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EDITOR
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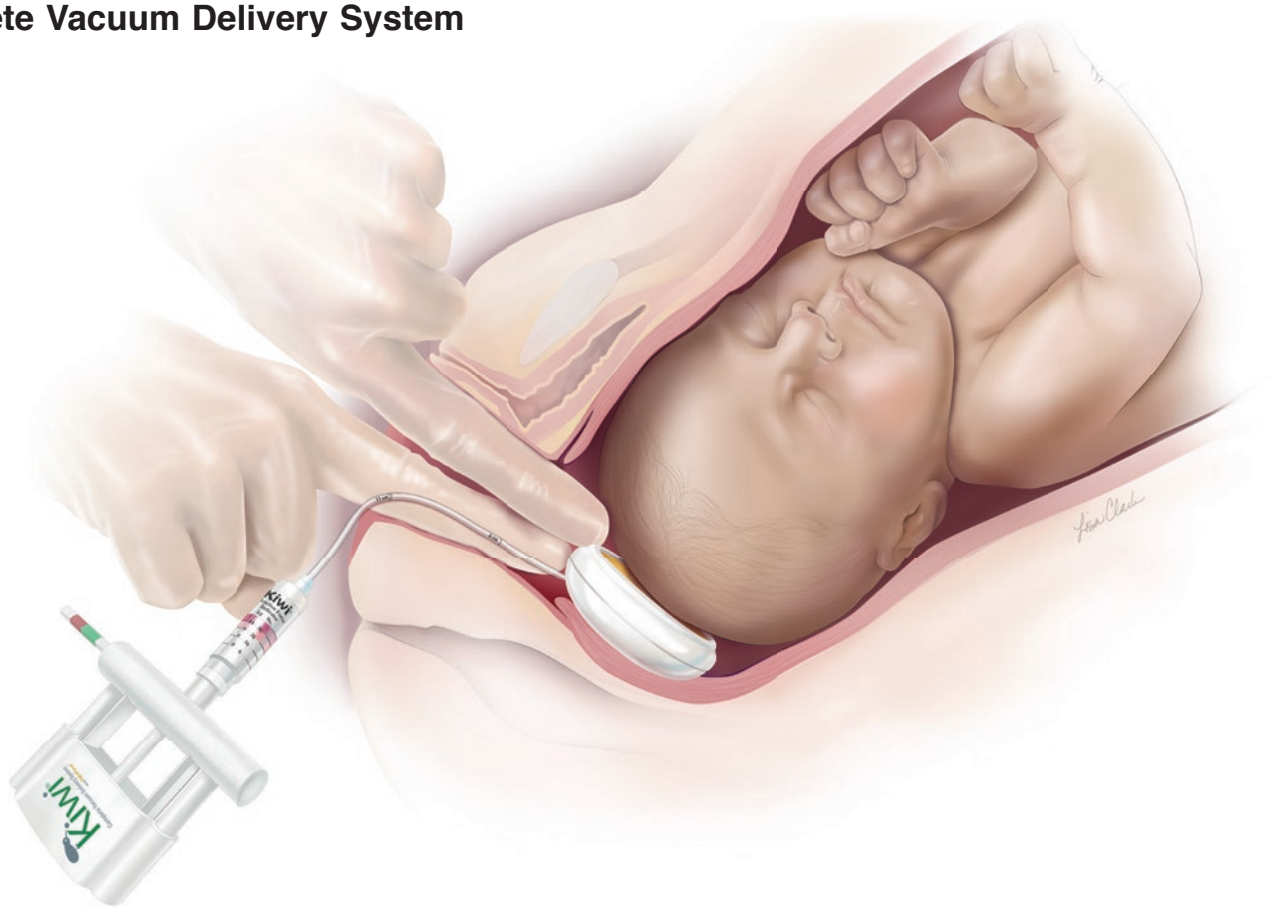

