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TOPIC:

MATERNAL MEDICINE:
JOURNEYS OF WOMEN
IN PREGNANCY, DELIVERY
AND SICKLE CELL DISEASE

By

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MATERNAL MEDICINE: JOURNEYS OF WOMEN IN PREGNANCY, DELIVERY AND SICKLE CELL DISEASE

An Inaugural Lecture Delivered at the University of Lagos J.F.
Ade Ajayi Auditorium on 8th May 2019

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Protocol

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Distinguished Academic and Professional Colleagues,
Non-academic Colleagues (Administrative and Technical),
Dear Patients and Students,
Members of the Press (Print and Electronic Media),
Distinguished Ladies and Gentlemen.

Preamble

I am honoured to be standing here today with the permission of the Vice-Chancellor, before such an esteemed audience, to deliver my inaugural lecture, which happens to be the 4th from my Department of Obstetrics and Gynaecology and the 341st Inaugural of this great university. This inaugural is an opportunity to share my academic and professional work over the past 20 years in the College of Medicine, University of Lagos, the University of First Choice and the Nation's (Indisputable) Pride, with my colleagues, family and members of the public. I am grateful for this opportunity.

Being an academician, I am going to start with a question. Are pregnancy and delivery natural occurrences? As this is an Inaugural lecture and I am aware that you are not allowed to respond, I will debate

this issue and you can then decide for yourself what the answer to the question is.

When we say something is natural, we infer that it is uncomplicated and that it occurs readily and with ease. Incidentally, we can say that to an extent with pregnancy. Approximately sixty to seventy per cent of women have a normal pregnancy and delivery, without the need for any medical intervention. This is the reason women often arrive in hospitals dragging their placentas behind them in one hand and a wailing baby in another, having delivered in the taxi that conveyed them with the poor taxi driver looking a bit confused. It is also, unfortunately, the reason many women have severe complications during pregnancy and childbirth as they are often told how all the people in their mother in laws' cohorts delivered themselves at home and did not need any doctors or nurses.

If we did the maths up there, we would have realised that thirty to forty per cent of pregnancies are actually not "normal" and even in a small country where 100,000 women get pregnant every year, it means 30,000 – 40,000 women could have minor to severely complicated pregnancies, some of which they could potentially die from. In Nigeria where more than 7 million babies are reportedly born every year, we are talking about between 2.1 and 2.8 million women every year, potentially exposed to complications. This is a scary concept especially as we cannot usually predict which women would deliver safely and which ones would not. By this, I mean that even amongst the women who seem to have had a normal pregnancy, problems can develop either towards the end of the pregnancy, at delivery or soon after delivery. So despite the fact that a relatively small proportion of women end up with complications at

delivery, it is important for ALL women to get care during pregnancy and especially during delivery as that is when most complications occur. Yorubas say 'eku ewu omo' which roughly translated means Congratulations on surviving the dangers of childbirth, and 'a gbo ohun iya, a gbo ohun omo' – We will hear the voice of the mother and that of the baby – both of which refer to the perceived danger of the procedure.

Maternal medicine is a fascinating subspecialty as it bridges the disciplines of Internal medicine and pregnancy; surgical conditions and pregnancy; and pregnancy-induced conditions such as preeclampsia (a condition unique to pregnancy where the blood pressure rises, protein appears in the urine and several organs of the body are affected) and gestational diabetes. Internal medicine deals with many conditions like hypertension, diabetes, heart disease, kidney disease, liver disease, neurological disease (e.g. stroke), blood conditions like sickle cell disease, thrombocytopaenia, (to name a few!), in non-pregnant women and men. When pregnant women develop these conditions, maternal medicine specialists are the ones who look after them. There are thus several sections of maternal medicine e.g. problems encountered during pregnancy and problems encountered during delivery - either during vaginal or caesarean delivery. Another and more common method of classification is to use the different organ systems e.g. heart disease in pregnancy, lung or respiratory disease in pregnancy, liver disease in pregnancy and so on. The unique thing about an academic maternal medicine specialist is that not only does she carry out the clinical aspects, which involve looking after the pregnant women and helping to prevent, diagnose and treat their complications, she also does the research. The aim of this is to look further into the minute details of the

possible causes or mechanisms of some of the conditions or into how to treat them or at least reduce the complications that occur from them. The academic maternal medicine specialist standing before you today has been privileged to do all the above but still has a long way to go and a great deal to learn. However, she also has a number of stories to share from the past experiences of 20 years and will unravel this over the next 45 minutes.

Mr Vice-Chancellor sir, I stand here today to talk about a number of journeys. The journey of pregnancy and delivery is solely by women as to date and to the best of my knowledge, only women can become pregnant and they only can deliver babies. These journeys are life-affirming and magnificent but also treacherous and unpredictable because each one potentially breeds and produces new and ever so precious life and because each one has the potential to be very full of twists and turns. My journey as a maternal medicine specialist, supporting the journey of pregnancy and delivery and researching into some of its aspects, is what I will concentrate mostly on today. I will also touch briefly on my journey as a specialist in medical education, which is an interesting one that I might have spent more time on except for the fact that I was reminded a few times that the University of Lagos would only promote me to a Professor of Obstetrics and Gynaecology and not of Medical Education. Permit me therefore, to divide my lecture into sections, in order to address the different aspects of my work as well as to attempt to keep the audience from sleeping or gazing at their mobile phones. I will start with a few medical conditions in pregnancy, move on to research surrounding delivery, discuss my work in sickle cell pregnancy and end with a few words about medical education.

Diabetes in pregnancy

My research has dwelt heavily on medical problems during pregnancy and I will start with diabetes mellitus. Diabetes is a disease that results from the lack of insulin, either because the body is not producing enough or because it is resistant to what is being produced. Pregnancy is potentially a diabetogenic state as there are several hormones that are produced that oppose insulin, particularly in late pregnancy. Thus those who have risk factors for diabetes such as obese women or women with a strong family history e.g. mother, father or sibling with diabetes, have a higher risk of developing the condition in pregnancy. However, in early pregnancy, there is an increased sensitivity to insulin, and fasting and random blood sugar levels are usually relatively low. We conducted a study on fasting blood glucose of women in pregnancy and found it to be lower than normal non-pregnant women as expected (Table 1), and significantly lower than the WHO recommended criteria for diagnosing diabetes at the time (5.3mmol/l vs. 7.8mmol/l). Our results suggested a possible need for different populations of pregnant women to have their own reference values for fasting blood glucose and for the revision of the WHO criteria for gestational diabetes and diabetes in pregnancy, which has since happened, not as a direct result of our study but as a collective result of many similar studies.

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nepitA itmrgsqjwq esctmseb vancocellt mnsosm
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edited by Prof. Akin Aigbenigbe and Dr. Mulatu Joab
Mellitus, Pregnancy induced hypertension, pre-eclampsia
and chronic hypertension, hydramnios and low birth
weight

Table 1: Mean fasting plasma glucose in all patients studied

	<i>Control (n = 60)</i>	<i>1st trimester (n = 60)</i>	<i>2nd trimester (n = 100)</i>	<i>3rd trimester (n = 100)</i>	<i>Significance*</i>
Mean fasting	(4.64 ± 0.79)	(3.72 ± 0.58)	(3.78 ± 0.81)	(3.81 ± 0.85)	<i>P < 0.001 (C: 1,2,3)</i>
Plasma		(3.72 ± 0.58)	(3.78 ± 0.81)		<i>P = 0.66</i>
Glucose		(3.72 ± 0.58)		(3.81 ± 0.85)	<i>P = 0.51</i>
(mmol/l ± SD)			(3.78 ± 0.81)	(3.81 ± 0.85)	<i>P = 0.79</i>

*One-way analysis of variance. SD = standard deviation. (C: 1,2,3) = P value for difference between control group and all pregnant patients.

B.B. Afolabi et al. Journal of Obstetrics and Gynaecology, November 2003.

Hypertension and preeclampsia

Preeclampsia is a condition associated with hypertension that is unique to pregnancy and has been studied for decades in the field of maternal medicine. It has been studied so extensively because it can lead to severe complications including kidney failure and liver disease and can also lead to eclampsia – in which the patient with preeclampsia develops convulsions. It is one of the commonest causes of maternal death in Nigeria and worldwide. My team and I decided to examine whether a particular type of immunity was different in preeclampsia than in normal pregnancy. We measured adenosine deaminase, which is a marker of cell-mediated immunity, in non-pregnant controls and in three groups of women with normal pregnancy, gestational hypertension and preeclampsia respectively. We found a lower level in pregnancy than in non-pregnant women as expected (Table 2). We also found a higher level in women with gestational hypertension and preeclampsia than those with normal pregnancy. This was the first study to measure adenosine deaminase in pregnant African women, to the best of our knowledge and added to the body of literature on the topic.

Table 2: Adenosine deaminase activity in various study groups

Group	Number	Mean ± SD ADAActivity
Non-Pregnant	35	23.21 ± 6.3
Normal Pregnant	35	14.69 ± 3.2*
Pregnancy Induced Hypertension	35	17.72 ± 4.9**
Pre-eclampsia	20	17.92 ± 5.5**

*Compared to non-pregnant group. p<0.01; **Compared to normal pregnancy, p<0.01

O.O. Oladipo, B.B. Afolabi, A.O. Okorodudu. West African Journal of Medicine, 2009

Still on preeclampsia, we also tried to see if we could find a marker to predict the development of the condition, a feat that has been difficult worldwide. We examined two markers that had been studied outside Nigeria, plasminogen activator Type I, and fibrinogen in pregnant women before 20 weeks of pregnancy. We picked that time because preeclampsia develops after 20 weeks of pregnancy and because for our resource poor environment, a single measurement would be more cost-effective. We found that neither of them could predict preeclampsia when examined in a single sample before 20 weeks of pregnancy.

We also wrote 4 chapters on different maternal medicine topics in the much read textbook – Textbook of Obstetrics and Gynaecologists for Medical Students, edited by Prof Akin Agboola, namely on Diabetes Mellitus, Pregnancy induced hypertension, pre-eclampsia and chronic hypertension, Hydramnios and Low birth weight.

Nutrition during pregnancy

Before I move to the aspect of delivery, I will touch briefly on some uncommonly researched areas in our environment. Vitamin D is a fat-soluble vitamin that is produced when the skin is exposed to the sun. As we live in a very sunny environment, it is assumed that most of us would produce a lot of Vitamin D, at least enough of what we need for our health. However, as our skin is dark, the increased melanin prevents exposure to the Ultraviolet B rays of the sun required for the production of Vitamin D. To top it all, we are also often hiding from the sun and are either inside one form of transportation or the other before we get into our protected destinations.

