I would like to thank you for your participation to the 46th International Congress on Pathophysiology of Pregnancy and the 35th Meeting of Japan Society for the Study of Hypertension in Pregnancy, which was held from September 18 to 20 in Tokyo, Japan. I hope you enjoyed the Congress and your stay in Tokyo.

More than 380 participants including about 40 participants from overseas (16 countries) attended the Congress. I assure that, thanks to you, sessions by prominent speakers and chairs abroad stimulated lively discussions at the conference and motivated participants.

I also reaffirmed the significance of face-to-face discussions with doctors and specialists in various backgrounds and partnership with the society in each country.

We deeply appreciate your kind consideration and cooperation, and your generous support to the 46th Congress. I sincerely hope that our friendship and continued collaboration will last forever.

I’m looking forward to seeing you again and I wish you continued success and happiness in the future.

Sincerely yours,

Masao Nakabayashi, MD.
President of the 46th International Congress on Pathophysiology of Pregnancy
Professor, Director, Imperial Gift Foundation AIIKU Maternal and Child Health Center
Uterine tamponade in management of postpartum hemorrhage — Malaysian experience

Carol Karkoong Lim

Maternal Fetal Medicine Consultant Temerloh Hospital, Malaysia

Introduction

Obstetric hemorrhage is estimated to cause 25% of all maternal deaths and is the leading direct cause of maternal mortality worldwide and accounts for 34% of maternal deaths in Africa, 31% in Asia, and 21% in Latin America and the Caribbean.\(^1\) Although active management of the third stage of labor can prevent up to 60% of postpartum hemorrhage (PPH) cases,\(^2\) PPH continues to have a devastating impact on women in low-resource settings.

In Malaysia, PPH contributed to 15.5% of maternal mortality for the years 2006–2011 (128 cases out of 826), with atony uterus comprising majority of the PPH cases. For the similar period in Japan, PPH also contributed to 15% of maternal mortality (40 cases out of 267).\(^3\) Even though the absolute number was small, PPH was nevertheless still a significant cause of maternal mortality in Japan. For the year 2010, as many as 23% of maternal deaths were a result of PPH (7 cases), of which 2 were uterine rupture, 2 uterine inversion 1 cervical laceration, 1 abruptio and 3 listed as miscellaneous.\(^4\)

Uterine tamponade

In cases of atony uterus, uterine tamponade has been advocated as one of the methods to arrest PPH. There are various uterine tamponade methods, such as external uterine compression, a combination of both external and internal uterine compression (bimanual uterine compression), uterine packing and uterine balloon tamponade using various devices.

Uterine packing was described in the 1800s. It is usually done using roller gauze or abdominal pack and has since being rarely used due to doubt on its efficacy, risk of concealed continuous bleeding, infection and traumatic insertion and removal.

Since Goldrath\(^5\) first reported the use of foley catheter for the purpose of uterine tamponade in 1983, various balloon devices have emerged to affect uterine tamponade. Some were non-specific for uterus such as urological balloons, eg Foley catheter, Rusch catheter, Sanstaken-Blackmore Esophageal Tube and condom catheter, while the newer ones were specifically designed for uterus eg. Bakri postpartum balloon, BT-Cath balloon or ebb balloon.\(^6\)–\(^11\)

The postulated mechanisms for uterine balloon tamponade include direct pressure of the balloon on placental bed to stop the bleeding from placental bed. Similarly, the balloon’s exerted pressure exceeding the arterial pressure will stop the bleeding from an arterial source in the endometrium and promote clot formation. Lastly, presence of the balloon in the uterine cavity may cause it to contract reflectively, helping to stop further bleeding.\(^12\)

Malaysian experience

Uterine balloon tamponade was first introduced in the Likas Hospital, Sabah, Malaysia in 2008, using Rusch catheter. As the department gained confidence in uterine balloon tamponade, we switched to Bakri Postpartum Balloon in April 2011. By late 2011, it was introduced to all 21 first-referral level hospitals in the state, to stabilise patients and facilitate transfer to tertiary hospitals. The same strategy was later accepted as a national policy by September 2012.

