

IJOPARB

Indian Journal of
Perinatology and Reproductive Biology

Vol. 09 | No. 02 | April - June 2019 | ISSN 2249-9784

INDEX  COPERNICUS
I N T E R N A T I O N A L



Official Journal of
INDIAN SOCIETY OF PERINATOLOGY AND
REPRODUCTIVE BIOLOGY (ISOPARB)



Indian Society of Perinatology and Reproductive Biology

Estd. 1978

(Reg No. 71 of 1978-1979 under the Societies Registration Act 21 of 1860)

Executive Committee (2018-2019)

President	DR SUCHITRA N. PANDIT	09820416474
Secretary General	DR MEENA SAMANT	09334105945
Immediate Past President	DR MILIND R. SHAH	09822096280
Editor-in-Chief	DR HIRALAL KONAR	09433033225
Vice Presidents	DR ARUP KUMAR MAJHI DR NARAYAN JANA DR GANGADHAR SAHOO DR SHANTI H. K. SINGH	
Treasurer	DR PRAGYA MISHRA CHAUDHARY	09835273668
Communicator	DR SUPRIYA JAISWAL	09431207284

Zonal Chairpersons

East Zone	DR OJASWANI PATEL
West Zone	DR PARUL KOTDAWALA
North Zone	DR ANJOO AGARWAL
South Zone	DR ROOMA SINGH

Executive Members

Patna	DR ABHA RANI SINGH
Patna	DR AMITA SINGH
Ranchi	DR Archana Kumari
Kolkata	DR BISWAJYOTI GUHA
Chennai	DR LAKSHMI RAVINDRAN
New Delhi	DR MALA SRIVASTAVA
Lucknow	DR RAJUL TYAGI
Patna	DR RITA KUMARI JHA
Hyderabad	DR S. MADHUMATHI
Kolkata	DR SUKUMAR BARIK
Chennai	DR VIJAY LAKSHMI SESHADRI
Lucknow	DR YASHODHARA PRADEEP

Head Office:

IMA Building, Dr A. K. N. Sinha Path, South East Gandhi Maidan, Patna 800004

Web: www.isoparb.org

Secretary General's Office

Dr Meena Samant, Secretary General, ISOPARB

21/D, Road No 10, Rajendranagar, Patna - 800016

Phone: +91 93341 05945 | E-mail: meenasamant@rediffmail.com



Indian Journal of Perinatology and Reproductive Biology

CD 55, Sector I, Salt Lake City, Kolkata 700 064

E-mail: ijoparb1978@gmail.com

ISSN 2249-9784 RNI No. WB ENG/2010/39056

EDITORIAL BOARD

Editor-in-Chief

Kolkata Dr Hiralal Konar

Emeritus Editor

Kolkata Dr Arup Kumar Majhi

Editorial Advisory Board

Kolkata Dr K M Gun
Kolkata Dr Gita Ganguly Mukherji
Jamshedpur Dr A K Debdas
Mumbai Dr Bandana Walvekar
New Delhi Dr Sunita Mittal
Cuttack Dr S N Tripathy
Kolkata Dr Sudip Chakravarti

Associate Editors

Kolkata Dr Picklu Chaudhuri
Dr Gita Basu Banerjee
Dr Sukumar Barik
Dr Subrata Lal Seal

Joint Editors

Kolkata Dr Sajal Datta
Kolkata Dr Ramprasad Dey
Kolkata Dr Pallab Kumar Mistri
Kolkata Dr Sudhir Adhikari

Members of Editorial Board

Patna Dr Abharani Sinha
Kolkata Dr Nalini Arora
Kolkata Dr Mamta Sanghamita
Bengaluru Dr Jayanthi
Kolkata Dr Aftabuddin Mondal
Kolkata Dr Shyamal Banerjee
Kolkata Dr Rathindra Nath Roy

Members of Editorial Board

Lucknow Dr Anju Agarwal
Hyderabad Dr Sampat Kumari
Hyderabad Dr Swaraj Lakshmi
Kolkata Dr Chaitali Datta Ray
Silchar Dr Pranoy Nath
Kolkata Dr Somajita Chakraborty
Kolkata Dr Sebanti Goswami
Puducherry Dr Sayed Habeebullah
Kolkata Dr Arindam Halder
Vellore Dr Abraham Pedicyle

Members of National Advisory Board

Kolkata Dr Narayan Jana
Delhi Dr Asoke Kumar
Delhi Dr Deepika Deka
Cochin Dr V P Paily
Cuttack Dr P C Mahapatra
Delhi Dr Arun Singh
Manipal Dr Murali Dhar Pai
Bengaluru Dr Shila Mane
Belgaum, Karnataka Dr M B Bellard
Dibrugarh Dr Rina Ahmed
Lucknow Dr Vinita Das
Burla, Odhisa Dr Gangadhar Sahoo

Members of International Advisory Board

Kolkata Dr B N Chakravarty
UK Dr S Arulkumaran
Japan Dr Kiyoko Kato
Korea Dr Joong Shin Park
Malaysia Dr Ravi Chandran
Sri Lanka Dr Rohana Haththotuwa
Nepal Dr Gehanath Baral
Bangladesh Dr Firoza Begum

Ex-Officio Members

President, ISOPARB Dr Suchitra N Pandit
Secretary General, ISOPARB Dr Meena Samant

Editorial Office:

CD-55, Salt Lake City
Sector-I, Kolkata 700064
Email: ijoparb1978@gmail.com

Contents

Editor's Choice	37
<i>Prof (Dr) Hiralal Konar</i>	
Views and Reviews	
Vaginal Cuff Disruption and Visceral Prolapse	39
<i>Prof (Dr) Hiralal Konar</i>	
Review Article : Obstetrics	
Predicting Pre-term Birth: Ideal Method	41
<i>Dr. Mala Srivastava, Dr. Ankita Srivastava</i>	
Original Article: Obstetrics	
Cesarean Myomectomy – Case Series and Review of Literature	46
<i>Dr. T. Ramani Devi, Dr. C. Archana Devi</i>	
Maternal Proteinuria in Twin Pregnancies Compared with Singleton Pregnancies	53
<i>Arunasish Mallick, Abhijit Rakshit, Anindya Das, Ajanta Samanta, Arup Kumar Majhi</i>	
Case Report - Gynaecology	
A Case of Vaginal Vault Dehiscence with Bowel Evisceration following Abdominal Hysterectomy	59
<i>Dr Baisali Roy, Dr Himadri Sekhar Das, Dr Sujoy Dutta, Dr Subrata Samanta, Prof (Dr) Picklu Chaudhuri</i>	
Instruction to Authors	62

Disclaimer: The Editor/Publisher disclaims any responsibility or legal liability for statements made and opinions or views expressed by the author(s) and contributors and any claims made by the advertisers.

© IJOPARB. All rights reserved. No part of this publication should be reproduced or stored in a retrieval system, or transmitted in any form, by any means: electronic, mechanical or photocopying, recording, or otherwise, without written permission from Editors or Publishers.

Editor's Choice



This issue of the journal is a must read. The articles in this issue are very contemporary and pertinent in current gynecological practice. The authors of the articles are well known in their respective field of specialty. Management issues that are much debated in current practice of obstetrics and gynecology, are discussed. The editorial board look forward the feedbacks from the readers with their views and any queries, if that need to be clarified. The place of cesarean myomectomy is of much interest. (p.46). Debate till continues as regard its place. It appears, decision of cesarean myomectomy should be made with due consideration to patient counseling, size, site, type of myoma, surgeon's expertise, and above all the availability of resources. The author has the experience of doing cesarean myomectomies. In one case it was a compulsion to deliver the baby. The myoma was fairly large and occupied the whole of lower uterine segment. It weighed 830 gram. In one international conference (2019), author had the opportunity to listen to Sir, Prof. S. Arulkumaran (past president FIGO), to comment on cesarean myomectomy. Myoma situated on the line of incision and sub-serous pedunculated myoma are the unambiguous indications.

The case report in this issue (p.59) is of major attraction for many of our readers and especially for me that I have discussed it elaborately in 'Views and Reviews' of this issue. In both the articles, the respective authors' views must be carefully noted to make our practice safe. The photographs presented, need much appreciation for the quality and the reproduction. For our readers the editor has expressed the reviews and his personal views with this topic of case report (p.59), though it is a rare one.

Besides the academic part, we the members of ISOPARB are just back from the festive mood of Durga Puja, Navaratri and the Dussehra (Ram lila). October heralds the onset of autumn and it is the festive season in India, especially in Bengal and more so in Kolkata. The Bengalees' main festival 'Durga Puja' is celebrated with great pomp and grandeur. As the Hindu mythological doctrine proclaims the earth was once troubled by the demons. Goddess Durga was created by Gods to kill the Asuras (demons) and to restore peace and harmony on the earth. Goddess Durga was empowered with divine strength and the weapons from the Gods under the leadership of Lords Vishnu, Brahma, and Maheswara (Shiva). Ultimately Mahishasura (demon king) was killed in a great war by Goddess Durga and peace prevailed on the earth.

It is believed, this time, the October, Goddess Durga with her family members descend on the earth to her maternal home. These five days of her stay on the earth are celebrated in a big way. This is to commemorate the victory of Goddess Durga over the Asuras otherwise, it is the victory of good over the evil. City Kolkata undergoes a major change during these days. Every neighborhood builds a pandal as the home for the Goddess. She is regarded as the source of power and strength against all the evils. These five days the mantras and shlokas of Sri Sri Chandi, calm the heart and soul of the citizens..

With the progress of science and culture, the puja has brought a major societal change over the years. The artistic work on the idol Durga is superb to express the theme of each Pandal. Embodiment of Durga and Lord Krishna is presented in one of such deity

this year, to show the reflection of a classic artistic work. Thousands of visitors from home and abroad throng around the pandals throughout the days and nights.

Pandals are decorated with wire-framed sculptures of diverse religious architecture. The sounds of mantras and Chandipath are interspersed with the azzan, catholic hymns and readings from Guru Granth Sahib. It is recognized that, Kolkata becomes a huge open air art gallery and museum when the best of creativity and artistry is displayed at this puja. Puja days are also the days of culinary delights. Innumerable varieties of lip smacking Bengaline, national (south and north Indian) and the international cuisines are available, on the top is the famous Kolkata sweets.

The fifth day (Dashami) is the Sindoor (vermilion) Khela. It takes place when Goddess Durga travels to river Ganga for immersion. The immersion procession on the Dashami day with the beats of Dhaks leaves a mixed feelings amongst the hearts of all. On one side we are to bid farewell to Her and at the same time welcoming Her for an early return in the next year.

Durga Puja is more than a religious festival, it is a festival of daughter's homecoming. It gives us of togetherness, upholding of culture, artistic work, creativity and above all, a sense of inclusiveness in the present days' spirit of life.

Prof (Dr) Hiralal Konar

Editor-in-Chief

MBBS (Cal), MD (PGI), DNB, MNAMS, FACS (USA) FRCOG (London)

FOGSI Representative to Asia Oceania Federation of Obstetricians and Gynaecologists (AFOG)

Chairman, Indian College of Obstetricians and Gynaecologists (ICOG), 2013

Prof. & Head, Dept. OB-Gyn Agartala Govt Medical College and G B Pant Hospital, Tripura



Views and Reviews

Vaginal Cuff Disruption and Visceral Prolapse

Prof (Dr) Hiralal Konar

Vaginal Cuff Disruption (VCD) and Visceral Prolapse (VP), is an uncommon gynecological complication following hysterectomy. It is the small bowels with or without the omentum, often come out through the gaping of the vaginal vault. It is a surgical emergency that need urgent diagnosis, evaluation and prompt intervention. A wide range of vaginal vault disruption rates have been reported in the literature, overall incidence as mentioned are as follows: total abdominal hysterectomy - 0.28%; vaginal hysterectomy - 0.15%; laparoscopic assisted vaginal hysterectomy - 0.20%; total laparoscopic hysterectomy 0.87% and the highest being with robotic assisted laparoscopic hysterectomy 2.33%.¹ This clinical problem of VCD and VP (VCD & VP) is difficult for evaluation as the studies are very sparse. Majority are the case reports with retrospective observation. Author has met with no such instance of VCD & VP, with the long phase of working in the state, national and international centers. Risk factors, described for this emergent clinical scenario are many. Basic underlying of pathology is the quality of wound healing following surgery and the severity of strain on the vaginal cuff to cause disruption and expulsion of the viscera through the opened vaginal cuff. The risk factors may be broadly seen under the heads of patient's characteristics: anemia, malnutrition, presence of sepsis, tissue atrophy, associated co-morbid conditions (chronic air way obstructive disease, constipation) and hysterectomy done for malignant conditions. Premature resumption to intercourse has been considered as an important risk factor.²

Surgical procedures specially the use of electro surgery for hemostasis and tissue dissection is considered as a risk factor. It is thought to be due to more tissue necrosis and devitalization resulting in poor wound healing.^{3,4} Factors are yet unknown to explain the procedure of laparoscopic assisted robotic surgery.

However available studies are limited and till date the subsequent studies have not supported this theory.⁵

Many centres have used the barbed suture during laparoscopic vaginal vault closure to ensure the perfect tissue apposition and healing.⁶ Based on currently available data, the true impact of various risk factors is difficult to determine.⁶ Author's own experience on using electro surgical procedures, harmonic ace, barbed suture, compared with traditional suture (delayed absorbable suture) has not made any difference in the outcome specially in relation to vaginal cuff healing.