One of my former resident doctors, who is now a Consultant Obstetrician and Gynaecologist in my department – Dr Emmanuel Owie worked with me on a study examining the prevalence of Vitamin D deficiency and insufficiency in pregnant women as well as in their newborn babies. We measured Vitamin D levels in the mother's venous blood and for the baby, in the cord blood. We found that Vitamin D deficiency i.e. levels lower than 20ng/ml was relatively low in the women but that Vitamin D insufficiency i.e. levels between 21 and 29 ng/ml was about 28.3%, which is higher than expected for our climate. What was more surprising was that despite the relatively low levels of deficiency in the mothers, the babies had a deficiency of 29.5% and an insufficiency of 36.1% (Fig. 1).

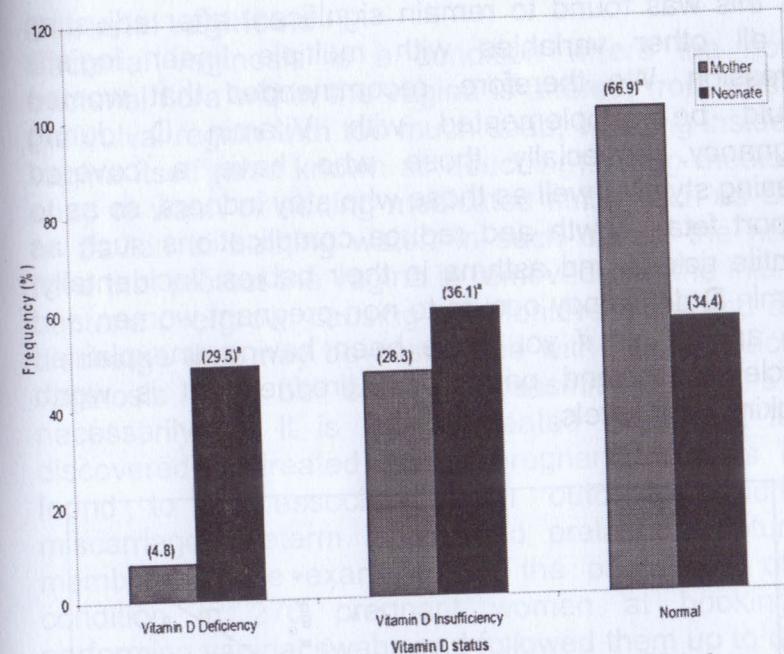


Fig. 1: The comparison of Vitamin D status based on serum concentrations of 25(OH) Vitamin D in the mothers and their neonates (figures in parenthesis on each bar represent the percentage frequency). The disparity in frequency between mother and neonates by Vitamin D status was evaluated by chi-square test.
^ap<0.05.(mother vs. neonate)

Owie E, Afolabi, B.B. Vitamin D deficiency in pregnant women and newborns in Nigeria. J. Obstet Gynaecol, 2018.

Thus although we found a positive correlation between maternal and cord blood Vitamin D levels (Fig. 2), it appears there is something preventing the full transfer of Vitamin D between mothers and their neonates and this is a situation that requires further exploration. We also found that women who had a covered dressing style and those who spent less than one hour a day outside, were more likely to have lower Vitamin D levels, whilst those who had Vitamin D supplementation had higher levels

and this was found to remain significant after adjusting for all other variables with multiple linear logistic regression. We therefore, recommended that women should be supplemented with Vitamin D during pregnancy, especially those who have a covered dressing style as well as those who stay indoors, so as to support fetal growth and reduce complications such as infantile rickets and asthma in their babies. Incidentally, Vitamin D deficiency occurs to non-pregnant women and men as well so if you have been having unexplained muscle aches and pains, and tiredness, it is worth checking your levels.

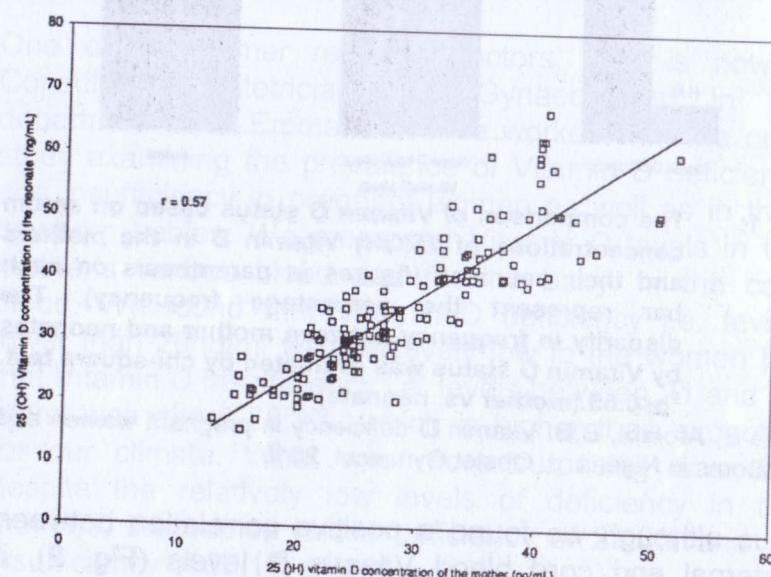


Fig. 2: The relationship between serum 25(OH) Vitamin D concentrations of the mothers and their neonates (solid line shows linear regression)

Owie E, Afolabi, B.B. Vitamin D deficiency in pregnant women and newborns in Nigeria. J Obstet Gynaecol 2018.

Bacterial vaginosis

Bacterial vaginosis is a condition where the normal bacterial flora within the vagina is altered, from washing the vulval region with too much soap, washing inside the vagina itself (also known as douching), using medicated soap to wash or adding medicated fluids such as Dettol or Savlon to bathing water. In such cases, the normal flora that protect the vagina is removed and the injurious bacteria overgrow, causing an offensive smell and a thin discharge that may be associated with itching. Bacterial vaginosis can be sexually transmitted but is not necessarily so. It is usually treated easily but if not discovered or treated before pregnancy, it has been found to be associated with outcomes such as miscarriage, preterm labour and prelabour rupture of membranes. We examined for the prevalence of the condition in 270 pregnant women at booking by performing vaginal swabs and followed them up to detect any complications in them and in their newborn babies. We were the second published study in Nigeria to look at BV in pregnancy in relation to outcome and we felt the need to carry out our study because the previous one did not find any association with pregnancy outcome as has been reported in many other countries. We used the Nugent score in our study, which has been shown to have a higher specificity and sensitivity for the diagnosis of BV, compared to the AMSEL criteria used in the previous study, and we also studied more women. We found a prevalence of BV in 26% of the women studied as well as significantly higher incidences of preterm delivery, low birth weight and premature rupture of membranes in the women with BV, compared to those without (Table 3).

The question is how do we prevent bacterial vaginosis in women before they get pregnant? This is because

treatment during pregnancy has not been shown to prevent the outcomes. We treated all women diagnosed with the condition in our study but some of them still developed the outcomes. We therefore, recommend that women avoid developing or get treated for bacterial vaginosis before getting pregnant. This means there might be a case for having a swab test before pregnancy in women at high risk for the condition. Something to take note of here is that bacterial vaginosis and other common vaginal infections especially the most common one called candidiasis and also known as yeast infection or thrush are not necessarily sexually transmitted. They are also not acquired from the toilet as a lot of people think. It is actually very rare to acquire vaginal infections from the toilet as the organisms that cause them do not thrive on such surfaces. However, other infections can be acquired so do continue to wash your hands carefully after using the toilet.

Table 3: BV status and pregnancy outcome

Pregnancy Outcome	BV Positive (N = 64)	BV Negative (N = 182)	RR (95% CI)	P Value
Preterm delivery N (%)	16 (25)	17 (9.3)	2.68 (1.44–4.98)	.002
LBW	9 (14.1)	8 (4.4)	3.2 (1.29–7.94)	.008
PROM	19 (29.7)	8 (4.4)	6.75 (3.11–14.67)	<.001
Miscarriage	3 (4.7)	6 (3.3)	1.42 (0.37–5.52)	.307
Neonatal Unit Admission	12 (18.8)	24 (13.2)	1.42 (0.75–2.67)	.145

Abbreviations: BV, bacterial vaginosis; CI, confidence interval; LBW, low birth weight; PROM, premature rupture of membranes; RR, risk ratio.

Afolabi. B.B. et al. Bacterial vaginosis and pregnancy outcome in Lagos, Nigeria. Open Forum Infectious Diseases, 2016.

Delivery: Anaesthesia for caesarean section

Anaesthesia is the method used by trained doctors known as anaesthetists to render a person insensitive to

pain before a surgical procedure is performed. When I first came into the College of Medicine and the Lagos University Teaching Hospital 20 years ago, I realised that most of the caesarean sections were being done under general anaesthesia. I found this surprising as I had recently finished training in the UK where most caesarean sections were done under regional anaesthesia. To explain this simply, general anaesthesia is the type of anaesthesia where you are put to sleep and rendered immobile while regional is the type where an injection is put in a particular area to numb that area. For the regional used for caesarean section, the injection is put in the woman's back to numb her from the waist down so she doesn't feel any pain during the surgery. The types used are spinal and epidural anaesthesia, spinal being used more commonly. I decided to examine the difference in the outcome of the babies of mothers who had general anaesthesia for their caesarean section compared with those who had spinal anaesthesia. We therefore carried out a prospective comparative study of women who had general compared with spinal anaesthesia. We found that their babies' need for assistance with breathing was less, their Apgar scores (a score that gives an idea of babies' well being in the first few minutes after birth) were higher and that the need for transfusing the mothers was less when the women had spinal anaesthesia compared with general anaesthesia. We were the first to carry out such a comparative study in West Africa and since then, most of our caesarean sections have been done using spinal anaesthesia.

We further examined our findings in another study published by Professor Ronke Desalu and myself in this area; here we found just a year later, that more caesarean sections were performed under regional anaesthesia (67%) compared with general (33%). The

question we were asking on that occasion was what informed the choice of one of the techniques over the other. We examined 196 caesarean sections and found that general anaesthesia was used more in cases where the baby was in distress whilst regional anaesthesia was used more for women with co-existing medical problems such as preeclampsia (Table 4).

Table 4: Anaesthetic techniques used for patients with medical problems (n=37)

Anaesthetic technique No. (%)	Medical problems (no.)
General anaesthesia	10 (27%) Pre-eclamptic toxæmia – 8 Diabetes mellitus – 2
Regional anaesthesia	27 (73%) Pre-eclamptic toxæmia – 22 HIV – 2 Cerebral malaria – 1 Sickle Cell disease – 1 Active herpes - 1

Desalu I, Afolabi BB. 'Urgency of Surgery...' Nigerian Postgraduate Medical Journal, 2007.