The effectiveness of uterine balloon tamponade has been reported to be 80% and above, without need for additional procedures.\(^6\)–\(^8\) In our series of initial 31 patients in Sabah, postpartum haemorrhage was controlled in 16 of 22 cases (72.7%). Of the remaining 6 patients, five required hysterectomy. There were 2 maternal deaths, one of which underwent hysterectomy while the other did not. Both were referred cases, having delivered prior to and arrived at our institute in a moribund state. In Temerloh Hospital, the second largest hospital in the state of Pahang, Bakri balloon was introduced in April 2013. The effectiveness was 90.9% (10 out of 11 cases successfully controlled) in 2013 and 100% thus far this year (12 out of 12 cases controlled).

Both Likas and Temerloh Hospitals are major hospitals in their respective states, with the former the busiest maternity hospital in the country, having more than 16,000 deliveries every year, and the latter manages about 8,000 deliveries every year. After the introduction
of Bakri balloon, the two hospitals showed a reduction in hysterectomy rate among the massive PPH patients (ie blood loss of more than 1,500 ml), which were halved after first year of Bakri postpartum balloon usage. The hysterectomy rate continued to drop in the subsequent years, as illustrated in the tables below:

There was a drop in maternal mortality following PPH in Sabah, ie from a total of 20 PPH deaths in 2011 (20 out of a total of 42 maternal mortality, 47.6%) to a total of 9 PPH deaths in 2012 (9 out of 33 maternal mortality, 27.3%). As uterine balloon tamponade was the only new changes introduced to PPH management in the state it was postulated with caution, that uterine balloon tamponade was instrumental in reducing the numbers of PPH deaths in Sabah.

**Guidelines**

As uterine tamponade was easy to apply and does not require anaesthesia, we are also in the opinion that paramedics can be trained to use uterine tamponade method, with perhaps the aid of ultrasound machine to ensure that the balloon is inserted into uterine cavity.

We also mandate vaginal packing following balloon insertion, as our initial experience had taught us that the Bakri balloon does not hold well without it. Furthermore, uterine contraction may expel the balloon. Antibiotic coverage would be on board for the duration of balloon being in-situ.

As recommended by manufacturer, we do not keep Bakri balloon beyond 24 hours. Again for our series of 31 patients, the duration of balloon insertion ranged between 2.5 hours to 54 hours (mean 18.6 hours).

Uterine tamponade is now one of the recommended measures in PPH management by many international and national authorities, such as WHO, Royal College of Obstetrics & Gynaecology (RCOG), American College of Obstetrics & Gynaecology (ACOG), Australia and more.

Beside using uterine tamponade for atony uterus case, we had also used it to manage PPH secondary to morbidly adherent placenta, placenta previa, midtrimester miscarriage, cervical ectopic pregnancy, uterine inversion and idiopathic thrombocytopenic purpura. Very often, uterine tamponade was all it needed to control the bleeding.

As for any procedure, there were reported complications with uterine tamponade. These included uterine rupture/perforation and migration of balloon following perforation. We also do not apply Bakri balloon in cases of secondary.

PPH as the etiology is often infection in origin.

**Conclusion**

From our experience of using Bakri balloon, both in the states of Sabah and Pahang, we found uterine tamponade a useful, easy and effective method. We recommend that all maternity units should equip themselves with this life-saving device as an essential part of PPH management. Beside making available the Bakri balloon, more importantly is the training and practice of application to ensure proper placement of device in time of PPH.

**References**

3. CEMD
Peri-implantation origins of pregnancy complications

Jan Brosens

Division of Translational & Systems Medicine, Warwick Medical School, University of Warwick, Coventry, CV4 7AL, United Kingdom

Peri-implantation origins of pregnancy complications

The hallmark of the human endometrium is spontaneous decidualization, a phenomenon shared with only a handful of other mammalian species. The term ‘spontaneous’ decidualization refers to the fact that this differentiation process, characterized by the transformation of endometrial stromal cells into specialized secretory cells, is under the control of endocrine rather than embryonic cues. In the human endometrium, this process is driven by the postovulatory rise in progesterone levels and increasing local cyclic AMP production. Hence, decidualization is a feature of the mid-luteal phase in all ovulatory cycles, whether they lead to conception or not.

