AOGD BULLETIN

Volume 22 I January 2023 I Monthly Issue 9

Safeguarding women and their Doctors

Issue Theme:
Hypertension in Pregnancy-Optimising outcomes

AOGD SECRETARIAT

Department of Obstetrics and Gynecology
Maulana Azad Medical College & Lok Nayak Hospital
Jawahar Lal Nehru Marg, Delhi-110 002
Email: aogdmamc2022@gmail.com | www.aogd.org | M: 9717392924

Abbott

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

Women FIRST

The trusted progestogen completes **60 years**#

IF IT'S **ORALLY** EFFECTIVE, IT'S†

Duphaston®

Dydrogesterone Tablets IP 10 mg

BACKED BY **EVIDENCE**

We have supplemented our range with

Estrabet™
Estradiol (as Hemihydrate) Tablets USP 1mg/2mg
A Novel^ Safer+ Estrogen

Estrabet gel
Estradiol Transdermal Gel 0.06% w/w
A Novel^ Safer+ Estrogen

Solfe*
Sodium Feredetate, Folic Acid & Vitamin B_{12} Tablets
MADE FOR HER, CARES FOR HER

Mirza F, et al. Dydrogesterone use in early pregnancy. Gynecol Endocrinol. 2016;32(2):97-106. † Schindler AE. Progestational effects of dydrogesterone in vitro, in vivo and on human endometrium. Maturitas. 2009;65(1):S3–S11.
^ Novel-Estradiol hemihydrate first time in India. +Safer-As compared to conjugated equine estrogens. Smith NL et al Lower risk of cardiovascular events in postmenopausal women taking oral estradiol compared with oral conjugated equine estrogens. JAMA Intern MED. 2014; 174(1):25-31. * As Prescribing Information of Solfe, version 1; Dated: 25th July 2013
For full prescribing information, please contact: Abbott India Limited, Floor 16, Godrej BKC, Plot C-68, 'G' Block, Bandra-Kurla Complex, Near MCA Club, Bandra East, Mumbai-400 051. www.abbott.co.in

And strengthened our portfolio with

Novelon®
Desogestrel & Ethinylestradiol Tablets USP
Each uncoated tablet contains: Desogestrel BP: 0.15mg, Ethinylestradiol IP: 0.03mg

Femilon®
Desogestrel & Ethinylestradiol Tablets USP
Each uncoated tablet contains: Desogestrel BP: 0.15mg, Ethinylestradiol IP: 0.02mg

MSD INVENTING FOR LIFE

Organon (India) Pvt Ltd.,
Platina Building, 8th Floor, C-59, G-Block, Bandra Kurla Complex, Bandra (East), Mumbai 400051. Tel.no: 022-67898888
IN-XHB-00017 19/1/2021 to 14/1/2022
Please refer to full prescribing information before prescribing Novelon & Femilon
For reporting an Adverse Event visit contact us at www.msdindia.in

Abbott

Marketed and distributed by: **Abbott India Limited,**
Floor 16, Godrej BKC, Plot C-68, 'G' Block, Bandra-Kurla Complex, Near MCA Club, Bandra East, Mumbai - 400051
For Product Complaints/Adverse events or Queries please write to webmasterindia@abbott.com

IND2177598 16 Feb 2021

AOGD Office-Bearers 2022-23

Dr. Asmita M. Rathore
President

Dr. Y. M. Mala
Vice President

Dr. Deepti Goswami
Secretary

Dr. Renu Tanwar

Dr. Poonam Kashyap

Joint Secretaries

Dr. Shakun Tyagi

Dr. Chetna A. Sethi

Treasurer

Editorial Board

Dr. Madhavi M. Gupta
Editor

Dr. Nalini Bala Pandey

Dr. Chetna A. Sethi

Dr. Reena Rani

Co-Editors

Dr. Pushpa Mishra
Web Editor

Dr. Nidhi Garg
Co-Web Editor

Dr. Niharika Dhiman

Dr. Shalini Shakarwal

Public Relation & Media Management

Committees

Dr. Gauri Gandhi

Dr. Sangeeta Gupta

Dr. Krishna Agarwal

Dr. Latika Sahu

Dr. Preeti Singh

Scientific Committee

Dr. Sangeeta Bhasin

Dr. Rachna Sharma

Dr. Poonam Sachdeva

Dr. Bidhisha Singha

Dr. Shikha Sharma

CME and Sub Committee Co-ordinator

AOGD Office Bearers 2022-23

AOGD Secretariat
Room No OG 14, Department of Obstetrics & Gynaecology, MAMC & Lok Nayak Hospital, New Delhi – 110002.
Tel: 9717392924
Email:aogdmamc2022@gmail.com | www.aogd.org

AOGD Bulletin

Volume 22 • Monthly Issue 9 • January 2023

Publisher/Printer/Editor
Dr. Madhavi M Gupta on behalf of Association of Obstetricians & Gynaecologists of Delhi.

Concept, Design & Page Layout
Process & Spot C-112/3, Naraina Industrial Area, Phase-1, New Delhi 110028

Published from
Department of Obstetrics & Gynaecology
Maulana Azad Medical College & Hospital, New Delhi -110002

Editor
Dr. Madhavi M Gupta
Ph. No. 9968604351; Email: aogdeditor22@gmail.com

Foreword

This issue of AOGD Bulletin delves upon – Hypertensive disorders of pregnancy (HDP)and non technical skills in medico-legal safety.

Out of all HDP's, pre eclampsia (PE) is responsible for 10-15% of 5 million annual maternal deaths, besides being a major contributor to severe maternal morbidity. Universal screening for PE becomes more relevant after the publication of ASPRE Trial, which states that Aspirin started before 14 weeks of pregnancy causes a 62% reduction in PE<37 weeks and 78% in <32 weeks.Therefore an ideal screening test should identify women at risk by the end of 1st trimester. Over the years PE screening has moved from risk factor based approach to 2nd trimester uterine artery Doppler to 1st trimester uterine artery Doppler to angiogenic/anti angiogenic marker, their ratio, ophthalmic artery Doppler and various combined screening models. Article entitled "Predicting PE- what the future Holds" gives an in depth analysis of all the prediction modalities including the newly launched PIERS MODEL, and our own GESTOSIS SCORE , which is the most reliable, practical and cost effective model to follow.

Out of all bio markers, sFlt-1/PlGF ratio is the most promising one in 2nd and 3rd trimester with a NPV of 99.8% at a level of ≤38 for ruling out PE within 1 week in women with signs and symptoms of PE - The Prognosis Trial. A post-hoc analysis of this trial highlights that a ratio of ≤ 38 can rule out PE within 4 weeks at NPV of 94.3%. Based on available literature it is recommended that repeat risk stratification can be carried out in 2nd/ 3rd trimester by using this ratio alone or in combination with uterine artery Doppler. Article on sFlt-1/ PlGF ratio elaborates on its role.

Regarding chronic hypertension there is a sea change in management after the publication of CHIPS AND CHAP'S trial- which suggest that treating Mild hypertension and maintaining tight control reduces severity of hypertension, superimposed PE , related morbidities with NO INCREASE in incidence of low birth weight. Article by Dr. Kapur does a commendable job on management of hypertension in pregnancy.

Dr. Chitra's article on 'Nontechnical skills in medico-legal safety' is very informative, a must read for all clinicians. The author highlights that nearly 50% of surgical errors are due to non technical issues. It is time that non technical skills should be a part of teaching armamentarium right at the beginning of training. To conclude, articles in this bulletin will help us to form our own protocols to improve upon patient care.

Prof. Dr. Kanwal Gujral
Chairperson & HOD
Institute of Obstetrics & Gynaecology
Sir Ganga Ram Hospital

From the AOGD Office


Dr. Asmita M. Rathore


Dr. Y. M. Mala


Dr. Deepti Goswami

Dear AOGD members

Warm greetings to all on the occasion of the 74th Republic Day!

January 26th is the day when India declared itself a sovereign, democratic, and republic state with the adoption of the constitution and is a proud moment for all Indians. As we celebrate, let us also remember those who have fought and continue to fight for the rights and freedom of all citizens.

All India Congress of Obstetrics and Gynaecology was held at Kolkata from 4-8th January 2023 with many AOGD members actively participating in the Congress and winning awards. Heartiest congratulations to all-star AOGD achievers at AICOG 2023.

The present issue of the bulletin is on Hypertensive Disorders in Pregnancy (HDP). Hypertensive disorders in pregnancy are associated with severe maternal morbidity and mortality, suggesting that strategies to address rising maternal morbidity rates should include early recognition and management of hypertension. In this bulletin, various aspects of screening and prediction of this disorder in pregnancy have been covered. We hope it will be of use to all as none of us practicing obstetrics can escape a woman with hypertension.

The AOGD Risk Management Support group is functional for all AOGD members.

On the start of another year let's reaffirm our pledge to work for women's health.

Dr. Asmita M Rathore, President
Dr. Y M Mala, Vice President
Dr. Deepti Goswami, Secretary

AOGD Risk Management Support [ARMS] Group

One of the ways to ensure the stress-free work environment and optimal patient care is mutual support among professional colleagues. We propose to form an advisory group of senior AOGD members that can be contacted if one of us is caught in a complex clinical dilemma / dealing with aggressive clients or is apprehensive about how to document or effectively troubleshoot a potential problem. This group will provide the timely advice and will be led by-

Convener- **Dr. Vijay Zutshi** - 9818319110

Co convener- **Dr. Aruna Nigam** - 9868656051

We invite suggestions from all members regarding functioning of this cell which will guide us forming the SOPs. Any member interested in being part of Advisory group may contact the convener.

Pl mail to aogdmamc2022@gmail.com

From the Editor's Desk

Dr. Madhavi M. Gupta
Editor

Dr. Nalini Bala Pandey

Dr. Chetna A. Sethi

Dr. Reena Rani

Co-Editors

Hello Friends,

Warm Greetings in this cold weather !

We are happy to bring to you the first AOGD Bulletin for the year 2023.

This month the Game Changer section brings to you the PROGNOSIS Study and the CHAP Project as we cover Hypertensive Disorders in Pregnancy (HDP).

Hypertension in pregnancy accounts for serious maternal morbidity and mortality along with preterm birth and neonatal complications. Optimizing outcomes in HDP will improve the health of the mother. Hypertension being the second most important killer of mothers requires special attention in terms of screening, diagnosis and treatment. sFlt-1/PlGF Ratio has emerged as a evidence based tool for early prediction of Preeclampsia. All the nuances of the use of this ratio including use in predicting adverse outcomes have been covered. The management of mild chronic hypertension during pregnancy has undergone a significant change. The strategy of treating mild chronic hypertension during pregnancy with a blood pressure goal of less than 140/90 to lower the incidence of adverse maternal and perinatal outcomes have been discussed. Predicting preeclampsia is the way forward. The article touches all the aspects-screening, use of various markers along with maternal characteristics which are helpful in predicting this killer disease.

Risk Management under 'Safeguarding the Doctors' section is dedicated to Non Technical Skills in Medicolegal Safety. We have always laid stress on acquiring and polishing our technical skills but the present time calls for working on various cognitive and interpersonal skills alongside. The relevance of these skills can be well understood by the improvement in patient safety. The author walks us through these various skills and how to use them in our daily practice.

My heartfelt gratitude to all the authors for their efforts in putting together an interesting and informative read.

As always, we look forward to receiving your feedback to help us bring out a better version each time.

Yours in health

Dr. Madhavi M Gupta
Editor

GAME CHANGER:

PROGNOSIS (Prediction of Short-Term Out come in Pregnant Women with Suspected PreeclampsiaStudy) and Chronic Hypertension and Pregnancy (CHAP) project

Madhavi M Gupta*, Reena Rani**
*Director Professor, **Assistant-Professor, Department of Obstetrics & Gynaecology, MAMC & Lok Nayak Hospital, Delhi

Abstract of the research articles are available free at the journal websites and on Pubmed (http://www.ncbi.nlm.nih. gov/PubMed)

Preeclampsia, a heterogeneous, multisystem disorder, affecting 2 to 5% of pregnancies worldwide.[1,2] Preeclampsia is associated with high risks of iatrogenic preterm delivery, intrauterine growth restriction, placental abruption, and perinatal mortality, along with maternal morbidity and mortality.[3,4] Although the pathogenesis of preeclampsia is not completely understood, altered levels of angiogenic factors appear to play a role.[5]

There is a need for a reliable predictor of preeclampsia (particularly its absence) in the short term in women with suspected preeclampsia.

Predictive Value of the sFlt-1:PlGF Ratio in Women with Suspected Preeclampsia

Zeisler H, Llurba E, Chantraine F, Vatish M, Staff AC, Sennström M, Olovsson M, Brennecke SP, Stepan H, Allegranza D, Dilba P, Schoedl M, Hund M, Verlohren S.. N Engl J Med. 2016 Jan 7;374(1):13-22. doi: 10.1056/NEJMoa1414838.

PROGNOSIS (Prediction of Short-Term Outcome in Pregnant Women with Suspected Preeclampsia Study) was designed to investigate the value of using the sFlt-1:PlGF ratio for the prediction of the presence or absence of preeclampsia in the short term.

Background:

This study was undertaken to establish the predictive value of the ratio of soluble fms-like tyrosine kinase 1 (sFlt-1) to placental growth factor (PlGF) which is elevated in pregnant women before the clinical onset of preeclampsia.

Methods

PROGNOSIS was a prospective observational study conducted in 14 countries.

The study aimed to derive and validate a ratio of serum sFlt-1 to PlGF that would be predictive of the absence or presence of preeclampsia in the short term. The target population were women with singleton pregnancies in whom preeclampsia was suspected (24 weeks 0 days to 36 weeks 6 days of gestation).

Primary objectives were to assess whether low sFlt-1:PlGF ratios (at or below a derived cutoff) predict the absence of preeclampsia within 1 week after the first visit and whether high ratios (above the cutoff) predict the presence of preeclampsia within 4 weeks.

Result

In the development cohort (500 women), an sFlt-1:PlGF ratio cutoff of 38 was identified as having important predictive value. In a subsequent validation study among an additional 550 women, an sFlt-1:PlGF ratio of 38 or lower had a negative predictive value (i.e., no preeclampsia in the subsequent week) of 99.3% (95% confidence interval [CI], 97.9 to 99.9), with 80.0% sensitivity (95% CI, 51.9 to 95.7) and 78.3% specificity (95% CI, 74.6 to 81.7). The positive predictive value of an sFlt-1:PlGF ratio above 38 for a diagnosis of preeclampsia within 4 weeks was 36.7% (95% CI, 28.4 to 45.7), with 66.2% sensitivity (95% CI, 54.0 to 77.0) and 83.1% specificity (95% CI, 79.4 to 86.3).

