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A – 9/7, Kalyani, Nadia, West Bengal 741235 India

Email: jiaog2017@gmail.com

website: www.iaog.in

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To
All Medical Fraternity

As a Editor of Journal of Indian Academy of Obstetrics & Gynaecology I feel proud and glad to inform you that 1st edition of Journal of Indian Academy of Obstetrics & Gynaecology is going to release during second convocation of IAOG at The Stadel, Salt Lake stadium, Kolkata on 3 Dec 2017.

We have focused on many evidence based scientific research papers covering review article, original article, case reports, book review, video presentation etc.

It is the total team effort of IAOG to make this Journal one of the best medical journal in the world in future.

My sincere and wholeheartedly believe that scientific world of our fraternity will be benefited from this journal.

Our moto is to make this journal a Pubmed indexed journal as well as having good impact factor and more so.

Thanking you

Dr Dilip Kumar Dutta

Chief Editor

Journal of Indian Academy of Obstetrics & Gynaecology

Contents

Editorial:

Strategies to reduce MMR by advocating Dutta's innovative techniques <i>Dilip Kumar Dutta</i>	1
--	---

Original Article:

A pilot study to evaluate the cffdna as a predictive marker of preeclampsia <i>Mriganka Mouli Saha, Utpal Ghosh, Nitai P Bhattacharya, Subir Kumar Das, Deepshikha Mukherjee, Subikas Biswas</i>	5
Comparative efficacy of intravenous iron sucrose versus intravenous iron sucrose and erythropoietin therapy in moderate and severe anemia of pregnancy <i>JB Sharma, Sirisha D Bumma, Renu Saxena, Sunesh Kumar, Prerna Gupta, KK Roy, Neeta Singh, P Vanamail</i>	10
A study on the sex ratio at birth in institutional deliveries in a tertiary care hospital in Kalyani, West Bengal <i>Ranita Roy Chowdhury, Srijoni Chowdhury, Manidip Pal</i>	16
Evaluation of awareness, acceptance and expulsion rate of post-placental intrauterine device (ppiucd) in a tertiary care centre <i>Banasree Bhadra, Sougata Kumar Burman</i>	20
Impact of global epidemic of cesarean section in a district medical college of West Bengal: an observational study <i>Srijoni Chowdhury, Ranita Roy Chowdhury, Manidip Pal</i>	24
Incidence of HIV infection in antenatal mothers <i>Suvabrata Sarkar</i>	29

Stillbirths and its causes in a tertiary care teaching hospital of West Bengal <i>Amitava Pal, Debobroto Roy, Rupali Modak</i>	31
--	----

Review Article:

Placenta & intrauterine fetal death <i>Soma Bandyopadhyay</i>	35
---	----

MTP beyond 20 weeks: time for policy change <i>Ramprasad Dey, Subhash Chandra Biswas</i>	39
--	----

Pharmacotherapy of hypertension in pregnancy <i>Keshab Mukhopadhyay, Chanchal Kumar Dalai, Kishore Mazumdar</i>	42
---	----

Case Reports:

Acute fatty liver of pregnancy: A case report of an uncommon disease <i>Abhijit Halder, Mainak Nath</i>	46
---	----

Video Presentation:

OASIS 3B repair <i>Manidip Pal, Srijoni Chowdhury, Joydeep Neogi</i>	50
--	----

<i>Book Review</i>	52
---------------------------	----

<i>Author's Guidelines</i>	53
-----------------------------------	----

<i>Subscription Form</i>	56
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Editorial

STRATEGIES TO REDUCE MMR BY ADVOCATING DUTTA'S INNOVATIVE TECHNIQUES

Dilip Kumar Dutta

MD, PhD, FRCOG (Hon), FICOG, FIAMS, FICMCH, MAMS, DACOG (USA), DPS (Germany)
Chairman, Indian College of Obstetrics & Gynecology (2015)
Dean, India Academy of Obstetrics & Gynecology (IAOG) 2017
Vice Chairman, ISAR Bengal 2015-2017
National Editor of 'Jogi Journal' (2015-2017)
Director, GICE, Kalyani, Nadia, WB Author of 36 books (Obstetrics and Gynaecology)
Honorary Editor, Journal of the Indian Medical Association (JIMA)

It's a known fact that 500 lakh pregnant mother die each year in the world, in developing countries the MMR is approximately 30/1 lakh live birth which spirals upwards to approx. 350-450 per 1 lakh maternal deaths in developing countries.

Hence considering this above fact, it is the developing country which requires utmost attention to reduce maternal deaths which are preventable. India being a diverse country with rich being super rich and poor being extremely poor with minimal or no access to quality healthcare.

Problems in India:

Cause of morbidity to pregnant mothers – Direct causes include eclampsia, anemia, sepsis, PPH, others include obstructed labour and other indirect causes.

Where is the lacking? – failure in health care, lack of transport facility, lack of manpower, and other socio-political commitments How to improve this scenario? – solving rural health problem by making outreach and awareness programmes to them, making skilled doctors available to rural population, provide them proper care during child birth and post partum care. Prevention, early detection and treatment of complication of pregnancy, provision of

clean and safe vaginal delivery and prompt action and management of obstetrical emergencies. Following are the commonest problems faced in rural India and various methods have been adopted by authors for preventing MMR.

Problem 1 (Atonic Uterus noted during Caesarean section)

Uterine atony was found to be the most common cause of PPH. The ability to identify which women will experience atony is limited and with or without risks factors. Till date a lot of work have been done to prevent uterine atony and also develop evidence based medical and surgical interventions to save the uterus for fertility preservation in future. Paramount importance for every obstetrician is to prevent PPH due to uterine atony during emergency LSCS by early detection, assessment of the severity and search for specific causes. Life threatening PPH can be a nightmare to the obstetrician and requires an active multidisciplinary management to prevent maternal morbidity and mortality.

Dutta's Scoring:^{1,2} Scoring method to be used during caesarean section was formulated keeping rural India in head. As it is known that to prevent uterine atony various methods are being used but in a haphazard manner, medical management if fails then B lynch sutures, step wise devascularisation, vertical sutures, tamponade or finally internal iliac artery ligation is done. But Dutta's technique involves an easy observational method and scoring system which enables the surgeon to identify grave

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risk patients or uteruses which are atonic and treat in a systematic manner. So here the uterus is divided in various parameters like shape and size, rugosity, tone, placental localisation, and time of placental expulsion and scoring were given (Tables 1-3). Approximately 130 women were selected for Group A, 100 for Group B, and 70 for Group C. Early diagnosis and management of uterine atony during emergency/elective LSCS after adopting Dutta's score were found to be not only reduce intra and post operative blood loss but also was found to maintain a satisfactory hemoglobin level and hemodynamic status. Maternal mortality was found to be nil. This randomised trial highlighted the importance of prompt treatment in Group C to reduce intra and post operative blood loss and maternal morbidity and mortality.

Problem 2 (Placenta previa-except increta and percreta detected during caesarean suddenly)

Placenta previa, abruption placenta and uterine rupture are three important causes of ante partum hemorrhage seen frequently at ter-tiary care level hospital claiming high maternal mortality and morbidity. Till date present existing different surgical techniques adopted during LSCS to deal with excessive bleeding after placental separation site from Major degree Placenta Previa have not been found to be effective method to control intra- operative hemorrhage. This has led to high incidence of maternal mortality and morbidity. Hence to prevent intra-operative hemorrhage during LSCS operation due to major degree placenta previa Author had advocated new surgical technique (Dutta's)^{3,4} in a stepwise manner to reduce maternal mortality and morbidity.

Existing technique includes following steps :

BABY DELIVERED → PLACENTA DELIVERED → OXYTOCIN /ERGOMETRINE GIVEN → IF BLEEDING NOT CONTROLLED THEN SURGICAL TECHINUES USED LIKE B/L UTERINE LIGATION/ B/L INTERNAL ILLIAC LIGATION / HYSTERECTOMY.

Dutta's Technique :

BABY DELIVERED → BILATERAL UTERINE ARTERY LIGATION → INJ TRANEXAMIC ACID

Table 1 — Criteria of scoring

Uterus	0	1	2
Shape and size	Broad and flat (discoid)	Less elevated, narrow, hard and globular shape	More elevated, narrow Hard and globular shape Present in both surfaces
Rugosity	Absent	Present either in anterior or posterior surface	
Tone	Soft	Firm	Hard, contracted
Placental Localisation	Lower segment	Fundo anterior	Fundo posterior
Time of Placental Expulsion	>5 min	3-5 min	<3 min

Table 2 — Distribution of scoring in Groups

Groups	Pattern of Scoring	Total Score
Group A	Shape and size-2 Rugosity-2 Tone-2 Placental Localisation-1 to 2 Placental expulsion – 1 to 2	8 to 10
Group B	Shape and size-1 Rugosity-1 Tone-1 Placental Localisation-1 to 2 Placental expulsion – 1 to 2	5 to 7
Group C	Shape and size-0 Rugosity-1 Tone-0 Placental Localisation-1 to 2 Placental expulsion – 1 to 2	<5

1000MG STAT → OXYTOCIN INFUSION 15-20U STAT → PLACENTA PLUS MEMBRANES DELIVERED AND CHECKED → IF TEAR / LACERATION THEN SUTURE ACCORDINGLY → UTERINE WOUND CLOSED IF NO BLEEDING.

It was observed from a study (done in tertiary care hospital in rural india) that good effectiveness to control bleeding and intra operative blood loss less than 300 cc were seen in 89 (94.68%) cases respectively. Six (6.3%) cases required underlying interrupted suture for bleeding from placental bed. Subtotal cesarean hysterectomy was advocated in 3 (3.28%) cases due to fail-ure to control uterine atony. Immediate post operative bleeding less than 200 cc

Table 3 — Management Protocol

	Oxyt*	Methy erg**	Carbo-prost	Lateral compression on upper segment of uterine wall	Anterior posterior uterine wall compression	Isthmus compression	Misoprostol 800mcg per rectal
Group A (Score 8-10)	10U	-	-	-	-	-	-
Group B (Score 5-7)	15U	0.25mg	-	-	Yes	-	-
Group C (Score <5)	20U	0.5mg	250mcg	Yes	Yes	Yes	Yes

was found in 81 (86.16%) cases. Maternal mortality was found to be absent. Maternal morbidity was seen in 12 (12.76%) cases. Subsequent menstrual cycles were found to be normal in 80 (87.91%) cases and repeated pregnancy was observed in 26 (28.57%) cases indicating non effect on gonadal function.

CONCLUSION

Dutta's new surgical technique during LSCS for major degree placenta previa was found to be simple, safe and quick procedure. It reduces perfusion pressure, permits time for further steps, thereby avoiding unnecessary ligation of bilateral internal iliac arteries and caesarean hysterectomy. Maternal mortality and morbidity were also found to be reduced. This technique is suitable for rural based hospital in absence of adequate blood transfusion facility.

Problem 3 (third stage complications during vaginal delivery at low resource settings)

Low resource setting problems may arise due to nonavailability of experienced doctor or lack of medications. Hence low resource setting can be a challenging place to manage emergencies. Hence proper utilization of existing staff and nurses so that they can be of help to prevent PPH or in a wider sense help in reaching our goals of reducing MMR.

So keeping above in head author had devised an easy protocol which can help in achieving the above goal to some extent. Three groups of patients were divided in a study done in low resource setting as mentioned below⁵ (Table 4).

Group A (N-100) : After delivery baby is put on mother's abdo-men till placental expulsion.

Group B (N-100) : After delivery baby is put on labour cot till placental expulsion with misoprostol 600µg orally.

Group C (N-100) : Baby is separated before the expulsion of placenta (i.e. following cessation of cord pulsation) with 10U oxytocin IM within 1 min of placental expulsion.

So what are the advantages of above method ?

- (1) Sustained uterine contraction and retraction (92%) probably due to Fetal weight on mother's abdomen (acts as fundal pressure),
- (2) Fetal movement (acts as massage to uterus), psychological change of mother after seeing the baby on her abdomen that leads to early (<5 min) and sustained uterine contraction and retraction,
- (3) Early expulsion of placenta (98%), minimal (immediate) post partum blood loss (92%),
- (4) Non requirement of drugs (misoprostol or oxytocin) and instrumentation,
- (5) Avoidance of unnecessary clamping and pulling of cord when uterus is still not contracted,
- (6) Normal temperature of the baby will be maintained due to contact with mother skin,
- (7) Baby can be easily put on breast for early sucking, after placental separation, Postpartum transfer of blood to fetus is rapid, Technique is safe and do not interfere normal progress of vaginal delivery of placenta, Do not interfere with the psychology of mother,
- (8) Minimum training of midwife / health worker will help to apply this technique.
- (9) Suitable technique for rural women of Asian countries where women are ill nourished having less blood volume and lower antenatal haemoglobin value.

Table 4 Showing the number of patients along with the uterine contraction and retraction followed by placental expulsion time required

Groups & No of Patients	Uterine Contraction and Retraction (minute)			Placental Expulsion (minute)		
	Excellent (<5mins)	Good (5-10mins)	Moderate (>10mins)	<5 min	5-10min	10min
Group A (N=100)	92% (92)	8% (8)	-	98%	2%	-
Group B (N=100)	76%	24%	-	-	10%	90%
Group C (N=100)		16%	84%	-	12%	88%

Comparative Analysis of Clinical Observation of Three Different Groups

Observations	Group A (N - 100)	Group B (N - 100)	Group C (N - 100)
Uterine contraction & retraction	Excellent (92%) <5 min	Good (76%) >10min	Moderate (84%) >10min
Placental expulsion	Early (98%) < 5 min	Late (90%) >10 min	Late (88%) > 10 min
Post partum blood loss	Less (92%) < 100 cc	More (76%) >100-150 cc	More (84%) > 150 cc
Retained placenta	Nil	Yes (2.1%)	Yes (3%)
Inversion of uterus	Nil	Nil	Yes (1%)



Fig 1 — AP Compression



Fig 2 — Lateral compression



Fig 3 — Isthmic compression

CONCLUSION

This study clearly shows that placing the baby on mother's abdomen after delivery till the expulsion of placenta, early breast feeding and misoprostol (600 mg) minimize the complications of third stage of labour at low resource setting. And it also implies that this method can reduce the PPH and MMR where active management of third stage of labour is not adopted routinely.

Hence these are the small effort taken by author to prevent maternal death and periodic training of doctors either through CME's or conferences along with training of nursing staff and ANM's are done to learn small tricks and techniques to prevent preventable causes of maternal death specially in rural outreach areas.

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Original Article

A PILOT STUDY TO EVALUATE THE CFFDNA AS A PREDICTIVE MARKER OF PREECLAMPSIA

Mriganka Mouli Saha,¹ Utpal Ghosh,² Nitai P Bhattacharya,³ Subir Kumar Das,⁴ Deepshikha Mukherjee,² Subikas Biswas⁵✉

ABSTRACT

Objectives: Preeclampsia often complicates pregnancy resulting in adverse impact on maternal and fetal health. Early detection helps in intervention and avoiding adverse outcome of pregnancy. Detection of cell free fetal DNA (cffDNA) in maternal plasma opens the possibility of non-invasive probe into health of fetus.

Methods: Total 50 pregnant women had been recruited from the Antenatal OPD with and without preeclampsia. The women with preeclampsia were considered as case and without preeclampsia were considered as control. cffDNA had been utilized for prenatal diagnosis of adverse pregnancy outcomes.

Result: Among 50 participants, 27 were in preeclampsia group and 23 were in control group. Cell free fetal DNA was $55.34 \pm 7.232 \times 10^{10}$ genomic equivalents in preeclampsia group and $11.076 \pm 2.345 \times 10^{10}$ genomic equivalents in control group which is fivefold higher in study group.

Conclusion: Elevated amount of cffDNA in maternal plasma is associated with preeclampsia.

Key words: Cell free fetal DNA, Maternal plasma, Preeclampsia, Pregnancy outcome

INTRODUCTION:

Preeclampsia (PE) complicates some 2%-8% of pregnancies worldwide. Hypertensive disorder in pregnancy is the leading cause of maternal death in developed countries and its incidence is increasing. Worldwide approximately 830 pregnant women die every day from preventable causes which accounts for maternal mortality ratio (MMR) 239 per 100,000

live births in developing countries and 12 per 100,000 live births in developed countries.¹ World health organization has demonstrated that 85% maternal death is contributed by the African and South-East Asian countries.¹ The MMR in India is 174 in 2015 and it contributes up to 20% of maternal deaths worldwide due to preventable causes.² Sustainable development goals (SDG) after millennium

1. Dept. Obstetrics & Gynaecology, College of Medicine & JNM Hospital, Kalyani
2. Dept. Biochemistry and Biophysics, University of Kalyani, Kalyani
3. Biomedical Genomics, Kolkata
4. Dept. Biochemistry, College of Medicine & JNM Hospital, Kalyani
5. (✉)Dept. Surgery, College of Medicine & JNM Hospital, Kalyani, WB, India, PIN 741235, E-mail: drsubikasbiswas@gmail.com

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development goals (MDG) have been aimed at reducing MMR below 70 per 100,000 live births by the year 2030.³

Early detection of pregnancy complications may dictate appropriate intervention. Several randomized controlled trials have been carried out to show that aspirin, an anti-platelet agent, prevents preeclampsia effectively and safely among women with high or moderate risk of PE.^{4,5,6} It has been shown that aspirin reduces relative risk of preeclampsia by as much as 53% when administered at 12-16 weeks' of gestation.⁷

Cell Free Fetal DNA (cffDNA) originates from the trophoblastic cells and enters in to the maternal circulation invading the feto-placental barrier. It was detected in maternal plasma in early eighties. Placental origin of cffDNA can be detectable as early as 5 weeks of gestation and it constitutes about 10% of cell free DNA, which is cleared rapidly from maternal circulation after delivery.⁸ It thus offers potential source of prenatal diagnosis for various genetic conditions namely achondroplasia, autosomal recessive disorders, fetal thalassemia, aneuploidy, and RHD genotyping.

This gender-independent detection of cffDNA in maternal plasma using RASSF1A/beta-actin has curtailed off a new dimension regarding its utility to predict the adverse pregnancy outcomes. Recent studies have shown the utility of cffDNA using the methylation-dependent DSCR3 and RASSF1A markers along with total cell free DNA (cfDNA) in maternal serum by HYP2 marker, are useful in predicting preeclampsia, intrauterine growth restriction.⁹ The higher concentration of cffDNA in maternal serum is found in preeclampsia and particularly cffDNA and cfDNA ratio is twofold higher in severe preeclampsia group.¹⁰

Given the observation that cffDNA in maternal plasma can be detected in early weeks of gestation and elevated in some studies, we have contemplated to test the hypothesis that increased cffDNA is associated with PE. We shall further establish relationship between elevated amount of cffDNA and adverse outcome of pregnancy in terms of preterm birth, low birth weight, stillbirth and spontaneous abortion among pregnant women once the study is completed. The aim of the study was to test the hypothesis that increased amount of cell free DNA in maternal plasma is correlated with preeclampsia (PE) and to determine the outcome of pregnancy with preeclampsia. Outcome was measured in terms of preterm birth, low birth weight, stillbirth and spontaneous abortion was determined.