Decidualization is a dynamic process. For pregnancy to be successful, decidualizing cells must transit through distinct functional phenotypes, characterized initially by an acute pro-inflammatory response (Phase I), which is followed by a profound anti-inflammatory response (Phase II), and finally reactivation of the inflammatory phenotype leading to tissue destruction (Phase III). The inflammatory phenotype in phase I renders the endometrium transiently receptive to embryo implantation, whereas acquisition of a mature secretory phenotype in phase II enables the endometrium to respond to individual embryos in a manner that either supports further development or facilitates early rejection. This process has been termed ‘embryo selection’. In response to a developmentally competent embryo, decidual cells induce a microenvironment that protects the conceptus against stress signals, confers maternal immune tolerance to the fetal allograft, provides a nutritive matrix for trophoblast expansion, and ensures tissue hemostasis during endovascular trophoblast invasion. By contrast, signals emanating from developmentally impaired human embryos trigger a proteotoxic stress response in decidual cells, thus enabling prompt maternal recognition and rejection.

The emerging concept of active selection of human embryos at implantation provides new insights into the cause of recurrent miscarriages. In order to sense, support or reject implantation, decidualizing cells surrounding the conceptus must expand their endoplasmic reticulum and be fully secretory. Emerging evidence indicates that failure of decidualizing cells to transit from Phase I to Phase II will lead to a prolonged window of implantation, out-of-phase implantation, and early pregnancy loss. Beyond the early stages of the implantation process, decidual cells play an important role in ensuring timely rejection of a failing pregnancy. For example, duplication of an ancestral β-luteinizing hormone gene enabled human embryos to avoid guaranteed maternal destruction by ensuring continuous ovarian progesterone production in the early stages of pregnancy through the production of beta human chorionic gonadotropin (hCG). Hence, decidual cells are a priori programmed to select against embryos that are perceived to lack fitness because of insufficient hCG production. Similarly, the transition from histiotrophic nutrition of the early conceptus to active maternal perfusion of the placenta towards the end of the first trimester of pregnancy causes dramatic changes in local oxygen tension and production of free radicals. More recently, attention has focused on the role of premature decidual senescence in the pathophysiology of preterm labor. Cellular senescence is increasingly recognized as a prominent mechanism for tissue remodeling. It is defined by stable cell-cycle arrest and senescence-associated secretory phenotype (SASP), which refers to the characteristic production of various pro-inflammatory cytokines, chemokines, and proteases. The importance of this pathway was confirmed by animal studies demonstrating that uterine deletion of tumor suppressor TP53 causes preterm birth due to premature decidual senescence. In human samples, expression in the decidua of senescence markers, such as senescence-associated beta-galactosidase or phosphorylated histone H2AX, is reportedly a hallmark of PTL and not associated with other obstetrical disorders, such as preeclampsia.

The direct consequence of spontaneous decidualization is cyclic tissue destruction and menstruation in response to falling progesterone levels. As a consequence, the human endometrium undergoes waves of shedding and regeneration, which depends — as is the case for most tissues — on recruitment, mobilization and differentiation of resident stem cells. While as yet speculative, it seems likely that deficiency or impaired programming of stem/progenitor cells in the endometria...
niche compromises the responsiveness of stromal cells to decidualogenic cues, accelerates replicative senescence, and predispose for subsequent pregnancy failure. If substantiated, than assessment of the endometrium prior to conception may identify women at increased risk of pregnancy complications.

References

Pathways to preterm birth

David M. Olson

Department of Obstetrics and Gynecology, University of Alberta, Canada

Synopsis: Preterm birth is a syndrome involving the inflammatory pathway. New, effective, and inexpensive diagnostics and therapeutics based on convergence points of this pathway are being developed to predict and mitigate risk for preterm birth.

Preterm birth is a complex problem or syndrome of several etiologies; it is not one disease. These include stress, inflammation or infection, placental abruption, multiple births, genetics or others. Regardless of the original insult or causal origin, these various etiologies will converge on a common series of steps or a ‘birth cascade’ of pathways that will result in transforming the uterus of pregnancy to the uterus of delivery.

