Spontaneous preterm birth and cervical length in a pregnant Asian population

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Declaration of interests

• None
Introduction – Preterm Birth

• All births before 37 weeks of completed gestation
• Incidence: 5-13%
• Etiology: multifactorial
  – Syndrome initiated by multiple mechanisms
  – Many clinical risk factors (low isolated or combined predictive value)
  – Cause unidentified in up to half of all cases
Prematurity - Burden of disease

- Leading cause of neonatal death.
- Babies born a few weeks early are 6 times more likely to die in their first week of life than full-term babies.
- Many survivors of preterm birth are at increased risk for neonatal health complications and lasting disabilities.

Causes of neonatal mortality, year 2001-2010, KKH. Data courtesy of Department of Neonatology, KKH.
Aims of study

• To determine the rate of spontaneous preterm birth
• To analyse the distribution of cervical length
• To analyse the relationship between preterm birth and cervical length

in the pregnant Asian population
Methods - Participants

- Neonatal and Obstetrics Risk Assessment (NORA) prospective cohort study
- Women with single viable pregnancies at less than 14 weeks of gestation recruited between September 2010 and November 2013
- Exclusion criteria:
  - Multiple gestation
  - Chronic medical conditions such as renal disease or autoimmune diseases
  - Pregnancies complicated by aneuploidy or fetal anomaly
Methods - Follow-up

• From recruitment till their postnatal discharge from the hospital

• Antenatal visits:
  1. Visit 1 (V1) – less than 14+0 weeks of gestation
  2. Visit 2 (V2) – 18+0 to 22+0 weeks of gestation
  3. Visit 3 (V3) – 28+0 to 32+0 weeks of gestation
  4. Visit 4 (V4) – 34+0 weeks of gestation and above
Methods - Cervical length measurement
(Fetal Medicine Foundation protocol)

- Empty bladder
- Place woman with legs abducted for full range of movements whilst scanning.
- Ultrasound transducer: 5MHz transvaginal probe. Disposable sheath to cover the probe and use of sterile lubricating gel.
- Gently place probe in the anterior vaginal fornix for sagittal view of the cervix
- Identify internal os, external os, cervical canal and endocervical mucosa. Endocervical mucosa used to define level of internal os. Distinguish between cervical canal and thickened lower uterine segment coming together in the midline, which can give false impression of a longer canal.
- Do not exert undue pressure on the cervix as this will falsely elongate the cervix.
- Magnify picture so that cervix occupies at least 75% of image
- Measure distance between internal and external os. Take 3 measurements (and pictures) over 3 minutes and record best shortest measurement of cervical length.
- Note possible presence of funneling at the internal os. Endocervical mucosa will give an accurate definition of the amount of funneling. Occasionally a thickened lower uterine segment can mimic a funnel and this can be identified by the absence of mucosa extending along the walls of the funnel.
- Note dynamic changes in the cervix, defined by the appearance and disappearance of funneling during the scan.
3271 (100%) patients were screened for eligibility (September 2010 to November 2013)

2820 patients were eligible

1013 (35.9%) patients recruited

934 (92.2%) patients completed all 4 antenatal follow-up visits

Antenatal visits
V1: 11-14 weeks
V2: 18-22 weeks
V3: 28-32 weeks
V4: >34 weeks

451 (13.8%) ineligible patients

1807 (64.1%) patients refused

68 (6.5%) patients lost to follow-up
Before V1: 15 (22.7%)
After V1: 32 (48.5%)
After V2: 12 (18.2%)
After V3: 7 (10.6%)

13 (1.3%) patients had miscarriages
Before V1: 8 (61.5%)
After V1: 4 (30.8%)
After V2: 1 (7.7%)

17 (1.8%) patients delivered at other institutions

917 (98.2%) patients delivered at our institution

926 (99.1%) patients with study outcomes

9 (52.9%) patients had delivery data retrieved via phonecall
Prevalence of spontaneous preterm birth

**PATIENTS WITH COMPLETED VISITS**

*n= 926 (100%)*

- **Preterm Birth (PTB)**  
  - ≤ 37 Weeks  
  - *n= 62 (6.7%)*

  - **Iatrogenic PTB**  
  - 24 (38.7%)

  - **Spontaneous PTB**  
  - 38 (61.3%)

- **PPROM**  
  - 13 (34.2%)

- **Spontaneous onset of labour**  
  - 25 (65.8%)

- **Term Birth**  
  - *n= 864 (93.3%)*

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**Gestational Age at Delivery (weeks)**

<table>
<thead>
<tr>
<th>Gestational Age at Delivery (weeks)</th>
<th>Extreme preterm</th>
<th>Very preterm</th>
<th>Moderate preterm</th>
<th>Late preterm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous Preterm Birth</td>
<td>2 (5.1%)</td>
<td>1 (2.6%)</td>
<td>7 (17.9%)</td>
<td>29 (74.4%)</td>
</tr>
</tbody>
</table>

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**Obstetrics & Gynaecology**