Review of literature and the current practice of vaginal vault closure showed different procedures depending upon the region, institute and the surgeon.⁷ History of hysterectomy is long. The procedures are different since the time of Hippocrates. Most American centres practice 'figure-of-eight' stitches with or without incorporation of the cardinal or uterosacral ligaments. UK practice with which the author is more familiar, uses mattress sutures or interrupted sutures to close the vaginal vault. The angles of the vagina are closed with Heaney's stitch. A continuous suture is not used to close the vaginal vault as it narrows down the vault and leads to dyspareunia.

The author has the varied experience since the beginning. During the residency in PGI-Chandigarh, American practice has mostly been followed. Use of three clamps to hold a vascular pedicle was the practice. Period of registrarship in Calcutta, the leading teaching institute, British practice of mattress or interrupted sutures had been followed. We also learned, the third method of British practice e.g. not to close the vagina vault. The vaginal cut edges are encircled by a continuous suture similar to a blanket stitch (reef stitch). Pelvic peritoneal closure is done over the vaginal cuff. Suture material used is delayed

absorbable (vicryl) 2-0 so that there is minimal foreign body reaction. Follow up report showed no difference in terms of cuff dehiscence and visceral prolapse. Many surgeons practise multilayer closure to improve vaginal vault disruption.⁹ However, till date the hypothesis of multilayer closure has not been supported by subsequent studies.

Based on the current available data and with personal experience, it is difficult to determine the true impact of various surgical procedures on the risk of vaginal cuff dehiscence. Moreover studies are too small to draw any statistically significant differences between the comparison group.

Diagnosis of VCD & VP is mostly clinical. Women with VCD and VP need surgical intervention as an emergency. Cases without evisceration can be managed with continuous bladder drainage (Foley catheterization) and packing the vagina. Patient should lie down with a pillow under the back to minimize pelvic pressure. Patients with evisceration, the bowels are gently reduced and a moist pack is placed in the vagina. When the bowels are irreducible, woman needs resuscitation and immediate surgical intervention.

Vaginal cuff disruption is commonly managed with laparotomy. Presently reports of managing such cases

with repair of the cuff, are by vaginal or abdominal or with combined route.¹⁰ However cases with expulsion of the viscera need abdominal approach. Coverage with broad spectrum antibiotics including the anaerobes (bacteroides and bacterial vaginosis) with metronidazole are important. The principles of surgery are to approximate the healthy edges of the vaginal cuff. The necrotic tissues at the edges if any, need to be excised before closure. Delayed absorbable suture and interrupted stitches are preferred. Vaginal estrogen cream may be used specially for post menopausal women. On post operative discharge, patient is advised for pelvic rest for 6-8 weeks without any strenuous activities. Couple need counselling to prevent the recurrence of cuff disruption. Prevention of vaginal infections and delaying sexual activities are the important ones. Examination of vaginal cuff in the post operative follow up to assess the cuff integrity is of doubtful value.

Vaginal cuff disruption with or without visceral expulsion is a rare complication of hysterectomy. Several risk factors have been mentioned in relation to patient characterization and surgery. It is yet to develop evidence based data to correlate the risk factors and to modify the existing clinical practice. VCD and visceral expulsion needs to be managed as an emergency.

REFERENCES

1. Uccella S, Ceccaroni M, Cromi A, et al. Vaginal cuff dehiscence in a series of 12,398 hysterectomies: effect of different types of colpotomy and vaginal closure. *Obstet Gynecol* 2012; 120:516–523.
2. Cronin B, Sung VW, Matteson KA. Vaginal cuff dehiscence: risk factors and management. *Am J Obstet Gynecol* 2012; 206:284–288.
3. Chan WS, Kong KK, Nikam YA, Merkur H. Vaginal vault dehiscence after laparoscopic hysterectomy over a nine-year period at Sydney West Advanced Pelvic Surgery Unit: our experiences and current understanding of vaginal vault dehiscence. *Aust N Z J Obstet Gynaecol* 2012; 52:121–127.
4. Fanning J, Kesterson J, Davies M, et al. Effects of electrosurgery and vaginal closure technique on postoperative vaginal cuff dehiscence. *JLS* 2013;17:414–417.
5. Nick AM, Lange J, Frumovitz M, et al. Rate of vaginal cuff separation following laparoscopic or robotic hysterectomy. *Gynecol Oncol* 2011; 120:47–51.
6. Siedhoff MT, Yunker AC, Steege JF. Decreased incidence of vaginal cuff dehiscence after laparoscopic closure with bidirectional barbed suture. *J Minim Invasive Gynecol* 2011; 18:218–223.
7. Kashani S, Gallo T, Sargent A, et al. Vaginal cuff dehiscence in robotic assisted total hysterectomy. *JLS* 2012; 16:530–536.
8. Hur HC, Donnellan N, Mansuria S, et al. Vaginal cuff dehiscence after different modes of hysterectomy. *Obstet Gynecol* 2011; 119:382–383.
9. Iaco PD, Ceccaroni M, Alboni C, et al. Transvaginal evisceration after hysterectomy: is vaginal cuff closure associated with a reduced risk? *Eur J Obstet Gynecol Reprod Biol* 2006; 125:134–138.
10. Fuchs Weizman N, Einarsson JI, Wang KC, et al. Vaginal cuff dehiscence: risk factors and associated morbidities. *JLS* 2015; 19:e2013.00351.

Predicting Pre-term Birth: Ideal Method

Dr. Mala Srivastava,¹ Dr. Ankita Srivastava²

The Pre-term Birth (PB) is defined as delivery occurring before 37 completed weeks of gestation. Pre-term Birth are caused by multiple etiologies which makes the prediction and prevention of preterm delivery difficult. But PB is an important cause of neonatal mortality as well as cause of long term neurologic and developmental problems of the newborn.

Since etiology of preterm labor is not clear, identification of the risk factors is important. It is also necessary to determine the individual risk factor for pregnant women for preterm birth, so that the obstetric management of the pregnant women can be done.

Risk Factors

Maternal Factors

- Family history of preterm birth
- Low socio-economic status
- Low educational attainment
- Maternal age (low and high)
- Ethnicity
- Stress
- Depression
- Tobacco use
- Low body mass index
- Infections (genitourinary or extra genital)
- Periodontal infection
- Uterine anomalies

- History of cervical excisional procedures/surgery (LEEP/Conization)

Obstetric History

- Prior preterm birth
- Prior stillbirth/Pregnancy loss >16 weeks GA
- Induced abortion
- Cervical insufficiency

Present pregnancy features

- Vaginal bleeding
- Pregnancy conceived after ART
- Multiple gestation
- Polyhydramnios
- Short cervical length

It is a known fact that women with h/o preterm birth in previous pregnancy have an increased risk for preterm birth in subsequent pregnancy. In a study by Iams et al risk of recurrent PB (<35 weeks) was 14-15% while women with a previous history of uncomplicated term delivery had 3% risk for spontaneous pre-term delivery.¹

Induced abortion is not a risk factor for PB in subsequent pregnancy for first time mothers. But repeated terminations of pregnancy were associated with high risk for extremely PB whereas interpregnancy interval less than 6 or more than 6 months, following dilatation and evacuation did not increase the risk of PB.

Maternal underweight is a risk factor for PB and being low birth weight. A study which examined 12,526 women reported that, among underweight and normal weight women, neither low gestational weight gain

1. Senior Consultant, Institute of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, New Delhi
2. Senior Resident, Department of Obstetrics and Gynaecology, Jai Prakash Lok Nayak Hospital, New Delhi
Corresponding author: Dr. Mala Srivastava. E-mail: malasrivastava2001@yahoo.co.in

nor gestational weight gain pattern in first and second trimester of pregnancy was associated with PB.²

Alkaline vaginal PH due to bacterial vaginosis is proposed as a predictor of PB. The risk of PB was found increased by 3-fold when vaginal PH was >5. Also alkaline vaginal PH was found to be more accurate in predicting late PB (34–37 weeks) than early PB (<34 weeks). The urogenital infections also increase the risk of preterm birth. There is a correlation between HPV, especially high-risk genotypes (HPV 16 and 18), and spontaneous preterm labor in a study from Egypt. The viral load of HPV was positively correlated with the rate of Matrix Metalloproteinase 2 (MMP2) gene expression and both had significant effect on gestational age.³

Periodontitis is the most common chronic infection harboured by women and is a significant multibacterial reservoir and source for pro-inflammatory cytokines. No reduction has been demonstrated in PB with treatment of periodontal disease in pregnancy. Regarding maternal Vitamin D Deficiency, a meta-analysis, including 10,098 subjects from 10 studies, reported that risk of PB was higher in pregnant women with vitamin D deficiency (<20 ng/mL).⁴

Cervical Length: Screening of cervical length by transvaginal ultrasound is a good predictor of PB risk in singleton pregnancies. Threshold of cervical length in 24 weeks of gestation for PB risk was defined as 25 mm (10th percentile), with 37.3% sensitivity and 92.2% specificity. But cervical length assessed in mid-trimester asymptomatic twin pregnancies was a poor predictor of PB <32 weeks' gestation. If in 3-week period there is a shortening in cervical length >10% then it is found associated with increased risk of PB.⁵

A cervical length ≤15mm is reported as the most optimal cut-off with 81% specificity and 83% positive predictive value for predicting the preterm labor.

Cervical Consistence: Cervical length is only a morphologic analysis and cervix has consistency and structural changes during labor. Two methods have been described for assessment of cervical elastography: **strain elastography and shear wave elastography**. Therefore cervical elastography, which is not yet a clearly identified subject, is proposed to be a possible alternative in the future which may be combined with cervical length. Cervical consistency index (CCI), formulated as $(AP'/AP) \times 100$, measuring anteroposterior cervical diameter

before (AP) and after (AP') is reported as being more effective than cervical length in prediction of PB.

Anteroposterior cervical diameter is measured before (AP) and after (AP') application of pressure on the cervix using the transvaginal probe. The index is calculated using the formula: $CCI = ((AP'/AP) \times 100)$. Cervical length is also measured as a screening for Pre-term birth.

Newer Tools. Uterocervical angle (the angle taken between lower uterine segment and cervical canal) $\geq 95^\circ$ and $\geq 105^\circ$ detected in second trimester indicated an increased risk for PB at <37 and <34 weeks, respectively.⁶

Uterine artery pulsatility index during peak uterine contraction in women with threatened preterm labor was found significantly higher in women who delivered within seven days.⁷

Placental strain ratio, when measured with real-time sonoelastography, was found negatively correlated with gestational age at birth and it is suggested to be an effective predictor for PB.⁸

Measurement of central zone of fetal adrenal gland is found effective in predicting PB within seven days with a similar accuracy to cervical length measurement.

Cervical Fluid. Fetal fibronectin is a glycoprotein which is produced by amniocytes and cytotrophoblasts that binds chorionic membranes to maternal decidua. It is normally found in cervicovaginal fluids before 22 weeks of gestation but its presence in cervicovaginal fluid between 24 and 34 weeks of gestation indicates a risk for PB. A systematic review reported that although the accuracy of fetal fibronectin in predicting spontaneous PB varied, it is most accurate in predicting preterm birth in women with threatened preterm labor without advanced cervical dilatation within 7-10 days after testing.⁹

The value of quantitative fetal fibronectin measurement combined with cervical length was compared with qualitative fetal fibronectin combined with cervical length and it was found that it did not improve the prediction of PB within 7 days. The fetal fibronectin for predicting PB in nulliparous patients was reported to be low.

The IL-6 and IL-8 levels in cervicovaginal fluid were associated with PB within 7 days and successfully predicted preterm birth if combined with cervical

length. The combination of IL-8 levels and cervical length had a specificity of 92.8% for predicting PB in 7 days; however its relatively low sensitivity (56.4%) was a limitation for its clinical use.¹⁰

The placental alpha macroglobulin-1 (PAMG-1), which is assessed by a bedside test, Parto Sure, was compared with fetal fibronectin and cervical length measurement and it was reported that PartoSure was more accurate in predicting PB within 7 days with 80% sensitivity and 95% specificity and it was reported that PartoSure had the greatest utility in patients when cervical length was 15–35mm.¹¹

Cervical Fluid, Insulin-like growth factor binding protein-1 (IGFBP-1) was requested as a marker for predicting PB for being positive at significantly higher rates in cervical fluids of patients with PB. Premaquick[®], developed as a triple biomarker of native and total IGFBP-1 and IL-6, was reported as a successful test with 87.1% sensitivity, 92.4% specificity, 84.4% PPV, 100% NPV, and 95% accuracy in predicting PB in 7 days.¹²

When combined with cervical length, ActimPartus test (IGFBP-1) was suggested as an alternative for fetal fibronectin to identify the women who are at risk of delivering in 7 days.

Another study reported that bedside test for IGFBP-1 was more reliable in prediction of PB than fetal fibronectin test. A recent meta-analysis compared PAMG-1, fetal fibronectin, and phosphorylated IGFBP-1 in symptomatic women, and PAMG-1 was reported to have the highest positive predictive value and positive likelihood ratio (LR+) while negative predictive value and LR- remained similarly high within the three biomarkers.¹³

Amniotic Fluid: Low amniotic fluid glucose was found associated with preterm delivery in patients who had undergone amniocentesis at 16-22 weeks of pregnancy for other indications. The Interleukin-6 (IL-6) in amniotic fluid in second trimester was found negatively correlated with gestational age at delivery.¹⁴

In asymptomatic mid-trimester women undergoing amniocentesis, rapid bedside test of matrix metalloproteinase- 8 (MMP-8) was reported to predict nearly half of spontaneous preterm births. In amniotic fluid, increased vascular endothelial growth factor (VEGF), placental growth factor (PGF), and decreased

soluble VEGF receptor-1 (sFlt-1) at 16–19 weeks of gestation, which were indicating angiogenesis and tendency for inflammation, were predictive for PB.