Conclusion

The investigators concluded that a sFlt-1:PlGF ratio of 38 or lower can be used to predict the short-term absence of preeclampsia in women in whom the syndrome is suspected clinically.

The study was funded by Roche Diagnostics

Treatment for Mild Chronic Hypertension during Pregnancy

Tita AT, Szychowski JM, Boggess K, Dugoff L, Sibai B, Lawrence K, Hughes BL, Bell J, Aagaard K, Edwards RK, Gibson K, Haas DM, Plante L, Metz T, Casey B, Esplin S, Longo S, Hoffman M, Saade GR, Hoppe KK, Foroutan J, Tuuli M, Owens MY, Simhan HN, Frey H, Rosen T, Palatnik A, Baker S, August P, Reddy UM, Kinzler W, Su E, Krishna I, Nguyen N, Norton ME, Skupski D, El-Sayed YY, Ogunyemi D, Galis ZS, Harper L, Ambalavanan N, Geller NL, Oparil S, Cutter GR, Andrews WW; Chronic Hypertension and Pregnancy (CHAP) Trial Consortium. Treatment for Mild Chronic Hypertension during Pregnancy. N Engl J Med. 2022 May 12;386(19):1781-1792. doi: 10.1056/NEJMoa2201295. Epub 2022 Apr 2

Chronic hypertension in pregnancy is associated with three to five times the risk of preeclampsia, placental abruption, preterm birth or small-for gestational- age birth weight, or perinatal death.[6,7]

The condition is also associated with 5 to 10 times the risk of maternal death, heart failure, stroke, pulmonary edema, or acute kidney injury.[6,7]

Background

This project was undertaken to evaluate the benefits and safety of the treatment of mild chronic hypertension (blood pressure, <160/100 mm Hg) during pregnancy and generate data on whether a strategy of targeting a blood pressure of less than 140/90 mm Hg reduces the incidence of adverse pregnancy outcomes without compromising fetal growth.

The investigator-initiated Chronic Hypertension and Pregnancy (CHAP) project was a multicenter, pragmatic, open-label, randomized, controlled trial conducted at more than 70 recruiting sites in the United States.

Methods

Pregnant women with mild chronic hypertension and singleton fetuses at a gestational age of less than 23 weeks were assigned to receive antihypertensive medications recommended for use in pregnancy (active-treatment group) or to receive no such treatment unless severe hypertension (systolic pressure, ≥160 mm Hg; or diastolic pressure, ≥105 mm Hg) developed (control group).

The primary outcome was a composite of preeclampsia with severe features, medically indicated preterm birth at less than 35 weeks' gestation, placental abruption, or fetal or neonatal death. The safety outcome was small-for gestational-age birth weight below the 10th percentile for gestational age. **Secondary outcomes** included composites of serious neonatal or maternal complications, preeclampsia, and preterm birth.

Result

A total of 2408 women were enrolled in the trial. The **incidence of a primary-outcome event was lower in the active-treatment group than in the control group** (30.2% vs. 37.0%), for an adjusted risk ratio of 0.82 (95% confidence interval [CI], 0.74 to 0.92; P<0.001). The percentage of small-for-gestational-age birth weights below the 10th percentile was 11.2% in the active-treatment group and 10.4% in the control group (adjusted risk ratio, 1.04; 95% CI, 0.82 to 1.31; P = 0.76). The incidence of serious maternal complications was 2.1% and 2.8%, respectively (risk ratio, 0.75; 95% CI, 0.45 to 1.26), and the incidence of severe neonatal complications was 2.0% and 2.6% (risk ratio, 0.77; 95% CI, 0.45 to 1.30). The incidence of any preeclampsia in the two groups was 24.4% and 31.1%, respectively (risk ratio, 0.79; 95% CI, 0.69 to 0.89), and the incidence of preterm birth was 27.5% and 31.4% (risk ratio, 0.87; 95% CI, 0.77 to 0.99).

Conclusion

In pregnant women with mild chronic hypertension, a strategy of targeting a blood pressure of less than 140/90 mm Hg was associated with better pregnancy outcomes than a strategy of reserving treatment only for severe hypertension, with no increase in the risk of small-for-gestational-age birth weight.

(Funded by the National Heart, Lung, and Blood Institute; CHAP ClinicalTrials.gov number, NCT02299414.)

References

1. Ananth CV, Keyes KM, Wapner RJ. Pre-eclampsia rates

in the United States, 1980-2010: age-period-cohort analysis. BMJ 2013; 347: f6564.

2. World Health Organization. The World Health Report 2005: make every mother and child count. November 1, 2014 (http://www .who .int/ whr/ 2005/ en/).
3. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet 2008; 371: 75-84.
4. McClure JH, Cooper GM, Clutton- Brock TH. Saving mothers' lives: reviewing maternal deaths to make motherhood safer: 2006-8: a review. Br J Anaesth 2011; 107: 127-32.
5. Hod T, Cerdeira AS, Karumanchi SA. Molecular Mechanisms of Preeclampsia. Cold Spring Harb Perspect Med. 2015 Aug 20;5(10):a023473
6. Bateman BT, Bansil P, Hernandez-Diaz S, Mhyre JM, Callaghan WM, Kuklina EV. Prevalence, trends, and outcomes of chronic hypertension: a nationwide sample of delivery admissions. Am J Obstet Gynecol 2012; 206(2): 134.e1-8.
7. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins — Obstetrics. ACOG practice bulletin no. 203: chronic hypertension in pregnancy. Obstet Gynecol 2019; 133(1): e26-e50.

sFlt-1: PlGF Ratio in Preeclampsia

Neha Varun[1], Paridhi Gupta[2]
[1]Assistant Professor, [2]Senior Resident, Department of Obstetrics & Gynecology, AIIMS, Delhi

Introduction

Preeclampsia (PE) is a disorder specific to pregnancy, it is characterized by hypertension with or without proteinuria and it is associated with maternal organ dysfunction and uteroplacental insufficiency after 20 weeks period of gestation. It affects 2-8% of all pregnancies.[1] It is a multisystem disorder associated with significant maternal and fetal morbidity and mortality. It also represents a considerable burden of healthcare resources in both developing and developed countries. Early, accurate detection and diagnosis of disease is important not only to prevent complications but also to decrease unnecessary hospitalization, overdiagnosis and overtreatment of patients. World Health Organization (WHO) figures indicate that hypertension during pregnancy accounts for 16% of maternal deaths in industrialized countries[2] and it is almost up to 25% in developing countries[3] and these maternal deaths can be avoided via timely diagnosis and management.

Predictors of preeclampsia

There are four main categories

- Maternal demographic characteristics
- Mean arterial pressure
- Biochemical marker
- Ultrasound makers

Maternal demographic characteristics: Maternal age, body mass index (BMI), race, ethnicity, parity of patient, low socioeconomic status, history of preeclampsia, history of poor perinatal outcomes (Small for gestational age or preterm baby), large inter-conceptional period (>10 years), family history of preeclampsia, chronic hypertension, diabetes mellitus, autoimmune disorders like SLE, APLA, chronic renal disease, family history of preeclampsia and assisted reproduction.

Mean arterial pressure (MAP): It is calculated from systolic (SBP) and diastolic blood pressure (DBP) readings and is defined by DBP + (SBP-DBP)/3.

Biochemical markers: Definite pathogenesis of PE is unclear, but the imbalance between angiogenic factors like vascular endothelial growth factor (VEGF) or placental growth factor (PlGF) and anti-angiogenic factors like soluble fms-like tyrosine kinase 1 (sFlt-1) are well known to be related to the presentation of PE. In PE, circulating maternal serum levels of sFlt-1are increased, and PlGF levels are decreased.[4] An antagonist of PlGF and vascular endothelial growth factor, sFlt-1 causes vasoconstriction and endothelial damage that may lead to fetal growth restriction and preeclampsia.[5] This alteration begins before the onset of disease and stays during the course of the disease. In PE, sFlt-1 rises approximately 5 weeks prior to disease onset while the level of PlGF starts to decrease before sFlt-1 increases.[6] Hence, to improve the accuracy of diagnosis, various studies suggest that the ratio of sFlt-1/PlGF is a better predictor than measuring sFlt-1 or PlGF alone for the diagnosis of PE.[7]

Ultrasound marker: Uterine artery pulsatility index (PI) > 95th percentile at 11-13+6 weeks period of gestation has 60% sensitivity for early onset PE. Uterine artery notching at 22-24 weeks is also used for screening and it indicates maternal endothelial dysfunction.

There is a calculator available free of cost at https://fetalmedicine.org/research/assess/preeclampsia/first trimester to calculate PE risk in first trimester based on above mentioned variables.

sFlt-1: PlGF ratio in PE

sFlt-1 acts as an antagonist of PlGF and VEGF. It causes vasoconstriction and endothelial dysfunction which further leads to PE and fetal growth restriction.[5] These alterations are more pronounced in early-onset rather than late-onset disease and are associated with severity of the clinical disorder. Current definitions of PE are

poor in predicting PE-related adverse outcomes. A diagnosis of PE based on blood pressure and proteinuria has a positive predictive value of approximately 20% for predicting PE-related adverse outcomes.[9] Estimation of sFlt-1: PlGF ratio not only predicts onset of PE but also correlates with adverse maternal and perinatal outcomes.

In our practice, we diagnose PE mainly by measurement of BP and proteinuria which have poor predictive value in detecting adverse maternal and fetal outcomes. Due to this potential severity of adverse outcomes and unpredictable behavior of PE, women with suspected PE may need to be hospitalized for close observation and monitoring. However, some women with diagnosed PE may carry pregnancy to term without any adverse outcomes. The ability to rule out the likelihood of PE developing in at risk women through a negative predictive test would be an important advancement in the pregnancy care and would enable valuable health care resources to be directed towards the patients who need them.

Predictive Value of sFlt-1:PlGF Ratio in PE

Currently, there are no recommendations regarding the use of sFlt-1: PlGF ratio in predicting PE. However, numerous studies support its use in women with suspicion of PE to not only predict PE but also to estimate adverse perinatal and maternal outcomes.

The ***PROGNOSIS trial*** is a landmark trial in evaluating the importance of sFlt-1:PlGF ratio in short term prediction of PE and its associated adverse outcomes in women with suspicion of PE syndrome.[10] It was a global, prospective, multicenter, double blinded and non-interventional, observational study conducted in 14 countries from December 2010 till 2014 including around 1273 participants. It included women from 24 weeks to less than 37 weeks of gestation with only suspicion of preeclampsia. (Table 1)

This study aimed to derive and validate cutoffs for the sFlt-1/PlGF ratio, to rule out (for 1 week) or rule in (within 4 weeks) the occurrence of PE/ eclampsia/HELLP syndrome. (Table 2)

Table 1. Criteria which contribute to suspicion of clinical diagnosis of PE [10]

- New onset of increased BP
- Aggravation of pre-existing hypertension (HTN)
- New onset of protein in urine
- Aggravation of pre-existing proteinuria
- One or more other reason(s) for clinical suspicion of PE
- Preeclampsia-related symptoms:
  1. Epigastric pain
  2. Excessive edema/severe swelling, (face, hands, feet)
  3. Headache
  4. Visual disturbances
  5. Sudden weight gain (>1 kg/week in the third trimester)
- PE-related findings:
  1. Low platelets
  2. Elevated liver transaminases
  3. (Suspected) intrauterine growth restriction
  4. Uterine perfusion detected by Doppler sonography with mean PI >95th percentile in the second trimester and/or bilateral uterine artery notching

Table 2: Validation of a Cutoff Point of 38 for sFlt-1:PlGF Ratio in Predicting PE

PE	Result (Validation cohort) %
Within 1 week	
NPV (Negative predictive value)	99.3
Sensitivity	80.0
specificity	78.3
Within 4 weeks	
PPV (Positive predictive value)	36.7
Sensitivity	66.2
Specificity	83.1

In another trial, conducted by Bian X et al (2019)[11] also known as ***PROGNOSIS Asia***,

Asian counterpart of PROGNOSIS Trial. It was a prospective, multicenter study conducted at 25 cities of Asia (China, Japan, Singapore, South Korea, Hongkong, Thailand) from 2014- 2016. A Total of 764 women were included from 20 weeks to 36+6 weeks POG. They have concluded that the sFlt-1: PlGF ratio ≤ 38 is associated with high NPV of 98.6% to rule out preeclampsia within 1 week. (Table 3)

Table 3: NPV, PPV, Sensitivity and Specificity of sFlt-1/PlGF ratio to predict PE

sFlt-1/PlGF Ratio ≤ 38/>38	NPV, %	PPV, %	Sensitivity, %	Specificity, %
Within 1 wk	98.6	17.9	76.5	82.1
Within 4 wks	95.1	30.3	62.0	83.9

Cerdeira AS et al in 2019, [12] conducted an ***INSPIRE Trial*** at the John Radcliffe Hospital in Oxford, United Kingdom from 2015 to 2017 including 370 women. It was an interventional, parallel-group, randomized clinical trial that evaluated the use of sFlt-1/PlGF ratio in women presenting with suspected PE. They have showed that the low ratio of sFlt-1:PlGF (<38) was found to have 100% NPV to rule out PE within 7 days.

Soundararajan R et al conducted the ***ROBUST study*** [13] in 2020, it was a prospective pilot study conducted in Bengaluru including 50 women. They have showed that the incidence of PE with severe features was found to be significantly high in patients with high sFlt-1:PlGF ratio as compared to those with low ratio (90 % vs 8.00%, p < 0.0001) and also observed higher maternal complication rate and delivery at earlier gestation in women with high ratio.

Caillon H. et al (2018),[14] conducted study in the Nantes University Hospital, France from January to May 2014 and included 67 high-risk pregnant women from 20 week to 37 weeks POG. They have observed that the sFlt-1/PlGF ratio < 38 has 100% NPV, positive predictive value was 21% at one week and 18% at four weeks.

Diagnosis

Raised BP and Proteinuria are diagnostic criteria for PE, but the clinical presentation is variable, and the diagnosis of PE is very difficult. The sFlt-1: PlGF ratio has been approved as a diagnostic aid for preeclampsia in conjunction with other clinical findings.[15]

Discovery of circulating angiogenic factors in the pathogenesis of PE has been a major advance for both diagnosis and prognosis. The sFlt-1 and PlGF can be measured in plasma and serum and are usually reported as a ratio, which specifically relates to the onset and severity of PE. The sFlt-1/PlGF ratio has a very high NPV in ruling out the development of PE within 7 days among women with high risk of developing PE. Currently, there is no clear consensus on the practical use of angiogenic biomarkers in the detection and management of PE in routine clinical practice. While major international clinical guidelines exist, they do not define which specific parameters suggests patient admission, or outpatient evaluation of suspected PE, and most clinicians follow their own local practices.