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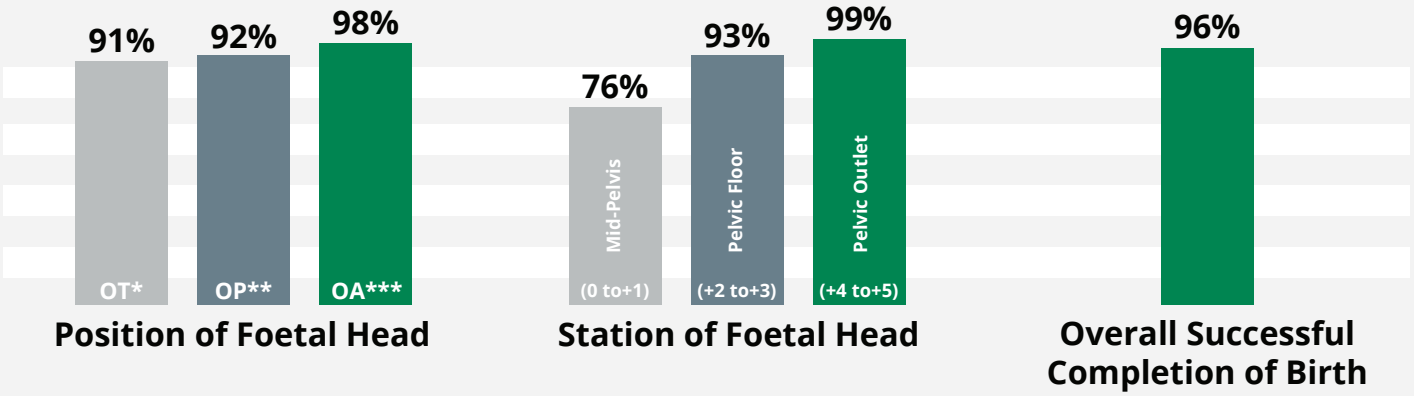

OT* = Occipito-transverse; OP** = Occipito-posterior; OA*** = Occipito-anterior

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Working against gender-based violence is our responsibility

GBV is a profound and widespread problem in South Africa, impacting on all aspects of life. While the damage done by violence cuts across gender, ethnicity, class, and education level, it disproportionately affects women and the LGBTQ+ community as the result of systemic, deeply entrenched attitudes within South Africa as a whole. In the Obstetrics and Gynaecology community we are frequently confronted by the fall-out of GBV when treating injuries, managing unwanted pregnancies, and listening to confidential disclosures of partner violence. As such it is part of our duty as medical professionals, and as moral individuals, to confront the realities in our country and try and enact change. Gender equality and personal safety is a prerequisite for sustainable health and prosperity.

Gendered power dynamics often stem from patriarchal history, and the ways that normative expectations of gender roles continue to foster unequal power relationships within society. The belief in some form of male superiority, whether physically, socially, or fiscally, can manifests in men feeling entitled to sex and maintaining a hierarchy which gives them the power to prescribe aspects of their partners' lives and punish them for transgressions.[1]

The term GBV is used specifically to describe the violence that occurs due to gender dynamics -however, many South African women who never experience extreme physical or sexual violence can still attest to the ways in which prescriptive gender roles have constrained, othered and humiliated them.

"Othering" is a common phenomenon in which individuals or groups are defined primarily by the ways in which they differ from prevailing social norms; the ways they are "not like us". It creates a false perception of what "normal" society looks like and discriminates against those who do not conform to the expectations that this perception raises. The process of othering goes hand in hand with social inequality - in most cases it is the 'non-male', 'non-straight' and 'non-wealthy' who are seen as different.

Gender discrimination can range from overt to extremely subtle, and those who offend might be entirely unaware of the ways in which their language or actions reinforce existing systemic problems. As carers, it is thus crucial that we seriously reflect on how we think and speak about gender roles, and how our expectations of colleagues and patients are influenced by how we perceive their gender. We must identify and combat discriminatory language and actions, both in ourselves and in the environment around us.

How can we as the O&G community make a difference?

There is a relative lack of good-quality evidence about best practice in dealing with GBV. If we wish to be ready to help our patients, we must first collect data and learn from other countries to find effective strategies. It is not enough to prevent GBV in our own practices and homes; we must develop the tools to prevent GBV everywhere.

