PRIMARY PULMONARY ARTERIAL HYPERTENSION AND PREGNANCY
HOW PREPARED ARE WE?

“When you change the way you view birth, the way you birth will change.”

~Marie Mongan

DR TARAKESWARI S
DR SUBHASHINI Y
• **Pulmonary hypertension** (PH) is an increase of blood pressure in the pulmonary artery, pulmonary vein, or pulmonary capillaries, together known as the lung vasculature

• It was first identified by Ernst von Romberg in 1891

• The estimated incidence of PAH in pregnancy is 1.1/100000
WHO Definition: Group I PAH

• Upon cardiac catheterization:
  – Pulmonary artery mean pressure $\geq$ 25 mm Hg
  – Pulmonary capillary wedge pressure (or left atrial or left ventricular end-diastolic pressure) $< 15$ mm Hg,
  – Pulmonary vascular resistance $> 3$ Wood units (or 240 dynes-second-cm)

No significant pulmonary parenchymal, airway, or thromboembolic disease

Clinical Classification of Pulmonary Hypertension (Dana Point)

1. PAH
   - Idiopathic PAH
   - Heritable
   - Drug- and toxin-induced
   - Persistent PH of newborn
   - Associated with:
     - CTD
     - HIV infection
     - portal hypertension
     - CHD
     - schistosomiasis
     - chronic hemolytic anemia

1'. PVOD and/or PCH

2. PH Owing to Left Heart Disease
   - Systolic dysfunction
   - Diastolic dysfunction
   - Valvular disease

3. PH Owing to Lung Diseases and/or Hypoxia
   - COPD
   - ILD
   - Other pulmonary diseases with mixed restrictive and obstructive pattern
   - Sleep-disordered breathing
   - Alveolar hypoventilation disorders
   - Chronic exposure to high altitude
   - Developmental abnormalities

4. CTEPH

5. PH With Unclear Multifactorial Mechanisms
   - Hematologic disorders
   - Systemic disorders
   - Metabolic disorders
   - Others

The physiologic changes that occur during pregnancy & the peripartum period are poorly tolerated in these patients.
Maternal Mortality

- High maternal mortality: 30 - 56%

- Acute conditions associated with pregnancy: pulmonary and amniotic fluid embolism.

- Majority of maternal deaths occur during labor or within 1 month postpartum

Practice guidelines from the European Society of Cardiology and the American College of Cardiology/American Heart Association strongly discourage pregnancy in these patients and advise termination should pregnancy occur.

• Earlier recognition of the underlying disease
• Improved understanding of cardiopulmonary pathophysiology
• Better obstetric/anaesthetic management
• Introduction of a multidisciplinary approach
Aim

- We present our clinical experience with idiopathic pulmonary arterial hypertension complicating pregnancy and their outcomes.
Material and methods

- Retrospective analysis
- Electronic database
- January 2000 to 2014
- Fernandez Hospital, Hyderabad
- Tertiary referral perinatal unit
- 8000 deliveries annually
The Team

• Obstetrician
• Cardiologist
• Anaesthetist
• Critical care
• Physician
• Neonatologist
Diagnosis

• 2D ECHO

• ECG

• CHEST XRAY
2D ECHO

- Echocardiography is a crucial screening tool in the diagnosis of PAH.

- An estimated RVSP $\geq$ 35 mm Hg

- Evidence of right heart pressure overload
  - Right atrial enlargement
  - Right ventricular enlargement
  - Hypertrophy or dysfunction
  - Significant tricuspid regurgitation

- Normal left heart structure and function, especially normal left atrial size

• Right heart catheterization is required for a definite diagnosis of PAH, to determine the severity of the disease, to assess the prognosis and to select the appropriate treatment.

• Pulmonary Arterial Hypertension (PAH) is a disorder defined by measuring mean pulmonary arterial pressure above 25 mmHg on Right Heart Catheterization (RHC).
Statistical Analysis

• Numerical values are presented as median(range) and categorical variables as number(percentage of total available group)
## Patient Population

<table>
<thead>
<tr>
<th>MEDIAN AGE</th>
<th>23 YR (22-28)</th>
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<tbody>
<tr>
<td>GRAVIDA</td>
<td>2 (1-4)</td>
</tr>
<tr>
<td>PARA</td>
<td>1 (0-2)</td>
</tr>
<tr>
<td>REFERALS</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>LATE BOOKING</td>
<td>3 (50%)</td>
</tr>
<tr>
<td>PRE-PREG COUNSELLING</td>
<td>1 (16%)</td>
</tr>
<tr>
<td>Δ BEFORE PREG</td>
<td>2 (33%)</td>
</tr>
<tr>
<td>Δ DURING PREG</td>
<td>4 (67%)</td>
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<tr>
<td>SEVERE PAH</td>
<td>4 (67%)</td>
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## Baseline Characteristics