A consensus report has been developed in 2022 following a meeting of international experts and aims to guide clinicians in the management of pregnant women at risk of PE using the sFlt-1/PlGF ratio test.[15]This report has given different risk categories of PE on the basis of sFlT-1:PlGF ratio. Which is as follows:

1. **sFlt-1/PlGF < 38 (low risk):** This value rules out PE within the next 1 week at least, irrespective of gestational age. Further management is according to the clinician's discretion. Monthly assessment by ratio could be carried out after 20 weeks of POG if clinically appropriate, based on individual case circumstance. In the PROGNOSIS trial [13], 2% of women with sFlt-1/PlGF ratio of ≤38 developed preeclampsia.
2. **sFlt-1/PlGF ratio 38–85 (early-onset PE) or 38–110 (late-onset PE):** These women are at intermediate risk and require enhanced monitoring, with a repeat test after 1–2 weeks or immediately if the clinical situation worsens. It provides extra information as to which women are at moderate risk or at high risk of developing PE within 4 weeks.
3. **sFlt-1/PlGF ratio > 85 (early-onset PE) or > 110 (late-onset PE).** These women are at high risk of developing PE. Women in this group are most likely to develop or will develop PE and require intensive monitoring.

Highly elevated sFlt-1/PlGF ratios (> 655 at <34 + 0 weeks; > 201 at ≥ 34 + 0 weeks) have been observed to deliver early, mostly within 48 hours. Close surveillance and if < 34 weeks prompt initiation of antenatal corticoids to accelerate fetal lung maturation are mandatory. Repeat measurement at 2-4 days can be done depending upon severity of disease and according to clinician's discretion. A repeat measurement of the sFlt-1/PlGF ratio may help to distinguish whether a patient is at moderate, high, or at very high risk of developing a future complication. Currently, there are no recommendations regarding the time intervals for a follow-up test. Conversely, women with abnormal sFlt-1/PlGF ratios should be considered as having suspected PE and to be managed accordingly.

Clinical Application

PE is a disorder which is very difficult to diagnose. There is no single parameter available which suggests that whether the patients who are suspected PE needs admission or can be followed up on out-patient basis. A better guidance is needed on risk stratification among women with suspected PE, as well as among women at high risk for PE. Prediction of adverse outcomes in women, after the clinical diagnosis of PE, is also important. The sFlT-1:PlGF ratio is a reliable factor to not only predict the incidence of PE but also to detect maternal and fetal complications. Also, patients with a very high ratio have shortened time to delivery. The rate of change of the sFlt-1/PlGF ratio (or delta) indicates severity of disease and is an important marker for the progression of disease.

The use of this ratio may enable better patient management for women with suspected PE, as clinicians can identify low and high-risk patients and ensure that they are managed appropriately. This may help to reduce unnecessary hospitalization, extended monitoring and thereby cost saving for the healthcare system.

In the study by Hodel M et al (2019), [16] the economic impact of using sFlt-1: PlGF ratio in addition to standard of care for women with suspected preeclampsia in switzerland was estimated among 6084 pregnant women. They observed annual savings of €2,105,064 (Rs. 93,115,83) (€346/patient) after implementation of sFlt-1: PlGF ratio mainly because of reduction in unnecessary hospitalization.

Frusca et al (2017) [17] also estimated the financial impact of using sFlt-1:PlGF in women with suspicion of preeclampsia versus standard care, the healthcare cost associated with standard care was €2384 (Rs. 2,11,288.50) as compared to €1714 (Rs. 1,51,907) when using sFlt-1/PlGF ratio test.

Various large scale and robust studies have proved applications of sFlt-1:PlGF ratio in the identification and management of PE but its clinical utility still needs to be established.

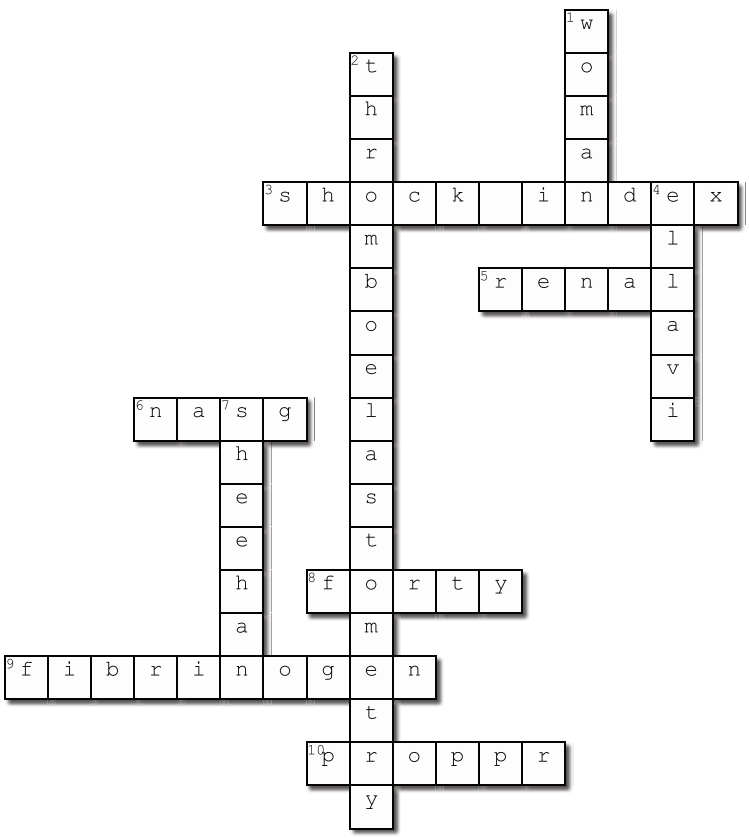
References

1. Abalos E, Cuesta C, Carroli G, Qureshi Z, Widmer M, Vogel JP, Souza JP; WHO Multicountry Survey on Maternal and Newborn Health Research Network. Pre-eclampsia, eclampsia and adverse maternal and peri- natal outcomes: a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health. BJOG. 2014;121(suppl 1):14–24.
2. Khan KS, Wojdyla D, Say L, Gulmezoglu AM, Van Look PF: WHO analysis of causes of maternal death: a systematic review. Lancet 2006, 367:1066–1074
3. Polsani S, Phipps E, Jim B: Emerging new biomarkers of preeclampsia. Adv Chronic Kidney Dis 2013, 20:271–279.
4. Levine RJ, Lam C, Qian C, et al. Soluble endoglin and other circulating antiangiogenic factors in preeclampsia. N Engl J Med 2006;355:992-1005.
5. Lu FX, Longo M, Tamayo E, et al. The effect of over-expression of sFlt-1 on blood pressure and the occurrence of other manifestations of preeclampsia in unrestrained conscious pregnant mice. Am J Obstet Gynecol 2007;196:396.e1-396.e7
6. Levine RJ, Maynard SE, Qian C, Lim K-H, England LJ, Yu KF, et al. Circulating angiogenic factors and the risk of preeclampsia. N Engl J Med. 2004;350(7):672–83.
7. Handa S, Pujar Y. Evaluation of Uterine Artery Doppler at 11–13+6 Weeks of Gestation for Prediction of Preeclampsia: A Descriptive Observational Study. J South Asian Feder Obst Gynae 2019;11(5):305–308.
8. Powe CE, Levine RJ, Karumanchi SA. Preeclampsia, a disease of the maternal endothelium the role of antiangiogenic factors and implications for later cardiovascular desease. Circulation. 2011;123(24): 2856-69.
9. Zhang J, Klebanoff MA, Roberts JM. Prediction of adverse outcomes by common definitions of hypertension in pregnancy. Obstet Gynecol. 2001; 97:261–267. doi: 10.1016/s0029-7844(00)01125).
10. Zeisler H, Llurba E, Chantraine F, Vatish M, Staff AC, et al. Predictive Value of the sFlt-1:PlGF Ratio in Women with Suspected Preeclampsia. N Engl J Med. 2016 Jan 7;374(1):13-22.
11. Bian X, Biswas A, Huang X, Lee KJ, Li TK, et al. Short-

Term Prediction of Adverse Outcomes Using the sFlt-1 (Soluble fms-Like Tyrosine Kinase 1)/PlGF (Placental Growth Factor) Ratio in Asian Women With Suspected Preeclampsia. Hypertension. 2019 Jul;74(1):164-172.

12. Cerdeira AS, O'Sullivan J, Ohuma EO, Harrington D, Szafranski P, et al. Randomized Interventional Study on Prediction of Preeclampsia/Eclampsia in Women with Suspected Preeclampsia: INSPIRE. Hypertension. 2019 Oct;74(4):983-990.
13. Soundararajan R, Suresh SC, Mueller A, Heimberger S, Avula S, et al. Real life outpatient biomarker use in management of hypertensive pregnancies in third trimester in a low resource SeTting: ROBUST study. Pregnancy Hypertens. 2021 Mar;23:97-103.
14. Caillon H, Tardif C, Dumontet E, Winer N, Masson D. Evaluation of sFlt-1/PlGF Ratio for Predicting and Improving Clinical Management of Pre-eclampsia: Experience in a Specialized Perinatal Care Center. Ann Lab Med. 2018 Mar;38(2):95-101.
15. Verlohren S, Brennecke SP, Galindo A, Karumanchi SA, Mirkovic LB, et al. Clinical interpretation and implementation of the sFlt-1/PlGF ratio in the prediction, diagnosis and management of preeclampsia. Pregnancy Hypertens. 2022 Mar;27:42-50.
16. Hodel M, Blank PR, Marty P, Lapaire O. sFlt-1/PlGF Ratio as a Predictive Marker in Women with Suspected Preeclampsia: An Economic Evaluation from a Swiss Perspective. Dis Markers. 2019 Aug 14;2019:4096847.
17. Frusca T, Gervasi MT, Paolini D, Dionisi M, Ferre F, Cetin I. Budget impact analysis of sFlt-1/PlGF ratio as prediction test in Italian women with suspected preeclampsia. J Matern Fetal Neonatal Med. 2017 Sep;30(18):2166-2173.

Answer key of Quiz of December 2022



Winners of the monthly quiz, December Issue 2022

1. Dr Neerja Varshney

Mild Chronic HT in Pregnancy- What to do? When to do?

Aishwarya Kapur
Associate Professor, Department of Obstetrics & Gynaecology, LHMC & SSKH, New Delhi

Hypertensive disorders of pregnancy (HDP) encompass chronic hypertension, gestational hypertension, preeclampsia/eclampsia, and chronic hypertension with superimposed preeclampsia. Hypertension in pregnancy is defined using a thres hold blood pressure (BP) ≥140/90 mm Hg (American College of Obstetricians and Gynecologists (ACOG), 2013).[1] HDP are the second most common cause of maternal mortality worldwide, next to maternal hemorrhage and are an important cause of short and long-term maternal and fetal morbidity. Elevated systolic BP during pregnancy, even below the diagnostic threshold for hypertension, is associated with increased risk of preterm delivery, small for gestational age and low birth weight.[2]

Chronic hypertension affects 0.9–1.5% of pregnant women is a major cause of maternal, fetal, and neonatal morbidity and mortality.[2] The incidence of maternal chronic hypertension has increased by 67% from 2000 to 2009, maximum increase (87%) among African American women, primarily due to the epidemic of obesity and increasing maternal age.[3] The trend is expected to continue owing to the change in lifestyle and socio demographic fabric.

The threshold for initiating antihypertensive treatment varies amongst different expert bodies. This is attributable to uncertain maternal benefits of reducing BP, and the potential fetal risks from medication- induced decrease in utero-placental circulation and in utero exposure to antihypertensive medications.[2]

Preconceptional and early pregnancy evaluation [4]

Women with chronic hypertension should be ideally evaluated and counseled preconceptionally. This should be done with a multidisciplinary approach involving an obstetrician, physician, dietician and other specialists as per requirement. The duration of hypertension, degree of blood pressure control and current therapy should be ascertained. General health, daily activities, diet and adverse behavior have to be assessed. History of prior adverse events, such as cerebrovascular accidents, myocardial infarction, renal or cardiac dysfunction has to be noted and necessary evaluation of present status has to be done accordingly. Ophthalmological examination, echocardiography and renal function testing are recommended in women with long standing hypertension.

Lifestyle modifications[4]

Lifestyle modifications play an important role in long term management of patients with hypertension, even after pregnancy. These include

- Weight reduction
- DASH eating plan- Diets rich in fruits, vegetables, whole grains, low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils, and nuts; limit sweets and red meat.
- Lower sodium intake—not more than 2400 mg sodium/day; 1500 mg/day desirable.
- Engage in aerobic physical activity three to four sessions per week, lasting average 40 minutes per session, and involving moderate-to-vigorous intensity physical activity.
- Moderation of alcohol consumption.

Antihypertensive therapy

Antihypertensive treatment is the standard of care for hypertensive nonpregnant patients with a blood pressure of 140/90 mm Hg or higher (American Heart Association)[2], but treatment during pregnancy is controversial. The benefit of Antihypertensive treatment during pregnancy is the reduction in frequency of severe hypertension (blood pressure ≥160/110 mm Hg). However, it does not improve maternal,

fetal, or neonatal outcomes. Also, there is an increased risk of small-for-gestational-age fetuses.[5]

Treatment recommendations for pregnant women with chronic hypertension vary among international organizations. It is universally agreed to treat pregnant women with severe hypertension, but for women with mild chronic hypertension (defined as blood pressure <160/110 mm Hg), it is unclear when to start antihypertensive and what is the target of BP control.

The CHAP study[5]

The landmark Chronic Hypertension and Pregnancy (CHAP) study was an open label, multicentric, randomized trial published in 2022. This study was undertaken to evaluate the benefits and safety of pharmacologic antihypertensive therapy during pregnancy.

Women with mild chronic hypertension (accounting for 70 to 80% of pregnant women with chronic hypertension) were enrolled in the study and randomized into active treatment group (received anti hypertensive in mild chronic hypertension) and control group (no treatment till severe hypertension).

The primary outcomes were preeclampsia with severe features, medically indicated preterm birth (<35weeks), placental abruption, or fetal/ neonatal death. The safety outcome was small-for gestational- age (birth weight<10th centile). Secondary outcomes were serious neonatal or maternal complications, preeclampsia, and preterm birth.