Elevated levels of interleukin-1 β (IL-1 β) in amniotic fluid and cervicovaginal fluid, were suggested as a potential predictor of PB. However, investigations do not have an active role yet in clinical practice in prediction of PB and further studies are needed for clinical use of IL-1 targeting therapies for prevention of PB. Duration of pregnancy was reported significantly longer in patients after emergent cerclage when neutrophil elastase levels in amniotic fluid were <180 ng/mL.¹⁵

IL-8 and Annexin-A2 levels were measured in amniotic fluid that developed PB <32 weeks either with or without preterm premature rupture of membranes (PPROM); combination of amniotic fluid IL-8 and Annexin-A2 for predicting PB within 2 weeks was reported to have a sensitivity of 81.25%, specificity of 88.89%, and positive predicting value (PPV) of 92.86%

Maternal Serum Markers: The ratio of maternal serum alpha fetoprotein (AFP)/amniotic fluid AFP was suggested as a potential predictor for intrauterine growth restriction and preterm delivery in a small sample sized study. The maternal salivary estriol, measured in 25-34 weeks, had 82% negative predictive value on identifying women who will not deliver preterm, which could be used for avoiding unnecessary interventions to prevent PB.¹⁶

The production of 25 proteins in maternal serum at 16-17 weeks of gestation was analyzed and the proteomic imbalance (downregulation and upregulation) in 25 proteins as antioxidant enzymes, chaperons, cytoskeletonproteins, celladhesionmolecules, and proteins involved in angiogenesis, proteolysis, transcription, inflammation, binding, and transportation of various ligands was detected. This means that changes that promote PB start as early as second trimester.¹⁷

Preterm SAMBA study was intended to study metabolomics techniques in multiethnic populations to investigate multiple complex underlying determinants in etiology of spontaneous PB which have not been enlightened yet. MicroRNA profiles were assessed in

maternal blood and it was reported that a correlation with PB was not detected.¹⁸

Conclusion

Recently, the prophylactic use of progesterone, pessary, and cerclage in women with high risk of PB has been reported to reduce the incidence of PB and improve neonatal outcomes. These results highlight the importance of prediction models in order to establish preventative strategies early in pregnancy. Currently, there are no tools that enable early prediction of those women susceptible to PB and more research is needed to develop new strategies to identify women who may benefit from prophylactic therapy.

Identification of risk factors early in pregnancy is an essential component of obstetric care, since early

interventions may be effective in reducing the risk of PB. The preconceptional counselling regarding these factors may further reduce the risk of PB. Differentiation of severity of risk factors is important to assess the best strategy to prevent PB. The prevention of PB is a major public health priority aiming to reduce the infant and childhood morbidity and mortality.

Many findings such as maternal risk factors, ultrasound markers, and biomarkers in maternal serum, amniotic fluid, or cervical fluid are defined in literature that can be effective in predicting PB. There is not a routine method recommended for screening PB in asymptomatic low risk population. Measurement of cervical length by transvaginal ultrasound is the only cost-effective method in women with history of previous PB or with symptoms of threatened PB.

REFERENCES

1. J. D. Iams, R. L. Goldenberg, B. M. Mercer et al., "The Preterm Prediction Study: Recurrence risk of spontaneous preterm birth," *American Journal of Obstetrics & Gynecology*, vol. 178, no. 5, pp. 1035–1040, 1998.
2. A.J. Sharma, K.K. Vesco, J. Bulkley et al., "Associations of Gestational Weight Gain with Preterm Birth among Underweight and Normal Weight Women," *Maternal and Child Health Journal*, vol. 19, no. 9, pp. 2066–2073, 2015.
3. A. Mosbah, R. Barakat, Y. Nabil, and G. Barakat, "High-risk and low-risk human papilloma virus in association to spontaneous preterm labor: a case-control study in a tertiary center, Egypt," *The Journal of Maternal-Fetal & Neonatal Medicine: The Official Journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet*, vol. 06, pp. 1–6, 2017.
4. L. Qin, F. Lu, S. Yang, H. Xu, and B. Luo, "Does Maternal Vitamin D Deficiency Increase the Risk of Preterm Birth: A Meta-Analysis of Observational Studies," *Nutrients*, vol. 8, no. 5, p. 301, 2016.
5. J. Blanc and F. Bretelle, "Outilspr' edictifs de l'accouchementpr 'ematur' edansune population asymptomatique 'a haut risque," *Journal de Gyn ecologie Obst' etriqueet Biologie de la Reproduction*, vol. 45, no. 10, pp. 1261–1279, 2016.
6. M. Dziadosz, T.-A. Bennett, C. Dolin et al., "Uterocervical angle: a novel ultrasound screening tool to predict spontaneous preterm birth," *American Journal of Obstetrics & Gynecology*, vol. 215, no. 3, pp. 376–376.e7, 2016.
7. S. Olgan and M. Celiloglu, "Contraction-based uterine artery Doppler velocimetry: novel approach for prediction of preterm birth in women with threatened preterm labor," *Ultrasound in Obstetrics & Gynecology*, vol. 48, no. 6, pp. 757–764, 2016.
8. E. Albayrak, H. Y. Dogru, Z. Ozmen et al., "Is evaluation of placenta with real-time sonoelastography during the second trimester of pregnancy an effective method for the assessment of spontaneous preterm birth risk?" *Clinical Imaging*, vol. 40, no. 5, pp. 926–930, 2016.
9. H. Honest, "Accuracy of cervico vaginal fetal fibronectin test in predicting risk of spontaneous preterm birth: systematic review," *BMJ*, vol. 325, no. 7359, pp. 301–301.
10. E. Y. Jung, J.W. Park, A. Ryu, et al. Park, "Prediction of impending preterm delivery based on sonographic cervical length and different cytokine levels in cervicovaginal fluid in preterm labor," *Journal of Obstetrics and Gynaecology Research*, vol. 42, no. 2, pp. 158–165, 2016.
11. T. Nikolova, O. Bayev, N. Nikolova, and G. C. Di Renzo, "Comparison of a novel test for placental alpha microglobulin-1 with fetal fibronectin and cervical length measurement for the prediction of imminent spontaneous preterm delivery in patients with threatened preterm labor," *Journal of Perinatal Medicine*, vol. 43, no. 4, pp. 395–402, 2015.
12. G. U. Eleje, E. C. Ezugwu, A. C. Eke et al., "Accuracy of a combined insulin-like growth factor-binding protein-1/interleukin-6 test (Premaquick) in predicting delivery in women with threatened preterm labor," *Journal of Perinatal Medicine*, vol.45, no. 8, pp. 915–924, 2017.

13. R. Tripathi, S. Tyagi, Y. M. Mala, N. Singh, N. B. Pandey, and P. Yadav, "Comparison of rapid bedside tests for phosphorylated insulin-like growth factor-binding protein 1 and fetal fibronectin to predict preterm birth," *International Journal of Gynecology & Obstetrics*, vol. 135, no. 1, pp. 47–50, 2016.
14. A. S. Ozgu-Erdinc, S. Cavkaytar, A. Aktulay, U. et al., "Mid-trimester maternal serum and amniotic fluid biomarkers for the prediction of preterm delivery and intrauterine growth retardation," *Journal of Obstetrics and Gynaecology Research*, vol. 40, no. 6, pp. 1540–1546, 2014.
15. M. Nadeau-Vallee, D. Obari, C. Quiniou, W. D. Lubell, D. M. Olson, S. Girard et al., "A critical role of interleukin-1 in preterm labor," *Cytokine & Growth Factor Reviews*, vol. 28, pp. 37–51, 2016.
16. R. Sharony, D. Dayan, D. Kidron et al., "Is the ratio of maternal serum to amniotic fluid AFP superior to serum levels as a predictor of pregnancy complications?" *Archives of Gynecology and Obstetrics*, vol. 293, no. 4, pp. 767–770, 2016.
17. V. O. Gunko, T. N. Pogorelova, and V. A. Linde, "Proteomic profiling of the blood serum for prediction of premature delivery," *Bulletin of Experimental Biology and Medicine*, vol. 161, no. 6, pp. 829–832, 2016.
18. J. G. Cecatti, R. T. Souza, K. Sulek et al., "Use of metabolomics for the identification and validation of clinical biomarkers for preterm birth: Preterm SAMBA," *BMC Pregnancy and Childbirth*, vol. 16, no. 1, 2016.

ISOPARB thankfully acknowledges the generous donations to the journal fund by the following.

1. Dr Sudip Chakraborty, Kolkata (Member)
2. Organizing Committee of ISOPARB National Conference 2019 held at Hyderabad

Why to Submit in IJOPARB?

- National and International recognition, readership and acceptance.
- Not to wait too long for publication.
- Quality feedback from the expert editors for your improvement.

How to Submit:

Instruction to authors IJOPARB in each issue. Page No. 62

Support to prepare your paper

For any support of composition before submitting article you may contact the IJOPARB Editorial Board.

Email: ijoparb1978@gmail.com

For any more information, please contact Editorial Board

Email: ijoparb1978@gmail.com

BE A LIFE MEMBER

of
**Indian Society of Perinatology
 and**

Reproductive Biology (ISOPARB)

*[Affiliated to the Federation of
 Asia and Oceania Perinatal Societies (FAOPS)]*

Website: www.isoparb.org

Members of ISOPARB interested to work in the editorial Board as reviewers, are requested to submit their names with their updated Curriculum Vite to the Editor in Chief. Kindly mention your interest in the subspeciality that you need to be involved (e.g. fetomedicine, oncology, general gynaecology, general obstetrics etc.)

Cesarean Myomectomy – Case Series and Review of Literature

Dr. T. Ramani Devi,¹ Dr. C. Archana Devi²

Abstract

Introduction: Fibroids are the most common benign tumors occurring in the reproductive age group. Incidence of fibroids is around 0.3-5% during pregnancy. 0.89% of cesarean sections are combined with myomectomies. Increase in the incidence is probably due to delay in child bearing. In the past, cesarean myomectomy was discouraged due to post-operative morbidity and risk of hysterectomy. Now cesarean myomectomy is a safe option with careful selection of cases.

Methodology: It is a retrospective study of 29 cases of cesarean myomectomy which were performed between Jan 2011 and March 2019 at Ramakrishna Medical Centre, LLP, Tiruchirapalli, Tamil Nadu, India. The following parameters were analysed: demographic pattern, associated complications, duration of surgery, number of myomas, and drop in hemoglobin, transfusion rates and post-operative morbidity.

Results: 29 patients considered in the study had a median age of 30 years and most of them were Primipara. Most of the cases were incidental findings, while the others were referred as pregnancy complicated with fibroids. Commonest indication of cesarean section performed was floating. Co-morbid conditions included gestational diabetes, PIH, positive for anti-phospholipid syndrome presenting as BOH. Most patients showed no marked variation in pre-operative and post-operative hemoglobin. However, only one patient had blood transfusion because of large tumor weighing 3.2kgs. All babies were above 2kg except one weighing 800gm. The mean post-operative stay of the patients was 7 days. Post-operative period was uneventful and there was no sepsis.

Conclusion: Studies have proved that cesarean myomectomy is a very safe procedure in low resource settings. It can be ideally done for all cases of sub serous myomas and lower uterine segment myomas where there is difficulty in delivery of the baby or when closure is not possible. Intra mural myomas for myomectomy should be selected carefully. Cesarean myomectomy does not seem to increase the morbidity when compared to cesarean alone.

Keywords: Cesarean myomectomy; cesarean section; myomas; myoma outcome.

1. Consultant Obstetrician & Gynecologist, Ramakrishna Medical Centre LLP, Director “Janani” Fertility Centre, Trichy, Tamil Nadu.
 2. Consultant Obstetrician & Gynecologist, Ramakrishna Medical Centre LLP, Trichy, Tamil Nadu.
- Corresponding author: Dr. T. Ramani Devi. Email: ramanidevidr@yahoo.co.in

Introduction:

Orthodox view of Sir Victor Bonney who is a pioneer in myomectomy in non-pregnant women is reflected in his writing as “It is tempting for the adventurous and sympathetic surgeon to condense the operation of LSCS and myomectomy into one undertaking and save his patient, the ordeal of second admission to hospital. This kindly but misguided policy we heartily deprecate”. The reason for not favoring cesarean myomectomy being technical difficulty or surgeon may not have expertise, need for blood transfusion due to intra operative blood loss,¹ post-operative febrile morbidity and need for hysterectomy.

The incidence of myoma is around 0.3 - 5% during pregnancy.^{2,3} One in ten of these women have complications. The incidences of cesarean myomectomies are found to be 0.89%.¹ Majority of the myomas are asymptomatic and no treatment is needed. 22 – 32% may increase in size mainly during 1st trimester. Myomas greater than 5 cm may grow and lead to complications. Myoma may undergo red degeneration (Necrobiosis), torsion if it is a subserous myoma and rarely superficial vessels upon the myoma can rupture leading to haemoperitonium during pregnancy or postpartum period. Larger myomas can have pressure symptoms.