As such, we must firstly acknowledge, protect, and restore the well-being of those who have suffered because of violence. Response efforts need to be informed by research and integrated into policy frameworks in such a manner that all medical professionals have some training in helping the survivors of GBV. Secondly, we must work towards long-term prevention, by addressing the underlying cultural and societal causes of inequality. Using our platform as practitioners of medical health, we must advocate the cause of gender equality whenever and wherever we can.

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THE CONSEQUENCES OF THE CONSEQUENCES:
Can higher-order thinking skills help us reconsider the criminalization of cases of alleged medical negligence?

First-order thinking is a reflexive, knee-jerk response to a cognitive "stimulus". It's primal. It is the seemingly most obvious solution to the problem at hand. The tragedy of acting on first-order thinking is that it often neglects its siblings, the consequences. On the other hand, higher-order thinking skills (HOTS) can be seen as essential cognitive skills that improve our thinking quality and resultant actions. Higher-order thinking skills include synthesizing, analysing, reasoning, comprehending, application, and evaluation. In simple terms, it also means considering the "consequences of the consequences". It means finding the answer to, "and then what, and then what?".

An example of the result of first-order thinking would be when someone ingests intoxicating amounts of alcohol without considering consequences beyond being drunk. This means that they disregard the fact that they may have to drive and possibly become involved in an accident. The inherent risk is that drunken driving could result in death or injury to themselves or others. Higher-order thinking under these circumstances would mean considering the possible consequences of drunken driving and, at best, deciding not to consume alcohol under the given circumstances.

Dr Abdul Munshi was an experienced anaesthetist who ran a private practice in Johannesburg. At the time of his murder on 16 September 2020, he was on bail. Dr Munshi and a pediatric surgeon were facing charges of culpable homicide for a young patient's tragic death. Zayyaan Sahed is the patient who died following the consequences of a surgical procedure wherein Dr Munshi was the anaesthetist.

The loss of any life, particularly by accident or deliberately, is regrettable. We all commiserate with both the families of Zayyaan Sahed and Dr Abdul Munshi. The sad reality is that the subsequent murder of Dr Munshi has only but doubled the number of families that have lost their loved ones in this regard.

The writer has no first-hand knowledge of either the surgical procedure's circumstances or the subsequent killing of Dr Munshi, but according to some media reports, the murder of Dr Abdul Munshi was assassins' work. The basis of the further discussion is the assumption that this murder was committed to avenge the death of Master Sahed and followed the charges of culpable homicide, which is a form of criminalization of medical negligence.

Events around the criminalization of medical negligence and the murder of Dr Munshi illuminate several unfortunate realities, which can have grave consequences on medical practice and care in our country. Down-stream consequences need to be carefully considered before decisions are taken regarding how best to deal with potential medical negligence, and with personal loss. This is where higher-order thinking is essential for the formulation of sound (and evidence based) responses.

It is widely accepted that any adverse outcome consequent to health-care workers performing their regular duties should be a subject of medical malpractice investigation. Exactly by whom and how this investigation should be done, can be debated and is not always evident. However, the institution of criminal charges rather than performing and completing such investigation, represents a departure from the regular handling of such enquiries.

Such harsh and premature legal action can be seen as a consequence of the need to investigate or even as a consequence of the failure to effectively investigate. Either way, this is not the first case dealt with in this manner; it represents a dangerous sliding slope. Very serious and potentially deleterious effects on the practice of medicine in South Africa is foreseen as a consequence of inappropriate legal action.

Firstly, the anxiety that confronts doctors as they ply their trade is not negligible. It is well-known that this anxiety has several unintended results, including the practice of overly 'defensive medicine' which is known to dramatically increase the costs of medical care and reduce efficiency. It may also have harmful effects on doctor-patient relationships due to a loss of trust.

Secondly, these two incidents (criminal charges and murder, or legal action and revenge) are likely to lead to an exodus of doctors from the discipline of medicine. In addition, it leads to an increase in the cost of indemnity insurance, leading to financial insecurity. The ones who are most likely to quit are doctors who have many years of experience. All of us will bear the brunt of the deficit if attempts to stem the tide are not effective.