The preliminary data suggested a stepwise increase in adverse pregnancy outcomes with increasing blood pressure above 140/90 mm Hg during the first half of pregnancy.

The authors concluded that in pregnant women with mild chronic hypertension, a strategy of targeting a blood pressure of less than 140/90 mm Hg was associated with better pregnancy outcomes as compared to the strategy of reserving treatment only for severe hypertension, with no increase in the risk of small-for-gestational-age birth weight.

Based on the CHAP study, ACOG has issued a Practice Advisory in April,2022, recommending initiation of antihypertensives above a threshold limit of BP 140/90mmHg, as against earlier recommendation of ≥160/110mmHg.

The recommendations of antihypertensive use during pregnancy is summarized in Table 1.

Table 1: Chronic Hypertension in pregnancy-BP target

Guideline	Year	Hyper-tension during pregnancy Diagnosis	Treatment threshold mmHg	Treatment target mm Hg
ACOG	2019[4]	Acute/ chronic	≥160/110	120-159/80-109
	2022 [12]	Chronic	≥140/90	Not specified
WHO	2020 [13]	Not specified		
NICE	2019 [6]		≥140/90	≤135/85
Society of Obstetricians & Gynae-cologists of Canada	2022[14]		≥140/90	DBP<85

Choice of antihypertensives

Initial antihypertensive therapy is widely established as monotherapy with an accepted first-line drug: labetalol or methyldopa.[2] There is no clear evidence that one drug is preferable to another.

Women who are taking angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) should be informed about an increased risk of congenital abnormalities if these drugs are taken during pregnancy and they should be advised to stop the same as soon as they conceive, in consultation with a specialist. Also, women who are on thiazide or thiazide-like diuretics should be informed about teratogenic risk and increased risk of neonatal complications if these drugs are taken during pregnancy.[9]

Prevention of preeclampsia

Various strategies to prevent development of superimposed preeclampsia have been studied extensively over decades. Still, no intervention has been proved unequivocally effective at mitigating the risk of preeclampsia.

Nutritional supplements:

As regarding nutritional interventions, there is insufficient evidence to demonstrate effectiveness of vitamins C, D and E, fish oil, garlic supplementation, folic acid, or sodium restriction for reducing the risk of preeclampsia.[7].

Calcium supplementation:

A Cochrane meta-analysis including 13 trials (15,730 women) had reported a significant reduction in preeclampsia with calcium supplementation (≥ 1 gram/day), with maximum effect amongst women with low-baseline calcium intake.[11] It also reduced preterm birth and the occurrence of the composite outcome 'maternal death or serious morbidity'.

Bed Rest:

There is no evidence to support the effectiveness of bed rest in reduction of development of HDP and thus, it should not routinely be recommended.[7]

Aspirin

It is hypothesized that an imbalance in the metabolism of prostacyclin and thromboxane A2 is involved in the pathogenesis of preeclampsia. Aspirin preferentially inhibits thromboxane A2 at lower doses and thus is beneficial in prevention of preeclampsia.[7] Low-dose aspirin, starting between 12 and 16 weeks of gestation, reduces the risk of preeclampsia and related adverse outcomes by 10% to 20% in high risk women. Most trials recommend 81 to 150 mg of aspirin daily, although the optimal dose has not been formally tested.[2]

As per ACOG (2019), Low dose aspirin (81 mg/day) for prevention of preeclampsia should be initiated between 12 weeks to 28 weeks of gestation (ideally before 16 weeks) and continued until delivery in the women having one or more risk factors for development of preeclampsia (Table 2).[7]

Table 2: Risk stratification & aspirin use.

Level of Risk	Risk Factors	Recommendation
High	1. History of preeclampsia, especially when accompanied by an adverse outcome 2. Multifetal gestation 3. Chronic hypertension 4. Type 1 or 2 diabetes 5. Renal disease 6. Autoimmune disease (ie, systemic lupus erythematosus, the antiphospholipid syndrome)	Recommend low-dose aspirin if the patient has one or more of these high-risk factors
Moderate	1. Nulliparity 2. Obesity (body mass index greater than 30) 3. Family history of preeclampsia (mother or sister) 4. Sociodemographic characteristics (African American race, low socioeconomic status) 5. Age 35 years or older 6. Personal history factors (eg, low birth weight or small for gestational age, previous adverse pregnancy outcome, more than 10-year pregnancy interval)	Consider low-dose aspirin if the patient has more than one of these moderate-risk factors
Low	Previous uncomplicated full-term delivery	Do not recommend low-dose aspirin

NICE[9] also recommends starting low dose aspirin (75-150mg/day) at 12 weeks of gestation in women at high risk of developing preeclampsia i.e. women with hypertensive disease during a previous pregnancy, chronic kidney disease, autoimmune disease such as systemic lupus erythematosus or antiphospholipid syndrome, type 1 or type 2 diabetes, chronic hypertension. Similarly, in women with more than one moderate risk factors, i.e., nulliparity, age 40 years or older, inter pregnancy interval of more than 10 years, body mass index (BMI) of 35 kg/m2 or more at first visit, family history of pre-eclampsia and multi-fetal pregnancy, it is recommended to give low dose aspirin.

Metformin

Anecdotal evidence [12] suggests that metformin

may prevent preeclampsia by reduction in the production of antiangiogenic factors (soluble vascular endothelial growth factor receptor-1 and soluble endoglin) and the improvement of endothelial dysfunction, probably through an effect on the mitochondria. Another potential mechanism whereby metformin may play a role in the prevention of preeclampsia is its ability to modify cellular homeostasis and energy disposition. But, these are isolated studies and further trials with larger number of women are needed to establish the efficacy of metformin in prevention of preeclampsia.

Pravastatin

There are promising results from a pilot trial[13] of pravastatin in prevention of preeclampsia but there are concerns regarding the fetal safety of the drug.

Lifestyle modification

Preconceptional health and its impact on both pregnancy outcomes and future health have been studied extensively in the past decade. A meta-analysis[14] of 44 randomized controlled trials reported that dietary interventions (diet, physical activity, and a mixed approach) reduce maternal gestational weight gain (mean 1.42kg) and improve pregnancy outcomes, including reduced the risk of pre-eclampsia (OR 0.74, 0.60 to 0.92). Exercise may reduce the risk of developing gestational hypertension and preeclampsia risk by 30-40% (metaanalysis,106 studies, 2018).[15]

Timing of Delivery[4,9]

Women with uncomplicated , well controlled chronic hypertension with normal fetal growth maybe allowed to go in spontaneous labour at term (38weeks). However, women with severe chronic hypertension and those with superimposed preeclampsia with severe features need to be closely monitored and early delivery should be considered in case of uncontrolled hypertension, derangement of renal/hepatic function or fetal indications. Vaginal delivery is preferred and cesarean section should be carried out for obstetric indications.

Long term risks[9]

In all women with pregnancies complicated by HDP, there is approximately 21% risk of recurrence in subsequent pregnancies. Women with chronic hypertension are at increased risk of major cardiovascular events (1.7 times) and stroke (1.8 times). It is advisable to adopt healthy lifestyle and maintain appropriate weight in order to reduce the risk of long term cardiovascular morbidity and mortality.

Points To Remember

- Chronic hypertension affects about 2% of all pregnancies and the incidence is on rise due to advancing maternal age and obesity epidemic.
- Women with chronic hypertension should have detailed preconceptional evaluation for assessment of BP control and end organ effects, with a multidisciplinary approach.
- Lifestyle modification is advised preconceptionally, during pregnancy and lifelong thereafter for an optimal maternal-fetal outcome and to reduce the risk of long term cardiovascular morbidity and mortality.
- Low dose aspirin should be started at 12weeks in women with chronic hypertension and continued till delivery.
- Antihypertensive therapy should be started at a threshold BP ≥140/90mmHg and BP should be maintained <130/85mmHg.
- Monotherapy with alphamethyldopa/ labetalol is preferred initial treatment. ACE inhibitors/ ARBs and thiazides/thiazide like diuretics should not be used during pregnancy.
- Women with uncomplicated pregnancies, well controlled BP and fetal complications should be delivered at term. Earlier delivery should be considered in case of uncontrolled BP, severe superimposed preeclampsia and fetal indications.
- There is almost 20% risk of recurrence in case of any HDP, in women with chronic hypertension, there is 1.7-1.8-fold risk of major cardiovascualar evenst and stroke in subsequent years.

References

1. Roberts JM, August PA, Bakris G, Barton JR, Bernstein IM, Druzin ML, et al. Hypertension in pregnancy:

report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol. 2013

2. Garovic VD, Dechend R, Easterling T, Karumanchi SA, McMurtry Baird

   S, Magee LA, et al. Hypertension in pregnancy: diagnosis, blood pressure goals, and pharmacotherapy: a scientific statement from the American Heart Association. Hypertension. 2022;79:e21–e41.
3. ACOG Practice Bulletin No. 203 Summary: Chronic Hypertension in Pregnancy. Obstet Gynecol Jan 2019; 133(1): p 215-219
4. Cunningham FG, Leveno KJ, Bloom SL, et al. Chronic Hypertension. In Williams Obstetrics , 25th Ed.New York, Mc Graw Hill, 2018; p2162-87
5. Tita AT, Szychowski JM, Boggess K, Dugoff L, Sibai B, Lawrence K et al.Treatment for Mild Chronic Hypertension during Pregnancy. N Engl J Med 2022; 386:1781-1792
6. Clinical Guidance for the Integration of the Findings of the Chronic Hypertension and Pregnancy (CHAP) Study. ACOG Practice Advisory. April 2022
7. ACOG Practice Bulletin No. 202. Gestational Hypertension and Preeclampsia. Obstet Gynecol Jan 2019;133(1); e1-e25
8. WHO Recommendations on Drug Treatment for Non-Severe Hypertension in Pregnancy. World Health Organization; 2020
9. National Institute for Health and Care Excellence. Hypertension in pregnancy: diagnosis and management: NICE guideline [NG133]. https://www.nice.org.uk/guidance/ng133/chapter/Recommendations#management-of-chronic-hypertension-in-pregnancy
10. Magee LA, Smith GN, Bloch C, Cotee AM, Jain V : SOGC Clinical Practice Guideline, Guideline No. 426 Hypertensive Disorders of Pregnancy: Diagnosis, Prediction, Prevention, and Management. J Obs Gyn Canada 44 (5), May 2022, p547-57
11. Hofmeyr GJ, Lawrie TA, Atallah ÁN, Duley L, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.:CD001059. (Systematic Review and Meta-Analysis)
12. Romero R, Erez O, Hüttemann M, Maymon E, Panaitescu B, Conde-Agudelo A et al. Metformin, the aspirin of the 21st century: its role in gestational diabetes mellitus, prevention of preeclampsia and cancer, and the promotion of longevity. Am J Obstet Gynecol. 2017;217:282–302
13. Costantine MM, Cleary K, Hebert MF, Ahmed MS, Brown LM, Ren Z et al. Safety and pharmacokinetics of pravastatin used for the prevention of preeclampsia in high-risk pregnant women: a pilot randomized controlled trial. Am J Obstet Gynecol. 2016;214:720. e1–720.e17.
14. Thangaratinam S, Rogozinska E, Jolly K, Glinkowski S, Roseboom T, Tomlinson JW et al. Effects of interventions in pregnancy on maternal weight and obstetric outcomes: meta-analysis of randomised evidence. BMJ. 2012;344:e2088.
15. Davenport MH, Ruchat SM, Poitras VJ, Jaramillo Garcia A, Gray CE, Barrowman N et al. Prenatal exercise for the prevention of gestational diabetes mellitus and hypertensive disorders of pregnancy: a systematic review and meta-analysis. Br J Sports Med. 2018;52:1367–1375.

Predicting Pre- Eclampsia - What the Future Holds?

Shashi L. Kabra Maheshwari*, Richa Madaan**
*Senior Specialist, **Senior Resident, Deen Dayal Upadhyay Hospital, New Delhi

PE (PE) is a progressive, multi-system disorder of pregnancy. It leads to significant maternal and perinatal morbidity and mortality. Currently, research is being done to identify early biomarkers of PE in order to predict its occurrence early in pregnancy. The most accepted theory about the pathogenesis of PE, suggests a two-stage process.

The first stage (Placental Syndrome) results in inadequate remodelling of the spiral arteries because of defective trophoblastic invasion.

The second stage (Stage II—Maternal Syndrome) reflects the maternal response to this endothelial dysfunction which leads to many specific clinical features of the disease.[1]

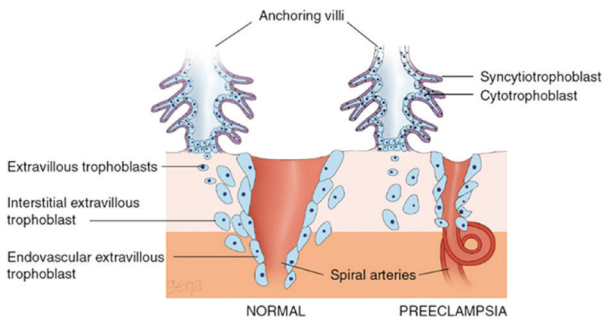


Figure 1: Normal placentation showing the proliferation of extra villous trophoblasts from an anchoring villus. These trophoblasts invade the decidua and extend into the walls of the spiral arteriole to replace the endothelium and muscular wall to create a dilated low resistance vessel. With preeclampsia, there is defective implantation characterized by incomplete invasion of the spiral arteriolar wall by extra villous trophoblasts. This results in a small-calibre vessel with high resistance to flow.[1]

Physicians are constantly striving to find out a method to predict PE early so that treatment can be started much before damage due to PE. Many biophysical and biochemical markers have been described, Mean arterial pressure (MAP), Uterine artery pulsatility (UTPI), soluble fms-like tyrosine kinase 1/placental growth factor (sFLT1/PlGF) ratio, soluble endoglin, and a subset of T-lymphocytes have shown promising results.

Screening for Pre-Eclampsia:

FIGO supports risk-based screening using biomarkers to predict first-trimester PE over screening methods that use only maternal demographic characteristics and medical history (maternal risk factors). All pregnant women should be screened for preterm PE in the first trimester with maternal risk factors and blood pressure.