Uterine transformation is the sum total genetic, cellular and physiological changes the uterus must undergo to transform from pregnancy to delivery. Approximately 800 genes change their expression (increase or decrease) in preparation for labour in the human myometrium (Dr. RL Jones, personal communication). We have summarized this complex process into three stages: positive feedback, synergy and amplification. Positive feedback (or feed-forward) occurs when agonists or stimulators that are central to the process of transformation affect their own synthesis and or action. For instance, Dr. Tomohito Ishiguro from Juntendo University demonstrated that over the last five days of pregnancy in the Long Evans rat that the uterine receptors for interleukin (IL)-1β, IL-1RI and its accessory protein, AcP, mRNA expression increased while IL-1RII (a decoy receptor) expression decreased.1) These changes were dependent upon progesterone status. Kelycia Leimert and Dr. Chen Xu demonstrated that IL-1β also induces a number of cytokines, chemokines and many prostaglandins (PGs) through its actions on their synthetic enzymes and on the receptors of these mediators, including the PGF2α receptor, FP.2,3) PG F2α, in turn, stimulates many of the same cytokines, including IL-1β, its IL-1RI and AcP, plus chemokines, and COX-2. Hence, positive feedback propels the transformation process toward labour.2,3)

Synergy occurs when the action of two or more agonists is greater than the sum of each agonist alone. Kelycia Leimert in our group demonstrated that PGF2α plus IL-1β stimulated increases of 240-fold for IL-6 and 80-fold for COX-2. This contrasts to 8- and 70-fold changes, respectively, when each agonist is administered alone for IL-6 and 5- and 40-fold changes for COX-2 when each is administered separately.4) It is highly probable that these agonists (and many more) are temporally synergistic during uterine transformation.

Amplification is defined as the increased or amplified effect of additional cytokine and PG mediators released from invading leukocytes. The release of chemokattractants during transformation attracts circulating peripheral leukocytes to the uterine tissues where they infiltrate, attach and release additional mediators. Our colleague, Prof. Xin Ni of the Second Military Medical University in Shanghai, has demonstrated that another of the mediators of uterine transformation, corticotrophin releasing hormone, or CRH, stimulates myometrial cells to release a chemokattractant that attracts monocytes.5) Dr. Nanlin Yin in our lab has similar data with IL-1β.

Dr. Jun Takeda from Juntendo University studied the release by the uterus of the chemokattractant that summons peripheral leukocytes for amplification before every delivery at term and preterm. He developed the Leukocyte Migration Assay6) by using an extracted chemokattractant from fetal membranes, peripheral leukocytes from pregnant or delivering women, and a Boyden chamber. He has shown that the migration of peripheral leukocytes from pregnant subjects increases the closer women get to delivery. The test has excellent positive (> 90%) and negative predictive values (> 75%) within 7 days of delivery. It can be used to assess risk not only in asymptomatic women, but it has considerable utility to be used in symptomatic women, of whom only 10–20% will deliver early. Those women who will not deliver preterm within a week should, in most cases, be sent home from hospital to continue their pregnancies to full term and save unnecessary hospital costs.

We have used these points of pathway conversion and key mediators in uterine transformation to identify targets for the prevention of preterm delivery. Drs. Christiane Quiniou, William Lubell and Sylvain Chemtob of the
Universite de Montreal have designed short peptide allosteric receptor antagonists using all-

-d amino acids (to diminish degradation) that block selected actions of key receptors and delay preterm delivery in mice. The heptapeptide, 101.10,7) antagonizes the IL-1β receptor accessory protein, IL-1RAcP in blocking LTA and IL-1β-induced preterm birth in mice. Also, it has been used as an anti-inflammatory to effectively block LTA-induced decreases in microvascular density in the brains of newborn mice, which suggests it could protect the human fetus against infection due to chorioamnionitis. Three generations of antagonists to the PGF2α receptor, FP,

also have been developed by this team: the octapeptide, PDC31,8) the azabicycloalkanone, 113.824,9) and the azapeptide, CAR 10.0.2) They all prevent LPS-induced preterm delivery in mice. With each generation, the FP antagonists have become more specific in their actions, synthesis becomes simpler, and the molecular size of the compound decreases, thereby raising its global access to women.

In summary, new diagnostics and new therapeutics work in tandem to identify and treat women at risk of preterm delivery.

