Maternal Anemia and Blood Loss at Childbirth and Postpartum in Zanzibar, Tanzania

MCHIP Nutrition Brown Bag

March 28, 2013

Justine A. Kavle, PhD, MPH
Senior Program Officer for Nutrition, MCHIP
Acknowledgements:

- Ministry of Health, Public Health Laboratory Ivo de Carneri, Mama na Afya study staff in Zanzibar, Tanzania
- Dr. Rebecca Stoltzfus, Cornell University, Division of Nutritional Sciences,
- Dr. Jim Tielsch, Dr. Laura Caulfield, Department of International Health, Johns Hopkins Bloomberg School of Public Health
- Dr. Frank Witter, Johns Hopkins University, School of Medicine
- Gates Foundation
- World Health Organization (WHO)
Hemorrhage (PPH) is the leading cause of maternal death. Anemia has been thought to underlie PPH.

Khan et al, WHO systematic review 2006
Data is scant on maternal deaths due to PPH in Africa
(Khan, WHO systematic review, 2006)
Maternal anemia is associated with poor birth outcomes, pregnancy complications and death

- Moderate to severe maternal anemia is associated with low birth weight and preterm deliveries

- Severe anemia is a cause of maternal mortality due to:
  - Heart failure
  - Excessive blood loss at delivery
Proposed biological mechanisms that play a role in PPH
Anemia is a plausible pathway

- Higher blood loss attributed to impaired uterine muscle strength for labor when prolonged
- Decreased resistance to infection, as infection may contribute to uterine dysfunction or inertia
- Decreased uterine blood flow or low uterine muscle strength may trigger inefficient uterine contractions, mediated by low body iron stores (serum ferritin) and iron deficiency anemia

Animal model, anecdotal evidence
What we know and don’t know about anemia, PPH, and maternal mortality

- PPH is the leading cause of maternal death
- Yet, most women survive PPH and likely suffer morbidities affecting productivity and care practices, and they may become or remain anemic postpartum
- Lack of evidence in less developed countries, on the relationship between maternal anemia and blood lost at childbirth
- Need for such data in a setting where maternal mortality and severe anemia are prevalent
We addressed the following unanswered questions:

- What is the distribution of blood loss at childbirth and postpartum in less-developed countries where 99% of maternal deaths occur? How much do women actually lose?

- Can a reliable and valid measurement technique be utilized to measure blood loss at childbirth and postpartum in a less-developed country?

- Do women lose more blood at childbirth and postpartum in areas where maternal mortality and severe anemia are prevalent, as in east Africa?

- What are the risk factors or determinants for greater blood loss at childbirth and postpartum? Is anemia related?
Mothers and Health “Mama na Afya” community-based trial
Prevention and Treatment of Severe Anemia in Pregnancy
Study site: Northern Pemba Island, Zanzibar

Population: ~300,000, Muslim

Maternal mortality rate: 449*

Staple foods: rice, cassava

P. falciparum malaria and soil-transmitted helminths endemic

* 2008 estimate, Hogan et al, 2010, Lancet
Treatment groups: preventing and treating maternal anemia

**Standard of Care**
- Iron folic-acid (60 mg, 400 ug), daily
- Anti-malarial: SP - 2 doses
- One dose deworming: 500 mg mebendazole

**Enhanced Care**
- Iron folic-acid, daily
- Antimalarial: SP – 2 doses
- Two dose deworming: 100 mg mebendazole, twice a day, 3 days
- Multivitamin (Vitamin A, C, E, B\(_1\), B\(_2\), B\(_3\), B\(_5\), B\(_6\), B\(_{12}\), folate)
Data collection was conducted in ANC clinics and through home visits.