In addition, society will pay a substantial premium to replace those leaving the profession, as the education of professionals costs the country millions. In the case of medical specialists, the costs are compounded by the many years of training. The fairest way for society to recoup its costs is for doctors to continue serving the populace for many years, an ideal threatened by the current trend.

Another seemingly obscure consequence is the possibility that fewer candidates may consider a career in medicine, given the risk of criminal charges and possibly physical attack or even murder in the event of severe adverse outcomes. This may lead to the training of less suitable candidates, or even shortages in the profession, especially in the specialities at higher risk for legal action, including Obstetrics.

The criminalization of medical negligence will place an increased burden on an already overloaded justice system. The consequences include more time lost for all involved as cases are postponed, and increased costs related to the investigations, prosecutions and possible incarceration of those found guilty.

The negative effects of the treat of incarceration on medical professionals performing their everyday job, is difficult to quantify. Jail sentence means complete loss of standing in society, families without an income, without their loved ones, with a subsequent significant impact on their standard of living and psychological well-being. A domino effect can be expected for the medical profession as a whole culminating in a loss of status and respect in society, and a loss of care givers to the nation.

One can go much deeper into the rabbit hole of the higher-order thinking due to the events of the case in point. It is not inconceivable that a murder to avenge the death of a loved one followed the institution of criminal charges for alleged but unproven medical negligence. Such a consequence of the criminalization of medical negligence may have been difficult to imagine before the current reality, but must be considered as a consequence of changed societal perceptions: "All poor outcomes are caused by faulty treatment and all mistakes are punishable; someone must pay."

Actions based on first-order thinking are often taken in "haste". They may seem to offer an "instant solution" to our deepest pain. Even those committed in pursuit of positive outcomes "chasing" instant gratification. The excessive consumption of alcohol and disregarding the potential negative consequences is one such example. Although spontaneous, primal thinking does not always result in disastrous outcomes, failure to consider and reconcile ourselves with the likely consequences of our actions therein may result in untold pain and regret.

Starting with the end in mind is a noble philosophy. When medical outcomes are undesirable, we shouldn't act on the "instinct" of our first-order thinking. With hindsight, we may not consider the actions taken in response to the unfortunate death of Zayyaan Sahed as the optimal choices under the circumstances.

Dr M Malebane
Founding director of Medical Advisory Group Services. MAGS is a strategy consulting firm to the private and public healthcare industry on risk management, business continuity, disaster management, and medicolegal matters.

IMPROVING
OF BACTERIAL VAGINOSIS, DYSBIOSIS, CANDIDA AND ANTIBIOTIC-ASSOCIATED SECONDARY INFECTION
WITH PROBIOTICS

Studies indicate only 20% to 40% of microbes, 'good bacteria', found in all but one of the probiotic medicines sold in South Africa survive the journey through the stomach to reach the lower intestine where they benefit their hosts.

The exception is Probitec, a recent newcomer to the market.

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The only probiotic available locally that is both stomach acid-resistant and 100% antibiotic-compliant, Probitec uses Duocap™ technology to protect probiotic bacteria from stomach acid, making it up to 2000 times more effective than other probiotic brands.In combination with the fact that it is Kosher, Halal and Vegetarian-friendly as well as clear of solvents, colourants, sugar, GMOs, gluten, preservatives and binders, Probitec's resilience to stomach acid and antibiotics facilitates the ease of practitioner recommendation and improves patient compliance. This article explains the technology and testing behind its claims.

Probiotics are the microbes, or 'good bacteria', that are naturally found living in the human body. These beneficial microbes make up part of the microbiome, specifically the gut microbiome.

A microbe must display several characteristics for it to be classified as a probiotic – being safe for consumption, having a proven clinical benefit to humans, being able to survive in the intestine after ingestion, and able to be isolated from a human.

There are also significant variables that must be considered to determine the clinically correct oral dosing formula of a probiotic medicine. These viability determinants significantly impact the efficacy of the probiotic, and therefore the therapeutic treatment outcomes for a patient.

VIABILITY & EFFICACY DETERMINANTS

Viability determinants are classified either as pre-oral or post-oral. Pre-oral determinants are classified by the manufacturing process and the oral dose form of the medicine, supplement or food product. Post-oral determinants are classified into the microorganism and the gastrointestinal tract.

