we used a combination of letrozole and misoprostol to compare between this combination and the usage of misoprostol alone. Would letrozole-misoprostol regimen induce complete abortion during the first 24 h better than misoprostol alone? Methods.

Patients and Methods :

This study was a Randomized control trial WITH allocation 1:1.No important changes have occurred to methods after trial commencement (such as eligibility criteria), Women were considered eligible to participate in the study if they were pregnant with gestational age of 13 weeks or less of missed abortion as confirmed by ultrasound scanning on day 1 of the study, in good general medical condition, and their age is between 20 – 40 years old were accepted, The study excluded women having living fetus, smokers, who gave history of bronchial asthma, IHD, liver or kidney diseases, and those who were receiving regular drug intake before admission to the study except medications for DM, HTN, SLE were accepted.

This study was conducted at Ain Shams University maternity hospital during the period from September2014 to September 2015

The subjects under the study underwent: history taking (Personal history, Complaint and present history, Obstetric history, Past history: Of Diabetes Mellitus (DM), Hypertension, Cardiac Problems, Renal Troubles, Bleeding Tendency, Blood Disease, Bronchial Asthma, Glaucoma, Allergy or Previous Operations (especially Previous Uterine Scar). Full physical examination was performed including General examination included: Abdominal examination, Vaginal examination, Ultrasound examination was performed on women who were eligible for participation in this study in order to confirm missed abortion and the gestational age. Lab was drawn from the patients including CBC, Renal and liver function (urea and creatinine and liver enzymes), Serum E2 concentrations was checked before and after the induction of abortion. Women then were sent home

for 3 days. In the letrozole group patients received 7.5 mg letrozole (Femara, Novartis) on Day 1 to Day 3. A designated research nurse supervised the subjects to take the first dose of letrozole on Day 1, and the subjects took the second dose themselves on Day 2. The third dose of letrozole was given on admission to our hospital on Day 3 then the patients were sent to another research nurse -who received subjects from both groups- to give them 400 mcg vaginal misoprostol soaked with saline every 4 hours up to a maximum of five doses. Administration of misoprostol was withheld if the woman had strong painful uterine contractions. Side effects, uterine contractions, blood pressure and pulse rate were recorded every 4 hours. Pelvic examination was performed every 4 hours to assess dilatation and effacement of the cervix before the next dose of misoprostol. The patient was reassessed if abortion has not occurred after 24 h. If there were no symptoms or signs suggestive of imminent abortion, the second dose of vaginal misoprostol was given (for a maximum of five doses). If abortion still failed to occur, the pregnancy was terminated by D&C.

After abortion, Pelvic ultrasound was done to confirm whether the abortion was complete or not. If necessary, Transvaginal evacuation and curettage of the uterus was performed under general anaesthesia if abortion was incomplete. The women were discharged 24 h after the abortion if there were no complications. Blood sample was taken for complete blood profile and estrogen level as stated above before administration of letrozole and after abortion before discharge.

The Primary outcome of this study was the rate complete abortion during the first 24 h, while the secondary outcomes were : Induction-to- abortion time interval (hours), No. of incomplete abortion, failure of induction of abortion, Doses of vaginal misoprostol (400mg tabs), side effects of drugs, estrogen levels in letrozole and non-letrozole groups.

NO changes occurred to trial outcome from the beginning till end of trial

Sample size calculation: The required sample size has been estimated using G*Power version 3.1.7 (Institute für Experimentelle Psychologie, Heinrich Heine Universität, Düsseldorf, German). The primary outcome measure is the difference between the letrozole-misoprostol protocol and the misoprostol-only group as regards the rate of complete abortion by 24 hours from the induction of abortion. It was estimated that a sample of 198 subjects equally randomized into either of the study groups (n=99 per group) would achieve a power of 80% (type II error = 0.2) to detect a small-to-medium effect size (w) of 0.2 between the two study groups as regards the outcome measures. The effect size (w) is calculated as follows: where $\chi 2$ is the chi square statistic and N is the total sample size. This effect size is chosen as it may be regarded as a clinically relevant difference to seek in this type of research.

The test statistic used for sample size calculation is the two-sided chi square test with one degree of freedom and significance is targeted at the 95% confidence level (type I error = 0.05)

No interim analyses and stopping guidelines: Randomization was done using a computer generated randomization table using Research Randomizer Version 4.0 software in a 1:1 ratio, using a case code written in a piece of paper and put in an opaque concealed envelope which carried the case number. The letter L referred to women randomized to Letrozole group; M refer to control group. Allocation concealment was ensured as the service nurse did not release the randomization code till the patient was recruited into the trial.

RESULTS

Fig 1 shows the flow chart of the patients for each group. For each group, the numbers of

participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome, no statistically significant difference among 2 groups as regard demographic data (Table 1). No Statistically significant difference between 2 groups as regard primary outcome and secondary outcomes as shown in table 2. Table 3 showed statistically significant difference among 2 groups as regard complication and side effects of drugs. Table 4 shows Comparison between estrogen levels in letrozole and non-letrozole groups. There was a high statistically significant difference between serum estradiol concentration in the letrozole group and that of the non-letrozole group on Day 3 and after abortion.

DISCUSSION

In this study, we used letrozole (a third-generation selective aromatase inhibitor) as an effective adjunct to misoprostol for termination of first trimester missed abortion; our Primary outcome in this study was the rate complete abortion during the first 24 h, while the secondary outcomes were : Induction-to- abortion time interval (hours), number of incomplete abortion, failure of induction of abortion, Doses of vaginal misoprostol (400mg tabs), side effects of drugs, estrogen levels in letrozole and non-letrozole groups.

Our results interpretation and its comparison to other studies

In the RCT study of lee et al., 2011; 168 were randomized into two groups. The patients in letrozole group were given letrozole 10 mg daily for 3 days then they received 800 micrograms vaginal misoprostol, while the patients in the placebo group were given placebo for 3 days followed by 800 micrograms vaginal misoprostol. The abortion rate of the studied letrozole group was significantly higher than that of the placebo group in gestations up to 49 days was significantly higher in the letrozole group than in the placebo group which apparently disagrees with our study but our study mean gestational age was about 8.6 weeks and 9.1 weeks in placebo group. In the study of Lee et al., 2011; the corresponding rates for gestation between 50 and 63 days were not significantly different between the two groups which agrees with our study. (5)

In another study of Lee et al. (2011), in accordance with our study they made a randomized placebo-controlled, double-blinded trial with 130 women between 12 and 20 weeks. Letrozole 7.5 mg vs placebo were given for 3 days, followed by misoprostol 400 microgram vaginally every 3 hours (up to a maximum of five doses on the third day). The abortion rate in 24 and 48 hours were similar either for the letrozole and placebo groups. The interval of induction-to-abortion was similar for both groups. Drug side effects were comparable between the both groups. They agreed with our results that the use of letrozole as an adjuvant to misoprostol in abortion does not significantly improve the abortion rate over the misoprostol-only group. (6)

In a RCT by Lee et al., 2012 ; 30 were randomized into two groups: in the letrozole group, the patients received 10 mg of letrozole daily for 3 days, and in the control group, the patients received a placebo for 3 days. Serum estradiol were measured before letrozole intake and then once daily for 6 days. Similar to our results the estradiol levels were significantly lower in the letrozole patients' group than in the control group. (7) In another RCT by Behroozi et al., 2018, they randomized 78 patients into two groups. First group received daily 10mg letrozole for 3 days followed by vaginal misoprostol. In second group the patients received the vaginal misoprostol only. Their results showed a higher complete abortion rate in favor of letrozole group over misoprostol only group. The main limitation of that study compared to our study is their small sample size. (8)

In their randomized controlled trail Naghshineh et al., 2015 randomized 130 patients eligible for legal abortions into two groups. Letrozole group received daily 10 mg letrozole for 3 days followed by misoprostol sublingually. Placebo group received daily oral placebo followed by misoprostol sublingually. The mean induction-to-abortion interval was 5.1 hours in letrozole group and 8.9 hours in placebo ($P < 0.0001$). These results differ from our study which may be explained by the different route used for misoprostol sublingually rather than oral. (9)

In a recent systematic review and meta-analysis, Zhou et al., 2021 analyzed 6 RCTs involving 555 patients (the studies previously mentioned in our discussion). They found that letrozole supplementation showed significantly increased complete abortion (in contrary to our study) and decreased estradiol and no significant effect on induction-abortion time (in accordance with our study.(10) From the point of view of Zhou et al., 2021 their meta-analysis have several limitations. First limitation is that their analysis is based on 6 RCTs, and 3 of them have a relatively small number of patients (number of patients <100) which could lead to overestimation of the letrozole effect. They concluded that more RCTs should be conducted with large sample size to investigate the letrozole effect. Another limitation were different doses and duration of letrozole supplementation which may have affected the pooling results. Last limitation was the different gestational age in all studied RCT which may have a role in judging the letrozole effect. (10).

Strengths and limitation of our study

Strength of our study in relation to other studies was adequate number of patients in both randomized groups while the main limitation of the trial is that it conducted in one hospital which may attribute to statistical bias.

Clinical implication of our study

From our study and in comparison, to other studies; we don't encourage the use of letrozole in clinical practice as adjuvant to misoprostol till more systematic review and meta-analysis study standardize its use.

Recommendations for Future research

Further studies using different regimens of aromatase inhibitors may be warranted

CONCLUSION

The regimen of letrozole pretreatment (7.5 mg daily for 3 days) does not improve the first trimestric abortion rate when compared with that of the misoprostol-only.

Consent for publication

NOT APPLICABLE

Availability of data and materials

All Data and ethical committee documents are available upon request

Competing interests

The authors report there are no competing interests to declare

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This study received no financial support.

Authors' contributions

All authors jointly contributed to conception and design of the study.

Ahmed Sherif Abdel hamid: Design of the study, helped in review of literature, revision of results and data analysis, writing the manuscript and submission to journal

Yaser Abu-Taleb; design of the study, revision of review of literature and revision of manuscript

Moustafa Ibrahim design of the study, revision of review of literature and revision of manuscript

Mohamed Omar Dakrory: registration of trial, obtaining ethical committee approval, reviewed the literature, shared in collection of Data, active participation in process of induction and labor.

AMR Sobhy: helped in review of literature, revision of results and data analysis and contributed in writing the manuscript

Acknowledgements

Not applicable.

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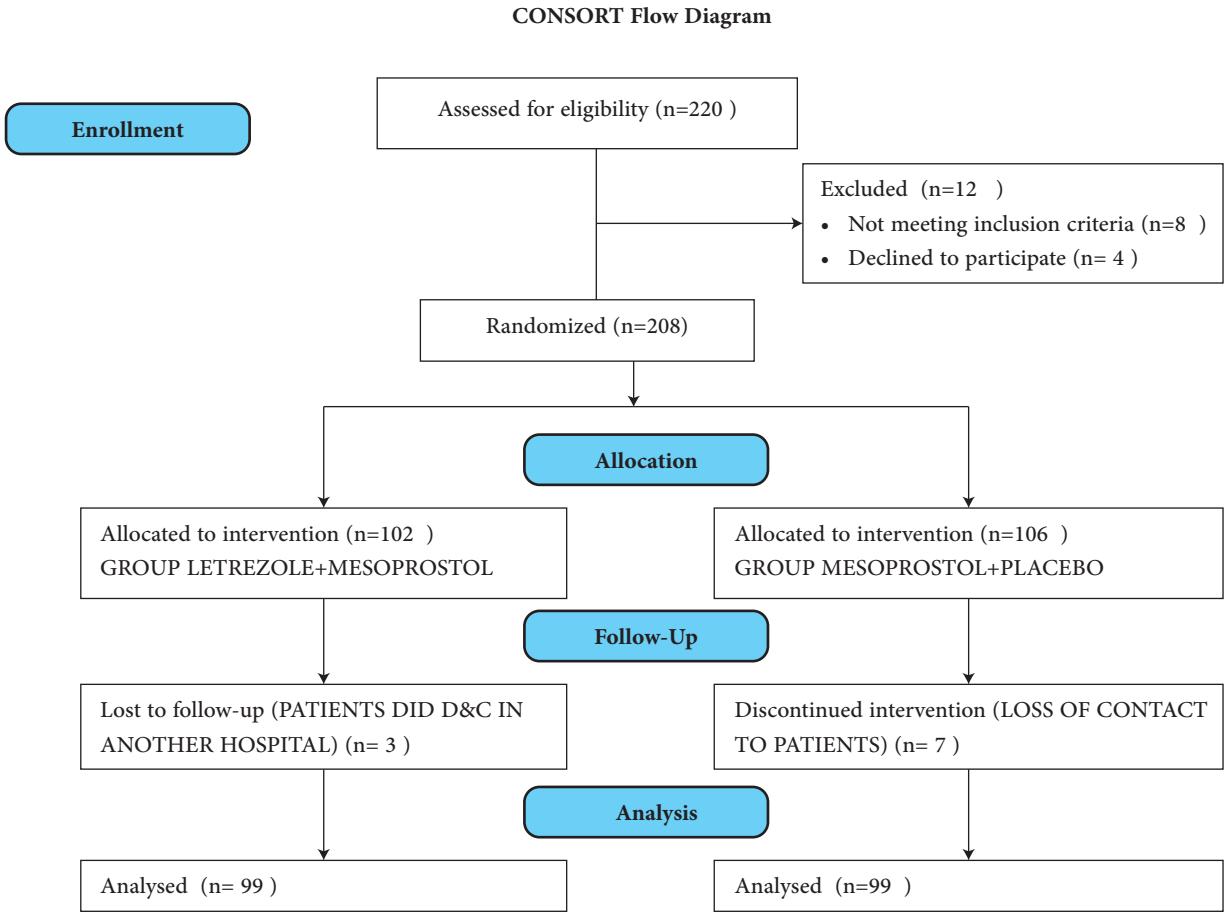

Table 1: Demographic data between the letrozole and non letrozole groups

	Group A (Letrozole) (n=99)		Group B (non Letrozole) (n=99)		p value
	mean	SD	mean	SD	
Age (years)	29.2	5.5	26.04	6.4	0.167
Age (years)	67.7	8.5	70.2	9.4	0.30
Height (cm)	167.6	5.5	165.0	5.1	0.179

Table (2): Comparison between both groups as regard the outcomes of study

	Group A (Letrozole)(n=99)	**Group B (non Letrozole)(n=99)**			**p value**
	mean	SD	mean	SD	
Gestational age by ultrasonography (weeks)	8.6	1.9	9.1	1.5	0.288
No. of subjects with previous pregnancy	number	percentage	Number	percentage	
	78	78.80%	75	75.70%	0.808
No. of subjects with previous abortion	29	29.30%	24	24.20%	0.49
Complete abortion rate in 24 h	78	78.80%	74	74.70%	0.746

	Median	range	Median	range	
Induction-to- abortion time interval (hours)	8.2	3–32	9.4	3.6–48	0.775
No. of incomplete abortion	7		11		0.491
	Range	mean	Range	mean	
Failure of induction of abortion	0		2		0.083
Doses of vaginal misoprostol (400mg tabs)	1-8 tablets	3.8	1-10 tablets	4.6	0.783

Table (3): Comparison between both groups as regard the appearance of side effects

	Group A (Letrozole)(n =99)	**Group B (non letrozole) (n =99)**	**p value**
Nausea	23	18	0.435
Vomiting	17	14	0.632
Fever (>38°C)	8	12	0.371
Dizziness	20	24	0.547
Fatigue	17	23	0.343
Breast tenderness	12	7	0.251
Headache	16	13	0.577
Diarrhea	15	22	0.249
Post abortive bleeding	7	14	0.126

Table (4): Comparison between estrogen levels in letrozole and non letrozole groups

Estradiol level (pg/ml)	Group A (Letrozole)(n =99)		Group B (non letrozole)(n =99)		p value
	mean	SD	mean	SD	
Before treatment	1324.5	456.3	1402.8	418.6	0.131
After three doses of letrozole	211.6	39.4	1347	387.6	0.0001
After abortion	85.8	14.5	148.1	26.2	0.0001

Immediate Post-placental Insertion of the Intrauterine Contraceptive Device during Cesarean delivery versus 6 Week Post-Cesarean Insertion: R.C.T

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Abstract

Background: Insertion of the IUCD immediately is likely to have a high motivation for accepting contraception, and the health-care center provides a convenient setting for inserting the IUCD. Aim of the study is to compare between immediate post-placental insertion of IUCD during cesarean delivery versus 6 weeks post-cesarean insertion delivery Design This study is a prospective randomized controlled trial study. Methods: This study was conducted at Ain Shams university maternity hospital. Women were randomly assigned into two groups; 1st group (Postplacental) containing 100 women in whom IUCD were inserted during cesarean section after delivery of the placenta, The second group (Postpartum) included 100 women where the IUCD were inserted after six weeks postpartum. Primary outcome was the expulsion rate while secondary outcomes were infection, perforation, bleeding, displacement for follow up visits at one month and three months. Data were analyzed by SPSS version 20.

Results: The result of the current study showed there is no significant difference between the two groups as regard expulsion rate also there is not any significant difference regarding infection, perforation, displacement and abnormal bleeding between the both groups. However, perforation rate between both groups is statistically insignificant, it is clinically high significant.

Conclusion: immediate post placental IUCD insertion during caesarean delivery is equal safe and effective method of contraception as IUCD insertion in puerperium, however it may be better as regard patient convenience because easy insertion, no expulsion no complications in using contraceptive method.

The paper was registered in clinicaltrial.gov NCT03404622

Keywords: IUD, post placental, perforation, displacement, infection, bleeding .

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Introduction

Each year, more than One Hundred million women make decisions about beginning contraception after child birth.

The main concern during the postpartum period is the occurrence of pregnancy in this short period of time, which may cause maternal-fetal complications and also have serious social, economic and psychological and repercussions. [1]

Intrauterine Contraception Device (IUCD) is the one of most frequently used method of reversible contraception in the world. Over One Hundred million women all over the world use it for contraception. It is regarded as one of the most reversible and effective contraceptive method. It is estimated that approximately 130 million women are using it worldwide. [2]

IUD is a very attractive to women as a contraceptive method because it is safe , reversible and effective. No follow up is required daily or monthly and it is a cost effective. The main drawback are failure, abdominal cramps, expulsion from the uterus, uterine perforation, menorrhagia , increased incidence of ectopic pregnancy, [3]

Instructions are given to the women to regularly feel the IUD strings, presence of the strings usually means that the IUD is in place. The first sign of perforation is the absence of threads in almost 80% of cases. The incidence of perforated uterus caused IUD is 0.87/1000 women and the perforation usually occurs during insertion.[4]

Previous studies assumed that Immediate post-placental application of intrauterine contraceptive device (IUCD) provides a more effective, reversible and long-term method of contraception . Previous trials of IUCD placement at the time of delivery by cesarean section have demonstrated low levels of complications and higher incidence of device retention.[5]

World Health organization (WHO) stated that risks generally outweigh benefits when insertion of IUD occurs between 2 days and 4 weeks. However, immediate post-placental IUCD insertion (within ten minutes) during delivery by cesarean section provides a good way to achieve minimal discomfort to the patient and also provides long-term contraception. There are no studies reporting any increase in the incidence of infection or any other complication related to immediate placement of IUD) during delivery by cesarean section.[6]

The aim of this study is to compare between immediate post-placental insertion of IUCD during cesarean delivery versus 6 weeks post-cesarean insertion delivery. The ethical committee at Ain Shams University has approved the study protocol. The paper was registered in clinicaltrial.gov NCT03404622

PATIENT AND METHODS

This study is a randomized clinical trial study conducted in Ain Shams University Maternity Hospital from May 2017 – December 2017 on 200 pregnant women.

Inclusion criteria of selected patients were; Age: 18-45, Singleton pregnancy at ≥32 weeks gestation at time of enrollment, voluntarily requesting to IUD placement for postpartum contraception. While the exclusion criteria were Uterine anomaly that preventing replacement of IUD, Chorioamnionitis (such as prolonged rupture of membranes >18 hours, prolonged labor >24 hours, fever >38C), Partum sepsis and unresolved postpartum hemorrhage, IUD allergy (copper), Systemic lupus erythematosus with severe thrombocytopenia.

Primary outcome

Expulsion [Time Frame:3 months] which is defined as the time until expulsion of the IUD beginning from the time of insertion until expulsion occurred, if known. If the date of expulsion was not known, this was documented as the day after the IUD was last known to be in place. If a pregnancy was detected and the IUD was absent (and the participant was unaware of expulsion), the expulsion was assumed to have occurred

at the time of conception, as determined by gestational age on ultrasound. Expulsions were measured as total expulsions and separately noted whether complete or partial,

Secondary outcomes

Displacement [Time Frame: 3 months]: The displacement was diagnosed by doing trans-vaginal ultrasound that showed IUCD that displaced up or down word

Infection [Time Frame: 3 months]: The diagnosis of PID was made based on the 2006 CDC guidelines and the criteria used in the PEACH study.

Bleeding [Time Frame: 3 months]: Irregular bleeding (including spotting, light bleeding, heavy or longer menstrual period) were common in the first 3 months and may persist.

Perforation [Time Frame: 3 months]: The diagnosis of a perforation was made by a transvaginal sonogram that shows no IUD within the uterus and an abdominal radiograph that show IUD within the abdominal cavity.

Sample Size calculation

Sample size was calculated using STATA program (Stata Corp. 2001. Statistical Software: Release 7.0. College Station, TX: Stata Corporation), setting the type-1 error (α) at 0.05 and the power (1-β) at 0.9. Results from a previous study (Lester et al., 2015) showed shows the IUD expulsion at 3 months was lower in the immediate insertion group compared to delayed insertion (93% vs. 50% after delayed Insertion $p<.0001$). Calculation according to these values produced a minimal sample size of 100 cases per each group.

Randomization

200 women have been allocated in this study, randomized in two groups: Group I (Postplacental): IUCD was inserted immediate post-placental removal during caesarean section and include 100 pregnant women. Group II (Postpartum): IUCD was inserted 6 weeks post cesarean delivery and include 100 pregnant women. Randomization was done using a computer-generated randomization table using Research Randomizer Version 4.0 software in a 1:1 ratio, using a case code written in a piece of paper and put in an opaque concealed enveloped which carried the case number. Closed opaque envelop method was applied as 100 envelops contained letter I (immediate insertion) and another 100 envelops would contain letter S (six weeks insertion). All patients with letter S (six weeks insertions) were followed up by phone to ensure they come to our hospital to insert the IUD by us. Allocation concealment was ensured as the service did not release the randomization code until the patient was recruited into the trial, which took place after all baseline measurements have been completed.

Procedures Done

Written consent Was obtained from all the participants and they were informed about the objectives of the study. Detailed complete history (personal, menstrual, obstetric and surgical history) taking, General and abdominal examination, Per vaginal examination and U/S before delivery were taken for all participants.

Surgical procedure: pre-operative antibiotics were given to all participants of both groups according to our hospital protocol. Group (1): this group included 100 women in whom IUCD were inserted during cesarean insertion, after delivery of the baby, placenta was removed then the IUCD was placed at the top of the uterine fundus with ring forceps or manually, Before closing the uterine Incision, the strings were placed in the lower uterine segment, The strings were usually descended spontaneously through the cervix during the partum period, If the cervix was closed, dilatation from above with ring

forceps and Strings were passed through the cervix with ring forceps, If this was done, rechecked to make sure IUCD was remained at the fundus of the uterus prior to closing the uterine incision, Trim strings at a follow-up visit. Group (2): this group included 100 of women who had elective lower segment cesarean section in whom the IUCD were inserted in the usual sterile fashion as described in the manufacturer's instructions at the 6-week postpartum visit.

All the participants were instructed about side effects, possible complications, and warning signs about the use of IUCD (TCu380) as a method of contraception and informed consent were taken from all recruited patients enrolled in the study. They were educated to recognize IUCD expulsion and to return to clinic for reinsertion or an alternative contraceptive method. Almost all expulsions occur in the first three months after insertion. She should also be advised that within several weeks, the IUCD strings may protrude through the internal os.

Follow up: Followed up was at interval of 1st week, one month and three months after insertion of IUCD. Follow up of participants was done by history taking, general and vaginal examination including speculum to visualize the strings of IUCD, CBC. In cases of missed IUCD an extra transvaginal ultrasound and pelvi-abdominal X-ray were done. Follow up was concise to primary and secondary outcomes.

Statistical methods: The collected data were revised, coded, tabulated and studies Statistical package for Social Science (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. Student T Test was used to assess the statistical significance of the difference between two study group means. Chi-Square test was used to examine the relationship between two qualitative variables. Fisher's exact test: was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of cells. P>0.05: Non significant (NS), P< 0.05: Significant (S) and P<0.01: Highly significant (HS).

Results

The mean of age in group I (Postplacental) was 25.74±4.29 years while it was 26.02±4.63 years in group II (Postplartum). The mean of body mass index (BMI) was 31.85±4.27 and 32.37±1.46 kg/m2 in Postplacental group and II respectively. The mean of hemoglobin was 10.02±0.81 gm/dl in Postplacental group versus 10.07±0.65 gm/dl in postpartum group . The mean of gestational age was 38.89±0.71 and 38.9±0.74 weeks in Postplacental group and postpartum group respectively. And all these differences were statistically not significant (data not tabulated).

Our results showed that Postplacental group included 85 multiparous patients (85%), 80 patients (80%) with history of cesarean section, 59 of them (59%) had 2 or more sections while postpartum group included 82 multiparous patients (82%), 81 patients (81%) with history of cesarean section, 61 of them (61%) had 2 or more cesarean section. These differences were statistically not significant (data not tabulated).

Table 1 shows the rates of primary and secondary outcomes in both groups in period of follow up (1 week, 1 month and 3 month). Comparison between the incidence of expulsion, infection bleeding and displacement in time of follow up in Postplacental group and postpartum group were statistically not significant.

The correlations between mean age, BMI, hemoglobin, gestational age and parity, and complications in Postplacental group (immediate post-placental IUCD insertion) and postpartum group (6 weeks postpartum IUCD insertion) as regards patients with complications 3 months after IUCD insertion

were statistically not significant. (Table 2)

The correlations between parity, previous number of cesarean sections, and IUCD expulsion in both groups were statistically not significant. (Table 3)

DISCUSSION

The copper-T IUD is considered a long-acting reversible contraceptive (LARC) and is recommended by the ACOG (American College of Obstetrics and Gynecology) as one of the best options contraceptive methods during early postpartum period . ACOG's guideline on using IUD aims to improve the pregnancy-spacing that leads to the improvement of child health and maternal care, especially in developing countries. [2]

Our results demonstrated that there was no statistically significant difference between 2 groups as regard the incidence of expulsion, infection bleeding and displacement in time of follow up (one week, 1 month and 3 month duration).

Also there was no statistically significant difference between 2 groups as regard the correlations between mean age, BMI, hemoglobin, gestational age and parity, and complications in Postplacental and postpartum group in period of follow up. The correlations between parity, previous number of cesarean sections, and IUCD expulsion in both groups were statistically not significant.