References

1. Ishiguro T, Bronson H, Takeda J, Fang X, Olson DM. Interleukin (IL)-1 receptor 1 and IL-1 receptor accessory protein increase at delivery in rat uterus. Reprod Sci. 2014; 21(3 Suppl): 238A. Abstract.

Figure 1. Summary of the process of uterine transformation from pregnancy to delivery.
Preeclampsia complicated by other medical disorders

Sanjay Gupte

Introduction

Hypertension in pregnancy can be a result of chronic disease or a new onset hypertension in the second half of pregnancy. In either situation there is an increased risk of maternal and perinatal morbidity and mortality. Prevalence of chronic hypertension in pregnancy is estimated to be about 3%.1–3)

Definition and magnitude of the problem

Chronic hypertension in pregnancy is defined as a blood pressure (BP) of at least 140 mmHg systolic or 90 mmHg diastolic before pregnancy, or before 20 weeks of gestation. 90 to 95% of cases of chronic hypertension are considered to be essential or idiopathic. Secondary causes account for approximately 5–10%.

Causes of secondary hypertension

Vascular Disorders
• Renovascular hypertension
• Aortic coarctation

Endocrine Disorders
• Diabetes mellitus
• Hyperthyroidism
• Pheochromocytoma
• Acromegaly
• Cushing’s syndrome
• Conn’s syndrome

Renal Disorders
• Diabetic nephropathy
• Reflux nephropathy
• Chronic glomerulonephritis
• Nephrictic and nephrotic syndrome
• Polycystic kidney

Connective Tissue Disorders
• Systemic lupus erythematosus
• Systemic sclerosis
• Polyarteritis nodosa
• Rheumatoid disease

I would like to share our experience with cases of chronic hypertension in three different categories
1. Hypertension in pregnancy as essential hypertension
2. Hypertension in pregnancy secondary to SLE
3. Hypertension in pregnancy with diabetes mellitus

5 years review of cases of chronic hypertension

Gupte Hospital & Centre for Research in Reproduction institute, 2008 to 2013

<table>
<thead>
<tr>
<th>Total number of cases</th>
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<tbody>
<tr>
<td>Chronic hypertension</td>
<td>185  (2.96%)</td>
</tr>
<tr>
<td>Essential hypertension</td>
<td>164  (88.64%)</td>
</tr>
<tr>
<td>Renal diseases</td>
<td>6    (3.2%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8    (4.32%)</td>
</tr>
<tr>
<td>SLE</td>
<td>4    (2%)</td>
</tr>
<tr>
<td>Others</td>
<td>3    (1.62%)</td>
</tr>
</tbody>
</table>

Cases of essential hypertension-sub groups

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Total number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosed preconceptionally</td>
<td>55 (33.53%)</td>
</tr>
<tr>
<td>Diagnosed during early pregnancy</td>
<td>98 (59.75%)</td>
</tr>
<tr>
<td>Diagnosed after pregnancy</td>
<td>11 (6.70%)</td>
</tr>
</tbody>
</table>

Outcome

| Developed preeclampsia                       | 32 (19.51%)           |
| Severe preeclampsia with early termination   | 8 (4.87%)             |
| Eclampsia                                    | 1 (0.6%)              |
| HELLP                                        | 3 (1.82%)             |
| Abruptio placentae                           | 2 (1.21%)             |

Risks to mother and fetus

Chronic hypertension during pregnancy can lead to major
maternal risks including—
• Increased frequency of preeclampsia (17–25%)
• Intrauterine growth restriction (IUGR) (10–20%)
• Preterm birth (30%)
• Placental abruption (RR 2.5)
• Stillbirth (RR 2.3)
• Increased rate of Cesarean delivery

Principles of Management of Chronic Hypertension In Pregnancy
Management of women with hypertensive disease in pregnancy aims at preventing further complications, avoiding unnecessary prematurity and optimizing maternal and infant outcomes. The treatment goals for chronic hypertension in pregnancy are different from the goals of the treatment of hypertension in non-pregnant patients. BP control is essential; so is aggressive attention to other cardiovascular risk factors, such as blood lipid & glucose levels, body weight, & smoking essential. The care of women with chronic hypertension should begin before pregnancy. Preconception-counseling and preparations are necessary for optimal control of BP. Medications may need to be changed before conception to reduce risk of fetal anomalies. In very high risk situations, pregnancy may need to be discouraged or postponed until maternal condition has improved. Management includes ruling out and treating secondary causes of hypertension. Careful evaluation for evidence of target organ damage may be required.