Cochrane systematic review – Evidence-based medicine

The two studies above were interesting but they still led to more questions. What type of anaesthesia did women actually prefer? And what was the real evidence determining the better type of anaesthesia? Did our findings hold in other climes? Were there other studies, perhaps performed more rigorously that might be different? In the world of research and data, it is very easy to find information that has been published somewhere that supports a particular bias. We see this in newspapers and social media all the time and it also

occurs in medicine, unfortunately. Fake news is everywhere and so are research questions that are answered by the wrong type of study, leading to inaccurate answers, even if inadvertent or due to lack of funding for high-quality research.

This is where evidence-based medicine comes in, which essentially is the practice of medicine, with the best available clinical evidence from **systematic** research, by an experienced practitioner. One of the best forms of evidence or the best method to clarify what treatment actually works better than another is by performing a type of robust research study called a systematic review. The Cochrane Group is one of the most respected repositories of systematic reviews worldwide and I happen to be a member of the Cochrane group and the author of 6 systematic reviews. We performed one of these reviews to answer the question on regional anaesthesia versus general for caesarean section (Fig. 3).



Regional versus general anaesthesia for caesarean section (Review)

Afolabi BB, Lesi FEA

Fig. 3: Front page of our Cochrane systematic review

We found that when it comes to important outcomes such as maternal death or neonatal death, there is no evidence of a difference between the two types of anaesthesia for caesarean section. We suspect that this is probably because caesarean section is very safe these days and in order to be able to prove such a rare finding as death from it, the numbers studied would have to be very large. As most researchers know, when you are trying to test a rare outcome, your sample size, i.e. the number of subjects in your study, has to be sufficiently large. In the case of the current question, there would be a need to study hundreds of thousands of women undergoing caesarean section, which would be a very expensive study indeed.

We did find that estimated blood loss during caesarean section was lower in those who had any of the two types of regional anaesthesia compared with being put to sleep i.e. general anaesthesia, and we also found evidence of an improved index of the well-being of the newborn babies, namely the Apgar score. Fewer babies of women who had spinal anaesthesia had an Apgar score of 6 or less at one minute than those who had general anaesthesia. However, by 5 minutes, there was no difference in the two groups. An interesting issue here is that we did not find evidence about what women actually preferred. One of the studies we looked at found that more women in the general anaesthesia group said they would use the same technique again than those in the spinal or epidural group.

Mr. Vice-Chancellor sir, I have dwelt on this publication not because it is about 86 pages long, virtually a book in its own right, but because together with its earlier version, it has been cited over 320 times by both international and national scholars. This means that more than 320

different groups of scholars worldwide have used our paper as a reference in their work. This is indeed very gratifying.

In addition to the above Cochrane reviews, I have co-authored 4 others on various topics attempting to answer the following questions:

Is intravenous antiD immunoglobulin as effective as intramuscular antiD in preventing Rhesus alloimmunization in Rhesus negative mothers i.e. forming antibodies against their subsequent babies? Is Mannitol or any other osmotic diuretic useful in the treatment of cerebral malaria – a very dangerous form of malaria that is often fatal? (We had two versions of this review as well). And is intramuscular arteether as effective as other antimalarial drugs such as quinine in treating severe malaria, including cerebral malaria?

As often happens with clinical scenarios, the answer to these questions was that more research needs to be done to add to the body of knowledge and further updates of the various systematic reviews would need to be done to discover the answer. In short, research, like a house, is never done and that is part of what makes it so exciting.

Delivery: Induction of labour

In 2002, a very intelligent resident doctor under my supervision, Dr Lawal Oyeneyin, who is now a senior obstetrician in his own right and currently a senior lecturer and the acting Head of Department of Obstetrics and Gynaecology at the University of Medical Sciences, Ondo, came to me to discuss a possible topic to work on for his dissertation. He wanted to do something different from what most people did and together, we decided on a

randomized controlled trial. This type of research needs a lot of resources and planning but he wasn't daunted and we went for it.

Induction of labour is the process where labour is started in the hospital using tablets or clinical devices, in patients who have gone past their due dates and have not fallen spontaneously into labour or who need to be delivered earlier than their due date for medical reasons. To induce labour, we often need to 'ripen the cervix' i.e. change it from a relatively long, firm structure to a thin, soft one (Fig. 4).

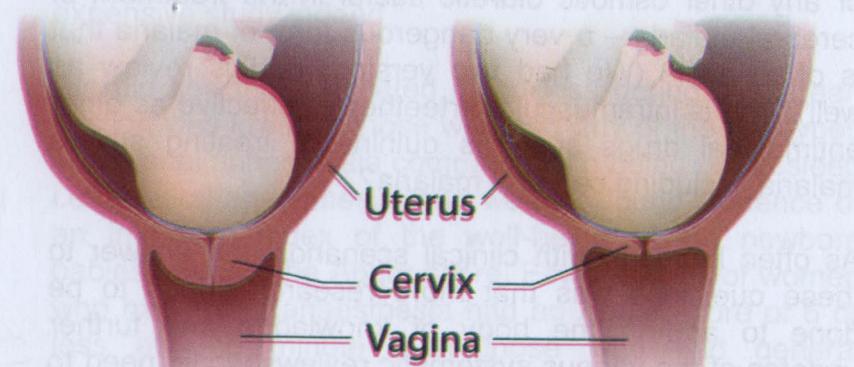


Fig. 4: The longer, tubular structure, effacing (or 'ripening') to a thin soft structure

In our centre, we usually used a rubber tube known as a Foley catheter that is inserted into the cervix of the woman through her vagina, a procedure that has been tried and tested but could be uncomfortable for the woman. We had recently started using a drug called misoprostol, inserted into the vagina, which did the same job by releasing a substance that softens the cervix. The study was to test one against the other and determine which was more effective in making the woman fall into

labour and deliver her baby as safely and as quickly as possible.

We found misoprostol to be more effective than our old technique with a shorter induction to delivery interval and a higher improvement in cervical ripening as assessed by the change in 'Bishop score'. However, we also found something ominous, something that made us tread carefully with the use of misoprostol. This was a time when misoprostol had only recently come into use in most of the world for this purpose and not enough research had been done to determine the appropriate dose. The dose we used in the study was a single 100mcg dose, which is half of one tablet of misoprostol. If this did not work i.e. if the cervix remained unfavourable after 12 hours, the protocol dictated that we switch to Foley catheter use. At the end of the study, we found that more women who had misoprostol had excessive contractions although not statistically significant. We also found that 2 women with misoprostol had silent small uterine ruptures, which were discovered during caesarean section after they failed to fall into labour or showed signs of fetal distress. There were no maternal or fetal losses thankfully and all the women and their babies did well. The results of the study, however, made us change our doses and indication for misoprostol use and the study has been cited over 50 times by national and international publications.

Table 5: Labour characteristics with a one-time successful induction

Characteristics	Misoprostol N=29	Foley Catheter N=28	Significance	95% C.I.
IDI (mean (h)± S.D.)	11.84±5.43	20.03±4.68	P<0.05	5.40, 10.98
Birth weight (mean (kg)± S.D.)	3.45±0.41	3.41±0.66	P>0.05	-0.25, 0.33
1st minute Apgar Score (mean ± S.D.)	8.17±1.56	9.93±1.72	P>0.05	-4.62, 8.15
Percentage delivered within 24 h	100.0	82.1	P<0.05	
Percentage of Oxytocin use	24.1	82.1	P<0.05	

IDI=Induction-Delivery Interval; SD=Standard deviation; kg=kilograms; mIU/min=milli international unit/minute; C.I.=Confidence interval.

Afolabi B.B. et al. Intravaginal misoprostol vs. Foley catheter for cervical ripening... International Journal of Gynecology and Obstetrics, 2004.

Table 6: Change in bishop score by method and parity in patients with a one-time successful induction

Parity	Misoprostol N=29	Foley Catheter N=28	Significance	95% C.I.
Nulliparae	N=13 $\bar{x}=6.6\pm 1.7$	N=13 $\bar{x}=4.4\pm 1.93$	P<0.05	0.71, 3.69
Multiparae	N=16 $\bar{x}=6.6\pm 2.50$	N=15 $\bar{x}=3.9\pm 1.62$	P<0.05	1.17, 4.23

\bar{x} =Mean change in score± Standard deviation; C.I.=Confidence interval; N=number in group.

Afolabi B.B. et al. Intravaginal misoprostol vs. Foley catheter for cervical ripening... International Journal of Gynecology and Obstetrics, 2004.

Journeying into sickle cell disease

Mr Vice-Chancellor sir, please permit me to begin the next aspect of my lecture – the part about sickle cell disease. Sickle cell disease is a condition that can cause terrible suffering and early deaths of young precious lives. It is a condition caused by an inherited abnormality of haemoglobin, which is the substance that carries oxygen within red blood cells. A specific genetic mutation causes the proteins in the haemoglobin to change and this affects the oxygen binding and causes a change in the shape of the normally bi-concave red blood cell during stressful conditions such as oxygen deprivation, dehydration or infection. The red blood cell then changes

to a sickle shape as depicted below (Fig. 5), hence the name of the condition. A sickle is a hand-held agricultural tool, which has a similar shape. Most of the complications of the disease occur because the abnormally shaped red blood cells break down easily and cause severe anaemia and because they also block the blood vessels that carry blood to tissues and therefore reduce the blood flow to those tissues (Fig. 6). The abnormal haemoglobin type is called SS while the normal one is called AA. People with AS are carriers but usually, do not have any symptoms. Inheritance of the condition is in a Mendelian fashion, such that if a carrier has a child with another carrier, the probability for each child to have Haemoglobin SS is 1 in 4 (Fig. 7).