Pre-oral determinants significantly impacting the mortality rate of probiotic organisms include pH and acidity, ambient temperature, ambient and encapsulated oxygen levels, incompatibility with other medicinal and food ingredients, strain compatibility, and the freeze/thaw operation. Probiotics are therefore manufactured within an optimal environment.

Post-oral viability determinants for probiotics include ability to adhere to the intestinal mucosa and colonise the intestinal tract, low oxygen levels, exclusion of pathogens, and ability to coexist with antibiotics in the gastrointestinal tract to prevent antibiotic-associated secondary infection.

The most significant factor affecting the mortality and viability of any probiotic – and therefore its efficacy – is the stomach acid survival rate. Studies indicate that survival rates vary between 40% to 20%, in some cases as low as 10%, when calculated as an average mean survival rate of probiotic strains across the four predominant genus classes.

Another vital efficacy consideration is patient behaviour. Probiotics are often prescribed for the prevention of antibiotic-associated secondary infection. Because virtually all probiotic genus and strain classes cannot survive being consumed simultaneously with an antibiotic, the standard probiotic dosing protocol is two hours before or after oral consumption of the antibiotic. This is inconvenient and impractical for most patients. As a consequence, they ingest them simultaneously, dramatically lowering the preventative health benefit for antibiotic-associated secondary infection.

CONSIDERATIONS FOR AN EFFECTIVE PROBIOTIC

An effective oral dosing form for a probiotic must possess both acid-resistant properties and antibiotic-compliant properties. It must overcome all the pre- and post-oral administration viability challenges, offer the patient the convenience of combinational dosing with an antibiotic and confer maximum efficacy through a minimal-to-no probiotic mortality rate. Finally, the probiotic strain must possess no 'acquired antibiotic-resistant characteristics'.

HOW DOES PROBITEC MEASURE UP?

Probitec is the first and only synbiotic product in South Africa to use DuoCap™ technology to protect probiotic bacteria from stomach acid. This ensures that, instead of delivering only 10% to 40% of the stated dose, it delivers 100% of its 10-billion Colony Forming Units (CFU) of bacteria to the lower intestine making it up to 2000 times more effective than other probiotic brands.

Probitec works by employing two acid-resistant capsules, one inside the other and both designed to dissolve at different pH environments. In this way, the probiotic is only released once it has passed through the stomach into the lower intestine.

Probitec also uses other proprietary oral dosage technological innovations to overcome pre- and post-administration viability challenges:

- The inner capsule containing the probiotic is a DR Cap™ (Delayed Release Cap) that shields the probiotic from the stomach acid and bile salts. DR Caps™ also contain low-to-no levels of moisture, reducing the chances of thawing hygroscopic probiotic substrates.
- The Licap™ (Liquid-filled caps) is filled with glycerin to suspend the prebiotic formula allowing for a quick release of the prebiotics once in the lower intestine, preserve the plant capsules and minimise the risk of thawing.
- LEMS® Sealing (Liquid Encapsulation Microspray Sealing) provides a hermetic air-tight seal and prevents oxygen and moisture from entering the product as well as an efficient tamper-proof system (the capsules would leak if tampered with).
- Nitrogen flushing creates an anaerobic environment for the probiotics, and keeps the product fresh and stable by preventing oxidation.

No other probiotic product in South Africa uses these technologies to ensure a probiotic is manufactured and received by a patient's gut the way it is clinically meant to.

PROBITEC'S APPLICATION IN GYNAECOLOGY AND OBSTETRICS PRACTICES

With cases of antibiotic-resistant pathogenic microorganisms on the rise, the use of probiotics has provided a natural and non-toxic modality, as well as cost-effective treatment, for Bacterial Vaginosis. The metabolites produced by probiotics have shown great antimicrobial potential not only for inhibiting proliferation of antibiotic-resistant strains but also killing these strains.

In particular, Lactobacilli play a significant role in the inhibition of growth, adhesion and spread of pathogenic microbes. They are able to form biofilms over the mucosal layer of the vagina and through competitive exclusion, compete for nutrients and receptors with pathogenic microbes. They also secrete lactic acid, hydrogen peroxide, bacteriocins, and biosurfactants which have good antimicrobial properties.