MATERIALS & METHODS:

Pregnant women have been recruited from the Antenatal OPD of College of Medicine & JNM Hospital, WBUHS, Kalyani, Nadia. Being a pilot study with the expected outcome to be relatively uncommon, we were not going in for a formal sample size calculation. Considering the constraint of logistics and time hence we have screened 50 pregnant women with and without preeclampsia. The women with preeclampsia were considered as case and without preeclampsia as control. The exclusion criteria were; pregnancy less than 20 weeks, cervical abnormalities (e.g. excessive friability, malignancy, polyps, and trauma), ectopic pregnancy, molar pregnancy, multiple pregnancies, any medical complication, chronic hypertension, renal disease, autoimmune disease (SLE), antiphospholipid syndrome, and diabetes mellitus. All participants have to sign an informed consent and a standard pro-forma was filled up by the doctor for recording the base line data.

Laboratory methods:-

Quantifying separation of maternal plasma:

About 5 ml peripheral blood was drawn into an EDTA tube. Plasma was separated by centrifugation at 1600xg at 4°C for 10 minutes. Plasma was collected and re-centrifuged once again at 1600xg at 4°C for 10 minutes. Plasma in the upper layer was distributed into 1.5ml tubes (300 µl in each tube, two such). About 300µl plasma could be used either immediately for cell free DNA or stored at -80°C for future use.

Methods for detection and quantification of cell free fetal DNA in maternal plasma:

Cell free DNA in maternal plasma could be extracted using various commercially available Kits as described by many authors. However, these KITS are expensive. Several methods have been described in literature for isolation of fetal DNA from maternal plasma. Comparisons of various methods for total yield were made. These methods consist of (a) Phenol/ chloroform DNA extraction method after SDS (Sodium dodecyl sulfate) and proteinase K lysis, (b) Phenol/ chloroform DNA extraction with addition of a polyacryl DNA carrier, (c) Salting-out protein precipitation method with 6M sodium chloride, (d) Guanidium isothiocyanate-based RNA extraction method and (e) Commercially available kits. It was observed that the yield was maximum with guanidium isothiocyanate-based RNA extraction method. Our initial result indicates that guanidium isothiocyanate-based RNA extraction was convenient and the yield was somewhat higher.

Promoter of RASSF1A is hypermethylated in trophoblast (maternal component) resulting in resistance to digestion by methylation sensitive restriction endonuclease *HhaI*, *HpaII*, *BstI*. On the contrary, RASSF1A promoter is hypomethylated in fetus (fetal component) and sensitive to digestion of the above restriction endonucleases. Thus digestion of cell free DNA purified as stated above is digested with the above restriction enzymes. Subsequent PCR amplification with specific primers around the promoter would detect the quantity of fetal DNA.

RESULTS:

In our study we have screened about 50 women till date which is 27 in preeclampsia group and 23 in control group. In Table 1, baseline parameters are; age (years) 24.37 ± 4.692 in preeclampsia group and in control group 22.87 ± 3.684 ($p = 0.220$); gravida (number) $1.85 \pm .864$ in preeclampsia group and in control $1.70 \pm .926$ ($p = 0.541$), Parity (number) $1.32 \pm .768$ in preeclampsia group and in control $1.28 \pm .875$ ($p = 0.398$), BMI (kg/m^2) $26.53 \pm .672$ in preeclampsia group and in control $25.42 \pm .764$ ($p = 0.286$); gestational age (days) 230.96 ± 18.135 in preeclampsia group and in control 256.91 ± 19.598 ($p = 0.452$), these all are comparable in both group. But the systolic blood pressure (mmHg) was significantly high in preeclampsia group 149.11 ± 13.993 than the control group 108.52 ± 11.805 ($p = 0.000$) and similarly diastolic blood pressure (mm Hg) was also higher in preeclampsia group 97.19 ± 12.481 than the control group 70.78 ± 9.530 ($p = 0.000$).

Table 1: Baseline Parameters

Demographic Characteristics	Case (n= 27)	Control (n=23)	p - Value
Age (years)	24.37 ± 4.692	22.87 ± 3.684	0.220
Gravida (number)	$1.85 \pm .864$	$1.70 \pm .926$	0.541
Parity (number)	$1.32 \pm .768$	$1.28 \pm .875$	0.398
BMI (kg/m^2)	$26.53 \pm .672$	$25.42 \pm .764$	0.286
Gestational Age (days)	230.96 ± 18.135	256.91 ± 19.598	0.452
Systolic Blood Pressure (mm Hg)	149.11 ± 13.993	108.52 ± 11.805	0.000
Diastolic Blood Pressure (mm Hg)	97.19 ± 12.481	70.78 ± 9.530	0.000

In Table 2, laboratory parameters; haemoglobin (g/dl) 10.456 ± 1.1453 in case group and 10.922 ± 1.1156 in control group ($p = 0.153$), platelet count (per cu mm) 208.74 ± 38.731 in case group and 261.65 ± 29.725 in control group ($p = 0.000$) which is lower in preeclampsia group; creatinine (mg/dl) $0.981 \pm .254$ in case group and 0.717 ± 0.111 in control group ($p = 0.000$) which is higher in preeclampsia group; serum bilirubin (mg/dl) 0.822 ± 0.210 in case group

and $0.761 \pm .167$ in control group ($p = 0.265$); SGPT (IU/L) 28.52 ± 9.283 in case group and 22.83 ± 2.674 in control group ($p = 0.007$); SGOT (IU/L) 33.48 ± 10.319 in case group and 26.70 ± 2.771 in control group ($p = .004$).

Table 2: Baseline Laboratory Parameters:

Laboratory Parameters	Case (n= 27)	Control (n=23)	p - Value
Haemoglobin (g/dl)	10.456 ± 1.1453	10.922 ± 1.1156	0.153
Platelet Count X 1000(cu mm)	208.74 ± 38.731	261.65 ± 29.725	0.000
Creatinine (mg/dl)	0.981 ± 0.254	0.717 ± 0.111	0.000
Bilirubin (mg/dl)	0.822 ± 0.210	0.761 ± 0.167	0.265
SGPT (IU/L)	28.52 ± 9.283	22.83 ± 2.674	0.007
SGOT (IU/L)	33.48 ± 10.319	26.70 ± 2.771	0.004

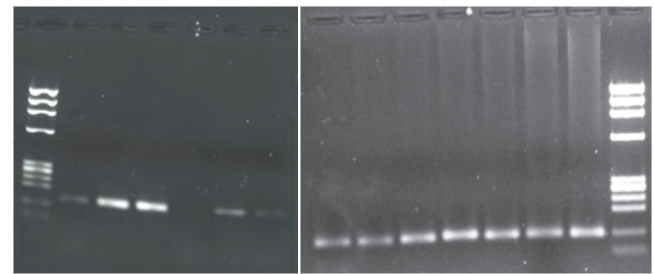


Figure 1: PCR amplification using Y chromosome specific locus DYS14 (for primers used please see Table 2). Lanes 1 (from left to right) ϕ X174 digested with restriction enzyme Hae III; from lowest to highest bands were of sizes 72bp, 118bp, 194bp, 234bp (other are not mentioned), lane 2, (3 and 4), 6 and 7 were from different samples. Lane 5 shows negative control (without template). The band intensities visibly vary indicating that different samples had different amount of cell free fetal DNA as mothers do not have Y chromosomes. PCR amplified DNA using markers (NCO1) for total cell free DNA (Panel B). First lane (from right to left) was maker as described for panel A, 2-5 same samples as that of in panel A. Negative control was not shown in the panel B. Lanes 6-8 other samples from mothers who did not deliver male child.

The outcome of pregnancy depicted in table 3 where case is $n=23$ as four patients were lost in follow up and similarly control group is $n=20$ where three patients were lost in follow up. The outcome parameters are gestational age (days) at birth 232.46 ± 18.932 in case group and 267.56 ± 15.958 in control group ($p = 0.000$) which is lower in preeclampsia group, birth weight (kg) $2.327 \pm .6672$ in case group and $2.581 \pm .4520$ in control group ($p = .171$), APGAR Score at birth 5.71 ± 1.654 in case group and $6.31 \pm .602$ in control group ($p = .191$). The total numbers of still born were five in preeclampsia group and only one in control group.

Table 3: Pregnancy Outcomes Parameters

Outcomes Parameters	Case (n= 23)	Control (n=20)	p - Value
Gestational Age (days) at birth	232.46 ± 18.932	267.56 ± 15.958	0.000
Birth weight (kg)	2.327 ± 0.6672	2.581 ± 0.4520	0.171
APGAR Score at birth	5.71 ± 1.654	6.31 ± .602	0.191
Still Born	5	1	0.000

Regarding the quantification of cell free fetal DNA in preeclampsia group as shown in figure 2A & 2B, it was $55.34 \pm 7.232 \times 10^{10}$ genomic equivalents in preeclampsia group and $11.076 \pm 2.345 \times 10^{10}$ genomic equivalents in control group which is fivefold higher in study group.

DISCUSSION:

In a recent study with 107 pregnant women having clinically established PE at their third trimester and 93 normotensive pregnant women, it has been shown that total cell free DNA, cell free fetal DNA and soluble endoglin (sEng) increased significantly among women with PE. It has also been observed that elevated total cell free DNA and cfDNA were also significantly higher among women with preterm labour and adverse fetal outcome groups compared to the full- term and favourable outcome groups. These three markers were almost equivalent with regard to the area under the curve for predicting adverse fetal outcome in the severe PE group.¹¹ No significant difference in levels of cfDNA was observed in the first trimester in women who subsequently developed preeclampsia. Levels of cell-free total DNA in the first trimester are increased in African American and

Hispanics compared to the white women, and levels increase with increasing BMI. Interestingly, total cell free DNA in pregnant women has been shown to be dependent on the ethnicity. Cell-free total DNA was higher in African American (median; 25-75%; 6.15; 0.14-28.73; $p=0.02$) and Hispanic (4.95; 0.20-26.82; $p=0.037$) compared to white women (2.33; 0.03-13.10). This result shows that cell free DNA in maternal plasma may depend on ethnic background. No systematic study has been carried out so far, hence requires further studies. In a study with 8 women with preeclampsia and 8 normotensive control with singleton male pregnancy between 28 and 32 gestational weeks, it has been shown that cell free fetal DNA concentrations were higher in early preeclampsia women than control subjects.¹² To determine relationship between maternal and fetal characteristics and pregnancy outcomes on fetal and maternal cell-free DNA in maternal plasma at 11-13 weeks' gestation, it has been observed that cell free DNA in maternal plasma was not significantly altered in pregnancies complicated by preeclampsia, early spontaneous preterm birth (SPB) delivery of small for gestational age (SGA) neonates. However, fetal cfDNA level has been seen to be inversely related to maternal weight and uterine artery pulsatility index while maternal cfDNA has been seen to be increased with maternal weight.¹³ It cannot be ruled out whether the cfDNA increases in the advance stage of gestation. In a meta-analysis of several studies elevated cfDNA was observed in preeclampsia.

CONCLUSION:

In summary, increased cfDNA was identified in many studies; while in some studies negative result was also

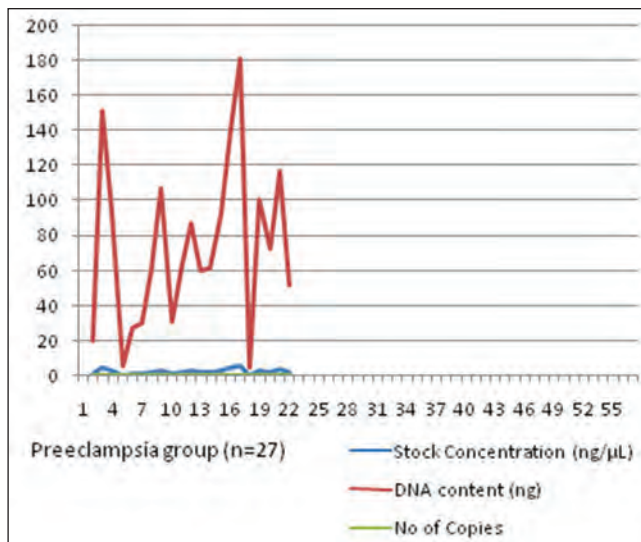


Fig 2A: Cell free fetal DNA quantification in preeclampsia group

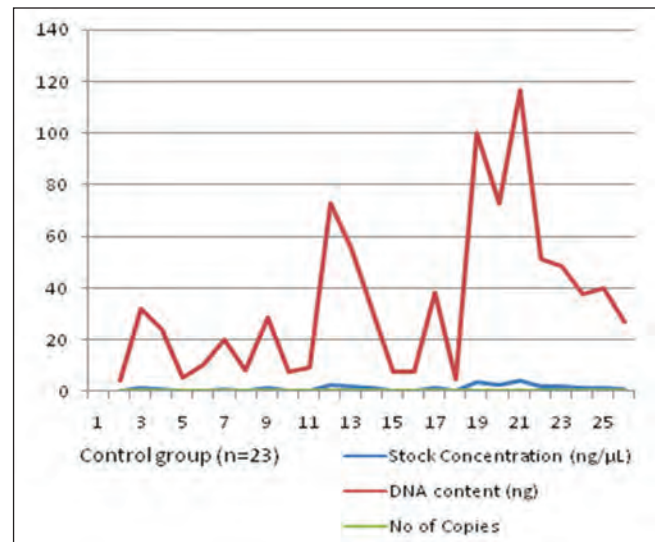


Fig 2B - Cell free fetal DNA quantification in control group

reported. In most of the studies, small numbers of samples were used and one or two loci were used to detect cffDNA. Amount of cffDNA may depend on the gestational period, parity, obesity, ethnicity and age of women. Though in our study we have found fivefold higher cffDNA in the study group, but we have planned to screen about 500 women in future for larger study.

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Original Article

COMPARATIVE EFFICACY OF INTRAVENOUS IRON SUCROSE VERSUS INTRAVENOUS IRON SUCROSE AND ERYTHROPOIETIN THERAPY IN MODERATE AND SEVERE ANEMIA OF PREGNANCY

JB Sharma,¹✉ Sirisha D Bumma,¹ Renu Saxena,² Sunesh Kumar,¹ Prerna Gupta,¹ KK Roy,¹ Neeta Singh,¹ P Vanamail¹

ABSTRACT

Aim: The aim of the study was to evaluate the efficacy of intravenous iron sucrose versus intravenous iron sucrose and erythropoietin in moderate and severe anemia of pregnancy.

Methods: A total of 50 women with hemoglobin of less than 8 g/dl in the second or third trimester of pregnancy were enrolled to receive either 1000 mg of intravenous iron sucrose as 5 doses of 200 mg on alternate days (Group I) or to 500 mg of parenteral iron as above with 3 doses of subcutaneous 6000 units each of erythropoietin (Group II).

Results: There was a mean rise of 1.4 g with intravenous iron sucrose there was a mean increase of 2.8 g/dl with intravenous iron sucrose and erythropoietin therapy. There was significantly high rise in serum iron, serum ferritin, and transferrin saturation. There was no anaphylaxis in any group with iron sucrose and erythropoietin therapy as compared to iron sucrose alone.

Conclusion: Addition of erythropoietin to intravenous iron sucrose gives superior results in improving hematological parameters in moderate and severe anemia during pregnancy and can obviate the need for blood transfusion.

Keywords: Anemia, Pregnancy, Erythropoietin, Intravenous iron sucrose

INTRODUCTION

Iron deficiency is the most common nutritional disorder in the world, affecting approximately 25% of the world's population.¹ Pregnant women are particularly at high risk for iron deficiency and iron-deficiency anemia because of increased iron needs

during pregnancy. Anemia during pregnancy causes significant maternal mortality and morbidity and may be responsible for up to 40% of maternal deaths in low income countries.^{2,3} It also causes perinatal mortality and morbidity due to increased risk of preterm deliveries, low birth weight infants, small

1. (✉) Dept. Obstetrics & Gynecology, Teaching Block, 3rd Floor, All India Institute of Medical Sciences, Ansari Nagar, New Delhi – 29.
Email: jbsharma2000@gmail.com
2. Dept. Hematology, All India Institute of Medical Sciences, New Delhi

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gestational age infants, low iron stores in infants, cognitive and affective dysfunction and lower mental development in infants.^{4,5} The global prevalence of iron-deficiency anemia in pregnant women is 38.2% being 3-4 times higher in lower income countries as compared to high income countries. The prevalence is 24.4% in America, 25.8% in Europe, 43.6% in Africa and 48.7% in South east Asian regions.⁶ India has one of the highest incidence of anemia with small incidence being 55.3% (38.6% mild anemia, 15% moderate anemia, 18% severe anemia).⁷ It is probably due to dietary habits, consumption of low iron bioavailability cereal diet with vegetarian diet low in vitamin C with low excess of inhibition of iron (Fe) absorption (like phytaes), high prevalence of worm infestations and repeated pregnancies at shorter intervals.⁸⁻¹⁰ Diet alone cannot supply the 30-40 mg Fe that is required for absorption of the 4-6 mg iron per day needed during the latter stages of pregnancy.¹¹

Iron supplementation is therefore recommended for all pregnant women in developing countries.¹⁰ Oral iron intake is the treatment of choice, and almost all women can be treated effectively with oral preparations.

However oral Iron supplementation is not always sufficient for a quick and effective treatment of anemia in pregnancy. Ministry of Health, Government of India recommends 200 mg elemental iron with 1 mg folic acid for treatment of anemia until Hb levels come back to normal, followed by 100 mg per day as maintenance therapy during 3 months of puerperium for replenishing the iron stores.¹² Parenteral iron therapy is only indicated when the pregnant woman is unable to take oral iron due to side effects or is non-compliant as both oral iron and parenteral iron have been found to be equally efficient in the studies.¹³ The advantage of parenteral iron is its certainty of administration while iron sorbitol can only be given intramuscularly. Iron dextran can be given both intramuscularly and intravenously.^{10,13} However, both these preparations though economical, run the risk of allergic and anaphylactic reactions and are going out of favor. Currently, intravenous iron sucrose is the preferred treatment due to its efficacy and safety (rare chance of anaphylaxis) although more expensive than iron dextran and iron sorbitol as 200 mg intravenously twice or thrice weekly. It raises Hb and Ferritin levels significantly and faster.¹⁴⁻¹⁶ Newer iron preparations like ferric carboxymaltose has no iron dextran and has high molecular weight and high stability. It can be given as 1000 mg high dose intravenously in one sitting. Although found

to be safe for use even during pregnancy, it has not yet been approved for use during pregnancy by US FDA and drug controller of India.^{17,18} However, it has been approved for postpartum anemia where it is considered to be drug of first choice as single injection can be used and patient can be discharged early.^{17,18} Blood transfusion is widely used as a last resort, despite its controversial use and safety and the risk of complications, such as viral infections, or noninfectious and immunological adverse effects. Synthetic agents such as recombinant human erythropoietin (rHuEPO) have traditionally been used as therapeutic means for anemia of chronic renal disease with low endogenous erythropoietin production.¹⁹

During the last decade, rHuEPO supplementation has also been used in the treatment of anemia in pregnancy and postpartum.²⁰⁻²³ However, such treatment during pregnancy still remains controversial and of limited use.

The objective of this study was to investigate the therapeutic efficacy of rHuEPO combined with intravenous iron sucrose, in the treatment of moderate and severe iron deficiency anemia of pregnancy that didn't respond to iron supplementation alone.

MATERIALS AND METHODS

It was a prospective, randomized study consisting of 60 women in second or third trimester of pregnancy with a hemoglobin value <8 g/dL. It was conducted between Jan 2006-May 2012. The study was approved by ethics committee and all women gave informed consent.