Myomas can lead to infertility or early pregnancy loss (mainly submucous myomas). They can also lead to preterm labour, preterm premature rupture of membranes, obstructed labour, malpresentation, pressure symptoms leading difficulty in micturition and defecation, hydronephrosis, retained placenta, postpartum endomyometritis, sub involution and postpartum hemorrhage. Rarely uterine torsion can happen. Katz et al reported 10 - 30% of women can have these complications. Cesarean section rate is increased up to 73% mainly due to obstructed labor.^{4,5,6,7}

The incidence has increased of late as women delay their child bearing. In African women, the incidence may be further high. Subserous myomas can be easily removed during caesarean section without harming the mother. Many pregnancies with fibroids in the recent days are seen, which make us think about the need for cesarean myomectomy. By careful selection of cases for cesarean myomectomy may be safe.^{9,10}

Materials & Methods:

The data collected from Ramakrishna Medical Centre which is a 40 bedded hospital were analyzed. The records of the hospital were used to retrieve the cesarean myomectomy patient history and case details between Jan 2011 March 2019. Informed consent was obtained from the patients for publication. Following parameters were analyzed: age, parity, associated history, weeks of gestation, indications for caesarean section, number of fibroids, type of fibroids, location of fibroids, volume of fibroids, duration of surgery, duration of hospitalization, weight of the baby and pre-operative and post-operative haemoglobin levels (Table: 1). SPSS (IBM SPSS Statistics for Windows, Version 20.0) was used to analyze data.

Discussion

Routine thinking is that myoma regresses after delivery and hence there is no need for myomectomy. Evidence shows 30 - 40% of myomas grow during pregnancy, especially in the 1st trimester. Fibroids greater than 5 cm grow rather than smaller myomas. The size of the myoma regresses by 50% during postpartum period. But once when lactational period is over myoma starts increasing in size under the influence of hormones. Hence, it is logical to remove the myomas during cesarean section. In the era of current day techniques it is very safe to do cesarean myomectomy. Few studies have shown high incidence of hysterectomy for postpartum hemorrhage during delivery and post natal period and post-partum sepsis in which myomas were not removed during cesarean section.

This gives an idea that it may be ideal to remove the myoma during cesarean section.^{11,12} Burton et al reported 13 cases of cesarean myomectomy in which he has reported only one case of intra operative hemorrhage.¹³ Few other studies show there is only slight increase in the intra operative hemorrhage as well as operative timing.^{14,15,16}

Result

29 cesarean myomectomy patients were considered in our study, with median age 30 years (range being 25 – 40 years) (Fig. 1). 18 of the patients were primigravida and the rest were multi gravida (Fig. 2). 26 patients were delivered between 36-40 weeks of gestation and the rest were pre term (two falling between 31-35

weeks because of IUGR and one <30weeks owing to the huge size of the myoma and reverse diastolic flow) (Fig. 3). Myoma mapping was done by USG in most of the cases prior to surgery and blood and blood products were reserved.

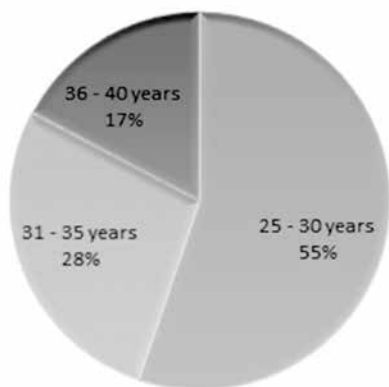


Fig. 1: Age

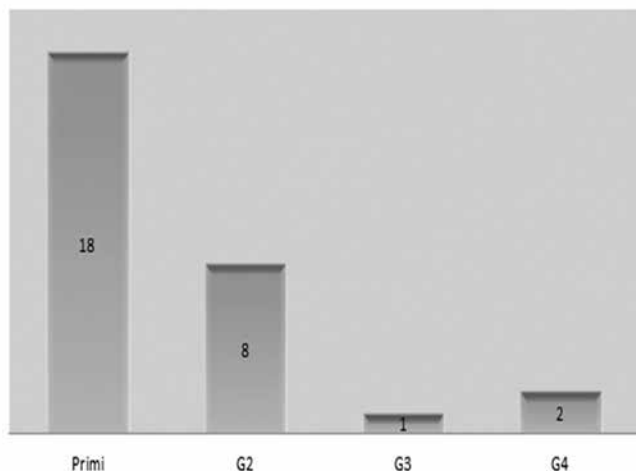


Fig. 2: Parity

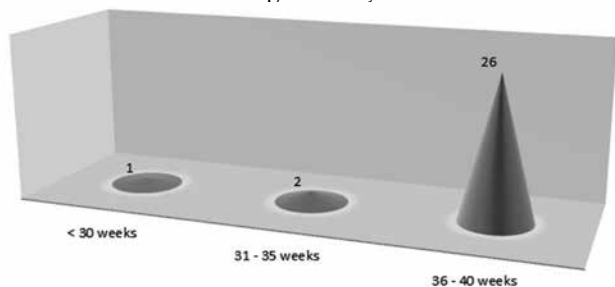


Fig. 3: Weeks of Gestation

Cesarean section was indicated in the following situations: (Fig. 4)

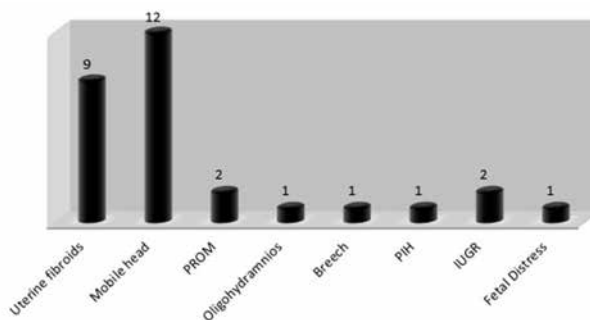


Fig. 4: Indications for Caesarean Section

Myomedotomy was done due to the following reasons:

1. Elective cesarean section when patients insist on concurrent myomectomy
2. Emergency myomectomy is done, when the myomas are in the lower uterine segment causing difficulty in delivering the fetus or difficulty in wound closure
3. Red degeneration causing pain during antenatal period.
4. Unusual appearance of myoma
5. Pedunculated myomas

17 cases were associated with conditions complicating pregnancy like PIH, GDM, Breech presentation, obstructed labor, IUGR, BOH and previous myomectomy (Fig. 5)

Delivery of fetus was usually by Pfannenstiel incision except for two cases where Right Paramedian incision was used as the myomas were large. LSCS was preferred over classical cesarean section.²⁰ After the delivery of the fetus, high dose of oxytocin or prostaglandin or local vasopressin were given. Vasopressin 20 units diluted with 200ml of normal saline were instilled between the serosa and the myoma. BP was monitored carefully when vasopressin was used. Tourniquet can be used to occlude the uterine vessels. Bleeding can further be reduced by using electro-cautery,²¹ tourniquets,¹⁷ clamping uterine artery and infundibulopelvic ligament (or) stepwise devascularisation²² and in centres where facilities are available, uterine artery balloon catheter to be kept in situ and embolization can be done soon after the delivery of the baby. (Figs. 6 – 8)

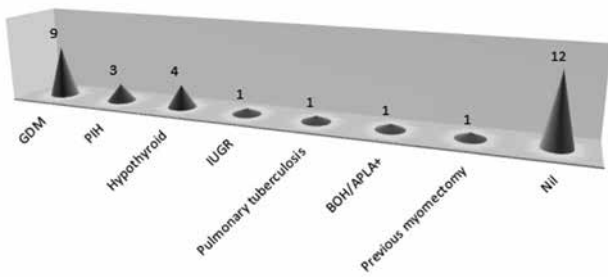


Fig. 5: Associated History



Fig. 6: Sub-serous myoma



Fig. 7: Intra-mural myoma

Subserous myomas and intramural myomas <5 cm are very safely removed. Intramural myomas >5 cms should be done carefully by experienced surgeons. Myomas were located in subserous, intramural and submucous planes. (Fig. 9). Myomectomy is done by conventional way where incision is placed over the myoma and it is enucleated. Dead space is closed with 1-0 vicryl in layers. Those myomas in lower uterine segment are enucleated and then baby is delivered. The incision can be revised and suturing can be done with 1-0 vicryl. 2-0 vicryl can be used to close the serosa. Baseball suturing can help to prevent the adhesions. Multiple myomas are handled in the same way. Tunnelling incision is not ideal. Postoperative adhesion preventing barriers can be used. Submucous myoma

can also be removed very safely and the dead space is closed. Ideal way to reach the submucous myoma is to go through the cavity. If submucous myomas are tackled from outer layer, there is involvement of the full thickness of the myometrium and the scar may be weakened. In cases of the location of the myoma being in the lower uterine segment there may be difficulty in delivery of the fetus. In such cases, myoma has to be enucleated initially followed by the delivery of the baby.²³



Fig. 8: Surgical Procedure

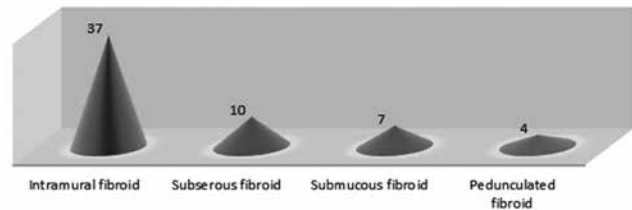


Fig. 9: Plane of fibroids

Prophylactic antibiotics were given for all cases. Hemoglobin was checked post-operatively. Mean drop in hemoglobin was 1.22gms (ranging between 1.07 and 1.36) (Fig. 10). Total no of myomas removed were 59 (Fig. 11). Volume of myomas ranged between 10.5 and 2100cms³ (Median = 60cms³) (Fig. 12). Weight of the babies delivered in our study is given in Fig. 13. Mean duration hospitalization was 7 days (Fig. 14)

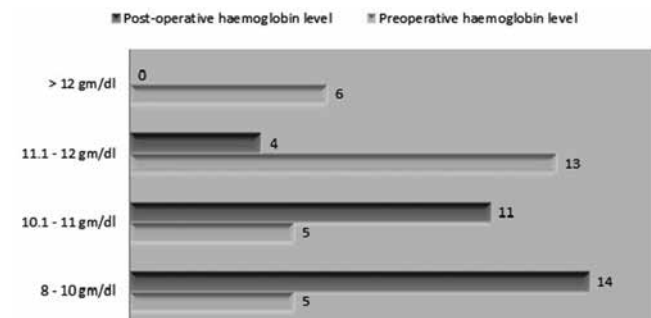


Fig. 10: Pre-operative and post-operative haemoglobin levels

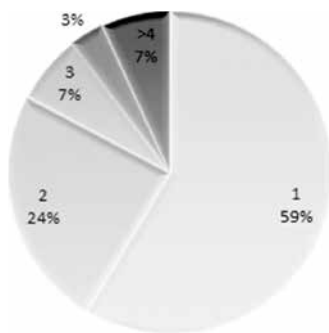


Fig. 11: No. of myomas

■ 1 - 50 ■ 51 - 100 ■ 101 - 200 ■ 201 - 300 ■ > 300

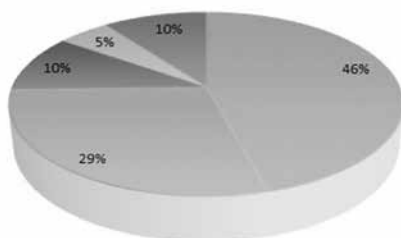


Fig. 12: Volume of fibroids (cm³)

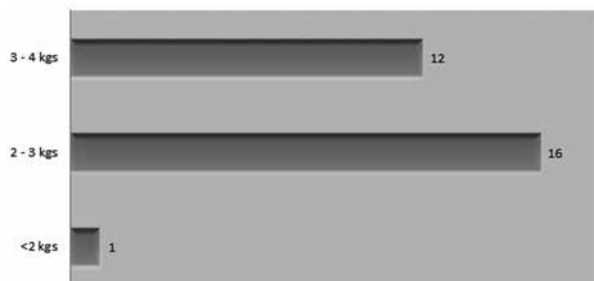


Fig. 13: Weight of the baby

All the specimens were sent for HPE. They were found to be simple leiomyoma or leiomyoma with degenerative changes. None of our patients had undue bleeding needing transfusion except one patient. She was having a very large myoma weighing 2.3kg (Fig. 15, 16) and was treated with elective transfusion. She also had history of Pulmonary Tuberculosis which was treated during the ante natal period. None of the patients needed hysterectomy.