Interpretation of our results and their comparison to similar studies

The CS rate was estimated at 55.1% for the 2019, 2020 and 2021 , the highest rate reached 67.8% in Behira and the lowest rate was 49.0% in Assiut. This higher rate of CS should encourage obstetricians to apply IUD immediate after delivery of placenta in CS, the main objection of obstetricians is that uterus size in immediate postdelivery is large and their increased rate of expulsion compared to 6 weeks insertion. The Expulsion was the was the primary outcome in our study in 3 month follow up. In Postplacental group, expulsion rate was about 6.0%, in three of those cases IUCD was not found at one month follow up and in the other three cases IUCD was not found at three month follow up but fortunately pregnancy had not occurred in any them may be due to exclusive breast lactation. The expulsion of IUD differs according to parity and number of previous CS as it increases in cases of postpartum insertion, but in our study, we found no statistically significant difference in rate of expulsion and previous number of CS which favors the insertion of IUD in post placental. The study done by levi et al. (2015), 112 women were randomized into their trial for post placental insertion vs 6 weeks insertion, they had four expulsions in the post placental group that occurred in the first three weeks postpartum which is almost similar to our study that 3 patients in Postplacental insertion had her IUD expelled. They explained that these women had a dilated cervix of 0-1cm at the time of cesarean section and IUD insertion [7] In the study of Zaconeta et al., (2019), which was a prospective cohort study including 100 women where Postplacental IUD was inserted during CS (it included only one group). The expulsion rate in the first 6 weeks was not different from that between 6 weeks and 6 months (9 vs 9.1%, respectively) which is different from our study 3% after first month and 6% after 3 rd month. Five of 9 patients in Zaconeta at al., study had spontaneous IUD expulsion, while one patient had the IUD removed due to PID. The remaining 4 cases were as follow 2 women IUD were removed due to excessive bleeding, and one was removed because was rotated to a transverse position and one patient asked removal to change to another way of contraception. During their 6 month follow up only 3 (3.4%) of 88 patients had IUD expulsion, so these results are in line with our results in both 6 weeks and 6 months follow up.[8]

In postpartum group , the expulsion rate was about 9.0%, six of those cases IUCD was not found at one month follow up and other three cases IUCD was not found three month follow up and by comparing both groups in our study; there was no statistical significant between both groups as regard expulsion of IUCD in the present study, these results are in line with RCT of Lester et al., 2015 where there was no statistical significant difference between 34 Postplacental women versus 18 women in postpartum period.[9] while in study by Mohamed et al. (2015) immediate postpartum IUCD insertion had higher expulsion rate 6.2% compared to 1.2% among post partum which is statistically significant. [10] In contrary to our study is the study of Gupta et al., (2016) where the Expulsion rate was significantly higher in Postplacental group as compared to postpartum insertion group (4.3% v/s 2.0%; p value< 0.05).[11]

In the present study there were no cases of perforation in Postplacental group while there was only one case in our study of uterine perforation in postpartum group (1%) had been occurred during insertion and managed conservatively. The comparison between both groups revealed no statistically significant difference which is comparable to study by Gutgutia et al. (2017) in which there were no cases of perforation in Postplacental insertion of IUCD. [12]

In Postplacental group, there was 15% of women complained of abnormal bleeding, eight of those cases were at one month follow up and other seven cases at three month follow up. 5% of those women were required removal of IUCD, in postpartum group there were about 19% complained of bleeding, ten of those cases at one month follow up and other nine at three month follow up. only 9% of those women were required removal of the IUCD and shifting to another method because of this complaint. There was no statistical difference between both groups as regard abnormal bleeding. Our results agree with study by Gupta et al. (2016) where number of women complain of bleeding was 5.3% and all of them remove the IUCD because of this complaint [11]

In Postplacental group, the displacement rate was about 9%, five of those cases IUCD were displaced at one month follow up and other four cases were displaced at three month follow up, so transvaginal and abdominal ultrasound were done to exclude perforation. While in postpartum group, the displacement rate was about 11%, nine of those cases IUCD were displaced at one month follow up and other two cases were displaced at three month follow up. No statistical significant difference was found between 2 groups , similar results were recorded in the study of Lester et al., 2015 where no statistical significant difference was found between 34 Postplacental women versus 18 women in postpartum period as regard rate of displacement (p>0.05). [9]

Regarding vaginal infection, in Postplacental group , the infection rate was about 5% at three month of follow up, although in postpartum group, the infection rate was 10%. Five of those cases were at one month follow up and other five cases were at three month follow up, in this study there was no cases of PID, comparable to study by Gupta et al. (2016) [11]. As regard cases of PID; the present study revealed that there was no statistically significant difference in both groups. This may be attributed to that 6-weeks postpartum participants resuming their sexual life after puerperium that make them risk for pelvic infection, also immediate post placental participants recently had a complete course of antibiotic that decrease the incidence of their risk of have pelvic infection. These results are in line with Gupta et al. (2016),[11] and Zaconeta et al., (2019). [8]

Strength and limitation of our study

The current study had the advantages of having a high power (90%) and of being randomized controlled trial; however. The

main weak point of this study is the absence of long term follow-up after the second visit between seven and ten days after birth, and the use of pain -which is a subjective measure- as the only variable for patient's satisfaction; however, efforts were made to minimize this bias by explaining how to fill the follow up sheet another limitation of the study is that it is not multicenter which may cause statistical bias

Clinical Implication of our study

We highly recommend the doctors to insert the IUD immediately post placental delivery in CS to decrease the fear felt by the patients as many patients refuse to insert IUD just from fear, also due to easier application during CS

Recommendations for future studies

Further studies are needed with a long term follow up and to study satisfaction of the patient towards the post placental IUD insertion and the decrease of psychological fear of pain from the inserting the IUD

Conclusion: immediate post placental IUCD insertion during caesarean delivery is equal safe and effective method of contraception as IUCD insertion in puerperium, however it may be better as regard patient convenience because easy insertion, no expulsion no complications in using contraceptive method

Ethics approval

Study approved by Research Ethical Committee, faculty of medicine , Ain shams University

Registration

The paper was registered in clinicaltrial.gov NCT03404622

Consent for publication:

Non applicable

Availability and data material:

The datasets used and/or analyzed during the current study are available from

the corresponding author on reasonable request.

Competing interests:

The authors report there are no competing interests to declare

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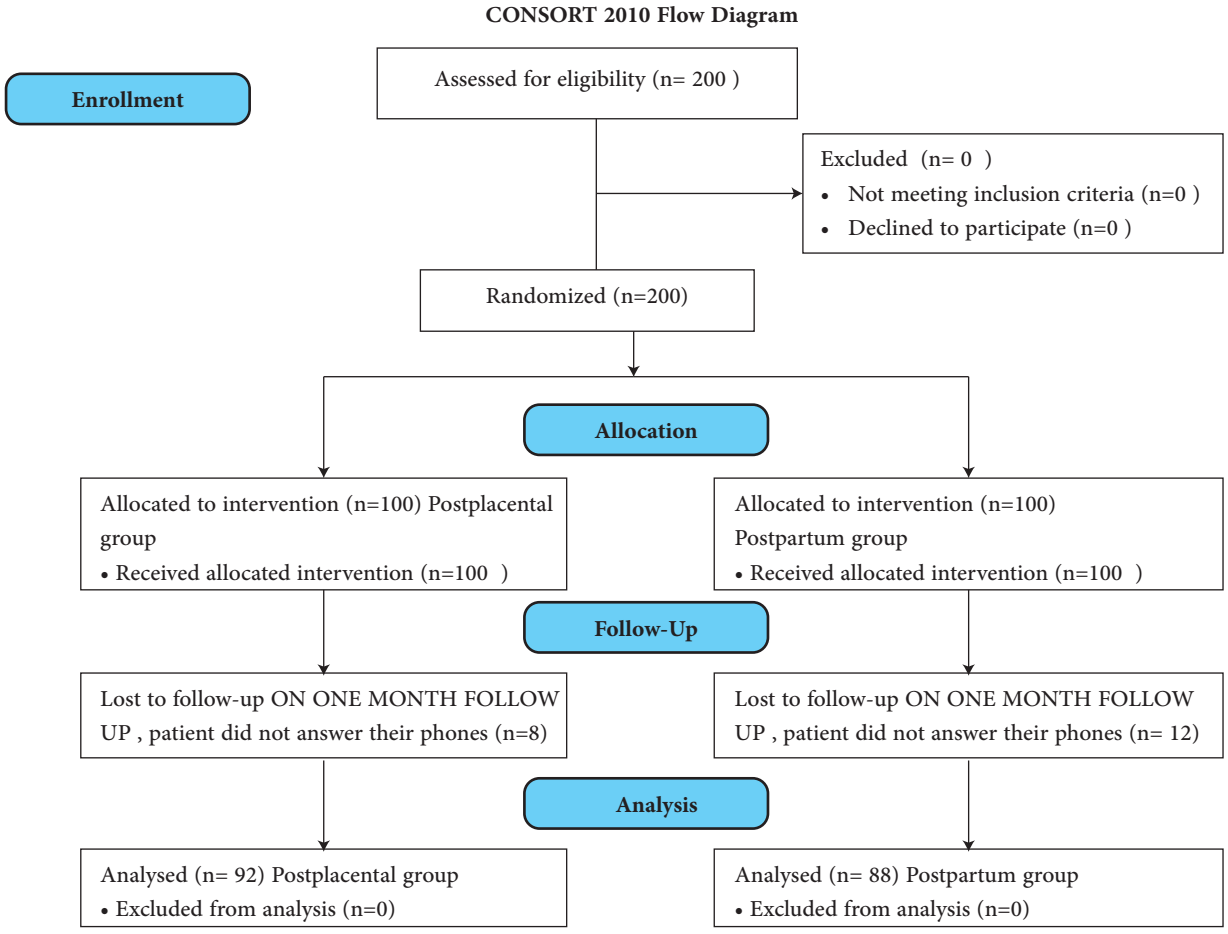

Table (1): Comparison between group I and Group II as regard Primary and secondary outcomes; one week, 1 month and 3 month duration.

Group I (n=100)	**1 week after insertion (n=100)**	**1 month after insertion (n=100)**	**3 months after insertion (n=92)**	
Expulsion	0 (0%)	3 (3.0%)	6 (6.5%)	
Infection	0 (0%)	0 (0%)	5 (5.4%)	
Bleeding	0 (0%)	8 (8.0%)	15 (16.3%)	
Perforation	0 (0%)	0 (0%)	0 (0%)	
Displacement	0 (0%)	5 (5)	9 (9.8%)	
Group II (n=100)	**1 week after insertion (n=100)**	**1 month after insertion (n=100)**	**3 months after insertion (n=88)**	
Expulsion	0 (0%)	6 (6.0%)	9 (10.2%)	
Infection	0 (0%)	4 (4.0%)	10 (11.4%)	
Bleeding	0 (0%)	10 (10.0%)	19 (21.6%)	
Perforation	0 (0%)	0 (0%)	1 (1.1%)	
Displacement	0 (0%)	9 (9.0%)	11 (12.5%)	
	Post placental Group I (n=100)	**Post puerperal Group II (n=100)**	**P**	**Sig**
Expulsion 1 month after IUCD insertion	3 (3.0%)	6 (6.0%)	0.307	NS
Infection 1 month after IUCD insertion	0 (0%)	4 (4.0%)	0.053	NS
Bleeding 1 month after IUCD insertion	8 (8.0%)	10 (10.0%)	0.622	NS
Perforation1month after IUCD insertion	0 (0%)	0 (0%)	---	---
Displacement 1 month after IUCD	5 (5.0%)	9 (9.0%)	0.269	NS
	N=92	**N=88**		
Expulsion 3 month after IUCD insertion	6 (6.5%)	9 (10.2%)	0.370	NS
Infection3 month after IUCD insertion	5 (5.4%)	10 (11.4%)	0.147	NS
Bleeding3 month after IUCD insertion	15 (16.3%)	19 (21.6%)	0.365	NS
Perforation3 month after IUCD insertion	0 (0%)	1 (1.1%)	0.315	NS
Displacement 3 month after IUCD	9 (9.8%)	11 (12.5%)	0.566	NS

Using: Chi-square test; with p-value >0.05 is insignificant

Table (2): Correlations between mean of age, BMI, Hemoglobin (HB) , Gestational age (GA) and parity in post-placental group I (immediate post-placental IUCD insertion) and post puerperal group II (6 weeks postpartum IUCD insertion) as regards patients with complications 3 months after IUCD insertion.

	Groups		p-value	Sig
	Post placental Group I	Post puerperal Group II		
	Mean ± SD	Mean ± SD		
Correlation between mean of age of the patients and 3-month complications				
Expulsion	25.83 ±3.87	28.33 ±6	0.386	NS.
Infection	25 ±3.81	24 ±4.69	0.687	NS
Bleeding	27.07 ±3.26	25.53 ±3.92	0.230	NS
Perforation	--	27.0±0.0	--	--
Displacement	28 ±4.64	30.55 ±3.91	0.199	NS
Correlation between mean of BMI of the patients and 3- month complications				
Expulsion	31.94 ±1.45	32.63 ±1.58	0.404	NS.
Infection	31.86 ±1.44	32.09 ±1.42	0.778	NS
Bleeding	30.31 ±7.6	32.69 ±1.31	0.188	NS
Perforation	--	32.47±0.0	--	--
Displacement	32.56 ±0.85	33.37 ±1.02	0.074	NS
Correlation between mean of HB of the patients and 3- month complications				
Expulsion	10.25 ±0.99	10.06 ±0.58	0.637	NS.
Infection	10.2 ±0.91	10.15 ±0.63	0.902	NS
Bleeding	9.43 ±0.59	9.42 ±0.56	0.951	NS
Perforation	--	9.5±0.0	--	--
Displacement	9.56 ±0.88	10.14 ±0.6	0.096	NS
Expulsion	39.17 ±0.98	39 ±0.71	0.707	NS.
Infection	39 ±0.71	38.9 ±0.88	0.829	NS
Bleeding	38.93 ±0.26	38.63 ±0.68	0.089	NS
Perforation	--	39±0.0	--	--
Displacement	38.89 ±0.78	38.73 ±0.65	0.619	NS
Correlation between mean of parity of the patients and 3- month complications				
Expulsion	1.67 ±1.63	2 ±1.32	0.670	NS.
Infection	1.6 ±0.89	1.6 ±1.26	1.000	NS
Bleeding	2.27 ±1.1	1.95 ±0.85	0.346	NS
Perforation	--	3±0.0	--	--
Displacement	2.56 ±1.81	3±1.1	0.506	NS

Using: Independent sample t-test; with p-value >0.05 is insignificant

Table (3): Comparison between two groups according to outcome relation with history of previous CS after 3 months.

			Group				p	Sig
			Post placental Group I		Post puerperal Group II			
			N	%	N	%		
Expulsion	History of previous CS	No	3	50.0%	2	22.2%	0.280	NS
		Yes	3	50.0%	7	77.8%		
Infection	History of previous CS	No	1	20.0%	3	30.0%	0.690	NS
		Yes	4	80.0%	7	70.0%		
Bleeding	History of previous CS	No	0	.0%	1	5.3%	0.373	NS
		Yes	15	100.0%	18	94.7%		
Perforation	History of previous CS	No	0	.0%	0	.0%	----	----
		Yes	0	.0%	1	100.0%		
Displacement	History of previous CS	No	2	22.2%	0	.0%	0.108	NS
		Yes	7	77.8%	11	100.0%		

Using: Chi-square test; with p-value >0.05 is insignificant

Table (4) Relation between expulsion at 3 months with parity and previous number of cesarean section in all patients (n=180).

		Expulsion				Chi square test	P value
		Yes (n=15)		No (n=165)			
		N	%	N	%		
Parity	PG	2	13.3%	38	23.0%	8.461	0.076
	One	5	33.3%	17	10.3%		
	Two	4	26.7%	50	30.3%		
	Three	4	26.7%	40	24.2%		
	>three	0	0.0%	20	12.1%		
Previous number of cesarean section	1	8	53.3%	82	49.7%	0.239	0.887
	2	5	33.3%	65	39.4%		
	3	2	13.3%	18	10.9%		
	4	0	0.0%	0	0.0%		
	More 4	0	0.0%	0	0.0%		

Using: Chi-square test; with p-value >0.05 is insignificant

Pre-incisional Oxytocin infusion in elective cesarean section delivery, maternal and neonatal outcome

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Abstract

Background: Best timing for giving prophylactic oxytocin during cesarean section (CS) to prevent post-partum hemorrhage (PPH) is still a debatable issue.

Objectives: Assess maternal and neonatal effects of starting prophylactic oxytocin infusion just before uterine incision during CS.

Methods: This study is a randomized controlled trial, evaluating best timing of oxytocin administration in cesarean deliveries as regard amount of intraoperative and postoperative estimated maternal blood loss, also evaluated change of pre-operative to post-operative hemoglobin levels, intraoperative maternal nausea and vomiting and immediate postpartum neonatal condition. One hundred and fifty patients had done pre-labor cesarean section, half of participants received oxytocin immediately before uterine incision and the other half received oxytocin in the third stage of labor. The study hypothesized that administering oxytocin immediately before uterine incision, resulted in less overall maternal blood loss, better maternal and neonatal outcome.

Results: Results were pooled, mean, standard deviation, P value and 95% confidence intervals (CI) were calculated. There was a significant reduction in the need for additional uterotonics and also reduced intra-operative and postoperative blood loss and need for blood transfusion, when oxytocin was given immediately before uterine incision versus after fetal delivery.

Conclusion: Immediately pre-incisional oxytocin infusion was superior to post-placental delivery oxytocin infusion as regard additional use of ecbolics in elective cesarean sections, further studies with large sample sizes are needed for further evaluation of other maternal and neonatal parameters.

Keywords: Oxytocin, cesarean section, postpartum hemorrhage, maternal outcome, neonatal outcome.

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Introduction

Inability to have an efficient uterine contractions post-delivery, accounts for 1 every 40 deliveries and accounts for approximately seventy-five percent of postpartum hemorrhage

(PPH) [1]. This is one of the uppermost five reasons for maternal mortality [2].

In the developing countries, around 1.2% of births are complicated by PPH and around three percent of these ladies died [3]. Worldwide, PPH happens 8.7 million times and causes death in 44,000 to 86,000 yearly [3][4][5].

Blood loss and blood transfusion are major problems of CS [2, 6]. The huge hyper-perfusion of uterus (750 mL/min) in third trimester of gestation which is around (10–12% of cardiac output) [1] clarifies the high blood loss during CS (500–750 mL) [7].

In developing countries the rate of CS is high, and Females who deliver by CS are at a greater possibility for postpartum hemorrhage than those who deliver by vaginal delivery [8, 9] [10,11].

The surgeons often undervalued the amount of blood lost during CS [12]. Undervaluing blood loss during CS make ladies at danger of uncorrected blood loss and uncorrected anemia, poor wound healing, surgical site infection (SSI), fatigue, and physical debility [13, 14].

PPH is considered when the amount of blood loss is ≥500 mL after vaginal birth or ≥1000 mL after cesarean delivery [15]. Oxytocin is routinely given in cesarean and vaginal deliveries during the third stage of labor in the United States [15].

The current WHO recommendations, published in 2018, for prevention PPH is 10 IU of intravenous or intramuscular oxytocin for preventing PPH for all deliveries [16].

As the evidence is still lacking, as regards the best timing of oxytocin infusion in cesarean section, this raised the need to perform this randomized controlled study.

Patients and methods

Ethical committee approval of Al Gazeerh hospital was obtained before the study start (Ethical committee approval number 0024886 NTR), also obtaining an informed consent before enrollment of each woman accepting to participate in the study was done, after complete explanation of the procedure to the participant woman.

This randomized controlled trial included one hundred and fifty patients, who were planned to deliver by elective cesarean section in Al Gazeerh hospital, Giza, Egypt. The study started in December 2017 and ends in January 2022. Patients were assigned to one of 2 groups; group A (study group), 75 patients were infused by oxytocin immediately before uterine incision and group B (control group), 75 patients were infused by oxytocin in the third stage of labor.

Pregnant women age 20 years or older, with average BMI (not including those with morbid obesity) and undergoing elective cesarean section at gestational age 37-41 weeks were included in the study. Women with anemia (hemoglobin < 10 gms%), coagulopathies, gestational or chronic medical disorders, anticoagulant therapy, risks of thrombo-embolism, and/or post-partum hemorrhage, uterine over distension (fetal macrosomia, multiple pregnancy, polyhydramnios), history of antepartum hemorrhage, placental abnormalities as previa or accrete were excluded from the study.

All patients underwent full history taking, thorough clinical examination, obstetric ultrasound and routine preoperative laboratory investigations. Neonatal evaluation after delivery included recording APGAR score, neonatal weight, incidence of transient tachypnea of newborn (TTN), respiratory distress syndrome (RDS), neonatal hypoglycemia and NICU admission.

Randomization and blinding was done through a computer generated model, and a closed-envelope system was implemented where subjects were divided into 2 groups; Group A and B as the ward nurse opened the envelope after the women were enrolled,

while the participant and outcome assessor were blind.

This study evaluated best timing of oxytocin administration in cesarean deliveries as regard amount of intraoperative and postoperative estimated and quantitative maternal blood loss, also evaluated change of pre-operative to post-operative hemoglobin levels, intraoperative maternal nausea and vomiting and neonatal immediate postpartum condition.

Uncomplicated CS was defined when the duration of the CS was < 45 min with < 750 mL intra-operative blood loss, no bladder, ureteral, intestinal, or uterine artery injuries, and no uterine atony [17].

Intervention

All patients received regional spinal anesthesia. One bag of 500 ml 0.9% NaCl (normal saline) with 10 units of Oxytocin (Syntocinon, NOVARTIS Pharmaceutical, Egypt) (Oxytocin solution) was hung by the anesthetist at an infusion rate 10 ml/min immediately before uterine incision in group A, this amount of fluid is part of standard of this group of patients care.

A transverse uterine incision was done in LUS, then the amniotic fluid (AF) was drained by suction to minimize soaking of the towels and gauzes by the AF as possible. After draining of the AF and delivery of the fetus, the umbilical cord was clamped and placenta was delivered. Group B patients were infused by One bag of 500 ml 0.9% NaCl (normal saline) with 10 units of Oxytocin (Syntocinon, NOVARTIS Pharmaceutical, Egypt) (Oxytocin solution) at an infusion rate 10 ml/min, this amount of fluid is part of standard of this group of patients care as an active management of the third stage of labor to avoid uterine atony [18-20].

After delivery of the placenta, the uterus was exteriorized and the uterine incision was repaired in 2 layers using no. 1 absorbable polyglycolic sutures (Vicryl-Ethicon, NJ, USA) [17].

After excluding any adnexal abnormalities, the uterus was entered back to the abdominal cavity, peritoneal toilet was done and rectus sheath was repaired after making sure that the uterine tone was retained, (considering it to be of delayed tone if not retained at start of rectus sheath repair). Additional uterotonics, ergometrin (Methergin 0.2 mg ampules, NOVARTIS Pharmaceutical, Egypt) intramuscular injection and/or misoprostol (Misotac 200mcg tablets, SIGMA Pharmaceutical, Egypt) given intrauterine, were used if retaining uterine tone was delayed, most of these cases needed continuing postpartum uterotonics.

Postoperative blood samples were taken from participants 6 hours after delivery and or before discharge (48 hours after delivery) to measure hemoglobin and hematocrit values.

Intraoperative blood loss was obtained through measuring the volume of blood in the suction machine reservoir and weighing the swabs (surgical towels) as soon as possible. The weights of dry swabs were subtracted from the weights of swabs used during the operation. The weight of swabs found in grams was translated to ml by using blood density (1.050 g/ml) [21].

Postoperative blood loss in the first and after 24 hours was measured by subtracting intraoperative blood loss from total blood loss. Total blood loss was measured using pre and postoperative hematocrit values, by multiplying the calculated pregnancy blood volume by percentage of blood volume lost.

- Pregnancy blood volume = (0.75 × {[maternal height (inches) × 50] + [maternal weight in pounds × 25]})
- Percent of blood volume lost = ({predelivery HCT − postdelivery HCT}/ predelivery HCT)
- Total blood loss = pregnancy blood volume × percent of blood volume lost [22].

Outcomes

The primary outcome measures were total blood loss (both estimated blood loss and quantitative blood loss) after completing the surgery and incidence of intraoperative or postoperative nausea and or vomiting (that could occur from early use or excessive uterotonic drugs). The secondary maternal outcome measures included incidence of primary postpartum hemorrhage (women who lose 1000 milliliters or more blood from cesarean delivery), need for blood transfusion (if hemoglobin level is below 7 g/dl or there is acute blood loss), unacceptable change in pre-operative to post-operative hemoglobin levels in the immediate 24 hours post-surgery (average post-cesarean drop in hemoglobin was 1.52±1.27 gm/dl and drop in hematocrit was 5.49±4.1% [23]) and neonatal condition (incidence of transient tachypnea or respiratory distress of newborn and neonatal Intensive care unit admission).

Sample size justification

Sample size calculation was done using the comparison of total intraoperative blood loss between women undergoing elective Cesarean delivery treated with prophylactic oxytocin infusion before uterine incision and treated with conventional oxytocin infusion. Accordingly, we calculated that the minimum proper sample size was 66 mothers in each group to be able to reject the null hypothesis with 80% power at $\alpha = 0.05$ level using Student's t test for independent samples. Sample size calculation was done using PS Power and Sample Size Calculations Software, version 3.1.2 for MS Windows [24]. Accounting for possible withdrawal after randomization, we increased each group to 75 women in each group (Figure I).

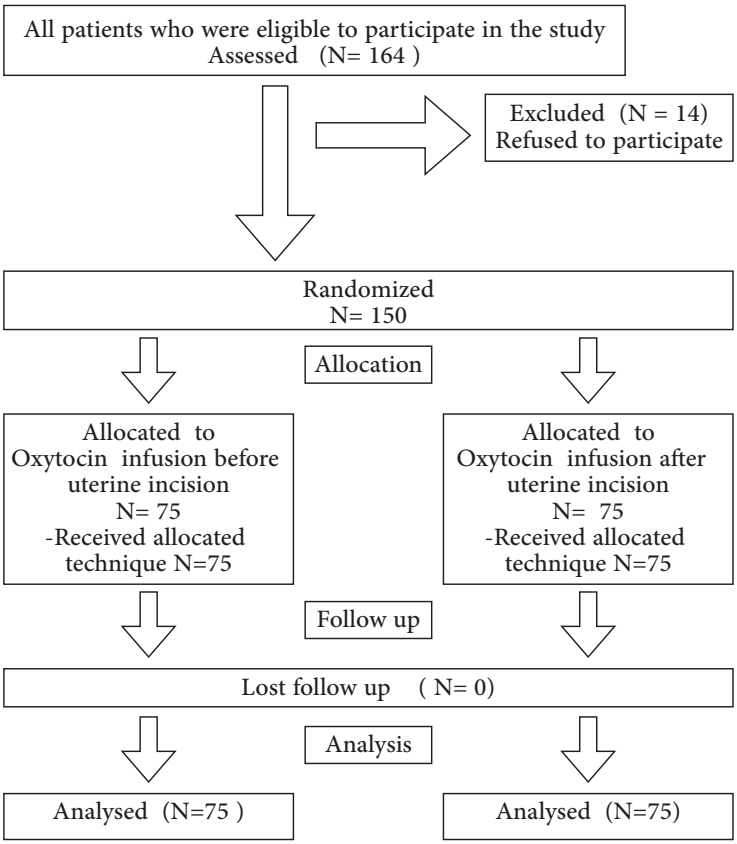

Figure I: Consort flow diagram

Statistical analysis

Data was coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired t test (Chan, 2003a). For comparing categorical data, Chi square (c2) test was performed. Exact test was used instead when the expected frequency is less than 5 (Chan, 2003b). P-values less than 0.05 were considered as statistically significant [25] [26].

Results

One hundred and fifty pregnant females, planned to terminate their pregnancy by elective cesarean section, participated in the study and were divided into two equal groups. Table I and II show the baseline characteristics of the studied groups, there were no significant difference in the baseline terms as regard age, education, profession, residence and gravidity (p-value > 0.05). Indications of cesarean section showed no significant differences between both groups, with repeat lower segment cesarean section being the commonest indication in both groups.

As regard intraoperative findings, figure II shows incidence of intraoperative nausea and vomiting in both groups, being more in group A (cases), but with no significant statistical difference between both groups (p-value; 0.24) (Table III).

Additional uterotonics (ergometrin and prostaglandins) were used if retaining uterine tone was delayed till starting rectus sheath repair, only 8 cases of group A showed delayed retaining uterine tone, while 15 cases of group B showed delayed retaining of uterine tone (Figure IV). This was reflected on use of additional intraoperative and postoperative uterotonics, in both groups, where only 12 cases in group A while 18 cases in group B need intraoperative additional uterotonics (Figure V) and 15 cases in group A while 28 cases in group B need postoperative uterotonics (Figure VI) with a statistical significant difference between both groups (p-value; 0.019) (Table III and Table IV).

As regard intraoperative blood loss, 14 cases in group A while 18 cases in group B showed excess intraoperative blood loss, this was reflected objectively by measuring postoperative hemoglobin and comparing it to preoperative measurements (Figure III). 2 cases in group A showed signs of postpartum hemorrhage, while 5 cases in group B showed signs of postpartum hemorrhage (blood loss more than 1000 cc) (Figure VII). Unacceptable drop in pre-operative to post-operative hemoglobin levels in the immediate 24 hours post-surgery being more than 1.52±1.27 gm/dl [24] was observed in 8 cases of group A while being observed in 12 cases of group B (Figure VIII) (Table III and Table IV).

2 cases in group A need blood transfusion, while 3 cases in group B need blood transfusion. Only one case in the study, being in the control group (group B) necessitated doing cesarean hysterectomy as the patient was 40 years old, multigravida, with history of repeat LSCS, showed delayed retaining uterine tone and excess intraoperative blood loss and had been counseled preoperatively for doing hysterectomy if there is surgical risk on maintaining the uterus (Table III).

Table V showed data of neonatal outcome in both groups, with no statistically significant difference between both groups as regard neonatal APGAR scores and incidence of TTN or RDS. 5 cases in group A need NICU admission while 7 cases in group B need NICU admission (Figure IX).