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<tr>
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<tr>
<td><strong>NYHA CLASS III-IV</strong></td>
<td>3 (50%)</td>
</tr>
<tr>
<td><strong>SpO2 DURING PREG(%)</strong></td>
<td>96 (93-100)</td>
</tr>
<tr>
<td><strong>Hb DURING PREG</strong></td>
<td>9.4 (8-11.8)</td>
</tr>
<tr>
<td><strong>RVSP (mm Hg)</strong></td>
<td>85 (43-100)</td>
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<tr>
<td><strong>PAP systolic (mmHg)</strong></td>
<td>94-103</td>
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## Management

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<tbody>
<tr>
<td><strong>GESTATIONAL AGE AT HOSPITALIZATION</strong></td>
<td><strong>32 (29-37)</strong></td>
</tr>
<tr>
<td><strong>DELIVERY(WEEK)</strong></td>
<td><strong>33 (30-37)</strong></td>
</tr>
<tr>
<td><strong>MODE: CS</strong></td>
<td><strong>6 (100%)</strong></td>
</tr>
<tr>
<td><strong>MODE: VD</strong></td>
<td><strong>0 (0%)</strong></td>
</tr>
<tr>
<td><strong>ANTENATAL STEROIDS</strong></td>
<td><strong>4 (66%)</strong></td>
</tr>
<tr>
<td><strong>TUBECTOMY</strong></td>
<td><strong>1 (17%)</strong></td>
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</tbody>
</table>
An arterial line and a central venous catheter for the monitoring of right atrial pressure should be considered for parturients with PAH.

Invasive pulmonary arterial pressure monitoring remains controversial, owing to associated complications such as pulmonary artery rupture.
Anti – Thrombotic Therapy

- Low-dose subcutaneous heparin prophylaxis is generally recommended in pregnant women as warfarin is teratogenic

- Patients with a history of thromboembolic events or atrial fibrillation require higher dose

- All pt received postpartum thromboprophylaxis

- Warnes CA. Pregnancy and pulmonary hypertension. Int J Cardiol 2004;97(Suppl.1)
## Therapeutic Options for PAH

<table>
<thead>
<tr>
<th>Traditional Rx</th>
<th>FDA Approved for PAH</th>
<th>Investigational Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplemental O₂</td>
<td>Prostanoids - epoprostenol - treprostinil - inhaled iloprost</td>
<td>Prostanoids - inhaled treprostinil</td>
</tr>
<tr>
<td>Diuretics</td>
<td>ERAs - bosentan</td>
<td>ERAs - sitaxsentan - ambrisentan</td>
</tr>
<tr>
<td>Oral vasodilators - (CCB)</td>
<td>PDE-5 inhibitors - sildenafil</td>
<td></td>
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<tr>
<td>Anticoagulants - warfarin</td>
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<tr>
<td>Inotropic agents - digitalis</td>
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</tbody>
</table>
Sildenafil Citrate Therapy for Pulmonary Arterial Hypertension

Nazzareno Galiè, M.D., Hossein A. Ghofrani, M.D., Adam Torbicki, M.D., Robyn J. Barst, M.D., Lewis J. Rubin, M.D., David Badesch, M.D., Thomas Fleming, Ph.D., Tamiza Parpia, Ph.D., Gary Burgess, M.D., Angelo Branzi, M.D., Friedrich Grimminger, M.D., Marcin Kurzyna, M.D., and Gérald Simonneau, M.D., for the Sildenafil Use in Pulmonary Arterial Hypertension (SUPER) Study Group

Sildenafil inhibits phosphodiesterase type 5, an enzyme that metabolizes cyclic guanosine monophosphate, thereby enhancing the cyclic guanosine monophosphate–mediated relaxation and growth inhibition of vascular smooth-muscle cells, including those in the lung.

Sildenafil improves exercise capacity, WHO functional class, and hemodynamics in patients with symptomatic pulmonary arterial hypertension.
• Animal studies on sildenafil and two case reports on humans have reported no deleterious effects on the mother or offspring.

_Villanueva-Garcia D, Mota-Rojas D, et al_.
In our series

• Five of the patients were on sildenafil and 1 was on tadalafil (both cGMP-specific phosphodiesterase type 5 inhibitors).