Inclusion Criteria

All subjects had severe iron deficiency anemia with hemoglobin 8 g/dL. All patients had received oral iron (elemental iron=100 mg) for at least fourweeks before starting injectable therapy.

Exclusion Criteria

Women with anemia due to other causes than iron deficiency and those not willing to participate in the study were excluded.

Study Group

All patients were recruited on a consecutive and prospective basis from our antenatal clinic if they fulfilled our inclusion and exclusion criteria. Sixty patients were randomly assigned to two treatment groups of 30 patients each. The aim was to include enough patients so that a true difference of 1 g/dL in haemoglobin increase from baseline to day 7 would have a 90% chance of giving significance in a 2-sided

test at the 5% risk level. Since, enough empirical evidence with respect to haemoglobin levels changes due to intravenous iron sucrose vs iron sucrose and erythropoietin therapy were not available, the adequate sample size could not be calculated. Therefore, the present study was initiated by taking 30 patients in each group.

Group I: 200 mg of intravenous iron sucrose on alternate days for 5 injections.

Group II: Intravenous iron sucrose as above with 3 doses of subcutaneous 6000 units each of erythropoietin on day 1, 3 and 5.

The first dose of iron sucrose was administered in labor room keeping injection adrenaline, hydrocortisone and chlorpheniramine maleate and oxygen cylinder ready for any anaphylactic reactions. Further doses were given in labor room or in outpatient department.

Laboratory tests:

A detailed history was taken from all the women, and a complete physical examination and an obstetric examination were performed at the time of recruitment.

The study protocol was cleared by the Ethics Committee of the Institute. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. An informed written consent was taken from all the patients who were participating in the study after explaining to them in detail about the protocol in the local and regional language of the patient. Detailed history taking, complete physical and obstetrical examination and routine antenatal investigations were performed in all pregnant women. Among the patients who were detected as anemic, a hemoglobin electrophoresis study was carried out to rule out thalassemia and other hemoglobinopathies. Upon recruitment, a 5 ml blood sample was taken from each patient and was sent and processed in the Hematology Department laboratories of the Institute for the following investigations which were conducted free of cost.

1. The routine hematological indices (Hb, MCV, MCH, MCHC) were measured by the *Coulter H 750 Analyser*: MCV = PCV/RBC count, MCH = Hb/ RBC count, MCHC = Hb/PCV. A peripheral smear was also made.
2. Serum iron studies: for this test, the patients were asked to stop iron intake for 7 days. Around 4 ml of clotted blood was taken in an iron- free test tube provided, from which 1 ml of serum was taken for serum iron studies

and 2 ml of serum for serum ferritin levels. An ELISA kit for serum iron studies (serum iron, % saturation of iron, TIBC) from *FAR Diagnostics, USA* was used and the various concentrations of each component was measured with the *Genius WD 21B machine*.

3. Serum ferritin levels: a 2 ml serum sample was separated as discussed above. For measuring the serum ferritin levels, the *Ferritin Enzyme Immuno Assay* from *Orgentech, USA* was used (optical density was proportional to concentration).
4. Serum transferrin receptor level: A 2 ml serum sample was taken from the above sample and processed using the *Human sTfR ELISA kit* form *Bio Vendor LLC, Candler, NC 28715, USA*.

Oral Iron was given for haemoglobin of >8 g/dl while parenteral Iron was given for <8 g/dl. Apart from the iron treatment, all the women were advised dietary changes in terms of green leafy vegetables and other iron rich foods. The women were also regularly followed up in the antenatal clinic.

RESULTS

Baseline patient characteristics:

All patients had used oral iron for at least two weeks. There was no intolerance or noncompliance to oral iron. Hemoglobin in all these patients was ≤ 8 g/dL. Iron deficiency anemia was confirmed in all these patients by a serum ferritin value of less than 1.5 $\mu\text{g/dL}$. The mean age, parity and gestation were similar in two groups (Table 1). There were no significant differences between the groups (Student's *t* test or chi-square test). There was no history of blood transfusion or clinical evidence of infection.

Table1: Baseline patient characteristics in the 2 groups

Characteristic	Group I Iron sucrose alone N=30	Group II rhEPO+ iron sucrose N=30	P- Value
Age (year)			
Range	19-33	20-38	
Mean	22 \pm 3.8	24 \pm 2.8	0.0238
Body Mass Index			
Range	19-31	20-32	
Mean	22.5 \pm 2.8	23.1 \pm 2.4	0.3765
Gestation at initiation of treatment (week)			
Range	20-34 weeks	22-36 weeks	
Mean	28 \pm 3.6	29 \pm 2.8	0.2346

Table 2 shows the mean value and range of hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular

Table 2: Mean value and range of hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular Hb concentration (MCHC), serum iron, total iron binding capacity (TIBC), transferrin saturation and serum ferritin at recruitment and after completion of therapy

Parameters	Group I Iron Sucrose alone		Group II rhEPO+ iron Sucrose		Post-treatment rise/Fall*		P-value
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Group I	Group II	
Hb(g/dl)							
Mean	6.8±0.58	8.2±0.76	6.7±0.56	9.5±0.80	1.4±0.4	2.8±0.8	0.001
Range	5.2-8	6.3-9.1	5.0-7.5	6.5-10	0.7-1.9	2.0-3.1	
Hematocrit(%)							
Mean	22.4±3.2	27.2±3.6	21.8±2.9	32±3.8	4.8±0.5	10.2±0.7	0.001
Range	17.4-26.2	21-32	16.6-25.2	28-34	3.1-6.2	7.4-18.2	
Mean corpuscular volume (fl)							
Mean	77±5.1	83±2.8	76±4.5	88±2.1	9±0.8	12±0.9	0.001
Range	69-83	74-92	71-88	82-95	6-14	8-18	
Mean corpuscular Hemoglobin (MCH) pg							
Mean	21.8±2.4	28.2±2.6	21.6±2.3	32.4±2.6	6.4±1.2	10.6±1.8	0.001
Range	20-24.2	22.2-30.2	20.2-24.8	28.2-36.0	3.2-8.2	7.6-12.5	
Mean corpuscular Hb concentration (MCHC%)							
Mean	26.6±1.8	34.2±2.2	28.6±1.9	38.2±2.8	5.6±0.4	9.6±1.2	0.001
Range	22-30	27.6-38.0	25.8-32.2	30.2-42.2	31-72(**?)	5.2-11.2	
Serum iron µg/dl							
Mean	31.48±4.84	48.79±10.4	30.87±4.38	56.67±13.2	17.31±2.45	25.80±3.82	0.001
Range	26.37-40.85	38.42-59.45	25.88-39.42	42.54-67.38	12.45-24.25	19.48-38.45	
Total iron binding capacity (TIBC)* µg/dl							
Mean	368.2±39.4	324.4±12.6	362.6±38.7	321.3±11.8	43.4±2.8	41.3±2.4	0.003
Range	332.4-388.9	312.4-338.5	329.2-387.4	309.4-331.7	20.2-58.4	19.8-59.5	
Transferrin saturation (%)							
Mean	11.2±2.1	28.0±3.4	10.6±1.9	38.0±3.8	16.8±2.2	27.4±2.8	0.001
Range	9.2-18.4	12.8-39.5	7.8-19	14.8-44.7	11.5-23.2	20.2-32.5	
Ferritin concentration (µg/l)							
Mean	6.8±3.2	38.9±11.2	7.2±3.4	60.2±19.8	30.1±9.8	53.0±1.45	0.001
Range	4.8-12	9.2-52.8	3.4-14	11.2-90.2	12.3-45.2	22.5-68.5	

Hb concentration (MCHC), serum iron, total iron binding capacity (TIBC), transferrin saturation and serum ferritin at recruitment and after completion of therapy. At recruitments the two groups did not differ much in term of hemoglobin, hematocrit, blood indices, serum iron, TIBC or serum ferritin values.

Response to therapy:

After 2 weeks of therapy there was a significant improvement in all the parameters in both the groups. The range of post therapy hemoglobin was 6.3 to 9.1 g/dl with mean of 8.2 g/dl in-group I in contrast to 6.5 to 10.0 g/dl with mean of 9.4 in Group II (p=0.001). Thus while there was a mean rise of 1.4 gm with parenteral iron there was a mean increase of 2.8 g/dl with parenteral iron and erythropoietin therapy (p=0.001). Both groups showed an increased hematocrit response to therapy. At two weeks of therapy in Group II the mean hematocrit was 32 compared to 27.2 in Group I (p=0.001). Mean

corpuscular volume increased in both groups and was higher in Group II than Group I at two weeks (88 vs. 83 fl; p value=0.001). MCH and MCHC increased over two weeks in both the groups but, the increase was subsequently more in group II than in group I (p=0.001) Serum iron increased significantly more in group II than in group I (p=0.005) while TIBC decreased significantly more in group II than in group I (p=0.003). Transferrin saturation increased significantly in both the groups but the increase was higher in group II (p=0.001). Serum Ferritin concentration increased from 6.8±0.32 µg/dL in group I to 38.9±1.12 µg/dL while the increase was significantly higher in group II than in group I (p=0.001) (increased from 7.2±0.34 µg/dL to 60.2±1.98 µg/dL). There was no anaphylactic reaction in any group. One patient in intravenous iron sucrose group had thrombophlebitis at injection site which healed of its in one week. None of the women needed additional ante partum and postpartum blood transfusion.

DISCUSSION

Iron deficiency anemia during pregnancy continues to be a major public health problem especially in developing countries causing significant maternal and perinatal mortality and morbidity.¹⁻⁶ The prevalence is particularly high in India (55.3%) due to dietary habits, worm infections and repeated pregnancy at shorter intervals.⁷⁻¹⁰

Iron supplementation with folate is recommended to all pregnant women in dose of 100 mg oral iron with 1 mg folate per day while for treatment double dose (200 µg elemental iron and 200 mg folate) are recommended.^{11,12} Then efficacy of oral and parenteral iron is equal.^{13,14} The only advantage of parenteral iron is certainty of administration. Traditional parenteral iron preparations like iron dextran and iron sorbitol, though economical, can cause allergic reactions including anaphylactic reactions.¹³ New iron preparations like iron sucrose, though more expensive, is associated with least risk of anaphylaxis and is highly effective.^{15,16} Ferric carboxymaltose is a newer iron preparation which can be given as 1000 mg dose but is not licensed yet for administration during pregnancy but is suitable for postpartum anemia.^{17,18} For severe anemia, traditional treatment especially in late pregnancy is blood transfusion which can be associated with viral transmission and blood related reactions and should only be given for antepartum hemorrhage or severe anemia near term. Erythropoietin therapy has traditionally been recommended for renal disease with anemia but has been found to be safe for severe anemia during late pregnancy to avoid blood transfusions.¹⁹⁻²³

This study shows that combination of erythropoietin with intravenous iron sucrose increases the hematological response compared to intravenous Iron sucrose alone. Also the mean increase of hemoglobin and hematocrit was higher and anemia was corrected earlier in combination group. The hemoglobin increase observed after 2 weeks corresponds to the expected rise after transfusion of two units of blood, similar to that observed previously in a retrospective study of women with postpartum anemia.²⁴ As it was an outpatient therapy, no admission was required and treatment was completed in one week.

Several studies have described the role of recombinant erythropoietin in non-renal obstetric anemia during pregnancy.²⁵ The combination of erythropoietin with parenteral iron increases the efficacy by stimulating erythropoiesis at the time iron is delivered for hemoglobin synthesis and storage.²⁰ Continued

supplementation with oral iron after completion of parenteral iron therapy helps in replenishing iron stores. Because intravenous iron sucrose is also safe and effective, the combination of the 2 substances increases the efficacy of anemia therapy by stimulating erythropoiesis (rhEPO) at the same time that it delivers enough iron for hemoglobin synthesis and iron stores (iron sucrose). Indeed, it is now generally accepted that rhEPO should be combined with intravenous iron, especially when iron stores are empty before therapy. In our patients functional iron deficiency was already present before therapy, and it did not worsen during the observation period. The fact that functional deficiency was still present at the end of therapy, however, shows that iron must be supplemented until the end of pregnancy in patients such as ours with empty iron stores.

Recombinant erythropoietin might be most useful in severe anemia or in cases of anemia complicated by conditions like placenta previa, in Jehovah's Witnesses²⁶ and hemoglobinopathy (eg, thalassemia and sickle cell disease).^{27,28} Use of rhEPO could also serve as a second-line therapy if iron alone fails to increase the hematocrit within a defined interval. Because blood transfusions are a last resort, alternative strategies such as rhEPO plus parenterally administered iron are of considerable value. Our data show that adjuvant rhEPO combined with an optimized dosage schedule shortens treatment considerably while avoiding the gastrointestinal side effects and associated poor compliance found in as many as 30% of patients receiving oral iron therapy.¹³

CONCLUSION

To conclude recombinant human erythropoietin combined with intravenous iron appears to be an effective treatment for pregnancy anemia. The efficacy and safety of rhEPO during pregnancy warrants further evaluation, including cases of non-renal anemia.

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Disclosure of Interest: None

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Original Article

A STUDY ON THE SEX RATIO AT BIRTH IN INSTITUTIONAL DELIVERIES IN A TERTIARY CARE HOSPITAL IN KALYANI, WEST BENGAL

Ranita Roy Chowdhury,¹ Srijoni Chowdhury,¹✉ Manidip Pal¹

ABSTRACT

Background: The sex ratio at birth and the sex ratio in the population should remain constant without manipulation. However, several parts of the world, particularly some Asian countries including India, have shown a low sex ratio at birth due to the preference for a son and due to sex selective abortion.

Objectives: The objectives of our study were, to find out the trend of sex ratio at birth in institutional deliveries.

Methods: In the present study, the secondary sex ratio was analyzed from the birth records of all the deliveries which were conducted at the College of Medicine and JNM Hospital, WBUHS, Kalyani, Nadia during the period from January 2016 to September 2017.

Results: During the study period, 12,852 institutional deliveries took place, of which 6017 was female births, thus giving an overall sex ratio of 880.

Conclusion: In our study, a trend towards an alarmingly decreasing sex ratio was documented.

Key words: demographic indicator, literacy rate, sex composition

INTRODUCTION

Sex Ratio is a term used to define the number of females per 1000 males. It's a great source to find the equality of males and females in a society at a given period of time. In India, Sex Ratio was respectable till the time of Independence, thereafter it has declined regularly. According to Census of India 2011, Indian sex ratio has shown major signs of improvement in the last 10 years.¹ From a small number of 933 in 2001, the bar has been raised to 940 in the 2011 Census of India.¹ Although this improvement is fair

enough in a developing economy, but still there is a long way to go. India suffers from a huge inequality of male female child ratio due to poor sex ratio in some regions.

The sex ratio at birth (SRB) is an important demographic indicator that was initially studied in the late 17th century.² The sex composition of a population is determined, in part, by the number of male births which are relative to the number of female births. In humans, the sex ratio at birth is commonly assumed to be 100 boys to 105 girls

1. Dept. Obstetrics and Gynaecology, College of Medicine & JNM Hospital, WBUHS, Kalyani, Nadia, West Bengal, India
✉P-25/1, P.M. Sarani, P.O. Haltu, Kolkata – 78,
Email: sriju.chowdhury@gmail.com

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(which is sometimes shortened to “a ratio of 105”). However, the sex ratios at birth or among infants may be considerably skewed by sex-selective abortion and infanticide. The Central Intelligence Agency (CIA) has estimated that the current world wide sex ratio at birth is 107 boys to 100 girls.³

The data on the sex ratio at birth is necessary to understand the trends in infant morbidity like low birth weight and mortality, since male infants are more susceptible to illness and have higher infant mortality rates than females.^{4,5} The sex ratio at birth which is biased against female births can result in a gender imbalance, which in turn can have grave implications on the society in the form of lack of marriage-ability of the excess male population, thus resulting in social unrest, a demand driven increase in prostitution, kidnappings of women, etc.^{6,7} The sex ratio at birth can be affected by sex-selectivity at birth.⁸ The SRB for India for the period from 2004-06 (3 years average) has been estimated to be 892. It varies from 895 in the rural areas to 881 in the urban areas. In the rural areas, the highest and lowest SRBs are in the states of Tamil Nadu (970) and Delhi (810) respectively. The SRB in the urban areas varies from 962 in Kerala to 800 in Punjab.⁹

The various factors which are associated with declining sex ratios are social, economic and cultural in nature. Health institutions represent the health related behaviour of the population. It was thought that the sex ratio at birth would give some idea about the overall picture of the sex ratio in the society.

MATERIALS AND METHODS

This study was undertaken at the College of Medicine and JNM Hospital, WBUHS, which is a tertiary care government teaching hospital in Kalyani, Nadia, West Bengal, to find out the sex ratio at birth in institutional deliveries. It was a retrospective, record based, observational study. The birth records of all the deliveries which were conducted at the above mentioned institute during the study period were analyzed by using the study variables i.e. literacy rate and residential status of the state and Nadia district as per 2011 census.

RESULTS

In the present study, a total of 12,852 deliveries took place in this hospital, with 6835 male and 6017 female births, giving an overall sex ratio of 880. The sex ratio for the year 2016 was 902 and 852 for the year 2017 calculated till date. The results of the study has been interpreted using standard statistical methods. (Table 1, Fig. 1)

Table 1: Sex ratio in Kalyani, COMJNM hospital

Year	Male	Female	Total Birth	SRB
2016	3767	3401	7168	902.8
2017(till Sep 2017)	3068	2616	5684	852.7

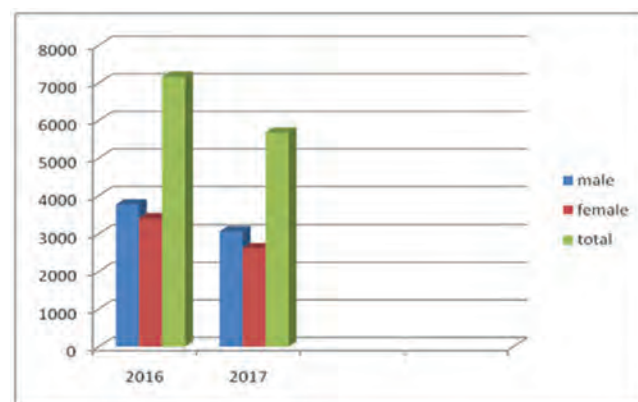


Fig. 1: Sex ratio in Kalyani, COMJNM hospital

The national sex ratio of India showed that in 2012 it was 940 and in 2016 it is 944. (Table 2)

Table 2: Sex ratio in India (yearly)

Year	Sex ratio
2012	940
2013	941
2014	942
2015	943
2016	944

<http://www.indiaonlinepages.com/population/sex-ratio-of-india.html>

As per the population census 2011, vast majority of the people of West Bengal stayed in rural area (Fig. 2) and literacy rate has been increased if we compare the report between 2001 and 2011 (Table 3).