Table I: Base line terms between both groups (cases and control)

	Cases		Control		
	Mean	Standard Deviation	Mean	Standard Deviation	P value
Age	30.81	5.69	30.12	5.23	0.439
Termin Gest age	38.25	1.07	38.12	0.84	0.396

Table II: Base line terms between both groups (cases and control)

		Cases		Control		P value
		Count	%	Count	%	
Educ.	**Illiterate**	18	24.0%	10	13.3%	0.299
	Educated	19	25.3%	17	22.7%	
	Graduate	36	48.0%	45	60.0%	
	Postgraduate	2	2.7%	3	4.0%	
Occup	**Occupied**	25	33.3%	32	42.7%	0.239
	Unoccupied	50	66.7%	43	57.3%	
	Rural	18	24.0%	20	26.7%	0.707
	Urban	57	76.0%	55	73.3%	
Gravidity	**Multipara**	55	73.3%	45	60.0%	0.083
	Primigravida	20	26.7%	30	40.0%	
Indication for CS	**Breech**	6	8.0%	9	12.0%	0.779
	contracted pelvis	7	9.3%	3	4.0%	
	delayed conception	7	9.3%	6	8.0%	
	failed vaginal delivery	4	5.3%	4	5.3%	
	Low liquor	5	6.7%	8	10.7%	
	Macrosomia	1	1.3%	4	5.3%	
	on demand	7	9.3%	7	9.3%	
	previous cs	35	46.7%	31	41.3%	
	small for gestational age	3	4.0%	3	4.0%	

Table I: Base line terms between both groups (cases and control)

		Cases		Control		P value
		Count	%	Count	%	
intra operative nausea and vomit	**Yes**	32	42.7%	25	33.3%	0.239
	No	43	57.3%	50	66.7%	
Intraoperative adhesions	**Yes**	9	12.0%	13	17.3%	0.356
	No	66	88.0%	62	82.7%	
Retain uterine tone	**Immediate**	67	89.3%	60	80.0%	0.113
	Delay	8	10.7%	15	20.0%	
use of other intraop uterotonics	**Yes**	12	16.0%	18	24.0%	0.221
	No	63	84.0%	57	76.0%	
Intraop blood loss	**Accepted**	61	81.3%	57	76.0%	0.425
	Excess	14	18.7%	18	24.0%	
Blood transfusion	**Yes**	2	2.7%	3	4.0%	1
	No	73	97.3%	72	96.0%	
Hystrectomy	**Yes**	0	0.0%	1	1.3%	1
	No	75	100.0%	74	98.7%	

Table I: Base line terms between both groups (cases and control)

use of other post op uterotonics	**Yes**	**15**	**20.0%**	**28**	**37.3%**	**0.019**
	No	60	80.0%	47	62.7%	
unacceptable	**Accepted**	67	89.3%	63	84.0%	0.337
	Excess	8	10.7%	12	16.0%	
change of pre-post op hb	**Yes**	2	2.7%	5	6.7%	0.442
	No	73	97.3%	70	93.3%	

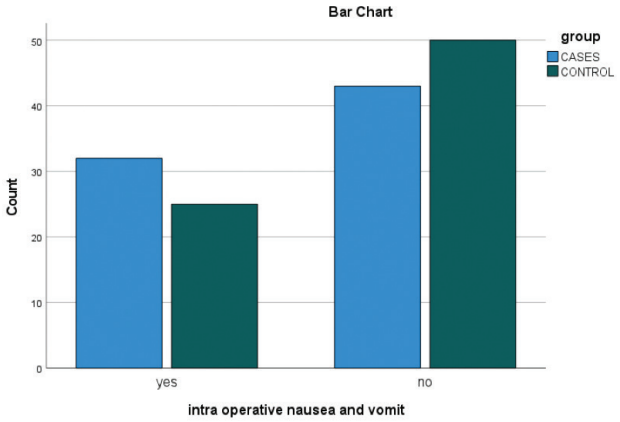

Figure II: Intra operative nausea and vomiting in the study groups

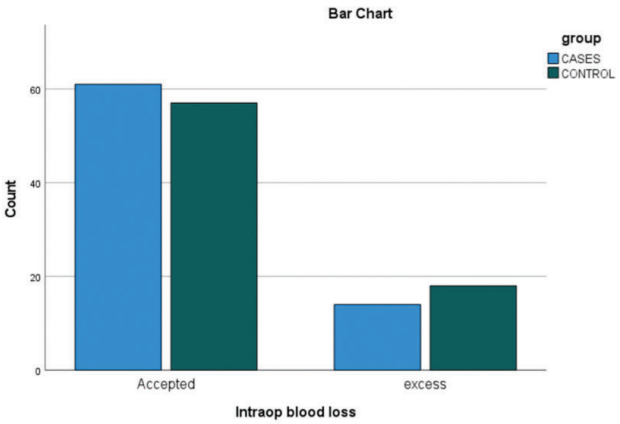

Figure III: Intra operative blood loss in the study groups

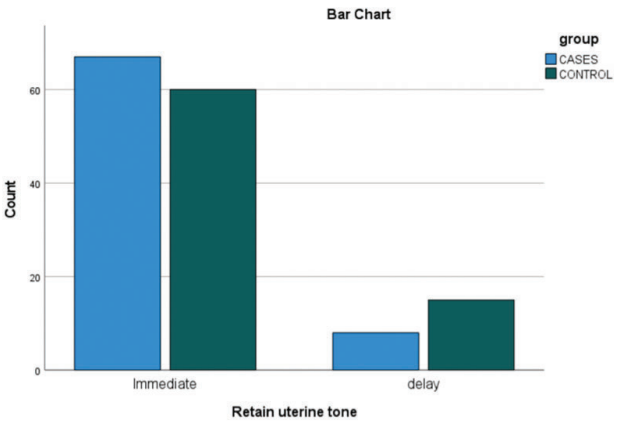

Figure IV: Retaining uterine tone in the study groups

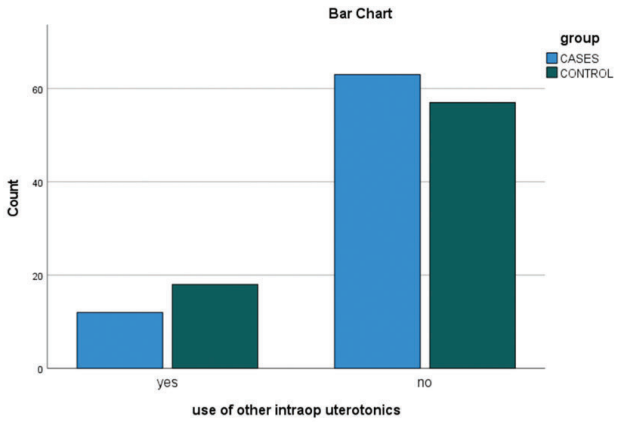

Figure V: Use of intra operative additional uterotonics in study groups

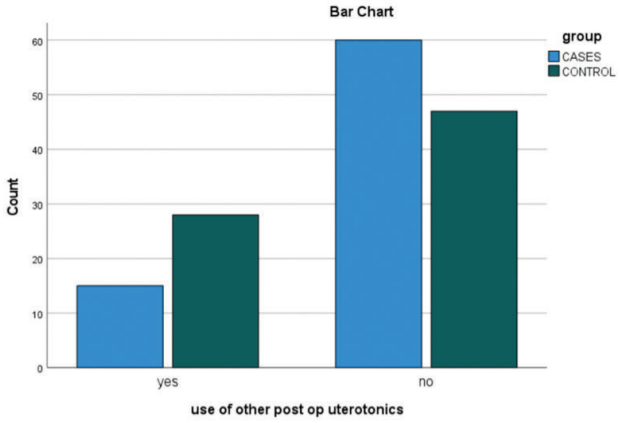

Figure VI: Use of postoperative additional uterotonics in study groups

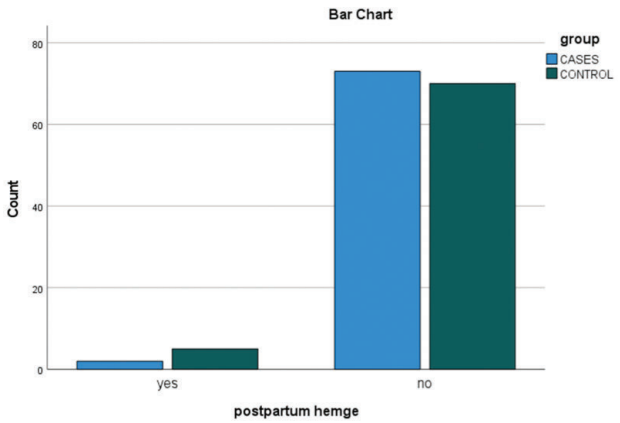

Figure VII: Postpartum hemorrhage in the study groups

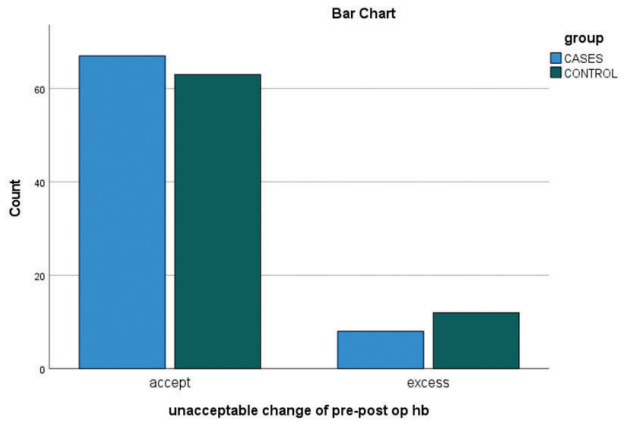

Figure VIII: Preoperative to postoperative change in hemoglobin in the study groups

Table V: Neonatal outcome

		Cases		Control		P value
		Count	%	Count	%	
TTN	**Yes**	2	2.7%	3	4.0%	1
	Absent	73	97.3%	72	96.0%	
RDS	**Yes**	3	4.0%	5	6.7%	0.719
	No	72	96.0%	70	93.3%	
ICU ADMIT >24 HRS	**Yes**	5	6.7%	7	9.3%	
	No	70	93.3%	68	90.7%	0.547

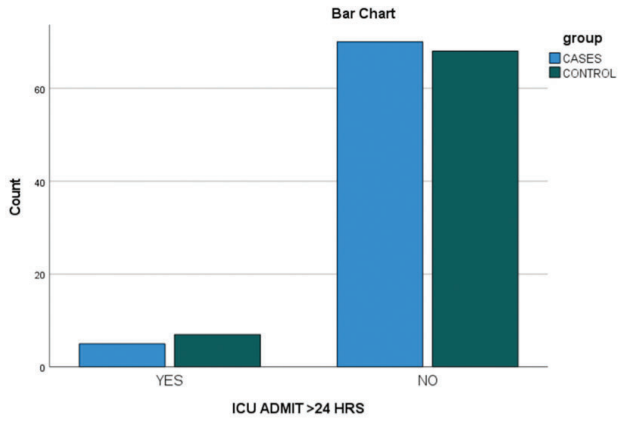

Figure IX: NICU admission in the study groups

Discussion

Prophylactic oxytocin at any dose with different regimens decreases both postpartum hemorrhage (PPH) and need for therapeutic uterotonics. Active management of the third stage of labor has been shown to reduce the risk of postpartum hemorrhage (PPH) greater than 1000 ML. Prophylactic uterotonics, as regard dose, timing and route of administration vary across the globe and may have an impact on maternal and neonatal outcomes.

Oxytocin is the routinely used and effective uterotonic drug, but still regimens of prophylactic oxytocin infusion to avoid peripartum hemorrhage in elective pre-labor cesarean section (CS) differ in various guidelines. Randomized controlled double-blind trials supported by expert opinions mainly and studies with low evidence rates are still the main source of evidence in this issue. Extra use of Oxytocin must be taken into consideration, especially among female patients with any pre-existing heart conditions. One of the important research priorities is the identification of the optimal regimen of intravenous oxytocin at caesarean section, as still there is no consensus on the best timing for prophylactic oxytocin administration during CS to prevent post-partum hemorrhage.

ACOG indorses postponing elective CS at spontaneous labor pains to let oxytocin secretion, and its helpful action on epithelial sodium channels (ENaC), which prepares the lung for gas exchange, and decreases the neonatal respiratory morbidity [27]. In addition, Abdelazim et al. reported significant decrease in neonatal respiratory morbidity when the elective CS is made at ≥ 39 weeks of gestation [27]. Blood loss > 750 mL is reflected as Class-I hemorrhage, in which minimal physiological changes happen [17, 28].

In a study done by Maria Torloni et al. 2021, nine databases were searched to identify relevant randomized controlled trials (RCT). They found no statistically significant differences between oxytocin given before versus after fetal delivery were found. There was a significant decrease in using additional uterotonics when oxytocin was administered immediately before uterine incision versus after fetal delivery.

Oxytocin given before fetal delivery significantly reduced intra-operative blood loss but did not change the incidence of blood transfusion. One trial (N = 100) compared prophylactic oxytocin before versus after placental separation and found no significant differences on PPH, additional uterotonics, or nausea/vomiting. There is very limited evidence suggesting no significant differences between prophylactic oxytocin given before versus after placental separation on PPH, need for additional uterotonic, or nausea/vomiting. The overall certainty of the evidence was mostly low or very low due to imprecision [29].

Future studies on larger sample of patients are still needed to expand our understanding and establish long-term safety regarding the pregnancy outcome in using prophylactic oxytocin starting just before fetal delivery. This may have an important impact on lowering hospital stay and a lot of maternal and fetal complications especially in countries with limited economic resources in which cesarean section rates are increasing. The strength point in this study, the consort statement of randomized study was followed. The limitation is the lack of settled data and evidence in the topic of our study.

Conclusions

In women having pre-labor CS, no significant statistical differences between prophylactic oxytocin given before versus after fetal delivery were found as regard the mother nausea/vomiting, incidence of intra-partum or postpartum hemorrhage or blood transfusion, or hysterectomy. Earlier oxytocin administration significantly reduces need for additional uterotonics and may reduce intra-partum and postpartum blood loss.

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Conflict of interest

The author declares no conflict of interest.

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Uterine Rupture in Third Trimester of Pregnancy in a Tertiary Centre: A Descriptive Observational Study

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Abstract

Background: Uterine rupture is a rare but serious obstetric complication that can have an adverse impact on the mother and the fetus.

Methods: This is a cross-sectional study conducted in a tertiary care centre over a one-year period, including all cases with uterine rupture occurring at or after 28 weeks of gestation. We collected demographic data, possible causes, diagnosis, management and feto-maternal outcome.

Results: We had 48 cases of uterine rupture in the study period; 42 cases with a scarred uterus, most commonly cesarean section (CS), and 6 cases with unscarred uterus most commonly due to labour-related causes. Adverse outcome included blood transfusion (n=25), hematoma formation (n=6) bladder injury (n=4) and one mortality. The perinatal death rate was 37.8%. Surgical repair of the uterus was possible in 79.2% of the cases. Those with unscarred uteri had significantly more bleeding and hematoma formation with more risk for blood transfusion than those with scarred uteri. No statistically significant differences in the rate of hysterectomy, bladder injury or perinatal death rate between both groups.

Conclusion: In our population, CS represents the most common cause of uterine rupture followed by labour-related causes. Uterine rupture in an unscarred uterus is associated with more bleeding, hematoma formation and more risk for blood transfusion than scarred uterus group. Surgical repair is possible in most cases. Reducing the rate of CS, optimizing care for women with previous CS and careful management of labour can help to reduce the incidence of uterine rupture.

Keywords: Uterine rupture, cesarean section, placenta percreta, obstructed labour, induction of labour, fundal pressure.

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Introduction

Uterine rupture is the disruption of the uterus during pregnancy or delivery. It can either be a complete rupture if the tear is involving the 3 layers of the uterus; namely (endometrium, myometrium and serosa) or partial

rupture if it doesn't involve all layers. The latter is referred to as uterine dehiscence and is usually an incidental finding in an asymptomatic patient (1).

Complete uterine rupture is a serious potentially life-threatening obstetric emergency with high maternal and fetal morbidity and mortality. The incidence of this complication and the feto-maternal outcome depends on the level of the maternal care women receive and thus has been reported to vary between nations with prevalence tending to be lower in countries classified by the United Nations as developed than the less or least developed countries (2). There is however, limited data on the magnitude of the problem, and more efforts are required to monitor its frequency, causes and management.

In this study, we aimed to evaluate the incidence of uterine rupture in a tertiary care referral centre, identify risk factors, diagnosis, management and feto-maternal outcome of this serious obstetric emergency.

Materials And Methods

This was a cross-sectional study in which we collected data of cases with complete uterine rupture occurring at or after 28 weeks of gestation (when chances of viability would be reasonable in a low resource setting) admitted to the Emergency Unit at the Department of Obstetrics and Gynecology at Cairo University Hospital in the period from 1st of August 2017 till 31st of July 2018. Our department is a tertiary centre providing care for high-risk pregnant women referred from other facilities. Only cases with complete uterine rupture at or after 28 weeks of gestation were included. We excluded cases with dehiscent scar (partial uterine rupture) and cases occurring before 28 weeks of gestation. We collected demographic data, gestational age, cause of uterine rupture, clinical presentation, surgical findings, management as well as feto-maternal outcome. We also collected information on the total number of deliveries during the time period of the study. This study was approved by the Research Scientific and Ethical Committee of the Department of Obstetrics and Gynecology – Cairo University Hospital with ethical approval number (O-170014).

Statistical analysis

Data were statistically reported in terms of mean ± standard deviation, or frequencies and percentages when appropriate. Comparison of numerical variables between 2 study groups was done using the student t-test. Welch's t-test was used if the study groups do not have equal sample size. Comparison of categorical data was performed using Chi square ($\chi 2$) test. p values less than 0.05 was considered statistically significant. All statistical calculations were done using SPSS for IBM (IBM Corp., Armonk, NY, USA).

Results

We encountered 48 cases of complete uterine rupture occurring during the third trimester of pregnancy (at or after 28 weeks of pregnancy) who were admitted to the Emergency Unit at the Department of Obstetrics and Gynecology at Cairo University Hospital, in the period from 1st of August 2017 till the 31st of July 2018.

In this time period, we had 14,994 total deliveries with 8084 vaginal deliveries (53.9 %) and 6910 cesarean deliveries (46.1 %). Thus, the incidence of uterine rupture in our study is 0.3%. The mean age of the patients was 31.75 ± 4.1 years with a mean BMI of 31.9 ± 5.8 kg/m2. All cases were parous apart from two cases were primigravidae and 60.4% of women in the study were para 3 or more. More than half of the women were obese (58.3%). The mean gestational age at which uterine rupture occurred was 35.9 ± 2.45 weeks, with rupture reported as late as 41 weeks. Most cases were term (66.7%) and

33.3 % of cases were preterm. There were 42 cases (87.5%) with scarred uterus while 6 cases only had unscarred uterus (12.5%). Co-morbidities were found in 25% of the cases, the most common of which was hypertensive disorders (12.5%). The baseline characteristics of women with uterine rupture in the third trimester are summarized in Table 1.

Table 1: The baseline characteristics of women with uterine rupture in the third trimester

Variable	Mean ± SD (Range)	N	%
Age (years) :	**31.75 ± 4.1 (19- 40)**	**48**	**100**
• 19-29		12	25
• 30-40		36	75
BMI (kg/m^2)	**31.9 ± 5.8 (24.9 - 60.3)**	**48**	**100**
• Normal weight (18.5-24.9)		2	4.2
• Overweight (25-29.9)		18	37.5
• Obese (>30)		28	58.3
Parity	**2.875 ± 1.36 (0 – 6)**	**48**	**100**
• P0		2	4.2
• P1		5	10.4
• P2		12	25
• P3 or more		29	60.4
Gestational age (weeks)	**35.9 ± 2.45 (31-41)**	**48**	**100**
• Singleton	36 ± 2.6 (31-41)	42	87.5
• Twins	34.6 ± 1.2 (33-36)	6	12.5
• 28-< 36 weeks		16	33.3
• 36 -<38 weeks		18	37.5
• 38-41 weeks		14	29.2
Associated co-morbidity:			
• No morbidity		**36**	**75**
• Co-morbidities (12)		**12**	**25**
• Hypertensive disorders		6	12.5
• Diabetes		4	8.3
• Cardiac condition		2	4.2
• Thyroid disorders		1	2.1
• Hepatic dysfunction		1	2.1
• Hepatitis C virus		2	4.2
• Severe anemia (HB<4)		1	
Placenta accreta		**2**	**4.2**
Inter-delivery interval (years) for parous women with previous CS	**2.7 ± 1.29 (1-8)**	**42**	**87.5**
• Less than 9 months		0	0
• 9-18 months 6		36	14.3
• More than 18 months 36		36	85.7

Mode of previous deliveries: • No previous delivery (primigravida)		2	4.2
• NVD		4	8.3
• Cesarean section		42	87.5
Unscarred uterus		**6**	**12.5**
• Primigravida		2	4.2
• Multigravida		4	8.3
Scarred uterus		**42**	**87.5**
• Previous 1 CS		9	18.7
• Previous 2 CS		13	27.1
• Previous 3 or more CS		20	41.7

**BMI = Body mass index, NVD = normal vaginal delivery , CS= cesarean section*

Causes of uterine rupture in our study population are summarized in Table 2. These included most commonly previous CS followed by labour-related causes (improper use of prostaglandins, obstructed labour, fundal pressure and one case had no identifiable cause apart from grand multiparity and induction of labour), rarely by placenta percreta, previous perforated uterus and abdominal trauma. None of the cases in our study population had a previous history of myomectomy or uterine rupture.

In cases with an unscarred uterus, uterine rupture was most commonly related to labour and only one case occurred during pregnancy due to abdominal trauma, while, in scarred uterus, half of the cases occurred with spontaneous onset of labour and the other half occurred during pregnancy. See Figure 1. In unscarred group, all cases related to labour, had induction with prostaglandins except one case that had spontaneous onset of labour but ended with obstructed labour. All cases received oxytocin. Uterine rupture occurred in the first stage of labour in 2 cases, and in the second stage in 3 cases. Figure 2 demonstrates the timing of uterine rupture in relation to pregnancy and stage of labour.

Table 2: Causes of uterine rupture in the studied population

	Causes of Uterine rupture	**N**	**%**
Scarred uterus (87.5%)	**Previous cesarean delivery**	**39**	**81.2**
	Previous perforated uterus	**1**	**2.08**
	Placenta percreta	**2**	**4.16**
Unscarred uterus (12.5%)	**Labour-related:**	**5**	**10.4**
	• Improper use of Prostaglandins	**2**	**4.16**
	• Assisted fundal pressure	**1**	**2.08**
	• Obstructed labor	**1**	**2.08**
	• No identifiable cause apart from high parity and induction of labour (P5)	**1**	**2.08**
	Trauma	**1**	**2.08**

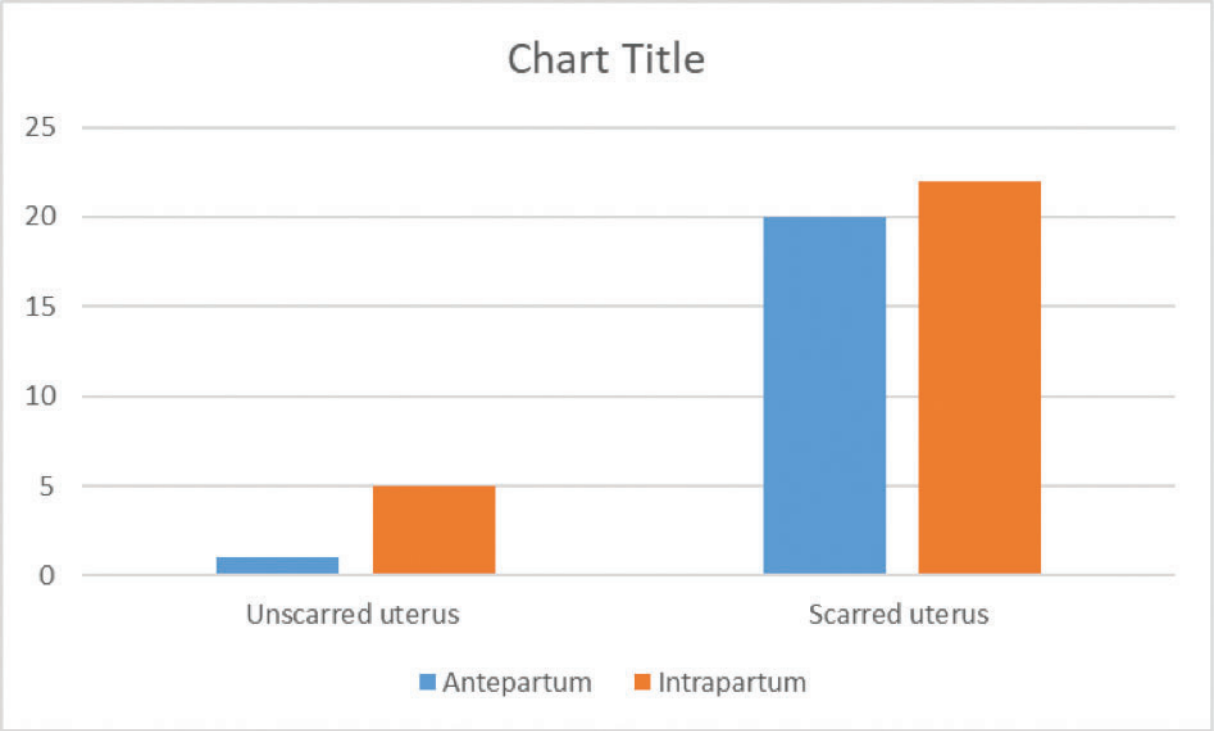

Figure 1: Onset of uterine rupture in relation to labour pains in scarred and unscarred uterus

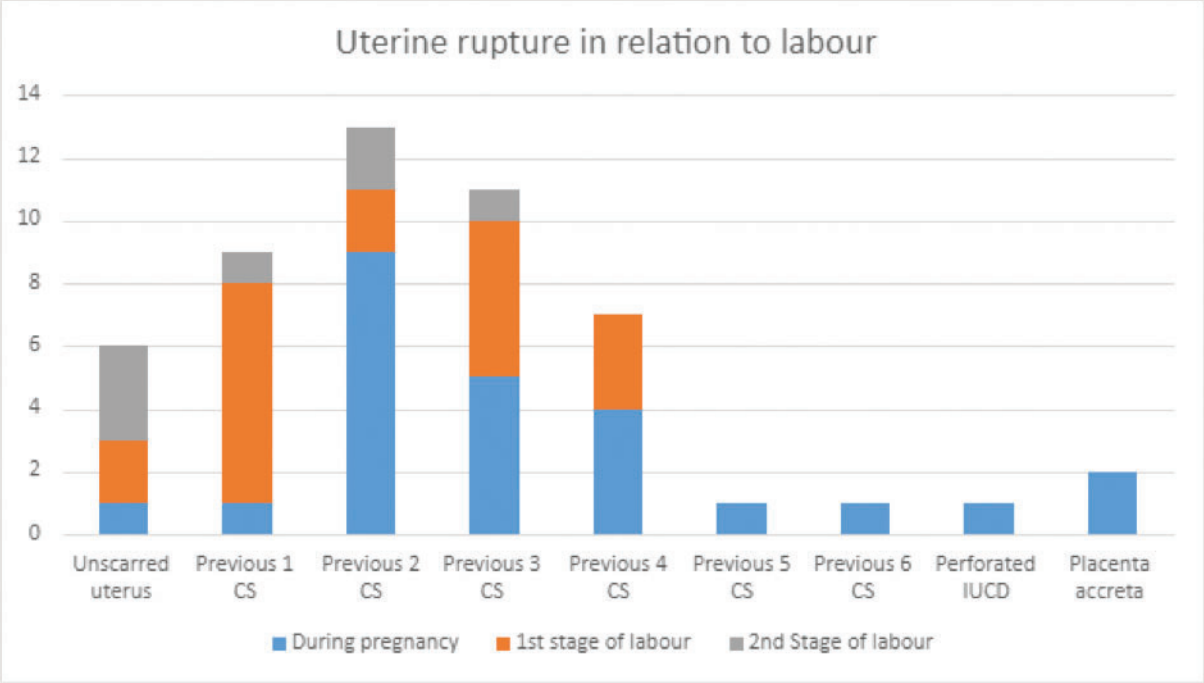

Figure 2: Timing of uterine rupture in relation to pregnancy and stage of labour

The most common presenting symptom was abdominal pain (68.75%) followed by vaginal bleeding (20.8%). However, 5 cases did not have significant symptoms. These cases had previous uterine scar (two cases had previous 3 CS presented at 38 weeks, one case had previous 4 CS and presented at 36weeks, another case had previous 5 CS presented at 37 weeks for delivery and one case with previous 2 CS was diagnosed after vaginal delivery during digital exploration of the uterus). Two cases in the unscarred uterus group were diagnosed after delivery during the management of traumatic postpartum hemorrhage. Table 3 shows clinical presentation of uterine rupture. Ultrasonography confirmed the diagnosis by visualization of the fetus outside the uterus. This was documented in 9 cases and in 2 cases the rupture was suspected by the ultrasound from the presence of hematoma.

Table 3: Clinical presentation of uterine rupture

Symptoms	N	Percentage
Abdominal pain	33	68.75
Vaginal Bleeding	10	20.8
Hypovolemic Shock	9	18.75
Asymptomatic	5	10.4
Vaginal bleeding	4	8.3
Abnormal CTG	4	8.3
Failure to progress	4	8.3
Loss of presenting part	2	4.2
Cessation of contractions	2	4.2

The diagnosis was confirmed in all cases intraoperatively. Pfannenstiel incision was used in 41 cases (85.4%) while midline incision was used in 7 cases (14.6%). In cases with a scarred uterus, the site of uterine rupture was at the site of previous CS scar except in 3 cases; one case had rupture in the posterior uterine wall and two other cases had rupture in the upper uterine segment; due to perforated intrauterine contraceptive device (IUCD) and the other due to previous hysterotomy. Figure 3 demonstrates uterine rupture at the site of previous CS scar in a woman with previous CS with intact amniotic membrane.

In cases with an unscarred uterus, uterine rupture involved the lower uterine segment in all cases. Surgical repair of the uterus was possible in 38 cases (79.2%); however, 10 cases had hysterectomy (20.8%). Figure 4: Total hysterectomy specimen in women with unscarred uterus showing lateral tear extending from cervix upwards. The mean estimated blood loss (EBL) was 1442.7 ± 753.7 ml (300-3800 ml) and the mean hospital stay 4.3 ± 2.1 (2-11). Table 4 shows operative findings and surgical procedures.