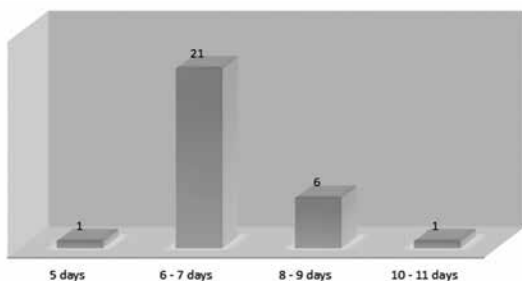


Fig. 14: Duration of hospitalization



Fig. 15 & 16: Large myoma weighing 2.3kg

Discussion

Review of literature by Douglas and Stromme reported 13 cases among which one patient had severe intra operative bleed. A series of 9 cases of caesarean myomectomy reported by Exacousts and Rosat showed three cases of severe haemorrhage necessitating hysterectomy.^{1,24}

Another study by Orac et al involving 22 patients who underwent caesarean myomectomy had no hysterectomy or internal iliac artery ligation.¹⁵ Burton et al reported 13 cases where only one patient had intra operative haemorrhage.²⁵ Similarly study by Kwawkume showed 12 cases of cesarean myomectomy with uneventful intra and post-operative period.²⁶ Other studies showed safe cesarean myomectomy with 11 minutes increase in surgical time.^{17,26} The mean surgical time in our study was 40 minutes (ranging between a maximum of 120 minutes to a minimum of 30 minutes) (Fig. 17). Till date the largest study of Li Hui et al comprising of 1242 cases showed that the mean hemoglobin change, frequency of haemorrhage, post-operative morbidity and length of stay are statistically not significant in cesarean alone or in cesarean myomectomy.²⁸

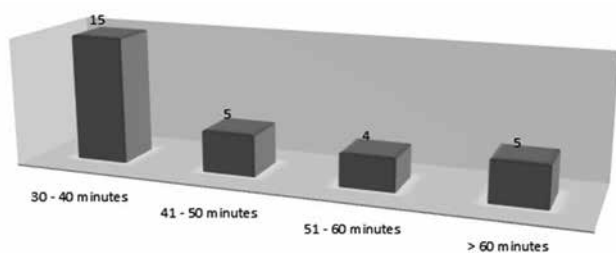


Fig. 17: Duration of surgery

Another study by Hassiakos et al showed an increase in mean surgical time by 15 minutes. There was no postoperative complications, need for blood transfusion, hysterectomy and hospital stay was same. Only when myomas greater than 10 cm and multiple myomas were removed, there was need for blood transfusion comprising of less than 10% of the patients.²⁹

Study by Owolabi et al showed reduction in the blood loss when tourniquet was used along with high dose oxytocin infusion.³⁰

There are studies of isolated cases of huge myomas removed, requiring blood transfusion which is similar to our case study (Yuddandi & Leanzi et al).³¹

Cesarean myomectomy reduces the risk of myoma related complications at a later date both non-pregnant and pregnant status. Sub involution and sepsis can be avoided in the post-partum period. It also reduces menorrhagia and anemia subsequently. In subsequent pregnancies also complications like red degeneration, pre-term labor, PROM and PPH can be avoided. Repeat surgery for myomectomy can be avoided and there is reduced risk of anesthesia. There is reduction in economical and work loss. Studies have shown, in experienced hands it is a safe procedure and there is also possibility of consequent vaginal birth as scar healing is better in caesarean myomectomy.

Disadvantage being slightly increased incidence of hemorrhage, infection, post-operative morbidity and need for hysterectomy in remote condition. In general, complications following cesarean myomectomy could

be need for blood transfusion, hematoma formation in the scar, need for hysterectomy due to postpartum hemorrhage and intraperitoneal bleed and puerperal sepsis.³²

Few cases have been reported in the literature regarding myomectomy during antenatal period.³³ We had incidentally operated 2 cases of myomectomy during 2nd trimester of pregnancy. The reason was, they were very large myomas weighing 2 kg and 1.8 kg causing difficulty in micturition to the patient. Both the myomas were subserous in the retro pubic region causing recurrent retention of urine. Both patients had uneventful post-operative period and antenatal period. They delivered by elective LSCS at 37+ weeks.

Future obstetric performance:

Subsequent pregnancy is spontaneous in 80% of the cases and the rest may need fertility treatment.³⁴ Antenatal complications are threatened abortion, malpresentation (10%) placenta previa (10%) and rupture of the previous scar which is remote.³⁴ The chance of vaginal birth is 44.8% according to a study by Adesiyun. Scar integrity following cesarean myomectomy is better than interval myomectomy as assessed by serial USG in subsequent pregnancies.³⁵

Conclusion:

Studies have proved that cesarean myomectomy is safe in low resource settings especially in sub Saharan African countries where fibroids are common. Cesarean myomectomy can be ideally done for all subserous myomas and lower uterine segment myomas when there is difficulty in delivery of the baby or when uterine closure are not possible. The post-operative morbidity is almost the same in both groups. Plan for caesarean myomectomy should be executed carefully in centres where there are experienced surgeons and availability of blood bank. However, proper consent should be taken including hysterectomy and need for blood transfusion to avoid antigation.

REFERENCES

1. Omigbodun AO, Fawole AO. Myomectomy during pregnancy and delivery: is it safe?: Commentary. *Tropical Journal of Obstetrics and Gynaecology*. 2005;22(1):1-3.
2. Agboghoroma CO, Efezie ER, Umezulike AC. Unavoidable caesarean myomectomy: a case report. *Tropical Journal of Obstetrics and Gynaecology*. 2005;22(1):81-2.

3. Baloniak B, Jasinski O, Prews K, Slomko Z. Morphologic pattern of uterine myomas enucleated at cesarean section. *Clinical Pol.* 2002 APR; 73(4): 255-259
4. Nwagha UI, Agu KA, Nwankwo TO, Egbuji CC. Emergency myomectomy during pregnancy: a case report. *Tropical Journal of Obstetrics and Gynaecology.* 2005;22(1):79-80.
5. O. Okoro and S. Onwere, "Myomectomy during pregnancy," *Pakistan Journal of Medical Sciences*, vol. 23, no. 5, pp. 771–773, 2007.
6. Rice JP, Kay HH, Mahony BS. The clinical significance of uterine leiomyomas in pregnancy. *American journal of obstetrics and gynecology.* 1989 May 1;160(5):1212-6.
7. Cunningham FG, Gant NF, Levenok KJ, Gilstrap LC, Hauth JC, Wenstrom KD, editors: Chapter 35: Abnormalities of the reproductive tract. In: *Williams Obstetrics.* 2001, New York: McGraw Hill, 930
8. Exacoustòs CA, Rosati P. Ultrasound diagnosis of uterine myomas and complications in pregnancy. *Obstetrics and Gynecology.* 1993 Jul;82(1):97-101.
9. Ehigilgha AE, Ande AB, Ojobo SI. Myomectomy during cesarean section. *Int. J. Gyn. & Obs.* 2001; 75: 21-25.
10. Brown D, Myrie M. Cesarean myomectomy a safe procedure. *WestInd. Med. J.* 1997; 46 (supp/2): 450.
11. Hasan F, Aromigm K, Sivanesaratnom V. Uterine leiomyomata in pregnancy. *Int. J. Gyn. Obs.* 1990; 34: 45-48.
12. Davis JL, Ray-Mazumder S, Hobel CJ, Boley K, et al. Uterine leiomyomas in pregnancy: A prospective study. *Obs. Gyn.* 1990; 75: 41-44.
13. Burton CA, Grimes DA, March CM. Surgical management of leiomyomata during pregnancy. *Obs. Gyn.* 1989; 74: 707-709.
14. Orac F, Gungor. M, Sonmezer M, Myomectomy during cesarean section. *Int. J. of Gyn. & Obs.* 1999; 67: 189-190.
15. Dimitrov A, Nikolav A, Stomenov G. Myomectomy during cesarean section. *Akush Ginekol (Sofia).* 1999; 38 (2): 7-9.
16. Hsieh TT, Chong BJ, Liov JD, Chiw TH. Incidental myomectomy in cesarean section. *Changgeng Yi Xueza Zhi Zomar.* 1989; 12 (1): 13-200.
17. Owolabi AT, Loto OM, Kuti O, Ehinmitan RR, Ibrahim AY. Unavoidable cesarean myomectomy: a case report. *Nepal Journal of Obstetrics and Gynaecology.* 2007;2(2):81-3.
18. Febo G, Tessarolo M, Leo L, Arduino S, Wierdis T, Lanza L. Surgical management of leiomyomata in pregnancy. *Clinical and experimental obstetrics & gynecology.* 1997;24(2):76-8.
19. Roman AS, Tabsh KM. Myomectomy at time of cesarean delivery: a retrospective cohort study. *BMC Pregnancy and childbirth.* 2004 Dec;4(1):14.
20. Ben-Rafael Z, Perri T, Krissi H, Dicker D, Dekel A. Myomectomy During Cesarean Section—Time To Reconsider?. *Clin Exp Obstet Gynecol.* 1997;24(2):76-8.
21. Cobellis L, Florio P, Stradella L, Lucia ED, Messalli EM, Petraglia F, Cobellis G. Electro-cautery of myomas during cesarean section—two case reports. *European Journal of Obstetrics and Gynecology and Reproductive Biology.* 2002 Apr 10;102(1):98-9.
22. Sapmaz E, Celik H, Altungül A. Bilateral ascending uterine artery ligation vs. tourniquet use for hemostasis in cesarean myomectomy. A comparison. *The Journal of reproductive Medicine.* 2003 Dec;48(12):950-4.
23. Igwegbe AO, Nwosu BO, Ugboaja JO, Monago EN. Inevitable cesarean myomectomy; a case report. *Niger J Med* 2010;19:329-31
24. Douglas RG, Stromme WB. *Operative Obstetrics,* Newyork. Appleton– Crafts. 1982; p289
25. Burton CA, Grimes DA, March CM. Surgical management of leiomyomata during pregnancy. *Obs. Gyn.* 1989; 74: 707-709.
26. Kwawkume EY. Myomectomy during cesarean section. *Int. J. of Gyn.& Obs.* 2003; 76: 183-184.
27. H. Li, J. Du, L. Jin, Z. Shi, and M. Liu, "Myomectomy during cesarean section," *Acta Obstetricia et Gynecologica Scandinavica*, vol. 88, no. 2, pp. 183–186, 2009.
28. Hassiakos D, Christopoulos P, Vitoratos N, Xarchoulakou E, Vaggos G, Papadias K. Myomectomy during cesarean section: a safe procedure?. *Annals of the New York Academy of Sciences.* 2006 Dec;1092(1):408-13.
29. Owolabi AT, Kuti O, Loto OM, Makinde ON, Adeyemi AB. Cesarean myomectomy—a safe procedure: A retrospective case controlled study. *Nepal Journal of Obstetrics and Gynaecology.* 2007;2(2):59-62.
30. Yuddandi N. Management of a massive caseous fibroid at Cesarean section. *J Obstet Gynaecol* 2004; 24:455–6.
31. Ehigiegba AE, Ande AB, Ojobo SI. Myomectomy during cesarean section. *International Journal of Gynecology & Obstetrics.* 2001 Oct;75(1):21-5.
32. Shafiee MN, Azlin MN, Arifuddin D. A successful antenatal myomectomy. *Malaysian family physician: the official journal of the Academy of Family Physicians of Malaysia.* 2012;7(2-3):42.
33. Adesiyun AG, Ojabo A, Durosinlorun-Mohammed A. Fertility and obstetric outcome after cesarean myomectomy. *Journal of Obstetrics and Gynaecology.* 2008 Jan 1;28(7):710-2.
34. Cobellis G, Messalli EM, Stradella L, Pecori E, Cobellis L. Restitutioadintegrum of myometrium after myomectomy. Different results in pregnant and non-pregnant patients. *Minerva ginecologica.* 2002 Oct;54(5):393-5.
35. Cobellis L, Messalli EM, Stradella L, Pecori E, Gioino E, De EL, Cobellis G. Myomectomy during cesarean section and outside pregnancy. Different outcomes of scars. *Minerva ginecologica.* 2002 Dec;54(6):483-6.

Maternal Proteinuria in Twin Pregnancies Compared with Singleton Pregnancies

Arunasish Mallick,¹ Abhijit Rakshit,² Anindya Das,³
Ajanta Samanta,⁴ Arup Kumar Majhi⁵

Abstract

Background: Although 24-hours urinary protein excretion is more in multiple pregnancies than singleton, the cut-off value for proteinuria in diagnosing preeclampsia is considered same for both singleton and twin pregnancies i.e. ≥ 300 mg /day.

Objective: To compare 24-hour urinary protein excretion in twin pregnancies with that of singleton pregnancies, not complicated by hypertension, diabetes mellitus or any renal disease.

Method: Pregnant women aged 18-45 years with either singleton (n= 43) or twin pregnancies (n= 43) between 24-36 weeks of gestation without hypertension, diabetes, autoimmune disease, renal disease, were asked to collect 24-hour urine. Thereafter urine protein was calculated by Esbach'salbuminometer. Blood samples were drawn at the time of urine collection for serum creatinine estimation. Urine sample suggestive of infection were excluded. Adequacy of the sample collection was assessed using creatinine excretion as per maternal body weight. All the participants were followed up to 6 weeks postpartum for development of new onset hypertension.

Results: After excluding 6 participants due to inadequate creatinine excretion, the final cohort comprised of 80 women (40 singleton, 40 twin) with similarities in most baseline demographic and clinical characteristics. Mean 24-hour urine protein excretion was higher in twin than singleton pregnancies (196.30 mg compared with 145.45 mg, $p < 0.0001$). The upper limit of the 95% CI for mean urinary protein excretion was 216.2 mg in twin and 157.69 mg in singleton pregnancies. Four twin pregnancies (10%) were found to have proteinuria ≥ 300 mg/day at the time of specimen collection but no singleton pregnancy had this level of proteinuria.

Conclusion: Twin pregnancies had significantly more proteinuria as measured by 24-hour urine protein than singleton pregnancies. They are more likely to have proteinuria

1. Senior Resident, College of Medicine & JNM Hospital, Kalyani
2. Associate Professor, Dept of Obs & Gyn, R G Kar MCH, Kolkata
3. Assistant Professor, Dept of Obs & Gyn, R G Kar MCH, Kolkata
4. Assistant Professor and HOD, Dept of Obs & Gyn, Medical College, Kolkata
5. Professor, R G Kar MCH, Kolkata
Corresponding author: Abhijit Rakshit. E-mail: drabhijitr81@gmail.com

in absence of hypertension and this value can exceed 300 mg/day. So a re-evaluation of the diagnostic criteria for preeclampsia in the twin pregnancy is needed.