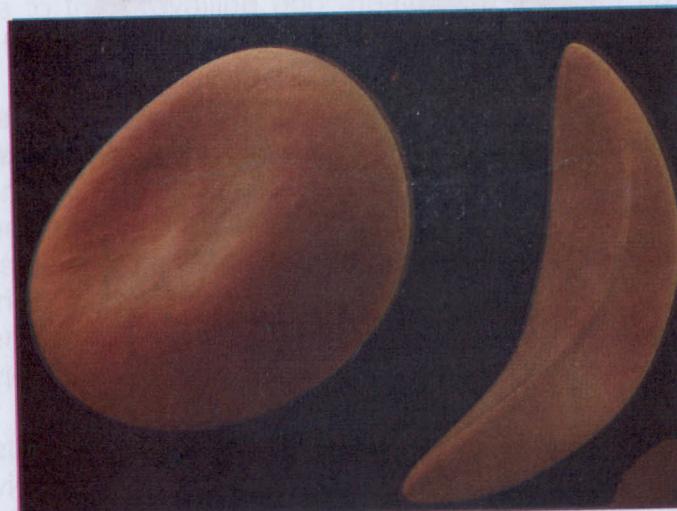


Fig. 5: A normal shaped red blood cell and a sickle-shaped red blood cell

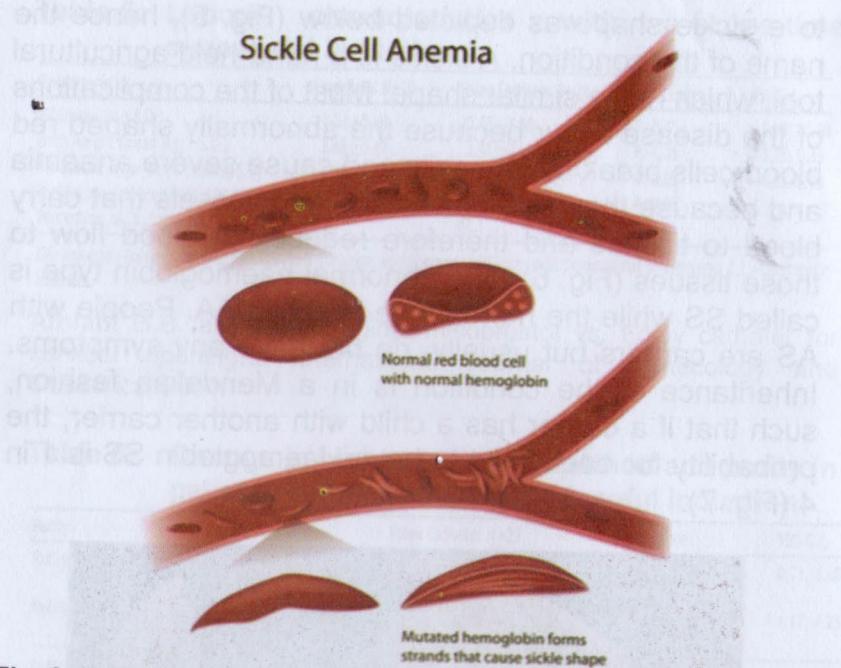


Fig. 6: Normal and sickle-shaped red blood cells within blood vessels

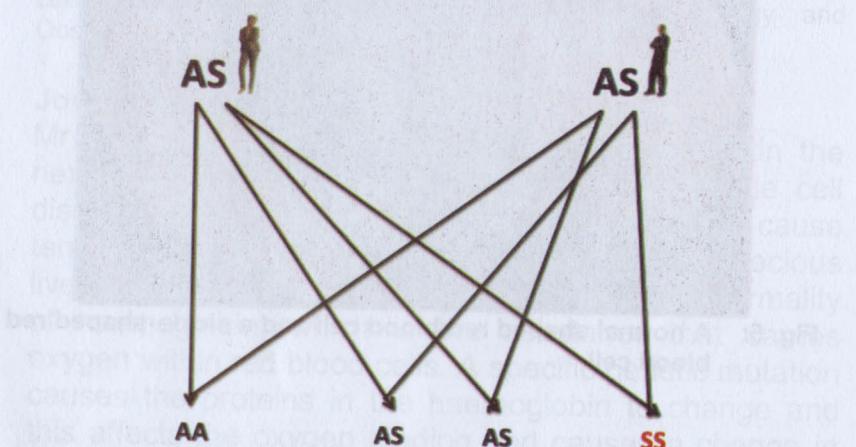


Fig. 7: Inheritance of sickle cell disease from two carrier parents. The probability of having a child with the genotype SS for each pregnancy is 1 in 4

In the past, children born with sickle cell disease hardly made it to age 5 and it was seen as a disease of childhood. Life expectancy was very low and this remains the case in low resource and poor public health areas. In areas with good public health facilities however, survival has increased dramatically over the years as a result of improved preventive and medical care. We have many individuals these days living with the condition till middle and elderly ages. Despite this, life expectancy is still relatively low, ranging from 53 years for men and 58.5 for women in Jamaica and 58 years on average in the USA. In Nigeria, where approximately 150,000 babies are born every year with sickle cell disease, the highest number in the world, there are no specific life expectancy figures. Due to the prevailing poor healthcare facilities however, we know it is likely to be lower than the figures above.

The first major review of sickle cell disease in pregnancy was by Kobak et al in 1941. They found a 33% maternal mortality rate as well as several complications such as preeclampsia, pneumonia and puerperal sepsis. There was also a high incidence of miscarriage and stillbirths – 6 in 37 pregnancies. However, even in those early days, there was a variability of the clinical course with one review finding a maternal mortality of 66% (four deaths in six women) and in the same year, another finding no maternal deaths in 11 deliveries. More recently some reviews have also found a reduction in the maternal and perinatal mortality though still a higher incidence of complications in both mother and fetus.

We ourselves have occasionally found some remarkably resilient women with this condition. We published a case report about a 38-year old woman with Haemoglobin SS whom we admitted at 28 weeks of pregnancy with recurrent episodes of severe anaemia i.e. a very low

level of haemoglobin, as well as occasional abdominal pain. This woman was in her fourth pregnancy, having had 2 normal deliveries 15 and 12 years respectively before presentation as well as an ectopic pregnancy for which she had to have surgery, 6 years before presentation. By the time she was referred to us, she had been transfused 8 pints of blood for the anaemia. She had also been diagnosed with a twin pregnancy, with one twin alive and the other one having died in-utero, i.e. within her womb. She later had a miscarriage of the dead 'twin' but the other baby remained alive and well. We managed to get her up to 34 weeks before we decided to deliver her as she kept having episodes of severe anaemia and abdominal pain. When we opened her up to deliver her, we found that the second pregnancy was actually not within her womb but in the abdomen i.e. it was what we call an abdominal pregnancy. She lost a lot of blood during the surgery and had to be transfused even more. She eventually went home after 4 months of admission and 25 pints of blood in total! What was remarkable about her case apart from the abdominal pregnancy, which was missed and thought to be in the uterus, was that she survived all the complications that arose from the pregnancy.

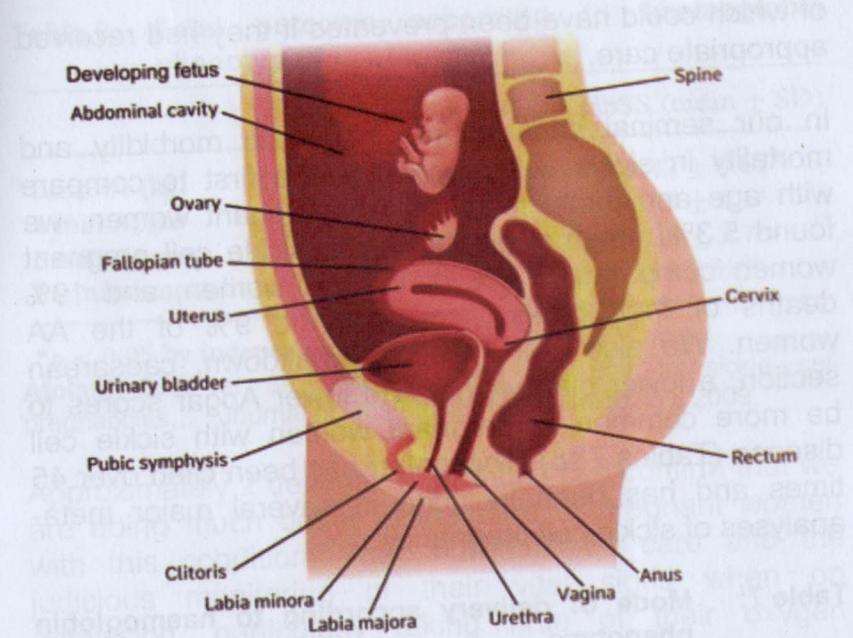


Fig. 8: Diagram depicting an abdominal pregnancy

Despite the variability, however, there is no doubt that the condition is still fraught with a high incidence of maternal and perinatal mortality, particularly in our environment. This is because healthcare indices are still poor and unevenly distributed as a result of inappropriate distribution and management of resources and manpower. Also, the majority of our people are still unaware of the need to cultivate healthy lifestyles and seek medical help when in the early stages of illness. Many individuals are not even aware of their haemoglobin phenotype either because they have never checked it or because they received an erroneous test result in the past. Thus by the time the females get to the reproductive age group, they are either unaware of the condition or have had several complications from it, some

of which could have been prevented if they had received appropriate care.

In "our seminal case control study on morbidity and mortality in sickle cell pregnancy, the first to compare with age and parity matched AA pregnant women, we found 5.3% maternal deaths in the sickle cell pregnant women compared to 0% of the AA women, and 19% deaths of their babies, compared to 9% of the AA women. We also found wound breakdown, caesarean section, a lower birth weight and lower Apgar scores to be more common in pregnant women with sickle cell disease (Tables 7&8). This paper has been cited over 45 times and has been included in several major meta-analyses of sickle cell pregnancy.

Table 7: Mode of delivery according to haemoglobin phenotype

Mode of delivery	HbAA (%)	HbSS (%)
Vaginal delivery	79.9	60*
Caesarean section	20.1	38.7*
Emergency CS	18.9	33.3*

* $p < 0.05$ by χ^2 -test. CS, caesarean section.

Afolabi B.B. et al. "Morbidity and mortality in sickle cell pregnancies...". Journal of Obstetrics and Gynaecology, 2009.

Table 8: Fetal outcome according to haemoglobin phenotype

	HbAA (mean \pm SD)	HbSS (mean \pm SD)
Birth wt (kg)	3.14 \pm 0.63	2.42 \pm 0.62*
1 min Apgar	7.3 \pm 2.4	5.7 \pm 3.1*
5 min Apgar	8.9 \pm 2.4	7.5 \pm 3.7*
Perinatal mortality	8.8 %	18.7 %**

* $p < 0.05$ by independent t -test, ** $p < 0.05$ by χ^2 -test.

Afolabi B.B. et al. "Morbidity and mortality in sickle cell pregnancies...". Journal of Obstetrics and Gynaecology, 2009.

Approximately 2 decades after this, I can confirm that we are doing much better in the care of pregnant women with this condition. With individualized care and the judicious monitoring of their vital signs when on admission, particularly taking note of their oxygen saturation using inexpensive handheld pulse-oximeters, we have recorded a zero per cent mortality during the past 5 years in pregnant women with sickle cell disease under our care. A prospective study by my team detailing this improvement in mortality indices was recently published in the reputable and indexed Nigerian Postgraduate Medical journal.