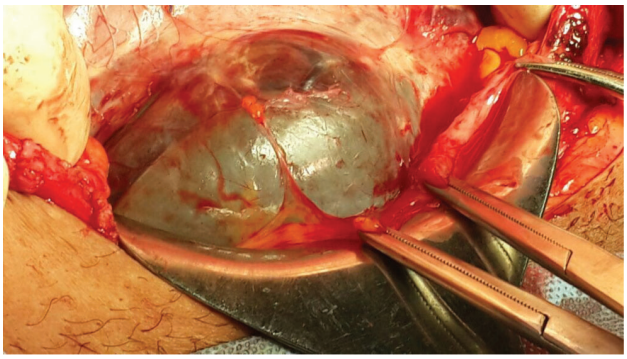

Figure 3: Uterine rupture at the site of previous cesarean scar in a woman with previous CS with intact amniotic membrane

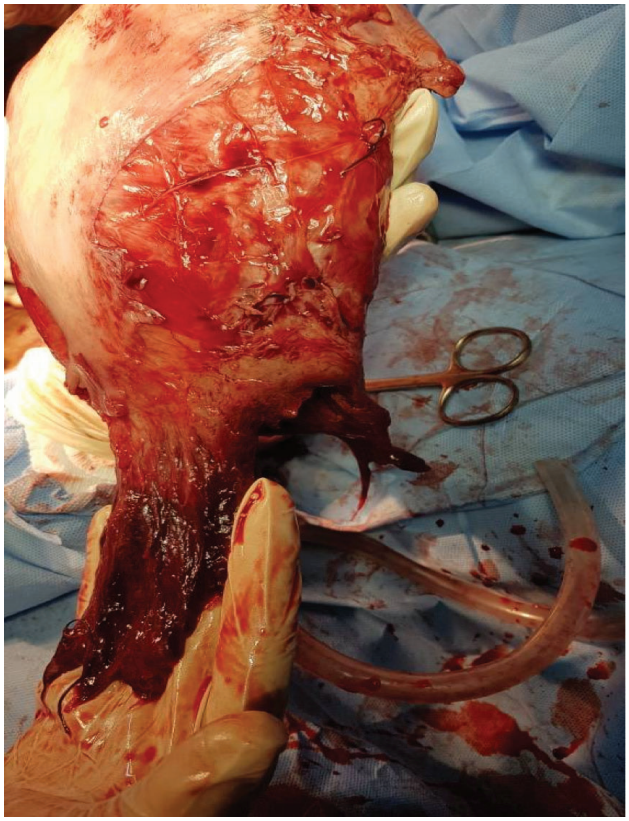

Figure 4: Total hysterectomy specimen in women with unscarred uterus showing lateral tear extending from cervix upwards

Table 4: Surgical findings and procedures:

Operative findings	Number	Percentage
Incision:		
• **Midline incision**	7	14.6
• **Pfannenstiel incision**	41	85.4
Site of the Uterine rupture		
• Upper uterine segment	2	4.1
• At site of CS scar (Extensions were seen in 7 cases)	39	81.3
• LUS	6	12.5
• Posterior uterine wall (scarred uterus)	1	2.1
Ruptured membranes	28	58.3
Intact membranes	17	35.4
Extrauterine fetus	15	31.2
Extrauterine placenta	11	22.9
Surgical management		
• **Repair of rupture uterus**	38	79.2
• **Hysterectomy**	10	20.8
• Additional procedures:		
o Internal iliac artery ligation	1	2.1
o Bilateral tubal ligation	1	2.1

The adverse maternal outcomes included blood transfusion in 25 cases (52.1%), bladder injury in 4 cases (8.3%), hematoma formation in 6 cases (12.5%). Nine cases were transferred to the ICU (18.75%). One mortality occurred due to shock with multisystem organ failure (2.5%). We evaluated the fetal outcome in singleton pregnancies after excluding twin pregnancies (n=6) and cases with intrauterine fetal death (IUFD) due to associated co-morbidities (n=6). The mean fetal weight was 2744.86 ± 710.54 (750 –4000 gm). Out of 37 singleton pregnancies, 12 fetuses were born dead (32.4%) and 25 fetuses were born alive (67.6%). Apgar score in 1 min was less than 7 in 13 cases (52%). NICU admission was required in 5 of the liveborn fetuses (20%), 3 were discharged and 2 died. Thus, the perineatal death rate was 37.8%. Table 5 demonstrates the feto-maternal outcome.

Feto-maternal outcome for the scarred uterus group was compared to that of the unscarred uterus group. The unscarred uterus group was associated with significantly more blood loss, more risk for hematoma formation and more risk of blood transfusion (but the latter was not statistically significant). There were no cases of bladder injury in the unscarred uterus group compared to 4 cases in the scarred uterus group, but the difference was not statistically significant. No statistically significant difference in rate of hysterectomy, NICU admission and perinatal death rates between both groups. Both groups showed no statistically significant differences in baseline characteristics including age, gestational age and BMI. See Table 6 Feto-maternal outcome in scarred vs unscarred uterus group.

Table 5: Feto-maternal outcome (Fetal outcome –excluding cases of IUFD due to associated morbidities, and cases with multiple pregnancies)

Feto-maternal outcome	Mean ± SD (Range)	Number	Percentage
Maternal outcome			
EBL (ml)	1442.7 ± 753.7 ml (300-3800 ml)	48	100
Blood transfusion		25	52.1
Bladder injury		4	8.3
Hematoma		6	12.5
ICU admission		9	18.75
Hospital stay (days)	4.3 ± 2.1 (2-11)		
Readmission		0	0
Mortality		1	2.1
Fetal outcome			
Fetal weight	2744.86 ±710.54 (750-4000 gm)	37	100
Live born		25/37	67.6
Dead		12/37	32.4
Perinatal death		14/37	37.8
NICU admission		5/25	20
Apgar in 1 min <7		13/25	52
Apgar in 5 min <7		2/25	8

Table 6: Feto-maternal outcome in unscarred vs scarred uterine rupture

	Unscarred uterus (n=6)	Scarred uterus (n=42)	p value
Age	31.5 ± 7.8	31.8 ± 3.45	0.93
Gestational age	37 ± 3.8	35.7 ± 2.31	0.45
BMI	31.2 ± 4.3	32.0 ± 6.026	0.713
EBL (ml)	1875 +/-534.5	1369.048 ± 747.27	0.045
Blood transfusion	6 (100 %)	19 (45.2%)	0.12
Bladder injury	0	4 (9.52%)	0.43
Hematoma	3 (50%)	3 (7.1%)	0.001
Hysterectomy	1 (16.7%)	9 (21.4 %)	0.78
NICU admission	0	5 (20%)	0.593
Perinatal death rate	1(out of 4 cases) (25%)	13/33 (39.39%)	0.575

Discussion

Uterine rupture is a potentially life-threatening complication that occurs between 1 and 280–12,000 births (3, 4). The incidence of uterine rupture in the current study was 0.3%. We expect this to be higher than the actual community-based incidence given that the data were collected from a tertiary care centre with referral of high-risk cases. The prevalence of uterine rupture was found in a WHO systematic review to be much lower in community-based (median 0.053, range 0.016-0.30%) than in facility-based research studies (0.31, 0.012-2.9%). The incidence of uterine rupture in our study is within the reported range for developed countries where the incidence was reported to be in the range from 1.9 to 38 cases per 10,000 births (0.019 - 0.38%) (3,4). The incidence reported in other parts of Africa is much higher (5,6,7).

In our study, 87.5 % of uterine rupture cases occurred in the scarred uterus while 12.5% occurred in an unscarred uterus. This is similar to the study conducted in USA by Finnsdottir et al. in which rupture occurred in 82.1% and 17.3% respectively (8). In developed countries, the uterine rupture was found to occur most commonly due to previous CS, while in developing countries, it was found to occur most commonly in the unscarred uterus (2,9).

Most cases of uterine rupture in our study were attributed to previous uterine scar, most commonly CS. In scarred uterus group, two cases had uterine rupture due to placenta percreta which has been reported as a rare cause of uterine rupture in all trimesters (10,11, 12, 13, 14, 15). It represents 5 % of the placenta accreta spectrum (16). Previous uterine surgery has been identified as the most important risk factor for placenta accreta (11), although it has been reported in the unscarred uterus (17).

One case in the scarred uterus group had a history of previous intrauterine contraceptive device (IUCD) perforation. Since uterine rupture, in this case, occurred at the upper uterine segment (fundus) rather than at site of previous cesarean scar, the cause was attributed to the history of perforated uterus rather than to the CS. The uterine fundus has been reported as the commonest site of uterine perforation with several reports described uterine rupture after perforation in an unscarred uterus (18, 19;20, 21).

In women without uterine scar, the uterine rupture was mostly related to labour with causes including improper use of

prostaglandins (n=2), fundal pressure during the second stage of labour (n=1), obstructed labour (n=1) and no cause was identified in one case apart from high parity and induction of labour (n=1). Assisted fundal pressure has been reported as a cause of uterine rupture in previous studies (22,23). Obstructed labour due to cephalopelvic disproportion is a major factor in uterine rupture (24).

Uterine rupture in the unscarred uterus group mostly occurred intrapartum, with only one case occurred during pregnancy as a result of abdominal trauma. This is unlike scarred uterus group in which cases were almost equally divided between labour and antepartum period. This agrees with the findings of the study by Schrinsky and Benson (25). Almost half of the uterine rupture in our study, occurred during or after the second stage of labour which is similar to the findings of the study by Miller et al who described a series of women with primary uterine rupture (26).

In our study, 75% of cases were above 30 years old. This agrees with the study by Ezechi et al in which the incidence was found highest in patients aged 30-34 years and lowest in those aged 25-29 years (27). Only 2 cases in our study were primigravidae and 60.4 % of cases were para 3 or more. Multiparity and particularly grand multiparity is considered a high risk for uterine rupture (23).

The most common clinical presentation in our study was acute abdominal pain. This agrees with the study by Savukyne et al., 2020 (28). Other presentations included vaginal bleeding, shock, CTG abnormalities, cessation of uterine contractions and loss of the presenting part. It has been reported that CTG changes (prolonged, persistent fetal bradycardia) are the most consistent early sign of uterine rupture according to Revicky et al., 2012. (29). However, we encountered 5 cases with no significant symptoms. Silent or asymptomatic uterine rupture has been described in the literature in a few case reports (30,31). Thus, clinicians must remain watchful for signs and symptoms of uterine rupture and a high index of suspicion is necessary for diagnosis to ensure prompt management. Ultrasound was diagnostic by finding the fetus outside the uterus or by the presence of hematoma. Three cases were diagnosed after delivery of the placenta; one in scarred uterus with previous 2 CS in which uterine rupture was diagnosed with digital exploration of the uterine cavity after delivery of the placenta and two cases in unscarred uterus during management of primary postpartum haemorrhage following vaginal deliveries.

In most cases of the scarred uterus, the uterine rupture occurred at the site of the previous cesarean scar except in 2 cases occurred at the upper uterine segment (one due to previous history of uterine perforation and another one due to previous history of hysterotomy). Another case had a rupture in the posterior uterine wall with intact CS scar. This case was para 4, had previous 2 CS and was in second stage of labour. There are few case reports describing rupture of the posterior uterine wall, the exact mechanism of which is unknown but could be due to element of obstruction associated with strong inelastic scar (32,33,34).

Surgical repair of the uterine rupture was possible in most cases (79.2%) and hysterectomy was done in 20.8 %. The mean estimated blood loss was 1442.7 ± 753.7 ml (300-3800 ml). The adverse outcomes included blood transfusion which was required in 25 cases, hematoma (n=6) and bladder injury (n=4). The perinatal death rate related to uterine rupture was 37.83 % (excluding cases with IUFD due to associated co-morbidities, and multiple pregnancies). The mortality rate in our study was 2.1% which is similar to the study by Fitzpatrick et al., 2012 and Guise et al., 2004 (3,4), but the stillbirth rate was higher (32.4%) compared to that reported by Fitzpatrick et al.2012 (12%) (3).

Cases with an unscarred uterus were found to

have statistically significant more EBL and more hematoma formation. The rate of blood transfusion was higher in the unscarred uterus group (but was not statistically significant). This is similar to the results of studies by Gibbins et al. 2016 (35) and Finnsdottir et al. (8). The lower EBL in scarred uterus group can be explained by the relatively reduced vascularity at the scar site.

On the other hand, bladder injury was encountered only in 4 cases in the scarred uterus group with no cases in the unscarred uterus group. This is unlike the study by Finnsdottir in which they found a higher risk for bladder injury in unscarred uterus (8). The bladder adhesions in cases with previous CS explain the increased risk of bladder injury in scarred uterus group. There was no significant difference in the rate of hysterectomy between scarred and unscarred uterus group. This is unlike the results of the study by Gibbins et al., 2016, and Finnsdottir et al, in which risk for hysterectomy was higher in the unscarred uterus group (35,8). In the series of Miller et al,in which primary uterine rupture was studied, the rate of hysterectomy was only 10% rate (which is similar to the rate of hysterectomy in women without uterine scar in our study 16%) (26). The neonatal outcomes did not show statistically significant difference between scarred and unscarred uterus group in our study. This is in contrast to the study by Gibbins et al., in which the rupture of unscarred uterus was found to cause significantly more neonatal morbidity than the rupture of a scarred uterus (35).

Conclusion

In our population, CS represents the most common cause of uterine rupture followed by labour-related causes. Uterine rupture in the unscarred uterus is associated with more bleeding, hematoma formation and more risk for blood transfusion than the scarred uterus group. Surgical repair is possible in most cases. Reducing the rate of CS, optimizing care for women with previous CS and careful management of labour can help to reduce the incidence of uterine rupture.

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Prediction of latency period in patients with PPROM by cervical measurements using Transvaginal Ultrasound; A Prospective cohort study

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Abstract

Background: Preterm premature rupture of membranes (PPROM) is a main cause of Preterm Labor (PTL) which is the most major cause of perinatal morbidity and mortality. Measurements of angle between cervix and uterus may play a role in prediction of PTL.

Aim of the Work: To assess the accuracy of cervical length, posterior and anterior cervical angles to predict the latency in PPROM.

Design: A cohort Prospective study on 150 patients with PPROM was done in 2 private hospitals in KSA.

Methods : patients with PPROM had underwent a transvaginal ultrasound examination to measure cervical length (CxL), posterior and anterior uterocervical angle.

Results: The latency period was within 2 days in 42 patients (28%) while was after 2 days in 108 patients (72%) of cases. The cervical length (CxL) cut-off value was 26.0 mm, while the sensitivity and specificity were (79.7% and 67.4% respectively), The Cut off value of posterior uterocervical angle (PCA) was 109.0˚ while the sensitivity and specificity were (94.0% and 62.3% respectively), The Cut off value of anterior uterocervical angle (ACA) was 107.0˚ while the sensitivity and specificity were (94.0% and 73.4% respectively).

Conclusion: The combination of the length of Cervix (CxL), PCA and ACA values can predict the latency period in patients with PPROM

key words: latency period, PPROM, length of the cervix, ACA, PCA

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Introduction

PPROM is defined as fetal membranes rupture before 37 weeks of pregnancy [1], It may reach 3% of all pregnancies and accounts for about 30% of preterm deliveries. Prematurity Can lead to respiratory distress syndrome, cerebral palsy after intraventricular hemorrhage, necrotizing enterocolitis and perinatal death [2].

Latency period in PPROM is defined as the interval between PROM and birth [3]. The measurement of Cervical length by transvaginal ultrasound (TVS) is used to assess the risk of preterm birth. At second trimester, the short cervix less than 26 mm is significantly correlated with preterm labor, it has a high negative predictive value. But its predictive accuracy as a single measure is limited [3].

Secondly, the posterior uterocervical angle (PCA), is defined as the angle between the cervical canal and the posterior uterine wall [4]. Furthermore, PCA was shown to be associated with an interval of specificity of 67.4% for the labor within 48 hours of PPROM. [5] The Anterior uterocervical angle (ACA) is defined as the angle between the cervical canal and the anterior uterine wall [6].

Aim of the Work

To assess the accuracy of cervical length (CxL), ACA and PCA in prediction of latency period in patients with PPROM.

Materials and Methods

A Cohort Prospective study was conducted at 2 private hospitals in Saudia Arabia during the period from January 2022 till August 2022. The ethical committee of both hospitals approved the study

Primary outcomes: ACA, PCA and latency period

Secondary Outcomes Cervical Length (CxL) and relevant obstetric outcomes

SAMPLE SIZE JUSTIFICATION

Sample size was calculated using software of SPSS® version 11, adjusting the type-1 error (α) at 0.05 and power of 80%. Results from Kathir et al., 2017 were taken as reference, they reported that PCA 113.0˚ achieved a sensitivity of 80.4% and a specificity of about 65.5% for the labor within 48 hours of ROM, with the assumption of labor within 48 hours among 63.8% of cases, assuming same findings for ACA, this study included 150 cases.

Eligibility Criteria

Patients with PPROM were included if they experienced rupture of membranes between 28 – 34 weeks diagnosed by eye visualization of amniotic fluid through the external cervical opening by speculum examination. The Exclusion criteria included fetal heart rate abnormalities, Antepartum hemorrhage, chorioamnionitis, history of cervical cerculage in this pregnancy and women who were in active labor at admission.

Clinical Protocol

All patients with PPROM were admitted, diagnosed Clinically and managed expectantly in the absence of criteria of chorioamnionitis. All Patients have received corticosteroids in the form of Dexamethasone 6 mg IM/12 hrs for 48 hrs (total 24 mg) and received antibiotics in the form of 1 gm oral Azithromycin as recommended by ACOG [7].

Obstetric Ultrasound was performed by senior sonographer to assess Fetal age, presentation, Biophysical profile, amniotic fluid volume and placenta location. Transvaginal ultrasound was performed after the patient has the sensation of full bladder, the probe was placed in the anterior fornix, decreasing the pressure on the cervix [8], In order to measure PCA and ACA, a line was drawn between the external and internal cervical os another was drawn parallel to the inner side of the posterior wall of the uterus (PCA) and anterior wall of the uterus (ACA), Cervical length is the measurement between the internal and the external cervical os. Termination of pregnancy was indicated in cases of chorioamnionitis, patient entered in labor of fetal distress determined by CTG, or reaching 34weeks.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA). The quantitative data were presented as mean± standard deviation and ranges. Also, qualitative variables were presented as number and percentages. ***The following tests were done:*** Independent-samples t-test of significance was used when comparing between two means & Chi-square (x2) test of significance was used in order to compare proportions between qualitative parameters. Receiver operating characteristic (ROC curve) analysis was used to find out the overall predictivity of parameter in and to find out the best cut-off value with detection of accuracy was represented using the terms sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy, the likelihood ratio of a positive test and the likelihood ratio of a negative test.

Results

Table 1 shows the demographic data of 150 patients including age, body mass index, parity, total leucocyte count, amniotic fluid index, the length of Cervix (CxL), (PCA) and (ACA)

Table 2 shows a high statistically significant difference between 2 groups as regard the length of Cervix (CxL), (PCA) and (ACA). No statistically significant difference between 2 groups as regarding age, body mass index, parity, total leucocyte count, amniotic fluid index.

Table 3 shows the diagnostic accuracy of data measured in prediction of latency period within the two days .Table 4 shows the diagnostic characteristics of measured item as cutoff points in the prediction of latency period within the 2 days.

Discussion

Interpretation of our results and their comparison to other studies

Our study has measured the cervical length, posterior uterocervical angle and anterior uterocervical angle by transvaginal ultrasound in order to predict the latency period in patients with PPROM. We found that ACA and PCA were significantly higher among patients that had labor within 2 days, while CXL was significantly lower among the same cases.

In our study, CXL had a cutoff value 26 mm, its sensitivity was 79.7% while its specificity was 67.4% in the prediction of latency period within 2 days.

Rizzo et al., who reviewed 92 patients with PPROM found that a CXL< 20 mm was associated with shorter latency. In Contrast, Carlan et al; Fischer and Austin found no statistically significant relationship between CXL and latency period with a 3 cm cutoff to characterize short CXL [9,10,11].

Our study proved that PCA and ACA parameters are highly statistically significant in prediction of latency period within 2 days in PPROM. In the study by Kathir et al., PCA was shown to be associated with latency period (p value = 0.003). PCA of 113.0˚ with a sensitivity 80.4% and specificity 65.5% for the labor within 2 days of PROM. [12]

Perez et al. in their study, ACA > 105˚ predicted the latency period ≤ 7 days with a

sensitivity 78% and latency period ≤ 2 days with a sensitivity 90%. These results might be affected by low number of cases that included in Perez' study (98 women).

Mean AFI in patients with the latency period within two days was 4.31±1.09 cm while in

patients with latency period after the two days was 4.92±1.38 cm (p value=0.011).

Mehra et al. found a positive correlation between short CXL and high labor rates within seven days (when cutoff value is < 20 mm and a sensitivity 44% with specificity 74%), [13]

In the study by Ayad et al; the mean TLC in cases with latency period < two days, the latency period between 2 - 7 days and the latency period > 7 days group, were 13.449 ± 2.959, 10.845 ± 2.432 and 9.389 ± 2.656, (103/μL) respectively. The ANOVA test showed a statistically significant difference in the mean of TLC among different PPROM groups with F = 16.755, p value < 0.001.

Clinical implication of our study

For clinical practice, the use of transvaginal Ultrasound in this study in patients with PPROM may assist in the decision of the transfer of pregnant women to other highly qualified hospitals with better neonatal facilities and for administration of corticosteroids for the enhancement of fetal lung maturation.

Limitations and strength of our study

The small sample size is the main limitation of this study and the lack of randomization of study while the advantage of study, it was carried in 2 hospitals which decrease the publication bias.

Recommendation for further studies

Further studies are needed to be multicentral and include large no of participants to study the effect of cervical angles in prediction of latency period in PPROM.

Conclusion

The combination of the length of Cervix (CxL), posterior uterocervical angle (PCA) and anterior uterocervical angle (ACA) measurements can predict the latency period in women with PPROM

Ethics approval

Study was approved by Ethical Committee of 2 private hospitals

Consent for publication

Non applicable

Availability and data material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors report there are no competing interests to declare

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Table 1. The Demographic and the Basal characteristics.

Demographic data	Mean±SD	Range
Age (years)	27.34±5.81	18-42
BMI (kg/m^2)	21.83±3.37	18-31
Parity	**No.**	**%**
Primi	56	37.3%
Multi	94	62.7%
Basal		
TLC (×10^3/mL)	8.77±2.75	4-18
AFI (cm)	4.69±1.43	2-8
Cervical length (mm)	25.91±2.96	15-32
Posterior uterocervical angle (˚)	110.26±5.20	93.6-121.4
Anterior uterocervical angle (˚)	108.63±5.41	96.2-124.4

Table 2. Comparison according to latency period (two days) regarding demographic and basal characteristics.

	Within (n=42)	After (n=108)	p-value
Demographic data			
Age (years)	27.13±4.59	27.44±6.22	0.770
BMI (kg/m^2)	23.87±3.77	21.01±2.75	0.08
Parity			
Primipara	12 (28.6%)	44 (40.7%)	0.232#
Multipara	30 (71.4%)	64 (59.3%)	
Basal			
Enrollment GA (week)	33.66±1.53	33.46±1.94	0.550
TLC (×10^3/mL)	9.38±2.08	8.57±2.14	0.038*
AFI (cm)	4.31±1.09	4.92±1.38	0.061
Cervical length (mm)	24.07±3.57	26.52±2.45	<0.001**
Posterior uterocervical angle (˚)	113.73±3.98	108.94±5.00	<0.001**
Anterior uterocervical angle (˚)	113.53±4.49	106.69±4.49	<0.001**

Using: Independent Sample t-test; #Chi-square test

*p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.001 is highly significant*

Table 3. Diagnostic performance of basal measurements in prediction of latency period within two days.

Factor	AUC	SE	P	95% CI	Cut off
TLC	0.530	0.050	0.632	0.433-0.628	-
AFI	0.620	0.043	0.020*	0.536-0.706	-
Cervical length	0.762	0.041	<0.001**	0.681-0.845	≤26 mm
Posterior uterocervical angle	0.812	0.034	<0.001**	0.745-0.879	≥109.0˚
Anterior uterocervical angle	0.897	0.025	<0.001**	0.849-0.946	≥107.0˚

*AUC: Area under curve, SE: Standard error, CI: Confidence interval, *significant.*

Table 4. Diagnostic characteristics of basal measures cutoff points in predicting latency period within two days.

Characters	Cervical length ≤ 26.0 mm		Posterior uterocervical angle ≥ 109.0˚		Anterior uterocervical angle ≥107.0˚	
	Value	95% CI	Value	95% CI	Value	95% CI
Sensitivity	79.7%	67.42%-90.37%	94.0%	84.66%-100.06%	94.0%	84.66%-100.06%
Specificity	67.4%	58.45%-74.66%	62.3%	52.84%-69.46%	73.4%	64.87%-80.27%
DA	70.69%	63.75%-77.01%	70.69%	63.75%-77.01%	79.15%	72.62%-84.76%
YI	45.39%	32.03%-58.75%	54.16%	43.66%-64.67%	65.89%	55.90%-75.89%
PPV	47.84%	37.33%-58.45%	48.25%	38.56%-58.14%	56.92%	46.10%-67.32%
NPV	90.78%	83.23%-96.08%	97.61%	91.19%-100.78%	98.33%	92.82%-100.98%
LR+	2.34	1.81-3.03	2.38	1.93-2.94	3.35	2.56-4.36
LR−	0.33	0.19-0.55	0.12	0.04-0.31	0.10	0.04-0.26
LR	7.27	3.54-14.96	20.39	7.01-59.33	34.11	11.62-100.16
Kappa	0.38	0.25-0.50	0.42	0.31-0.52	0.55	0.44-0.66

CI: Confidence interval, YI: Youden's index. DA: Diagnostic accuracy, PPV: Positive Predictive value, NPV: Negative Predictive value, LR+: Positive likelihood ratio, LR−: Negative likelihood ratio, LR: Diagnostic odd ratio.

Ovarian Reserve After Laparoscopic Ovarian Cystectomy For Endometrioma

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Abstract

The outcomes of laparoscopic cystectomy of endometriomas have been the subject of numerous investigations. Endometriosis is the term used when endometrial glands and stroma are seen outside of the usual uterine cavity. Ectopic endometrial tissue growing inside the ovary leads to pseudocysts known as endometriomas. The best course of treatment for women with symptomatic or expanding endometriomas is first surgery. Analyzing the serum level of anti-mullerian hormone (AMH) can be used to estimate ovarian reserve.

This study's objective was to evaluate how laparoscopic ovarian cystectomy for endometrioma affected ovarian reserve.

Methods: This prospective interventional study on96 patients of ovarian endometriomas candidate for laparoscopic ovarian cystectomy.

All patients included in the study were subjected to; detailed history taking and full examination, day 3Follicular Stimulating hormone (FSH) and Antimullerian hormone (AMH)measurement the cycle before operation then subjected to laparoscopic cystectomy and histological examination then the same tests were repeated on day 3 of the cycle three months postoperative.

Results: There was a statistically significant reduction in postoperative mean value of AMH (2.04+ 1.69) when compared to the preoperative mean value of AMH (2.59+ 1.85) and a statistically significant rise in postoperative mean value of serum FSH (7.23+ 1.48), when compared to preoperative mean value of FSH (5.50+ 1.85).

In this study, patients with endometriomas> 5 cm in diameter compared to smaller ones saw larger post-operative AMH declines (p value 0.001 and 0.01 respectively), as well as those with bilateral endometriomas compared to those with unilateral ones. (p value <0.001, 0.02 respectively), so endometrioma size and bilaterality of endometriomas were significant risk factors for diminished ovarian reserve.

Conclusion: Laparoscopic cystectomy of endometrioma has an adverse effect on ovarian reserve reflected by Anti-mul-

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lerian hormone that decreases significantly after Laparoscopic ovarian cystectomy and FSH level that increases significantly after Laparoscopic ovarian cystectomy.

Introduction

When the glands and stroma of endometrial are seen outside of the healthy uterine cavity, this referred to as endometriosis. It is equivalent to 0.8% to 2% of reproductive-age women (1).

Despite the lack of evidence linking endometriosis to infertility, the fact that over a third of endometriosis sufferers struggle with infertility suggests a connection (2).

Endometrioma is the term used to describe the development of an ovarian cyst lined by endometrial glands and stroma that is next to healthy ovarian tissue and is encased in a pseudocapsule. 20% to 40% of women with endometriosis have it. It might be connected to chronic pelvic discomfort, dysmenorrhea, and infertility (3).

Endometriomas affect the surrounding follicles in a way that is gonadotoxic, which results in fibrosis, diminished vascularization, loss of cortex-specific stroma, and atresia in the recruited follicles, all of which lead to a decrease in follicle number (4).

In order to treat ovarian endometrioma, laparoscopic excision of the cyst capsule using the stripping technique is typically used. Due to inadvertent loss or death of the healthy ovarian tissue near the pseudocapsule of the cyst, surgical removal may reduce ovarian reserve. Compared to standard surgery, laparoscopic surgery has the advantages of being quicker, requiring less time in the hospital, and causing less damage to the ovarian reserve (5).