• Prostacycline analogues (epoprostenol, treprostinil, iloprost)

• Endothelin receptor antagonists (Bosentan, Ambrisentan)

• Inhaled NO

• Calcium channel blockers (amlodipine, diltiazem, nifedipine)
Outcomes

- **Premature delivery:** 33.6 wks
- **Postpartum discharge (day):** 5(3-6)
- 2 pt went LAMA

- **Other complications**
  - No Pulmonary hypertensive crisis
  - No Pulm thromboembolism
  - RV failure (33%)
  - Fall in HB+ transfusion (30%)
Maternal mortality

- There was one maternal death in 2000 with severe therapy resistant circulatory collapse following postpartum hemorrhage within 5 hours of delivery.
Neonatal outcomes

- 33% of neonates had fetal growth restriction
- The average wt at birth was around 1.8 Kg with good APGARs
- Neonatal jaundice requiring phototherapy was the most common reason for stay along with need of preterm care.
Contraception

• Discussing methods of birth control is crucial

• Permanent methods such as tubal ligation can also be recommended

• Nulliparous- Progesterone IUCD, Barrier

• Tubectomised: 16%

Contemplating back…

- Higher rates of caesarean section and premature delivery compared with literature review

- Closer surveillance and a lower threshold for intervention with early signs of maternal or foetal distress may have resulted in same, however we speculate, better outcomes.
Long term follow up

• All the above mothers are continuing their lifelong medications under follow up with their cardiologist and did not report any new cardiac events warranting admissions.

• However one pt has had a second successful delivery elsewhere.

• All the six children are doing well with no morbidities or neurodevelopment delays.
## Literature review

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Type of delivery</th>
<th>Anesthesia</th>
<th>Medical treatment</th>
<th>Maternal mortality</th>
<th>Fetal mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedard et al. [5]</td>
<td>73 IPAH=29CHD=28OPH=15</td>
<td>Vaginal 7-30%; CS 70-93%</td>
<td>Regional 28-87%; General 29-43%</td>
<td>PC 20-62%; NO 24-33%; S 0-14%; CCB 21-31%</td>
<td>17-33%</td>
<td>10-13%</td>
</tr>
<tr>
<td>Kiely et al. [15]</td>
<td>10</td>
<td>CS</td>
<td>Regional</td>
<td>IV PC 40%; INH PC 100%; S 30%</td>
<td>10%</td>
<td>0</td>
</tr>
<tr>
<td>Smith JS et al. [32]</td>
<td>5</td>
<td>Vaginal 60%; CS 40%</td>
<td>NA</td>
<td>IV PC 100%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jais X et al. [18]</td>
<td>20</td>
<td>Vaginal 5%; CS 95%</td>
<td>Regional 80%; General 20%</td>
<td>IV PC 15%; SC PC 5%; INH PC 15%; S 20%; CCB 40%</td>
<td>20%</td>
<td>10%</td>
</tr>
<tr>
<td>Duarte et al. [16]</td>
<td>12</td>
<td>CS 100%</td>
<td>Regional 66%; General 25%</td>
<td>IV PC 41%; SC PC 8%; S 33%</td>
<td>16.7%</td>
<td>0</td>
</tr>
<tr>
<td>Rabin Medical Center [31]</td>
<td>9</td>
<td>CS 100%</td>
<td>Regional 20%; General 80%</td>
<td>IV PC 88%; S 55%</td>
<td>22%</td>
<td>0</td>
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</table>

IPAH: Idiopathic Pulmonary Arterial Hypertension; CHD: Congenital Heart Disease; OPH: Other causes of Pulmonary Hypertension; CS: Caesarean Section; PC: Prostacyclin; NO: Nitric Oxide; S: Sildenafil; CCB: Calcium Channel Blockers; NA: Not Available.

Table 1: Recent published series in the literature.
Conclusion

- Maternal mortality in parturients with PAH remains prohibitively high despite the enormous progress made in recent years' knowledge and therapy & lower death rates over previous era

- Early advice on the risks of pregnancy and methods of contraception is, thus, paramount
• Women must balance the best estimate of risk with the value they put on pregnancy

• The decision of patient to continue pregnancy should be supported by an empathetic group of health care professionals who would optimize the treatment and hopefully pregnancy outcomes and survival after delivery.
BATTLE CONTINUES....

- Mrs R, 27, G2A1, IDA
- Dec 2013 Combined obs med counselling - to avoid pregnancy
  was on bosentan, acitrom, NYHA-II
- Booked in July 2014 @ 7 WK
- Continued ANC on sildenafil, clexane, LDA.
- Admitted at 28 wk in v/o early RHF, RVSP-72
- EmCS > antenatal steroid cover on 23/02/15
- Restarted on bosentan postop along with sildenafil, lasix, inotrope support
- Mch, 1.48, 5/8/9 apgar, shifted to mother side on 11 pod.
Take home message

• Development of unexplained shortness of breath in pregnant woman may be the first symptom of PAH: Do 2D ECHO!

• In selected cases, despite the risk, follow-up and intensive therapy by a multidisciplinary team can control pulmonary pressure during pregnancy and allow the woman to give birth safely