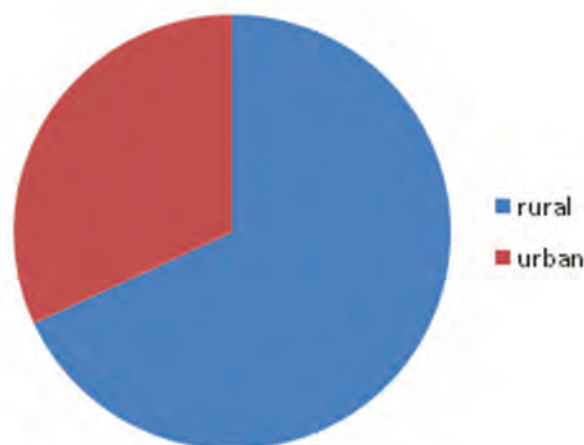


Fig. 2: Population of West Bengal

Table 3: Literacy rates (%) in West Bengal

Year	Male	Female	Total literacy rates
2001	77.02	59.61	68.64
2011	81.69	70.54	76.26

DISCUSSION

In our study, we tried to investigate the trend of SRB in our institute in background of local demographic factors such as female literacy and rural and urban status. In the present study, the SRB (880) was found to be well below the national average of 944. The sex ratio at birth for the year 2016 was 902.8 while SRB till Sep 2017 being 852.7. An alarmingly lower than the national average of the past few years. As per the census of the year 2011, the sex ratio in India was 940 girls per 1000 boys, whereas it was 976 in 1961, just five decades back. The sex ratio in West Bengal was 934 per 1000 males. According to NFHS 3, there was an accelerated decline in the sex ratio at birth from 1993-97 to 2000-04.^{10,11} The level of literacy was relatively low among the mothers from rural areas. According to the census of the year 2011, the female literacy in West Bengal was 70.5%.¹² The literacy rate in our study population is taken to be as per the last census, 2011. A similar observation was also made in other studies from India.⁶ It has been observed that female literacy is rising in this state but this does not seem to reduce the sad state of affair prevalent in this part of the country. A possible explanation could be explained by the fact that the women with higher education opted more for sex selection due to the preference for a son and a small family size. 6 The NFHS III data also showed that 56% of the women and 59% of the men considered the ideal family size to be two children or less, but there was a consistent preference for sons over daughters among both women and men. About one-third of the women and one quarter of the men wanted more sons than daughters, but only 2% wanted more daughters than sons.¹³ It showed that though female education could lead to some decrease in the gender disparities, it was not enough. Hence, with increased female education, there had to be an increased awareness regarding the adverse consequences of the declining sex ratio, particularly among females. The sex ratio at birth was 909 for urban mothers and it was 820 for rural mothers. In institutional deliveries, the sex ratio at birth was low in both urban and rural areas as compared to the state average. Studies by other groups also showed that the preference for a son and the discrimination against the girl child were common among the rural population and that it mainly arose out of social attitudes and the

society's prejudices, myths and beliefs. It could be explained that smaller families had a significantly higher proportion of sons than the larger families and that socially and economically disadvantaged couples not only wanted but also attained a higher proportion of sons, if the effects of the family size are controlled. A low sex ratio at birth in the rural areas was a point of concern. It possibly reflected an increased access of prenatal diagnostic techniques among the rural population who were possibly more biased against women due to an agriculture based male dominant society.^{14,15} There was a decline in the SRB from the second birth onwards. The variation of SRB with the birth order (or parity) was seen in Asia and in all the other countries where the SRB was increased. It showed that after the first child, a large number of couples availed of the prenatal techniques for sex selection. Similar findings were observed in other studies too.¹³

Limitations of the study

The present study was conducted in only one teaching hospital taking into account the local demographic features prevalent in that part of the state. SRB determination calls for involvement of other hospitals along with the socio-religious and residential status of the patients.

CONCLUSIONS

An extremely complicated situation is existent regarding the sex ratio at birth in India due to diverse demographic, cultural, and socio economic factors. These have shown a variable influence over the sex ratio in different studies. It is necessary to understand these complex mechanisms before making policies and programmes to decrease the gender discrimination. The effective implementation of a legislation which prevents sex selective abortion should be combined with proper education with respect to the declining sex ratio and its future adverse consequences. All forms of gender inequality with equal social and economic rights for males and females, including the rights of inheritance, need to be addressed. The PCPNDT Act should be effectively implemented, so as to discourage female foeticide. Both print and electronic media, should be mobilized to percolate the relevant information to prevent female foeticide. In addition, further studies are recommended to explore the reasons of the unhealthy sex ratio at birth. The women especially those from the rural areas should be targeted to be educated, which could make both men and women accept female births. So the target is not only to achieve adult literacy but proper education in real terms.

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ABBREVIATION

NFHS – National family health survey

Original Article

EVALUATION OF AWARENESS, ACCEPTANCE AND EXPULSION RATE OF POST-PLACENTAL INTRAUTERINE DEVICE (PPIUCD) IN A TERTIARY CARE CENTRE

Banasree Bhadra,¹✉ Sougata Kumar Burman¹

ABSTRACT

Background: During the postpartum period both woman and newborn need a special integrated package of health services as morbidity and mortality rates are quite high. Advantages of immediate postpartum intrauterine contraceptive device insertion (PPIUCD) include convenience, safety, client motivation, facilitates proper birth spacing, does not interfere with lactation, immediately reversible and does not require repeated health care visits for refill of contraceptive.

Methods: This prospective longitudinal study was conducted in the Department of Obstetrics and Gynaecology, College of Medicine & JNM Hospital, Kalyani, West Bengal from 1st January 2016 to 31st December 2016.

Results: During the study period from 1st January 2016 to 31st December 2016, 9441 women were counseled and 61.1% women were aware about PPIUCD. 7410 patients delivered during this period. Overall 3889 patients had PPIUCD insertion in the study period. Acceptance rate was 52.5%. Majority of the insertions were post placental insertions (63.7%). Majority of the cases who had PPIUCD insertion were between the age group of 18-25 years (40.52%). Most of the clients were para-2 (34.89%). PPIUCD with expulsion rate was of 0.6%.

Conclusion: Immediate postpartum IUCD insertion is safe, effective, low cost, long acting and reversible contraceptive method. Awareness of PPIUCD should be increased to create a positive impact. The feasibility of accepting PPIUCD insertion can increase with proper antenatal counselling and awareness programs in rural and urban areas. With proper insertion techniques expulsion rate can be kept low.

Key words: contraception, post placental insertion, PPIUCD

INTRODUCTION

During the postpartum period both woman and newborn need a special integrated package of health care services, as morbidity and mortality rates are still quite high. Women are also vulnerable to unwanted

pregnancy, which often leads to illegal abortions. In developing countries, delivery is probably the only time when a healthy woman comes in contact with health care provider and the chances of her returning for contraceptive advices are uncertain.¹ In

1. Dept. Obstetrics & Gynaecology, College of Medicine & JNM Hospital, WBUHS, Kalyani
✉8A/2 Anupama Housing Complex, Phase 1 VIP Road, Kolkata; West Bengal (India). PIN- 700052.
Email: banasree22@yahoo.com

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spite of availability of wide range of contraceptives, the unmet need for family planning is estimated to be 12.8%.² The common reasons for unmet need maybe unsatisfactory services, lack of knowledge or information, and fear about side effects of contraceptive method.

WHO medical eligibility criteria state that PPIUCD is safe in postpartum lactating women with advantages outweighing the disadvantages.³ Advantages of immediate postpartum insertion of the IUCD include convenience, safety, client motivation, ensuring proper birth spacing, unrelated to lactation, immediate reversibility and last but not the least it does not require repeated visits to health center for further contraceptive administration. PPIUCD insertion gives the women an additional advantage of leaving the hospital with appropriate long-term contraception after institutional delivery thereby decreasing the overall costs borne by patients and the Government.

MATERIALS AND METHODS

This prospective longitudinal study was conducted in the Department of Obstetrics and Gynaecology, College of Medicine & JNM Hospital, Kalyani, West Bengal from 1st January 2016 to 31st December 2016. The study was approved by the ethics committee of the institution.

Inclusion Criteria: All women attending antenatal clinic or labour room in early labour were counseled for post partum insertion of IUCD either at vaginal delivery or during caesarean section.

Exclusion Criteria: All women with chorioamnionitis, puerperal sepsis, PROM for > 18 hours,

known distorted uterine cavity, past history of PID or ectopic pregnancy and PPH.

All antenatal patients, irrespective of maternal age, risk factor and proposed mode of delivery at antenatal clinic of the Institution were counseled about contraceptive options. Women were asked whether they were aware of PPIUCD before or not. Women were sensitized about advantages and importance of family planning methods during ANC visits and also at the time admission (before delivery but not when in active labour). Pros and cons of PPIUCD were explained. Cu T 380 A was inserted within 10 minutes of placental expulsion in vaginal deliveries and during caesarean section in women who gave informed consent. Follow up schedule was at 6 weeks after insertion and the patient was asked to revisit after 3 months.

RESULTS

During the study period from 1st January 2016 to 31st December 2016, a total of 9441 women were counseled and of them 61.1% women were found to be aware of PPIUCD (Table 1).

Table 1: Awareness of PPIUCD

Women counselled	Aware of PPIUCD	Not aware of PPIUCD
9441	5773 (61.1%)	3668 (38.9%)

7410 patients delivered during this period. A total of 3889 patients had PPIUCD insertion in the study period. Mean Acceptance rate was 52.5% (Table 2). Majority of the insertions were post-placental 63.7% as compared to 36.3% of PPIUCDs, which were inserted during caesarean section.

Table 3 shows that majority of cases who had PPIUCD insertion were between the age group of

Table 2: Acceptance of PPIUCD insertion

Month (2016)	Total Deliveries	Total Insertions (Accepted)	Intra Caesarean	Vaginal (Post placental)	Acceptance(%)
January	607	58	50	8	9.5%
February	546	180	133	47	33%
March	573	213	138	75	38.65%
April	551	257	104	153	46.64%
May	638	209	83	126	32.75%
June	482	325	120	208	67.42%
July	581	367	123	244	63.16%
August	651	391	123	268	60%
September	623	415	139	276	66.6%
October	731	478	132	346	65.4%
November	683	508	131	377	73.37%
December	744	488	139	349	65.5%
Total	7410	3889	1415 (36.3%)	2477 (63.7%)	52.5%

18-25 years (40.52%). The rate of acceptance amongst varied parity were seen to be almost identical.

Table 3: Distribution of PPIUCD acceptors according to age and parity

Age (in years)	Accepted (Number)	Percentage (%)
18 yr-25 yrs	1576	40.52
26-30 yrs	1383	35.56
31 - 35 yrs	916	23.55
>35 yrs	14	0.35
Parity		
Primipara	1286	33.06
Para 2	1357	34.89
Multipara	1246	32.03

Analysis amongst the acceptors, based on the level of education, revealed that uneducated and primary level educated were far more in number than those who were secondary level and beyond. Hindu community contributed around 56% whereas Muslim community contributed around 44% (Table 4).

Table 4: Distribution of PPIUCD acceptors according to education and religion

Education	Accepted (Number)	Percentage (%)
Illiterate	1394	35.84
Primary	1503	38.64
Secondary	958	24.63
Higher Secondary and above	34	0.87
Religion		
Hindu	2174	56
Muslim	1715	44

Reason behind continued acceptance of PPIUCD was dependent on the level and competence of counseling regardless of the fact whether done during antenatal period, early labour or before caesarean section. As many as 61.86% cases came for follow up and out of these cases 90.77% cases showed willingness to continue PPIUCD (Table 5).

Table 5: Follow up of PPIUCD acceptors

Follow up	Number	Percentage (%)
Presented at 6 weeks	2406	61.86
Willingness to continue	2184	90.77
Spontaneous Expulsion	14	0.6
IUCD removed	8	0.33
Missing thread	139	5.77

DISCUSSION

The postpartum period is the ideal time to begin contraception as women are more strongly motivated

to do so at this time. It is also convenient for both patients and healthcare providers. The PPIUCD is highly effective, long acting, reversible, cost effective and easily accessible family planning method. It is safe for use by most post partum women and has no adverse impact on breast feeding.⁴

We found that 61.1% women were aware of PPIUCD. Shahbaz F et al found in their study that 75% of women were aware of PPIUCD.⁴ Regular awareness and sensitisation programs arranged by our post-natal unit in nearby villages and health centres helped in creating awareness about PPIUCD. In our study we found acceptance rate to be 52.5% which is quite high. This was possible because of extensive counseling by trained counselors, Nurses and doctors in antenatal clinic and in wards using pictorial flip cards and posters. Videos on family planning and PPIUCD were played in the television, installed in the antenatal clinic and ward. Kharkwal S et al also found acceptance rate of PPIUCD to be 60%.⁵ whereas Kanhere AV et al found acceptance rate of PPIUCD insertion to be 36% which was significantly low as compared to preference to use of other methods of contraception at a later date (64%).⁶

In our centre majority of the PPIUCD insertions were post placental insertions (following vaginal delivery). Whereas some studies found maximum insertions to be Intra Caesarean.^{5,7} As the nurses of our maternity ward were also given training, they did the insertions efficiently and contributed to the increase in post placental insertions.

Majority of the patients who accepted PPIUCD were of age group 18-25 years (40.25%). Katheit G et al also found acceptance rate higher in age group 21-25 years (50.88%).² But in a study by Borthakur S et al acceptance was maximum in the age group 26-30 years.⁷

In our study we found that para 2 women accepted PPIUCD more than the primipara. This was in concurrence with the study by Katheit et al where they found higher acceptance in para 2 clients (35.76%). Some other studies found higher acceptance in multiparous^{7,8} whereas in another study majority (44%) of the insertions were in para 1 patients.^{6,9}

As many as 38.64% of the PPIUCD acceptors were primary level educated which is similar to the findings of other studies where majority of the insertions were in patients who had primary level of education.^{5,9} Jairaj S et al found acceptance to be more in those patients who had completed their secondary school level education (23.3%).¹⁰ Various other studies

concluded that educational status has definitely high influence in acceptancy of PPIUCD.^{2,6,10}

The willingness to continue this method during follow up was 90.7% in our centre which is similar to the study conducted by Shahbaz F.⁴ Regular counselling in antenatal clinic and wards were effective in sensitizing the would-be mothers. Awareness created by our family planning staffs in villages and educating the ASHA workers and nurses in the primary care centre also helped to achieve this objective.

Expulsion rate was low (0.6%) in our study. In our centre we arranged PPIUCD workshops with hands-on-training at regular intervals to train the doctors and nurses in the PPIUCD insertion techniques. The expulsion rate in a study by Shahbaz F et al was 4.5% whereas Katheit G et al and Jairaj S found the expulsion rate to be 10.5% and 14.28% respectively.^{2,4,10} Removal of Copper T was done in 0.33% cases in our study period for various reasons while in the study by Gautam R et al and Shahbaz F et al removal was done in 4% and 5% cases respectively.^{4,11} In this study, 5.77% cases presented with missing threads which is similar to the findings of Kanhere AV et al where 3% cases had missing thread.⁶

CONCLUSION

Awareness was quite high in our centre (61.1%) leading to more acceptance of PPIUCD (52.5%). In our centre expulsion rate was very low (0.6%).

Immediate postpartum IUCD (PPIUCD) insertion is safe, effective, cheap, long acting and reversible contraceptive method. Awareness of PPIUCD needs to be increased to have a positive impact. The likelihood of accepting PPIUCD insertion can increase with rigorous antenatal counseling and

emphasizing on regular awareness programs in rural and urban areas. With proper insertion techniques expulsion rate can be reduced to minimum.

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Original Article

IMPACT OF GLOBAL EPIDEMIC OF CAESAREAN SECTION IN A DISTRICT MEDICAL COLLEGE OF WEST BENGAL: AN OBSERVATIONAL STUDY

Srijoni Chowdhury,¹ Ranita Roy Chowdhury,¹✉ Manidip Pal¹

ABSTRACT

Background: In developing countries, increasing use of medical technologies during childbirth is now the matter of keen interest. Though the application of reproductive technologies has significantly improved clinical obstetric care but this has generated unintended health issues for women and increased costs to family and eventually nation. According to the latest data from 150 countries, currently 18.6% of all births occur by CS. In 2010 in India, the incidence was around 8.5% but a phenomenal increase of 40 % was seen in Kerala and Tamil Nadu. Keeping in view the above facts, the present study tries to explore the trends of caesarean section delivery in College of Medicine & JNM Hospital, Nadia West Bengal (the only tertiary care hospital in this predominantly rural district) and its comparison with the state and national data.

Methods: Over a study period of Oct 2016-Sept 2017 the rate of caesarean section was obtained from COM JNM Hospital Nadia, West Bengal and comparison was made with the latest available national and regional data.

Results: Our study over the period of Oct 2016-Sept 2017 in College of Medicine & JNM Hospital found CS rate increased annually from 34.4% (October 2016) - 41.1% (September 2017) which is quite high among whole Nadia District (15%) and West Bengal (18.2).

Conclusion: The high CS rate can be accounted to the fact that this is the only tertiary referral centre in the district, however due consideration has to be given to reduce the rate to some extent.

Key words: CS on demand, CS rate, Nadia, NFHS, West Bengal

INTRODUCTION

In developed and developing countries, including India, increasing use of medical technologies during childbirth is now the matter of keen interest. Though

the development and application of reproductive technologies have significantly improved clinical obstetric care but this phenomenon can generate unintended health issues for women. With the increasing numbers of institutionalised births in

1. Dept. Obstetrics & Gynaecology, College of Medicine & JNM Hospital, WBUHS, Kalyani, Nadia, West Bengal
✉7, Port Blair Lane (N), Near Subhas Sangha Club, Barrackpore, Kolkata – 120
Email: ranitasinha@gmail.com

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India, the trend of caesarean delivery is also sharply rising. Obstetricians, Government and social scientists worldwide are concerned of this enigmatic rise because of the lack of consensus on the appropriate CS rate and the associated additional short and long-term risks and costs to family and eventually nation. In 2008, the cost of the global excess/unnecessary

C-section delivery was estimated approximately 2.32 billion US dollar.¹ Rapid increase of CS rate throughout the world has become a serious public health issue because several studies have found that the high rate of caesarean section does not necessarily contribute to an improved maternal health and pregnancy outcome. We present here the latest CS rates and trends over 1 year among global, national and regional estimates. According to the latest data from 150 countries, 18.6% of total births are performed by CS. Latin America and the Caribbean region have the highest CS rates (40.5%), followed by Northern America (32.3%), Oceania (31.1%), Europe (25%), Asia (19.2%) and Africa (7.3 %).²

Caesarean section rate varies in different places depending on type of caregiver and type of facility. In the last decade, the rate has increased by almost double.

Proportion of CS to the total births is considered as one of the important indicators of emergency obstetric care (World Health Organization, 2009).³

In developing countries like India too many women are undergoing caesarean section. This trend is rising in urban as well as in rural population of India. In 2010, the incidence was around 8.5% but a phenomenal increase to a level of 40 % was seen in Kerala and Tamil Nadu.⁴ A substantial proportion of this increase was due to unnecessary operations attributable to non-evidence based indications, professional convenience, maternal request, and over enthusiastic media propaganda of childbirth by CS. Based on the presentations in the conference and a systematic review of literature, the conference panel stated that though there was lack of sufficient evidences to evaluate fully the benefits and risks of planned caesarean delivery over planned vaginal delivery, the following outcomes were supported by at least some evidences. Compared to planned vaginal delivery and unplanned CS, planned caesarean delivery was associated with:

- (1) A lesser risk of postpartum haemorrhage and stress urinary incontinence,
- (2) An increased risk of infection, anaesthetic complications and placenta previa,

- (3) Greater complications in subsequent pregnancies,
- (4) Longer hospital stay of mothers and neonates,
- (5) Higher risk of respiratory morbidity for infants and
- (6) A lower rate of foetal mortality, birth injury, neonatal asphyxia and encephalopathy.⁵

The increasing trend of CS has generated much controversy regarding the causes of such tendency. The factors which are responsible for this trend include increased institutional deliveries, inadequate use of electronic foetal monitoring devices, inadequate care and apprehension of patients as well as doctors, importuning family and social pressure, clinical status. Rising litigation, insurance, preterm caesarean section to salvage the premature babies in an era of modern NICU facility & doctor's anxiety and apprehension are to a large extent responsible for increasing number of operative deliveries

Keeping in view the above facts, the present paper tried to explore:

1. The levels and trends of caesarean section delivery in College of Medicine & J.N.M Hospital, WBUHS, Kalyani, Nadia, West Bengal (the only tertiary care hospital in this predominantly rural district) and its comparison with the state and national data.
2. To update previously published estimates, present the latest data on CS rates nationwide and to modify obstetricians view on performing caesarean delivery.