Anti-Mullerian Hormone testing is the most accurate way to gauge ovarian reserve because it is menstrual cycle independent and unaffected by hormonal supplementation. Assuming that AMH is a good indicator of the size of the ovarian follicle pool, a decline in the number of tiny developing follicles is followed by a decline in the amount of AMH that circulates in the body (6).

Ultrasonographic follicle count (AFC) is a valid alternative to AMH, which is a systemic blood marker and expresses the ovarian reserve of both ovaries. It is a direct indicator of the number of follicles and has a positive relationship with the ovarian reserve of a single ovary (7). The loss of ovarian reserve caused by surgery may be somewhat countered by an improved ability to detect small follicles after the endometriomas have been removed because ovarian reserve may be underestimated by AFC when endometriomas are present (8).

Aim of work

to evaluate the impact on ovarian reserve after ovarian cystectomy performed laparoscopically for endometrioma.

Patients

The 96 cases in this prospective interventional trial were selected from the period from January2021 to December 2021.

Inclusion criteria:

- Females who are sexually active (21-39 years).
- Had an endometrioma diagnosed by ultrasonography that was unilateral or bilateral and measured >3 cm.

Exclusion criteria:

- Younger than 20 years and older than 40 years.
- Previous chemotherapy, pelvic radiation, or ovarian surgery.
- Unusual menstrual cycles.
- The existence of additional ovarian abnormalities in addition to polycystic ovary syndrome.

- Using any drugs that might impair ovarian function in the three months before to the surgery, such as oral contraceptives or GnRH analogues..

All cases were subjected to the following:

1. **Complete history taking**
2. **Physical examination**
3. **Transvaginal ultrasound (TVS)**
4. **Hormonal assay:**

For AMH and day3 FSH in the cycle before laparoscopic cystectomy.

All hormonal measurements of hormonal were performed in the same reference laboratory.

5. **Laparoscopic ovarian cystectomy**
6. **Histopathologic Analysis:** All resected cyst walls were sent to the pathology laboratory to confirm endometrioma and exclude any possibility of malignancy.
7. **Follow up of** all cases till 3 months post-operative then reassay of AMH and FSH at the day 3 of the cycle for the patients had endometriomas confirmed by histopathology.

Outcome measures: Measurement of AMH and day3 FSH before and 3months after ovarian cystectomy.

Statistical Analysis: The data were coded, entered and processed on computer using SPSS (version 18).

Results

Table (1) shows demographic data of included women whose age mean 28+ 5.53years and their BMI mean 27.65+ 5.53 kg/m2

The chief complain in many cases in this study was infertility by 83.3% either primary by 58.3% or secondary by 25%(table 2).

During laparoscopy, Endometrioma was present either unilateral in 66.7% or bilateral by 33.3% in the studied cases, its mean size was(5.84+ 1.60cm) and there was other endometriotic lesions in uterus by 6.25%, douglas pouch by 8.33 and adhesions by 25% (table 3).

There was statistically significant reduction in postoperative mean value of serum AMH compared to preoperative measurement (2.04, 2.59 respectively, p <0.001) and statistically significant rise in postoperative mean value of serum FSH compared to preoperative measurement (7.23, 5.50 respectively, p <0.001) (table 4).

Table (I): Demographic data of included women.

		patients	
Age (years)	**Range**	21 – 39	
	Mean +SD	28+5.53	
BMI (kg/m^2)	**Range**	18.69- 42.97	
	Mean +SD	27.65+5.53	
Parity		No.	%
	Nulligravida	64	66.7
	P1	16	16.7
	P2	18	16.7

SD standard deviation **BMI** body mass index

Table (2): Clinical presentation of the studied women.

	Patients (No=96)	
	16	16.7
Pain	8	8.3
Pain + Infertility	80	83.3
Infertility	56	58.3
• **Type of infertility** **- Primary** **- Secondary**	24	25.0
• **Duration of Infertility (years)** **- Range**	1 – 10	
- Mean +SD	2.96+1.76	

Table (3): Distribution of laterality of endometrioma, average dimension of endometrioma and other endometriotic lesions assessed during laparoscopy among the studied women (Operative Findings).

		Patients	
		No.	%
Laterality of Endometrioma	**Unilateral**	32	66.7
	Bilateral	64	33.3
Average dimension of Endometrioma (cm)	**Range**	3.50-10	
	Mean +SD	5.84+ 1.60	
Associated other endometriotic lesions	**uterus**	6	6.25
	Pelvis (Douglas pouch)	8	8.33
	Adhesions	24	25

Table (4): Comparison between preoperative measurement and postoperative measurement among the studied women.

Hormone		Mean +SD	Range	Paired t.test	P. value
AMH	Preoperative	2.59+ 1.85	0.29 - 8	13.50	<0.001
	Postoperative	2.04+ 1.69	0.15- 7.14		
FSH	Preoperative	5.50+1.85	3.55- 8.80	20.97	<0.001
	Postoperative	7.23+ 1.48	4.70- 9.50		

Discussion

Infertility and pelvic pain are the typical complaints of endomertriosis, a frequent benign condition that impacts fecundity rates. However, it may be asymptomatic and unintentionally discovered during laparoscopy or any other exploratory operation (9).

A variety of surgical procedures, including de-roofing, stripping, excision, and ablation using either a "cold knife,"electrosurgery, or laser, have been suggested to treat ovarian endometriomas (10).

In this study, the laparoscopic cystectomy was done for ovarian endometriomas. A total of 96 women had ovarian endometriomas were included in the study. The mean age of included women was 28+5.53years and it was found in this study that endometrioma was mostly present in women whose age ranged between 20 to 25 years by 41.6%. The mean BMI was 27.65+ 5.53kg/m2 and endometrioma was mostly present in overweight women by 66.7%.

The included women complained of infertility, pain or both. The majority of the studied cases complained of infertility that represented 83.3%, either primary that represented 58.3% or secondary that represented 25.0%.

Endometrioma in the included women by laparoscopy were bilateral in 66.7% or unilateral 33.3% in and its mean size was 5.84+ 1.60.

There was a statistically significant reduction in post-operative mean value of AMH (2.04+ 1.69) when compared to the preoperative mean value of AMH (2.59+ 1.85) and a statistically significant rise in postoperative mean value of serum FSH (7.23+1.48), when compared to preoperative mean value of FSH (5.50+1.85).

The current study's findings are consistent with a systematic review by Kitajima et al.

(2014) that found that surgical removal of endometriomas had a detrimental impact on ovarian reserve as measured by AMH levels. AMH levels considerably decreased from preoperative values (3.86± 3.58 ng/mL) in the first week (1.66± 1.92 ng/mL), third month (2.06 ±2.5 ng/mL), and ninth month (1.77± 1.76 ng/mL) after surgery, according to a larger follow-up research by Alborzi et al. (2018), which included 193 women. FSH levels significantly increased during the course of a three-month follow-up from baseline to the third postoperative month because FSH was underestimated in endometrioma patients. Three months after surgery, the FSH levels had dramatically increased from the preoperative level (6.28± 3.79)to (6.99 ± 3.92)postoperatively(11).

Ergun et al. (2015) showed in his study that after a laparoscopic ovarian cystectomy, serum AMH levels dropped, and this finding might be interpreted as a sign of a depleted ovarian reserve. Postoperative AMH levels were statistically significantly lower after operations for ovarian endometrioma or other ovarian cysts than endometrioma. The rate of AMH level drop for both groups was comparable. A reduction in ovarian reserve was not consistently supported by pre- and postoperative serum FSH and E2 levels (12).

Then, Saliholu et al. (2016) supported these results, showing that removal of the endometrioma resulted in a non-significant change in FSH levels but a significant decrease in AMH levels (P 0.001). Saliholu explained this result by stating that FSH is irrelevant to ovarian reserve and the clinical outcomes of fertility (13).

Studies have evaluated that ovarian reserve markers, follicle-stimulating hormone and estradiol, were not impacted by laparoscopic surgery, according to certain studies that assessed the impact of endometrioma removal on these markers (14).

Ercan et al. (2016) failed to demonstrate how surgery adversely impacts the ovarian reserve and claimed that this is a safe approach when carried out by a trained physician who recognizes the cleavage of the cyst capsule and appropriately excises the endometrioma (15).

Then, the disagreement to our results based on revising the literatures which documented that the mere presence of benign ovarian cysts was already shown to be associated with low serum AMH levels from the start, particularly with endometriomas.

In a study conducted on 102 women with ovarian endometriomas and 48 women with mature cystic teratoma, Kim et al. (2013) showed that preoperative serum AMH levels were significantly low in such two groups of women, when compared to age-and BMI-matched control group of women (16).

In a second study conducted on 172 women with benign ovarian cysts (122 with endometriomas and 50 with nonendometrioticcysts), Somigliana et al. (2014) showed that serum AMH was significantly low in bilateral ovarian cysts (17).

The pathogenesis underlying the adverse impact of surgical management of ovarian endometrioma has been a matter of research. The most accepted explanation by Matallotakis et al. (2017) and Bongioanni et al. (2018) is the use of electrocoagulation for hemostasis after ovarian cystectomy (18,19).

In the present study, post-operative AMH decrease was greater in patients with endometriomas> 5cm in diameter compared with smaller ones (p value <0.001, 0.01 respectively) and in patients with bilateral endometriomas compared with unilateral ones (p value <0.001, 0.02 respectively).

These results are in agreement with Kashi et al. (2017) who concluded from his study that Laparoscopic cystectomy was associated with post-operative decrease in serum AMH, particularly with bilateral involvement (p value in bilateral = 0.029 and in unilateral =

0.046) and endometriomas at least50 mm in diameter (p value in ≥ 50mm was < 0.001 and in <50mm was 0.015) (20).

Conclusion

Laparoscopic cystectomy for endometrioma has an adverse impact on ovarian reserve reflected by Anti-mullerian hormone that decreases significantly after laparoscopic ovarian cystectomy and FSH level that increases significantly after laparoscopic ovarian cystectomy.

Bilaterality and size of endometrioma increase the adverse effect of laparoscopic ovarian cystectomy on the ovarian reserve.

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Fetal Ultrasound Scanning at 11-13 weeks Gestation for Detection of Fetal Abnormalities at Low Risk Pregnancy

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Abstract

Background: Fetal structural anomalies are present in up to 2- 3% of all pregnancies. Worldwide, second trimester scan between 18 and 22 weeks is the standard of care for fetal anatomical assessment; however, first-trimester screening can detect almost half of all severe fetal anomalies at an early stage of pregnancy. The prenatal detection of fetal anomalies during first trimester of pregnancy allows for optimal perinatal management, providing expectant parents with opportunities for additional imaging, genetic testing, and the provision of information regarding prognosis and management options.

Objective: To determine the effectiveness of the fetal ultrasound scanning at 11-13 weeks gestation in the early diagnosis of structural fetal anomalies in an unselected low-risk population.

Patients and Methods: This prospective follow-up study included 195 pregnant women at first trimester with low risk pregnancy at the fetal medicine unit of Obstetrics and Gynecology Department in Mansoura University Hospital during 2021. Ultrasound screening was performed at 11-13 Weeks in all pregnant women. For those who had normal scans a follow up scan was done at 18-22 weeks. Fetal viability was examined and crown rump length was measured.

Results: In this study, we have shown the prevalence and types of congenital anomalies in the studied cases during 11-13 weeks gestation and the associations of such anomalies with the demographic characteristics, obstetric history and CRL.

Conclusion: This study shows that ultrasound diagnosis at 11–13th week gestational age is possible for some severe anomalies. We recommend the introduction of an 11–13th week scan as first part of the routine anomaly screening in pregnancy, as this enables early identification of severe anomalies.

Keywords: First trimester, Fetal anomalies, Low risk pregnancy.

INTRODUCTION

Fetal structural anomalies are found in up to 2- 3% of all pregnancies. The etiology is unknown in about two –thirds of cases. A revolutionary technological achievement and the use of high-frequency ultrasound enabled detailed and accurate imaging of the structure of the fetus, such as fetal viability, dating, development, any chromosomal or structural abnormalities, and multiple pregnancies, even in early pregnancy at 11-13 weeks. (1)

Ultrasound-based screening is an integral part of routine prenatal care. The prenatal detection of fetal anomalies allows for optimal prenatal management, providing expectant parents with opportunities for additional imaging, genetic testing, and the provision of information regarding prognosis and management options. (2)

In majority of countries worldwide, second trimester scan between 18 and 22 weeks remains the standard of care for fetal anatomical assessment; however, most recent literature shows a significant improvement in detection of fetal abnormalities in first trimester of pregnancy. (3)

First-trimester screening can detect almost half of all severe fetal anomalies at an early stage of pregnancy with positive predictive values of 90% and more. Sensitivities varied depending on the organ system and reached the highest figures for anomalies of the heart, the abdomen, the spine and the skeletal system. (4)

Major abnormalities are classified into three groups according to the probability of their detection rate by 11-14th weeks' ultrasound. The first group includes anomalies that can be easily detected in the first trimester such as anencephaly, the second group comprises anomalies that reveal ultrasonography signs later in gestation and have no possibility of early detection such as hypoplasia of cerebellum. The third group anomalies can be detected in first trimester with meticulous examination using high-tech devices. This group of anomalies includes spina bifida occulta, skeletal dysplasia, and some kinds of cardiac defects, which sometimes need to be examined using transvaginal ultrasound. (5)

Screening in the first and early second trimester and early detection of major anomalies will lead to early decisions of pregnancy termination. Moreover, doing it before the 16th gestational week brings the advantage of early termination before women feel movements of the fetus. This is important for women, especially in cultures in which beliefs strongly affect social life rules. Furthermore, early termination of pregnancy has physical and physiological advantages for women and their families compared with late termination. (6)

AIM OF THE WORK

The aim of the present study was to determine the effectiveness of the fetal ultrasound scanning at 11-13 weeks gestation in the early diagnosis of structural fetal anomalies in an unselected low-risk population.

PATIENTS AND METHODS

This prospective follow-up study included 195 pregnant women at first trimester with low risk pregnancy at the fetal medicine unit of Obstetrics and Gynecology Department in Mansoura University Hospital during 2021.

Sample size justification: The calculated sample size of the study was 176 participants at 5% level of significance and 95% power of the study, using G*Power 3 sample size calculator. The estimation of sample size based on the previously reported incidence of Fetal non-chromosomal abnormalities detected in the first trimester= 27.6% and percentage of Fetal non-chromosomal abnormalities detected in the second trimester = 53.8%. The sample size was increased to 195 participants to compensate

for the incomplete data and to increase the study power.

Ultrasound screening was performed at 11-13 Weeks in all pregnant women. For those who had normal scans a follow up scan was done at 18-22 weeks for confirmation. Fetal viability was examined and crown rump length was measured.

Inclusion Criteria: Age between 19-40 years old. Healthy pregnant women with singleton pregnancy attending for a routine hospital visit at 11-13th week gestation.

Exclusion Criteria: Gestational age <11 weeks or >14 weeks. Multiple gestations. Maternal disease/ disorder, IVF or induced pregnancies. Incomplete pregnancy outcome information, unexplained miscarriages, and fetal death.

Full medical history including: Personal history. Past history of common medical disorder such as hypertension, diabetes, chronic kidney disease and cardiac patients. Past history of parity and gravidity. Family history of fetal anomalies.

Physical examination: a careful general and obstetric examination was done.

Ultrasound protocol: subjects were asked to remove their clothes and put on a gown or cover for the procedure. Ultrasound screening was performed by experienced radiologist transabdominally using ultrasound machine (Samsung H60, Korea). Whenever visualization of fetal structure was suboptimal or a structural abnormality was suspected during transabdominal scan, transvaginal scan was always performed. Ultrasound screening was performed at 11-13 Weeks in all 195 pregnant women. For those who had normal scans a follow up scan was done at 18-22 weeks for confirmation. Fetal viability was examined and crown rump length was measured. Evaluation of fetal anatomy was done according to the following check list.

- Skull and brain
- Face (Facial Profile, Nasal Bone and orbits)
- Neck (Nuchal translucency measurement, presence of Cystic hygroma)
- Spine (Examination of overlying skin and neural tube in longitudinal and transverse planes)
- Heart (Four chamber view, three vessel view, and heart rhythm)
- Stomach (its existence in left upper abdomen)
- Abdominal wall defect
- Kidney (existence, size, and shape)
- Urinary bladder (existence, size, and shape)
- Extremities (existence, size, and shape)

Along with the evaluation of the anatomy, the Nuchal translucency measurement was done according to the guidelines established by the Fetal Medicine Foundation, in fetuses with CRL between 45mm and 84mm at 11 to 13 weeks gestational age. The cut off value of NT measurement was taken as ≥ 3 mm. When NT measurement was abnormal a further confirmatory test was combined. The following confirmatory that were offered are, first trimester serum markers (free βhCG, PAPP-A), chorionic villous sampling, amniocentesis and triple screening or quadruple screening and it was left to the patients choice.

Women were fully counselled before their ultrasound examination and written informed consent was obtained. Based on the anomalies detected, the patients were counselled regarding termination or continuation of pregnancy. All the patients were followed up till delivery.

Pregnancy outcome was obtained from our maternity unit or the patients themselves.

Analytical statistics: Data were analyzed using the Statistical Package of Social Science (SPSS) program for Windows

(Standard version 21). The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Qualitative data were described using number and percent. Associations between categorical variables were tested using Fisher exact and Monte Carlo tests when expected cell count less than 5. Continuous variables were presented as mean ± SD (standard deviation) for normally distributed data and compared with independent t test. The results was considered significant when $p \leq 0.05$. The smaller the p-value obtained, the more significant are the results.

Results

Table 1: Demographic data among the studied group

Demographic data	The study group (n=195)
Age (years) Mean ± SD Min-Max	 27.67±4.21 20-40
Age classes 20-25 y >25-30 y >30-35 y >35-40 y	 65 (33.3%) 85 (43.6%) 39 (20.0%) 6 (3.1%)
Residence Urban Rural	 66 (33.8%) 129 (66.2%)
Consanguinity Positive Negative	 59 (30.3%) 136 (69.7%)

Table 2: Anthropometric measurements among the studied group

Anthropometric measurements	The study group (n=195)
Weight (kg) Mean ± SD	 78.41± 8.75
Height (cm) Mean ± SD	 166.78± 4.95
BMI (kg/m^2) Mean ± SD	 28.19± 2.70

The present results demonstrated that at the mean gestational age of 12.16±0.68, the mean CRL was 68.95±12.57. Normal US represented 97.9% while abnormal US represented 2.1% as illustrated in table 3.

Table 3: First two dimensional ultrasound scan results among the studied group .

First two dimensional ultrasound scan	The study group (n=195)
Gestational age(wk) Mean ± SD	 12.16±0.68
US Normal US Abnormal US	 191 (97.9%) 4 (2.1%)
CRL(mm) Mean ± SD	 68.95±12.57
Gestational age(wk) Mean ± SD	 12.16±0.68

The present results demonstrated that at the mean gestational age of 20.51 ± 1.42, the mean FL was 34.71±3.94. Normal US represented 91.8% while abnormal US represented 2.6%, terminated pregnancy, missed abortion occurred in 1% of cases and 4.6% of cases lost follow-up, as seen in Table 4.

Table 4: Second two dimensional ultrasound scan results among the studied group.

Second two dimensional ultrasound scan	The study group (n=195)
Gestational age(wk) Mean ± SD	 20.51 ± 1.42
US Normal Abnormal Terminated/ missed abortion Lost follow up	 179 (91.8%) 5 (2.6%) 2 (1.0%) 9 (4.6%)
FL(mm) Mean ± SD	 34.71±3.94

In this study, The present results demonstrated that the agreement percentage between the first and second US scans was 83.9% as demonstrated in Table 5.

Table 3: First two dimensional ultrasound

Table 5: Agreement % between first and second US scan.

	First US scan (n=195)	Second US scan (n=186)	Agreement %
Normal US	191 (97.9%)	179 (96.2%)	83.9%
Abnormal US/ terminated	4 (2.1%)	7 (3.8%)	

Table 6: First two dimensional ultrasound scan results among the studied group.

Fetal abnormality	Total	Increased NT	1st US scan	2nd US scan	TOP	Missed abortion IUFD	Live birth
Nervous system							
-Occipital encephalocele	1	--	1	0	0	0	1
-Bilateral ventriculomegaly	1	--	0	1	0	0	1
Congenital heart defect							
-VSD	1	--	0	1	0	0	1
Urogenital system							
-Bilateral hydronephrosis	1	--	0	1	0	0	1
Skeletal							
-Mermaid syndrome	1	--	1	0	1	0	0
Multiples -Echogenic kidney with dilated renal pelvis, Bilateral club foot, AVSD (Trisomy 13)	1	1	1	0	0	0	1
Others							
-Cystic hygroma with fetal hydrops	1	1	1	0	0	1	0

TOP: Termination of pregnancy. IUFD: Intrauterine fetal death

The present results demonstrated a significant increase in age among abnormal US in comparison with the normal US (P value>0.001). The results also demonstrated a significant increase in positive consanguinity among the abnormal US in comparison with the normal US as illustrated in Table 7.

Table 7: Association between abnormal US / terminated and demographic data.

Demographic data	Normal US (n=179)	Normal US (n=179)	p value
Maternal age			
20-25 y	61 (34.1%)	2 (28.6%)	
>25-30 y	80 (44.7%)	0 (0%)	0.001*
>30-35 y	34 (19.0%)	3 (42.9%)	
>35-40 y	4 (2.2%)	2 (28.6%)	
Residence			
Urban	60 (33.5%)	3 (42.9%)	0.609
Rural	119 (66.5%)	4 (57.1%)	
History of Consanguinity			
Positive	50 (27.9%)	5 (71.4%)	0.025*
Negative	129 (72.1%)	2 (28.6%)	

P-value< 0.001: highly significant, P-value <0.05: significant, P-value >0.05: Non-significant.

The present results demonstrated a statistically significant increase in CRL among the abnormal US group in comparison with the normal US group as illustrated in Table 8.

Table 8: Association between abnormal US / terminated and CRL.

	Normal US (n=179)	Abnormal US/terminated (n=7)	p value
CRL Mean ± SD	68.25±12.62	79.28±9.12	0.023*

DISCUSSION

Fetal structural anomalies complicate 2-3% of all pregnancies. Screening for fetal abnormalities at 11 to 13 weeks' gestation can provide a detailed fetal anatomic evaluation, with the aim of identifying fetuses with major structural anomalies early in pregnancy. (7)

Screening for structural abnormalities is routinely performed by ultrasound between 18–22 weeks of gestation. However, increasing evidence has suggested that about half of fetal structural abnormalities can be detected during the first trimester of pregnancy with low false-positive rates. (8)

Regarding the demographic characteristics of the studied cases, our results indicated that the mean age was 27.67±4.21 years old. Our result revealed that 30.3% of the cases were positive consanguinity. Regarding the anthropometric measurements among the studied group, our results revealed that the mean weight, height and BMI of the studied were 78.41± 8.75 kg, 166.78± 4.95 cm and 28.19± 2.70 respectively.

Such findings are in agreement with Snaifer et al. (9) in Lebanon that indicated that the patients' mean age was 27.5 ± 8.5 years with a 35% consanguinity rate that lead to increased anatomical and chromosomal fetal anomalies. Additionally, Aloui et al. (10) study in Tunisia indicated a marked association of parental consanguinity with increased congenital anomalies rates. Syngelaki et al. (11) studied the diagnosis of fetal non-chromosomal abnormalities on routine ultrasound examination at 11–13 weeks' gestation and indicated that median maternal age was 31.0 years old and median maternal weight was 67.5 kg.

Our results indicated that the prevalence of congenital anomalies in the studied cases during 11-13th pregnancy ultrasound was 2.1% and during second trimester ultrasound was 3.8% and the agreement % between first and second US scan was 83.9%. A previous study by Ding et al. (13) demonstrated that the reason for not all structures being visible in the first trimester is not the failure of the resolution of the ultrasound, but the fact that several structures are not yet formed and therefore, cannot be seen. Therefore, first trimester ultrasound examination could not replace the mid-trimester scan and the 16–20 weeks follow-up examination by conventional second-trimester transabdominal scan should always be performed. Simula et al. (14) indicated that approximately 40% to 66% of fetal anomalies can be identified during the 11−14 week prenatal sonographic examination and all women should be offered a routine complete 11−14 week prenatal sonographic examination.

Two cases were diagnosed with central nervous system anomalies (one case has occipital encephalocele and one case has bilateral ventriculomegaly). One case was diagnosed with ventricular septal defect. One case was diagnosed with bilateral hydronephrosis. One case was diagnosed with mermaid syndrome. One case was diagnosed with Echogenic kidney with dilated renal pelvis, bilateral club foot, atrioventricular septal defect (AVSD, Trisomy 13) and one

case was diagnosed with cystic hygroma with fetal hydrops. Such findings are in agreement with Onyambu and Tharamba, (15) that indicated that the prevalence of congenital anomalies in the sampled population was 3%. The most frequently observed fetal anomalies involved the head (1.6%). Each of the remaining anomalies affected less than 1% of the fetuses and included anomalies of the spine, pulmonary, renal and urinary tract and skeletal systems and majority of the fetuses with anomalies detected on prenatal ultrasound resulted in postnatal mortality within days of delivery. Kenkhuis et al. (16) indicated that the prevalence of early detected anomalies was 0.95% and during 11-13th scan, all particularly severe anomalies were detected (all cases of neural tube defect, omphalocele, megacystis, and multiple severe congenital and severe skeletal anomalies), moreover, the number of false positives and markers is much lower at the early scan, limiting parental anxiety.

Regarding the association between abnormal US / terminated and demographic data, our results indicated a statistically significant increase in abnormal US / terminated among the pregnant women with age group >35-40 years old (42.9%) (P value<0.001) and with positive history of consanguinity (P value=0.025). Such findings are in agreement with Dai et al. (17) that revealed that the kinds of fetal abnormalities, numbers of abortions, and chromosomal abnormality rates increased with increasing maternal age. Additionally, Gul et al. (18) revealed that parental consanguinity is one of the major risk factors for structural, neurological and cardiac anomalies. Similarly, Ozawa et al. (19) indicated that the maternal age, history of miscarriage, and embryonic/fetal size at miscarriage may be independently associated with the frequencies or profiles of cytogenetic abnormalities in early miscarriages.

Regarding the association between abnormal US , terminated pregnancy and obstetric history, our results indicated a significant increase in the history of miscarriage among the abnormal US / terminated group in comparison with the normal US group (P value=0.048). Such findings are in agreement with Visconti et al. (20) that indicated that pregnancies complicated by fetal congenital malformations in patients with two or more pregnancy losses were significantly associated with maternal thrombophilic disease and previous birth defects.

Our results indicated a statistically significant increase in CRL among the abnormal US / terminated group in comparison with the normal US group (P value=0.023). Balsane et al. (21) indicated that at the first transvaginal ultrasound, the mean Z- score for CRL was significantly lower in pregnancies that subsequently aborted compared to pregnancies that remained viable. A recent study by Li et al. (22) indicated that the increased fetal crown-chin length / crown-rump length ratio at 11–14 weeks' gestation is associated with an increased risk of skeletal dysplasia and may be useful in first-trimester screening for this condition. Contrarily, a previous study by Sagi-Dain et al. (23) indicated that low first-trimester CRL might be associated with a significantly increased risk of chromosomal anomalies. Thus, invasive prenatal testing or cell-free DNA screening might be offered in such pregnancies, particularly if dating is certain.

CONCLUSION

This study shows that ultrasound diagnosis at 11–13th week gestational age is possible for some severe anomalies. We recommend the introduction of an 11–13th week scan as first part of the routine anomaly screening in pregnancy, as this enables early identification of severe anomalies.

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Social support and pregnancy outcomes among Egyptian women

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Abstract

Purpose: Determine the relationship between social support and unfavorable pregnancy outcomes.

Patients and Methods: This was a cross-sectional study conducted at the emergency department of the obstetrics and gynecology department. We recruited women admitted for delivery. Women were asked to fill in the Arabic validated Interpersonal Social Support questionnaire (short form 12). Adverse pregnancy outcomes (preterm birth, preeclampsia, antepartum hemorrhage, postpartum hemorrhage, and fetal growth restriction) were reported. Fetal birth weight, fetal sex, and fetal head circumference were also reported.

Materials and methods: A randomized clinical trial conducted in the obstetrics and gynecology department of a tertiary hospital. Patients were recruited according to inclusion and exclusion criteria. 70 Patients were allocated into two groups: a study group who had hysteroscopic resection of the scar defect and a control group who were managed expectantly. Patients were assessed for postmenstrual spotting amount and duration. Evaluation of spotting related discomfort and dysmenorrhea was done using a visual analogue scale. Quality of life was evaluated using the Arabic validated SF 36 quality of life questionnaire. Patient satisfaction was measured using a five- point Likert scale.

Results: The total support score was 17.83 ± 4.01. Individual domain scores were 5.45 ± 1.65, 6.08 ± 1.84, and 6.3 ± 1.88 for belonging, appraisal, and tangible. Seventy-three (71.6 %) women had no adverse pregnancy events. There was a negative correlation between the social support total score and fetal weight, fetal head circumference, and adverse pregnancy outcomes, yet it was insignificant (p-value 0.559, 0.421, and 0.413, respectively). Social support did not predict adverse pregnancy outcomes. Also, patients' education, occupation, parity, and fetal sex did not predict it either.