Table 1: Maternal characteristics, Medical History and obstetric History for pre-eclampsia screening in the first trimester.[2]

Maternal Age
Maternal Weight
Maternal height
Ethnicity: White, Afro-Caribbean, South Asian, East Asian, Mixed
Past Obstetrics History: Nulliparous, Parous without prior PE, Parous with prior PE
Interpregnancy interval in years between the birth of the last child
Gestational age at delivery (weeks) and birthweight of previous pregnancy beyond 24 wk
Family History of PE (Mother)
Method of Contraception: Spontaneous, ovulation induction, in vitro fertilisation.
H/O Smoking
History of chronic hypertension
History of diabetes Mellitus: type 1, type 2, insulin intake
History of systemic lupus erythematosus or anti phospholipids syndrome

Risk factors of PE are important for its early detection:

1. A **history of PE** is the **most predictive factor** for the development of subsequent PE and is associated with an **8.4-fold** increased risk compared with women with a previous uncomplicated pregnancy.[3]
2. **Maternal pre-existing comorbidities** such as pre-existing chronic hypertension (relative risk (RR)=5.1), pre-gestational diabetes (RR=3.7), antiphospholipid syndrome and systemic lupus erythematosus (RR=2.5) play a role as well.[3] Women with both chronic hypertension and pre-gestational diabetes are **eight times more likely to be diagnosed with PE.**
3. **Nulliparity**- Nulliparous women had an increased risk of PE compared to parous women (OR 3.6, 95% CI 2.6 - 5.0). One systematic review reported that the risk of PE is increased three-fold in nulliparous women.[4]

4. **Maternal age beyond 35 and age under 19 years** -

   Maternal age >= 35 years at the time of delivery is associated with 1.2 to 3-fold increased risk of developing PE. Using multivariate logistic regression analysis, adjusting for confounders, the risk for late-onset PE has been shown to increase by 4% with every 1-year increase in maternal age above 32 years.

5. **Maternal birth weight** -Women with low birth weight (<2500 g) have been shown to have double the risk of experiencing pre-eclampsia (OR 2.3, 95% CI 1.0–5.3) when compared with women who weighed 2500–2999 g at birth.[5] A Danish cohort study reported that there was an increased frequency of pre-eclampsia in women who were born prematurely and were small-for-gestational age.

6. **Assisted reproductive techniques (ART)** - ART doubles the risk of PE. In a cohort study of more than 1 million pregnant women, the risk of PE was increased in women exposed to **hyperestrogenic ovarian stimulation** drugs regardless of ART type compared with those with spontaneous conception. The use of **non hyper-estrogenic ovarian stimulation** drugs is not associated with an increased risk of PE. High estrogen levels during implantation may lead to:

   - Impaired placentation
   - Reduced uteroplacental circulation
   - Decreased number of uterine spiral arteries with vascular invasion.

Risk of developing PE is higher in women conceived with donor ovum. Evidence from IVF pregnancies with ovum donation suggests that there are altered extra villous trophoblast and immunological changes in decidua basalis, which may impede the modification of the spiral arteries.

7. **Multifetal gestations** - PE is **2.9 times** more likely to develop in a multifetal pregnancy.[3]

8. **Prepregnancy body mass index**: O**besity (BMI ≥30 kg/m2) increases the risk of developing PE by 2 to 4-fold.**[6] It is considered a state of low-grade chronic inflammation, also (meta-inflammation). This inflammation induces endothelial dysfunction and placental ischemia by immune mechanisms, which in turn leads to the production of inflammatory mediators, leading to an exaggerated maternal inflammatory response and the development of PE.

9. **kidney disease**- PE may occur frequently in pregnant women with chronic kidney disease, lupus nephropathy and diabetic nephropathy. For women with diabetes, proteinuria of either 190–499 mg/day or +2 on urine dipstick at booking is associated with a significantly higher risk.

10. **Short duration of sperm exposure**-A landmark study by Robillard et al. in 1994 showed that conception within the first 4 months of a couple's sexual relationship carries a high risk (incidence of 40-50%) that hypertension will complicate the pregnancy. However, this risk significantly decreased in women after at least 1 year of cohabitation before conception.[7]

11. **Interpregnancy interval** -Both short and long interpregnancy intervals are associated with an increased risk of PE. A recent large multicentric retrospective study of 894 479 women reported that **interpregnancy intervals < 12 months or >72 months** are associated with higher risk of PE development compared with interpregnancy intervals of 12–23 months.

The risk of PE with short intervals may be due to factors related to:

- Socioeconomic status
- Postpartum stress
- Malnutrition
- Inadequate access to healthcare services

The risk of PE with long intervals may be due to:

- Advanced maternal age
- Infertility
- Underlying maternal medical conditions.

12**. Mental disorders-** Depression and anxiety in the first trimester of pregnancy are known to increase the risk of pre-eclampsia by two- to three-fold.[8] In addition, lifetime stress and perceived stress during pregnancy may

double the risk of developing pre-eclampsia; an interaction that may be mediated by the neuropsych immunological pathway.[9]

13. **Family history of PE**: **Daughters or sisters of women with PE are 3–4 times more likely to develop** the condition than women without a family history.[2] The mode of inheritance seems to be complex, including numerous variants, which individually have small effects, but collectively contribute to an individual's susceptibility to the disorder.

PREDICTORS FOR PE:

BIOPHYSICAL MARKERS-

1. **MEAN ARTERIAL PRESSURE:** MAP is calculated from systolic (sBP) and diastolic blood pressure (dBP) readings.
   The formula for measuring MAP is:
   MAP=dBP+(sBP−dBP)/3.

POINTS TO REMEMBER:

1. MAP should be measured by validated automated and semi-automated devices.
2. Women should be in a sitting position, with their arms well supported at the level of their heart and an appropriate-sized adult cuff (small <22 cm, normal 22–32 cm, or large 33–42 cm) used depending on the mid-arm circumference.
3. After resting for 5 minutes, blood pressure is measured in both arms simultaneously and two sets of recordings are made at 1-minute intervals.

Four sets of sBP and dBP measurements are required to enter the risk calculator, and the final MAP measurement (average of four sets of measurements) will be automatically calculated to calculate patient-specific risk.

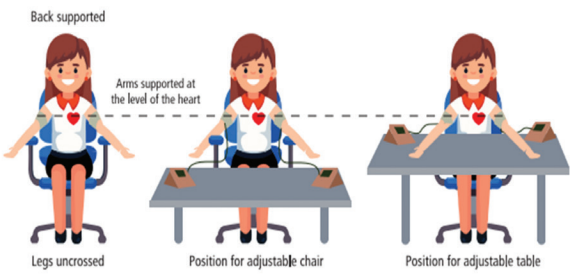


Figure 2: Correct positioning of a woman for blood pressure measurement. Courtesy of PerkinElmer Life and Analytical Sciences.[2]

Several factors can affect MAP values in pregnant women. A cohort study of nearly 70,000 pregnancies was conducted to evaluate the relationship between MAP and maternal characteristics. Significant independent contributions to MAP were made by gestational age, maternal weight, height, Afro-Caribbean ethnicity, cigarette smoking, family history provided by gestational age , maternal weight, height, Afro-Caribbean ethnicity, cigarette smoking, family history of PE. History of PE in previous pregnancy, interpregnancy interval, chronic hypertension and diabetes mellitus.

2. UTERINE ARTERY DOPPLER:

PULSATILITY INDEX: The **pulsatility index** (**PI**) (also known as the **Gosling index**) is a calculated flow parameter in **ultrasound**, derived from the maximum, minimum, and mean Doppler frequency shifts during a defined cardiac cycle.

It is calculated by the following equation:

PI = (peak systolic velocity - minimal diastolic velocity) / (mean velocity)

HOW TO DO?

Transabdominal scan in the first trimester

A midsagittal section of the uterus should be obtained and the cervical canal identified. The ultrasound probe should be gently tilted from side to side and colour Doppler should be used to identify each uterine artery along the side of the uterus at the level of the internal os.

Transabdominal scan in the second or third trimester

The ultrasound probe should be placed in turn on the left and right lower lateral quadrant of the abdomen just above the inguinal ligament to visualize the external iliac artery. Each uterine artery is identified using the color Doppler as a vessel crossing the external iliac artery pulsed wave sample volume should be placed on the uterine artery about 1 cm above the cross-over of the vessels to avoid contamination from the iliac artery.

Transvaginal scan in any trimester: The bladder must be empty. The woman should be placed in the dorsal lithotomy position. The ultrasound probe should be placed in turn into the left and right lateral fornix. The uterine arteries are identified using colour Doppler at the level of the internal cervical os.

After the identification of each uterine artery

Use pulsed wave Doppler. The sampling gate should be 2 mm so that it covers the whole vessel. The angle of insonation should be <30º. The peak systolic velocity should be >60 cm/s to ensure that the uterine artery, rather than the arcuate artery, is being examined. When three similar consecutive waveforms are obtained the PI should be measured. This can be done by automatic or manual tracing of the waveform.

The UTPI of the left and right arteries is recorded. The application uses the average value of the two.

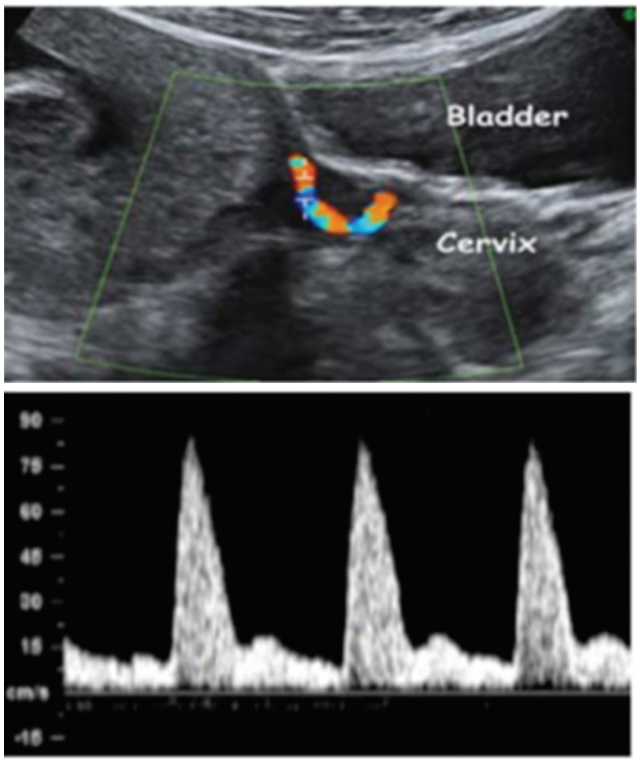
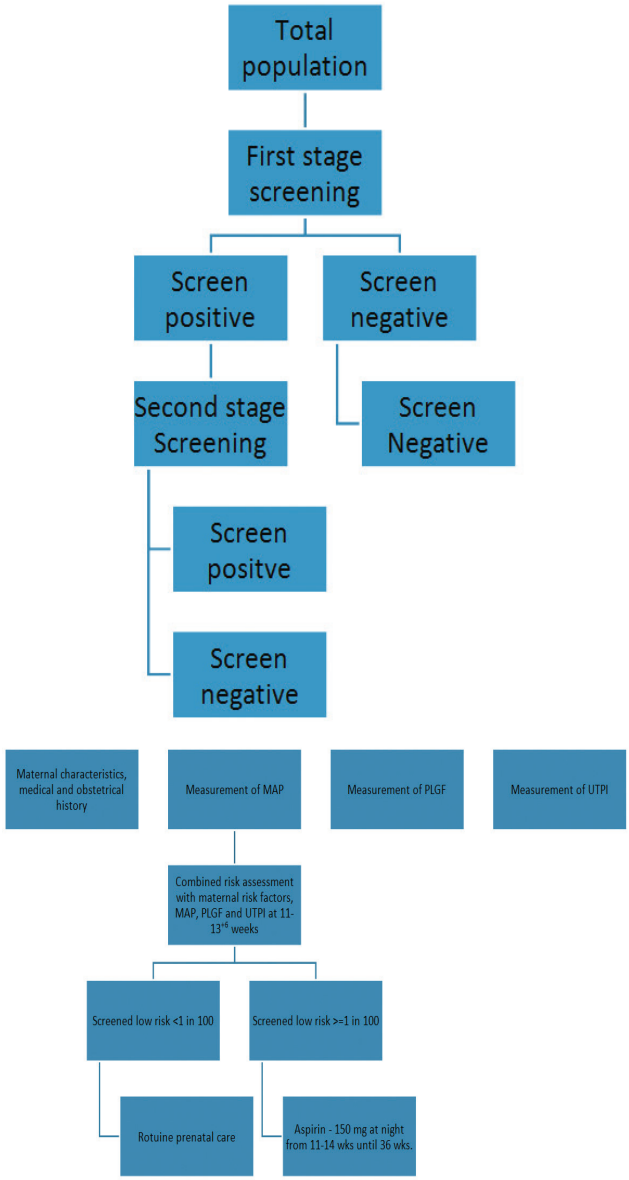


Figure 3: Identification of the uterine artery at the level of the internal os (left) and typical waveforms of the uterine artery Doppler in the first trimester of pregnancy. Courtesy of the Foetal Medicine Foundation.[2]

All measurements for biophysical and biochemical markers are expressed as multiples of the normal median (MoMs), adjusting for maternal factors that provide a substantive contribution to their value. This application allows calculation of MoMs from the measurements of biomarkers.

Pathway to Preterm Pre-eclampsia screening and prevention:[10]

Two stage screening strategy for preterm PR in which the whole population undergoes first-stage screening by maternal factors and MAP and a selected proportion of those considered to be at intermediate risk undergo second stage screening by PLGF and UTPI:[2]



BIOCHEMICAL MARKERS:

Measurement of biochemical markers requires validated equipment and reagents. At present these are provided by DelfiaXpress from PerkinElmer, Kryptor from Thermo Fisher and Elecsys from Roche.

In first-trimester screening, the best biochemical marker is PLGF. PAPP-A is useful if measurements of PLGF and UTPI are not available. Maternal serum concentrations of PLGF and PAPP-A are measured by commercially available automated devices. The measurements of PLGF and PAPP-A should be converted to MoMs, adjusting for

these associated maternal characteristics, analyzers, and gestational age.

PAPP-A:

1. **PAPP-A** is a metalloproteinase insulin-like growth factor (IGF) binding protein secreted by the syncytiotrophoblast that plays an important role in placental growth and development.[8] Therefore, as a single marker it is not an accurate predictive test for PE.

   Pregnancy-associated plasma protein A (PAPP-A) and **alpha fetoprotein (AFP)**: **Low maternal serum levels of PAPP-A in the first trimester and high levels of AFP in the second trimester have been reflective of placental insufficiency complicating pregnancy as in small for gestational age, preterm birth and PE.**

2. **Vascular endothelial growth factor (VEGF)**: VEGF is an important angiogenic factor, which acts on endothelial cell growth. This action is promoted by NO and vasodilatory prostacyclins, thus resulting in overall decrease of vascular tone and blood pressure.Therefore, VEGF antagonism may have a role in hypertension and proteinuria. Levine et al. studied the angiogenic factors in PE and normal pregnancies; sFLT-1 levels were approximately 2.5 times higher, and VEGF levels 2 times lower in PE pregnancies.