MATERIALS & METHODS

The data about the rates of CS was obtained primarily from three sources:

i) Representative nationwide surveys, ii) routine vital statistics, and iii) reports from health authorities. The data available from our hospital (College of Medicine & J.N.M Hospital, WBUHS, Kalyani, Nadia, West Bengal) were compared with the latest available global and regional rates of CS.

RESULTS

On analysis of the data of one year it was found that the caesarean section rate as increase from 34.4% (October 2016) to 38.4% (September 2017) with a peak in June 2017, 46.1% (Table 1).

Table 1: Total percentage of caesarean section performed from a period of October 2016 to September 2017 in COM & JNM Hospital, Kalyani

Month (October 2016 To September 2017)	Total Deliveries	Caesarean Deliveries	Percentage
October	710	244	34.4
November	677	221	32.6
December	748	259	34.6
January	623	201	32.3
February	620	227	36.6
March	623	248	39.8
April	608	235	38.6
May	598	264	44.1
June	583	269	46.1
July	641	279	43.5
August	765	299	39.1
September	762	313	41.1
TOTAL (in 12 months)	7958	3059	38.4

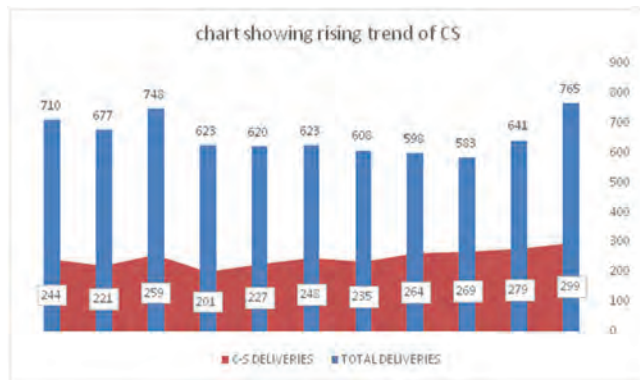


Fig. 1: Incidence of caesarean section over total deliveries from October 2016 to September 2017 in College of Medicine & J.N.M Hospital, WBUEHS, Kalyani, Nadia, West Bengal

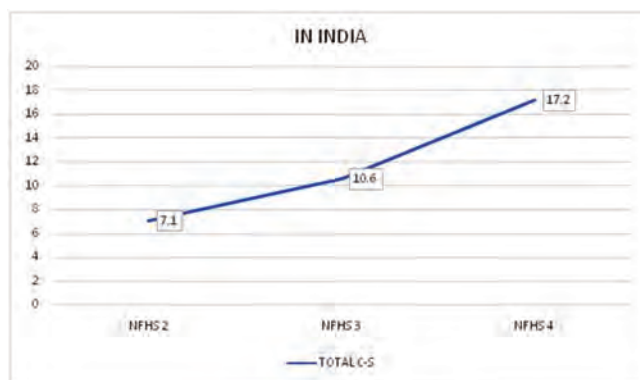


Fig. 2: Graph showing rising trend (In Percentage) of Caesarean Section in India (From 1998 to 2017 based on NFHS data)^{6,7,8}

Caesarean section rate was compared between national, state and district level. It was found that as per NFHS 4 Nadia District's caesarean section rate has been increased to 16.9% from 11.8% (NFHS 3) (Table 2).

Table 2 Increasing rates of Caesarean Section in India, West Bengal and Nadia District (Based on NFHS 3, NFHS 4, DLHS 3 and DLHS 4 Data)^{7,8,9,10}

Percentage of C-S among total Institutional Deliveries			
Based on Survey	India	West Bengal	Nadia
NFHS and DLHS 3	10.6	16.6	11.8
NFHS and DLHS 4	17.2	18.8	15.9

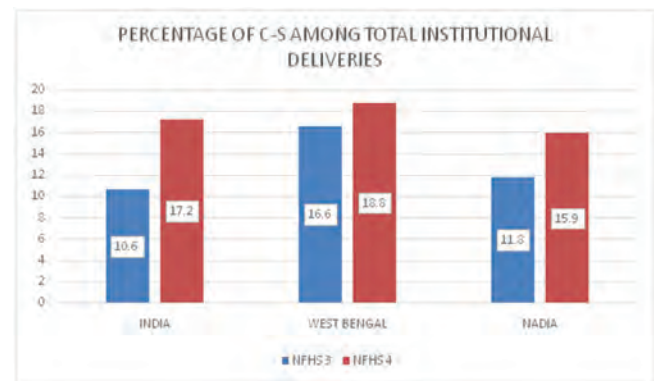


Fig. 3: Percentage of caesarean section among total institutional deliveries

DISCUSSION

Most of the Caesarean Sections (CS) are currently performed keeping the benefit of the fetus in mind not that of the mother. Changes in maternal characteristics and individual practice styles, increasing tendency of malpractice, profit-oriented attitudes, fear of litigation, social and cultural attributes and sometimes pressure from the families, have all been attributed in this increasing trend. In India, the rate of caesarean section delivery has increased by a whopping 10% in 10 years from 7.1% (NFHS 2 1998) to 17.2% (NFHS 4 2016-17).^{6,8} However, this is much lower compared to some developing nations like Brazil and China. But as India is the second most populous country in the world, even a small increase in the incidence pose a huge impact on the vital statistics and health infrastructures. If the 1985 guidelines of WHO (as in 2009 WHO stated that 'optimum rate is unknown' and world regions might want to continue to use a range of 5-15% or set their own standard), are followed it will be noticed that at national level the present rate of CS does not appear to be that alarming but at regional level the scenario is quite different. Our study over one year from Oct 2016 to Sept 2017 in College of Medicine & JNM Hospital has revealed that CS rate has increased from

34.4 to 41.1%, which is quite high compared to that of whole Nadia District (15.9%) and West Bengal (18.8%) statistics. This can be accounted for by the fact that there is individual institution specific rate at many places and more importantly it is the only tertiary referral centre in the entire district. Using the data of National Family Health Survey (NFHS) India, 1992-93, Mishra and Ramanathan (2002) found that among 18 large states, two states (Goa and Kerala) had CS rate near 15 per cent whereas the rest of the states had less than 5 per cent.¹¹ On the contrary, data from a large teaching hospital in Kolkata revealed that between 1990 and 1995, of all deliveries, caesarean deliveries were done in 50 per cent cases.¹² Another study analyzing the data of 30 medical colleges found that the rate of CS increased from 21.8 percent (1993-94) to 25.4 per cent in 1998-99.¹³ Another study revealed that in Madras city (Chennai), between June 1997 and May 1999, the CS rate was 32.6 per cent.¹⁴ They also found that private sector deliveries had a higher odds ratio of a primary C-section delivery in comparison to public sector after covariate adjustment. Similar findings have been observed in several other studies.¹⁵

The proponents of CS claim that CS is an extremely safe operation with a negligible mortality and morbidity. But on the contrary, elective CS had a 2.84 fold greater chance of maternal death as compared to vaginal birth.¹⁶ So CS-on-demand threatens national resources, and is an expensive and dangerous luxury. Obstetricians should abide by ethics in clinical practice and carefully evaluate the indication in every CS and take an unbiased decision before performing CS-on-demand/request. Actually, inadequately informed women choose CS to avoid painful natural childbirth who should be given proper preparatory knowledge of childbirth during antenatal check-up by trained health care provider and professional groups.

A trial for vaginal birth after a previous CS (VBAC) is considered safer than a routine repeat CS. But, it is unfortunate that there is currently less enthusiasm for VBAC by trial of scar or of labor. It is evident that whereas CS is doctor friendly but VBAC is not. RCOG recommends that all women, previously delivered by one lower segment CS, should be offered an opportunity to vaginal delivery during their subsequent pregnancy by promoting a trial of scar or of labor. Carefully supervised vaginal delivery after CS needs to be enthusiastically encouraged by promoting trial of scar or trial of labor.¹¹

Routine practice of external cephalic version is recommended during antenatal period in selected cases of breech presentation.

The question of seeking a second opinion from a senior and experienced obstetrician before performing a CS for a controversial indication is debatable but may be seriously considered or debated in the best interest of the profession and of the women as well. The prevalent practice of “defensive obstetrics” among obstetricians for fear of litigation claims should be duly addressed by law enforcing authority and respective government after paying due attention to the pros and cons of such practices.

CONCLUSIONS

Financial allocation for maternal health care should be enhanced and incentives for vaginal deliveries should be promoted. Provision of proper infrastructures, facilities of EFM (Electronic Fetal Monitoring) devices in rural set up too, along with trained man-power will certainly have a positive impact in terms of increased vaginal delivery rate. Health education activities highlighting the advantages of vaginal deliveries also should be promoted. A hospital-based audit system should be kept in place in order to closely monitor the incidences of and indications for Cesarean Sections in both private and public health care institutions. By doing so, it is possible to maintain CS rate within a respectable range (somewhere between 10-15%) while maintaining a fairly low maternal and perinatal morbidity & mortality ratio.

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Original Article

INCIDENCE OF HIV INFECTION IN ANTENATAL MOTHERS

Suvabrata Sarkar

ABSTRACT

Objectives: To determine the number of mothers detected as HIV positive during the period of April 2016 to September 2017 in COM&JNM Hospital Kalyani Nadia attending ICTC unit.

Methods: This is a retrospective cohort study. All antenatal mothers attending antenatal OPD for first time was counselled for HIV testing. Antenatal patient after giving consent was tested for HIV in ICTC. Confirmative test was done for positive patients.

Results: Total 1557 patient was tested for HIV during the time period of 18 months. Only 2 mothers came positive. So, 0.12% patient was detected with HIV.

Conclusion: HIV incidence is less in compare to west Bengal and India in our institute.

Key words: HIV, antenatal, ICTC, PPTCT.

INTRODUCTION

Despite being home to the world's third largest population suffering from HIV/AIDS (with South Africa and Nigeria having more) the prevalence in India is lower than in many others country. In 2016 HIV prevalence in India was 0.3%.¹ But with a huge population (1.324 billions) - 2.1 million people in India is suffering from HIV.¹ New HIV infection in India in 2016 is 80000 (62000-100000)² and new infection in children <15 years is 9100 (7200- 12000).³

Prevention of parent to child transmission (PPTCT) in India was started in 2002. Based on 2013 WHO guidelines the programme aims to initiate anti retro viral treatment for all pregnant and breast feeding women living with HIV regardless of CD4 count or stage of HIV infection.⁴

However, in 2015 only 38% of pregnant in India living with HIV received PPTCT treatment⁵ and in

2016 only 41% pregnant mothers received treatment³. There is a wide variation of HIV in adults as well as pregnant women in different states.

The present study aims at finding out incidence of HIV among the pregnant mothers undergoing testing in our set up. The determination of HIV incidence in a population is important to a) monitor the epidemic b) to improve the target population for intervention. c) to evaluate the effectiveness of HIV prevention and treatment programmes in our community.

MATERIALS & METHODS

This is a retrospective cohort study done for a period of 18 months from April 2016 to September 2017. The data was collected from the registry of ICTC (Integrated counselling and testing centre) of college of medicine and JNM Hospital, Kalyani, Nadia, West Bengal.

Dept. Obstetrics & Gynaecology, College of Medicine & JNM Hospital, WBUHS, Kalyani, Nadia, West Bengal
✉18, Dinendra Street, Kolkata - 700004
E-mail: sarkar_suvobrat@yahoo.com

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The following parameters were seen a) number of antenatal mothers screened b) number of antenatal mother received pretest counselling. c) number of test done in our centre d) number of HIV positive mothers, their period of gestation at detection and starting of ART prophylaxis.

Antenatal mothers after proper pretest counselling and consent was tested for HIV antibodies (HIV 1 and 2). If detected positive confirmatory test was done. Post-test counselling done in positive mothers maintaining confidentiality of the report. If the mother was found positive after confirmatory test HAART (highly active anti retro viral therapy) was started irrespective of viral load or CD 4 count. Baby born of HIV positive mother was given single dose of Niverepine Syrup (2 mg/kg) immediately after birth. HAART was continued in mother after delivery.

RESULT

In our set up total antenatal mothers tested after pretest counselling was 1557. From April 2016 to March 2017 mothers screened was 873, and from April 2017 to September 2017 was 684. This shows number of counselling and testing is increased per month in 2017 than 2016. 2 mothers was detected HIV positive and confirmed by confirmative test. One case was detected in June 2017 and other July 2017. Both mother's age was less than 30. One was at 27 weeks gestation and other at 40 weeks. HAART was started in both cases. Both women was housewife with one being illiterate. One was delivered by caesarean section and baby being fine received syrup Niverepine on delivery. Another is yet to deliver.

Table 1: Particulars of the 2 positive mothers

Age	Gravida	Occupation	Education	Gestational Age at detection
26 yrs	2	Housewife	Illiterate	27 weeks
20 yrs	1	Housewife	Secondary school	40 weeks

In our study shows in the last 18 months only 0.12 % of mother is detected positive in our set up.

DISCUSSION

The Indian Government is committed to eliminate new HIV infection in children. In India prevention of parent to child transmission of HIV/AIDS started on 2002.

Perinatal transmission of HIV infection occurs in absence of any intervention. The risk of transmission from mother to child is proportional to the plasma viral load of the mother. Untreated mothers with viral load >100000 copies/ml have a transmission risk over 50%.⁶ When viral loads are < 1000 copies/ ml

the transmission risk is less than 1 %.⁷ So HAART for mother both before and during delivery and ART for new born of positive mothers after delivery are recommended to substantially reduce risk of transmission.

India technical report for HIV estimation 2015 shows that there is a declining trend in the number of mother needing PPTCT care. In 2007 it was estimated as 52806 (lower 41208 higher 67575) women needed PPTCT whereas in 2015 mothers needed was 35255 (27351-45965). The trend is also declining in West Bengal. 3539 (2664-4638) needed in 2007 and 1777 (1258-2427) had a need of PPTCT care in 2015.⁸

All states in the country (except Nagaland) and all district in our state have shown less than 1% HIV prevalence among ANC clinic attendees in 14 th round (HSS 2014-15).⁹

The West Bengal AIDS prevention and control society (WBSAPCS) report shows cumulative number of people found positive in ICTC in WB still September 2015 is 65478. Among them 49665 have registered to ICTC and 31021 have enrolled and ever started ART in WB.⁹

However people living in India with HIV and AIDS continue to experience high level of discrimination in a variety of society including household, communities and workplaces. While ART is free the uptake remains low and requires a dramatic scaling up especially in the wake of new 2013 WHO treatment guidelines. Moreover stigma and discrimination remain a significant barrier preventing key affected groups and those at high risk of high risk of HIV transmission preventing from accessing vital health care services.

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Original Article

STILLBIRTHS AND ITS CAUSES IN A TERTIARY CARE TEACHING HOSPITAL OF WEST BENGAL

Amitava Pal,¹ Debobroto Roy,¹ Rupali Modak²✉

ABSTRACT

Objective: To evaluate stillbirth rate and obstetric risk factors and its trend in a referral hospital.

Methods: A hospital based retrospective analysis of stillbirths was done in all pregnant women admitted in the antenatal ward over the years of 2016 and 2017 in Burdwan Medical College and Hospital. Changing trends of stillbirth rates and associated risk factors were assessed.

Results: The overall stillbirth rate in the present study is 25 per 1000 total births. Incidence of macerated stillbirth was high (70.39%). The present study also noted the overall stillbirth rate below 2500 gm was 36% (336/929). Severe prematurity contributed 9% of stillbirths and other factors responsible for fetal salvage are maternal diseases (11%), intrapartum asphyxia (17%), preeclampsia and eclampsia (11.12%).

Conclusion: Poor antenatal check-up, lower socioeconomic status were the major contributing factors for stillbirths which can be reduced by proper antenatal care, judicious and early referral of high risk cases and good obstetric care during delivery.

Key words: stillbirth rate, stillbirth ratio, antenatal care

INTRODUCTION

Stillbirth and early neonatal death pose a major problem in the developing countries. It varies widely in various geographic locations. Each year more than 3.3 million stillbirths are reported worldwide and a vast majority (98%) takes place in developing countries.¹ In developing countries improper reporting is a common problem.² Stillbirth rate is 5 per 1000 or less in the US and other developed countries, while the stillbirth rates of 30-40 per thousand of live births are common in developing countries and in

India the stillbirth rate varies from place to place and from urban to rural areas. Complications during pregnancy are associated with high stillbirth rate in developing countries.^{3,4} It is an important indicator of the quality of antenatal services in a community. Hence critical analysis of every stillbirth will go a long way in reducing its incidence over a period.

The objectives of our study were to analyze the stillbirth rate and find out factors associated with it through a retrospective hospital based study.

1. Dept. Obstetrics & Gynaecology, Burdwan Medical College, Burdwan, West Bengal
2. (✉)Dept Obstetrics & Gynaecology, R. G. Kar Medical College, 12/3J, Northern Avenue, Kolkata 700037.
Email: amitava.628@rediffmail.com

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MATERIALS AND METHODS

The hospital based retrospective study was undertaken from data received from January, 2016 to September, 2017 (21 months) in the department of Obstetrics & Gynaecology, Burdwan Medical College, Burdwan. Data were taken from hospital records of admission and delivery of pregnant mothers. A total of 38,955 maternity admissions were recorded in the maternity department during the last 21 months and of these 4.58 % (1786/38955) were not delivered during the study period. All stillbirths with gestational age of ≥ 28 weeks and birth weight of more than 1000 gms were included in the study. The out come was measured in terms of stillbirth rate calculated as late fetal death (≥ 28 weeks) in a year divided by live births plus stillbirths multiplied by 1000. The stillbirth ratio as the late fetal death divided by live births multiplied by 100. Stillbirths taking place in the intrapartum period are generally normal in appearance and are, therefore, regarded as fresh stillbirths whereas when the skin is not intact or macerated, it implies that death has taken place anything beyond 12-24 hours before delivery.

Different demographic variables like age in years, parity, residence and obstetric factors like status of admission (booked/not booked or referred), mode of delivery, birth weight and factors associated with stillbirths were analyzed. Gestational age was calculated from history, obstetrical examination and supported by ultrasonography.

The data were analyzed using Epi Info (version 3.32). Descriptive analysis was performed and odds ratio with 95% confidence interval was calculated for the retrospectively identified variables associated with stillbirths. A p-value less than 0.05 is designated as statistically significant.

RESULTS

Table 1 demonstrates the total deliveries in the year 2016 were 21330 of which 557 were stillbirths. The stillbirth rate was highest during the span of July-September (27.08 per 1000 births). Seventy percent of total stillbirths were macerated in nature. The total deliveries and stillbirths from January to September in the year 2017 was 15879 and 372 respectively. The stillbirth rate was higher (26.34 per 1000 births) in the first 3 months of the year, 2017.