Keywords: Proteinuria, Singleton, Twin Pregnancy

Introduction

The concept of maternal proteinuria and its diagnosis in pregnancy is utmost important. The exact amount of albumin filtered each day by kidneys is controversial. Normal rate of albumin excretion is less than 20 mg/day. The upper limit of the urinary protein excretion is 150 mg/d in normal non-pregnant woman.¹ Total protein excretion, however, increases to 150-250 mg daily in normal pregnancy due to increase in blood volume and, therefore, the glomerular filtration rate. The cut-off value for pathologic proteinuria in pregnancy was accepted as 300 mg of total protein per 24 hours without preexisting medical conditions and prior to the onset of labor.^{2,3} Proteinuria is an important criterion in diagnosing pre-eclampsia in pregnancy.⁴ Pre-eclampsia is best described as a pregnancy-specific syndrome that can affect virtually every organ system. Although pre-eclampsia is much more than simply gestational hypertension with proteinuria, appearance of proteinuria remains an important diagnostic criterion. Thus, proteinuria is an objective marker and reflects the system-wide endothelial leak, which characterizes the pre-eclampsia syndrome.

Although one study suggests urinary protein excretion, as measured by urinary protein –to-creatinine ratio, is higher in twin pregnancy,⁵ the same cut off value for proteinuria for diagnosis of pre-eclampsia is used for both twin and singleton pregnancy. No clear cut off value of proteinuria for diagnosis of pre-eclampsia in twin is mentioned in the literature. In a recent study done by Osmundson et al⁶ shows that mean 24-hour urinary protein excretion in twin pregnancies is greater than in singletons. These data suggest a re-evaluation of the diagnostic criteria for pre-eclampsia in twin pregnancies. Hence more study is needed to address this issue. The objective of this study will be to determine 24 hour urinary protein excretion and the prevalence of proteinuria in twin and singleton pregnancies, which is not complicated by hypertension and this will give a clue whether urinary protein excretion value (in 24 hours) for the diagnosis of pre-eclampsia to be re-evaluated differently or not, in singleton and twin pregnancy.

Materials and Methods

The present study is conducted at the Department of Obstetrics and Gynaecology, R.G. Kar Medical College and Hospital, Kolkata, during June 2015 - May 2016. Pregnant woman aged between 18 yrs and 45 yrs, carrying singleton or twin pregnancy with gestational age 24-36 weeks attending antenatal clinic / admitted in antenatal ward were the study population.

Women with Urinary Tract Infection, any hypertension at initial check up, Chronic hypertension, Known kidney diseases, Vaginal bleeding, higher order multiple gestations, Autoimmune disease, Diabetes mellitus, and Participants who were expected to deliver within 2 weeks of submitting the 24 hour urine sample were excluded.

In a study by Osmundson et al⁶ proteinuria (300 mg /day protein excretion or greater) occurred in 38% of twin and 8.2% of singleton pregnancies. Keeping in alpha error of 0.05 and 80% power, minimum 28 patient will be required in each arm of study; considering an attrition of 50% a total sample size of 86 will be required with 43 in each arm.

Ethical committee of R.G. Kar Medical College approved study and all participants gave informed consent. Blood pressure was measured and normotensive participants between 24 weeks to 36 weeks were asked to submit 24 hour urine sample. Blood samples were drawn at the time of urine collection, for serum creatinine estimation.

Participants were advised to discard the first morning urine sample and collect all urine in dark container for 24 hour period ending with the next morning's void. They were instructed to avoid strenuous exercise and intercourse during the time of collection. Adequacy of collection were assessed using creatinine excretion with a range of 11-25 mg/kg.

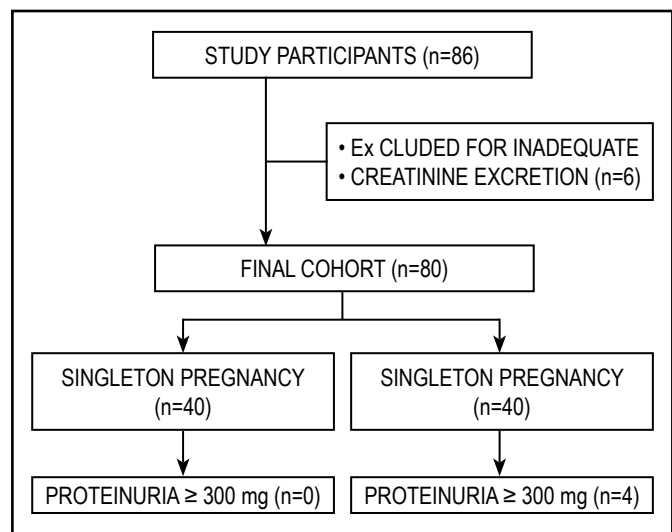
Women admitted in antenatal ward were eligible only during the first 3 days of admission, before prolonged recumbency, because of concern that posture may affect protein excretion with less protein excreted in

supine position.⁸ Total urinary protein excretion was measured by the pathology department. Dye-binding colorimetric method was used. The reportable range for this assay is 2–250 mg/dL with intra- (n20) and interassay (n20) coefficients of variation of 2.5% and 4.3% at 18.98 mg/dL and 4.1% and 4.7% at 61.90 mg/dL, respectively. All urine specimens were processed within 1 hour of arrival to the laboratory. To determine the total protein concentrations in the 24-hour urine specimens, the total urine volume (dL) was multiplied by the total urine protein concentration (mg/dL). Demographic and clinical characteristics were noted. Participants were followed for up to 6 weeks postpartum to monitor for the development of hypertension, which was defined as new-onset blood pressure of greater than or equal to 140 mmHg systolic or 90 mmHg diastolic. Gestational hypertension was defined as the development of hypertension without proteinuria. Mild preeclampsia was defined as blood pressure of 140 – <160 mmHg systolic and 90 – <110 mmHg diastolic with proteinuria. For the purpose of preeclampsia diagnosis, proteinuria was defined as 300 mg or more of protein excreted in a 24-hour urine collection or, when a 24-hour collection was not available, a urine protein-to-creatinine ratio of greater than or equal to 0.3 mg/dL. Severe preeclampsia was defined as blood pressure \geq 160 mmHg systolic or \geq 110 mmHg diastolic with proteinuria. The primary outcome was mean 24-hour urinary protein excretion. Secondary outcomes included proteinuria (300 mg protein or greater in 24 hours) and the development of any hypertensive disorder during pregnancy. In a study by Osmundson et al 6 proteinuria (300mg /day protein excretion or greater) occurred in 38% of twin and 8.2% of singleton pregnancies.

Plan for Analysis of Data

Continuous variable was analysed by independent student t test or Mann-Whitney U test depending on the data normally. Categorical data were analysed by Chi square or Fisher exact test, as appropriate p value of <0.05 will be considered to be statistically significant. Analysis was done by intention to treat principle. Statistical analysis was done by Medcalc version 15.3.0. (Mariakerke, Belgium: Medcalc software 2015).

Results and Analysis



A total of 86 women (43 twin and 43 singleton pregnancies) participated in this study. Six collections were inadequate based on creatinine excretion and were excluded. So 80 women (40 twin and 40 singleton pregnancies) comprised the final cohort.

Table 1 depicted that two groups were similar in most baseline demographic and clinical characteristics. Twin pregnancies delivered at an earlier gestational age compared to singleton pregnancies. Mean 24-hour urinary protein excretion was higher in twin than singleton pregnancies (196.30 mg compared with 145.45 mg, $P < 0.0001$). The upper limit of the 95% confidence interval (CI) for the mean urinary protein excretion was 216.2 mg in twin and 157.69 mg in singleton pregnancies. Four twin pregnancies (10%) were found to have proteinuria \geq 300 mg/day at the time of the specimen collection but no singleton pregnancy had this level of proteinuria. 10% of singleton (4 participants) and 15% of twin pregnancy (6 participants) subsequently developed hypertensive disorder in pregnancy (total 10 participants). When the data were reanalyzed excluding these 10 participants ($n = 70$), the findings were consistent with the overall analysis i.e. mean 24-hour urinary protein excretion was higher in twin than singleton pregnancies (193.11765 mg compared with 141.33333 mg, $P < 0.0001$) and 75% of twin who had 24 hour proteinuria \geq 300 mg were normotensive.

Discussion

This study supports the hypothesis that baseline urinary protein excretion is greater in twin pregnancies. In this study mean 24-hour urinary protein excretion was higher in twin than singleton pregnancies (196.30

mg compared with 145.45mg, $P < 0.0001$). The upper limit of the 95% confidence interval (CI) for the mean urinary protein excretion was 216.2 mg in twin and 157.69 mg in singleton pregnancies. And even after excluding the subjects who subsequently develop hypertension mean 24-hour urinary protein excretion was still higher in twin than singleton pregnancies (193.12mg compared with 141.33 mg, $P < 0.0001$).

Previously Osmundson et al⁶ compared 24-hour urinary protein excretion in singleton and twin pregnancies without hypertension. 24-hour urinary protein excretion was evaluated between 24 weeks and 36 weeks of gestation in twin and singleton pregnancies. Mean urinary protein excretion was higher in twin compared with singleton pregnancies (269.36 mg compared with 204.36 mg, $P = 0.004$). Published studies comparing urinary protein excretion in twin and singleton pregnancies are limited. Smith et al⁵ compared urine protein-to creatinine ratios in 51 twin and 51 singleton pregnancies at three time points across gestation. They found that the urine protein-to-creatinine ratio increased significantly over gestation in all pregnancies and the odds of an elevated urine protein-to-creatinine ratio—defined as greater than 0.19 was significantly higher in twin compared with singleton pregnancies only in the late third trimester (34–38 weeks of gestation). Despite the lack of published studies comparing twin and singleton renal physiology, it is biologically plausible that urine protein excretion is higher in twin pregnancies. Pregnancy increases filtration of urinary proteins resulting in increased urine protein excretion compared with the nonpregnant state.⁹ This is thought to occur as a result of progesterone-induced permeability of the glomerular basement membrane and a 50% increase in the glomerular filtration rate established as early as the first trimester.⁸ In twin pregnancies, cardiac output increases by an additional 20% and blood volume increases by an additional 10% compared with singleton pregnancies.¹⁰ Theoretically, increased cardiac output could lead to an increased glomerular filtration rate resulting in more filtration of protein and more protein excretion. Alternatively, greater proteinuria in twin pregnancy might represent slightly greater accumulation of placental derived vasoactive factors such as sFlt-1, which has been associated with albuminuria in normal pregnancies.¹¹

So our study strengthens the hypothesis that baseline urinary protein excretion is greater in twin pregnancies.

Although 300 mg/day of urinary protein excretion is considered as abnormal in pregnancy, it is not clear how this threshold originated.⁸ In a study by Higby K3, 270 healthy pregnant women ≤ 35 years without a history of diabetes, hypertension, pyelonephritis, preeclampsia, or renal or connective tissue disease were evaluated and found a mean urinary protein excretion of 117 mg and an upper 95% CI limit of 260 mg. Kuo and colleagues¹² reported an upper limit of the 95% CI of less than 150 mg among their population of 205 women with singleton pregnancies. But mean 24-hour urine protein excretion was not reported in this study. So our study also adds to the current literature regarding normal values for urinary protein excretion in pregnancy.

In our study four twin pregnancies (10%) were found to have proteinuria ≥ 300 mg/day at the time of the specimen collection but no singleton pregnancy had this level of proteinuria. And only one of these twin pregnancies (who had proteinuria ≥ 300 mg/day) subsequently developed hypertensive disorder in pregnancy. Rest three twin pregnancies were normotensive, yet they showed proteinuria ≥ 300 mg/day. Though statistical analysis of 24 hour urine protein ≥ 300 mg in singleton and twin pregnancies did not show significance ($P = 0.1238$) in our study, in the study by Osmundson et al⁶ proteinuria ≥ 300 mg/day occurred in 38.0% of twin and 8.2% of singleton pregnancies and statistical analysis of their study showed significant proteinuria (≥ 300 mg/day) in twin pregnancies compared with singleton pregnancies ($P < 0.001$). Proteinuria ≥ 300 mg/day is the cut off value for the diagnosis of hypertensive disorder in pregnancy and currently this value stands for all pregnancies \geq singleton/ twin/ higher order multiple gestations. Our study showed three normotensive twin pregnancies had proteinuria ≥ 300 mg/day. And similar finding was noted in the study by Osmundson et al.⁶ Hypertensive disorder in pregnancy is an important cause of maternal morbidity and mortality in pregnancy. So an appropriate criteria for its diagnosis is utmost important. These data suggest a re-evaluation of the diagnostic criteria for preeclampsia in twin pregnancies. Hence more study is needed to address this issue.

In our study four singleton and six twin pregnancies developed hypertensive disorder in pregnancy later in study period. So a total of ten pregnancies out of eighty participants developed hypertensive disorder in pregnancy. Incidence of hypertensive disorder in pregnancy in our study is eight percent which correlated with the reported incidence of pre-eclampsia (2 - 8% of pregnancies worldwide).

Limitation and strength

The primary limitation of our study is the lack of published norms for assessing adequacy of 24-hour urine collections in pregnancy. In the non pregnant state,¹³ collection adequacy is assessed using 24-hour urine creatinine excretion per kilogram of body weight. Because weight changes throughout pregnancy, it is unknown whether pre pregnancy weight, or weight at the time of the urine collection should be used in. We choose only weight recorded at the time of the urine collection because this information was available for all participants.

Second limitation is the lack of non pregnancy information regarding protein excretion. Although every attempt was made to avoid recruiting patients with medical complications that predispose to proteinuria, it is possible that some participants had undiagnosed renal disease. Ideally, to identify such patients, study participants would need to perform a

24-hour urine collection postpartum to assess whether proteinuria persisted or resolved.