Some grey areas—Exercise
Pregnant hypertensive women, in contrast to their non-pregnant counterparts, are not advised to exercise vigorously. They can be advised to do moderate exercise e.g. walking 3–5 times a week. The main concern in this is that women with chronic hypertension are at risk for preeclampsia, and as such vigorous exercise may compromise blood flow.

Antihypertensive therapy
Currently guidelines for antihypertensive therapy during pregnancy are less clear than those for non-pregnant hypertensive women. For the later, compelling data from large population studies document the benefits of lowering blood pressure with medication, even in women with only mild hypertension. During pregnancy maternal safety remains the primary concern; there is also a desire to minimize exposure of fetus to drugs.4)

Controversy
There is a controversial issue whether lowering blood pressure prevents superimposed preeclampsia. No convincing evidence is available to support this contention. It is permissible to tolerate higher blood pressure levels during pregnancy in such cases that do not harm in the short term while limiting use of antihypertensive drugs.

A Cochrane systematic review with meta-analysis of 28 randomized trials comparing anti-hypertensive treatment either with placebo or with no treatment showed that antihypertensive treatment significantly reduced the risk of severe hypertension. However, treatment did not reduce the risk of superimposed preeclampsia, placental abruption or growth restriction, nor did it improve neonatal outcomes.5)

CHIPS Trial
Recently completed control of hypertension in pregnancy study (CHIPS) - a multicenter randomized controlled trial looking at non-severe, non-proteinuric hypertension has concluded that “tight” control (target diastolic BP 85 mmHg) was better than “less tight” control (target diastolic BP 100mm of Hg); as far as hypertensive complications are concerned. And “tight” control does not lead to adverse effect on the feto-maternal circulation.6)

The goal of antihypertensive therapy in women with essential hypertension is to keep the systolic BP between 130/155 mm of Hg and diastolic BP between 80/105 mm of Hg. For pregnant women with end organ damage secondary to hypertension, the aim should be to keep the BP lower than 140/90 mmHg. For women whose antihypertensive therapy is continued, aggressive lowering of BP should be avoided.

Fetal Surveillance
Hypertension in pregnancy can have significant impact on fetal well-being. Chronic utero-placental insufficiency may result in FGR and oligohydramnios. Oligohydramnios in turn may result in loss of protection of the umbilical cord from mechanical compression.7)

Intrapartum & Post-Partum Care
Early delivery may become necessary in cases of maternal complications such as worsening hypertension or disease, non-assuring fetal testing or severe fetal growth restriction. Syntometrine or ergometrine should be avoided for the active management of third stage to avoid its pressor effects.

Secondary hypertension due to Autoimmune problems during pregnancy
Systemic lupus erythematosus
It is a chronic inflammatory disease with potential multisystem involvement. For SLE Female affection is 9 times more than males. It may first appear during pregnancy. It is seen that women who have had an unexplained II trimester stillbirth, a fetus with growth restriction, preterm delivery, or recurrent spontaneous
abortions are often later diagnosed with SLE. It may worsen, particularly immediately postpartum.

The case

There was a patient 28 yrs. old female married since 1 yr k/c/o SLE since 2007, on Prednisolone and Azathioprine with no complaints then. She was primi-gravida with 16 weeks pregnancy. Her Past history was–She was diagnosed to have SLE in Feb. 2007 when she had fever, anorexia. She was then detected to have proteinuria, hemolytic anaemia and dsDNA antibody positive status. She was admitted and started on injectable steroids and then shifted to oral prednisolone 60 mg/day. She developed Cushingoid features which resolved after tapering the dose. She had a relapse in 2009 and she required blood transfusion. She had convulsions during the same course for which CT brain was done. It showed venous infarcts. She also developed hypertension for which she was put on envas and stamlo. She was given eptoin and endoxan. She developed non healing ulcer on right foot for which debridement and later on skin grafting was done. Since then she is in a remission phase and taking prednisolone 5 OD and Azathioprine 50 OD.