Table 1. Quarter-wise distribution of stillbirths of December, 2016 and January to September, 2017

Details	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Total
Year- 2016					
Total births	4680	5029	5612	6009	21330
Live births	4554	4905	5460	5854	20773
Intrauterine fetal death	95	100	118	134	447 (80)
Intrapartum stillbirths	31	24	34	21	110 (20)
Stillbirth ratio (%)	2.76	2.53	2.78	2.64	
Still birth rate (per 1000 birth)	26.92	24.66	27.08	25.79	
Year 2017					
Total births	4669	5104	6106	NA*	15879
Live births	4546	4988	5973		15507
Intrauterine fetal death	102	92	101		295 (79)
Intrapartum stillbirths	21	24	32		77 (21)
Stillbirth ratio (%)	2.71	2.33	2.23		
Still birth rate (per 1000 birth)	26.34	22.73	21.78		

* NA: not available

Table 2. Labor and delivery (January 2016 to September 2017)

Characteristics	Total birth n (%)	Still births n (%)	OR (95% CI)	p value
Total enrolled	37,209	929 (2.50)		
		Macerated: 654 (70.39)		
		Fresh: 275 (29.61)		
Mode of delivery				
Vaginal	21776 (58.52)	732 (3.36)	2.63 (2.24-3.10)	0.0001
Forceps	992 (2.67)	20 (2.02)	0.80 (0.50-1.28)	0.3364
Cesarean section	13070 (35.13)	130 (0.99)	0.30 (0.25-0.36)	0.0001
Assisted breech	1371 (3.68)	47 (3.43)	1.39 (1.02-1.89)	0.2872
Type of birth				
Multiple	708 (1.90)	29 (4.10)	1.66 (1.12-2.45)	0.0076
Singleton	36501 (98.10)	900 (2.47)	0.60 (0.41-0.89)	0.0076
Birth weight				
<2500gm	7527 (20.23)	336 (4.46)	2.23 (1.95-2.57)	0.0001
>2500 gm	29682 (79.77)	593 (1.99)	0.45 (0.39-0.51)	0.0001

OR: odds ratio, CI: Confidence interval

Table 2 depicts assisted breech delivery (OR 1.39, CI: 1.02-1.89), cesarean section (35.13 percent of total birth of which 1% were still birth), multiple births (OR 1.66, CI: 1.12-2.45, $p=0.0076$) and birth weight >2500 gm (80 % of total births of which 1.99% were stillbirths). Fresh stillbirth was found in 29.61 % of cases.

Table 3 Obstetric factors associated with stillbirths

Factors	n (%)
Antepartum hemorrhage	72 (8)
PIH and eclampsia	100 (11.12)
Intrapartum asphyxia	153 (17)
Congenital fetal anomalies	9 (1.0)
Gross Prematurity	81 (9)
Maternal diseases	99 (11.0)
Cord prolapse	10 (1.1)
Post dated	144 (16)
Unexplained	152 (16.89)
Maternal Infection	80 (8.89)
Total	900

Obstetric complications were noted in 900 cases of total stillborn fetuses. The stillbirths were noted commonly with antepartum hemorrhage (8%), intrapartum asphyxia (17%), and maternal diseases (11%). One hundred and fifty two fetal deaths (16.89%) were classified as unexplained deaths and majority of those (59.21%, 90/152) were macerated (Table 3).

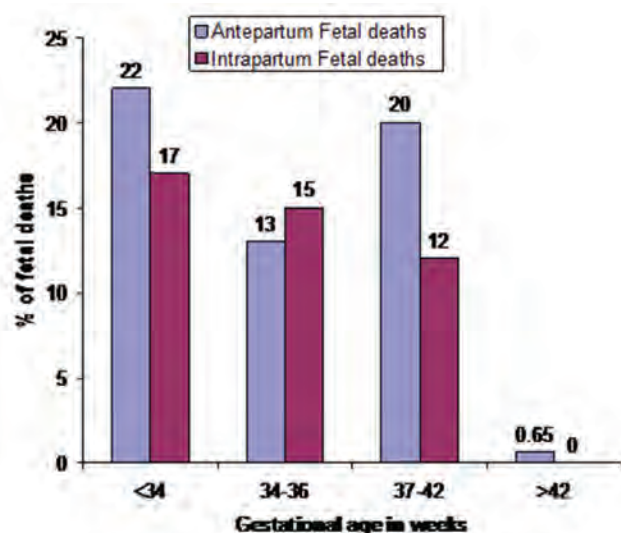


Fig. 1: Gestational age of the antepartum and intrapartum fetal deaths (n=929)

Fig. 1 Shows 20 percent of antepartum and 12 % of intrapartum fetal deaths were at term.

Sixty seven percent (622/929) were preterm (<37 weeks), post maturity was associated in 0.65 % of the stillbirths and all the deaths occurred in the antepartum period.

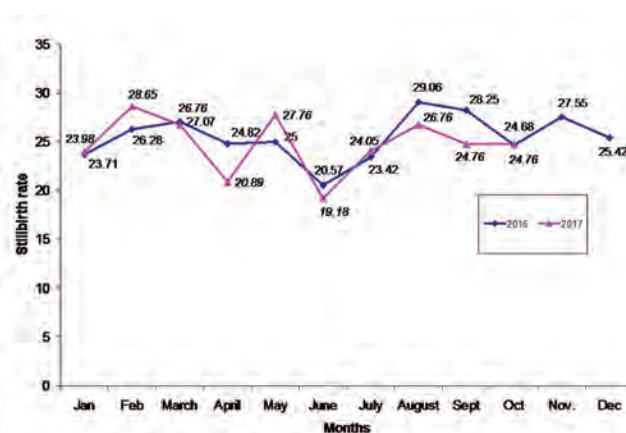


Fig. 2: Month-wise trends of stillbirth rate in the year 2016 and 2017

Fig. 2 shows that the stillbirth rate was comparatively lower in the months of April (20.89), June (19.18), August (26.76) and September (24.76) in the year 2017 as opposed to the corresponding months of the previous year.

DISCUSSION

Stillbirth rate is a painful experience to both mother and obstetrician. It is an indicator of both quality of antenatal service and delivery care of a country. The overall stillbirth rate in the studied period is 25 per 1000 total births. This figure is lower to 35.1/1000 births as reported by Kameshwaran et al⁴ and higher than 23.⁴ per 1000 births studied by Nayak and Dalal.⁵ The probable reasons of high stillbirth rates in our study is due to the fact that it is a referral hospital which serves rural populations with large catchments areas and caters a lot of districts, subdivisions and rural hospitals of west Bengal and Jharkhand. The present study showed that 39% of stillbirths were below 34 weeks. Our study is comparable with the study of Shrestha and Yadav⁶ who noted 40% of stillbirths occurred below 34 weeks of gestation. The present study also noted the stillbirth rate below 2500 gm was 36 % (336/929) which is also comparable with the findings (41%) of Jammeh et al.⁷ Most of the delivery in our study was vaginal (59%), which was associated with stillbirth in 3.36% of cases. The association of stillbirth with cesarean section was low (1%). Intrapartum monitoring with partography and timely cesarean section can reduce the intrapartum fetal death during labor. The present study also noted that severe prematurity contributed 9% of stillbirths and other factors responsible for fetal salvage are maternal diseases (11%), intrapartum asphyxia (17%), Preeclampsia and eclampsia (11%) and unexplained (17%) [Table 3]. Korde-Nayek and Gaikwad⁸ in a hospital based study showed the commonly associated factors for stillbirths are

antepartum hemorrhage (23.95%), medical disorders (20.8%), asphyxia (8.4%) and prematurity (8.4%) and unexplained (18.8%). Jehan et al⁹ reported 63% of fresh still birth in their report whereas it was thirty percent in our study.

CONCLUSION

The stillbirth rate in our analysis is high. This is an apex level rural based teaching hospital that caters to a very large geographical area. Poor antenatal care, lower socioeconomic status of the women, under nutrition and late or no referral, to our opinion, are the major contributory factors responsible for a large number of stillbirths. A significant number of stillbirths are preventable by adopting the following means: adequate and dedicated antenatal check-up by trained health care providers, timely identification of high risk factors and referral to the nearest higher center, having essential obstetric services including cesarean section by trained obstetricians. Strict clinical observation, including CTG monitoring during first stage of labor and application of partography are very essential components in monitoring of labor. Periodic facility audit, perinatal

mortality & morbidity meetings involving all stakeholders and personal supervision by the Head of the Department (O&G) would certainly reduce the stillbirth rate substantially.

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Review Article

PLACENTA & INTRAUTERINE FETAL DEATH

Soma Bandyopadhyay

ABSTRACT

Placenta has a significant role in etiopathology of fetal death. About 11.6% cases of fetal death are due to placental pathology. CORM system of fetal death classification has reduced the unclassified category to 8.5%. Maternal vascular malperfusion, fetal vascular thrombosis, umbilical cord pathologies contribute a lots. Understanding these pathologies can help us to manage the subsequent pregnancies by evaluation of maternal cardiovascular status, diabetes & thrombophilia screening, prophylactic aspirin, early delivery etc.

Key words: fetal, malperfusion, pathology, stillbirth, vascular

INTRODUCTION

Causal relationship between fetal death and placental pathology has traditionally been given less importance. The placenta is the gateway between mother and the fetus. It supplies essential nutrients to the growing fetus, and also provides a protective environment. Fetal nutrition depends on the vascular tree of the placenta, which is continuously growing and developing as the gestation advances. Whenever any external threat comes an inflammatory response against that happened (placental protective function). Such responses may occur at feto-maternal junction where organisms may enter the placental environment whilst fetal antigens may be presented to the maternal immune system allowing a response leading to the release of mediators of inflammation.¹

Histopathological examination of the placenta is to be done to determine the cause of stillbirth/fetal death.² Placental examination alongwith autopsy of the fetus can give a good highlights towards the etiology of fetal death.³ Routine examination of placenta at birth and genetic studies in suspicious

cases will enable us to counsel the parents about the possibility of recurrence of fetal death or congenital abnormality.⁴ Placental pathology contributing to fetal death is 11.6%.⁵

FETAL DEATH CLASSIFICATION SYSTEM

A new fetal death classification system [CORM system {Condición Obstétrica Relevante de la Muerte (Spanish) (relevant obstetric death condition)}]⁵ based on obstetrical history and placental biopsy is been developed in Chile. The histopathological evaluation of placenta revealed the damage that occurs to placenta as a consequence of original obstetric condition, ultimately leading to fetal death. The causes are been classified under the following headings –

- 1) Maternal conditions
- 2) Fetal conditions
- 3) Placental conditions
- 4) Uterine conditions
- 5) Asphyxia during labor
- 6) Conditions not classifiable

Dept. Obstetrics & Gynaecology, Katihar Medical College,
Bihar
✉ Tolly Twin, Block-C, 2nd Floor, B-1, Kabardanga More, 327,
M.G. Road, Kolkata – 700104
Email: somapb@gmail.com

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The placental pathologies have been categorized as –

1. *DPPNI* {Desprendimiento Prematuro de Placenta Normo Inserta (Spanish)}: Separation of the placenta from the uterus, in the absence of maternal-fetal pathology and with placental lesions: hematoma and retroplacental hemorrhage, subcorial hemorrhage, villous infarcts, intervillous thrombosis
2. *Maternal and fetal circulatory disorders and IUGR*: Absence of maternal-fetal pathology, with IUGR, with or without DPPNI, with placental lesions: thrombotic fetal arteriopathy, intervillous and fetal arterial thrombosis, increased deposit of perivillous fibrinoid, villous infarcts, hematoma and retroplacental hemorrhage
3. *Deciduitis, chronic vellositis and IUGR*: Absence of maternal-fetal pathology, with IUGR and placental lesions: chronic lymphoplasmacytic deciduitis, chronic chorioamnionitis, perivillous and chronic vellositis, intervillous thrombosis
4. *Other and IUGR*: Absence of maternal-fetal pathology, with IUGR and with placental lesions: villous edema, corangiosis.
5. *Pathology of the umbilical cord*: Circular knot, with thrombosis and / or rupture, cord hyperrotation, procidentia/prolapse, hematoma, velamentous insertion

The advantage of this classification system is that the non-classifiable or non-explainable condition is only 8.5%. For more detailed information refer to the original article @ reference no 5.

Most frequently encountered primary placental conditions responsible for fetal death are abruptio placentae (5.3-12.9%) followed by placental insufficiency (2.6-8.1%) and placenta praevia (1.7%).^{2,6} Placental insufficiency is considered when infarction of “about 25% placental mass” has occurred,⁷ though it is described as “>30% parenchymal loss” in another study.⁸ Pathology of placenta responsible for fetal death are chorioamnionitis, cord abnormalities, delayed villous maturation (DVM), fetal thrombotic vasculopathy (FTV), hemorrhagic endovascularitis (HEV), villitis of unknown aetiology (VUE).²

VASCULAR PATHOLOGY

Maternal vascular underperfusion – due to inadequate spiral artery remodeling or pathology of spiral artery (decidual vasculopathy). Commonly seen in case of PIH. The parenchymal pathology seen are placental hypoplasia, increased syncytial knots, villous agglutination, increased perivillous fibrin,

distal villous hypoplasia, abnormal villous maturity, infarction, retroplacental hematoma.⁹

Fetal thrombotic vasculopathy – Thrombosis in the umbilical cord, chorionic plate or stem villus vessels (recent or remote) and / or secondary degenerative pathology in the fetal vasculature by thrombotic obliterated vessels (e.g. avascular chorionic villi). Pathologies seen are hemorrhagic endovascularitis, intimal fibrin cushions, fibromuscular hypertrophy, villous stromal-vascular karyorrhexis.⁹

Massive perivillous fibrin deposition (MFD) on placenta has a deleterious effect on pregnancy. Severe cases (MFD extended over more than 50% of the placenta) are more often associated with fetal death and abnormal umbilical artery Doppler velocimetry in compare to moderate cases (MFD extended over between 25% and 50% of placenta).¹⁰

FETAL GROWTH RESTRICTION (FGR)

In FGR, fetal death has increased syncytial nuclear aggregates (SNAs) & trophoblast area and reduced proliferation & villous vascularity. Applying quantitative assessment in addition to qualitative assessment may help us to reduce the proportion of unexplained fetal death.¹¹ Low weight placenta and oligohydramnios are found in early fetal death.¹² Placental pathology due to maternal vascular underperfusion is the main contributor of fetal death (34-38)% which is most prominent during preterm period, in PIH, and declining after that. At term gestation, fetal death is mostly due to developmental pathology of placental parenchyma.⁹

In search of placental pathology responsible for fetal death and fetal growth abnormalities among 319 singleton stillbirths and 1119 singleton live births at ≥24 weeks, 25 suspected placentas were investigated. Out of these 25, 15 placentas were significantly associated with fetal death. Ten of the 15 were also associated with fetal growth abnormalities (single umbilical artery; velamentous insertion; terminal villous immaturity; retroplacental hematoma; parenchymal infarction; intraparenchymal thrombus; avascular villi; placental edema; placental weight; ratio birth weight/placental weight) while 5 of the 15 associated with fetal death were not associated with fetal growth abnormalities (acute chorioamnionitis of placental membranes; acute chorioamnionitis of chorionic plate; chorionic plate vascular degenerative changes; perivillous, intervillous fibrin, fibrinoid deposition; fetal vascular thrombi in the chorionic plate).¹³ A diagnostic challenge sometimes encountered in cases with prior intrauterine fetal death, since degenerative changes post demise result

in a similar histomorphologic picture. The diffuse versus focal nature of the lesions may help in the distinction.¹⁴

LARGE FOR GESTATIONAL AGE

In case of large –for-gestational age (LGA) fetuses, the causes of fetal death are grouped as fetal (43.5%), placental (22.6%), and maternal (11.2%). Among placental causes abruption and infarct are most common and this is more common in diabetic mothers (33% vs 18% in the entire LGA group). Most fetal death in diabetic mothers occurs after 28 weeks.¹⁵

Regarding intrapartum fetal death, except in cases of intrauterine infection, placental vascular abnormalities are unlikely to be associated with intrapartum asphyxia leading to fetal death during labor.¹⁶

UNEXPLAINED FETAL DEATH

The risk of unexplained fetal death increases late in pregnancy – aging of the placenta may play a role. Aging causes oxidative damage to DNA, RNA, and lipids. There is a role for aldehyde oxidase 1 and G-protein-coupled estrogen receptor 1 in mediating placental aging that may contribute to stillbirth.¹⁷ In unexplained stillbirth, there is an association between elevated amniotic fluid chemokine ligand (CXCL)10 and chronic placental inflammatory lesions. An elevated amniotic fluid CXCL10 concentration (above the 95th centile) was present in 60% of the cases, and a receiver operating characteristics (ROC)-derived cut-off of 2.9 ng/mL had a sensitivity of 73% and a specificity of 75% in the identification of chronic placental inflammatory lesions.¹⁸

COMMON UNDERLYING PLACENTAL CAUSES¹⁹

- 1) **Preterm fetal death:** Global/partial maternal vascular malperfusion (accelerated maturation), global/partial fetal vascular malperfusion (umbilical cord accident), abruptio placenta
- 2) **Term fetal death:** Abruptio placenta, global/partial fetal vascular malperfusion (umbilical cord accident), fetomaternal hemorrhage, delayed villous maturation

MANAGEMENT IMPLICATIONS¹⁹

Knowledge of the placental pathology and their possible consequences will help the obstetricians to tackle the situation in better way. Some of the pathologies are due to the vascular malperfusion of the maternal aspect of the placenta whereas some are

due to the vascular malperfusion of the fetal aspect of the placenta.

- 1) **Severe global/partial maternal vascular malperfusion:**
Evaluation of maternal cardiovascular status, glucose tolerance test, thrombophilia, renal function; uterine artery Doppler, early third trimester placental ultrasonography
Treatment options - weight loss, aspirin therapy, early delivery in subsequent pregnancies
- 2) **Complete/segmental fetal vascular malperfusion**
Maternal thrombophilia workup, diabetes screening, platelet count

Placental examination alongwith fetal autopsy can bring more information regarding the cause –effect relationship of placenta in causing intrauterine fetal death. However fetal autopsy is less performed in many instances due to parental refusal.²⁰ Proper passionate counseling and public awareness programme may change the scenario and help in realizing the etio-pathology so as to research for more avenues for prevention fetal death.

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Review Article

MTP BEYOND 20 WEEKS: TIME FOR POLICY CHANGE

Ramprasad Dey,¹✉ Subhash Chandra Biswas²

ABSTRACT

Unsafe abortion is one of the most common cause of maternal mortality and morbidity. Illegal abortions are performed frequently in India with their disastrous results even today in spite of liberalization of the Medical Termination of Pregnancy Act, The Act does not permit termination of pregnancy beyond 20 weeks. This has been challenged by so many times. The Supreme court of India allowed medical termination of pregnancy after 20 weeks in many times. With the advancement of technology, foetal abnormalities are diagnosed more precisely where termination may be indicated due to lethal anomaly even after 20 weeks. After years of legal advocacy, the Government of India has proposed amendments in MTP Act that would extend the legal time limit for abortion. Termination of pregnancy can be performed surgically before 15 weeks of pregnancy. After this gestational age, medical termination is performed by medical methods with mifepristone followed misoprostol or gemeprost. Although risks of medical termination increase with gestational age, result of the MTP is likely to be beneficial where it is truly indicated

Key words: Medical Termination of Pregnancy, Unsafe abortion, Fetal anomaly

“No woman can call herself free until she can choose consciously whether she will or will not be a mother”.