3. **Placental growth factor(PIGF):** Discussed in detail in another chapter of this bulletin.

4. **Soluble endoglin**: Endoglin is a cell surface receptor found on the cell membranes of the vascular endothelium and syncytiotrophoblast-explosions. It acts as an anti-angiogenic factor by inhibition the action of angiogenic growth-transforming factor (TGF)-bl and TGF-b3. This also inhibits the role of endothelial NO synthase, thereby interfering with the vasodilatory effects of NO mediated by TGF. Several studies have shown the association between endoglin and there is PE and its severity.

5 **Glycosylated fibronectin**

   These above markers in combination increase the predictive value but are not cost-effective at present. While it is clear that maternal characteristics combined with biochemical and biophysical markers are more sensitive in predicting PE than maternal characteristics alone, there is currently insufficient evidence to support a recommendation on any particular approach.

FIGO recommends the use of risk-based screening using biomarkers for first-trimester prediction of PE over screening methods that use maternal demographic characteristics and medical history (maternal risk factors) only.

It is worth mentioning two commonly used prediction models for the assessment of P E integrated estimate of risk.

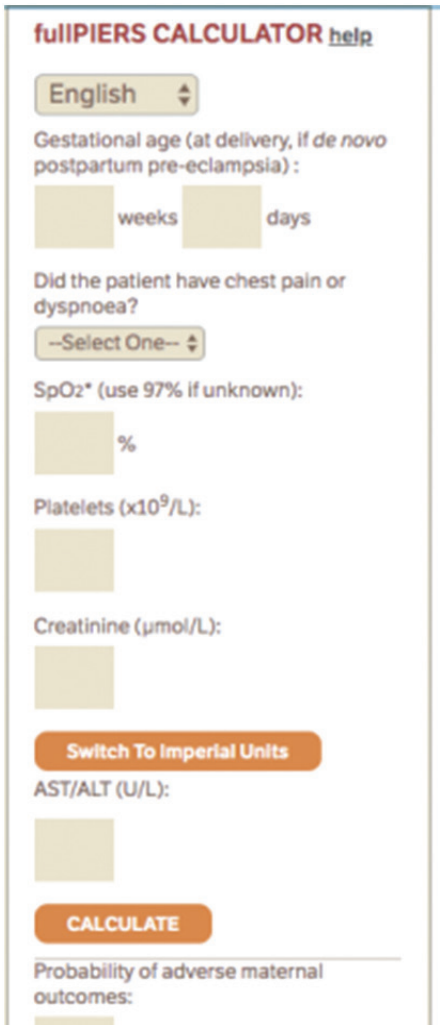
- Recently designed tool which assesses maternal signs, symptoms, and laboratory findings to generate a valid and reliable algorithm for predicting adverse maternal and perinatal outcomes in patients with PE.
- Identifies women at increased risk of adverse outcome up to 7 days before complications arise.
- Helps to plan the timing of delivery and place of care.
- Developed and internally validated in the prospective, multi-center study across Canada, New Zealand, Australia and UK using data from a cohort of 2023 women with pre-eclampsia admitted to tertiary perinatal units.

1. FullPIERS:

Factors included in the model:

1. Gestational age
2. Presence or absence of chest pain or dyspnea
3. Oxygen saturation
4. Platelets
5. Creatinine
6. AST/ALT

Full PIERS CALCULATOR[11]



2. PREP-S Prediction model

Aims to predict the risk time of adverse outcomes at a number of time periods.

- Can be used in women up to 34+6 days.
- Factors in the model include

1. Maternal age.
2. Gestational age at diagnosis.
3. Presence or absence of tendon reflexes.
4. Presence or absence of pre-existing conditions.

   (hypertension, renal disease, diabetes mellitus, autoimmune disease, previous pre-eclampsia)
5. Systolic blood pressure.
6. Oxygen saturation .
7. Platelets
8. Urea .
9. Creatinine .
10. PCR .
11. Whether woman receives antihypertensive or MgSo4 at diagnosis or 24hr.

Recommendations given by FOGSI-GESTOSIS- ICOG Hypertensive Disorders in Pregnancy (HDP) 2019 guidelines, for Indian population:[12]

According to them, though Universal screening is recommended, still there is no single good screening test yet for the general population.

A careful history early in the first trimester is very useful for the effective prediction and prevention of PE early..

This can be done by any healthcare worker by using HDP-Gestosis Score.

HDP-Gestosis score:

- Effective and feasible prediction policy.
- Easy to use

Process of risk scoring:

- This score incorporates all the existing and emerging risk factors in the pregnant woman.
- Score 1, 2 and 3 is allotted to each clinical risk factor as per its severity in the development of PE.
- With careful history and assessment of women a total score is obtained from time to time.
- When total score is =/> 3; a pregnant woman should be marked as 'At risk for PE'.

Age more than 35 years	1
Age less than 19 years	1
Maternal anaemia	1
Obesity (BMI> 30)	1
Primigravida	1
Short duration of sperm exposure (cohabitation)	1
Woman born as small for gestational age	1
Family history of cardiovascular disease	1
Polycystic ovary syndrome	1
Internal pregnancy interval more than 7 years	1
Conceived with assisted reproductive (IVF/ ICSI) Treatment	1

MAP> 85 mm of Hg	1
Chronic Vascular disease (Dyslipidemia)	1
Excessive weight gain during pregnancy	1
Maternal Hypothyroidism	2
Family history of PE	2
Gestational diabetes mellitus	2
Obesity (BMI> 35 kg/ M^2)	2
Multifetal Pregnancy	2
Hypertensive disease during previous pregnancy	2
Pregestational diabetes mellitus	3
Chronic Hypertension	3
Mental disorders	3
Inherited/ acquired thrombophilia	3
Maternal chronic kidney disease	3
Autoimmune disease (SLE/ APLAS/ RA)	3
Pregnancy with assisted reproductive (OD or surrogacy) treatment	3

Newer approaches:

1) Messenger RNA

Placental biomarkers Given the two-stage theory of PE proposing placental disease precedes maternal endothelial dysfunction, placenta-released molecules offer a rational starting point. Placenta-enriched molecules (those highly expressed in the placenta), including messenger RNAs (mRNAs), microRNAs (miRNAs) and proteins can be studied more as potential biomarkers for the development of PE.

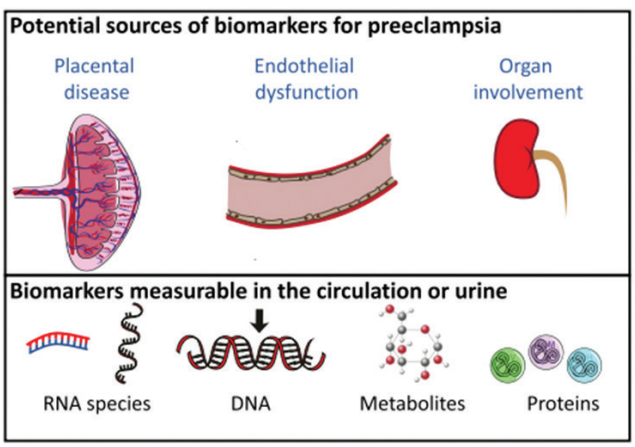


Figure 4: Schematic outlining the potential sources of biomarkers for PE and types that may be measured. PE is associated with placental insufficiency that leads to significant endothelial dysfunction and organ involvement. As such, the placenta and endothelial cells represent potential sources of potential biomarkers that may be in the form of RNAs, DNA, and metabolite proteins.[13]

2) Cell-free DNA

Liquid biopsies measuring plasma Cell-free DNA(cfDNA) have shown promising results for the prediction of PE much before onset . cfDNA of placental origin can be detected in maternal plasma. It is hypothesized that cfDNA is released in preeclampsia by accelerated apoptosis of cytotrophoblasts. However, one MFMU Network study found no correlation between total cfDNA levels and preeclampsia prediction (Silver, 2017).

3) Estimation of glycosylated hemoglobin A1c

4) Serum cystatin-c

5) 1st-trimester estimated placental volume.

6) Proteomic, metabolomic, and transcriptomic technologies can be employed to study serum and urinary proteins and cellular metabolites.

PREVENTION OF PE:

FIRST TRIMESTER PREVENTION OF PRETERM PE:

1. Proposed Aspirin regimen for preterm PE prevention.

Maternal Weight, Kg	Daily required dosage, mg	Administration, mg
<40	100	1*100
>=40	150	2*60
		2*75
		2*81
		1*100 + ½ * 100 (discard the other half)
		½ * 300 (discard the other half

2. In women with low calcium intake (<800 mg/d), either calcium replacement (≤1 g elemental calcium/d) or calcium supplementation (1.5–2 g elemental calcium/d) may reduce the burden of both early- and late-onset PE.

Conclusion

Currently, no screening tests for preeclampsia are predictably reliable, valid, and economical. However, it is feasible for low-resource countries to make use of maternal characteristics and MAP for screening for PE and patients with screen

positive should undergo uterine artery Doppler and test for biochemical markers.

References

1. Cunningham F, & Leveno K.J., & Dashe J.S., & Hoffman B.L., & Spong C.Y., & Casey B.M.(Eds.), (2022). Williams Obstetrics, 26e. McGraw Hill. https://obgyn.mhmedical.com/content.aspx?bookid=2977&sectionid=249396578
2. The International Federation of Gynecology and Obstetrics (FIGO) Initiative on Pre-eclampsia: A Pragmatic Guide for First-Trimester Screening and Prevention. Liona C. Poon, Andrew Shennan, Jonathan A. Hyett, Anil Kapur, Eran Hadar, Hema Divakar, Fionnuala McAuliffe, Fabricio da Silva Costa, Peter von Dadelszen, Harold David McIntyre, Anne B. Kihara, Gian Carlo Di Renzo, Roberto Romero, Mary D'Alton, Vincenzo Berghella, Kypros H. Nicolaides, Moshe Hod. IJGO Supplement Editor: Paul Fogarty. This project was funded by an unrestricted educational grant from PerkinElmer Inc, Waltham, USA.
3. Bartsch E, Medcalf KE, Park AL, et al. Clinical risk factors for PE determined in early pregnancy: systematic review and meta-analysis of large cohort studies. BMJ 2016;353:i1753. doi:10.1136/bmj.i1753.
4. Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking: Systematic review of controlled studies. BMJ.2005;330:565.
5. Khalil A, Syngelaki A, Maiz N, Zinevich Y, Nicolaides K. Maternal age and adverse pregnancy outcome: a cohort study. Ultrasound Obstet Gynecol 2013;42(6): 634–643.
6. Bodnar LM, Ness RB, Markovic N, Roberts JM. The risk of PE rises with increasing prepregnancy body mass index. Ann Epidemiol 2005; 15(7):475–482.
7. Bodnar LM, Ness RB, Markovic N, Roberts JM. The risk of PE rises with increasing prepregnancy body mass index. Ann Epidemiol 2005; 15(7):475–482.
8. Kurki T, Hiilesmaa V, Raitasalo R, Mattila H, Ylikorkala O. Depression and anxiety in early pregnancy and risk for PE. Obstet Gynecol 2000;95(4):487–490
9. Yu Y, Zhang S, Wang G, Hong X, Mallow EB, Walker SO, et al. The combined association of psychosocial stress and chronic hypertension with PE. Am J Obstet Gynecol 2013;209(5): 438.e1-e12
10. Wright D, Gallo DM, Gil Pugliese S, Casanova C, Nicolaides KH.Contingent screening for preterm pre-eclampsia. Ultrasound ObstetGynecol. 2016;47:554–559.
11. 20th World Congress in fetal medicine,Spain 2023
12. FOGSI-GESTOSIS-ICOG Hypertensive Disorders in Pregnancy (HDP) Good Clinical Practice Recommendations 2019
13. MacDonald TM, Walker SP, Hannan NJ, Tong S, Kaitu'u-Lino TJ. Clinical tools and biomarkers to predict preeclampsia. EBioMedicine. 2022 Jan;75:103780. doi: 10.1016/j.ebiom.2021.103780. Epub 2021 Dec 23. PMID: 34954654; PMCID: PMC8718967.

Non Technical Skills in Medicolegal Safety

Chitra Setya
Senior Consultant and Head of Department OBGY Apollo Hospitals Noida

What are non-technical skills?

Non-technical skills are the cognitive and interpersonal skills that complement practical and technical competences, such as decision making, leadership and team working. In surgical specialties, these behavioural or non-technical aspects of performance (e.g. communication failures) are often the underlying causes of adverse events, rather than a lack of technical expertise. Traditionally, these aspects of performances have been largely developed informally rather than explicitly addressed in training.

Patient safety improves when non-technical strategies, tools and behaviours are combined with proficient medical skills

It has been established that only 50% of surgical errors can be explained due to lack of technical skill. The other half is due to non-technical factors, such as communication problems (43%) and work overload (33%). In a retrospective review of 258 closed malpractice claims, systems factors contributed to error in 82% of cases & communication breakdown was responsible for 24% . NTS as a formal training system is derived from aviation Crew Resource Management (originally called Cockpit Resource Management). CRM was first adopted by United Airlines in 1981. In healthcare, after the 1990s the significance of human factors in patient safety became more widely publicized. Flin pioneered a behavioural marker system known as Anaesthetists' Non-Technical Skills (**ANTS**) followed by Non-Technical Skills for Surgeons (NOTSS). NTS is most important for anaesthesia, critical care and surgery.

NTS is basically defined as "cognitive and interpersonal skills that include: **situational awareness, decision making, communication, teamwork and leadership**".

Performance Shaping Factors (PSFs) can be classified according to a clinical adaptation of James Reason's 'Three Buckets' model, based on Self,Work and Context.

Performance shaping factors – James Reason's 3 bucket model

NOTSS skills taxonomy (RCOG)

Category	Elements
1. Situation Awareness	• Gathering information • Understanding information • Projecting and anticipating future state
2. Decision Making	• Considering options • Selecting and communicating option • Implementing and reviewing decisions
3. Communication and Teamwork	• Exchanging information • Establishing a shared understanding • Co-ordinating team activities
4. Leadership	• Setting and maintaining standards • Supporting others • Coping with pressure

Situational Awareness

This is being aware of what is happening around you now, what it means to you now and what is likely to happen soon, all based on previous experiences and knowledge. Eg: during a complex procedure, we pay attention and focus only on the task at hand and ignore the apparently irrelevant other side because activities continue to happen outside the spotlight and these can be missed, potentially leading to vital pieces of information being omitted from the decision-making process. 'Loss of situational awareness' is a term normally used to describe this phenomenon and often appears in adverse event investigation reports. Strategies to improve situational awareness, namely, honest, open and candid debriefs and delegation of 'oversight tasks' to others within the operating theatre when workload is expected to be high using a positive handover plays a major role.

