

## **Liver function testing and monitoring in preeclamptic women in Zanzibar**

### **Introduction**

- Background on preeclampsia
- Procedures in diagnosing preeclampsia
  - Mild/severe
- Procedures in monitoring
- How LFTs help monitor conditions of preeclamptic women
- Our potential impact of our ALT device

Preeclampsia is an obstetric condition that causes high blood pressure, proteinuria, and often edema in the legs, feet, and hands. It occurs at a gestational age of 20 weeks. If left untreated, preeclampsia may develop into eclampsia, which involves seizures, or cause failure of the liver, kidneys, and heart. Zanzibar's Ministry of Health implicates preeclampsia in 50% of maternal deaths in Zanzibar. Patients with severe preeclampsia are admitted to the hospital and must be constantly monitored in addition to given medication to lower blood pressure. If necessary, liver function tests (LFTs) and renal function tests (RFTs) are done to monitor organ damage. However, LFTs are done in a laboratory using a chemical autoanalyzer and results are often received the day after the test was ordered by the doctor. This delay is also caused by lack of reagents, broken equipment, and lack of technicians to repair broken equipment. Since preeclamptic patients should be monitored constantly, the procedures of LFTs are inconvenient and often avoided. Therefore, our point of care device to quantify alanine aminotransferase (ALT) has the potential to circumvent the longer procedures of monitoring liver function. Our device is designed to be used at the bedside of preeclamptic patient by physicians and nurses. With just a small amount of blood, our device will be able to quantify the amount of ALT in blood within 10-15 minutes. ALT is a liver enzyme and the level of elevation corresponds to the severity of liver damage.

### **Methods**

The first week we met with Dr. Saleh Jiddawi from the Ministry of Health and Dr. Tarek Meguid from MMH to learn about the overview of preeclampsia monitoring as well as suggestion on how to move forward with our device.

In the second week, we visited the Central Medical Store (CMS) to learn about the supply chain of drugs and medical devices, which is applicable in introducing our device in the future. We also visited the laboratories at Tasakhataa Global Hospital and Mnazi Mmoja Hospital to observe the workflow and process of LFTs.

In the third week, we met with Poppy Farrow to learn about maternal health in Zanzibar and her mobile application. We interviewed patients at the antenatal care clinic and at the maternity ward at Chake Chake Hospital, Pemba. In addition, we met with Dr. Natasha Housseine from MMH to learn more about the problems in the hospital and the limitations patients faced regarding antenatal care and delivery service.

The fourth week we interviewed patients, hospital staff, and a laboratory technician at Mwembeladu Maternal and Child Health (MCH) Clinic, and patients, hospital staff, and a laboratory technician at Mnazi Mmoja Reproductive and Child Health (RCH) Clinic.

The fifth week we interviewed patients and a physician at Fuoni Hospital Primary Health Care Unit.

## Results & Discussion

- Problems with LFTs and relation to preeclamptic women
  - LFT procedure- chemical analyser
    - Lack of reagents
    - Lack of equipment
    - Lack of training
    - Delay in workflow
  - Cost-how much patient pay for LFTs
  - Info patient-how much they can afford
  - Info doctors-tarek, natasha- government funding to hospital
  - Maternal health in Zanzibar (Poppy)
  - How our device will address the problems listed in results
    - Cost of glucometer, batteries-affordability
  - Observations that can help in designing our device to meet adoptability
    - Public Health Laboratory- include a control for device
    - How our device will be used in hospital
  - Where to initiate our device

In total, we interviewed 120 patients, 7 hospital staff, and 2 laboratory technicians: 6 patients at the ANC and 1 patient at the maternity ward in Chake Chake Hospital, 18 patients at Mwembeladu Maternal and Child Health (MCH) Clinic, \_ patients at Mnazi Mmoja Reproductive and Child Health (RCH) Clinic, \_ patients at Fuoni Hospital; 2 hospital staff at Mwembeladu Maternal and Child Health (MCH) Clinic, 5 at Mnazi Mmoja Reproductive and Child Health (RCH) Clinic, 1 at Fuoni Hospital; 1 laboratory technician at Mwembeladu Maternal and Child Health (MCH) Clinic, 1 at Mnazi Mmoja Reproductive and Child Health (RCH) Clinic.