In 1988, Abudu and Sofola published a paper titled 'Intravascular volume expansion and fetal outcome in pregnant Nigerians with Haemoglobin SS and SC'. This was the first paper to study the plasma volume in pregnant women with sickle cell disease. Plasma refers to the part of the blood that is liquid i.e. blood without the cells. Prior to this, Harrison had examined plasma volume in normal pregnant Nigerian women and found the changes in 20 such women, to be similar to that seen in Caucasian women. He also examined plasma volume

in pregnant women with severe anaemia (but not due to sickle cell disease) and found that the plasma volume is increased in them.

It is a known fact that the babies of pregnant women with sickle cell disease have birth weights and birth weight percentiles below average as a result of preterm delivery and IUGR. This was initially postulated to be due to their chronic anaemia. However the relationship between anaemia and birth weight is still not clear, and many studies report a U-shaped relationship between maternal haemoglobin and birth weight. Steer et al., noted that although severe anaemia is associated with a low birth weight, failure of plasma volume expansion also is and demonstrated this by showing that the optimal haemoglobin concentration for optimal birth weight was between 95 and 105 g/L. Haemoglobin concentrations greater than 120g/L were associated with a three-fold risk of intra-uterine growth restriction (IUGR) and preeclampsia. In another study closer to home by Professor Oluwarotimi Akinola and I, we also found high haemoglobin concentrations, which suggests a suboptimal plasma volume expansion, to be associated with lower birth weights i.e. smaller babies.

Table 9: Mean (SD) birth weight and incidences of low birth weight (<2500g) and preterm births (<37 completed weeks) by haemoglobin concentration

Haemoglobin concentration(g/L)	Mean (SD) birth weight(g)	Proportion < 2.5 kg at birth (%)
<100	3020 (480)	0
100-119	3060 (650)	14.3
120-139	3280 (480)	2.8
≥140	3040 (500)	23.1

Afolabi B.B., Akinola O.I. What is the optimum maternal haemoglobin concentration level for a normal birth weight in Lagos? *Trop J. Obstet Gynaecol*, 2004.

Plasma volume expansion in pregnancy was demonstrated about 40 years ago to be the most significant determinant of newborn size. It is also a determinant of good pregnancy outcome as pregnancies complicated by preeclampsia and IUGR are associated with reduced plasma volume expansion. With this background, Abudu and Sofola examined plasma volume in pregnant women with sickle cell disease as well as pregnant and non-pregnant HbAA controls and non-pregnant HbSS and SC women. They found that plasma volume in pregnant SS women was reduced by 36 weeks pregnancy when compared with the non-pregnant SS women. They suggested possible causes to include an alteration of the renin-angiotensin-aldosterone system in pregnancy associated with an increased sodium and water loss.

Fourteen years after this paper was written, I read and was fascinated by it. I applied and got an award from the

Royal College of Obstetricians and Gynaecologists to visit the University of Nottingham through introductions from Professors Abudu and Odum from my department. They had done some work with Professor Fiona Broughton Pipkin of the University of Nottingham, an academician par excellence who is a physiologist by training but became a professor of perinatal physiology and an honorary fellow of the Royal College of Obstetricians and Gynaecologists as a result of her extensive work in obstetrics. She is a co-author of the famous Dewhurst's Textbook of Obstetrics and Gynaecology and is more knowledgeable about preeclampsia and obstetric physiology in general than many clinicians. I mention her specifically here as she became my mentor and drew me into the laboratory, which was the beginning of another journey.

For a core clinician, the lab always seems like the other place where test tubes, pipettes and reagents hold sway as opposed to patients and we seldom go in there except to complain about not getting our results on time or to try to get blood for our patients. However, if you ever venture into it as part of your academic journey, it is the most fascinating and compelling place. There is very little as captivating as spinning your own samples in the centrifuge, discovering that the plasma that is spoken about can actually be separated from blood when you spin it fast enough, collecting the pale yellow supernatant and mixing it with reagents or inserting it into a spectrophotometer to measure the absorbance of light. The world of pipettes, test tubes, beakers, reagents, spectrophotometers and safety hoods is a special one and I am happy to have been able to add it to my journey. After finding out how much I enjoyed it and with encouragement from my mentors, I decided to do an additional Doctorate in Medicine, known as an MD or a

DM. I got a full scholarship to pursue this at the University of Nottingham and also got a doctoral assistance grant from the University of Lagos, our University of First Choice and the Nation's pride!, which helped with a few of the many trips I had to take to Nottingham to pursue a split site DM.



Fig. 9: Dr Bosede Afolabi conducting a plasma volume experiment

I started the DM in 2004 and worked on it on a part-time basis. I also got support from the British Federation of Women Graduates for living expenses for one year during my studies as well as a Central Research grant from the University of Lagos for some of the preliminary studies. In this time, at the same time as doing my full time job as a clinician and a lecturer in LUTH/CMUL, I had to recruit all the patients, carry out the experiments, analyse my samples both in Lagos and in Nottingham, sit through numerous compulsory small courses in research methodology and computer and statistical software methods, all in Nottingham. All my visits to Nottingham were during my annual or research leave except for a six-month period when I took study leave in order to try to complete my thesis writing. The whole process took six years and I was eventually awarded a Doctor of Medicine (DM) degree of the University of Nottingham in July 2011. I am the second person in my department to have an MD since its inception over 55 years ago, and to the best of my knowledge till date, fewer than 10 people in the core clinical sciences have completed one.

Thesis work

So what did I study and what were my findings? I looked at four different groups of women – Pregnant women with sickle cell anaemia i.e. HbSS as well as non-pregnant women also with sickle cell anaemia. The other two groups were pregnant and non-pregnant women with HbAA. All the women were in steady state i.e. for the HbSS women, no crises or transfusions in the four-week or six month period respectively prior to the study. The HbAA women were also well and none of the patients had any known medical illness.

I measured their plasma volumes using the Evans Blue dye dilution method, reconfirmed their haemoglobin

phenotype, measured parameters of the full blood count as well as plasma osmolality, sodium, potassium and creatinine; we also measured six hormones – plasma angiotensinogen concentration, plasma renin concentration (PRC), aldosterone, prolactin, progesterone and vasopressin (ADH). We didn't stop there but looked into their urine (24-hr urine collection) and measured the osmolality and sodium, potassium and creatinine as well. In total, we looked at 25 parameters in these four groups of women and are the first ever to measure all these substances in sickle cell pregnancy. This study was published in the Journal of the renin-angiotensin-aldosterone system, which is a prestigious international journal.

In the non-pregnant women, we found plasma volume (PV) to be higher in the HbSS women than their HbAA counterparts. We also found significant positive correlations between PV and plasma renin concentration and prolactin respectively and a significant negative correlation between PV and plasma progesterone, in HbAA non-pregnant women. For HbSS women, the only significant relationship was a negative one between PV and plasma Arginine Vasopressin (ADH). Thus it appears PV may drive ADH levels in them.

Table 10: Comparison of plasma volume in pregnant and non-pregnant women

HbAA	Non-pregnant (N=19)	16 weeks pregnant (N=10)	36 weeks pregnant (N=10)
PV, ml	2165 ± 497	2911 ± 1020*	3089 ± 1035*
PV/body weight, ml/kg	36.1 ± 8.3	40.1 ± 14.4	40.6 ± 16.1
PV/BMI, ml per kg/m ²	97.1 ± 24.4	108.9 ± 37.8	107.8 ± 40.0
PV/BSA, ml/m ²	1308 ± 281	1593 ± 564	1659 ± 603
HbSS	Non-pregnant (N=25)	16 weeks pregnant (N=11)	36 weeks pregnant (N=11)
PV, ml	2714 ± 949*	2758 ± 913	3003 ± 1382
PV/body weight, ml/kg	51.1 ± 16.8*	50.2 ± 19.7	48.9 ± 25.3
PV/BMI, ml per kg/m ²	131.4 ± 42.8*	126.5 ± 51.9	129.5 ± 66.0
PV/BSA, ml/m ²	1762 ± 593*	1768 ± 623	1801 ± 879

Data are reported as mean ± SD.

*Comparison with non-pregnant, $p < 0.05$.

*Comparison between HbAA and HbSS, $p < 0.005$.

N: number of women studied; Hb: haemoglobin; PV: plasma volume; BMI: body mass index; BSA: body surface area.

Afolabi BB et al. Volume regulatory hormones and plasma volume in pregnant women with sickle cell disorder. JRAAS, 2016.

In the pregnant women, plasma volume increased in pregnancy in HbAA compared to the non-pregnant as expected but there was no increase in HbSS at any stage of pregnancy. This is despite the fact that the hematocrit in HbSS pregnancy is significantly lower than in the non-pregnant state as we recorded in our paper on the evaluation of haematological parameters in pregnant sickle cell disease. When it came to relationships between hormones and plasma volume in HbSS pregnant women, we found a significant positive correlation between plasma renin concentration (PRC) and plasma volume per unit body surface area and between serum aldosterone concentration and plasma volume, both at 16 weeks gestation in HbSS women. There was also a significant positive correlation between aldosterone and PV in HbSS pregnancy in general. This suggests that PRC and aldosterone are very important in the control of PV in HbSS pregnancy. It was therefore not surprising to find that plasma renin concentration did not rise in late pregnancy and rose significantly less in early pregnancy in them.