Perception of Risk:

A **hazard** is anything that could potentially go wrong or cause harm, without any qualification of its likelihood or severity e.g., PPH. A **threat** is the subjective perception of a hazard. It is important to recognize, that a number of factors influence the perception of danger. A **risk i**s a calculated evaluation of the likelihood and impact of a hazard, based on objective assessments and measurements rather than subjective interpretation. Expert clinicians are

often called upon to make decisions in urgent and complex situations, and their '**threat assessments'** are usually better than a novice's 'risk assessments'.

Decision making

This is the process of reaching a judgement or choosing an option to meet the needs of a given situation. It requires an individual or a team to create or have a mental model of the situation, generate or determine one or more options which relate to that model, decide on a course of action and then review the outcome. The two key processes:

1. Sub-conscious perception, processing and 'choice'.
2. Logical and discrete steps where the problem, options and decisions are made in slow time.

Klein *et al.* showed that experts were able to identify key elements more quickly and subsequently made better, faster decisions. Novices often waited until they had a surplus of elements before deciding, and in some cases, this was too late.

First stage is situation assessment i.e. observation and identification of the problem. The second stage is the process of choosing a course of action to meet the needs of the situation assessment. Effectiveness of the response chosen will depend on the accuracy of the initial assessment and the experience of the individual making the decision. Finally, the result of implementing the chosen plan of action should be reviewed, checking that the desired outcome has been achieved and defaulting to a 'Plan B' if necessary.

Decision making may be degraded by fatigue, as it erodes working (short-term) memory, thereby reducing one's ability to retrieve problem solving information from the long-term memory.

Communication and Decision-Making:

Communication plays a pivotal role in this process, especially in healthcare as team members often perform sequentially and rely on information from the previous shift to guide their decisions and actions.

Team members let others in on their reasoning and inform them about their intentions and expectations Critically, expert teams ensure common ground and shared mental models by providing feedback. The SBAR format (situation, background, assessment, response) is also of use in transmitting critical information and is now commonplace on many delivery suites. The efficiency and safety of any healthcare setting is closely linked to the efficacy of the internal communication.

Stress:

Has a profound impact on decision-making which, in the medical context, could negatively affect clinical outcomes. Stress-related reductions in cognitive performance (e.g., accuracy, reaction time, attention, memory) resulted in poorer patient safety outcomes such as hospital acquired infections or medication errors. Healthcare professionals experience emotions differently, quantitatively, and qualitatively, and should be aware of their 'emotional intelligence' and trained on their ability to cope. Stressful conditions in the work environment must be identified and possibly mitigated, if not removed, in terms of both contents (working hours, monotony, participation and control) and context (job insecurity, teamwork, organizational culture, work-life balance etc.

Teamwork and Leadership Skills:

A team can be defined as 'a distinguishable set of two or more individuals who interact dynamically, adaptively, and interdependently; who share common goals or purposes; and who have specific roles or functions to perform' Successful teams are the product of time, effort, and trust. In multidisciplinary teams', people with diverse backgrounds and skills are brought together for a particular purpose. Eg. operating theatre team. Elements that are important to the good functioning of a team include the ability and willingness to support others, to solve conflict, to exchange relevant information and the coordination of activities. Effective leadership is essential for maintaining safe performance in the workplace and maintaining morale.

Leadership requires motivating, directing and organizing the team, encouraging individuals to work together, assessing performance, task assignment and generating a positive environment. Leadership skills may also be needed by other members of the team when necessary to plan, prioritize and manage workload.

Dramatics and Doctors: Emotional control and manipulation techniques are required to best cope with the psychological demands of patients. "Emotional labour"on a daily basis to appear reasonable all around , no matter how ragged we are really feeling**.**

Ten important Non-Technical skills:

Empathy, Communication Skills,

Be a Team Player, Dealing With Pressure, Strong Work Ethics, Positive Mental Attitude, Flexibility, Time Management, Self-Confidence and Dealing With Criticism.

References:

1. A A Watrelot, V Tanos, G Grimbizis , E Saridogan et al. From complication to litigation: The importance of non-technical skills in the management of complications: ESGE special interest group 'quality , safety and legal aspects' working group; Obgyn 2020 Aug 5.
2. Rhona Flin, Nicola Maran, Non-technical skills: identifying, training, and assessing safe behaviours https://doi.org/10.1093/med/9780198717621.003.0018 Pages 249–264 Published: October 2015
3. Bevinahalli N. Raveesh, Ragavendra B. Nayak, and Shivakumar F. Kumbar, Preventing medico-legal issues in clinical practice https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5109754/# 2016 Oct
4. Adaptation of non-technical skills behavioural markers. Medicolegal-Expert-Core-Competencies. by F Bracco·2017 pdf https://climoa.com/wp-content/uploads/2022/06
5. Khalid H Alzahrani, Ahmad M Elsheikh, Sohail S Bajammal, Wael S Taha et al., Non-technical training in orthopedic surgery: An unrecognized need Uhlman5 2019
6. Non-Technical Skills for Surgeons (NOTSS) RCOG. https://www.rcog.org.uk/careers-and-training/starting-your-og-career/specialty-training/assessment-and-progression-through-training/non-technical-skills-for-surgeons-notss/
7. Ailsa L Hamilton, Joanne Kerins, Marc A MacCrossan et al., Medical Students' Non-Technical Skills (Medi-StuNTS): preliminary work developing a behavioural marker system for the non-technical skills of medical students in acute care BMJ Simul Technol Enhanc Learn. 2019;

Events held in December 2022

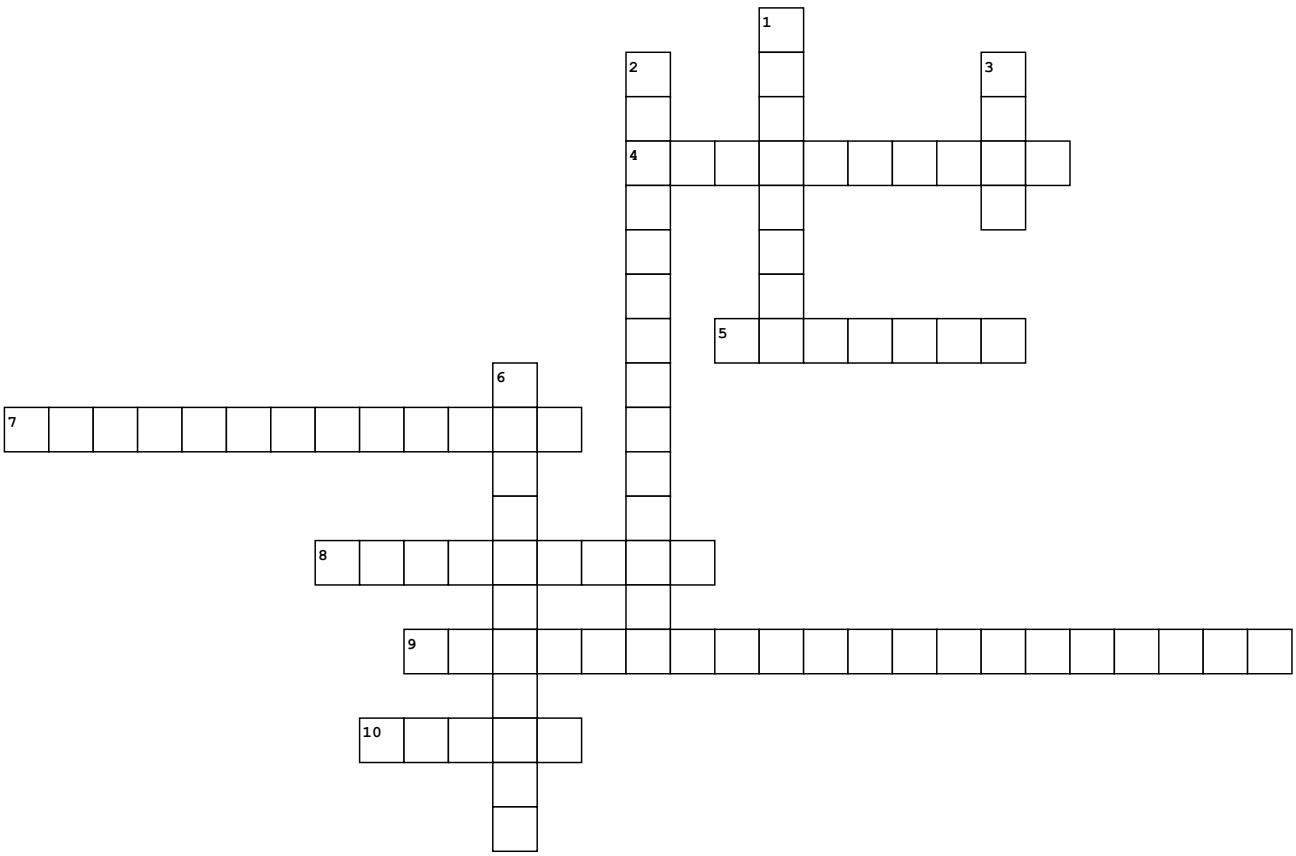
S. No.	Date	Events
1.	02.12.2022	Webinar on "Hyperglycaemia in pregnancy 3rd session; Care around birth" by AOGD Safe motherhood committee & NARCHI, Delhi
2.	03.12.2022	CME on "Practical approach to Gynaecological conditions" by FOGSI clinical research committee in association with AOGD
3.	18.12.2022	Public forum on Creating awareness and promoting health "BADLAAV" on 'Swasth Nari, Sukhi Nari' by Public awareness committee FOGSI in association with AOGD
4.	17.12.2022 18.12.2022	DGES Annual Conference by BLK – Max Hospital in association with AOGD
5	19.12.2022	PG Forum on 'Cancer Cervix' by Hamdard Institute of Medical Sciences (HIMSR)
6	30.12.2022	AOGD monthly clinical meeting at Sir Gangaram Hospital

Events in January 2023

S. No	Date	Events
1.	4th to 8th Jan 2023	**All India Congress of Obstetrics & Gynaecology (AICOG) 2023** at Kolkata
2.	16.01.2023	PG Forum on 'Renal disease in Pregnancy'
3.	27.01.2023	AOGD Monthly clinical meeting at ABVIMS & Dr RML Hospital
4.	28.01.2023	Live operative Hysteroscopic Workshop by Safdarjung Hospital

Cross Word Puzzle

Surbhi*, Nalini Bala Pandey**
*Senior Resident, **Consultant Department of Obstetrics & Gynaecology, MAMC & Lok Nayak Hospital, Delhi



Across

4. PROGNOSIS study based on which ratio

5. Drug for prophylactic use for prevention of pre-eclampsia

7. Diminished glomerular filtration, increased tubular reabsorption and decreased secretions cause what effect in preeclampsia

8. Which experimental drug may prevent preeclampsia by improving endothelial dysfunction?

9. Best predictive test for Gestational Hypertension

10. High levels of which antiangiogenic protein in the second trimester doubles the risk of pre-eclampsia

Down

1. Primary clinical assessment for screening and prediction of preeclampsia can be objectively performed by which 'easy to use'HDP-score

2. What is the mechanism of action of magnesium in preeclampsia

3. Glycoprotein synthesized in villous and extravillous cytotrophoblast and has both vasculogenetic and angiogenetic functions

6. Glycoprotein released from endothelial cells and extracellular matrix following endothelial injury

Mail the answers to aogdeditor22@gmail.com. The correct answers and names of the three winners will be announced in the next issue.

AOGD Sub-Committee Chairpersons 2022-2024

Committee	Chairperson	Contact No	Email.id
Breast and Cervical Cancer Awareness, Screening & Prevention Sub-Committee	Dr Mrinalini Mani	9811835888	drmrinal5@gmail.com
Infertility Sub-Committee	Dr Manju Khemani	9810611598	dr.manjukhemani@gmail.com
Rural Health Sub-Committee	Dr Shivani Agarwal	9868249464	dragarwal.shivani@gmail.com
Multidisciplinary Sub- Committee	Dr Kiran Guleria	9811142329	kiranguleria@yahoo.co.in

AOGD Sub-Committee Chairpersons 2021-2023

Committee	Chairperson & Co- Chairperson	Contact No	Email.id
Endometriosis Sub-Committee	Dr. Anjila Aneja	9810059519	anjilaaneja1966@gmail.com
QI Obst & Gynae Practice Sub-Committee	Dr K Aparna Sharma, Chairperson	9711824415	kaparnsharma@gmail.com
	Dr Jyoti Bhaskar, Co-Chairperson	9711191648	jytbhaskar@yahoo.com
Oncology Sub-Committee	Dr Sunita Malik	9818914579	svmalik@yahoo.com
Urogynaecology Sub-Committee	Dr Geeta Mediratta, Chairperson	9810126985	gmediratta@yahoo.com
Adolescent Health Sub-Committee	Dr Anita Rajouria, Chairperson	9711177891	anitarajorhia716@gmail.com
	Dr Sujata Das, Co- Chairperson	9971946064	drdas_sujata2110@yahoo.co.in
Reproductive Endocrinology Sub-Committee	Dr Surveen Ghumman, Chairperson	9810475476	surveen12@gmail.com
	Dr Deepti Goswami, Co-Chairperason	9968604348	drdeeptigoswami@hotmail.com
Safe Motherhood Sub-Committee	Dr Manju Puri	9313496933	drmanjupuri@gmail.com
Fetal Medicine & Genetics Sub-Committee	Dr Seema Thakur, Chairperson	9818387430	Seematranjan@gmail.com
	Dr Sangeeta Gupta, Co- Chairperson	9968604349	drsangeetamamc@gmail.com
Endoscopy Sub-Committee	Dr Kanika Jain	9811022255	dr.kanika@gmail.com

Proceedings of the AOGD monthly clinical meeting at Sir Ganga Ram Hospital on 30.12.2022

Large Vestibular Schwannoma in Pregnancy: Management Dilemma

Renuka Brijwal, K. Gujral, C. Mansukhani, A. Gupta, S. Nayar, A. Majumdaar.
Sir Ganga Ram Hospital

Case : A 28 year old, G2P1L1, Previous LSCS. First visited on 13/9/22 at 35+2 weeks with complaints of headache, vomiting since 3-4 Days. She also had complaint of vertigo, imbalance in walking, decreased vision and hearing loss on right side. She was booked elsewhere and had similar complaints at 29 weeks and was referred to SGRH (Neurosurgery Department). Then MRI Brain showed A Large Right cerebellopontine angle SOL measuring 4.7 x 3.4 cm with Hydrocephalus ? Vestibular Schwannoma. She had Laparoscopic assisted Left Parietal VP Shunt placed at 30 weeks (Neuro surgery Team, SGRH) OBGY consultation done, USG reported normal fetus with adequate liquor. The patient improved and was discharged with advice to follow up with OBGY team. However did not come back for follow with OBGY team till she had worsening of symptoms and reported in emergency at 35 weeks. On examination - patient conscious, oriented, followed commands with slurred speech. PR-120/min, BP - 120/80mmHg. The right facial palsy present, right sided hearing impaired. obstetrics examination: AGA foetus (35weeks), Cephalic, FHR 140 bpm, normal liquor. USG dating pregnancy, 2.5 kg normal liquor, normal dopplers. All routine investigations were normal. Patient was admitted in ICU. Neuro-Surgery consultation taken, urgent NCCT Head done which showed increased size of tumour with intra tumoral bleeding with mass effect. The treatment started with plan to do LSCS once patient stabilizes. However after one day she had one episode of vomiting and crashed. She was intubated immediately and emergency LSCS done within minutes of intubation. The baby delivered with APGAR score 6/8, shifted to NICU. Post LSCS patient remained vitally stable.

