Antihypertensive Medicines and Blood Pressure Devices: Uganda

**Background**

Hypertensive disorders of pregnancy (HDP) are an important cause of severe morbidity and mortality among mothers and babies. [1] In Africa and Asia, nearly 1 in 10 of all maternal deaths are associated with HDP. In Latin America, more than 1 in 4 of maternal deaths are associated with complications of hypertension (HTN). [2]

Treatment of severe hypertension in pregnancy reduces serious maternal complications such as cerebral edema and hemorrhage and blood pressure (BP) monitoring is a key component of antenatal and postnatal care.

The World Health Organization (WHO) recommends treatment with antihypertensive medications (hydralazine, labetalol, nifedipine immediate-release capsules, or alpha methyldopa) for acute treatment of severe hypertension in pregnancy. According to WHO, choice and route of administration of an antihypertensive drug for severe hypertension during pregnancy "should be based primarily on the prescribing clinician's experience with that particular drug and its cost and local availability, while ensuring that the medication has no adverse fetal effect." [3]

Barriers to effective treatment of HDP include problems with equipment (missing or dysfunctional blood pressure machines), medicines (stock outs of antihypertensives or inappropriate formulations or dosages), and policy (national guidelines that do not reflect the current evidence base or do not allow for stocking of medicines at facilities providing emergency obstetric care).

**Ugandan Context**

In Uganda, HDP were the second leading cause of maternal death in 2018. Among Ugandan women who received ANC for their most recent birth in the past 5 years, only 71.8% had their BP measured and 39.4% had proteinuria assessed. [4] Surveys of essential supplies for treatment of general hypertension have found poor availability of essential equipment including BP devices and urine test strips. [5, 6]
**PROJECT OVERVIEW:**

Gynuity selected three countries (Uganda, Mexico and India) for a focused assessment of the availability of essential supplies for the management and treatment of hypertensive disorders of pregnancy (specifically, antihypertensive medications and blood pressure devices). The landscaping exercise employed a mixed methods approach and collected global, national and sub-national data from three sources: document reviews, in-depth stakeholder interviews, and health facility readiness assessments.

**Goals:**

- To assess readiness of primary and secondary health facilities to diagnose, monitor and treat women with pre-eclampsia and eclampsia and other HDP.
- To identify gaps in equipment, medicines and policy and procurement practices that may pose barriers to recommended management.

**Methods:**

**Document review:**

- National treatment standards and guidelines for the diagnosis and management of HDP
- National and sub-national guidelines and reports for procurement and supply of oral AHT and BP cuffs (Including Essential Medicines Lists, forecasting reports of essential medicines and devices etc.)

**In-depth interviews** with 12-15 key stakeholders in each country including government health sector officials, members of professional medical societies, and non-governmental organizations and researchers working on maternal health

**Cross-sectional mixed methods facility survey** in a sub-sample of health care facilities and private pharmacies in two districts in each country

**UGANDA**

In Uganda, the survey was conducted in Butambala and Masindi regions by partners and Global Health Uganda. We sampled a total of 32 facilities in these two regions: 17 level II centers, 12 level III centers, 1 level IV center and 2 hospitals. This sample represents 50% of all operable government or mission facilities in these two regions. The survey team also surveyed 32 private pharmacies located in close proximity to each health facility.
**Antihypertensive Medications**

Table 1. Essential Medicine Lists

<table>
<thead>
<tr>
<th>Drug</th>
<th>WHO EML formulation and indication</th>
<th>Uganda EML</th>
<th>Types of medicines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyldopa</td>
<td>250mg tablet for acute management of severe hypertension in pregnancy (12.3)</td>
<td>HC III (Essential) +higher</td>
<td><strong>Vital</strong>: Used to diagnose and treat life-threatening conditions, or which are considered medicine of choice or &quot;first line&quot; items in their therapeutic category. Their unavailability would cause serious harm and side effects. They must be available ALWAYS.</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>Immediate release capsule 10mg for antioxytocic (tocolytics) (22.4)</td>
<td>HC III (Essential) +higher</td>
<td></td>
</tr>
<tr>
<td>Labetalol</td>
<td>Not listed</td>
<td>(IV) Regional Referral (Vital) +higher</td>
<td><strong>Essential</strong>: used to treat common illnesses, maybe less severe but nevertheless significant, or which are second line items in their therapeutic categories.</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>Powder for injection; 20mg (hydrochloride) in ampoule for acute management of severe hypertension in pregnancy (12.3)</td>
<td>HC IV (Vital) + higher</td>
<td></td>
</tr>
</tbody>
</table>


**Key Findings:**

**Uganda Essential Medicines List**

- No oral antihypertensive medicine is listed as a ‘vital’ medicine for supply at Health Centre IV or higher.
- Additionally, no antihypertensive medication is listed as a ‘vital’ medicine for supply at Health Center III level
**TREATMENT PROTOCOLS**

In Uganda, physicians, clinical officers, and midwives can prescribe antihypertensive medications. The UCG 2016 guidelines did not include a specific diagnostic criteria for severe hypertension in pregnancy or list a specific treatment of this indication. Rather guidance on antihypertensive treatment regimens was included in sections on treatment of chronic hypertension in pregnancy or preeclampsia/eclampsia. While methyldopa was listed on the EML, it was not included in the treatment guidelines for treatment of severe hypertension in pregnancy.

