HIV and high blood pressure in pregnancy: we're tracing the connections

By Sayuri Padayachee

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The vast majority of women dying from pregnancy-related conditions are in sub-Saharan Africa and Southern Asia. In 2017, about 86% of global maternal deaths occurred in these regions.

In South Africa, both HIV and pre-eclampsia are a burden to maternal health. GettyImages

The leading cause of maternal deaths is hypertension, or high blood pressure. This condition is also known as pre-eclampsia. It needs to be detected early through regular medical checkups, but developing countries don't always have the resources to offer these to pregnant women.

In South Africa, both HIV and pre-eclampsia are a burden to maternal health. The highest prevalence (41.1%) of HIV infection in pregnant women occurs in the province of KwaZulu-Natal. Pre-eclampsia is also common (12%) here.

Pre-eclampsia is the development of hypertension after the 20th week of pregnancy in a woman who previously had normal blood pressure. According to the latest guidelines of the International Society for the Study of Hypertension in Pregnancy, a diagnosis is based on a blood pressure reading greater than 140/90 mmHg. This is why it's vital that blood pressure is monitored throughout the pregnancy.

If left untreated, pre-eclampsia progresses to eclampsia. This can lead to severe high blood pressure associated with seizures. The baby has to be delivered as an emergency – which is why timely diagnosis is vital.

I am conducting research on HIV-positive women with pre-eclampsia. My findings should expand on the current science of high blood pressure in pregnancies complicated with HIV. As well as contribute to early detection of this condition in pregnant women.

Blood vessels

Pregnancy changes every organ in a woman's body. Most of these changes are associated with the placenta, which is attached to the wall of the uterus. The placenta is a network of blood vessels that provide oxygen and nutrients to the foetus and remove waste.

When the placenta develops normally, new blood vessels sprout from existing ones. Cells of the placenta infiltrate the vessels allowing them to become wider. As a result, there is a larger space for blood to flow. The process of creating new blood vessels is called angiogenesis and it's put in motion by special proteins called angiogenic factors. These proteins include the vascular endothelial growth factor (VEGF) and placental growth factor (PlGF).

In pre-eclampsia, the blood vessels of the placenta remain narrow as there aren't enough cells for invasion. There is less oxygen available and a reduced blood flow causes stress to the placenta. In response, the placenta produces excessive amounts of proteins known as anti-angiogenic factors. The most common protein is soluble fms-like tyrosine kinase 1 (sFlt-1), among others.

These proteins are released into the mother's blood and become harmful. The sFlt-1 protein is partly responsible for vessels not developing normally, leading to an increase in blood pressure as there is limited space in which the blood flows. At this point, both the mother and baby are at risk.

There are now higher levels of the protein sFlt-1 in the maternal blood than the proteins involved in normal vessel formation. This is known as an angiogenic imbalance. The sFlt/PlGF ratio is the first test for early detection of pre-eclampsia.

We assume that in the case of women with HIV, an additional factor interferes with the normal development of blood vessels. That is a protein called *Tat*. When the HIV virus enters the bloodstream in pregnant women, the *Tat* protein is able to recognise another protein similar to itself, VEGF. The *Tat* protein binds on to VEGF and VEGF can no longer perform its function. This lowers VEGF levels necessary for healthy vessel formation for normal blood flow.

Scientists investigate specific genes to determine if they are related to developing a disease. In the case of pre-eclampsia, there hadn't been many advances in the field of gene discovery until 2017. Using foetal blood, a group of scientists across Europe discovered that a gene called Flt-1 is associated with an increased risk of developing pre-eclampsia in a population from Norway and Finland.

In a bid to expand the knowledge base on the subject I chose to do my PhD research on the gene. It encodes the protein sFlt-1 which is the source of the trouble in placenta. To assess the risk, we are using a similar approach to this European study to investigate Flt-1 in maternal blood. This is the first time the gene is being studied in a population affected by HIV. All HIV-positive women in the study are on antiretrovirals.

Antiretroviral therapy in pregnancy

Part of our inquiry is to look into the effects of antiretroviral therapy on high blood pressure in pregnancy. Pre-eclampsia and HIV are both immune diseases so we assume there should be common link.

During pregnancy, changes in the immune system are a challenge to the placenta and foetus. For the mother, the foetus is now recognised as a foreign invader. Both the placenta and foetus need to be protected from the activation of the mother's

immune response. As a result, her immunity is increased during pregnancy to prevent rejection of the foetus as a foreign tissue.

The foetus needs to survive these changes and adapt to the mother's immune response. The incompatibility of both immune systems plays a role in the development of pre-eclampsia. The mother develops an abnormal immune response to the placenta with heightened immunity and an increase in inflammatory cells.

Research suggests that women receiving antiretroviral therapy may have a higher risk of developing pre-eclampsia. But the science remains unclear. Some studies found that antiretroviral therapy had no impact on pre-eclampsia development. More research is needed to confirm whether antiretroviral therapy is a risk indicator for pre-eclampsia.

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