### *Current standards of antenatal care in Zanzibar*

Antenatal clinics (ANCs) at hospitals provide routine diagnosis and monitoring tests for preeclampsia include blood pressure and a rapid diagnostic test for albumin in urine, in addition to other routine tests including HIV, syphilis, blood pressure, blood sugar, blood group, Hb level, malaria. Tests are usually done using rapid diagnostic tests (RDTs) to check for proteinuria in the doctor's office and the ANC lab, so results are known quickly. However, routine tests not always done completely because of stock outs. In addition, depending on whether there is a lack of consumables or not, patients may or may not have to pay. HIV and malaria are free, but for urine test for albumin, patients usually have to pay 1000 Tsh. Other patients do not recall the cost for each test, but recall the total cost for all tests to be 3000 Tsh in the first ANC visit, then 1500 Tsh for the following. Ultrasound is also recommended for patients. Since only MMH has ultrasound available in place, MMH provides a team to go to other hospitals to conduct ultrasounds for patients there. Patients are notified of the date beforehand. Ultrasound cost 10,000-15,000 Tsh. If blood pressure is above 120/80 but less than 140/90 and protein in the urine is +1 or +2, the patient is diagnosed with mild preeclampsia. She is given food and exercise advice and medication to lower blood pressure (such as aldomet). She is instructed to follow up at the clinic every week and to measure blood pressure every two days at pharmacies. If blood pressure is higher than 140/90 and protein is +3 or +4, the patient is diagnosed with severe preeclampsia, is given hydralazine and magnesium sulfate, and advised to deliver within 8-12 hours. These patients are referred to public tertiary care facilities in Zanzibar -either Mnazi Mmoja Hospital, Makunduchi Hospital, or Kivunge Hospital, depending on the patient's distance from the hospitals. Makunduchi and Kivunge Hospital are

cottage hospitals and should provide C-section for delivery of severe preeclamptic women. However, in our meeting with Poppy Farrow,, sometimes the doctor is not available at those facilities so patients are referred to Mnazi Mmoja Hospital as a last resort.

Also, she mentioned that expecting mothers with preeclampsia should have follow up appointments every week or two but do not usually go. In our meeting with Natasha, she offered some valuable insight as to how preeclampsia is treated at MMH. Most incoming referrals to MMH are severe cases. Many peripheral maternal health clinics do not have basic facilities needed for standard deliveries, resulting in mothers being referred to Mnazi Mmoja hospital even if there is no complication. This causes Mnazi Mmoja Hospital to be overwhelmed with patients, that they do not have the staff or supplies to treat. She mentioned that even for these more severe cases, liver function monitoring would only occur once per day. Current LFTs take 3-4 hours at least (if samples are delivered to the lab early in the morning). There is no emergency night testing. When supplies run out, or the lab closes, patients must go to a nearby facility - in most cases private hospitals, Al-Rahma Hospital, or Lancet Lab to get the lab testing and report the results back to Mnazi Mmoja. Severe pre-eclampsia causes unpredictable organ failure - it is unclear which organ will be affected first - if not monitored. Stroke is most common because of extremely high blood pressure. If high blood pressure sustain for long time, it can cause heart failure and pulmonary edema.

Furthermore, most patient use the Dala Dala as transportation to hospitals. They pay 300-500 Tsh one way.