Along with the antimicrobial property of lactic acid, Lactobacilli help in maintaining the pH level of the vagina within a 3.5 to 4.5 pH range for a non-conducive environment for the proliferation of pathogenic microbes. Commonly indicated for Bacterial Vaginosis, candida, dysbiosis and antibiotic-associated secondary infections, the La-14 strain is one of the most clinically researched strains of Lactobacillus Acidophilus worldwide and one of the only commercially available with a fully-sequenced annotated genome.

Probitec is concentrated with 10-billion CFUs of the La-14 strain. Its Licaps™ is concentrated with 10mg of fructo-oligosaccharide prebiotic fibre. Fructo-oligosaccharides (FOS) are used by probiotics and stimulate the production of probiotic bacteria in the gut, specifically lactobacillus bacteria (supplemental FOS can increase the number of lactobacillus bacteria by up to ten-fold). Probitec also offers patient-convenient combinational dosing to improve patient compliance. This is because its DuoCap™ technology allows for 'no antibiotic third-space contact' with the probiotic in the gastrointestinal tract. The La-14 strain is also clinically certified not to possess any 'acquired antibiotic- resistant' traits.

CONCLUSION

Probitec's resilience to stomach acid and antibiotics, and delivery of 10-billion CFUs of the La-14 strain in combination with the fact that it is Kosher, Halal and Vegetarian-friendly as well as clear of solvents, colourants, sugar, GMOs, gluten, preservatives and binders, facilitates the ease of practitioner recommendation and improved patient compliance.

ORIGINAL RESEARCH
O&G Forum 2021; 31: 08 - 11

The accuracy of spot urine protein-to-creatinine ratio in diagnosis or exclusion of significant proteinuria in pre-eclampsia.

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Abstract
Background: Proteinuria is a major component of preeclampsia. Urine protein measurement after 24-hour urine collection is the traditional standard method for the detection of proteinuria. It is time- consuming and costly. Prompt diagnosis of preeclampsia is necessary to prevent fatal maternal and foetal complications. As an alternative, random spot urine protein to creatinine ratio (PCR) has been investigated.
Objectives: To assess if spot urine protein-creatinine ratio can be used as an alternative diagnostic test to the traditional quantitative 24-hour urine protein excretion for significant proteinuria in pre-eclampsia.

Methods:
Study Design: Case-control study. Prospective cross-sectional study was conducted on pregnant women with equal to or more than 20 weeks' gestation, admitted for pre-eclampsia work-up at Pelonomi Regional Hospital from July 2020 to December 2020.
Results: In total, 99 patients were included. There was a high correlation rate (r=0.74, P<0.001.) between the two tests. The area under the curve (ROC) was 0.8506. The optimal PCR cut-off found was 30mg/mmol (sensitivity=81.45%, specificity=77.7 8%). The PPV was 81,48 % and the NPV was 77,78 %. The LR+ was 3.67 and LR- was 0.24.
Conclusion: The random urine spot protein-creatinine ratio is a good alternative diagnostic test for significant proteinuria in pre-eclampsia because of its high correlation rate (r=0.74, P<0.001.) with 24-hour urine protein. It is a cost-effective, easy, non-invasive, and faster test. This will reduce the patient's stay in hospital, prevent complications associated with pre-eclampsia and will shorten diagnosis-treatment interval.

Keywords: Hypertension, Pre-eclampsia, urine protein-creatinine ratio, proteinuria

Introduction

Hypertensive disorders of pregnancy contribute significantly to maternal mortality and morbidity. In the Saving Mothers report of 2017 by the National Committee for Confidential Enquiries into Maternal Deaths (NCCEMD) in South Africa, hypertensive disease of pregnancy caused 210 maternal deaths (17,7% of all deaths) and was the number one common direct cause of maternal deaths.[1] Most of the maternal deaths in low- and middle-income countries occur at the community level, where the majority of women do not have access to health-care facilities. Failure to identify preeclampsia, along with a delay in responding to the clinical signs and symptoms, is responsible for nearly half of maternal deaths and more than half of foetal deaths.[2]