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**Treatment Guidelines for Treatment of Severe Hypertension in Pregnancy**

<table>
<thead>
<tr>
<th>World Health Organization</th>
<th>Uganda Clinical Guidelines 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORAL</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Nifedipine</strong> 5-10mg immediate-release capsule oral with a repeat dose after 30 minutes if response is inadequate until BP goal achieved. Max dose in acute treatment setting: 30mg.</td>
<td><strong>Nifedipine</strong> 20mg-40mg every 12 hours until delivery (HC3 and HC4)</td>
</tr>
<tr>
<td><strong>Methyldopa</strong> 750mg oral with a repeat dose after 3h until BP goal achieved. Max dose: 3g in 24h</td>
<td><strong>IV</strong></td>
</tr>
<tr>
<td><strong>Labetalol</strong> 200mg. Repeat dose after 1h until BP goal achieved. Max dose: 1200mg in 24h.</td>
<td><strong>Hydralazine</strong> 5mg IV bolus every 30 min until dBP&lt;100Hg OR (HC4 only)</td>
</tr>
<tr>
<td></td>
<td><strong>Labetalol</strong> 20mg IV (Regional referral hospital only)</td>
</tr>
<tr>
<td><strong>Hydralazine</strong> 5mg IV repeated every five minutes until BP goal achieved. Repeat hourly as needed or give 12.5 mg IM every two hour as needed. Max dose: 20mg in 24 hours.</td>
<td></td>
</tr>
<tr>
<td><strong>Labetalol</strong> 10mg IV and, if the response is inadequate after 10 minutes, then 20mg IV. Maximum total dose: 300 mg.</td>
<td></td>
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</tbody>
</table>

**Note:** *No specific diagnostic criteria for severe hypertension alone listed in UCG 2016. The UCG 2016 defines as Severe Preeclampsia as Systolic BP > 160 mmHg and diastolic BP > 110 and >1+ proteinuria or any degree of hypertension with organ dysfunction (renal dysfunction, raised liver enzymes, thrombocytopenia)*

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**Registered Antihypertensive Medicines**

There are multiple formulations of nifedipine registered in Uganda. However, very few products are the 10mg immediate release formulation recommended by the WHO and other international guidelines. Additionally, there are no registered IV or oral labetalol products although IV labetalol is included on the national EML. [8]

**Figure 1.** Registered Antihypertensive Drugs Used for HDP (n=19)

**Figure 2.** Number of Registered Nifedipine Products per National Drug Registry (n=12)

Reference: Drug Register of Uganda, Human Medicines, August 2019

**Availability of Antihypertensive Medications**

“When you ask women to go and buy drugs, they say that they don’t have money. So, a midwife is limited. [There is] nothing to do apart from referring these cases.” – Ugandan provider

**Figure 3.** Availability of Oral Medications in Surveyed Facilities (%)

Note: In Uganda, nifedipine was available in 93% of HCIII+ facilities. Most common nifedipine formulation was 20mg retard.
**Key Findings: Antihypertensive Medicines**

- While IV hydralazine and methyldopa were listed as “vital” medications on the national EML, they were only available at the hospital level in government facilities.

- Methyldopa was supplied as part of a 'kit' (i.e. 3 month supply). As noted by key informants and health providers at facilities: If centers did not treat a lot of HDP patients -- either because they lacked BP monitors to assess blood pressure or because they referred patients directly to higher levels of care -- methyldopa supplies would become expired and/or procurement officers prioritized outpatient drugs for purchase.

- **Hydralazine** supply was erratic and the medication was not available for purchase at local drug shops.

- **Nifedipine** was the most commonly and consistently available antihypertensive drug in government health facilities and nearby drug outlets. The most commonly available formulation was 20mg nifedipine retard. Stockouts of nifedipine retard were reported to be relatively infrequent.

- **Labetalol** (IV or oral) was not available.

- Our survey found few problems with the storage of medications at healthcare facilities and almost all the available drugs were registered products. However, drugs for sale at drug shops were between 2 and 10 times as expensive as the government procurement price.

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"I think institutions should have the capacity to carry out emergency purchases."

-- Technical Expert

"Patient treatment is delayed because we send them out to buy medications."