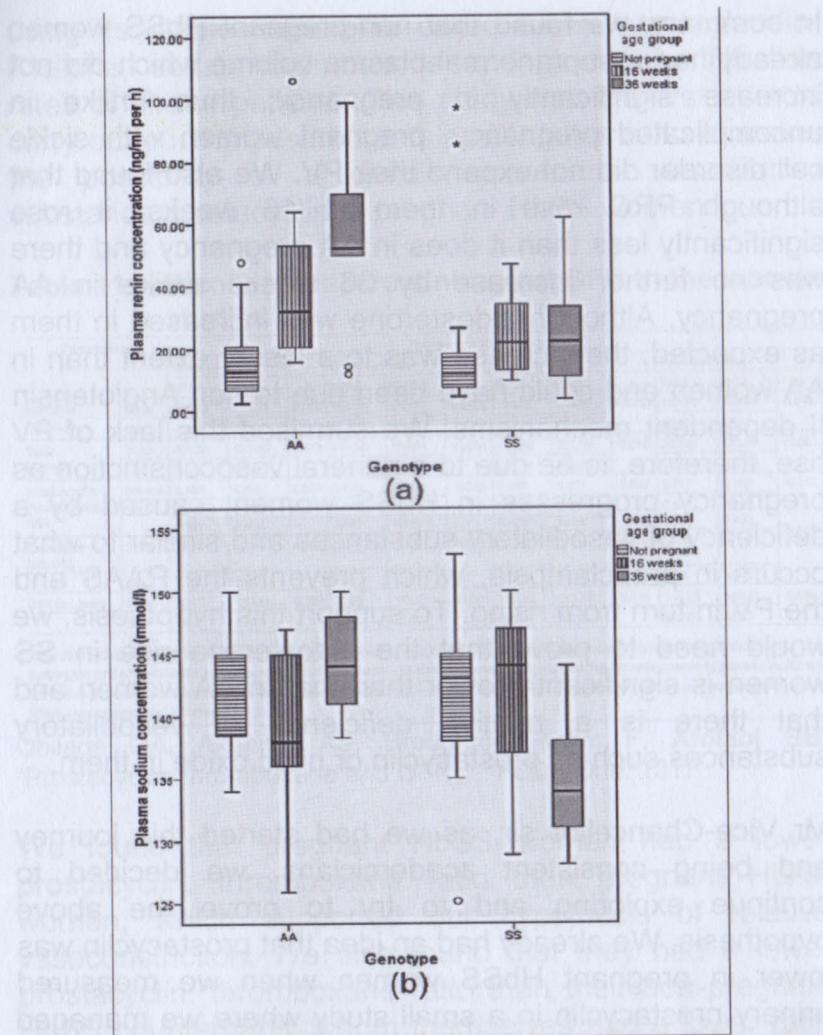


Fig. 10:(a) Plasma renin concentration rose throughout gestation in haemoglobin AA (HbAA) women ($p=0.0001$; Kendall's τ); it had risen by 16 weeks' gestation in HbSS women, but rose no more.

(b) Plasma sodium was not changed in pregnancy in HbAA women ($p>0.6$), but fell significantly in HbSS women ($p = 0.018$ Kendall's τ).

Afolabi BB et al. Volume regulatory hormones and plasma volume in pregnant women with sickle cell disorder. JRAAS, 2016.

In summary, we found that non-pregnant HbSS women already had a supranormal plasma volume which did not increase significantly in pregnancy; thus unlike in uncomplicated pregnancy, pregnant women with sickle cell disorder did not expand their PV. We also found that although PRC rose in them at 16 weeks, it rose significantly less than it does in AA pregnancy and there was no further increase by 36 weeks unlike in AA pregnancy. Although aldosterone was increased in them as expected, the increase was to a lesser extent than in AA women and could have been due to non Angiotensin II dependent mechanisms. We surmised this lack of PV rise, therefore, to be due to a general vasoconstriction as pregnancy progresses in HbSS women, caused by a deficiency of vasodilatory substances and similar to what occurs in preeclampsia, which prevents the RAAS and the PV in turn from rising. To support this hypothesis, we would need to prove that the aldosterone rise in SS women is significantly lower than that in AA women and that there is a relative deficiency of vasodilatory substances such as prostacyclin or nitric oxide in them.

Mr Vice-Chancellor sir, as we had started this journey and being consistent academicians, we decided to continue exploring and to try to prove the above hypothesis. We already had an idea that prostacyclin was lower in pregnant HbSS women when we measured urinary prostacyclin in a small study where we managed to recruit just a few pregnant HbSS women. Together with another bright resident doctor under my supervision, we carried out a truly remarkable study. We again recruited four groups of women, 20 women in each arm, specifically ensuring they were all women who had never previously given birth to ensure uniformity. We examined pregnant and non-pregnant HbSS women and HbAA women as before and measured serum prostacyclin

using its stable metabolite called 6-keto-prostaglandin-F1alpha, serum thromboxane and glomerular filtration rates of all the patients. This study was the first ever to carry out such measurements and to attempt to examine the possibility of a deficiency of the vasodilatory substance prostacyclin in pregnant HbSS women.

Table 11: Eicosanoids, creatinine and GFR in the women studied

Parameters	Groups (n = 20 in each group)*												
	NPAA vs NPSS			NPAA vs PrAA			NPSS vs PrSS			PrAA vs PrSS			
	NPAA	NPSS	p	NPAA	PrAA	p	NPSS	PrSS	p	PrAA	PrSS	p	
6kPGF1α (pg/mL)	Mean	208.75	174.35	0.004	208.75	132.71	<0.001	174.35	105.62	<0.001	132.71	105.62	0.019
	SD	47.09	45.61		47.09	22.40		45.61	20.44		22.40	20.44	
TxB2 (pg/mL)	Mean	419.59	473.80	0.173	419.59	203.84	<0.001	473.80	370.05	0.010	203.84	370.05	<0.001
	SD	85.38	125.34		85.38	111.59		125.34	163.23		111.59	163.23	
Prostacyclin: thromboxane ratio	Median	0.498	0.368	0.000	0.498	0.717	0.044	0.368	0.261	0.037	0.717	0.261	<0.001
	IQR	0.378,	0.278,		0.378,	0.481,		0.278,	0.199,		0.481,	0.199,	
		0.693	0.409		0.693	1.339		0.409	0.462		1.339	0.462	
Creatinine (μmol/L)	Mean	69.76	54.90	0.002	69.76	56.08	0.003	54.90	57.94	0.503	56.08	57.94	0.681
	SD	7.86	21.73		7.86	8.94		21.73	14.19		8.94	14.19	
GFR (mL/min)	Mean	99.23	130.24	0.008	99.23	165.23	<0.001	130.24	145.42	0.186	165.23	145.42	0.085
	SD	15.48	42.57		15.48	35.20		42.57	43.33		35.20	43.33	

#: n = 20 in each group except for 6-ketoPGF1α in the pregnant HbSS women in which two samples were inadvertently omitted during analysis thus prostacyclin (and prostacyclin:thromboxane ratio) for that group had n = 18. The other groups were unaffected and thromboxane on its own was unaffected.
6kPGF1α = prostacyclin metabolite, TxB2 = thromboxane metabolite. PrSS = pregnant HbSS, PrAA = pregnant HbAA, NPSS = non-pregnant HbSS and NPAA = non-pregnant HbAA women.

Obilade OA, Akanmu AS, Broughton Pipkin F, Afolabi BB. "Prostacyclin, thromboxane and GFR..." PLOS One, 2017.

We found that pregnant HbSS women had a lower prostacyclin: thromboxane ratio than pregnant HbAA women, which supported our hypothesis of relative vasoconstriction. We also found that they had a lower prostacyclin: thromboxane ratio than their non-pregnant HbSS counterparts, whom themselves had a lower ratio than the non-pregnant HbAA women. To clarify this, non-pregnant HbSS women are more vasoconstricted than non-pregnant HbAA women; but get even more vasoconstricted during pregnancy (Table 11 & Fig. 10).

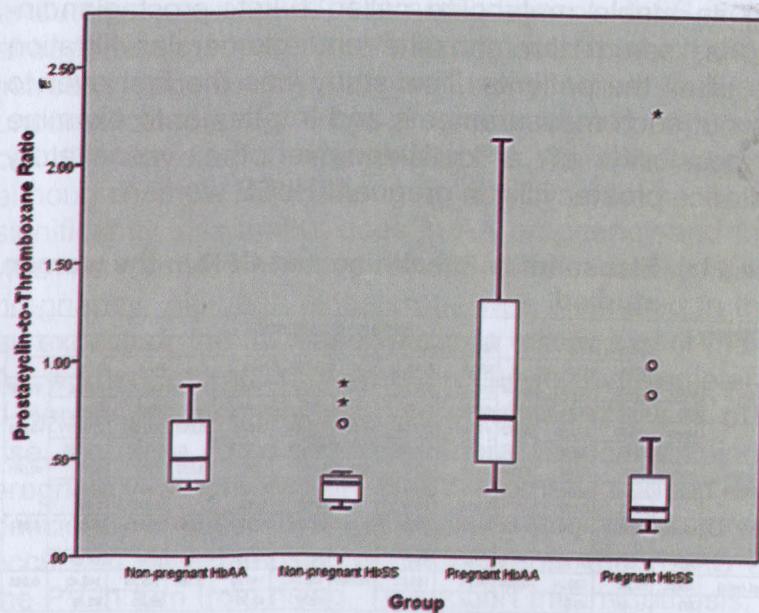


Fig. 11: Prostacyclin-to-thromboxane ratio in pregnant and non-pregnant HbSS and HbAA women

Obilade OA, Akanmu AS, Broughton Pipkin F, **Afolabi BB.** "Prostacyclin, thromboxane and GFR..." PLOS One, 2017.

We also found that their glomerular filtration rate, which is a measure of their renal function, did not increase in pregnancy compared with that of HbAA women, which increased significantly as expected. Even more interesting was the positive correlation between prostacyclin and glomerular filtration rate in the pregnant HbSS women (Fig. 11) and examining this further also confirmed effects of diastolic blood pressure and age on GFR in pregnant HbSS women. This is something we plan to examine in future, seeing as research is never done.

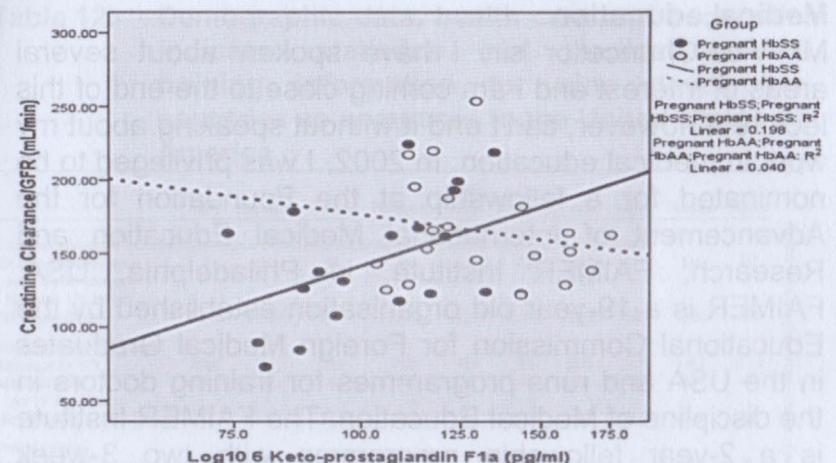


Fig. 12: Relationship between prostacyclin and GFR
A scatter plot showing the relationship between log₁₀ 6-keto-PGF1 α and estimated creatinine clearance in pregnant HbAA women (N=20), and HbSS (N=18) women. The computed best line of fit for both groups of women is displayed and there is a significant positive correlation in HbSS women as shown.

Obilade OA, Akanmu AS, Broughton Pipkin F, **Afolabi BB.** "Prostacyclin, thromboxane and GFR..." PLOS One, 2017.