Conclusion: Social support was not associated with adverse pregnancy outcomes nor predicted its occurrence.

Key words: Adverse pregnancy outcomes; Pregnancy; Social support.

Introduction

Pregnancy is a particular lifetime associated with significant changes requiring psychological adaptations (1). Social support represents social relationships influencing attitudes and behaviors, making women able to adapt to significant traumas and life stressors (2,3). It includes emotional, instrumental, and informational aspects (4). It acts as a protective buffer against these stressors, significantly impacting maternal well-being. It has been reported that pregnant women who received social support had less anxiety during pregnancy (5).

Additionally, less social support predicted significant antenatal depression and anxiety (6). Many studies reported on social support and antenatal depression, (6-8) with few data reporting on social support and unfavorable pregnancy outcomes (9,10). This study aimed to evaluate social support and adverse pregnancy outcomes among Egyptian women.

Material and Methods

This was a cross-sectional study conducted at the labor and delivery ward of the obstetrics and gynecology department, Suez Canal University hospital, from December 2021 to June 2022. We recruited women who had a birth in our institute following predetermined inclusion and exclusion criteria. Inclusion criteria were a) patients' age 18- 45 years, b) pregnant women from 28- 41 weeks, c) laboring women vaginally or by cesarean section, and d) any adverse pregnancy outcomes such as preterm birth, preeclampsia, antepartum hemorrhage, postpartum hemorrhage, and fetal growth restriction. Any patient refusing to participate in the study was excluded.

All participants gave oral and written informed consent prior to entering the study. Patients eligible for the study were asked to fill in a questionnaire to detect social support. This was done using Arabic validated Interpersonal Support Evaluation List: (11) (shortened version-12 items), developed by Cohen, Mermestein, & Kmarck, (12) was developed to measure the quality of interpersonal relationships and the presence of social support. Cronbach's alpha for the full scale is 0.70. The questionnaire had three different subscales designed to measure three aspects of Perceived Social Support; Appraisal Support, Belonging Support, and Tangible Support. Each is measured on a 4-point scale ranging from 'Definitely True' to 'Definitely False.' Each response item was scored as 0 = definitely false, 1= probably false, 2= probably true, and 3= definitely true. Reversed items included questions 1, 2, 7, 8, 11, and 12. The appraisal subscale included the sum of items 2R, 4, 6, and 11R. The belonging subscale included the sum of items 1R, 5, 7R, and 9. The tangible subscale included the sum of items3, 8R, 10, and 12R. The sum of the three subscales represented the overall support. The average score ranged from 0- 36, with higher scores representing high levels of support (12).

The study instrument consisted of three parts sociodemographic information, history of the current pregnancy to determine any adverse pregnancy outcomes, and the interpersonal support evaluation list. Data about the newborn included birth weight, sex, and head circumference. Adverse pregnancy outcomes included premature rupture of membranes (defined as spontaneous leakage of the amniotic fluid before the onset of labor) (13), hypertensive disorders in pregnancy (either gestational hypertension defined as elevated blood pressure ≥ 140/90 without proteinuria after 20 weeks gestation, preeclampsia defined as elevated blood pressure ≥ 140/90 with evidence of protein in urine + 1or more by dip stick method after 20 weeks gestation, or eclampsia which is characterized by the occurrence of convulsions) (14), preterm labor (defined as the occurrence of uterine contractions with cervical changes before 37

weeks gestation (15), antepartum hemorrhage (defined as any bleeding from the genital tract starting from the age of viability till the delivery of the baby) (16), and fetal growth restriction (defined as fetal weight below the 10% percentile for gestational age) (17) .

One of the study researchers interviewed each patient. Women were interviewed in a private room after delivery in the labor and delivery ward. The questionnaire was anonymous to guarantee confidentiality. A researcher was available to provide if needed. The questionnaire was filled in about 15- 20 minutes.

The sample size was calculated at a significance level of 5% with a margin of error of 9.1 %, and a prevalence/proportion of stress among pregnant women = 26.25 % (18). A 10% drop-out proportion was added to the raw results giving a total sample size of 100 women.

Ethical approval

This study was conducted after approval of the research ethics committee of faculty of medicine at Suez Canal university on 29/11/2021 with a number of 4672#.

Results

One-hundred and eleven women were eligible for the study. Nine women declined to participate leaving 102 women for the final analysis. The mean age of the studied population was 29.85 ± 6.77. The great majority of them were uneducated and housewives. They were recruited in the third trimester (38.4± 1.4 weeks) (Table 1).

The total support score was 17.83 ± 4.01. Individual domain scores were 5.45 ± 1.65, 6.08 ± 1.84, and 6.3 ± 1.88 for belonging, appraisal, and tangible. Seventy-three (71.6 %) women had no adverse pregnancy events. The most adverse event reported was preeclampsia affecting 11 (10.8%) women (Table 2).

There was a negative correlation between the social support total score and fetal weight, fetal head circumference, and adverse pregnancy outcomes, yet it was insignificant (p-value 0.559, 0.421, and 0.413, respectively).

Social support did not predict adverse pregnancy outcomes. Also, patients' education, occupation, parity, and fetal sex did not predict it either (Table 3).

Discussion

The mean social support scale was 17.83 ± 4.01 representing middle support levels. In another study, the social support scale was 66.74 ± 14.02, with about 60% of their studied population reporting childhood trauma (19) An earlier one reported a total score of maternal social support as 86.81 ± 14.84. However, this study used the medical outcome study social support survey (20) Inconsistent results would be explained by the different measuring tools used in each study, the variable educational level of the participants, and different socioeconomic levels.

The current study reported an insignificant correlation between social support and adverse pregnancy outcome and fetal growth. Besides, social support did not predict adverse pregnancy outcomes. Previous studies reported a significant negative correlation between social support and asymmetric fetal growth and fetal birth weight (1, 9, 18). This discrepancy would be rendered to the effect of adverse childhood experiences (ACE), which was not evaluated in this study. An earlier study reported a small significant association between social support and fetal birth weight. However, this study recruited pregnant teenage women (21).

Another study reported an insignificant association between exposure to acute life stressors and adaptive potential for pregnancy. However, this study recruited vulnerable women (wives of soldiers) and used a different instrument to evaluate the

adaptive response during pregnancy which is not representative of social support (22). Additionally, neither tangible nor emotional support was associated with any adverse pregnancy outcome (23). Also, partner support was not different between women who had preterm birth and those who delivered at term in a retrospectively conducted study (24). Social support represented by family functioning was not associated with fetal birth weight or gestational age (25).

Social support buffered the hazardous effects of low and moderate ACE but not among women with high ACE (18). The protective effect of social support is mediated through the hypothalamic-pituitary-adrenal axis leading to decreased glucocorticoid release during fetal development. These substances at higher levels lead to placental dysregulation, low birth weight, and preterm birth (26, 27). Decreased social support was associated with unfavorable pregnancy outcomes among women with significant life events (23).

Variable results were reported regarding the association between social support and adverse pregnancy outcomes. This would be rendered to different definitions for social support as the independent variable and pregnancy outcomes as the outcome from one study to another. Different studies considered adverse pregnancy outcomes as pregnancy complications, birth weight, and preterm birth. Additionally, lack of control for biomedical and behavioral risk factors influenced the integrity of the results. A variable statistical representation of the results did not allow for proper comparison between studies. Also, a lack of information about how social support influences pregnancy outcomes affected the results (28). Besides, lost cases during follow-up lead to overestimated associations (20).

Strength and limitation

The small sample size is a limitation. This was the first study to address social support among Egyptian pregnant women. No information was obtained about ACE. Being a hospital-based study, the generalizability of the results would be limited.

Conclusion

Social support was not associated with adverse pregnancy outcomes nor predicted its occurrence.

Acknowledgments

None

Disclosure

the authors report no conflicts of interest in this work.

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Table 1: Primary demographic characters of the participants

Age (years) (mean ± SD)		29.85 ± 6.77
BMI (kg/m^2) (mean ± SD)		30.19 ± 7.56
Education N (%)	None	55 (53.9%)
	Middle	33 (32.4%)
	High	14 (13.7%)
Occupation N (%)	Housewife	82 (80.4%)
	Worker	10 (9.8%)
	Employee	10 (9.8%)
Mode of delivery N (%)	Vaginal	52 (51%)
	C.S.	50 (49%)
Gestational age (weeks) (mean ± SD)		38.4± 1.4
Systolic BP (mmHg) (mean ± SD)		123.72 ± 12.89
Diastolic BP (mmHg) (mean ± SD)		79.9 ± 7.9

BMI, body mass index; CS, cesarean section; BP, blood pressure

Table 2: Social support score and adverse pregnancy outcomes

Adverse pregnancy events N (%)	None	73 (71.6 %)
	PROM	6 (5.9%)
	Preeclampsia	11 (10.8%)
	Eclampsia	1 (1%)
	Preterm birth	7 (6.9%)
	APH	1 (1%)
	FGR	1 (1%)
	Gestational hypertension	1 (1%)
Fetal sex N (%)	Male	63 (61.8%)
	Female	39 (38.2%)
EFW (gm) (mean ± SD)		3170.93 ± 424.96
HC (cm) (mean ± SD)		33.77 ± 1.47
ICI		0.011 ± 0.001
Belonging (mean ± SD)		5.45 ± 1.65
Appraisal (mean ± SD)		6.08 ± 1.84
Tangible (mean ± SD)		6.3 ± 1.88
Total social support score (mean ± SD)		17.83 ± 4.01

PROM, premature rupture of membranes; APH, antepartum hemorrhage; FGR, fetal growth restriction; EFW, estimated fetal weight; HC, head circumference; ICI, infant cephalization index

Table 3: Predictors for adverse pregnancy outcomes

Model	B	Coefficient standard error	Standardized coefficient beta	Significance
Constant	0.376	1.285		0.771
Education	0.305	0.366	0.110	0.407
Occupation	-0.397	0.411	-0.123	0.337
Parity	-0.026	0.131	-0.021	0.846
Fetal sex	0.321	0.441	0.078	0.469
Appraisal	-0.548	2.192	-0.487	0.803
Belonging	-0.386	2.240	-0.327	0.860
Tangible	-0.367	2.198	-0.345	0.868
Total score	0.443	2.195	0.878	0.841

The Relationship between Seminal Total Antioxidant Capacity and Idiopathic Repeated Pregnancy Loss

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Abstract

Background: Attempts to demonstrate a link between idiopathic recurrent pregnancy loss (RPL) and sperm quality have been contentious. Based on this debate, other factors such as the antioxidant capacity of seminal plasma and the amounts of free oxygen radicals known as seminal reactive oxygen spices (ROS) should be considered.

Objective: Evaluation of the role of seminal total antioxidant capacity (TAC), in idiopathic recurrent pregnancy loss.

Methods: One hundred men were enrolled. Wife of these men had undergone full gynecologic evaluation and basic investigations of infertility and recurrent pregnancy loss of them were normal. Cases were divided into two groups; group 1 "Recurrent pregnancy loss (RPL) group" composed of 50 male partners of couples who had previously experienced at least two clinical first trimesteric idiopathic miscarriages and group 2 "Control group"; composed of 50 fertile men, with at least one child without assisted reproduction treatments, normal karyotype, normal sperm parameters, and wives who had no history of miscarriage.

Results: Seminal total antioxidant capacity was significantly lower in RPL group; 1.25 ± 0.36 vs. 1.75 ± 0.64, $p<0.001$. Also, there was no significant correlation between seminal total antioxidant capacity and paternal age, BMI and seminal fluid examination. On the other hand, there was positive correlation between it and number of previous abortions. Regarding performance of seminal total antioxidant capacity to predict cases with RPL; statistical analysis of current results showed that AUC was 0.741 (95% confidence interval: 0.641-0.842). At a cut-off point > 1.46, the sensitivity was 70% and specificity was 64%.

Conclusion: Seminal total antioxidant capacity is a major contributor to idiopathic repeated pregnancy loss. At cutoff point > 1.46; it had sensitivity 70% and specificity 64% in prediction of cases of RPL.

Keywords: Seminal; Antioxidant Capacity; Repeated Pregnancy Loss

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INTRODUCTION

Based on the World Health Organization (WHO) guidelines, miscarriage has been defined as the loss of an embryo weighing 500g or less that occurs before 20 weeks of gestation and may vary with age and parity of the mother. Repeated pregnancy loss (RPL) is the loss of two or more consecutive clinical pregnancies in the first trimester of gestation. One percent of couples experience recurrent pregnancy miscarriage [1].

The main known etiological causes for RPL include uterine anatomical anomalies, genetic factors or chromosomal abnormalities, and infectious, immunological and endocrine disorders. Conversely, 40%−50% of RPL cases have no identified cause and are therefore classified as unexplained or idiopathic. Although pregnancy miscarriage is related to women, it is possible that the male partner has a role in these idiopathic cases. Since 50% of the embryonic chromosomes are paternal, and the male gamete contributes in placental and embryonic development so it is rational to analyze semen parameters to determine their role in idiopathic RPL [2].

It should be noted that routine semen analysis reveals only information about the concentration, motility and morphology of the sperm and does not provide information regarding sperm functional competence. Attempts to show a relationship between idiopathic RPL and sperm quality, evaluated through conventional internationally established guidelines for semen analyses, have been controversial. Based on this controversy, it is important to take into account other parameters, such as the antioxidant capacity of seminal plasma and the levels of free oxygen radicals known as seminal reactive oxygen spices (ROS) [3].

It is known that human spermatozoa generate reactive oxygen species ROS in physiologic amounts, which play a role in sperm functions during sperm capacitation, acrosome reaction, and oocyte fusion. However, uncontrolled and excessive production of ROS, when it overwhelms the antioxidant defenses in semen, results in seminal oxidative stress and sperm damage. Recently, a substantial body of growing evidence suggests that such seminal oxidative stress is involved in many cases of idiopathic RPL [4].

As it has been demonstrated that reactive oxygen species (ROS) can be detected and measured in human spermatozoa. Superoxide and hydrogen peroxide (H2O2) are the common forms of reactive oxygen species (ROS). They can interact with nearby molecules and thus play a key role in inducing sperm damage and even further damage of early gestation that may be involved in causing multiple or idiopathic loss of gestation [5].

The reduced ability of seminal reductive enzymes or reduced its amounts of antioxidants is called recently as Total antioxidant capacity (TAC) which is considered also as physiologic function of seminal plasma that maintains the balance between oxidation and reduction processes during sperm capacitation, acrosome reaction, and oocyte fusion. It has been demonstrated that the TAC can be useful as predictor for genetic alteration and sperm quality. In this study, relationship between amount of free radicals, and total antioxidant capacity (TAC) in semen have been considered as a risk factor for spontaneous miscarriage hypothesis [6].

METHODS

One hundred men were enrolled.

Study type

It was a case control study.

Study place

The study was conducted at Shebin El Kom infertility clinic (Benha University Hospital).

Study period

The study was conducted from February 2020 until February 2021.

Inclusion criteria

Couples had a history of at least two idiopathic first trimesteric miscarriages. Wife of these men had undergone full gynecologic evaluation and basic investigations of infertility and recurrent pregnancy loss and all of them were normal.

Exclusion criteria

Wives aged over 35 years, had gestational age more than 3 months or with known factors of RPL as sub mucous fibroid, congenital uterine malformation, sever intrauterine (IU) synechia, cervical incompetence, uncontrolled DM, hypothyroidism, antiphospholipid antibody syndrome, hydro-salpinx, PCO, endometriosis, hyper-prolactinemia or obesity. Also, husbands with a history of exposure to environmental or occupational toxicants as heavy metal or radiation exposure with proven toxicity on fertility or using medication with proven toxicity on fertility, infertility secondary to infections as orchitis due to mumps and sexually transmitted diseases, congenital defects as epididymis or vas deferens alterations and inguinal surgery.

Study procedures

This study was approved by the Committee for Clinical Research at Benha University Hospital and informed written consent was obtained from all participants. Additional clinical information were extracted from the records of each patient.

A complete medical history and clinical examination were performed for every patient. Their medical charts were reviewed for age, body mass index (BMI), primary or secondary infertility, and duration of infertility. A history of antioxidant and/or antibiotic prescription use was be also verified. Cases were divided into two groups:

- Group 1 "Recurrent pregnancy loss (RPL) group"; composed of 50 male partners of couples who had previously experienced at least two clinical first trimesteric idiopathic miscarriages.
- Group 2 "Control group"; composed of 50 fertile men, with at least one child without assisted reproduction treatments, normal karyotype, normal sperm parameters, and wives who had no history of miscarriage.

Semen Samples:

Semen samples were obtained by masturbation after 72 hours of sexual abstinence. After complete liquefaction of the sample, semen analysis was performed according to World Health Organization guidelines 2010.

Determination of total antioxidant capacity By TAC Kit

The determination of the antioxidative capacity was performed by the reaction of antioxidants in the sample with a defined amount of exogenously provide hydrogen peroxide (H2O2). The antioxidants in the sample eliminated a certain amount of the provided hydrogen peroxide. The residual H2O2 was determined colorimetrically by an enzymatic reaction which involved the conversion of 3, 5, dichloro –2– hydroxybenzensulphonate to a coloured product.

STATISTICAL ANALYSIS

All data were coded and analysed using the computer program SPSS (Statistical package for social science) version 23.0 to obtain descriptive data. Descriptive statistics were calculated.

RESULTS

There was statistical significant difference between RPL and control groups regarding age of wife and husband, while there was no significant difference between groups regarding duration of marriage (Table 1)

Table 1: Comparison between the studied groups regarding partners age and duration of marriage

		RPL group		Control group		Test	P value
		N=50	%	N=50	%		
Age of wife / years	**Mean ±SD**	32.4±4.3		28.2±2.5		t=5.9	<0.001*
	Range	26-41		23-34			
Age of husband /years	**Mean ±SD**	36.3±4.9		32.8±3.4		t=4.1	<0.001*
	Range	30-49		27-42			
Duration of marriage / years	**Mean ±SD**	7.7±2.7		7.4±3.3		t=0.56	0.57
	Range	4-13		2-15			

There was statistical significant difference between RPL and control groups regarding previous complete pregnancy and mode of delivery (Table 2)

Table 2: Previous complete pregnancy and mode of delivery in the studied groups

		RPL group		Control group		Test	P value
		N=50	%	N=50	%		
Previous complete pregnancy	0	24	48.0%	0	0.0%	X^2=65.4	<0.001*
	1	25	50.0%	11	22.0%		
	2	1	2.0%	14	28.0%		
	3	0	0.0%	18	36.0%		
	4	0	0.0%	3	6.0%		
	5	0	0.0%	4	8.0%		
Mode of delivery	C/S	26	100.0%	33	66.0%	X^2=11.3	<0.001*
	Vaginal	0	0.0%	17	34.0%		

There was statistical significant difference between RPL and control groups regarding previous abortion (Table 3).

Table 3: Previous abortion in the studied groups

		RPL group		Control group		Test	P value
		N=50	%	N=50	%		
Previous abortion	0	0	0.0%	50	100.0%	X^2=88.9	<0.001*
	1	0	0.0%	0	0.0%		
	2	7	14.0%	0	0.0%		
	3	23	46.0%	0	0.0%		
	4	19	38.0%	0	0.0%		
	5	1	2.0%	0	0.0%		

There was no significant difference between RPL and control groups regarding clinical assessment of females (Table 4).

Table 4: Clinical assessment of females in the studied groups

		RPL group		Control group		Test	P value
		N=50	%	N=50	%		
BMI	**Mean ±SD**	25±2.3		25.7±3.2		t=1.59	0.115
	Range	22-33.5		22.9-31.5			
Medical history	**Positive**	0	0.0%	0	0.0%	-	-
	Free	50	100.0%	50	100.0%		
Gynecological history of pain , bleeding , discharge	**Positive**	0	0.0%	0	0.0%	-	-
	Free	50	100.0%	50	100.0%		
Possible causes of RPL History	**Positive**	0	0.0%	0	0.0%	-	-
	Free	50	100.0%	50	100.0%		
General examination	**Positive**	0	0.0%	0	0.0%	-	-
	Free	50	100.0%	50	100.0%		
Local examination	**Positive**	0	0.0%	0	0.0%	-	-
	Free	50	100.0%	50	100.0%		

There was statistical significant difference between RPL and control groups regarding clinical assessment in males (Table 5).

Table 5: Clinical assessment of males in the studied groups

		RPL group		Control group		Test	P value
		N=50	%	N=50	%		
BMI	**Mean ±SD**	24.5±2.3		24.7±2.8		t=1.39	0.173
	Range	21-35		21.9-35			
Smoking	**Yes**	20	40.0%	19	38.0%	X^2=0.044	0.84
	No	30	60.0%	31	62.0%		
History genital surgery	**Positive**	0	0.0%	0	0.0%	-	-
	Free	50	100.0%	50	100.0%		
Exposure to toxicants of proven effect on fertility	**Yes**	0	0.0%	0	0.0%	-	-
	No	50	100.0%	50	100.0%		
General examination	**Positive**	0	0.0%	0	0.0%	-	-
	Free	50	100.0%	50	100.0%		
Local examination	**Positive**	0	0.0%	0	0.0%	-	-
	Free	50	100.0%	50	100.0%		

The mean volume of semen of RPL group was 4 ml, the mean liquefaction time was 20 min., the mean total sperm count was 46, the mean progressive motility was 42.4%, the mean abnormal shapes was 81.6%, and the mean vitality was 55.98%. (Table 6).

Table 6: Seminal fluid analysis in RPL group

	RPL group				
	Mean	**±SD**	**Median**	**Min.**	**Max.**
Volume /ml	4	1	4	2	5
Liquefaction time/ min.	20	1	20	16	23
Total sperm count/ mil	466	15	44	23	90
sperm concentration/ mil	46	15	44	23	90
Progressive motility %	42.44	7.81	43.00	28.00	57.00
Abnormal shape %	81.60	11.37	86.50	55.00	97.00
Vitality %	55.98	10.59	56.00	39.00	78.00

There was statistical significant difference between RPL and control groups regarding seminal total antioxidant capacity, as it was significantly lower in RPL group (Table 7).

Table 7: Seminal total antioxidant capacity in the studied groups

		RPL group		Control group		Test	P value
		N=50	%	N=50	%		
Seminal total antioxidant capacity	**Mean ±SD**	1.25±0.36		1.75±0.64		t=4.8	<0.001*
	Median	1.66		1.2			
	Range	0.32-2.97		0.32-1.95			

there was no significant correlation between seminal total antioxidant capacity and (Age, BMI, seminal fluid examination) (Table 8).

Table 8: Correlation between seminal total antioxidant capacity and clinical data in RPL group

		Seminal total antioxidant capacity	
		r	**P value**
Age/ years		-0.021	0.837
BMI		0.024	0.811
Seminal fluid examination	**Volume /ml**	0.107	0.467
	Liquefaction time/ min	0.067	0.599
	Total sperm count/ mil	0.028	0.845
	Sperm concentration/ mil	0.028	0.845
	Progressive motility %	0.159	0.270
	Abnormal shape %	-0.035	0.808
	Vitality %	0.099	0.493

There was statistical significant difference in seminal total antioxidant capacity, as regards number of previous complete pregnancy (Table 9).

Table 9: Seminal total antioxidant capacity according to previous complete pregnancy

		Seminal total antioxidant capacity				Test	P value
		Mean	±SD	Min.	Max.		
Previous complete pregnancy	0	1.75	0.67	0.75	2.97	F=3.1	0.010*
	1	1.60	0.62	0.32	2.79		
	2	1.28	0.38	0.32	1.73		
	3	1.27	0.37	0.75	1.95		
	4	1.43	0.15	1.26	1.55		
	5	0.94	0.11	0.79	1.06		

There was statistical significant difference in seminal total antioxidant capacity, as regards number of previous abortion (Table 10).

Table 10: Seminal total antioxidant capacity according to previous abortion

		Seminal total antioxidant capacity				Test	P value
		Mean	±SD	Min.	Max.		
Previous abortion	0	1.25	0.36	0.32	1.95	F=7.98	<0.001*
	2	2.14	0.75	1.13	2.97		
	3	1.71	0.62	0.32	2.79		
	4	1.61	0.60	0.75	2.63		
	5	2.49	.	2.49	2.49		

ROC analysis was done to assess the performance of Seminal total antioxidant capacity to detect cases with RPL; AUC was 0.741 (95% confidence interval: 0.641-0.842), p<0.001. At a cutoff point > 1.46, the sensitivity was 70% and specificity was 64% (Table 11).

Table 11: Performance of Seminal total antioxidant capacity to predict cases with RPL

	AUC	95% CI		Cut-off value	Sensitivity	Specificity	P value
Seminal total antioxidant capacity	0.741	0.641	0.842	>1.46	70%	64%	<0.001*

DISCUSSION

Current study disagreed with Kamkar and his colleague who conducted a case-control study that comprised 42 couples who had experienced idiopathic RPL and 42 fertile men as the control group. They stated that sperm motility in the patients was significantly less than the control group (P=0.001). On the other hand, they agreed with us and stated that the sperm count and morphology was not significantly different between the two studied groups [1].

Fazeli and Salimi aimed to determine the correlation between total antioxidant capacity (TAC) and malondialdehyde (MDA) as markers of oxidative stress in relation to idiopathic male infertility and sperm parameters. This case control study was conducted using 35 men with idiopathic infertility and 34 men with proven fertility. Seminal plasma TAC and MDA were measured by ferric reducing ability of plasma (FRAP) and thiobarbituric acid (TBA) reaction methods, respectively. They corresponded with current study and stated that seminal TAC levels were signifi-

cantly lower and seminal MDA levels were significantly higher in men with idiopathic infertility than in fertile men (P<0.0001 and P=0.004, respectively) [7].

Vatannejad and his colleague conducted a study to evaluate reactive oxygen species (ROS), total antioxidant capacity (TAC) and ROS-TAC score as indicator for oxidative stress status as well as 8-hydrodeoxyguanosine (8-OHdG) levels as a marker for DNA damage in the seminal plasma of asthenozoospermia patients compared to normozoospermia samples, however our study assessed TAC in normozoospermia samples only. They disagreed with current study and stated that no significant difference was observed in TAC levels between the groups. ROS-TAC score in astheno¬zoospermic men was lower than normozoospermic men (P = .02) [8].

Current study agreed with Kamkar and his colleague who stated that the total antioxidant capacity was 2.69 ± 0.88 in the RPL group compared to 3.63 ± 1.31 nm in the controls, respectively [1].

Huang and his colleagues conducted a systematic review and meta-analysis of observational case-control studies to evaluate markers of oxidative stress in seminal plasma of patients with male infertility. They agreed with current study and stated that the concentrations of GSH (SMD = –1.68, p < 0.00001), vitamin C (SMD = –1.12, p < 0.00001), and vitamin E (SMD = –1.48, p = 0.003), as well as the activities of catalase (SMD = –1.91, p < 0.0001), glutathione peroxidase (SMD = –1.96, p = 0.0002) and glutathione-S-transferase (SMD = –1.62, p = 0.009) declined remarkably, resulting in decreased total antioxidant capacity (SMD = –1.77, p < 0.00001) [9].

Twenty infertile men (test group) attending various fertility centers were recruited in the study and 20 fertile male volunteers (control group) were also recruited as procedural controls based on the biophysical analysis of semen in a study conducted by Riaz and his colleagues. They were in line with current study and stated that TAS concentration was lower in the infertile group compared to the fertile group. The results were shown as mean ± SD (95% CI), 0.65 ± 0.29 (0.51-0.79) vs. 0.98 ± 0.34 (0.82-1.14) respectively [10].

In a cross sectional study conducted by Issa Layali and his colleagues, 59 semen samples were provided by fertile (n=12) individuals as control, infertile patients with normal viscosity (n=25) and infertile patients with hyper viscosity (n=22). Seminal plasma TAC was measured by ferric reducing of antioxidant power (FRAP). They agreed with us and stated that the mean of seminal plasma TAC value in seminal plasma of non-hyper viscosity patients (1710.31 ± 458.67 μmol/l) was significantly (p<0.01) higher than that of hyper viscosity group (1230.25 ± 352 μmol/l) [11].

Fazeli and Salimi disagreed with current study and stated that a positive correlation was shown between sperm motility, sperm morphology, and TAC levels in men with idiopathic infertility (P=0.002 and P=0.002, respectively). In addition, there was a correlation between sperm motility and TAC levels in fertile men (P=0.005). There was no correlation between sperm count and TAC levels in either men with idiopathic infertility or in fertile men [7].

Same to current study, seminal plasma from 279 infertile patients and 46 normal healthy men referred to a male infertility testing laboratory were tested to measure TAC by a colorimetric assay kit in a study conducted by Roychoudhury and his colleagues. Infertile patients showed significantly lower levels (mean ± SEM) of total antioxidants (micromolar Trolox equivalents) in their seminal plasma (1863.84 ± 27.16 μM) compared to those from fertile men (2013 ± 56.04 μM, P = 0.019). A preferred cutoff TAC value of 1947 μM could facilitate better diagnosis of oxidative stress (OS) in men with male factor infertility. At this threshold, the specificity of TAC assay was 63.0 % and the sensitivity 59.5 % with a positive predictive value of 90.7 % and a negative predictive value of 20.4 % 12.