-- Hospital provider
**Blood Pressure Machines**

**Types of BP devices**

**Manual:** requires manual inflation, auscultatory, observer recording, and is subject to human error.

- Mercury sphygmomanometer (composed of inflatable bladder along with a column of mercury) and historically the gold standard device for BP measurement but poses an environmental and safety hazard if broken. [12]
- Aneroid which is mechanical (i.e. spring device and metal membrane) and must be calibrated often to avoid error.

**Digital** (e.g. oscillometric): These devices do not require stethoscopes and the power source may be solar or AC/DC power. While they may eliminate human error, they lack the precision of mercury devices and can yield inconsistent readings if not validated.

**Essential Health Supplies List**

Blood pressure devices are not included in the 2016 EMHSLU.[10] However, health sector development plans 2015/16 to 2019/2020, recognize the importance of ensuring availability of basic equipment for screening, management, and monitoring of non-communicable diseases (NCD) from HCII.[11] The National Drug Authority (NDA) monitors equipment imported for government and non-governmental health facilities.[12]

**Treatment Protocols**

National clinical guidelines recommend at least four ANC visits during pregnancy during which BP and urine protein should be measured.

Postpartum blood pressure should be monitored every 15min after delivery for 2h then at 3h, 4h and every 4h until discharge.[9]

“...where health providers have failed to make diagnosis of raised BP due to no BP monitor, they are going not to treat the patients and therefore the drugs are not utilized. The drugs end up expiring.”

--- Technical Expert

“Some women present with complaints, [we] are not able to make a good diagnosis because of lack of equipment so we just blindly refer.”

--- Provider at HCII

“One time we bought BP machines for some health facilities for about over 1000 health facilities but when we went around three quarters of those BP machines were not working.”

--- Key Stakeholder

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**KEY FINDINGS: BLOOD PRESSURE DEVICES**

**PROCUREMENT**
Respondents from government HC II, III IV reported supply of replacement devices was “not very easy”. The in-charge placed the request with the DHO but such requests were not processed quickly. Respondents at HC III facilities reported that the in-charge frequently stated that Primary Health Care funds were insufficient or unavailable for use.

**AVAILABILITY**
- At the most basic level, availability of blood pressure devices, cuffs, and stethoscopes look decent. However a closer look at the functionality and adequacy of the devices reveals concerns.
- Most facilities had only one BP device for the entire facility and many government HCII centers lacked functioning machines. One respondent at a HC II reported that it had been “over one year since they had a working device.”
- Both manual and digital devices were found at healthcare facilities. Many digital devices were fixed to the wall and difficult to move to a patient. Additionally, HC III and higher facilities with digital machines reported machines were frequently inoperable, lacked replacement batteries, or replacement batteries were of poor quality.
- One midwife reported that she purchased the batteries or requested a woman’s family to purchase batteries for their digital machine.

**Clinical management implications**
- Only 4% of providers in facility survey reported they had all supplies needed to diagnose and/or manage HDP patients.
- Almost all providers at higher facilities (HC III+) (88%) reported that stock outages hindered management of patients with HDP.

1/3 of Ugandan facilities with a working device on the day of the survey reported that the device has not been operable for more than 15 days in last two months.

![Figure 4. Availability of Blood Pressure Devices in Surveyed Health Facilities](image)
RECOMMENDATIONS

- Update national clinical guidelines to reflect recent WHO guidance on AHT dosing and management of HDP
- Include an oral antihypertensive as a vital drug on EML
- Provide job aids with practical guidance on use of different nifedipine formulations given their availability in the market and health sector facilities
- Improve registration and quality assurance mechanisms for procurement of blood pressure devices by government and donor agencies
- Improve and streamline procurement processes for BP devices
  - Provide District Health Officers technical guidance and specifications on types and characteristics of a ‘good quality’ BP device
  - Clarify whether and how replacement BP devices can be financed
- Improve and increase health sub-district (HSD), municipal and district health officers knowledge of HDP and importance of essential supplies for diagnosis and treatment (BP cuffs, oral AHT drugs, MgSO4, urine dipsticks)
- Improve refresher training on HDP for providers (midwives, clinical officers, ob/gyn) on the following:
  - Proper BP measurement techniques
  - Diagnosis of all HDP (chronic, acute severe HP in pregnancy, preeclampsia)
  - Treatment protocols with different AHT drugs (including information on use of different formulations of nifedipine)
  - Postpartum monitoring

...I feel that hypertension is not getting that prominence it deserves in terms of supplies. Advocacy is missing or inadequate.”
--Technical Expert

PROVIDER SUGGESTIONS FOR IMPROVEMENT OF HDP PATIENTS

- Provide adequate equipment (BP devices, urine catheters and collection bags) and medications
- Provide additional refresher or in-service training onsite on antihypertensive medication protocols
- Rotate midwives posted at HCIII or HCII facilities to general hospitals to obtain more experience and training in management of these cases
- Engage and inform clinical officers on HDP and treatment
REFERENCES


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