However, the more exciting pathway to embark on is to follow up on the finding of a lower prostacyclin thromboxane ratio, especially as this is something that has been found in preeclampsia and is the basis of the use of low dose aspirin to prevent preeclampsia in those with a high risk for it. My team and I have already developed a proposal for a trial to test the hypothesis that low dose aspirin might reduce the risk of growth restriction and preeclampsia in sickle cell pregnancy and have just submitted a grant application for funding to carry it out.

Medical education

Mr Vice-Chancellor sir, I have spoken about several areas of interest and I am coming close to the end of this lecture. I however, can't end it without speaking about my work in medical education. In 2002, I was privileged to be nominated for a fellowship at the Foundation for the Advancement of International Medical Education and Research, FAIMER Institute, in Philadelphia, USA. FAIMER is a 19-year old organisation established by the Educational Commission for Foreign Medical Graduates in the USA and runs programmes for training doctors in the discipline of Medical Education. The FAIMER Institute is a 2-year fellowship programme with two 3-week sessions in the USA, combined with a distance learning component back in one's own place of employment. This discipline involves the development of medical professionals into educationists who help teach or improve the skills of health professionals in all the aspects of teaching, assessment i.e. examinations and delivery of lectures. It also involves curriculum development and review, research into various aspects of medical teaching e.g. answering questions about which methods of teaching or assessment are more effective and efficient. A lot of universities in the USA and Europe now offer Masters and PhDs in Medical Education and there are many Professors of Medical Education in recent times.

I have 6 publications in medical education, 2 of which are in the prestigious "Education for Health" journal. Our paper titled "Accreditation of Undergraduate Medical Training Programs: Practices in Nine Developing Countries as Compared with the United States" is an interesting and detailed reference on undergraduate medical training programmes across the world and has been cited about 50 times.

Table 12: Demographic data, health care and economic indicator statistics and medical school training information for nine developing countries as compared to the United States of America

	USA	Argentina	Malaysia	Philippines	South Africa	Mongolia	India	Kenya	Pakistan	Nigeria
Overall and Economic indicators (Countries are listed from left to right in UN Human Development Index Rank)										
UN Human Development Index Rank* (range, 1, highest to 175, lowest)	7	34	58	85	111	117	127	134	144	152
GDP/capita (US\$)	34,320	11,320	8,750	3,840	11,290	1,740	2,840	980	1,890	850
Demographic and health data^b										
Population ($\times 10^6$)	288.0	37.5	23.5	77.2	44.4	2.5	1033.4	31.1	146.3	117.8
Infant mortality (per 10^3 live births)	7	16	8	29	56	61	67	78	84	110
Life expectancy at birth (years)	77.1	74.2	73.1	70.0	47.7	63.9	63.9	44.6	61.0	51.5
Medical training										
Number of medical schools (per country)	126	28	13	35	8	5	233	2	35	16
Number of doctors (per 10^6 population) 1990-2002	276	294	68	124	443	254	48	14	68	19

*The US and Argentina are listed as High Human Development; Malaysia, Philippines, South Africa, Mongolia and India are listed as Medium Human Development; and Pakistan, Kenya and Nigeria are listed as Low Human Development.

Accreditation of undergraduate medical training programs

Cueto J, Burch VC, Mohd Adnan MA, Afolabi BB et al. "Accreditation of Undergraduate Medical Training Programs..." Education for Health, 2006.

Another article, a feasibility study on Research on Medical Migration from sub-Saharan Medical schools revealed a great deal about the universal difficulties that arise from research in general and specifically when it comes to research about individuals within a Nigerian University system. The table below shows that a number of schools in 2 countries, including Nigeria, had whole years where no doctor graduated due to industrial activities shutting down the school for that whole year.

By virtue of this qualification and interest, I was appointed as one of the Coordinators of the pioneer Medical Education Development Unit, in 2011 and became the Deputy Director of the Unit in 2015. We have since helped to revise the old curriculum of our medical school

to a new student-centred “SPICCES” curriculum and are in the process of implementing it.

Table 13: Number of records of graduating medical students that would be involved in the originally proposed study

Country	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	TOTAL
DRC	26	34	*	*	15	*	72	29	*	54	34	50	40	*	69	423
Kenya	b	b	b	b	b	b	b	18	43	40	25	44	38	41	51	300
Nigeria	112	148	132	134	*	114	109	65	177	134	111	155	124	113	93	1721
Nigeria	149	143	155	127	*	177	*	128	171	188	231	226	299	16 ^a	186	2196
Nigeria	b	b	b	b	b	12	53	69	74	34	75	76	42	56	94	585
South Africa	143	125	139	167	146	114	111	165	184	136	143	163	167	155	156	2214
Tanzania	28	40	29	23	26	46	28	31	30	42	45	56	60	104	103	691
Uganda	75	58	58	45	98	67	63	106	89	198	103	119	1 ^c	173 ^c	122	1375
								Total 1990-2000 =	6313					Total =	9505	

^a None or few graduates due to local or national political unrest in the matriculation year, which resulted in the school being closed for all or part of the year.

^b Schools graduated first classes in 1995 and 1997.

^c School changed graduation time, so the 2002 class graduated during the 2003 class year.

Longombe A.O., Burch V., Luboga S., Mkony C., Olapade-Olaopa E.O., Otieno-Nyunyam B., **Afolabi B.** et al. “Research on medical migration...” Education for Health, 2007.

Last words

The last issue that I will talk about here is about women in general although it can also affect pregnancy and delivery. In 1994, when I first arrived in the UK to begin a specialty in the wonderful field of Obstetrics and Gynaecology, I discovered an interesting phenomenon in the African women that I helped manage. My first residency post was in an area of London with a substantial Somali community and it was here that I first discovered the condition of female circumcision, also known as female genital mutilation/cutting. I had never encountered it in my sheltered childhood and early adulthood in Nigeria, probably because it was not so

common amongst my peers or in the patients that I had encountered whilst in medical school. I was amazed at the proportion of them that had been circumcised. Theirs was not the simple Type I or II where the clitoris or the labia minora is removed; it was mostly the full Type III where everything that defines the female external genitalia i.e. the whole vulva, is removed and then the whole area is stitched together to leave a very small hole for passage of urine and menstrual flow. This is known as infibulation.

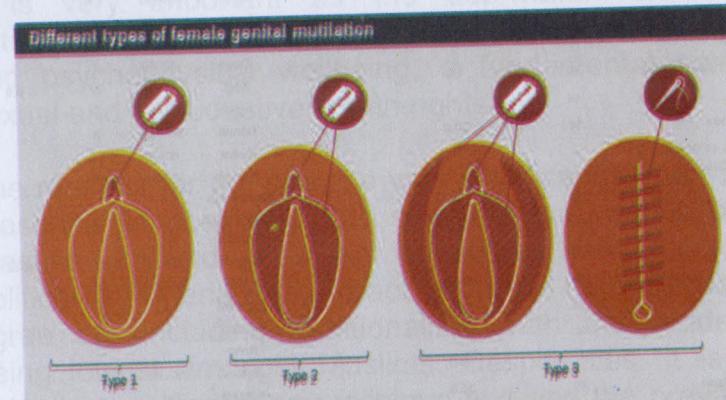


Fig. 13: Reproduced from END FGM European Network

The women would come in to be examined during pregnancy or at the time of delivery and it would be almost impossible to examine them properly. What I did not realise at the time was that this procedure was and is still also quite common in Nigeria, that Yoruba women are reported to have the highest prevalence of female circumcision, followed by Igbo women, and that Osun state, which happens to be my state of origin, has the highest prevalence of female circumcision in the country (Tables 14 & 15; NDHS 2013). In collaboration with colleagues from the University of Ibadan, we published a review paper on Female Genital Mutilation/Cutting in

Africa, with the hope of keeping the conversation about this abhorrent practice going in order to discourage and eventually eradicate it.

Tables 14 & 15: Prevalence rates of female genital mutilation

Table 1 Prevalence rates of female genital mutilation/cutting (FGM/C) in Africa by country and age periods

Country	Percentage of girls and women aged 15 to 49 years who have undergone FGM/C, 2004-2015	Percentage of girls aged 0 to 14 years who have undergone FGM/C, 2010-2015
Benin	9	0.2
Burkina Faso	76	13.0
Cameroon	1	-
Central African Republic	24	1.0
Chad	44	-
Côte d'Ivoire	38	10.0
Dem. Rep. of Congo (formerly Zaire)	-	-
Djibouti	93	-
Egypt	87	14.0
Eritrea	83	33.0
Ethiopia	74	24.0
Gambia	75	56.0
Ghana	4	1.0
Guinea	97	46.0
Guinea-Bissau	45	30.0
Kenya	21	3.0
Liberia	50	-
Mali	89	-
Mauritania	69	54.0
Niger	2	-
Nigeria	25	17.0
Senegal	25	13.0
Sierra Leone	90	13.0
Somalia	98	-
Sudan	87	32.0
United Republic of Tanzania	15	-
Togo	5	0.3
Uganda	1	1.0

Adapted from UNICEF, 2016 (8). Table 1 is a UNICEF document that does not need permission.

Table 2 Prevalence and types of female genital mutilation/cutting (FGM/C) in the various states of Nigeria

Geopolitical zone	State	2009 (15)		2013 (16) Prevalence (%) of women aged 15-49 years
		Prevalence (%)	Types of FGM	
South West	Oyo	60-70	I	47.5
	Ogun	35-45	I, II	
	Lagos	20-30	I	
	Ondo	90-98	II	
	Osun	80-90	I	
	Kogi	1	IV	9.9
	Niger	-	-	
	Benue	90-100	II	
	Kwara	60-70	I, II	
	Plateau	30-90	I, IV	
North Central	Nassarawa	-	-	
	Federal Capital Territory	-	-	
	Kaduna	50-70	IV	20.7
	Kebbi	90-100	IV	
	Zamfara	-	-	
North West	Sokoto	-	-	
	Kano	-	-	
	Jigawa	80-70	IV	
	Katsina	-	-	
	Taraba	-	-	2.9
	Borno	10-90	I, III, IV	
	Bauchi	50-60	IV	
	Adamawa	60-70	IV	
	Gombe	-	-	
	Yobe	0-1	IV	
South East	Ebonyi	-	-	40.0
	Enugu	-	-	
	Imo	40-50	II	
	Abia	-	-	
	Anambra	40-60	II	
South South	Akwa-Ibom	85-75	II	25.8
	Bayelsa	-	-	
	Edo	30-40	II	
	Cross River	-	-	
	Rivers	60-70	I, II	
	Delta	80-90	II	

Adapted from (15).