Preeclampsia belongs to the spectrum of hypertensive disorders of pregnancy; it is a progressive disease that, if undiagnosed and/or untreated, leads to fatal complications for both the mother and the baby.[3] Preeclampsia is defined as de novo hypertension after 20 weeks' gestation, and the new onset of one or more of the following:[4]

a) Proteinuria (≥300 mg/day or a spot urine protein-creatinine ratio, ≥30 mg/mmol)
b) Renal insufficiency (creatinine ≥ 0.09 mmol/L or oliguria)
c) Liver disease (raised transaminases and/or severe right upper quadrant or epigastric pain)
d) Neurological problems: convulsions (eclampsia), hyperreflexia with clonus, severe headaches with hyperreflexia, persistent visual disturbances (scotoma)
e) Haematological complications: thrombocytopenia, disseminated intravascular coagulation, haemolysis
f) Uteroplacental dysfunction marked by foetal growth restriction.

Proteinuria is a major component of preeclampsia. Regardless of

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difficulties encountered in obtaining a satisfactory urine collection, the 24-hour proteinuria remains the international gold standard for assessing the diagnosis of pre-eclampsia and ensuring its monitoring. [5] This method is time-consuming, and it is an inconvenience to the patient. The results may be inaccurate due to errors in the collection of urine, as the process may interfere with the patient's daily activities. The management of patients may be delayed during the period of urine collection and waiting for the laboratory urine analysis. A more rapid test that makes the accurate prediction of 24-hour urine protein excretion results possible, would be worthwhile. Random spot urine protein to creatinine ratio as a substitute for 24-hour urine protein excretion to detect significant proteinuria in patients with preeclampsia was investigated and the results are positive (4, 5).[5,6]

The aim of the present study was to determine the diagnostic accuracy and optimal threshold of the spot urine protein to creatinine ratio compared to 24-hour urine collection for the detection of significant proteinuria in patients suspected of pre-eclampsia because a rapid clinical decision is needed for expeditious treatment.

Severe preeclampsia is symptomatic; the challenge is in women with moderate preeclampsia, as they generally have no symptoms.[7]

Therefore, delays in diagnosis, adequate primary care, and late referral to a specialist care centre are likely to be important contributors to adverse maternal and foetal outcomes.[8]

Early detection and prevention of preeclampsia in the community is pivotal in reducing the morbidity and mortality related to hypertensive disease during pregnancy. Low-cost, user-friendly, sensitive screening tools for primary health care are part of the necessary armamentariums for reducing complications of hypertensive disease in pregnancy.

Significant proteinuria in pregnancy is defined as a protein-to-creatinine ratio (PCR) of 30 mg/mmol (0.3 mg/mg) or more (or a 24-hour proteinuria of 300 mg or more or a proteinuria of 1 g/L [2+] or higher on a dipstick test).[5]

Urine protein-creatinine ratio specimens can be obtained any time of the day after the first morning urine has been voided. 24-hour urine is usually started with the next voiding and carried on for the next 24 hours.

Preeclampsia is a multisystem disorder and can clinically manifest as maternal syndrome (elevated BP and proteinuria with or without multisystem disorder) or as a foetal syndrome (reduced amniotic fluid, foetal growth restriction, foetal distress). Pre-eclampsia is a major cause of maternal morbidity and mortality, preterm births, and perinatal deaths.[9]

Patients with preeclampsia are also at risk of developing cardiovascular disease later in life and their children are at risk of developing metabolic and cardiovascular complications later in life.

The exact cause of preeclampsia is unknown. Preeclampsia is thought to result from maternal response to abnormal placentation. The other theories suggest ischaemia, leading to oxidative stress within the placenta and immune maladaptation.[10] This leads to tissue anoxia at cellular level, which results in release of trophoblastic debris, apoptotic cells, and imbalance between angiogenic and antiangiogenic factors. The high levels of antiangiogenic factors lead to widespread endothelial vascular damage affecting all organs of the body; hence preeclampsia is a multisystem disorder. The risk factors for preeclampsia include nulliparity, advanced maternal age, previous history of pre-eclampsia, pre-existing diabetes mellitus, obesity, family history of hypertension and thrombophilias, assisted reproduction, race, and ethnicity (Afro-Carribeans and Asians). Patients at risk can be offered screening as early as the first trimester with serum biomarkers (PAPP-A DR 16%, PIGF DR 55%), mean arterial pressure (DR 76%), and uterine artery Doppler (DR 48%). Screening is continued throughout pregnancy with BP monitoring and urine dipstick being done at each antenatal visit.