#### *Current standards & availability of liver function testing in Zanzibar*

Liver functions test are conducted in clinical chemistry laboratories. Out of all the public hospitals we visited, Mnazi Mmoja Hospital has the only working clinical chemistry laboratory open to do tests for patients. Mwembeladu and Fuoni Hospital do not conduct LFTs, and the clinical chemistry laboratory in Chake Chake Hospital has not conducted any LFTs in over a year do to lack of control reagents. LFT result delivery may be delayed from 6 hours to over 1 day, due to lack of reagents, working equipment, and skilled technicians to repair broken equipment. Patients pay 6,000 to 8,000 Tsh for an LFT at Mnazi Mmoja Hospital and 40,000 Tsh for an LFT at Tasakhtaa Global Hospital.

The typical workflow of testing patient samples is: doctor orders test, patients provides samples at the reception, samples are given a barcode with patient information put into the reception computer, a laboratory technician takes the samples from the reception to the laboratory, tests are done on sample, results are obtained and entered into either the computer system or the paper-based registry whenever the system fails, results are reported back to the doctor and patient.

At Tasakhtaa Global Hospital, LFTs are done in the chemistry analyser (Mindray BS 200). The time to get results from chemistry analyser is 20-40 minutes. The analyser can run 35 tests per day. However, the cost is the barrier and thus, LFTs are not accessible to most of the patients in Zanzibar. Reagents for the chemical analyser are on a 6-month stock because transportation is slow. Reagents are ordered from Dar Es Salaam every month.

At the Mnazi Mmoja Clinical Chemistry Laboratory, LFTs composed 245 out of 643 total tests last month. The Mindray BS 200 is also used for LFTs, RFTs, and electrolytes. There are two machines in the lab, but only one is in use. It was observed that the amount of samples tested in the machine depended on how many samples were delivered to lab from reception. A quality control test is performed for each type of

test to compare to ensure the control values were within optimal ranges. The estimated turnaround time for samples in the BS200 seemed to be about an hour and a half. On the day of our observation, the laboratory did not have reagents for ALT, direct bilirubin, alkaline phosphatase, and phosphatase tests.

The Chake Chake hospital has the necessary reagents for the LFTs but lacks the control sample (Biosystem control/Elitrol I/Elitrol II). Thus, the laboratory has not been able to conduct the tests for over one year. The Public Health Laboratory is the only current facility, public or private, that can conduct the liver function test in Pemba, however this is in exceptional cases - they do not do routine LFTs. They are a research facility, and only do tests in emergency cases. Therefore, no LFTs are available in Pemba.

#### *Usability & Adoptability of a Glucometer-based test*

Regarding the glucometer, the CR2032 batteries used by most glucometers seem to be readily available in Stonetown, as do glucometers of various brands (OneTouch, Accu-Check, GlucoPlus). The prices of glucometers ranged from 30,000 to 60,000 Tsh, the price of one CR2032 battery ranged from 2000 to 5000 Tsh, while a pack of 50 test strips 35,000 to 60,000. At one pharmacy packs of 25 strips were 40,000 (Shamshu & Sons for OneTouch Ultra2). Generally patients bought the device and test strips for home use. The two most popular brands of glucometer were GlucoPlus and OneTouch SimpleSelect - all pharmacies also had test strips for these devices.

At the Public Health Laboratory, we spoke to Shaali Ame about our prototype. His main concern was the lack of a control - the device did not have a method of implementing a control as liver function tests in clinical chemistry lab do. However, we might need to do two controls: one control to validate the reagents on the chromatography paper and one control to validate the functionality of the glucometer.

From the Blood Transfusion Laboratory at Mnazi Mmoja Hospital, Ashura (the hematology laboratory director) noted that doctors in the maternity ward use Hemocue 201+ device to quickly do Hb count in order to detect anemia and order a blood transfusion for patient. The device requires acquiring a finger prick blood sample from the patient. Drawing blood in a ward or outside a lab is not allowed. This is the only exception. Usually, doctors make patients come to blood transfusion lab to use the Hemocue 201+ too. Since our ALT device will need to draw blood from patient, may need to consider whether will be acceptable as a bedside device.