—Margaret Sanger

INTRODUCTION

Unsafe abortion is one of the most common cause of maternal mortality and morbidity. It is estimated that 80 million abortions take place worldwide and half of them are performed illegally mostly in developing countries with grave consequences. Highest mortality is related to unsafe abortion in countries where abortion is not legalised. Today only 8% of the world's population lives in countries where the law prevents abortion. Although the majority of countries have very restricted abortion laws, 41% of women live in countries where abortion is available on request of women.

THE MEDICAL TERMINATION OF PREGNANCY ACT, 1971

In the year 1969 Medical termination of pregnancy bill was introduced in Rajya Sabha and Lok Sabha as per recommendation of Shantilal Shah Committee (1964).¹ 10th August 1971 was a historic day, a path breaking legislation was enacted by Parliament called the Medical Termination of Pregnancy Act. Medical Termination of Pregnancy Act, 1971 (MTP Act) was implemented from April 1972. The MTP Act, 1971 preamble states “an Act to provide for the termination of certain pregnancies by registered medical practitioners and for matters connected therewith or incidental thereto”. The preamble is very clear in stating that termination of pregnancy would be permitted in certain cases. The cases in which the termination is permitted are elaborated in

1. (✉) Dept. Obstetrics & Gynaecology, Chittaranjan Seva Sadan, College of Obstetrics, Gynaecology & Child Health, 37 S P Mukherjee Road, PO – Kalighat, Kolkata - 700026. Email: drprpdey@gmail.com
2. Dept. Obstetrics & Gynaecology, Institute of Post Graduate Medical Education & Research, Kolkata

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the Act itself. Grounds for termination of pregnancy are therapeutics, eugenics, humanitarian and socio-economic considerations. The Act does not permit termination of pregnancy beyond 20 weeks.

UNSAFE ABORTION-INDIAN SCENARIO

Illegal abortions are performed frequently in India with their disastrous results even today in spite of liberalization of the Medical Termination of Pregnancy Act.² The term “unsafe abortion” proposed by the World Health Organization (WHO) lately has been accepted by most other international health institutions. Unsafe abortion means “abortion not provided through approved facilities and/or persons”. Unsafe abortions are performed 15-20 times more often than safe legal abortions in India till now.²

It is estimated by the WHO (1994) that in the Indian subcontinent 15-24 unsafe abortions take place per 1000 women aged 15-49 years and 70-89 women per 100,000 live births die from unsafe abortion, the risk of death is 1 in 250 procedures.

TECHNOLOGICAL AND OTHER DEVELOPMENTS IN THE DIAGNOSIS OF FETAL ABNORMALITIES

Technical improvements in ultrasound equipment continue to be made – recently, 3D & 4D ultrasound technology has been introduced for diagnosis. Foetal Echocardiography detects cardiac anomaly around 22-24 weeks of gestation. MRI is an adjunct to ultrasound in diagnosing and evaluating structural abnormalities, particularly those involving the central nervous system. Although most of the anomalies can be detected before 20 weeks but patients seek medical advice beyond 20 weeks where termination may be indicated due to lethal anomaly. Amniocentesis, chorionic villous sampling and foetal blood sampling, noninvasive techniques (NIPT) remain standard methods for the diagnosis of aneuploidy.³ *In utero* treatment of some structural abnormalities has been practised for a number of years but such interventions are not available everywhere.

TERMINATION OF PREGNANCY FOR FETAL ABNORMALITY

UK scenario: When a fetal abnormality has been detected, the pregnancy can be terminated before 24 weeks of gestation under Ground 1(1)(a) of the Abortion Act but after 24 weeks of gestation it can only be Carried out if there is a substantial risk that the child if born would be seriously handicapped.^{4,5} Though there is no legal definition of of substantial risk and serious handicap.

Indian Scenario: As per Medical Termination of Pregnancy Act, 1971, pregnancy can be terminated i.e. up to twenty weeks of gestation. The Act does not permit termination of pregnancy beyond 20 weeks. This has been challenged by so many times. For years, the National Commission for Women, FOGSI, activists and prominent doctors have advocated for amendments to the MTP Act that would ensure protections of women’s mental and physical health throughout their pregnancies. After years of legal advocacy, the Government of India has proposed amendments in Medical Termination of Pregnancy Act (MTP Act) on 29 October 2014 that would extend the legal time limit for abortion.⁶ The amendments expand access to abortion and to extend the upper time limit on abortion to 24 weeks and excluding time limits all together where doctors have detected substantial foetal abnormalities.

Recently on 23rd June 2017 a petition file on Supreme court, this petition challenges the constitutional validity of section 3(2)(b) of the MTP Act 1972 restricted to the ceiling of 20 weeks therein. This petition argued that the 20 weeks stipulation to avail of abortion services under section 3(2)(b) may have been reasonable when the section was enacted in 1971 but has ceased to be reasonable today where technology has advanced and it is perfectly safe for a woman to even upto 24 weeks and thereafter. The ceiling of 20 weeks is therefore arbitrary, harsh, discriminatory and violative of article 14 (right to equality) & 21 (fundamental rights of life) of the constitution of India. On this basis, the Supreme Court allowed medical termination of pregnancy of a woman of 26 weeks gestation which was performed successfully without complication. Earlier this year, Apex Court allowed medical termination to a 24 weeks pregnant woman in Maharastra.

METHODS OF TERMINATION OF PREGNANCY IN LATE 2ND TRIMESTER

Termination of pregnancy can be performed surgically before 15 weeks of pregnancy, when uterine evacuation can usually be achieved by vacuum aspiration with an appropriate-sized curette after cervical preparation with misoprostol or gemeprost.⁷ After this gestational age fetal size precludes complete aspiration, dilatation and evacuation (D&E) becomes necessary. Medical termination can also be performed by mifepristone (200 mg) followed 36–48 hours later by either misoprostol or gemeprost (RCOG 2010).⁷ Risks of medical termination increase with gestational age. Complication rates (haemorrhage, uterine perforation, sepsis) increase from 5/1000 medical procedures at 10–12 weeks to 16/1000 at 20 weeks of gestation and beyond.⁷

Medical and surgical methods have similar outcomes. Wherever possible, women should be offered the choice of method. Medical termination offers the opportunity for pathological examination of an intact foetus. Live birth following medical termination of pregnancy before 21+6 weeks of gestation is very uncommon. Nevertheless, women and their partners should be counselled about this unlikely possibility and staff should be trained to deal with this eventuality. Instances of recorded live birth and survival increase as gestation at birth extends from 22 weeks.^{7,8} As per RCOG guidance, feticide should be routinely offered from 21+6 weeks of gestation.⁷

CONCLUSION

Today, MTP is legally available in most countries of the World. Most studies report psychologically favourable outcomes following MTP in the majority of women. With the advancement of technology, lethal foetal anomaly are diagnosed more precisely. Moreover with the availability of wonder drugs like mifepristone & misoprostol, MTP can be safely conducted beyond 20 weeks. Result of the MTP is likely to be beneficial particularly when the pregnancy is a result of rape, in an unmarried woman or with lethal anomaly irrespective of gestational age.

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Review Article

PHARMACOTHERAPY OF HYPERTENSION IN PREGNANCY

Keshab Mukhopadhyay,¹ Kishore Mazumdar,¹ Chanchal Kumar Dalai¹✉

ABSTRACT

Hypertension is a common disease in general population and among pregnant women leading to rise in morbidity and mortality. Hypertension among pregnant women even causes mortality of foetus. Therefore adequate treatment should be started in time to control it. Though a big list of antihypertensive drugs are there, the selection of antihypertensive in pregnancy is important, as because some may dampen the labor process, some may have teratogenic effect on foetus. At times quick lowering of BP is required, and at times drugs are prescribed during whole pregnancy period particularly who are known hypertensive and who are gestational hypertensives. Many molecules are in pipeline e.g. Heme oxygenase 1, G protein-coupled receptor (GPCR) targets, Aminopeptidase etc. and they are showing good result.

Key words: complications, drugs, eclampsia, hypertension, pregnancy.

Hypertension:¹ Sustained increase in blood pressure >140/90 mm Hg is defined as hypertension. Hypertension is a major risk factor for stroke, myocardial infarction, cardiac failure, renal insufficiency, dissecting aneurysm of aorta, peripheral arterial diseases.

Epidemiology: This is the most common cardiovascular disease and its prevalence increases with age. In United States², there is a 65.4% prevalence of hypertension in people between ages of 60-69 years which further increases with age. Diastolic blood pressure also increases with age until approximately 55 years of age, after which it tends to decrease. Systolic hypertension tends to increase after 60 years further while diastolic blood pressure may decrease because of decreased compliance of blood vessels with aging and atherosclerosis.

Whereas, in India, a study³ showed a prevalence of hypertension in India is 29.8%. About 33% urban

and 25% rural Indians are hypertensive. It means one third of urban population and one fourth of rural population are suffering from hypertension in India. Genetic and environmental factors may have an important role in hypertension prevalence. Obesity, weight gain, high dietary sodium chloride intake, alcohol consumption, stress, low physical activity may play important roles in hypertension.

Stages of hypertension²

	Systolic blood pressure	Diastolic blood pressure
Normal	<120 mmHg	and <80 mmHg
Pre-hypertension	120-139	or 80-89
Hypertension, stage 1	140-159	or 90-99
Hypertension, stage 2	≥160	or ≥100
Isolated Systolic Hypertension	≥140	And < 90

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1. Dept. Pharmacology, College of Medicine & JNM Hospital, WBUHS, Kalyani, Nadia, West Bengal, PIN - 741235.
✉Email: chanchal.dalai8@gmail.com

But very recently, blood pressure more than 130/80 mm of Hg is called as stage 1 hypertension and more than 140/90 mm of Hg is called as stage 2 hypertension.⁴

Hypertension also divided as primary hypertension also known as essential hypertension (~80-95% of all hypertensive patients) and secondary hypertension.

Primary hypertension is likely to be associated with environmental and genetic interaction.

Whereas secondary hypertension may be due to secondary causes like renal diseases (CKD, renal cysts *etc*), adrenal diseases (Primary Aldosteronism, Cushing's syndrome), preeclampsia, eclampsia, neurogenic, medications (high dose estrogens, adrenal steroids, MAO inhibitors, tricyclic antidepressants).

HYPERTENSION AND PREGNANCY⁵

During pregnancy blood pressure usually decreases in the latter half of first trimester to the mid half of second trimester due to decreased vascular resistance and start to increase in the third trimester till pre-pregnancy level.

In a cross sectional study⁶ carried out in 20 sub-centers under Community Health Center (CHC) Chiri, Block Lakhanmajra prevalence of hypertension in pregnancy was found to be 6.9%.

Hypertension in pregnancy may be chronic which she already has, before she got pregnant or may be induced by pregnancy (gestational hypertension, preeclampsia, eclampsia).

Preeclampsia: It includes presence of non dependant edema, hypertension and proteinuria in a pregnant woman which is generally nulliparous and these symptoms appears in the third trimester. Generalized arteriolar constriction being the patho-physiology causing decreased blood flow to the placenta leading to IUGR in the fetus and maternal complications like severe hypertension, seizure, stroke, oliguria, renal failure, pulmonary edema, DIC etc. Patient may develop HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets).⁷

Mild preeclampsia: (BP>140/90 or increase over pre-pregnancy BP of >30/15 with proteinuria >300mg/24hr) can be treated with induction of labor for term pregnancies. Antihypertensive medication like methyl-dopa, labetalol, hydralazine, nifedipine may be used.⁸

Severe preeclampsia: Magnesium sulfate for seizure prophylaxis and hydralazine for BP control can be used. The therapeutic level of magnesium will be between 4-7 mEq/L. If there is constant threat

of eclampsia, maternal interest should always be considered. If mother completed 37 weeks of gestation delivery should be considered. Corticosteroid is given if pregnancy is less than 34 weeks.⁸

Gestational hypertension: Blood pressure > 140/90 or systolic BP >30 of prepregnancy systolic BP or diastolic BP >15 of pre-pregnancy diastolic BP on two occasions 4-6 hours apart with 24 hour total urinary protein < 300mg.

Eclampsia: Generalized tonic clonic seizures occurring in a pre-eclampsia patient. Hypertension can be managed by hydralazine. Magnesium sulfate to be started for seizure management and to be continued continued for 24 hours after last seizure or delivery whichever is later.⁸

Chronic hypertension: It is defined as hypertension before conception, before 20 weeks of gestation or persisting more than 6 weeks postpartum. Patients with hypertension of 140/90 or less are managed expectantly. Above this level medications used are labetalol, nifedipine, methyldopa. If a woman is taking an antihypertensive medication before conception and her BP is well maintained, she can continue it during her pregnancy with exception of angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists. ACE inhibitors and ARBs are contraindicated in pregnancy sue to their association with adverse fetal effects.

Drugs used for severe hypertension in preeclampsia (SBP \geq 160 or DBP > 110)⁵

Hydralazine - 5mg IV or 10 mg IM \rightarrow repeat 5-10 mg at 20 min intervals as needed \rightarrow if no response after 20mg IV or 30 mg IM, consider another drug

Labetolol - 20 mg IV as bolus to start \rightarrow Further 40 mg 10 min later if needed \rightarrow further 80 mg every 10 min if needed for 2 doses \rightarrow maximum dose 220mg. switch to other drug if there is inadequate response.

If using nifedipine - 10mg PO to start \rightarrow repeat 10 mg in 30 min if needed \rightarrow do not use short acting calcium channel blockers.

Use sodium nitroprusside (rare cases) - Start with 0.25 μ g/kg/min to maximum dose of 5 μ g/kg/min \rightarrow fetal cyanide poisoning risk if used for > 4 hours.

Diazoxide – 30-50 mg IV bolus every 5-15 min

Commonly used antihypertensives during pregnancy

Methyldopa -It is a centrally acting α_2 adrenergic agonist. Methyldopa has long being used in pregnancy and doesn't appear to be teratogenic. According to FDA methyldopa is a class B drug. Dose: 0.5-3 gm/day orally in divided doses.

Clonidine - It is also a centrally acting α_2 adrenergic agonist and is a class C drug according to FDA. Dose: 0.1-0.6 mg/day in 2 divided doses (not commonly used)

Labetolol - It is a non selective β blocker and a vascular α_1 receptor blocker. Labetolol has shown equivalent efficacy and better tolerability compared to hydralazine. It is a class C drug according to FDA and has risk of fetal bradycardia and neonatal hypoglycemia. Dose: 200-1200 mg/day orally in 2-3 divided doses.

Beta blockers can be prescribed during pregnancy except atenolol. Atenolol is an FDA Class D drug. It is not recommended due to risk of IUGR and is not recommended if breast-feeding.⁹ Though another study recommend careful use of atenolol during breastfeeding because atenolol concentrations will be too low to be clinically relevant in majority of healthy, term infants. Premature infants and those with kidney disease require further study.¹⁰

Prazosin - It is a selective α_1 blocker. Prazosin has a useful role in chronic renal disease complicating pregnancy. It is associated with postural hypotension and palpitations. Dose: 0.5-5 mg tds

Calcium channel blockers - Nifedipine and verapamil doesn't appear to be teratogenic and frequently seen as 2nd line agents. According to FDA nifedipine and verapamil are Class C drugs. Commonly used calcium channel blockers may be avoided or withdrawn before parturition because it may delay labor and also may cause PPH in full term pregnancy. Nifedipine – 10-30 mg orally, Verapamil – 80 mg tds orally (not commonly used during pregnancy).

Diuretics - Diuretics are commonly prescribed in essential hypertension before conception and are used during pregnancy for treating hypertension and cardiac disease. Patients already on diuretics prior to pregnancy can continue during pregnancy. Hydrochlorothiazide, triamterene, and amiloride are not teratogenic according to a small number of case reports.¹¹ But diuretics are not part of the standard treatment for gestational hypertension and oedema. Use of diuretics is always limited. Methyldopa and prazosin can cause fluid retention, which can be prevented by using diuretics.¹¹ Furosemide may be used to manage heart or kidney failure.⁹

Drugs for prevention of preeclampsia

Aspirin - antiplatelet agent. Low dose aspirin (75mg orally daily) reduces the risk of preeclampsia by 17%, intrauterine fetal death or neonatal death by 14% and preterm delivery by 8%.¹² It should be stopped

once 34 weeks completed to avoid the possibility of premature closure of patent ductus arteriosus.

Calcium - calcium supplementation (1gm orally daily) may reduce the occurrence of preeclampsia, premature delivery etc.¹³ though the efficacy is doubtful.

Drugs in pipeline

Heme oxygenase 1 (HO-1) – In animal model HO-1 acts in 2 pathways, namely, normalization of angiogenic balance in the placenta, and reduction in oxidative stress. Both are potential pathway for treatment of preeclampsia.¹⁴

G protein-coupled receptor (GPCR) targets - GPCR-based therapies in preeclampsia, including calcitonin receptor-like receptor / receptor activity modifying protein 1 complexes, the angiotensin AT1, 2 and Mas receptors, and the relaxin receptor RXFP1 have good potential.¹⁵

Inhibitors of the enzyme poly ADP ribose polymerase (PARP) - PARP inhibitor, preventing the development of both endothelial dysfunction and hypertension have protective effect in preeclampsia in animal model.¹⁶

Angiogenesis - Placental cystathionine γ -lyase (CSE) expression is reduced in preeclampsia, resulting in reduction of plasma levels of the pro-angiogenic gaseous vasodilator, hydrogen sulfide (H₂S) and increment of sFlt-1. Targeting CSE/H₂S activity may be a potential therapy.¹⁷

Marinobufagenin & resibufagenin - (60-70)% of preeclampsia patients showed increased serum and urinary marinobufagenin. This changes can be prevented by the administration of resibufagenin beginning early in pregnancy.¹⁸

Aminopeptidase - both aminopeptidase A and placental leucine aminopeptidase could be potentially safe and effective drugs for patients and their babies in the treatment of preeclampsia and preterm labor.¹⁹ The changes of the balance between fetal angiotensin II (A-II) and vasopressin (AVP) and A-II and AVP degrading enzymes, between aminopeptidase A (APA) and placental leucine aminopeptidase (P-LAP) - in the placenta and maternal blood due to fetal stress such as hypoxia - are the provable causes of preeclampsia or preterm labor. Estradiol benzoate (E2) and progesterone (P) from placenta can induce APA & P-LAP. Sex steroid treatment with increasing dose manner by gestational week may be a good treatment option for severe preeclampsia and preterm labor.²⁰

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Case Report

ACUTE FATTY LIVER OF PREGNANCY: A CASE REPORT OF AN UNCOMMON DISEASE

Abhijit Halder,¹ Mainak Nath¹✉

ABSTRACT

A 36 years old G5P2A2L1 presented with pain abdomen and impending scar rupture at 34 weeks of pregnancy. Emergency LUCS was done and post operatively diagnosed as acute fatty liver of pregnancy (AFLP). Post operative period was complicated by hepatic encephalopathy, dyselectrolytemia, coagulopathy. Although all the complications were corrected by 7 days, but sudden onset of severe thrombocytopenia due to unknown reason (?Sepsis) led to cerebro-vascular accident and finally a maternal mortality occurred. Some aspects of AFLP are still unknown that are to be investigated and managed respectively in future.