Thirdly the 24-h urine collection takes an entire day to collect and it is cumbersome. Recently, the urine protein–creatinine ratio has been considered important for predicting proteinuria. It compares the spot urine protein excretion to the spot urine creatinine excretion, thereby normalizing protein excretion to the glomerular filtration rate. Thus, the urine protein–creatinine ratio is not subject to variation due to hydration status. In a study by Dwyer BK¹⁴ the urine protein–creatinine ratio showed better discriminatory power than urinalysis [95% confidence interval (CI) 0.83 to 0.95) vs 0.71 (95% CI 0.64 to 0.77, P<0.001]. Furthermore, the urine protein–creatinine ratio predicted the absence or presence of proteinuria in 64% of patients; urinalysis predicted this in only 19%.

Fourthly our study sample size is only 86 and study time period is one year and only those patients attending R.G.Kar Medical College were included. So a very selected population was included in this study which in true sense cannot depict a global population. A large multicentric trial is needed for a longer duration to overcome this.

Strength of our study was the prospective design which allowed us to exclude patients with disorders that

Table:

Characteristic	Singleton Pregnancies	Twin Pregnancies	P value
AGE (yrs.)	24.45 ± 3.741	24.85 ± 3.325	0.6147
RELIGION – HINDU	16 (40)	12 (30)	0.4819
RELIGION – MUSLIM	24 (60)	28 (70)	0.4819
NULLIPARITY	20 (50)	22 (55)	0.8228
MULTIPARITY	20 (50)	18 (45)	0.8228
GESTATIONAL AGE AT DATA COLLECTION (weeks)	28.98 ± 2.516	28.48 ± 2.230	0.3498
BMI (kg/m ²)	23.5625 ± 1.5561	23.7850 ± 1.1153	0.4689
SBP (mm hg)	119.15 ± 10.953	120.75 ± 10.961	0.5156
DBP (mm hg)	75.95 ± 6.118	77.40 ± 5.995	0.2876
URINE CREATININE (mg/dl)	17.25 ± 2.90667	18 ± 2.6602	0.2323
SERUM CREATININE (mg/dl)	0.72 ± 0.156	0.7 ± 0.165	0.5791
24 HOUR URINE PROTEIN (mg)	145.45 ± 38.276	196.30 ± 62.223	< 0.0001
TOTAL PROTEIN ≥ 300 mg	0	4 (10)	0.1238
GESTATIONAL AGE AT DELIVERY (weeks)	38.1 ± 2.318	35.43 ± 1.752	< 0.0001
HYPERTENSIVE DISORDER IN PREGNANCY	4 (10)	6 (15)	0.7353
24 HOUR URINE PROTEIN EXCLUDING THOSE WHO DEVELOP HYPERTENSION LATER	141.33333 ± 37.47761	193.11765 ± 59.76356	< 0.0001

might predispose them to proteinuria. In addition, it allowed us to follow patients throughout the remainder of gestation, delivery, and the postpartum period to correctly ascertain whether hypertension developed during the pregnancy.

Conclusion

This study demonstrates that women with twin pregnancies excrete significantly more protein as measured by a 24-hour urine collection. So in conclusion, twin pregnancy had significantly more

proteinuria as measured by 24 hour urine protein, than singleton pregnancy. And they are more likely to have proteinuria without hypertension and this value can exceed 300 mg/day. So a reevaluation of the diagnostic criteria for preeclampsia in twin pregnancies is needed.

Acknowledgement

Our sincere thanks to Head of the Department, Deptt. of O&G, Principal of R.G.Kar MCH, Kolkata.

REFERENCES

- Gosling P. In 'Clinical Biochemistry. Metabolic and Clinical Aspects. 2nd Ed'. Editors: Marshall WJ, Bangert SK. Churchill Livingstone. Elsevier. 2008. P: 156-73.
- Davey DA, MacGillivray I. The classification and definition of the hypertensive disorders of pregnancy. *Am J ObstetGynecol* 1988; 158: 892-898.
- Higby K, Suiter CR, Phelps JY, Siler-Khodr T, Langer O. Normal values of urinary albumin and total protein excretion during pregnancy. *Am J ObstetGynecol* 1994; 171(4): 984-989.
- Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *ObstetGynecol* 2013; 122(5): 1122-1131.
- Smith NA, Lyon JG. Protein to creatinine in uncomplicated twin pregnancy. *Am J ObstetGynecol* 2010;203:38 Lel-4.
- Osmundson SS, Lafayette RA, Bowen RA, Roque VC, Garabedian MJ, Aziz N. Maternal Proteinuria in Twin Compared With Singleton Pregnancies. *ObstetGynecol* 2014;124:332-7.
- Clark L, Thompson H, Beck E. The excretion of creatine and creatinine during pregnancy. *Am J ObstetGynecol* 1951;62:576-83.
- Lindheimer MD, Kanter D. Interpreting abnormal proteinuria in pregnancy: the need for a more pathophysiological approach. *ObstetGynecol* 2010;115:365-75.
- Roberts M, Lindheimer MD, Davison JM. Altered glomerular permselectivity to neutral dextrans and heteroporous membrane modeling in human pregnancy. *Am J Physiol* 270: F338-F343,1996.
- Cunningham F, Leveno K, Bloom S, Hauth J, Rouse D, Spong C. Multifetal gestation. Williams obstetrics. 23rd ed. New York (NY): McGraw-Hill Companies; 2010.
- Yoshimatsu J, Matsumoto H, Goto K, Shimano M, Narahara H, Miyakawa I. Relationship between urinary albumin and serum soluble fms-like tyrosine kinase 1 (sFlt-1) in normal pregnancy. *Eur J ObstetGynecolReprodBiol* 2006;128:204-8.
- Kuo VS, Koumantakis G, Gallery ED. Proteinuria and its assessment in normal and hypertensive pregnancy. *Am J ObstetGynecol* 1992; 167: 723-728.
- Cote AM, Firoz T, Mattman A, Lam EM, von Dadelszen P, Magee LA. The 24-hour urine collection: gold standard or historical practice? *Am J Obstet Gynecol* 2008 Dec;199(6):625.e1- 6.
- Dwyer BK, Gorman M, Carroll IR, Druzin M. Urinalysis vs urine protein-creatinine ratio to predict significant proteinuria in pregnancy. *J Perinatol* 2008; 28(7): 461-467.

IJOPARB is published four times per year

All India Circulation

ISOPARB have members in all the allied disciplines

A Case of Vaginal Vault Dehiscence with Bowel Evisceration following Abdominal Hysterectomy

Dr Baisali Roy,¹ Dr Himadri Sekhar Das,¹ Dr Sujoy Dutta,² Dr Subrata Samanta,³
Prof (Dr) Picklu Chaudhuri⁴

Introduction

Vaginal cuff dehiscence is a rare, but potentially morbid, complication of total hysterectomy (surgical removal of the uterus and cervix). After removal of the uterine specimen, the vaginal incision (vaginal cuff) is typically closed by continuous or interrupted absorbable sutures. Vaginal cuff dehiscence refers to separation of the vaginal incision. The term vaginal cuff dehiscence is frequently interchanged with the terms cuff separation or cuff rupture. All denote the separation of a vaginal incision that was previously closed at time of initial hysterectomy. After dehiscence of the vaginal cuff, abdominal or pelvic contents are at risk of evisceration (expulsion) through the vaginal opening. Bowel evisceration can lead to serious sequel, including peritonitis, bowel injury and necrosis, and sepsis. Prompt surgical and medical intervention is required. The present case is reported because of its rarity and to highlight the management.

Case Report

A 65 year old, Mrs. J B, was admitted via emergency in the department of gynaecology and obstetrics in

1. Senior resident, Department of G&O, Rampurhat Govt Medical College, Rampurhat, Birbhum
 2. Resident (post PG), Department of G&O, Rampurhat Govt Medical College, Rampurhat, Birbhum
 3. Assistant Professor, Department of G&O, Rampurhat Govt Medical College, Rampurhat, Birbhum
 4. Professor and HOD, Department of G&O, Rampurhat Govt Medical College, Rampurhat, Birbhum
- Corresponding author: Prof (Dr) Picklu Chaudhuri.
Email: picklu.chaudhuri@gmail.com

Rampurhat Govt Medical College on 1/7/2019 at around 9pm with complaint of feeling of mass coming out per vagina following a fall during lifting of heavy weight. She was a grand multipara (P5+0) with all vaginal deliveries. She had undergone total abdominal hysterectomy with bilateral salpingo oophorectomy due to fibroid uterus (documentations were unavailable) 8 months back at a private hospital.

On examination, patient was stable haemodynamically, abdomen was soft and non tender; vaginal examination revealed herniation of small gut through the introitus. There was no vaginal bleeding. Gut looked oedematous. (Fig 1)

Emergency Laparotomy was performed on the same day. Under GA abdomen was opened by midline vertical incision. Small gut was slowly pulled up through the rent in the vagina and exteriorised and examined by general surgeon (Fig 2). Wet mops were placed on the loops of the gut; vitality and peristalsis checked. There was no sign of gangrene and the prolapsed part of the gut was healthy, though it seemed to be edematous. Vault of the vagina was found to be open with well-delineated and healthy margins (Fig 3). Gut was repositioned back into the abdominal cavity. Margins of the vault were held with Allis tissue forceps. Anteriorly bladder was dissected down. Multiple interrupted mattress sutures were given over vault with 1-0 vicryl and vault was closed. Abdomen was closed after placing a Romson's ADK drain in the pelvis. Immediate post op period was uneventful. Drain collection in the first 48 hours was 200ml of



Fig 1: Expulsion of Gut through Vagina



Fig 2: Edematous loops of Gut

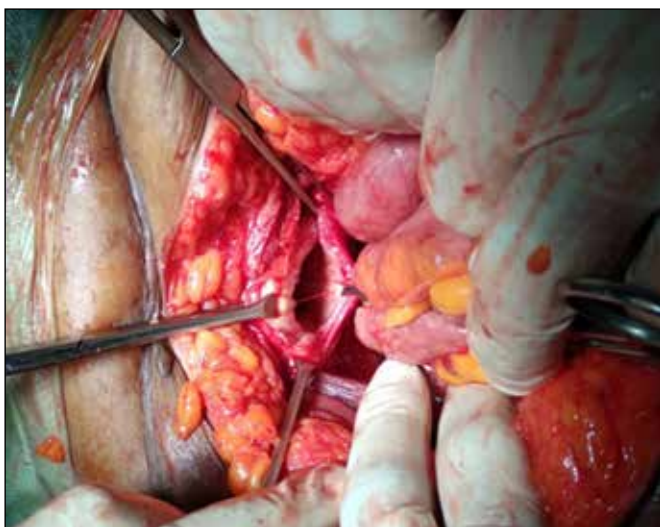


Fig 3: Open Vaginal Vault

reddish fluid. She was kept in CCU with drip and suction. Drain was omitted on 4 th post operative day. Stitches were removed on 10th post operative day and wound gaping was seen. Daily dressing was done and secondary suturing was done on 16/7/19.

Routine investigations were within normal limits. She was discharged on stable and healthy condition on 26/7/19.

Discussions

Vaginal cuff dehiscence following hysterectomy is a rare event with an estimated incidence of 0.39 percent (0.27 to 0.96 percent).¹⁻⁶ In a large single-center study, 28 cases of vaginal cuff dehiscence were reported among 11,606 patients (0.24 percent) who underwent total hysterectomy.² The largest multi-institution study included 12,398 patients and reported 38 cases (0.31 percent) of dehiscence after hysterectomy.³ Both studies included patients undergoing hysterectomy for benign and malignant indications. While one study reported a nearly 1 percent incidence of vaginal cuff dehiscence after total hysterectomy, the study sample size was much smaller (n = 2382 women), which may make the findings less reliable.⁴ The incidence of vaginal cuff dehiscence after any type of pelvic surgery (as opposed to hysterectomy) is approximately 0.03 percent and varies by surgical approach.^{5,6,7}

The true incidence of vaginal cuff dehiscence after hysterectomy is difficult to determine since this complication is likely underreported. Also, patients with cuff dehiscence may present to a different physician or hospital than for the initial hysterectomy, thereby making data collection difficult. Further, case reports of vaginal cuff dehiscence generally do not include for comparison the number of hysterectomies that were not associated with this complication. Lastly, the rate of dehiscence appears to vary by type of hysterectomy.⁸

Presentation and risk factors- Patients with vaginal cuff dehiscence can present with a combination of several different symptoms, most commonly pelvic or abdominal pain (58-100%), vaginal bleeding or watery discharge (33%-90%). Although one study reported two asymptomatic patients with a cuff dehiscence (in a series of 21 patients) who were diagnosed at a routine post-operative appointment, most patients with cuff dehiscence present for medical

care within 24 hours of the onset of symptoms.⁵⁻⁷ Patients with evisceration of bowel or intra-abdominal contents into the vagina often describe feeling a mass or pressure. Evisceration occurs in up to 70% of vaginal cuff dehiscence cases.⁵⁻⁷ Although intercourse, straining with defecation or valsalva manoeuvre can precede postoperative dehiscence of the vaginal cuff, many women who experience vaginal cuff dehiscence have no identifiable precipitating event. In the cases of vaginal cuff dehiscence reported in the literature, 8%-48% reported intercourse and 16%-30% reported defecation or valsalva (cough or sneeze) as the precipitating event. However, spontaneous vaginal cuff dehiscence has been reported to represent up to 70% of cases.⁷ Therefore, a high index of suspicion should be maintained for patients presenting after hysterectomy with sudden onset pelvic or abdominal pain accompanied by vaginal bleeding or watery discharge.