- Obstetric history
- Socioeconomic status
- Maternal morbidity
- Food Frequency
- Clinical Exam, treatments
- Pregnancy outcome
- Infant status
- Deliver treatments
- Compliance
- Birth weight
Mothers and Health study and Blood Loss Sub-study (2004-2005)

4 Standard of Care Clinics
4 Enhanced Care Clinics
N = 2369

Treatment:
Hb < 7.0 g/dl
1 & 4 weeks post-treatment
32, 36 wks GA, postpartum

Prevention:
Hb ≥ 7.0 g/dl
32, 36 wks GA, PP

Blood loss sub-study
34-36 wk venous sample (Hb, blood loss measurement)
1 Standard of care and 1 Enhanced care clinic
N = 268 (Wete town)

At delivery and 24 hours: blood loss sample

2 months postpartum:
Hb, anemia related symptoms
To determine the distribution of blood loss at childbirth and 24-hours postpartum, utilizing the alkaline hematin technique.
Diagnosing blood loss at childbirth is a challenge due to measurement

- Health workers rely on visual approximation for deciding if the amount of blood loss at childbirth is excessive
  - 30-50% under-estimation of blood loss
  - Can delay diagnosis, referral, and treatment

- Lack of consensus in research studies
  - No standard definition of excessive blood loss
  - Cutoff, duration and methods of measurement differ

(Brant 1967, Glover 2003)
Alkaline hematin method is the most widely used and most accurate method for objective quantification of blood loss in women.

- Simple, reliable, practical

- A few early studies used alkaline hematin to quantify excessive menstrual bleeding and blood loss at childbirth and none in developing country settings

Using the gold standard – the alkaline hematin method to accurately quantify blood loss at childbirth and postpartum

At delivery and 24 hours postpartum in Wete Hospital:

Collect pads at childbirth and postpartum, dilute with NaOH solution

Denature hemoglobin in blood loss to alkaline hematin

Measure concentration of alkaline hematin

Compute blood loss at childbirth

85% recovery rate

At > 34 weeks gestational age:

Collect venous blood

Dilute with NaOH

Measure concentration of alkaline hematin

17
Distribution of blood loss was lower in hospital-based deliveries (N= 158)

287 ml (97, 579)

Kavle, 2006
Why was blood loss at childbirth and postpartum lower than expected?

- No complications of 3\textsuperscript{rd} stage of labor
- Only two case of prolonged labor (3\textsuperscript{rd} stage > 30 min.)
- Incidence of PPH low (5%)
- Breastfeeding following birth is universal
- Active management of third stage of labor (AMTSL) routinely practiced in hospital-based deliveries

Kavle, 2006
Nurse-midwives estimated blood loss accurately, when compared to laboratory measurements, yet had lower precision at higher losses.

Kavle, 2006
To evaluate the determinants of blood loss at childbirth, and 24-hours postpartum, specifically focusing upon the purported relationship between maternal anemia and blood loss at childbirth and postpartum.
Little is known about factors which contribute to excessive blood loss at childbirth in less developed countries:

- Nulliparity
- Grand multiparity
- Cervical trauma
- Maternal obesity
- Maternal anemia
- Instrumental delivery
- Induced labor
- Prolonged labor
- Third stage complications
- Pre-eclampsia
- Previous history of PPH
- Birth weight > 4000 grams

Outcome: Total blood loss (mL) – childbirth and postpartum

- Bi-variate analyses
  - Nutritional factors
  - Socioeconomic factors
  - Obstetrical factors

- Multivariate regression analyses
  - Factors p< 0.10 in bi-variate analyses
  - Factors identified in previous literature
  - Universal confounders
### Selected background characteristics

**Zanzibari women, Wete town (N = 158)**

<table>
<thead>
<tr>
<th>Basic characteristics</th>
<th>50(^{th}) (5(^{th}), 95(^{th})) or %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.5 (18.0 - 38.0)</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>29.0 (20.0 - 37.0)</td>
</tr>
<tr>
<td>Hemoglobin category</td>
<td></td>
</tr>
<tr>
<td>No anemia (Hb &gt;110 g/L)</td>
<td>38.6</td>
</tr>
<tr>
<td>Mild anemia (Hb 90-109 g/L)</td>
<td>45.6</td>
</tr>
<tr>
<td>Moderate to severe anemia (&lt;90 g/L)</td>
<td>15.8</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>21.5</td>
</tr>
<tr>
<td>1</td>
<td>15.2</td>
</tr>
<tr>
<td>2-5</td>
<td>37.3</td>
</tr>
<tr>
<td>&gt;5</td>
<td>25.9</td>
</tr>
<tr>
<td>Not employed</td>
<td>80%</td>
</tr>
<tr>
<td>Malarial infection; intestinal helminths</td>
<td>Low rate</td>
</tr>
</tbody>
</table>