The reason this practice is abhorrent is that unlike male circumcision, it has no medical benefit whatsoever and instead leads to a high incidence of complications ranging from life-threatening bleeding and severe infections in the immediate period, to infertility, obstructed labour and maternal mortality in the long term. The reduction or lack of sexual pleasure the women are also predisposed to, depending on the type of circumcision, is often ignored since we like to pretend that this aspect of life is unimportant, especially for women. On the contrary, it is very important as the deprivation of sexual satisfaction denies women of their rights to sexual health and psychophysical wellbeing, a fundamental part of sexual and reproductive health rights.

The reasons for the practice vary significantly; the major reason is to control female sexuality but various other reasons abound such as traditional, religious and political. In Nigeria, it is a practice that all the major faiths agree on, including traditionalists, with the incidence being lowest amongst Muslims. Despite this, it is not actually specified in any religious text and the prevailing reasons for which it is practiced these days are largely economical as like traditional birth attendants, the practitioners tend to make a living from their practice. Research in Nigeria and Kenya has shown that there is no association between those who have been circumcised and sexual behaviour and the consensus is that it should be eradicated as there are no benefits; instead, it causes physical and psychological complications and sometimes death. So if anyone here is aware of those still carrying out this practice, please help spread the word to stop it.

Mr Vice-Chancellor sir, I alluded to something special earlier about our discipline – Obstetrics and

Reproduced from Odukogbe A.A., Afolabi B.B. et al. Female genital mutilation/cutting in Africa. Translational Andrology and Urology, 2017.

Gynaecology. I honestly don't think there is a better one. In fact, I am certain that there isn't. You get to look after women, listen to their issues, their highs and their lows, you help to bring life to the world, new and amazing life; yes you treat cancers of the reproductive system too and sometimes you lose people to that terrible condition. We also have some very large, recurrent fibroids and difficult to treat conditions such as severe endometriosis and infertility. However, most of the time, you are looking after people who respond to your treatment, your attention and your care. Beyond the treatment, women love being listened to, being heard and they respond to this as much as the medication. I have patients who, when the treatment is over, ask me – does that mean I won't see you again? I want another appointment o. And the feeling is mutual. To look after these people – in a manner that involves medical as well as surgical care, is to me quite the ultimate. Although general and other surgeons may dispute this, we also carry out quite amazing feats in the operating theatre and are the pioneers in areas like minimal access surgery (also known as keyhole surgery) as well as in fetal medicine and ultrasound. I always tell people that if I were to do it all over again, I would become an Obstetrician and Gynaecologist.

Recommendations

I have written on and I am passionate about the reduction of maternal mortality as most obstetricians and gynaecologists are. My main submission on this will be very succinct since we know all the reasons women are dying and what to do to stop them from doing so.

Government

1. For sickle cell disease, it is time we had a national policy on Universal Newborn screening such that everyone knows his or her genotype within a few

weeks of birth. One in four Nigerians has the sickle cell trait, i.e. is a carrier but many people are not even aware of their status. If they are aware and decide to carry on a relationship with another person with the sickle cell trait, then at least they do so with the knowledge of the consequence and can plan for it. The government also needs to commit more resources to the care of people with this disorder by contributing to research and counselling, and subsidising their healthcare expenses.

2. Ensure skilled health care at delivery for all women by removing the main barrier of cost, and allowing free antenatal and delivery care for all women, either by taxing specific consumer items or by developing a mobile phone subscription based community health insurance. Those two are just my suggestions because I know the money has to come from somewhere and I don't think government has the ability to pay for everything. The important point is to make maternal healthcare free and this has been attempted and shown to work in Ondo State where they met the Millennium Development Goals for the reduction of maternal mortality.
3. Ensure free access to family planning and contraception to reduce deaths from unwanted pregnancy and unsafe abortion. Limiting pregnancy also reduces deaths from pregnancy generally, as a maternal death can only occur if a woman gets pregnant. Whenever one discusses contraception with women, young or old, even some of them with medical training, the first thing they talk about is the side effects. Oh, I hear it has side effects, they say. I have news for you people – even paracetamol has

side effects; pregnancy has more side effects than all the contraceptives combined and so does unsafe abortion. And the truth is that contraception does not stop you from getting pregnant when you are ready to. It also does not cause weight gain in most women. Most of these statements are untrue so please encourage all women AND men of reproductive age to avail themselves of contraception and reduce maternal deaths.

University and Teaching Hospital

4. Drills and protocols to be put in place for training and retraining in emergency obstetric care. No matter how much you know, you need to practice carrying out the knowledge in emergencies. This is the reason the aviation industry is so successful in saving lives and why fire systems work in higher income countries. We are planning this in my department under my headship but I recommend that the University and Teaching Hospital make health care drills compulsory.

Individuals

5. The spirit of giving. There is nothing more rewarding than giving one's time or money, or both. It is part of the reason a lot of us in the healthcare and education profession tend to be so fulfilled, despite the difficulties of practicing in a challenging environment such as ours. Those who tend to go the extra mile enjoy the work more and that is part of what keeps us going. The truth is that despite the bad stories that come out of our hospitals and universities in this social media age, we do tend to help a lot more people and save a lot more lives than we are given credit for.

We are also aware that we have challenges and there are areas for improvement. We therefore, need the general public and private organisations to be more philanthropic and to give more. We need to give more to facilitate meaningful research, create foundations for destitute patients, purchase more equipment, and fund maintenance and repairs. Give time, give money – commit to a small amount every month, give blood – you don't need money to be able to do that. And the more you give, the more your life improves. It is the law of nature, it is in every single religious doctrine so let us all give a bit of ourselves. We do it for our family members but this is not enough, we also need to give to make our society better. I am charging even those of us in the health profession. Let us all give more and our reward will come while we are still here on earth.

ACKNOWLEDGEMENTS

On that note, I end but as you all know, I have only ended the formal aspect. This part is as important, if not more so. I know that I tend to appear very independent but no woman is an island. I thrive because I have a huge support network and I must give tribute to all.

The University Administration

Mr Vice-Chancellor sir, I would like to thank you and former VCs. It is of great value to this University of First Choice and the Nation's Pride, that we have had very progressive VCs. I was bowled away by your strategic plan for the University, which you have already started implementing. Your predecessor, Professor Rahman Bello was also the ultimate gentleman and very progressive as well. The sky is the limit for our great university.

I thank the Deputy Vice-Chancellors, Prof. Oluwole Familoni who always graces our invitations to the College of Medicine and Prof. Ben Oghojafor, who is a very amiable gentleman. My gratitude to Professor Folasade Ogunsola would probably stretch too long if you allowed me – my mentor, my role model and the mentor and role model of many. If there is anyone I want to be like when I grow up, it is you, the epitome of grace and intellect in one individual. Thank you for all that you are and for all that you do.

I thank the current registrar – Barrister Oladejo Azeez Esquire and the immediate past registrar – my friend Dr Taiye Ipaye, a woman of timber and calibre. I appreciate you both. I thank the bursar, also my friend – Mr Lekan Lawal, an upright and frugal individual.

My provost, my research collaborator, with whom I share a name – his first name is my last name, Professor Afolabi Lesi, thank you for everything from when I was a house officer till date. You are part of my success story.

The Deputy Provost, Acting College Secretary and Director of Finance CMUL, thank you all. We have been together so long – it is when you can walk in freely into admin offices that you realise how long you have been in an institution. Thank you for always responding to my many requests.

To all the administrative staff in the college and Unilag – Senate and ceremonies, Advancement office; CMUL Accounts department, Student affairs, and Academic office, thanks for always accommodating me.

LUTH

My CMD, Professor Chris Bode is a visionary, a gentleman and surgeon par excellence, who also appreciates art and nature. Thank you for the work you are doing in LUTH and for your encouragement and support. I thank the immediate past CMD as well – Professor Akin Osibogun, who was instrumental in helping us revive our gynaecological minimal access surgery and many other achievements. The CMAC – Prof Fasanmade and the DCMACs – Profs Daramola and Adeyemo, who are also my good friends, thank you for your hard work and your support.

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My teachers and mentors

I trained in OAU, otherwise known as Great Ife. This is where I developed as an individual and this is where I got my love for O&G. Professor Uche Onwudiegwu, a teacher of teachers – he put the love of O&G into me simply by teaching us relentlessly. I thank you. I am grateful to all my former teachers as well including Professors Fasubaa and Agbakuru. The latter were senior residents that were like consultants when we were training, as evidenced by the way they loved to teach us and ensure we retained the knowledge.

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other and support each other. Thank you ladies, I really appreciate you. Pass on the torch!

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Department of O&G

My department is an interesting one. It has evolved over the years and I am very impressed and happy about what it is today. We are quite cohesive now and have achieved a lot in the recent past. I am proud to be the head of this department and I thank all the members for their commitment and hard work. My mentor Professor Olalekan Abudu was one of those that inspired me to do an MD and he has been very supportive throughout my career in his own unique way. Professor Bomi Ogedengbe and Emeritus Professor Osato Giwa-Osagie have both been wonderful, encouraging and supportive to me in so many different ways. I am extremely grateful for this and I appreciate you both. I thank Professors Odum and Emuveyan for their support as well as my immediate past HOD – Professor Rose Anorlu. She has been so kind and gracious to me during her term and since the beginning of my Headship of the department. Thank you Prof.

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Babah, Owie, Ohazurike, Akinajo, Omisakin, Idiong and Osanyin. I also appreciate and thank you. Drs Makwe and Adegbola – I thank you also. I thank the departmental administrative staff in both CMUL and LUTH headed by Mr Otusanya, Mrs Adepoju and Mrs Summonu – you have made my work very easy. My right-hand woman, my assistant – Mrs Blessing Babatunde, I truly appreciate you.

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My patients, you are the other reason. Nothing makes me happier than when I have solved whatever it is that is hurting you or when we have come to the end of that pregnancy with a live mum and a live child. Thank you for allowing me to look after you.

Family

Coming home to family. I am so fortunate to have my parents still alive, hail and hearty to see this day. My mother – Mrs Bisi Ladipo-Fagbemi, AKA “Iya Egba”, the one from whose womb I emanated, the one who loves me like no other. Thank you for making me study medicine, for seeing that I was suited to it. I almost rebelled but I thank God that I did not. Thank you

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Finally, I would like to thank God. I have been extremely fortunate in life. I have been guided, supported and nurtured by something bigger than life itself and it is only grace that has made this happen. I have come to learn that whatever you believe in, even as a scientist, there are some things that can't be explained and that the pulling back and acknowledgement of gratitude to that greater being that is God Almighty begets even more grace. I am truly and deeply grateful.

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