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## Median cervical length - Overall

|  | Median cervical length (cm)  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=911)</td>
</tr>
<tr>
<td>V1</td>
<td>3.10 (± 0.63)</td>
</tr>
<tr>
<td>V2</td>
<td>3.19 (± 0.75)</td>
</tr>
<tr>
<td>V3</td>
<td>3.07 (± 0.73)</td>
</tr>
<tr>
<td>V4†</td>
<td>2.73 (± 0.82)</td>
</tr>
</tbody>
</table>

![Graph showing cervical length over gestation](image)
## Median cervical length - Ethnicity

<table>
<thead>
<tr>
<th></th>
<th>Chinese (n=462)</th>
<th>Malay (n=246)</th>
<th>Indian (n=99)</th>
<th>Others (n=104)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>V1</td>
<td>3.13 (± 0.65)</td>
<td>3.03 (± 0.61)</td>
<td>2.99 (± 0.67)</td>
<td>3.21 (± 0.58)</td>
<td>0.118</td>
</tr>
<tr>
<td>V2</td>
<td>3.22 (± 0.77)</td>
<td>3.13 (± 0.69)</td>
<td>2.97 (± 0.70)</td>
<td>3.33 (± 0.82)</td>
<td>0.009*</td>
</tr>
<tr>
<td>V3</td>
<td>3.11 (± 0.74)</td>
<td>2.95 (± 0.71)</td>
<td>2.94 (± 0.62)</td>
<td>3.13 (± 0.79)</td>
<td>0.045*</td>
</tr>
<tr>
<td>V4†</td>
<td>2.75 (± 0.82)</td>
<td>2.67 (± 0.81)</td>
<td>2.59 (± 0.85)</td>
<td>2.68 (± 0.86)</td>
<td>0.783</td>
</tr>
</tbody>
</table>

*significant at p<0.05, Mann Whitney test
ns=not significant
## Median cervical length – History of PTB

<table>
<thead>
<tr>
<th></th>
<th>Previous Preterm  (n=33)</th>
<th>No Previous Preterm (n=878)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>V1</strong></td>
<td>3.01 (± 0.66)</td>
<td>3.10 (± 0.63)</td>
<td>0.835</td>
</tr>
<tr>
<td><strong>V2</strong></td>
<td>2.92 (± 0.89)</td>
<td>3.20 (± 0.75)</td>
<td>0.050</td>
</tr>
<tr>
<td><strong>V3</strong></td>
<td>2.76 (± 0.85)</td>
<td>3.08 (± 0.72)</td>
<td>0.060</td>
</tr>
<tr>
<td><strong>V4†</strong></td>
<td>2.66 (± 0.81)</td>
<td>2.73 (± 0.82)</td>
<td>0.565</td>
</tr>
</tbody>
</table>

† only includes patients whose gestation at Visit 4 is ≤36 weeks

*significant at p<0.05, Mann Whitney test

ns=not significant
# Preterm birth and cervical length – Univariate analysis

<table>
<thead>
<tr>
<th>Median cervical length (cm)</th>
<th>Spontaneous PTB</th>
<th>Term birth</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.05 (±0.50)</td>
<td>3.10 (±0.64)</td>
<td>.425</td>
</tr>
<tr>
<td>V1</td>
<td>3.03 (±1.34)</td>
<td>3.20 (±0.71)</td>
<td>.028*</td>
</tr>
<tr>
<td>V2</td>
<td>2.43 (±0.88)</td>
<td>3.10 (±0.71)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>V3</td>
<td>2.21 (±0.73)</td>
<td>2.74 (±0.82)</td>
<td>.072</td>
</tr>
</tbody>
</table>

*significant at p<.05 using Mann-Whitney U test
† only includes patients whose gestation at Visit 4 is ≤36 weeks.
ROC analysis

• ROC curve for cervical length as a predictor of preterm birth at 18 to 22 weeks gestation

At cervical length cut-off of 2.48 cm:
Sensitivity = 29.0%,
Specificity = 90.1%,
NPV = 96.5%,
PPV = 12.0%
(Prevalence is 4.3%)

AUC = 0.605
**ROC analysis**

- ROC curve for cervical length as a predictor of preterm birth at 28 to 32 weeks gestation

  At cervical length cut-off of 2.49 cm:
  - Sensitivity = 54.8%,
  - Specificity = 82.5%,
  - NPV = 97.9%,
  - PPV = 11.1%
  (Prevalence is 4.3%)

  ![ROC Curve](image)

  - AUC = 0.725
Discussion

- First large prospective study in an Asian population regarding cervical length and preterm birth
- Results show a significantly shorter cervical length in the 2nd and 3rd trimester in the preterm birth group with a recommended cut-off value of 2.49cm (2.5cm) according to ROC curve analysis (AUC 0.725).
- Cervical length is a moderate predictor of preterm birth with specificity of 82.5% and negative predictive value of 97.9%.
- Suggests that while cervical length cannot be used to diagnose or confirm at-risk patients, it has a good negative predictive value and relatively good specificity to identify the lower risk patients for preterm birth
Future research

• Cervical length screening at 28 weeks gestation may be performed to identify patients at lower risk of preterm birth

• Allows identification of group requiring closer follow-up/intervention for the rest of the pregnancy
THANK YOU