



KATHMANDU

25-28 MARCH 2019 / KATHMANDU, NEPAL

**19TH GENERAL MEMBERSHIP MEETING OF THE
REPRODUCTIVE HEALTH SUPPLIES COALITION**



Oral Antihypertensive Therapy: A Pathway to Efficiently Reducing Maternal Complications from Severe Hypertension in Low Resource Environments

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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 associated with HDP.
 - In Latin America, more than 1 in 4 of maternal deaths associated with complications of hypertension.

- ❑ Treatment of severe hypertension in pregnancy reduces serious maternal complications such as cerebral edema and hemorrhage.

[1] Khan KS, Wojdyla D, Say L, Gülmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. *Lancet*, 2006 Apr 1;367(9516):1066-1074.



WHO recommendations for acute treatment of severe hypertension in pregnancy*

Drug	Treatment guideline
Methyldopa	750mg oral with a repeat dose after 3h until BP goal achieved. Max dose: 3g in 24 h
Nifedipine	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.
Labetalol	Oral: 200mg. Repeat dose after 1h until BP goal achieved. Max dose: 1200mg in 24 h. IV: 10mg IV and, if the response is inadequate after 10 minutes, then 20mg IV. Maximum total dose: 300 mg.
Hydralazine (IV)	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.

- “If antihypertensive medication for acute treatment of severe hypertension cannot be given intravenously, oral treatment can be given.”
- From: *Managing Complications in Pregnancy and Childbirth: A guide for midwives and doctors* - 2nd ed (WHO, 2017)



AHT Formulations typically used in pregnancy

Drug	WHO EML formulation and indication*	Typically available formulations	Storage
Methyldopa	250mg tablet for acute management of severe hypertension in pregnancy (12.3)	250mg and 500mg tablets	Dry conditions away from sunshine and light at room temp not to exceed 25 degrees C.
Nifedipine	Immediate release capsule 10mg for antioxytotic (tocolytics) (22.2)	10mg and 20mg immediate-and sustained-release capsules	
Labetalol	Not listed	200mg tablet and ampoule	
Hydralazine	Powder for injection; 20mg (hydrochloride) in ampoule for acute management of severe hypertension in pregnancy (12.3)	Ampoule	

* Note as per WHO Model List of Essential Medicines 20th List (March 2017)



Project Goals

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



Project Objectives

- ❑ **Objective 1:** Assess national standards and guidelines for
 - diagnosis, monitoring and treatment of HDP
 - procurement and supply of BP devices and the most commonly used AHT medications used in pregnancy (nifedipine, labetalol, methyldopa, hydralazine)

- ❑ **Objective 2:** Assess facility readiness
 - Measure availability, source, cost and procurement process of BP devices and AHT medications at a sample of public sector health care facilities and private sector medicine outlets in two districts or divisions

- ❑ **Project countries:** India, Uganda and Mexico
- ❑ **Project period:** June 2018-May 2019



Objective 1: Assessing National Standards and Guidelines

- Preliminary findings



Assessing national guidelines

□ 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 EMLs, forecasting reports of essential medicines and devices etc.)

□ In-depth interviews (IDIs)

- 12-15 IDIs with 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



Gaps in treatment and procurement guidelines

In **Uganda**, hydralazine (5mg) and nifedipine (20mg) included in treatment guidelines for preeclampsia management.

- ❑ Little guidance on acute treatment of severe hypertension alone (i.e. in absence of proteinuria)

Uganda EML does not list an AHT as ‘vital’ or a first priority for procurement for centers offering **basic** emergency obstetric care (EmOC)

- ❑ Hydralazine and labetalol (IV) classified as ‘vital’ for centers offering **comprehensive** EmOC
- ❑ Nifedipine and methyldopa considered ‘essential’ for centers providing basic EmOC. But, magnesium sulfate, also used for treatment of preeclampsia/eclampsia, is considered as ‘vital’ medication



Inclusion on EML may be inadequate to promote treatment of HDP

- ❑ *Methyldopa* only **oral drug** labelled specifically for HDP according to WHO EML and many NEML
 - ❑ In **Uganda**, respondents reported that the drug was not prioritized for purchase by staff at healthcare facilities because of preference to use allocated funds for “outpatient” drugs and/or the drug was not requested by health care providers
 - ❑ In **India**,
 - ❑ 250mg methyldopa considered as the drug of choice for HDP
 - ❑ But, not available.
 - ❑ Respondents reported that drug prices, formulation and availability variable and determined by the commercial interests of a limited number of manufacturers



Moving beyond the EML

- ❑ In both Mexico and India, **national practice guidelines** have helped **promote access to AHT** for treatment of HDP beyond the labelled indications in the EML
- ❑ In **India**, the Indian Public Health Standards (2016) were revised to **include nifedipine as** an essential supply at the **primary care level**.
- ❑ In **Mexico**, the Mexico Practical Guidelines for Obstetric Triage (2016) allow for inclusion of nifedipine and hydralazine in an **obstetric “red box”** located in the Emergency Room or close to Labor and Delivery



Objective 2: Assessing Facility Readiness

- Preliminary findings



Assessing facility readiness

- ❑ Facility survey in 2 districts in each country
- ❑ Sampling frame:
 - ❑ Sub-set of operable primary and secondary health centers including both urban and rural areas in each district.
- ❑ Data collection complete in Uganda and ongoing in Mexico and India



Uganda: Availability of operable BP measurement devices

	Secondary Health Centers		Primary health center
	<i>General hospital or HC IV</i> (n=4)	<i>HC III</i> (n=11)	<i>HC II</i> (n=16)
At least 1 operable BP apparatus at time of facility survey	3/4	8/11	7/16

- **Most public primary care (9/12) and many secondary facilities (4/11) did not have an operable BP apparatus.**

Note: Sample represents approximately 50% of health facilities in 2 districts and includes public, NGO and private health centers.



Uganda: Procurement of BP devices

- ❑ Most facilities had only one device for the entire facility
- ❑ Many public secondary facilities had a digital device on site but lacked batteries rendering the device inoperable
- ❑ Respondents at all levels of public health facilities reported supply of replacement devices was “not very easy”
 - ❑ Requests to district officials were not processed quickly. One respondent at a HC II reported that it had been “**over one year since they had a working device.**”



UGANDA: Availability of antihypertensive (AHT) medications

	Secondary Health Centers		Primary health center
	<i>General hospital or HC IV (n=4)</i>	<i>HC III (n=11)</i>	<i>HC II (n=16)</i>
At least one AHT in stock at time of survey	4/4	9/11	3/16

- Most common AHT in stock was 20mg nifedipine tablet.
- **Hydralazine**, categorized as a ‘vital’ drug by the NEML for supply at HC IV and higher, was **not available** in any **public hospital or HC IV facilities** (n=3)
- Private and NGO primary care centers (n=3) in both districts did have an AHT in stock



Preliminary conclusions

- ❑ National EMLs alone insufficient to promote access for HDP
 - ❑ Labelled indications for AHT may require further clarification in practice guidelines to promote use for HDP
- ❑ Even when funds are available, de-centralized procurement policies may not ensure availability of essential supplies
 - ❑ AHT listed for use in pregnancy may not be prioritized for purchase by sub-national officials responsible for procurement or AHT may be purchased in insufficient quantities resulting in frequent stock outs
 - ❑ Replacement of lost or broken BP devices may be possible with use of untied local funds or through requests to district procurement officials but replacement may not be timely



Research team

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THANK YOU!