Investigations

<table>
<thead>
<tr>
<th>Haemogram:</th>
<th>WNL</th>
<th>HIV</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>NAD</td>
<td>VDRL</td>
<td>Negative</td>
</tr>
<tr>
<td>LFTs</td>
<td>WNL</td>
<td>HbsAg</td>
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</tr>
<tr>
<td>RFTs</td>
<td>NAD</td>
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<tr>
<td>ANA</td>
<td>Neg</td>
<td></td>
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</tr>
</tbody>
</table>

She was allowed pregnancy. She developed early onset severe preeclampsia and also had fetal growth restriction with severe oligohydramnios. She was delivered at 29 & half weeks. The baby did well in NICU. She remained in remission but required increased doses of anti hypertensives.

Presentation

SLE may present to the obstetrician as, a known case or as symptoms for the first time in pregnancy, symptoms for the first time in the puerperium, subfertility or recurrent abortions, abnormal laboratory results like false positive VDRL, Neonates with congenital heart block or lupus like syndrome.

Exacerbations during pregnancy is seen in 33% patients.

Diagnosis

American Rheumatism Association criteria (Presence of at least 4 of following 11 criteria is necessary)
1. Facial butterfly rash.
2. Discoid lupus.
3. Photosensitivity.
4. Oral or nasopharyngeal ulceration.
5. Non-erosive arthritis involving 2 or more peripheral joints.
6. Pleurisy or pericarditis.
7. Proteinuria > 0.5 g/day or cellular casts.
8. Psychosis or convulsions.
9. Hematological abnormalities e.g. Thrombocytopenia, leucopenia,
10. Immunological disorder.
11. Antinuclear antibody.

Complications

Complications may include
• Fetal wastage- 10% (highest in females with LA)
• IUGR and intrauterine death-8%.
• Severe preeclampsia
• Congenital heart block due to maternal antibodies that cross the placenta.
• Significant preexisting renal or cardiac complications increase risk of maternal morbidity and mortality.
• Diffuse nephritis, hypertension, or the presence of circulating antiphospholipid antibodies increase risk of perinatal mortality.

Management

There is an unfortunate myth that pregnancy is contraindicated in SLE. The early work of Merrel and Schulman reported median survival of less than 4 yrs in SLE. Several advances like corticosteroids, immunosuppressants, serological analysis, early diagnosis and improved antenatal and neonatal care and surveillance have transformed long term outlook for women with SLE.

Our experience-

Gupte Hospital & Centre for Research in Reproduction institute

36 cases of SLE have been managed in last 32 years.
• 3 were advised to avoid conception.
• 18 developed Preeclampsia
• 5 had adverse fetal outcome.
• 4 showed post-partum exacerbation.
Rest all were in remission and had an uneventful course.
Diabetes and Hypertensive Disorders of Pregnancy
The pregnant women with diabetes are at considerable higher risk for HDP than women without diabetes. About 20% of pregnant diabetic women suffer from Gestational Hypertension or Pre-eclampsia. The patients at the highest risk are those with underlying microvascular complications, pre-existing hypertension or poor glycemic control.

Pre-eclampsia was five times more frequent & GH was twice as frequent in women with T1DM without nephropathy as nondiabetic control in a Finnish study. Gestational diabetes mellitus also increases a women’s risk for HDP. After adjustment for maternal age & BMI, GDM predisposes to an approximately 1.5-fold increase risk of GH or pre-eclampsia.

Kventy et al. noted that the serious complications (perinatal mortality, malformations, acute cesarean section) appeared with a higher frequency in women with GH & GDM (10%) than in women with GH but with normal OGTT (2%) \( (P=0.0083) \).

To Summarize
GDM & Diabetes Mellitus are significant high risk factors for Preeclampsia during pregnancy.

In Conclusion
Chronic hypertension during pregnancy either idiopathic or due to secondary causes like autoimmune diseases or diabetes mellitus increases chances of complications & perinatal mortality & morbidity. Hence every woman should be evaluated prior to conception or earliest in her pregnancy to define her BP status, and if hypertensive, one should assess its severity, possible secondary causes, and the presence of target organ damage, and to plan treatment strategies carefully.

References
1. WHO recommendations for Prevention & treatment of pre-eclampsia and eclampsia.