Strengths

The strengths of current study were due to every effort was made to ascertain that all data were documented, and only complete information was included in data analysis. All clinical evaluations and assessment of study outcomes were done by the same team.

Limitations

The limitations of current study were due to COVID 19 pandemic and relatively small sample size regarding accuracy of study outcomes.

CONCLUSION

Seminal total antioxidant capacity (TAC) is a major contributor to idiopathic repeated pregnancy loss (RPL). Seminal total antioxidant capacity is significantly lower in RPL patients. There was positive correlation between TAC and number of previous abortions. TAC at cutoff point > 1.46 had sensitivity 70% and specificity 64% in prediction of cases of RPL.

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The effect of L-carnitine and vitamin D supplementation on intracytoplasmic sperm injection outcomes in patients with polycystic ovarian syndrome

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Abstract

Background: Polycystic ovarian syndrome (PCOS) represents the most common endocrine pathology in women of reproductive age globally. There is a link between vitamin D deficiencies; lower levels of L-carnitine and PCOS. The purpose of this study is to see how L-carnitine and vitamin D supplementation affects intracytoplasmic sperm injection outcomes in patients with polycystic ovarian syndrome.

Patients and methods: The current study included (40) PCO patients who were arranged to perform ICSI owing to resistance to various methods of induction of ovulation. They were divided into two groups; Group (I) involved (20) patients received 3 grams l-carnitine with 20mcg vitamin D3 daily for 3 months before the ICSI cycle and during the ICSI cycle till the time of HCG measurement. Group (II) involved (20) patients who didn't receive L-carnitine and vitamin D3 neither before nor during ICSI cycle. The patients in this group continued receiving traditional metformin.

Results: After treatment, there was a significant decrease in HOMA IR in group I more than group II (p 0.01), and a significant decrease in HOMA IR after treatment in group I compared to group II (p 0.05). There was a significant increase in number of oocytes; the mean number of M2 oocytes and the mean injected number of oocytes in group I more than group II. Furthermore, the high quality of embryos and the pregnancy rate showed a significant increase in group I more than group II.

Conclusion: This study's findings add clinical support to the evidence that vitamin D and L-carnitine may play a role in intracytoplasmic sperm injection success rates in PCOS patients.

Keywords: Intracytoplasmic sperm injection, L-carnitine, polycystic ovarian syndrome, Vitamin D.

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Introduction

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder in women that causes a variety of signs and consequences.(1,2) It has already been for a long time that the disease has a likelihood of 8-13% in all breeding age categories.(3,4) Polycystic ovarian syndrome (PCOS) is a complicated condition inside which hereditary, hormonal, environmental, and behavioral characteristics all interact to produce a heterogeneous phenotype with reproductive, energy metabolism, and psychological variables that impact women's well-being and life quality throughout their lives.[5,6,7]

According to specialty society recommendations, the existence of at least two of the following three parameters is required for the diagnostic workup: chronic anovulation, hyperandrogenism (clinical or biological), and polycystic ovaries.(6,7) It is an exemption diagnosis, and abnormalities that simulated clinical characteristics of PCOS must always be ruled out. Thyroid issues, hyperprolactinemia, and non-classical congenital adrenal hyperplasia are examples.(8) If clinical manifestations point to another causative agent, some patients may require more comprehensive diagnostic procedures.[8,19]

Insulin resistance and compensating hyperinsulinemia are found in about 80% of obese women with PCOS and 30-40% of lean women, according to published studies.(9,20) There are numerous choices for treatment to decrease the extent of clinical characteristics in PCOS patients. Each doctor should be capable of selecting the most appropriate guidelines for PCOS and the possibility of childbirth.[10]

Vitamin D deficiency was linked to a significant decrease in ovulation frequency, pregnancy rate, and possibility of a live birth in PCOS women receiving ovarian stimulation for fertility problems.(21) An increasing body of research indicated that vitamin D could well be linked to PCOS-related symptoms such as ovulatory dysfunctions, hyperandrogenism, insulin resistance, dyslipidaemia, and metabolism-related risk factors (Muscogiuri et al., 2017).(25) One other study found that taking vitamins D and E together for two months before embryo transfer enhanced the clinical pregnancy rate from 23% to 62% and the live birth rate from 16% to 43% in women with PCOS experiencing IVF (Fatemi et al., 2017).[12]

L-carnitine is essential for glucose metabolism and oxidative stress.(29,30,32) Low serum L-carnitine amounts, also in non-obese women, have been linked to insulin resistance and hyperandrogenism, based on the research (Celik et al., 2017).(5) Researchers have discovered lower concentrations of L-carnitine in PCOS patients, as well as potentially major correlations among reduced ranks of L-carnitine and an increased risk of hyperinsulinemia in PCOS patients (Jamilian et al., 2017 Samimi et al., 2016).[15,28]

The present study aims to determine the impact of L-carnitine and vitamin D supplementation on intracytoplasmic sperm injection outcomes in polycystic ovarian syndrome patients.

Patients and Methods

This is single - blinded randomized placebo-controlled study included (40) PCO patients who were arranged to perform ICSI after unsuccessful ovulation induction using various routines.

- Eligibility criteria of participants were assessed by personal interviews and based on their medical records. The participants' age ranged between 20 to 38 years, BMI ranged between 20-34 kg/m², and serum FSH is lower than 10 m IU/ml in 3rd day of menstrual cycle.
- Exclusion criteria were; heart diseases, liver or kidney deficiencies, known cases of endometriosis (approved histologically), any uterine anomalies, hydrosalpinx,

and severe male factor infertility (sperm count < 5 million per milliliter or total azoospermia, normal morphology <4%). Those consumed vitamin and antioxidant supplementations in the last three months before the trial start date were excluded from the study.

The study's patients were divided into two groups:

- **Group (I):** involved (20) patients received 3 grams l-carnitine with 20mcg vitamin D3 daily for 3 months before the ICSI cycle and during the ICSI cycle till the time of HCG measurement.
- **Group (II):** involved (20) patients did not receive l-carnitine and vitamin D3 neither before nor during ICSI cycle. The patients in this group continued receiving traditional metformin therapy.

The HOMA index (marker of insulin resistance IR) was calculated as [baseline glucose] x [baseline insulin]/22.5 for all included patients in both groups after a complete history was taken, including that of the length of infertility, physical examination, and evaluation of male partners. Early findings in all patients were analyzed and after 3 months of l-carnitine and vitamin D therapies. All women underwent ICSI using either agonist or antagonist protocol with their basic elements according to the case.

- The primary outcomes measures were the quality of oocyte, number of oocytes, quality of embryos and number of embryos transferred.
- Secondary outcomes were clinical pregnancy, rate of miscarriage, multiple pregnancy rate and ectopic pregnancy rate.

The metabolic changes and the outcome of ICSI cycle were recorded and analyzed.

Statistical analysis of the data

- Data were fed to the computer using IBM SPSS software package version 24.0.
- Qualitative data were described using number and percent. Comparison between different groups regarding categorical variables was tested using Chi-square test.
- Quantitative data were described using mean and standard deviation for normally distributed data.
- For normally distributed data, comparison between two independent populations was done using independent t-test.
- Significance test results are quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

Results

Table (1) had shown the basic demographic and hormonal screening test of the two studied groups, with the mean age, BMI, and FSH levels showing insignificant differences ($p > 0.05$).

Table (1): Comparison between two groups as regard to demographic and basic laboratory findings

	Group I	Group II	P value
Age			
Range	23-38	22-37	0.155
Mean	30.1	28.8	N.S.
SD	3.67	4.31	
BMI			
Range	25-30.9	26-31.8	0.064
Mean	27.965	28.82	N.S.
SD	1.709	1.77	
FSH			
Range	6.7-9.33	7.06-9.84	0.074
Mean	8.03	8.45	N.S.
SD	0.905	0.908	

Regarding HOMA IR, it was discovered that the mean HOMA IR in the two groups before treatment was high (>2.5), and there was no significant difference when comparing the two groups before treatment. However, after treatment, there was a significant decrease in HOMA IR in group I more than group II

(p 0.01), and there was also a significant decrease in HOMA IR after treatment in group I when comparing with group II (p 0.05), as shown in table (2). Table (2): Comparison

Table (2): Comparison between the two studied groups regarding pretreatment and posttreatment HOMA IR values.

HOMA IR	Group I	Group II	P1 value
Pretreatment Range Mean SD	2.6-3.8 3.28 0.370	2.9-3.7 3.34 0.246	0.275 N.S.
Post treatment Range Mean SD	0.8-2.4 1.49 0.467	2-2.5 2.25 0.176	0.001*
P2	0.001*	0.061 N.S.	

P1 comparison between group I and II at the same time

P2 comparison between before and after treatment in the same group.

Table (3), showed the number and quantification of oocytes in the two studied groups, it was found that there was a significant increase in the number of oocytes retrieved in group I more than group II (p <0.01), also the mean number of M2 oocytes was significantly higher in group I more than group II, the mean injected number of qualified oocytes was significantly higher in group I more than group II.

Table (3): Comparison between two groups as regard to patient's oocytes number and quantification

Oocyte	Group I	Group II	P value
Number retrieved Range Mean SD	8-14 11.55 1.986	5-8 6.45 1.234	0.001*
M2 oocyte Range Mean SD	6-12 8.7 2.055	3-8 6.25 1.51	0.001*
Number of injected oocytes Range Mean SD	6-10 7.5 1.504	3-5 4.1 0.852	0.001*

Table (4), showed the quality of embryos in the two studied groups, the grade A embryos were significantly higher in group I more than group II (p <0.01), the embryos transferred at day 5 are significantly increase in group I more than group II.

Table (4): Comparison between two groups as regard to patient's embryo

Embryo	Group I		Group II		P value
Grade A embryos Range Mean SD	4-8 6.1 1.483		2-4 3 0.858		0.001*
	No	**%**	**No**	**%**	
Transfer at D3	9	45.0	14	70.0	0.05*
Transfer at D5	11	55.0	6	30.0	0.031*

Table (5), showed the final outcome, it was found that the pregnancy rate in group I was 60.0% and in group II was 30.0%, with a significant increase in group I more than group II, while the incidence of twin pregnancy, ectopic pregnancy and abortion shows insignificant difference between the two groups (p >0.05).

Table (5): Comparison between two groups as regard to patient's outcome

Outcome	Group I		Group II		P value
	No	%	No	%	
Pregnant					
Yes	12	60.0	6	30.0	0.029*
No	8	40.0	14	70.0	
Twin	4	33.3	2	33.3	0.194
Ectopic	0	0.0	0	0.0	-
Abortion	2	16.7	2	33.3	0.500

Discussion

Polycystic ovarian syndrome (PCOS) represents the most common endocrine pathology in women of reproductive age globally. There is a link between vitamin D deficiencies; lower levels of L-carnitine and PCOS. The purpose of this study is to detect the effect of L-carnitine and vitamin D supplementation on intracytoplasmic sperm injection outcomes in patients with polycystic ovarian syndrome.

Our results revealed a significant decrease in HOMA IR in patients received l-carnitine with vitamin D3.

Women with PCOS have indeed inadequate levels of vitamin D, and vitamin D treatment could have a favorable impact on IR in obese women with PCOS (Selimoglu et al., 2010). (29) Several investigators had proposed the correlation among both vitamin D status and metabolic dysfunctions particularly insulin resistance in women with PCOS. Finding from randomized controlled trials indicated that providing PCOS patients with constant smaller concentrations of vitamin D (< 4000 IU/d) or vitamin D as a co-supplement could enhance insulin sensitivity in terms of fasting glucose concentration and HOMA-IR (Łagowska et al., 2018).[18]

Maleki et al., (2019)(22) discovered that carnitine may aid in weight loss, glycemic control, and oxidative stress. Sharkwy and El-Din, (2019)(11) proved that co-treatment with L-carnitine and metformin improved reproduction rate, insulin resistance, and lipid profile in clomiphene citrate-resistant obese PCOS women.

The molecular mechanism underlying the relationship among treatment and PCOS improved performance is uncertain. Even so, according to a previous research, vitamin D3 replacement therapy advanced some biochemical parameters in women with PCOS by raising the amount of soluble receptor for Advanced Glycosylated Ends (AGEs). As a result, vitamin D3 inhibits the progression of inflammation in the pathogenesis of PCOS. Furthermore, vitamin D3 treatment is essential in folliculogenesis because it lowers elevated anti-mullerian hormone levels (Irani et al., 2014).[13]

According to the current study results, the number and quantification of oocyte was significantly improved in patients received l-carnitine and vitamin D3 supplementation.

Recent time, research in (PCOS) rat models was investigated to assess vitamin D effects in the ovary. Dietary vitamin D supplementation increased follicle viability and growth, as well as follicular E2 and P production (Behmanesh et al., 2019).(4) Vitamin D3 injection improved follicle morphology and ultrastructure (e.g., cell junctions, endoplasmic reticulum, and lipid droplets), as well as serum levels of testosterone (Kuyucu et al., 2020).[17]

In prospective studies, serum vitamin D concentration levels strongly associated with the number of mature oocytes retrieved and oocyte fertilization levels in patients undergoing IVF cycles, which was recommended to

be due to anti-inflammatory impacts of vitamin D (Abadia et al. 2016; Liu et al. 2019; Wu et al. 2018).[1]

Considerable lot in vitro studies have noted the pathways by which carnitines promote oocyte and embryo development; underlying mechanisms involve beta-oxidation, antioxidant power, and protection against apoptosis (Placidi et al., 2022).[26]

Dunning and Robker, (2012) (10) stated that L-carnitine impacted oocyte quality since it transports fatty acids and regulates energy production, both of which are crucial in enhancing oocyte maturation. Immature oocytes can cause metabolic and endocrine problems in PCOS (Dumesic and Abbott, 2008). (9) Oral dosing of L-carnitine (5 mg/mL) enhanced the count of oocytes ovulated as well as their competence in contexts of mitochondrial mass and dispersion, as well as oxidative damage in the oocyte and ovary in a mouse model of repetitive ovulation cycles (Miyamoto et al., 2010). [23]

Results of the present study showed significantly embryo transfer increases, pregnancy rate as well as, the grade A embryo significantly increased in patients received l-carnitine and vitamin D3.

Vitamin D could play an essential part in rising ovulation and pregnancy rates in PCOS women (Trummer et al., 2018). (31) Vitamin D supplementation might very well assist pregnant women with PCOS and insulin resistance reinstate normal vitamin D levels in their serum, boosting embryo performance and massively increasing clinical pregnancy rates (Irani et al., 2015). (14) A further study found that obtaining vitamin D six weeks before intracytoplasmic sperm injection improved endometrial quality and clinical pregnancy rate (Polyzos et al., 2014). [27]

In a new analysis, supplements were added to the IVF treatment of women with PCOS. It was discovered that implantation and clinical pregnancy incidence were significantly higher in patients with normal vitamin D levels especially in comparison to those with lowered vitamin D levels (< 20 ng/mL 25(OH)-vitamin D); vitamin D levels correlate strongly with the probability of implantation and clinical childbearing ($p < 0.01$); they enhance embryo quality and the number of high-quality embryos that after vitamin D therapies equals that happening in women with normal vitamin D status (Zhao et al., 2019). [33]

It was found that adding L-carnitine to clomiphene citrate in the follicular till the luteal phase in clomiphene-resistant PCOS cases could contribute significantly in enhancing ovulation performance and clinical pregnancy rate according to Abd-Elfattah et al., (2019) (2) study.

Human embryos exposed to L-carnitine after fertilization had higher implantation rates as well as clinical and continuous childbirth (Kim et al., 2018). (16) The addition of L-carnitine to culture media enhances mitochondrial function in human embryos at the morula stage by raising oxygen consumption rate and ATP production while having no impact on mitochondrial copy numbers (Morimoto et al., 2021). (24)

The current study's findings suggested that taking Vitamin D and L-carnitine supplements could help improve the clinical outcome of ICSI in PCOS patients.

condition

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Use of Tranexamic Acid for prevention of Postpartum hemorrhage after Cesarean section in high risk patients: A Randomized Controlled Trial

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Abstract

Background: Postpartum hemorrhage (PPH) is an obstetric emergency. It is one of the leading five etiologies of maternal deaths worldwide, although the absolute risk of death from PPH is much higher in low-resource countries. It accounts for at least 100,000 deaths each year worldwide and contributes up to 28% of maternal deaths. Timely diagnosis and proper management are essential for preventing PPH-related maternal deaths,

Aim and objectives: to assess the efficacy of administration of Tranexamic Acid in Prevention of postpartum hemorrhage in high risk women for PPH undergoing cesarean section,

Subjects and methods: Our study was conducted at Obstetrics and Gynecology department, in Benha University & Nasr City police Hospitals. A comprehensive sample was taken including all women who are at medium and high risk for PPH after cesarean section birth. Cases were divided into two groups: a study group and a control group. (25 cases in each group),

Result: There was high significant difference between the two studied groups according to blood loss (150cc/pack) and blood transfusion after using tranexamic acid,

Conclusion: Tranexamic Acid is effective in Prevention of postpartum hemorrhage in high risk women for PPH undergoing cesarean section,

Keywords: Postpartum hemorrhage (PPH) and Tranexamic Acid (TXA).

Introduction

Postpartum hemorrhage (PPH) is an obstetric emergency. It is one of the leading five etiologies of maternal deaths worldwide, although the absolute risk of death from PPH is much higher in low-resource countries. It accounts for at least 100,000 deaths each year worldwide and contributes up to 28% of maternal deaths. Timely diagnosis and proper management are essential for pre-

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venting PPH-related maternal deaths (1). Postpartum hemorrhage (PPH) is classically defined as "Blood loss from the genital tract either from placental or extraplacental sites greater than or equal to 500 mL following a vaginal delivery, or greater than or equal to 1000 mL following Cesarean Section". It can also be defined as "Cumulative blood loss which is greater than or equal to 1000 mL or accompanied by a state of hypovolemia within 24 h after the birth process regardless of the route of delivery" (2), or "Any blood loss sufficient to compromise hemodynamic status after delivery". More recent evidence suggests fibrinolysis may also play a role (3). According to the recent Confidential Enquiries into Maternal and Child health (CEMACH) Report, obstetric hemorrhage occurs in around 3.7 per 1000 births with uterine atony being the commonest cause (4), but it is often accompanied by a coagulopathy that may be consumptive in nature (5). Tranexamic Acid (TXA); Trans-4-aminoethyl cyclohexanecarboxylic acid is a synthetic derivative of the amino acid lysine. It is a competitive inhibitor of plasminogen activation. It binds to plasminogen and exerts its antifibrinolytic effect through the reversible blockade of the lysine binding sites on plasminogen molecules, blocking activation to plasmin which is the leading accelerator of fibrinolysis and fibrinogenolysis. This study aimed to assess the efficacy of administration of Tranexamic Acid in Prevention of postpartum hemorrhage in high-risk women for PPH undergoing cesarean section.

Patients and Methods

This was an interventional randomized control trial (RCT) for prevention of postpartum hemorrhage after cesarean section conducted on a comprehensive sample of all women who were at medium and high risk for PPH after cesarean section birth at Obstetrics and Gynecology department, in Benha University & Nasr City police Hospitals. Randomization was performed by using closed envelope technique for selection of the cases.

Sample technique: Systematic random sample.

Sample size: as TXA reduces the risk of blood transfusion in postpartum hemorrhage by a percent of 39 % (6) so sample was 44 cases which was divided into two groups: a study group and a control group. (22 cases in each group), sample was calculated using open EPI program with confidence level 95 % and power 80 %. The dropout incidence was expected to be 10%; therefore 3 participants were added to each group. Finally, each group included 25 women.

Inclusion criteria: Scheduled or unscheduled cesarean delivery, singleton or twin gestation. Women at high risk for PPH after cesarean section (ACOG, 2017): Placenta previa, accreta, increta or percreta, HCT < 30, bleeding at admission, history of Postpartum hemorrhage and Abnormal vital signs (hypotension or tachycardia). Women at Medium Risk for PPH after cesarean section (ACOG, 2017): Previous Cesarean or uterine surgery, more than four previous deliveries, multiple Gestation, Large Uterine fibroids, chorioamnionitis, magnesium sulphate use and prolonged use of oxytocin. Exclusion criteria: Age less than 18 years, women who are not at high risk for PPH, women attending for normal vaginal delivery and recent diagnosis or history of venous thromboembolism or arterial thrombosis because TXA is a risk factor for thromboembolism, its use is contraindicated, need for therapeutic dose of anticoagulation before delivery, because the risk of thrombosis may be increased with TXA, hypersensitivity to TXA or any of its ingredients. Transfusion or planned transfusion of any blood products during the current admission because the primary outcome is already pre-determined and the need for transfusion will be unrelated to perioperative hemorrhage, seizure disorder (including eclampsia) because TXA is a GABA receptor antagonist, and its use has

been associated with postoperative seizures and if there is no hemoglobin and hematocrit result available from the last 4 weeks since it is necessary to measure the post-operative change in hemoglobin and hematocrit.

Operational Design: All patients were subjected to: An informed consent was taken from every patient. Complete history taking: Personal history, any complaint, obstetric history, menstrual history, past medical and past surgical history and family history, complete physical examination. General examination: Vital signs (Blood pressure, Temperature, Heart rate, Respiratory rate). Patient monitoring included non-invasive blood pressure measurement, electrocardiography, and pulse oximetry. Anesthesia was administered according to the anesthesiologist's instructions. Any hypotension likely to be due to the anesthetic agents was treated by intravenous ephedrine as required. All women underwent cesarean section according to this technique: TXA Administration: Participants were divided into two groups: a study group & a control group. In addition to the standard management, the study group was given TXA 1 gm (100 mg/ml) slowly intravenous infusion during delivery after clamping of the cord (administered over 10 minutes at 1 ml/minute). Second dose of TXA 1 g Intravenous was given if: Bleeding continued after 30 minutes and bleeding restarted within 24 hours of completing the first dose While the control group was not given TXA, and we compared the results in both groups (amount of blood loss during operation to assess efficacy of TXA in prevention of PPH and reduction of intra and postoperative blood loss and to assess its safety and benefit in reduction of incidence of hysterectomy or blood transfusion requirements). Following placental delivery by controlled cord traction, the uterus was exteriorized and massaged. Estimation of blood loss was done by Cochrane Database Syst Rev. (7): Counting or weighing: Counting the number of saturated pads, or by weighing all towel and material used to absorb blood (gauze, pads, sheets, etc.)

Blood Loss = (Weight of materials used - weight of material before use) + volume included in the suction container. In direct blood collection, all blood lost during the third stage of labor (except for the placenta and membranes) was contained in a disposable, funneled, plastic collector bag, which was attached to a plastic sheet, and placed under the woman's buttocks. When the bleeding stopped, there were two options: the bag was weighed (gravimetric technique), or the bag was calibrated, allowing for a direct measurement. Taking in consideration the volume of irrigation fluids, subtracting this volume from the measured blood loss to estimate the final blood loss.

Outcomes:

Primary Outcome: Volume of blood loss.

Secondary outcomes: Transfusion requirements: transfusion of 1 or more units of packed red blood cells or other blood products such as fresh frozen plasma, cryoprecipitate, or platelets or any factor concentrates [Time Frame: within 7 days postpartum].Additional medical intervention through use of uterotonics other than oxytocin such as prostaglandins or methergine, [Time Frame: within 48 hours postpartum]. Additional surgical or radiological interventions to control bleeding and related complications such as: laparotomy, hysterectomy, evacuation of hematoma, uterine packing, intrauterine balloon tamponade, interventional radiology [Time Frame: within 7 days postpartum]. Change in maternal hemoglobin and hematocrit concentration. [Time Frame: from 4 weeks before delivery to 48 hours postpartum]. TXA side effects (nausea, vomiting, dizziness, headache, seizures) or skin reactions) [Time Frame: within 24 hours postpartum]. Thromboembolic events (venous or arterial) [Time Frame: within 7 days postpartum]. Maternal death [Time Frame: within 7 days postpartum]. Administrative Design: The protocol was ap-

plied for approval of Research Ethics Committee. Written consent was taken from all participants before including them in the study and they had the right to refuse without effect on their management.

Statistical Analysis: Data were checked, entered and analyzed using SPSS version 23 for data processing. The following statistical methods were used for analysis of results of the present study. I- **The student "t"** test for comparison of means of two independent groups. **II-Mann Whitney test** was used to calculate difference between quantitative variables in not normally distributed data in two groups. **III- Chi- square test (X2):** Used to find the association between row and column variables.

Results

Table (1): Comparison between the two studied groups according to age (years) and BMI

	Study (n = 30)		Control (n = 30)		t	P
Age (years)						
Min. – Max.	21.0 – 39.0		22.0 – 42.0		1.585	0.119
Mean ± SD.	30.23 ± 5.02		32.20 ± 4.58			
Median (IQR)	30.0 (26.0–34.0)		32.0 (30.0–36.0)			
BMI (kg/m²)	**No.**	**%**	**No.**	**%**		
<18.5	0	0.0	0	0.0	χ^2=1.071	^{MC}p=0.612
18.5 – 24.9	3	10.0	1	3.3		
>25	27	90.0	29	96.7		
Min. – Max.	24.0 – 35.0		25.0 – 33.0		t=1.315	0.194
Mean ± SD.	28.40 ± 2.58		29.13 ± 1.63			
Median (IQR)	28.0 (27.0–30.0)		29.50 (28.0–30.0)			

tχ^2: Chi square test MC: Monte Carlo test , t: Student t – test
p: p value for comparing between the two studied groups
*: Statistically significant at p ≤ 0.05
There was no significant difference among the two studied groups as regards age (years) and BMI (kg/m²).

Table (2): Comparison between the two studied groups according to Hemoglobin & HCT before and after using tranexamic acid

Hemoglobin	Study (n=30)	Control (n=30)	t	p
Hemoglobin Before TXA				
Min. – Max.	7.70 – 12.60	7.70 – 11.10	1.989	0.051
Mean ± SD.	10.60 ± 1.23	10.04 ± 0.94		
Median (IQR)	10.50 (10.0–11.20)	0.30 (9.70–10.60)		
After TXA				
Min. – Max.	7.0 – 12.30	7.0 – 9.90		
Mean ± SD.	10.33 ± 1.20	8.90 ± 0.76	5.507*	<0.001*
Median (IQR)	10.30 (9.80–11.0)	9.10 (8.90–9.30)		
p_1	<0.001*	<0.001*		

HCT				
Before TXA				
Min. – Max.	28.0– 37.50	27.60 – 34.10		
Mean ± SD.	33.15 ± 2.07	32.16 ± 1.74		
Median (IQR)	33.40 (32.0–34.0)	32.65 (31.90–33.20)		
After TXA				
Min. – Max.	28.0 – 35.60	28.0 – 32.0		
Mean ± SD.	32.91 ± 1.90	30.50 ± 1.16		
Median (IQR)	33.05 (32.10–34.0)	31.0 (29.80–31.10)		
p_1	0.049*	<0.001*		

t: Student t-test
p: p value for comparing between the two studied groups
p1: p value for Paired t-test for comparing between Before and After in each group
*: Statistically significant at $p \leq 0.05$

There was no significant difference between the two studied groups before administration of TXA. There was high significant difference between the two studied groups after administration of TXA. In the control group there was high significant difference between Hemoglobin before administration of TXA and Hemoglobin after administration of TXA. In the study group there was high significant difference between HCT before administration of TXA and HCT after administration of TXA.

Table (3): Comparison between the two studied groups according to Outcome after using of TXA

Outcome	Study (n=30)		Control (n=30)		Test of seg	p
	No.	%	No.	%		
Blood loss 150cc/pack						
Min. – Max.	5.0 – 8.0		8.0 – 18.0		U=1.500*	<0.001*
Mean ± SD.	6.30 ± 0.65		10.70 ± 2.78			
Median (IQR)	6.0 (6.0–7.0)		10.0 (9.0–12.0)			
Complications						
Blood transfusion	3	10.0	29	96.7	χ^2=45.268*	<0.001*
Hysterectomy	0	0.0	3	10.0	χ^2=3.158	^{FE}p=0.237
Death	0	0.0	0	0.0	–	–

U: Mann Whitney test χ^2: Chi square test FE: Fisher Exact
p: p value for comparing between the two studied groups
*: Statistically significant at $p \leq 0.05$

This table shows that there was high significant difference between the two studied groups according to blood loss (150cc/pack) and blood transfusion after using tranexamic acid.

Discussion

Our study was conducted at Obstetrics and Gynecology department, in Benha University & Nasr City police Hospitals. Comprehensive samples were taken including all women who are at medium and high risk for PPH after cesarean section birth. Cases were divided into two groups: a study group and a control group. (25 cases in each group).

This study demonstrated that there was no significant difference among the two studied groups as regards age (years) and BMI (kg/m2). Jianjun et al. (8) performed a randomized, double-blind, case-controlled study conducted on 174 primipara undergoing CS. 88 of them given 10 mg/kg TXA immediately before CS were compared with 86 others to whom TXA was not given. In agreement with our results, there was no significant difference among the two studied groups as regards age (years) and weight (kg).