Kavle, 2006
## Selected labor and delivery characteristics, Zanzibari women, Wete town (N= 158)

<table>
<thead>
<tr>
<th>Characteristics at childbirth</th>
<th>50(^{th}) (5(^{th}), 95(^{th})) or %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received oxytocin</td>
<td>44.9</td>
</tr>
<tr>
<td>Received ergometrine</td>
<td>95.6</td>
</tr>
<tr>
<td>Received oxytocin and ergometrine</td>
<td>40.5</td>
</tr>
<tr>
<td>Tear</td>
<td>7.6</td>
</tr>
<tr>
<td>Episiotomy</td>
<td>16.5</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>39.1 (36.4 – 43.5)</td>
</tr>
<tr>
<td>Birthweight (grams)*</td>
<td>3,410 ± 434</td>
</tr>
</tbody>
</table>

* Mean ± SD, singleton births only

Kavle, 2006
### Determinants for total blood loss: childbirth and 24-hrs postpartum

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>β estimate</th>
<th>SEM</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate - severe anemia vs. no anemia</td>
<td>90.63</td>
<td>28.38</td>
<td>0.002</td>
</tr>
<tr>
<td>Mild anemia vs no anemia</td>
<td>11.47</td>
<td>20.51</td>
<td>NS</td>
</tr>
<tr>
<td>First stage of labor (hr)</td>
<td>7.09</td>
<td>2.79</td>
<td>0.012</td>
</tr>
<tr>
<td>Placental weight (grams)</td>
<td>0.11</td>
<td>0.05</td>
<td>0.030</td>
</tr>
<tr>
<td>Oxytocin received</td>
<td>39.64</td>
<td>19.66</td>
<td>0.046</td>
</tr>
<tr>
<td>Pre-term birth &lt; 37 weeks</td>
<td>-52.52</td>
<td>29.91</td>
<td>0.081</td>
</tr>
</tbody>
</table>

*NS = not significant p > 0.10

Kavle, 2008
## Determinants for total blood loss: childbirth and 24-hrs postpartum

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>β estimate</th>
<th>SEM</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parity (0, Reference)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>34.19</td>
<td>34.18</td>
<td>NS</td>
</tr>
<tr>
<td>2 - 5</td>
<td>30.34</td>
<td>32.99</td>
<td>NS</td>
</tr>
<tr>
<td>≥ 5</td>
<td>59.61</td>
<td>35.17</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Tear</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>25.01</td>
<td>37.61</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Episiotomy</strong></td>
<td>18.77</td>
<td>34.00</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Standard of Care vs. Enhanced</strong></td>
<td>1.90</td>
<td>19.32</td>
<td>NS</td>
</tr>
</tbody>
</table>

*NS = not significant p > 0.10

Kavle, 2008
Identified maternal anemia as determinant of blood loss, supports hypothesized relationship

**Strong relationship between maternal anemia and blood loss**

- Influence of maternal anemia on blood loss is more pervasive - affects a normal range of losses
- Relationships persisted following adjustment of confounding factors
- Internal validity due to rigorous prospective data collection of women during pregnancy delivery and postpartum
- Conducted in population where anemia and iron deficiency are prevalent
Study limitations

- Study sample restricted to semi-urban setting who were able to afford hospital delivery
- Access to health care may have contributed to lower blood loss
- Some loss to follow-up experienced
  - Delivered prior to obtaining venous sample
  - Delivered at home, could not get to hospital in time
  - Did not stay through 24 hours postpartum
Research and programmatic Implications

- Our findings likely underestimate the effect of anemia on blood loss in rural Africa, especially where anemia is untreated and in home births.
- Accurate measurement of blood loss can guide limits for “normal” blood loss and “excessive blood loss” which may vary by setting.
- Consistency and accuracy of other measurement techniques vs. the gold standard needs further study.
- Further exploration of the link between maternal anemia and postpartum hemorrhage.
- Prevention of anemia is key.
Thank you (Asante sana)!