Conclusion

Vaginal cuff dehiscence and evisceration are serious complications of pelvic surgery, specifically hysterectomy. Continuing to identify and definitively investigate surgical techniques that may decrease the risk of cuff dehiscence is paramount. Though the data are limited, minimally invasive approaches to

hysterectomy, such as TLH and robotic hysterectomy may be associated with higher risk of vaginal cuff dehiscence.^{9,10} Judicious use of electro-cautery at the vaginal cuff and utilization of two layer cuff closure or bidirectional barbed suture may potentially decrease the risk of cuff dehiscence, the extent of the effect that these surgical techniques have on reducing the incidence of dehiscence is uncertain.

There is no one standard method of managing vaginal cuff dehiscence; the cases reported in the literature illustrate that vaginal, laparoscopic, abdominal, and combined approaches are all appropriate methods for secondary cuff closure. Each patient and each cuff dehiscence is different and the surgical approach should be dictated by the clinical circumstances and surgeon's judgment as to which approach will allow assessment for other problems (examination of the bowel, when there is concern about compromise) and allow optimal tissue approximation.

We suggest that gynaecologic surgeons need to discuss this complication with patients and provide them with information about possible symptoms of post-operative cuff dehiscence (pelvic pressure, sudden fluid leaking from the vagina, vaginal bleeding, or pelvic pain).

REFERENCES

- Iaco PD, Ceccaroni M, Alboni C, et al. Transvaginal evisceration after hysterectomy: is vaginal cuff closure associated with a reduced risk? *Eur J Obstet Gynecol Reprod Biol* 2006; 125:134.
- Hur HC, Donnellan N, Mansuria S, et al. Vaginal cuff dehiscence after different modes of hysterectomy. *Obstet Gynecol* 2011; 118:794.
- Uccella S, Ceccaroni M, Cromi A, et al. Vaginal cuff dehiscence in a series of 12,398 hysterectomies: effect of different types of colpotomy and vaginal closure. *Obstet Gynecol* 2012; 120:516.
- Fuchs Weizman N, Einarsson JI, Wang KC, et al. Vaginal cuff dehiscence: risk factors and associated morbidities. *JLS* 2015; 19.
- Hur HC, Lightfoot M, McMillin MG, Kho KA. Vaginal cuff dehiscence and evisceration: a review of the literature. *Curr Opin Obstet Gynecol* 2016; 28:297.
- Ceccaroni M, Berretta R, Malzoni M, et al. Vaginal cuff dehiscence after hysterectomy: a multicenter retrospective study. *Eur J Obstet Gynecol Reprod Biol* 2011; 158:308.
- Croak AJ, Gebhart JB, Klingele CJ, et al. Characteristics of patients with vaginal rupture and evisceration. *Obstet Gynecol* 2004; 103:572-6.
- Choosing the Route of Hysterectomy for Benign Disease. ACOG Committee Opinion No. 444. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2009;114:1156-8. [PubMed] [Google Scholar]
- Kho RM, Akl MN, Cornella JL, Magtibay PM, Wechter ME, Magrina JF. Incidence and characteristics of patients with vaginal cuff dehiscence after robotic procedures. *Obstet Gynecol*. 2009;114:231-5.[PubMed] [Google Scholar]
- Nick AM, Lange J, Frumovitz M, Soliman PT, Schmeler KM, Schlumbrecht MP, dos Reis R, Ramirez PT. Rate of vaginal cuff separation following laparoscopic or robotic hysterectomy. *Gynecol Oncol*. 2011;120(1):47-51. [PMC free article] [PubMed] [Google Scholar]

Instruction to Authors

The Journal of Indian Society of Perinatology and Reproductive Biology which is the official publication of the Indian Society of Perinatology and Reproductive Biology (ISOPARB) invites original research articles in gynaecology / obstetrics / related subjects in the following category: Clinical Articles; Review Articles; and Brief Communications (including Case Reports).

All manuscripts should be prepared according to the guidelines detailed below. Any manuscript that has not been formatted as per the ISOPARB requirements will be returned to the author for correction. All manuscripts should be created and submitted in Word format.

1. SUBMISSION

Authors must submit manuscripts by Email ID –
picklu.chaudhuri@gmail.com
dr_gita_banerjee@yahoo.co.in
hkondr@gmail.com

Hard-copy submissions will not be considered.

Please submit a cover letter to the Editor-in-Chief mentioning the following:

- Each author's name, address, and email address.
- Each author's affiliation and qualifications.
- The name of the author who is to deal with correspondence and proofs.

Once submitted, manuscripts undergo initial screening by the editorial staff and editors and then papers will undergo peer review.

2. Authors must give a separate "Author Guarantee" document mentioning the following:

- (1) that all authors have met the criteria for authorship and have participated sufficiently in the work to take responsibility for it;
- (2) that all authors have reviewed the final version of the manuscript and approve it for submission to the ISOPARB journal.
- (3) that neither this manuscript nor one with substantially similar content by the authors has been published elsewhere or is being considered for publication elsewhere;
- (4) that the manuscript has been submitted with the full knowledge and approval of the institutions or organizations given as the affiliation(s) of the author(s);

- (5) that the authors have informed the editor in a cover letter and in the manuscript itself of any conflicts of interest; and
- (6) that the corresponding author affirms the manuscript to be an honest and transparent account of the study being reported.

In line with ICMJE standards, the criteria for authorship are as follows:

- (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- (2) Drafting the work or revising it critically for important intellectual content; AND
- (3) Final approval of the version to be published; AND
- (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

3. CLINICAL TRIALS AND REVIEW ARTICLES

Clinical trials

Submission of clinical trials must include reference to ethics approval (or explanation of why ethics approval was not received). Authors must consult the CONSORT statement and checklist and submit a CONSORT flow chart as an editable figure in Word/PowerPoint format.

The clinical trial registration is preferable and information should be included at the end of the abstract of the submitted manuscript.

Review articles

Reviews based on the recent and relevant subjects of clinical interest should be considered.

4. LAYOUT OF MANUSCRIPTS

Manuscript text should be in English (US spelling), double-spaced, font size 12, in Arialmmes New Roman font.

First page

The first page of the manuscript should contain the following: (1) title; (2) full names of authors (6 maximum, although listing more authors may be considered on an individual basis if authorship requirements have been met and a request has been included in the cover letter); (3) affiliations of authors (i.e. department, section or unit of

an institution, hospital or organization, city, and country (4) full contact details (postal address, email address) of the corresponding author ; (5) a list of up to 8 keywords for indexing and retrieval:

Footnotes linking author names to affiliations should be listed as 1,2,3 etc..

The first page should also list the type of article: Clinical Article; Brief Communication: or Review Article.

Abstract

Clinical Articles

A structured abstract not exceeding 200 words is required for all full-length clinical articles. It should contain all and only the following headings: Objective; Methods; Results; and Conclusion.

The Objective reflects the purpose of the study: that is, the hypothesis that is being tested. The Methods should include the setting for the study, the participants (number and type), the treatment or intervention, and the type of statistical analysis. The Results include the outcome of the study and statistical significance, if appropriate. The Conclusion states the significance of the results.

Review articles

An abstract not exceeding 200 words is required for all review articles.

Narrative reviews require an unstructured abstract. Systematic review articles should have a structured abstract with the headings; Background; Objectives; Search strategy; Selection criteria; Data collection and analysis; Main results; and Conclusions.

Brief communications

Brief communications should not include an abstract.

Main text

In full-length articles, subject matter should be organized under the following headings, with no subheadings: Introduction; Materials and methods; Results; Discussion; Acknowledgments; Conflicts of interest; and References.

Brief communications should not have any headings separating the text.

Clinical articles

The main text of clinical articles should not exceed 2500 words, excluding the first-page information, abstract (no more than 200 words), author contributions, acknowledgments, Conflicts of interest, references (no more than 25), figure legends, and tables and figures. Please include the word count in the cover letter and on the first page of the manuscript.

Review articles

Review articles should have no more than 3000-3500 words in the main text and 40 references. Please include the

word count in the cover letter and on the first page of the manuscript.

Brief communications

Brief communications should be no more than 400 words, excluding the first-page information, synopsis, keywords, author contributions, acknowledgments, conflicts of interest, references, figure legends, and tables and figures. There should be no more than 4 references and no more than 1 table or 1 figure.

Power calculations, statistics, and reporting of numbers.

Power calculations

Where appropriate (e.g. for clinical trials), power calculations should be performed as part of the study design, and a statement providing the power of the study should be included in the Materials and Methods. Authors should state how the power calculation was determined, including what type of difference the calculation was powered to detect and on what studies the numbers are based.

Statistics

The statistical tests used and the significance level set should be listed in the methods for all studies that employed statistical analysis. Information regarding the statistical software programs used should be included in the methods: for example, "SPSS version 20 (IBM, Armonk, NY, USA)." This information should not be included in the reference list.

P values should be provided where calculated. The largest P value that should be expressed is $P > 0.99$. The smallest P value that should be expressed is $P < 0.001$.

For measures of effect (e.g. relative risks, risk ratios, odds ratios), authors should also report confidence intervals (e.g. 95%) so that the precision of the effect estimate can be assessed.

5. Ethics approval and informed consent

Studies of patients, patient records, or volunteers require Ethics Committee approval and informed consent.

Ethics approval

Include a statement in the methods that the research protocol was approved by the relevant Institutional Review Board or Ethics Committee before the study began; if such approval was not needed/obtained, include an explanation. Authors must provide copies of the appropriate documentation if requested.

Informed consent

Include confirmation in the methods that all human participants gave written informed consent before the study began; if consent was not needed/obtained, include an explanation. Authors must provide copies of the appropriate documentation if requested.

6. Acknowledgments

Sources of funding should be acknowledged by the author(s), along with the names of individuals who do not fulfil the criteria for authorship, but who have made a substantial contribution to the manuscript.

7. Conflicts of Interest

A conflict-of-interest statement must be included in the cover letter and before the reference list in the manuscript. It should list any relationships (for any author) that may be deemed to influence the objectivity of the paper and its review, or state that no such relationships exist. Commercial associations, either directly or through immediate family, in areas such as expert testimony, consulting, honoraria, stock holdings, equity interest, ownership, patent-licensing situations or employment that might pose a conflict of interest should be stated. Conflicts for other reasons, such as personal relationships or academic competition, should also be stated.

8. References

The number of references should not exceed 25 for clinical articles, 40 for review articles, and 4 for brief communications; in general, they should be limited to the past decade. They must be numbered and listed as they are cited in the article, using Index Medicus abbreviations for journal titles. Cite the names of all authors when there are six or fewer; when there are seven or more, list the first three authors followed by “et al.” Include the volume number.

Journal article

- [1] Vellacott ID, Cooke EJ, James CE. Nausea and vomiting in early pregnancy. *Int J Gynecol Obstet.* 1988;27:57-59 .

Book

- [2] Speroff L, Glass BH, Kase NG. *Clinical Gynecologic Endocrinology and Infertility.* Baltimore: Williams and Wilkins; 1982.

Chapter in a book

- [3] Disaia PJ, Creasman WT. Invasive Cancer of the Vulva. In: Disaia PJ, Creasman WT, eds. *Clinical Gynecologic Oncology.* St Louis: C.V. Mosby; 1984:214-219.

Web reference

- [4] World Health Organization. WHO Recommended Surveillance Standards, Second Edition [WHO website]. 1999. <http://www.who.int/csr/resources/publications/surveillance/whocdscsr992.pdf>.

Text references can be indicated by Arabic numerals in superscript. abc¹

Tables

Each table should be titled, numbered (with Arabic numerals), and placed on a separate page after the reference list (not embedded within the main text).

All tables must be cited in numeric order in the main text as “Table 1” etc.

Footnotes to tables should be listed as a, b, c etc.

9. Figures and photographs

Figures and photographs should be submitted as jpg format. CONSORT flow charts should be created and submitted as editable Word/ Power Point files. All figures must be cited in numeric order in the main text as “Figure 1” etc.

Figure permission

All authors wishing to use figures (or any material) that have already been published must first obtain the permission of the original author and publisher and/or copyright holders, in addition to giving precise reference to the original work. This permission must include the right to publish in electronic media. Confirmation should be included in the cover letter (the actual permission correspondence from the copyright holder does not need to be submitted).

Photograph/video consent

If photographs or videos of identifiable people are used, authors must obtain and submit a signed statement of informed consent from the identifiable person(s) or their next of kin. Authors should not try to conceal identity with black bars over eyes etc.

9. Drugs

Give generic names of all pharmaceutical preparations and, where appropriate, include the trade name and manufacturer’s name and address. Review drug names and dosages with care. The author is responsible for all recommended dosages.

10. Plagiarism

Plagiarism entails the “use or close imitation of the language and thoughts of another author and the representation of them as one’s own original work.” Self-plagiarism, a form of misconduct in which an author reuses his/her previously written text, data, or ideas, wholly or in part, without indicating previous dissemination, will also be considered plagiarism. Verbatim copying of sentences, even if a citation is provided (unless the sentence appears in quotation marks), is considered to be plagiarism.

11. ON ACCEPTANCE

If your paper is accepted for publication, you will receive an email informing you of this decision.

12. Copyright

Once accepted and published, all copyright will belong to ISOPARB. No part of the article could be published without permission. All disputes are subjected to Indian Jurisdiction.

- 13. It is desirable that the, author(s) submitting article in IJOPARB be a member of ISOPARB.

If undelivered, return to:
Indian Journal of Perinatology and Reproductive Biology
CD-55, Salt Lake City, Sector - 1, Kolkata 700064