Discussion

Intracranial neoplasms are rare in pregnancy. Incidence is one in 100,000 person. The diagnosis and management present significant challenges. The Vestibular Schwannomas is a slowly growing tumor. Vestibular portion of the eighth cranial nerve is benign tumor with female dominance may appear for the first time in pregnancy or flared up symptoms with pregnancy. It may be because of increased blood volume during pregnancy or hormonal influence (Estrogen/Progesterone) but still. The reason is unclear. Symptoms usually are due to compression of 8th cranial nerve and cerebellar compression. They are mostly diagnosed in the second or third trimester, only six required surgical resection prior to delivery. About 31 cases of vestibular Schwannoma in pregnancy are reported till 2014.

Managing 'Growing Teratoma Syndrome' in pregnancy : A rare case scenario

Rahul D Modi
Consultant-Gynaecological Oncology
Sir Gangaram Hospital, New Delhi

Mrs. S, 26 years-old, G3P1L1A1, was referred to Gynaecological Oncology Division, Sir Gangaram Hospital (SGRH) at 13+1 weeks POG with right adnexal mass and 2-3 episodes of severe torsion-like pain abdomen. MRI (abdomen/pelvis) showed a single intra-uterine fetus, right adnexal mass, solid-cystic with fat fluid levels and calcific areas measuring 6 x 7 cms. There was no ascites, enlarged nodes or disease elsewhere. On evaluation, her tumour marker profile was AFP – 28.42 ng/ml, CA 125 – 78.7 U/ml, beta HCG – 113875 mIU/ml and LDH – 244 U/ml. She was already a diagnosed case of Stage IA Grade 3 – immature teratoma, completely staged with adjuvant of 4 cycles of BEP (Bleomycin, Etoposide and Cisplatin). The above said surgery had followed fertility sparing protocol with complete staging including omentum and nodal assessment done at SGRH in September 2017. Intra-operatively, there was

a left adnexal mass – 25 x 20 cms, mild ascites and no gross disease elsewhere. She completed her chemotherapy in Feb 2018. There were 3 instances of follow-up in Medical Oncology Department, SGRH; tumour marker levels were normal at all instances. She then defaulted for follow-up. In 2020, she delivered a full-term girl child vaginally at local place. As per history, pregnancy was uneventful and no records or sonograms were available. The differentials considered as per her present history were recurrent immature teratoma vs growing teratoma syndrome (GTS). A plan for staging laparotomy with salpingo-oopherectomy was formalised. Patient was not willing for open surgery and complete salpingo-oopherectomy as she with her family were apprehensive about continuation of present precious pregnancy as removal of the only existing ovary and open route of surgery worried them. They were repeatedly counselled but were adamant on their decision with a strong desire of completion treatment after child-bearing. Laparoscopic staging was done with right ovarian cystectomy with peritoneal washings. Intra-operatively, there was a 6 x 6 cms of solid-cystic right adnexal mass with flimsy midline incision. There was no suspicious disease elsewhere and cyst enucleation was done in endobag with no spillage. Final histopathology report was mature cystic teratoma with negative cytology of peritoneal washings. She was planned for observation and is presently 26+4 weeks POG with no significant findings on follow-up sonograms.

GTS is a rare condition, which presents with benign (mature) teratoma masses either during or after chemotherapy. Incidence is approximately 12% after immature teratoma of ovary. Diagnostic criteria for GTS includes normalisation of serum tumour markers after initial treatment, visualisation of enlarging or new masses and exclusive presence of 'mature teratoma 'components only in resected specimen. Our case fulfilled all the three criteria. The challenges faced by us included – diagnosing GTS Vs recurrence as pregnancy too elevates similar tumour marker profile, patient's unwillingness for open surgery and complete salpingo-oopherectomy. As per our review on GTS, this is the first time – management of the same is being reported during ongoing pregnancy.

Enoxaparin Induced Skin Necrosis

Huma Ali, G. Mediratta
Sir Ganga Ram Hospital.

Enoxaparin induced skin necrosis is a rare complication of heparin injections either at the injection site or distant sites, in which there is the death of skin cells (necrosis) due to the inadequate blood supply. Three likely mechanisms causing the necrosis exist:

1. Immunologically mediated intravascular thrombosis resulting from heparin-induced immune aggregation of platelets (heparin-induced thrombocytopenia syndrome, HIT) 0.2% of cases.
2. Formation of antigen-antibody complexes in cutaneous blood vessels (type III hypersensitivity syndrome).
3. The LMWH persisting in the subcutaneous tissue, due to poor circulation within the adipose tissue.

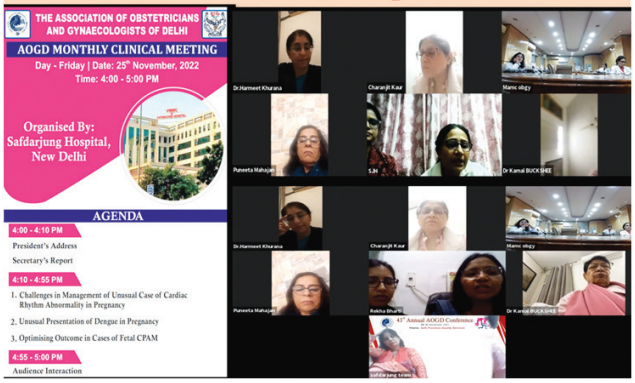
Case: A 24 year old Primigravida with 30+3 week POG with gestational hypothyroidism with oligohydramnios presented with swelling and pustular lesions in upper left limb and pustular lesions in bilateral thighs and anterior abdominal wall since 10 days. Patient was booked outside in a private nursing home. During her ANC, patient was started on tab. Ecospirin 75 mg in first trimester. Her anomaly scan was done on 09/08/2022, which reported AFI 4 cm and was inadequate for gestational age. Hence dose of tab. Ecosprin was increased to 150 mcg once daily and on 13/08/2022 she was started on Inj. Lonopin 40mg s/c on bilateral thighs with Argipreg sachet was started. She was administered Inj. Amino Acid IV along with 10% dextrose on 01/10/2022 and 05/10/2022 following which she developed swelling pain in left upper limb followed by bilateral thighs and anterior abdominal wall and was given Sumag dressing and thrombophob ointment. Her swelling progressed gradually to pustular lesions over bilateral thighs (5 x 4 cm and 6 x 4 cm) and left forearm (5 x 4 cm) and over umbilicus (6 x 4 cm) and another 5x4 cm lesion on anterior abdominal wall. This gradually progressed to tender abscess present above the elbow joint

with pus oozing out. Her gel HIT card test and CRP was positive. Inj. Lonopin was stopped and patient was given IV antibiotics and incision and drainage of pus with wound debridement was done. HPE reported edematous and congested dermis with collection of mixed inflammatory cell infiltrate in deep dermis and non specific acute inflammatory lesion with neutrophils. Hence the diagnosis was confirmed, patient was taken up for wound debridement and closure by plastic surgery team and she responded well to the treatment. Her pregnancy continued and she delivered at 38 weeks. So, LMWH should be used judiciously to avoid such dreadful complications.

Skin necrosis after administration of enoxaparin is rare. Most patients areadult women with an age range of 18 to 89 years, with 43% being older than 55 years. These patients are often overweight, diabetic, and receiving broad-spectrum antibiotics. Approximately 50% have a history of recent heparin exposure. The skin reaction begins between 1 and 25 days after these patients received the drug, and they typically presented with areas of erythema and tenderness at the injection site, which evolved into plaques and then skin necrosis. Antiheparin platelet factor 4 antibodies are present in 90% patients, and approximately 50% cases are associated with thrombocytopenia.

Events held under Aegis of AOGD in December 2022

AOGD Monthly Clinical Meeting on 25th November 2022
VMMC & SJH Hospital



Hyperglycemia in Pregnancy 3rd Session; Care around Birth on 2nd Dec,2022
AOGD Safe Motherhood Committee & NARCHI Delhi

DGES Annual Conference on 17th & 18th Dec
BLK – Max Hospital in association with AOGD

Practical Approach to Gynaecological Conditions on 3rd Dec 2022 FOGSI clinical research committee association with AOGD

FOGSI Clinical Research Committee

Invites you to

Practical Approach to Gynaecological Conditions

Hosted by

Association of Obstetricians & Gynaecologists of Delhi

Saturday 3rd Dec 2022 at 1:00 pm

Hotel The Royal Plaza (Royale Hall, 2nd Floor)
19, Ashoka Road, New Delhi – 110 001

Dr. Asmita M. Rathore President, AOGD	**Dr. Deepti Goswami** Secretary, AOGD
Dr. Alka Pandey Vice President, FOGSI	**Prof. (Dr.) Surekha Tayade** Chairperson - FOGSI, CRC
Dr. Hrishikesh Pai President, FOGSI	**Dr. Madhuri Patel** Secretary General, FOGSI

Applied for ICOG Credit Points

PG Forum on "Cancer Cervix" on 19th Dec,2022
Hamdard Institute of medical Science (HIMSR)

Swasth Nari , Sukhi Nari on 18th December 2022
Public Awareness Committee FOGSI with AOGD

Association of Obstetricians & Gynaecologists of Delhi

MEMBERSHIP FORM

Name:.....

Surname: .....

Qualification (Year): .....

Postal Address: .....

City:..... State: ..... Pin code: .....

Place of Working:.....

Residence Ph. No. ..... Clinical / Hospital Ph. No.....

Mobile No:.....Email: .....

Gender: Male:.....Female:.....

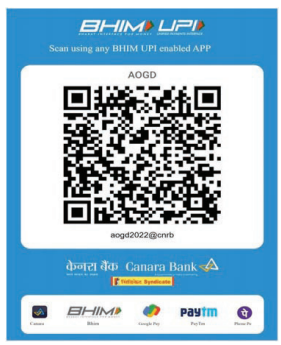
Date of Birth: Date..... Month ..... Year .....

Member of Any Society:.....

Proposed by: .....

Cheque/DD / No: .....

Cheque/Demand Draft should be drawn in favour of: **AOGD 2022**



For Online Transfer Through NEFT/RTGS
Name of Bank: **Canara Bank**
Branch: **M A Medical College New Delhi**
Name of Account: **AOGD 2022**
Account No: **110045692016**
IFSC Code: **CNRB0019068**
MICR Code: **110015415**

For Life Membership : Rs. 11,000 + Rs. 1,980 (18% GST applicable) = Rs. 12,980
For New Annual Membership* : Rs. 2,000 + Rs. 360 (18% GST applicable) = Rs. 2,360
For Old Renewal Membership+ : Rs. 1,200 + Rs. 216 (18% GST applicable) = Rs. 1,416

Encl.: Attach Two Photocopies of All Degrees, DMC Certificate and Two Photographs (Self attested)
***-Annual Membership is for the calendar year January to December.**
+ - In case of renewal, mention old membership number.
Note: 18% GST will be applicable as FOGSI requires it.

Send Complete Membership Form Along With Cheque / DD and Photocopy of required documents.

AOGD SECRETARIAT

Room No. OG-14, Department of Obstetrics & Gynaecology
Maulana Azad Medial College & Lok Nayak Hospital, New Delhi-110002
Email: aogdmamc2022@gmail.com | www.aogd.org

ACTGACTGACTGACTGACTGACTGACTGACTGACTGACTGACTGACTGACTGACTGACTGACTGACTGACTG

MEDGENOME | Claria Reproductive Genetics

CAP ACCREDITED COLLEGE of AMERICAN PATHOLOGISTS

DELIVERING PRECISION WITH CHROMOSOMAL MICROARRAY

Chromosomal Microarray (CMA) analysis has emerged as a primary diagnostic tool for the evaluation of structural abnormalities detected during pregnancy and for developmental delay and structural malformations in children.

How CMA can help you?

- Determine cause of fetal demise or still birth by analyzing products of conception
- Detect the cause of structural abnormalities in fetus[1]
- Offer more diagnostic clarity even in structurally normal fetus[2]

How CMA is superior to Karyotyping?

- Offering superior yield (23.3%)
- 6% increased diagnostic yield when karyotype is normal in structurally abnormal fetuses[3]
- <0.25% failure rate
- High resolution screening
- No need for live cells
- Screens for UPD/LOH
- Syndromic evaluation involving micro-deletion/ duplication

Why Choose MedGenome?

- CAP accredited reports
- Strict adherence to ACMG guidelines
- All prenatal samples being evaluated for maternal cell contamination (MCC)
- Reports reviewed and approved by clinical geneticist
- Free genetic counselling
- Comprehensive CMA offering including Optima, 750K, HD and XON array

Source:

1. Dugoff L, Norton ME, Kuller JA. The use of chromosomal microarray for prenatal diagnosis. J Obstet Gynecol 2016;215(04):B2-B9
2. Microarrays and Next-Generation Sequencing Technology: The use of Advanced Genetic Diagnostic Tools in Obstetrics and Gynecology. Obstet Gynecol 2016;128(06):262-268
3. N Engl J Med. 2012 December 6; 367(23): 2175–2184. doi:10.1056/NEJMoa1203382.

Talk to the Experts 1800 103 3691 diagnostics@medgenome.com www.medgenome.com