Key words: AFLP, coagulopathy, CVA, sepsis,

INTRODUCTION

Acute Fatty Liver in Pregnancy (AFLP) may be defined as acute liver failure with reduced hepatic metabolic capacity in the absence of other causes. The incidence of AFLP is reported to be 1 in 13000 pregnancies according to UKOSS (United Kingdom Obstetric Surveillance System). Fatty liver is more common in nulliparous with a male fetus and in 15% of cases there is a multifoetal gestation.¹ It usually occurs in late third trimester, rare cases have been reported as early as 23 and 26 weeks.² It is characterized by microvesicular steatosis in the liver.

The precise etiology of AFLP is not known. It is thought to be due to a mitochondrial dysfunction in the oxidation of fatty acids leading to an accumulation in hepatocytes. The infiltration of fatty acids causes acute liver insufficiency. Some, if not all, cases of maternal fatty liver are due to recessively inherited mitochondrial abnormalities of fatty acid oxidation. Hallmarks of the disease include jaundice, coagulopathy and encephalopathy.

Women who develop AFLP are more likely to have a heterozygous long-chain 3-hydroxyacyl-coenzyme A dehydrogenase (LCHAD) deficiency.^{1,2,3,4} LCHAD is found on the mitochondrial membrane and is involved in the beta oxidation of long-chain fatty acids. This gene mutation is recessive; therefore, outside of pregnancy under normal physiological conditions, women have normal fatty acid oxidation. However, if the fetus is homozygous for this mutation, it will be unable to oxidize fatty acids. These acids are passed to the mother, who, because of diminished enzyme function, cannot metabolize the additional fatty acids. Fatty liver is characterized by accumulation of microvesicular fat that literally 'crowds out' normal hepatocyte function. Symptoms and signs are vague and nonspecific such that making an early diagnosis is challenging. It usually develops over several days to weeks and includes malaise, anorexia, nausea and vomiting, epigastric pain and progressive jaundice. The presence of 5 among 14 **Swansea criteria** represents a validated method of supporting the diagnosis of AFLP. Though thrombocytopenia is not

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1. Dept. Obstetrics & Gynaecology, College of Medicine & JNM Hospital, WBUHS, Kalyani
✉ Email: mainak.nath.nbmc.mn@gmail.com

Table 1: Relevant Blood Reports done at the Hospital Central Laboratory Consecutively

DAY	HB	TC	PLATELET	Ur (mg/dl)	Cr (mg/dl)	BIL (mg/dl)	DIRECT BIL (mg/dl)	SGOT (U/L)	SGPT	ALP	Na+	K+	INR
DAY 1	11	15,000	2.1 LACS	56	2.3	10.68	9.52	120	45	644	152	3.5	2.6
DAY 2	11.2	19,400	1.98 LACS	79.7	1.6	13.12	10.8	70.4	36.8	663	137.62	3.29	3.1
DAY 3	12.7	25,000	2.0 LACS	92	1.2	15.5	8.5	51	RNA	203	182	2.8	2.8
DAY 4	12.9	25,000	1.5 LACS	110	0.7	14.4	7.7	ND	ND	204	High vaue	Low	2.0
DAY 5	ND	ND	ND	28	0.8	12.97	8.37	93	61	162	137	2.8	1.2
DAY 6	12.5	18,500	ND	107	0.8	8.1	6	89		184	143.36	2.94	ND
DAY 7	12.8	24,300	30,000	ND	ND	ND	ND	ND	ND	ND	ND	ND	1.2
DAY 8	ND	ND	60,000	23	0.8	4.8-M	3.67	49.7	37.4	396	133.0	3.31	1.3

• RNA- Reagent Not Available in lab, High and Low Value is reported in hospital if out of measuring range in available testing tools. ND – Not done

included in the Swansea criteria and is considered as a hallmark of HELLP syndrome, it is often found in AFLP, due to unknown reason.

Among various causes of pathological hepatic dysfunction, acute fatty liver of pregnancy (AFLP) is uncommon compared to pre-eclampsia and hemolytic anaemia, elevated liver enzymes and low platelets (HELLP) syndrome. Early diagnosis and prompt termination of pregnancy is necessary for better maternal and foetal outcomes.¹

We present a case report of a 36-year-old woman with AFLP complicated by sepsis and multiple organ dysfunction syndrome (MODS) requiring intensive care in spite of prompt termination of pregnancy and the fatal outcome, in spite of all of our efforts due to the various complications of AFLP with surprising thrombocytopenia and DIC.

CASE REPORT

A 36 year old woman, G5P2A2L1 at 34 weeks of gestation was admitted to the hospital with a history of lower abdominal pain and bleeding per vagina from previous night. Her first abortion occurred at 5 months, delivered vaginally. Second pregnancy was a case of IUFD at 7 months, delivered a boy baby vaginally followed by check evacuation. Third pregnancy was successful by caesarean delivery of a girl baby who is living. The next pregnancy got aborted at 3-4 months.

This time she presented only with severe lower abdominal pain. She was oriented to person, place, and time. She had icterus, with no pedal oedema and non-hypertensive. No foetal heart sound on auscultation. Bedside USG proved it to be a case of IUFD and increased echogenicity of maternal liver. As she had severe scar tenderness at admission decision of immediate caesarean section was taken with the suspicion of impending rupture of previous caesarean

scar. Bedside clotting test done and caesarean section was performed with delivery of a stillborn boy baby. It was found to be a case of impending rupture of previous scar during CS. She was transfused 4 units of FFP before operation and 2 units packed red cells transfused during operation. Her blood loss was 600 ml (approx.). Post operatively another 4 units of FFP was transfused. Patient was monitored at HDU and vitals were stable for 12 hours following delivery.

The blood reports on admission (Day 1) were Hb - 11g/ dl, TLC - 15,000/cm³, and platelet count - 210000/cu mm. Liver function tests showed aspartate aminotransferase 120 U/l, alanine aminotransferase 45 U/l, total bilirubin 10.68 mg/dl, direct bilirubin 9.52 mg/dl, alkaline phosphatase 644 U/l, total protein 6g/dl, and albumin 2.6 g/dl. Biochemical tests revealed blood urea 56 mg/dl, serum creatinine 2.3 mg/dl, serum glucose 80 mg/dl, Na⁺ 152 mmol/L, K⁺ 3.5 mmol/L, INR 2.6.

On 2nd postoperative day (Day 2) she suddenly developed restlessness and abnormal behaviour. Hepatic encephalopathy suspected and transferred to ICU though ventilator support was not needed. prothrombin time raised to 28 seconds with international normalized ratio (INR) of 3.1. Urine analysis showed mild proteinuria. All hepatitis profiles (hepatitis A, B, C, E) were negative. A presumptive diagnosis of AFLP with Hepatic Encephalopathy was made.

Twelve hours following admission to ICU, she became markedly tachycardic and tachypnoeic. USG whole abdomen showed increased echogenicity of liver, mild ascites and no gall bladder pathology. Arterial blood gas sample showed pH 7.520, PCO₂ 41.1mmHg, PO₂ 110 mm Hg, bicarbonate 35.0 mEq/L, and standard base deficit of 11.6 mEq/L. Her renal failure was corrected by volume replacement. It normalized in 2 days. Dialysis was not needed.

FFP of total 20 units over 6 days was transfused to correct coagulopathy. Although her renal failure improved, her serum bilirubin, sodium and potassium level was very much resistant to be corrected. Her bilirubin level started to decrease from day 6. During this period, she also received 5 units of packed red blood cells (PRBC) and was put on broad spectrum antibiotics. On 6th postoperative day INR was 1.2. She was making a gradual recovery even she didn't need any oxygen support to maintain normal SpO₂. Hepatic encephalopathy was corrected. She became well oriented with time, place and person. And we hoped her complete recovery in few days.

On 7th postoperative day suddenly she became drowsy again and on clinical examination she was found to have Cerebro Vascular Accident (CVA). Immediate CT scan was done and it was proved to be a case of left sided hemorrhagic CVA. Platelet count was surprisingly found to be 30,000 though INR was 1.2. Her leucocyte count also increased from 18500/cm³ to 24300/cm³. Platelet was transfused but it was too late to save the patient with a big size cerebral hematoma with ventricular extension. The patient died on 9th post-operative day due to CVA making all of us disappointed. (Table 1)

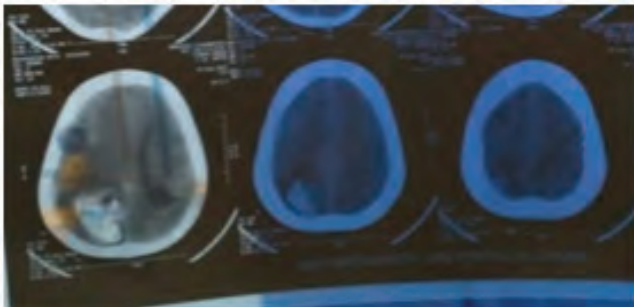


Photo 1 - Left sided hemorrhagic CVA

DISCUSSION

At presentation the bad obstetric history of our patient raised the suspicion of any genetic causes for liver dysfunction of the patient. She may be heterozygous carrier of LCHAD deficiency as she had history of one third trimester and one second trimester pregnancy losses of male fetuses. One living female child may be due to the genetic predisposition of AFLP. But this needs genetic testing which is not available in our hospital.

In our case, the clinical features of severe liver dysfunction appeared at the gestational age of 34 weeks. The symptoms initially mimicked those of acute viral hepatitis but clinical and laboratory evidence of severe coagulopathy, modest elevation of serum transaminase and bilirubin levels, hypoglycemia, an elevated ammonia value, and a low albumin level favoured the diagnosis of AFLP over

HELLP syndrome. The liver biopsy is diagnostic but is not always feasible especially in patients with severe coagulopathy⁸ and it seldom influences acute management.

The definitive management of AFLP is rapid delivery of the foetus and supportive care. Usually jaundice, liver dysfunction, and DIC may progress for one to two days after delivery but will then improve.⁹ Before 1980, both the maternal and foetal mortality rates were about 85% and major causes were cerebral oedema, gastrointestinal haemorrhage, renal failure, coagulopathy, and sepsis. Mortality has been reduced to less than 10% at present because of better recognition and appropriate management.

In our case, the obstetric history of the patient is very much suggestive of AFLP as she had jaundice in pregnancy, in both the cases of 2nd trimester pregnancy losses with delivery of male fetuses, so the patient may have been heterozygous carrier of LCHAD deficiency. The patient went to the phase of encephalopathy even after termination of pregnancy. Surprisingly the bilirubin level was too high but transaminase levels were even lower than normal. Probably it may be due to extensive hepatocyte damage leading to underproduction of liver enzymes. Our patient presented rather late to us due to poor antenatal visit to hospital. Although we performed an early caesarean section, we were unable to interrupt the progression of the disease and her condition continued to deteriorate even after delivery.

In conclusion, AFLP is an uncommon, life-threatening complication of third trimester with variable presentation. While the natural history of the disease is improvement within 24–48 hours of delivery, it is recommended that patients who are critically ill at the time of presentation, who develop complications, or who continue to deteriorate despite emergency delivery, should be managed in the intensive care unit. Daily clinical assessment along with pathology and biochemistry reports are mandatory for detecting any abnormality as AFLP may turn not only to hepatic failure but associated coagulopathy even if corrected by FFP transfusion may not stop the underlying DIC. In present case sudden fall of platelet count from 2 lacs/cm³ to 30,000/cm³ may be due to underlying DIC that may have been provoked by sepsis. Though we suspected the case to have underlying DIC, it could not be substantiated by the relevant investigations like FDP, D-dimer and Fibrinogen levels (as FDP, D-dimer test facilities are not available in our hospital). Sudden fall of platelet count with increase in leucocyte count suggests that the new onset DIC may be provoked by

septicemia. Hepatorenal failure, Dyselectrolytemia, metabolic abnormality, DIC, CVA in a same patient proves that AFLP is very much challenging entity to deal with. It indicates that further case reports and researches are needed to gather more information regarding the spectrum of the disease and its all possible complications. In our case sudden fall of platelet count if would have been detected earlier, the CVA could have been avoided and the patient may have been saved.

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Video Presentation

OASIS 3B REPAIR

Manidip Pal,¹ Srijoni Chowdhury,¹ Joydip Neogi¹✉

Any breach in the continuity of the perineum is known as perineal injury / tear.

Classification of perineal injury –

OASIS classification (Obstetric Anal Sphincter Injuries)

First degree - Injury to perineal skin only.

Second degree - Injury to perineum involving perineal muscles but not involving the anal sphincter.

Third degree - Injury to perineum involving the anal sphincter complex:

3a: Less than 50% of EAS (External anal sphincter) thickness torn.

3b: More than 50% of EAS thickness torn.

3c: Both EAS and IAS (Internal anal sphincter) torn.

Fourth degree - Injury to perineum involving the anal sphincter complex (EAS and IAS) and anal epithelium

In case of doubt regarding grade of third degree injury, assign higher grade.

Procedure - Third degree perineal injury repair

- Routine aseptic & antiseptic precaution. Thorough irrigation of the perineum with normal saline to remove any fecal material.
- An inverted 'U' shaped incision is made at the junction of posterior vaginal mucosa and anal skin. Lower limbs of 'U' extend upto the torn ends of external anal sphincter.
- A midline incision is made at the posterior

vaginal mucosa starting from the centre of the 'U' incision.

- Posterior vaginal mucosa is separated from the underlying structures and reflected laterally.
- Repair of the sphincters is done. Sphincter repair is done with '2-0' polyglactin suture.
- The internal anal sphincter is identified (The IAS (smooth muscle), overlaps and lies superior to the EAS (skeletal muscle), is continuous with the smooth muscle of the colon. The anal sphincter complex extends for a distance of 3-4 cm). Few fibres are torn which are approximated.
- Next bilaterally torn ends of EAS are hold with Babcock's forceps. EAS repair can be done either by overlapping technique and end-to-end anastomosis technique. We did it by overlapping technique.
- The EAS is released from its surrounding structures. Free ends of left EAS are brought below the right EAS so as to overlap each other. Needle passed from right EAS end (upper) to left EAS end (lower) and come out. Again back from inferior surface of left EAS end to superior surface of right EAS end. Both ends are tied snugly. Be careful – don't strangulate the EAS. Then 2 more sutures are placed in same way and tied.
- Superficial transverse perineal muscles and bulbospongiosus are then approximated to strengthen the perineal body.
- Vaginal mucosa is then closed.
- Additional interrupted hemostatic suture applied
- Lastly the perineal skin is closed.

1. Dept. Obstetrics & Gynaecology, College of Medicine & JNM Hospital, WBUHS, Kalyani, nadia, West Bengal.
PIN 741235
✉ Email: neogi.joydip@gmail.com

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EXTERNAL ANAL SPHINCTER REPAIR

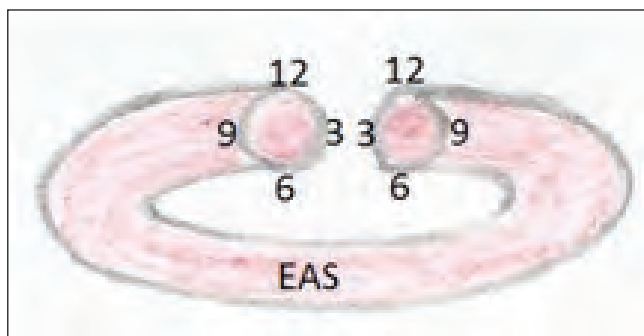


Fig. 1 - End-to-end anastomosis - respective numbers on either side will be attached with their counterparts. Start with 6 o'clock position. Both torn ends of EAS will get apposed to each other.

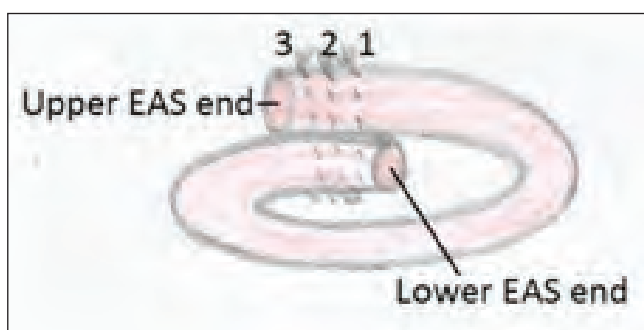


Fig. 2 - Overlapping technique - Freed ends of EAS will be made to overlap. Medial most suture is passed first (No. 1) from above downwards and come back to above again. Tie it snugly, but don't strangulate the EAS. Same way another 2 sutures are placed. Overlapping technique appears to yield better result in terms of post operative risk of developing fecal urgency and anal incontinence.¹

ACKNOWLEDGEMENT

We are very much thankful to Dr Mainak Nath for doing the video recording of the procedure.

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Video available at journal online version.
(www.iaog.in)

Book Review

“Urogynecology & Pelvic Reconstructive Surgery” is a textbook published by Jaypee Brothers Medical Publishers (P) Ltd, New Delhi and edited by Manidip Pal. The book has good front & back cover; clear, informative, colorful pictures, diagrams and photos; good quality paper with easy to read font size. ISBN 978-93-85891-98-4

“The book covers all aspects of urogynecology, ranging from anatomy and embryology to diagnosis and management of urinary incontinence and pelvic organ prolapsed. This book also includes chapters on fecal incontinence, treatment of congenital abnormalities and management of fistulas. There are many book on urogynecology is available. The characteristic of this book is that it focuses on the needs of patients in India to increase pelvic health in all women.

I am convinced this book will be well-received and considered useful to all those involved in making lives better for women in India.”

- Paul Riss, MD (Obs & Gyne), Master of Advanced Studies (Hospital Management) Professor, Division of Urogynecology, Dept. of Obstetrics & Gynecology Medical University Vienna, Vienna, Austria Ex Editor-in-Chief, International Urogynecology Journal e-mail: paul.riss@gmail.com

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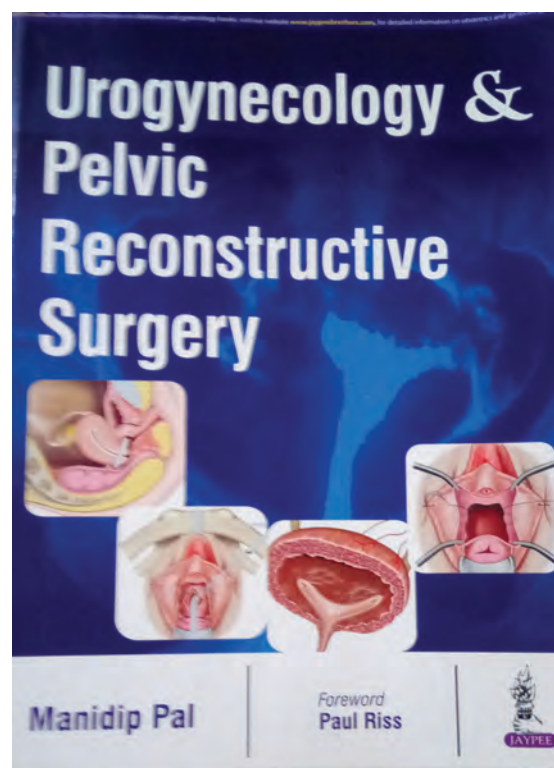
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- Narwadkar Mangesh
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431602
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“This book helps me to know the pelvic anatomy clearly and also about the examination procedure & operative procedure.”

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