Previous study by Ononge et al. (9) suggest that maternal age, number of maternal births, and child size are risk factors for postpartum hemorrhage. In Yang et al. (2021) study, their univariate analysis found that maternal age, number of maternal births, and fetal macrosomia were significantly associated with PPH. Although these factors have not been shown to be independently related to PPH in multivariate logistic regression analysis, they still have a suggestive role in the occurrence of postpartum hemorrhage.

In clinical practice, cesarean delivery for older women, multigravida and large fetuses still require close attention. The number of cesarean sections and fetal position are independent risk factors for PPH (10). Sentilhes et al. (11) enrolled 4551 eligible participants and randomly assigned them to receive tranexamic acid (2276 women) or placebo (2275); 112 women were excluded because they withdrew consent or were found to be ineligible after randomization. In agreement with our results, the baseline characteristics of the women, protocol adherence, and other aspects of management of the third stage of labor were similar in the two groups.Abdel-Fatah et al. (12) showed that the mean age of tranexamic acid intervention group was 28.62 ± 6 years (ranging from 20-40 years) and mean age of control group was 27.38 ± 7.1 years and ranged from (20-48). The difference was statistically non-significant.

In agreement with our results, Perveen et al. (13) found that mean age of tranexamic acid intervention group was 28.80 ± 3.72 years with no significant difference between the studied groups. Average gestational age was 38.94 ± 0.814 weeks in TXA group and 39.02 ± 0.864 weeks in control group with no statistical difference.

Yehia et al. (14) reported 28.4 ± 4.9 years mean age in women with postpartum hemorrhage. Xu et al. (15) also reported that mean age was 26.7 ± 3.7 years. Besides, Goswami et al. (16) reported 23.6 ± 2.5 years mean age in women having PPH.

This study illustrated that there was no significant difference among the two studied groups as regards gravidity, parity, abortion and number of CS. In agreement with our results, Abd El-Gaber et al. (17) illustrated that no statistically significant difference regarding the baseline criteria; parity and gestational age of both groups.

This study reported that there was no significant difference in hemoglobin between the two studied groups before administration of TXA. There was high significant difference in hemoglobin between the two studied groups after administration of TXA. In the study group there was high significant difference in hemoglobin before and after using of tranexamic acid.

In agreement with our results, Jianjun et al. (8) reported that there was no significant difference in hemoglobin between the two studied groups before administration of TXA. After admission in TXA group Hemoglobin declined by 1.1 ± 0.3. Decrease was significantly ($P<0.01$) less than Control group as

hemoglobin declined by 1.6 ± 0.6 in control group.

According to Bekassy et al. (18) the incidence of thrombosis during pregnancy and puerperium is five to six times higher than that in the general population, so it is interesting to observe that no significant difference was found in the incidence of thrombosis in these two groups. In another 100 women, including 50 pregnant women given TXA to prevent blood loss during and after cesarean delivery, thrombotic complications were absent (19).

Also, in Jianjun et al. (2013) study no significant abnormal vital signs occurred after TXA administration as BP, HR, RR, hemoglobin, platelet count, postoperative PT and PPT did not change very much in the TXA group compared with the control group.This has been validated by other studies. Abd El-Gaber et al. (17) demonstrated that as regard to change in hemoglobin level and hematocrit value pre and 24 hours postoperative were highly statistically significant differences between the two groups.

Jianjun et al. (8) demonstrated that there was no significant difference in postoperative PT ($p = 0.23$), PTT ($p = 0.40$), serum hemoglobin concentration ($p = 0.14$) and platelet count ($p = 0.75$) 24 h after surgery. In addition, serum hemoglobin concentration and platelet count show a decline in the control group than in the TXA group. Though the decline in hemoglobin was significantly different between these two groups, no statistical difference in platelet count could be found as bleeding in control group was not high enough to perform a significant change in blood components or criteria other than hemoglobin level.

Jianjun et al. (8) demonstrated that it is evident that the risk of postpartum hemorrhage increases in the control group than the TXA group ($p = 0.04$) from placental delivery to the end of CS, whereas rarely patients suffer PPH from the end of CS to 2 h postpartum in both TXA and control groups. Moreover, more patients in the control group ($n = 19$) had PRBCs infused than in the TXA group. Abd El-Gaber et al. (17) showed that as regard to changes in hemoglobin level and hematocrit value 24 hours postoperative in their study, the changes were significantly high in placebo group than tranexamic group. Also the need for additional uterotonic drugs, additional surgical interventions or blood transfusion were significantly less in tranexamic group. These results were agreed with many previous studies as what had been reported by the meta-analysis by Simonazzi G et al. (20) of the 9 RCTs for evaluation the efficacy of prophylactic tranexamic acid in decrease postpartum hemorrhage at cesarean delivery. Tranexamic acid was associated with a significant reducing postpartum blood loss (low incidence and low severity), a significantly lower hemoglobin level drop postoperative and less need for additional uterotonic drugs.

This study showed that there was high significant difference between the two studied groups according to blood loss 150cc/pack and blood transfusion after using tranexamic acid. In agreement with our results, Abdel-Fatah et al. (12) showed that the mean blood loss during CS of tranexamic acid intervention group was 484 cc and mean blood loss during C/S of control group was 705 cc, where the difference highly statistically significant ($p=0.000$). According to the study by Gungorduk et al. (21) a reduction in postoperative bleeding of around 17 % at 2 h was found in the intervention participants who received 1 g of TXA regardless of their weight.

A multi-center, randomized trial was conducted by Gai et al. (22) suggesting that approximately 18 % reduction of blood loss was found in the experimental group.

Two meta-analyses by Peitsidis et al. (23) and Novikova et al. (24) reported that the TXA effect compared with placebo showed 32.5 and 75.1ml reduction in blood loss, respectively.

In agreement with our results, Abd El-Gaber et al. (17) showed that amounts of blood loss had a highly statistically significant difference between the two groups (less in group A). Another study by Campbell et al. (25) reported that in Egypt the main causes for avoidable deaths were suboptimal care, delay in the recognition of the case, improper antenatal care and finally lack of supplies include blood and its derivatives e.g. fresh frozen plasma and platelets. Many medications have been tried in prevention of postpartum hemorrhage, authors used tranexemic acid in their study because it has affordable price, easily administered and has rare side effects.

CONCLUSION

TXA, with its antifibrinolytic properties, is increasingly being used worldwide to treat PPH. Tranexamic Acid is effective in Prevention of postpartum hemorrhage in high-risk women for PPH undergoing cesarean section.

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Early versus Delayed Oral Liquids and Soft Food after Elective Cesarean Section: A Randomized Control Clinical Trial

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Abstract

Background: When medically needed, caesarean section (CS) is one of the most frequent major surgical operations, saving the lives of both mother and child.

Aim of the work: This randomised controlled clinical experiment was done on a total of 150 pregnant women getting elective CS under spinal anaesthesia at the Ain Shams University Maternity Facility, a tertiary hospital, between June 2021 and March 2022.

Results: The current analysis revealed no statistically significant differences in age, gestational age, or parity between the analysed groups. The time to ambulation, intestinal sound, passing flatus, and passing faeces were statistically substantially shorter in the early eating group, according to this study. Consequently, the early feeding group had a considerably greater rate of ambulation and bowel movements. Only variations in abdominal distension were statistically significant. In neither group was ileus paralysis recorded. This study revealed that patients in the early feeding group were much happier.

Conclusion: Early feeding following an uncomplicated caesarean delivery was associated with a lower frequency of ileus symptoms, a shorter mean time to the first bowel movement, and greater mother satisfaction. This, together with the absence of gastrointestinal issues, indicates that early oral feeding is preferable to late oral feeding. In light of these encouraging findings, it is suggested that we abandon the customary approach to eating.

Keywords: Oral Liquids, Soft Food, Cesarean Section.

Introduction

Each year, the number of caesarean sections done worldwide is increasing dramatically. Consequently, it became necessary to lay a larger emphasis on their postoperative treatment [(1)].

In addition to anaesthesia, wound healing, and nursing, the restoration of intestinal motility and the passage of flatus are recognised as significant variables determining the duration of postoperative hospitalisation [(2)].

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The conventional practice of giving the patient nothing orally after surgery until bowel function (in the form of a bowel movement or flatus) returns, followed by progressive eating, is being questioned and has become controversial [3].

The importance of early postoperative feeding is contingent on the capacity of food intake to induce a reflex that supports synchronised propulsive motion and stimulates the release of gastrointestinal hormones. These effects have an overall positive effect on intestinal motility, hence shortening the duration of postoperative ileus (4). Early feeding may also be associated with less protein depletion, improved wound healing, and a faster recovery [5].

It was believed that oral intake following surgery without the return of bowel motions might cause nausea, vomiting, and abdominal distention, which could result in wound deterioration. This perspective has changed, however, as the length of surgical procedures has decreased, regional anaesthesia has become more available, and intestinal manipulation has decreased. All of these factors promoted early oral consumption prior to the commencement of bowel movements [2].

There have been several comparative studies on postoperative hydration and nutrition strategies(2). There have been a number of studies on the effects of early hydration after caesarean surgery, but less on the effects of fast hydration.

Within the first two hours following surgery, haemorrhage is considered one of the most severe complications. Before commencing oral hydration soon after Caesarean operation, it should thus be extensively assessed [2].

Therefore, early oral hydration, namely the quick administration of oral fluids after caesarean sections, warrants more study. Additionally, its impact on surgical recovery and hospital duration of stay must be examined in depth.

Moreover, early oral hydration after Caesarean section may be advantageous in a number of ways, it may facilitate early return of intestinal movements and reduce the risk of hospital infections, leading to early hospital discharge (2), it may decrease the cost of hospital stay as it decreases the duration of intravenous fluid administration with less use of cannulae with evidence of its association with breastfeeding success and less suffering of the mummy, and it may facilitate early return of intestinal movements(3).

Aim of the Work

The goal of this trial is to examine the safety of early vs delayed oral feeding following a caesarean section (CS) conducted under spinal anaesthesia and without complications.

Patients and Methods

Study design

A Randomized Controlled trial.

Study location

This study was conducted at the university's maternity facility.

Participants Women who had caesarean delivery at the Ain Shams University Maternity Hospital and satisfied the aforementioned criteria.

Criteria for inclusion

- Previous 1,2,3 cs women
- Caesarean section by choice with no complications.
- Uncomplicated pregnancy Spinal anaesthesia

Exclusion criteria

- Medical disorders in the form of HTN, DM.
- History of bowel surgery, intraoperative or immediate postoperative complications

- Contraindications to spinal anesthesia
- Women refused to participate in the study
- Patient receving medical treatment which interfere with intestinal motility e.g buscopan

Sample Size calculation

Using PASS 11 for sample size calculation with 80% power and 0.05 error, and based on earlier research by 'Guoetal,' the estimated mean time until flatulence for the Eof group is 20.18 hours and for the Lof group it is 24 hours. To establish a difference between the two groups, 75 women are required for each group.

Using a computer-generated list of random numbers, patients were randomised to either the "early feeding" or "delayed feeding" group. On opaque envelopes with consecutive numbers, the group's name was printed. In the maternity ward, a box containing sealed envelopes was put, and the envelopes were withdrawn serially until the conclusion of the research.

Ethics and legal considerations

This investigation was carried out at Ain Shams University's Faculty of Medicine after receiving permission from the department that specialises in obstetrics and gynaecology. Before any person was enrolled in the study, informed agreement was obtained from that individual by first outlining the objectives and procedures of the research.

Under the influence of regional anaesthesia, a simple caesarean section was done on each of the 150 women who participated in this study. Following the process, participants were randomly assigned to one of two groups. Women who satisfied both the inclusion and exclusion criteria were asked to participate in the study when the protocol was approved. Patients who were eligible for the trial were randomly allocated to either the early feeding group or the delayed feeding group using a computer-generated sequence. The identifier for this research on clinicaltrials.gov is NCT05233280.

3- Intervention:

First group (early feeding group): (n=75) allowed oral fluids and soft foods (2-4hrs) postoperatively regardless of intestinal sound, flatus, or stool. The second group (the delayed feeding group) was permitted oral fluids and soft foods. 6 hours after surgery.

1: Personal data

After the patient had been moved to the recovery area, her age, parity, gestational age, and the reason for the caesarean section were all noted. After that, the woman was briefed on the purpose of the research, as well as its advantages and potential drawbacks.

2: History taking

The entrance form and the lady were evaluated to ensure that all inclusion requirements were met and exclusion factors were eliminated:

To exclude the following from the medical history: hypertension and diabetes. Her obstetric history was reviewed to confirm that her pregnancy was without complications.

4: Oral fluids regimens

In the "early hydration" group, the woman received a few sips of water to urge her to drink. Then, a cup of clear, warm anise-flavored liquid was given to her, and she was free to drink according to her needs (but not milk or soda containing drinks). In the "delayed hydration" group, the woman was allowed to take liquids six hours after the start of treatment. When both groups tolerated oral fluids well, soft foods were subsequently added.

5: Intravenous fluids regimen:

All of the women received 500 millilitres of glucose solution with 5% concentration intravenously every six hours, 500 millilitres of Ringer lactate solution every twelve hours, and 500 millilitres of normal saline solution every twenty-four hours. These intravenous fluids were no longer administered since they were terminated after the lady had bow-

el movements early on and her feeding was well-established before 24 hours had passed. This occurred after the mother gave birth.

Outcomes;

Primary outcome:

Time of passage of flatus

Secondary outcomes:

Patient satisfaction using a 5-point Likert scale (satisfied, unsatisfied, neutral, completely satisfied, completely dissatisfied), time of stool passing, development of paralytic ileus symptoms such as non-audible intestinal sound, abdominal distention, nausea, and vomiting, and patient satisfaction using a 5-point Likert scale (satisfied, unsatisfied, neutral, completely satisfied, completely dissatisfied).

Statistical methods:

The collected data were encoded, tabulated, and submitted to statistical analysis utilising IBM SPSS statistics software version 28.0, IBM Corp., Chicago, United States of America, 2021. If the Shapiro-Wilk test for normality has been passed, the data have been provided as meanSD (standard deviation) along with the lowest and maximum values of the range, and the test has been successful, a t-test is performed to compare the quantitative data. The Chi-square test and Fishers Exact test are effective when analysing qualitative data given as numbers and percentages for variables with extremely tiny expected values. In order to compare the rates, the log rank test was utilised. A p-value of 0.05 or less was necessary for the result to be declared statistically significant; otherwise, the threshold for significance was not fulfilled.

Results

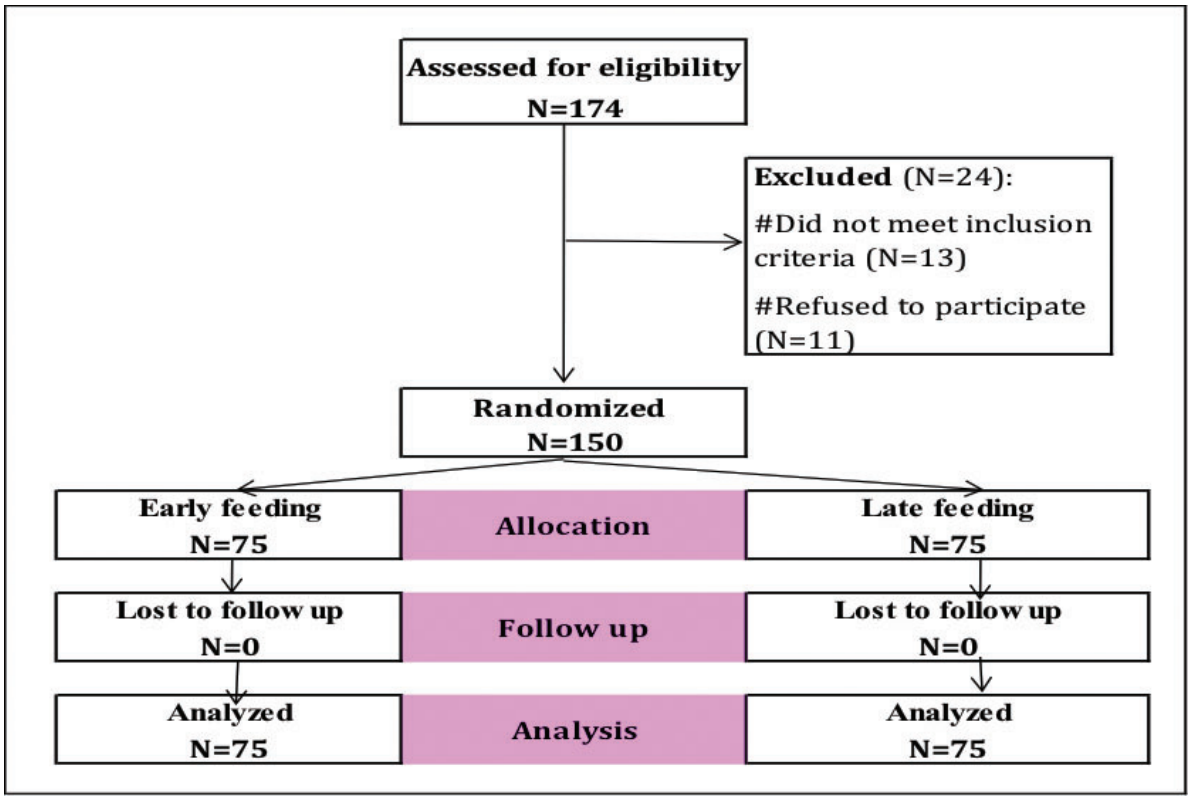

Figure 1: Flow chart of the studied cases

Table 1: Baseline traits in the groups under study

Vatiables		Early feeding (N=75)	Late feeding (N=75)	p-value
Age (years)	**Mean±SD**	29.7±5.9	29.9±5.3	^0.805
	Range	21.0–40.0	18.0–41.0	
GA (weeks)	**Mean±SD**	37.6±1.2	37.4±1.0	^0.274
	Range	34.0–40.0	34.0–40.0	
Parity	**One**	43 (57.3%)	24 (32.0%)	#0.104
	Two	24 (32.0%)	32 (42.7%)	
	Three	8 (10.7%)	19 (25.3%)	
Operation duration (minutes)	**Mean±SD**	57.8±14.2	61.3±14.8	^0.137
	Range	40.0–90.0	40.0–90.0	

GA: Gestational age. ^Independent t-test. #Chi square test

According to Table, there are no statistically significant differences in the ages, gestational ages, or parities of the research groups (1).

Table 2: The study groups' time spent walking (in hours).

Measures	Early feeding (N=75)	Late feeding (N=75)	^p-value	Relative effect Mean±SE 95% CI
Mean±SD	5.7±1.4	6.7±1.4	**<0.001***	-1.1±0.2
Range	2.7–11.0	3.0–9.2		-1.5–-0.6

*^Independent t-test. *Significant. SE: Standard error. CI: Confidence interval. Relative effect: Effect of early relative to late feeding*

As seen in Table 2, the early feeding group had a significantly shorter time to ambulation, as measured statistically.

Table 3: compares the study groups' times to intestinal sounds in hours

Measures	Early feeding (N=75)	Late feeding (N=75)	^p-value	Relative effect Mean±SE 95% CI
Mean±SD	2.7±0.7	3.4±0.7	**<0.001***	-0.7±0.1
Range	2.0–4.0	2.0–5.0		-0.9–-0.5

*^Independent t-test. *Significant. SE: Standard error. CI: Confidence interval. Relative effect: Effect of early relative to late feeding*

As shown in Table 3, the time to intestinal sound was statistically shorter in the early feeding group.

Table 4: Time to flatus (hours) among the studied groups

Measures	Early feeding (N=75)	Late feeding (N=75)	^p-value	Relative effect Mean±SE 95% CI
Mean±SD	4.2±1.1	6.2±1.2	**<0.001***	-2.0±0.2
Range	1.7–9.0	2.7–8.0		-2.4–-1.7

*^Independent t-test. *Significant. SE: Standard error. CI: Confidence interval. Relative effect: Effect of early relative to late feeding*

As seen in Table 4, the time to flatus was statistically considerably shorter in the early feeding group.

Table 5: Time to stool (hours) among the studied groups

Measures	Early feeding (N=75)	Late feeding (N=75)	^p-value	Relative effect Mean±SE 95% CI
Mean±SD	8.1±1.8	10.0±1.8	**<0.001***	-1.8±0.3
Range	4.0–13.0	6.7–15.6		-2.4–-1.3

*^Independent t-test. *Significant. SE: Standard error. CI: Confidence interval. Relative effect: Effect of early relative to late feeding*

As seen in Table 5, the time to first bowel movement was statistically substantially shorter in the early eating group.

Table 6: Postoperative complications among the studied groups

Complication	Early feeding (N=75)	Late feeding (N=75)	p-value	Relative effect Relative risk 95% CI
Nausea	4 (5.3%)	9 (12.0%)	#0.147	0.44 (0.14–1.38)
Vomiting	1 (1.3%)	4 (5.3%)	§0.367	0.25 (0.03–2.18)
Distension	10 (13.3%)	22 (29.3%)	**#0.017***	0.45 (0.23–0.89)
Paralytic ileus	0 (0.0%)	0 (0.0%)	NA	NA

*#Chi square test. NA: Not applicable. *Significant. CI: Confidence interval. Relative effect: Effect of early relative to late feeding*

In the early feeding group, vomiting, nausea, and stomach distension were more common, with statistically significant differences in abdominal distension. In neither group was paralytic ileus documented.

Table 7: Postoperative patients' satisfaction among the studied groups

Satisfaction	Early feeding (N=75)	Late feeding (N=75)	p-value	Relative effect Relative risk 95% CI
Satisfied	61 (81.3%)	45 (60.0%)	**#0.016***	1.36 (1.09–1.68)
Neutral	8 (10.7%)	18 (24.0%)		
Not satisfied	6 (8.0%)	12 (16.0%)		

*#Chi square test.. *Significant. CI: Confidence interval. Relative effect: Effect of early relative to late feeding regarding being satisfied*

Patients in the early feeding group reported significantly better levels of satisfaction, as seen in Table (7).

Discussion

The most common surgical operation performed worldwide is a C-section, which involves a laparotomy, hysterotomy, and the birth of the foetus [6].

Two to three hours after abdominal surgery, the small intestines begin to work and fully recover within six to twelve hours. The stomach recovers to normal function within 12 to 24 hours following surgery, whereas the large intestines recover completely within 48 to 72 hours. The recovery of bowel function can be determined by a patient's gut sound, flatus production, and stool movements (as judged by a physician). These factors are affected by incision size, surgical site, operating time, blood loss, anaesthetic type, opioids, the patient's overall health, diet, and mental health state [7].

The major goal of the typical diet following abdominal surgery is to prevent ileus. It is now advised that women who have just had a caesarean section ingest food orally as soon as feasible rather than sticking to the suggested diet. Early oral intake has raised questions about how it may affect postoperative ileus and other complications after caesarean delivery [8].

Given that postoperative bowel movements complications following caesarean section are a major problem and are frequently associated with nausea, vomiting, and prolonged hospital stays, it was determined that comparing the return of bowel movements in regionally anaesthetized women undergoing caesarean section who were given early oral feeding versus those who were given late oral feeding would be of particular interest [6].

This study compared the safety of early oral feeding following a simple caesarean section (CS) under spinal anaesthesia to delayed oral feeding six hours after audible intestinal sounds.

Between June 2021 and March 2022, 150 pregnant women undergoing elective CS under spinal anaesthesia at the Ain Shams University Maternity Facility, a tertiary hospital, participated in this randomised controlled clinical intervention.

Before recruiting began, this effort was authorised by the Ain Shams University Faculty of Medicine's ethical committee. This investigation may be found at https://clinicaltrials.gov/ct2/ show/NCT05233280. With the identification NCT05233280, it was registered at clinical.trial.gov. This research examined the eligibility of 174 individuals and enrolled 150 patients (75 in each group). Thirteen individuals failed to meet the study's eligibility standards, while eleven patients withdrew to participate.

The study included two groups of 150 pregnant women who delivered via elective CS under regional anaesthesia. No statistically significant differences were identified between the groups in terms of age, gestational age, or parity (p values = 0.805, 0.274, 0.104, and 0.137, respectively).

During the prior decade, a number of studies evaluated early vs delayed oral feeding after a caesarean section and found no negative consequences. However, their results were variable [6].

According to the findings of this study, the early-eating group had quicker times to ambulation, intestinal sound, flatus production, and faeces production (p 0.001).

Consequently, the group that was fed earlier had a much higher rate of ambulation and bowel motions.

Mawson et al. [6] conducted a randomised controlled trial with 148 singleton pregnant women undergoing elective caesarean section (C-section) with regional anaesthesia in order to compare the return of bowel movements in those who were given Early Oral Feeding (EOF) versus those who were given Late Oral Feeding (LOF). They observed that EOF was linked to increased bowel movement.

Mawson et al. [6] found no difference in the time it took to pass stool and flatus following surgery (EOF 3,213868.8 min, LOF 3,084660 min, P = 0.504; LOF 1,589.4 802.8 min, LOF 1,621.8756.6 min, P = 0.809). Considering the possible homogeneity of our sample population.

Ogbadua et al. [9] compared the safety of early vs delayed oral feeding in 152 women who received an uncomplicated CS under spinal anaesthesia. Their findings are congruent with ours. The early-fed group had substantially shorter postoperative time intervals for bowel sound restoration (7.3 h vs. 11.5 h; P = 0.005) and flatus passage (30.7 h vs. 61.5 h; P = 0.005).

Salehian et al. [10] conducted a randomised clinical study with 120 primiparous women who underwent elective caesarean section to examine the effect of early oral hydration on the restoration of bowel function and woman's satisfaction after surgery. They discovered statistically significant differences between the postoperative interval before the lady first heard regular intestinal noises, the postoperative interval before she first passed flaccid stools, and the woman's happiness level.

Chantarasorn et al. [11] conducted a randomised controlled study with 107 women undergoing an uncomplicated caesarean section under regional anaesthesia to examine the benefits and drawbacks of early postoperative feeding vs conventional nutrition for caesarean section patients. It was revealed that the early eaters had considerably less voiding intervals.

In a trial involving 200 moms, Bandyopadhyay [12] assessed the effectiveness of early oral feeding following caesarean birth. 12–14 hours; mean 13 hours; 30-36 hours; mean 33.2 hours (control group; p 0.01); flatus passed 36–40 hours; mean 37.9 hours; stool passed 36–40 (p 0.01); flatus passed 36–40 (p 0.01); stool passed 36–40 (p 0.01). (8.75 hours for bowel noises, 7.3 hours for flatus passage, and 6.27 hours for a bowel movement).

Vomiting, nausea, and abdominal distension were not substantially more prevalent in the early feeding group; only abdominal distension was statistically significant (p = 0.017). In neither group were any signs of ileus paralysis seen.

This study found that patients in the early feeding group were significantly happier than those in the control group (p = 0.016).

Mawson et al. [6] found that while there was no difference in gastrointestinal problems (EOF 42.03 percent, LOF 41.01 percent, P = 0.977), mother satisfaction with postoperative consumption was significantly higher in the EOF group (P = 0.049). Other reported symptoms, including nausea, vomiting, and bloating, did not diminish significantly after 6 to 8 hours, 24 hours, or after the patient was discharged (P-value 0.05).

Ogbadua et al. [9] observed that the early feeding group had significantly shorter hospital stays, which is consistent with our findings (P 0.001; 4.2 days vs. 4.9 days). Women who consumed meals earlier in the day were significantly happier.

In addition, Huang et al. [7] revealed that EOF was not linked with an increased risk of nausea (RR, 0.95; 95% CI, 0.69-1.33), abdominal distension (RR, 0.68; 95% CI, 0.43-1.07), diarrhoea (RR, 0.63; 95% CI, 0.28-1.41), moderate ileus symptoms (RR, 0.82; 95% CI, 0.53-1.10), or vomiting (RR). Salehian (0.960.18 vs 1.134 days; P0.05) (0.960.18 versus 1.134 days; P0.05). The group receiving early feeding had more patient movement than the intervention group (14.1 hours versus 18.8 hours; P0.05). Prefed mothers reported much greater maternal happiness (P0.05).

This is in accordance with the findings of Teoh et al. [13], who discovered that the mothers of EOF participants were much happier. It impacts postpartum depression, future

pregnancy decisions, and the reputation of medical professionals and institutions.

In addition, Chantarasorn et al. [11] found that postoperative nausea and vomiting were not seen, and the rate of mild ileus symptoms in the early feeding group was considerably lower than in the traditional feeding group (19.6% versus 31.5%, p = 0.03).

Teoh et al. [13] found that nausea increased in EOF patients who had orange juice 30 minutes after surgery. Despite a significantly higher incidence of nausea in the EOF group (10.2% vs. 2%, P0.05), mother satisfaction was much greater (P0.0001).

It is noteworthy to note that Izbizky et al. [14] observed no difference in satisfaction ratings between the two groups when they compared the early introduction of regular meals 8 h following surgery to the fluids used in the current experiment, which contradicts our findings. An earlier study hypothesised that the introduction of solid as opposed to liquid meals, which are significantly more pleasant for the great majority of women undergoing CS, might account for the observed difference in outcomes.

Conclusion

Following a caesarean birth without difficulties, early feeding was related with better bowel function recovery, a shorter mean time to first bowel movement, and greater mother satisfaction. In addition to the absence of gastrointestinal difficulties, this supports the idea of early oral feeding as opposed to delayed oral feeding.

On the basis of these optimistic findings, it is suggested that we alter our eating habits.

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