The traditional method to diagnose significant proteinuria is quantitative protein excretion over 24 hours. This test is time-consuming, requires a specific specimen bottle, is inconvenient, and may delay management of the patient. This can negatively impact maternal and perinatal outcomes.[10]

The urinary spot protein: creatinine ratio on a mid-day sample was investigated as an alternative diagnostic test to traditional quantitative 24-hour protein excretion, with the cut-off value of 30 mg/mmol (0.3 mg/mg) or more being found to correlate well with 24-hour urine collection for quantitating urinary protein loss. The evidence is, however, conflicting. This is a rapid test, results can be obtained within a day at most, and it is cheaper.[11]

Material and methods

Study Design: Case-control study.

Prospective cross-sectional study was conducted on pregnant women who are equal to or more than 20 weeks' gestation, admitted for pre-eclampsia work-up at Pelonomi Regional Hospital from July 2020 to December 2020.

The research was a prospective cross-sectional study conducted from July 2020 to December 2020 in Pelonomi Regional Hospital. The study included patients who were equal to or more than 20 weeks' gestation, admitted for pre-eclampsia work-up and exclusion thereof. Patients who qualified for work-up but needed urgent delivery, were also included in the study.

Patients with the following pre-existing medical conditions without baseline quantification of proteinuria before 20 weeks' gestation were excluded from this study: diabetes mellitus, chronic renal disease, chronic hypertension, and urinary tract infection.

The spot urine sample for performing the PCR could be collected at any time during the day, after the first voided morning specimen and before bedtime. The 24-hour protein collection was started from the next urination. The National Health Laboratory carried out both tests for every patient. The results were obtained electronically within 48 hours after submission of both tests via the NHLS TrakCare application.

With the 24-hour urine protein results as the gold standard, sensitivity, specificity, positive and negative predictive values were determined, as well as the positive and negative likelihood ratios of the PCR at several cut-off values for the prediction of significant proteinuria (>300mg/24 h). The diagnostic performance of the PCR test was evaluated with receiver-operating characteristic curves. A p value of less than 0.05 was considered significant.

Ethical approval to conduct the study was granted by the University of the Free State Health Sciences Research and Ethics committee (HSREC). The Free State Department of Health Research Committee granted permission for the research. Data was collected and entered into an Excel spreadsheet. Data analysis was done by the Department of Biostatistics, University of the Free State, Bloemfontein.

Results

A total of 270 patients were admitted during the study period. 167 patients met the exclusion criteria, 4 patients' specimen bottles were lost and therefore had no results. 99 patients were included in the study. The characteristics of the patients are presented in Table 1.

Table 1. Characteristics of patients

Variable[a]	n=99 patients
Maternal age (years)	31.8 ± 5.4
Parity	1.8 ± 1.1
Gravidity	3.1 ± 1.2
Gestational age (weeks)	30.7 ± 4.5
Nulliparous	13 (13.1)
HIV status	
Positive	37 (37.4)
Negative	62 (62.6)
Rhesus status	
Positive	89 (89.9)
Negative	10 (10.1)
Syphilis	
Positive	5 (5.0)
Negative	94 (95.0)

[a] Values are given as number (percentage) or mean ± SD

The average maternal age was 31.8±5.4 years, the average parity was 1.8±1.1, the average gravidity was 3.1±1.2, the average gestational age was 30.7±4.5 weeks, 13,1% of patients were nulliparous, 62,6% of patients were HIV negative and 37,4% were HIV positive, 89,9% were rhesus positive and 10,1% were rhesus negative, 5,0% tested positive for syphilis and 95% tested negative for syphilis.

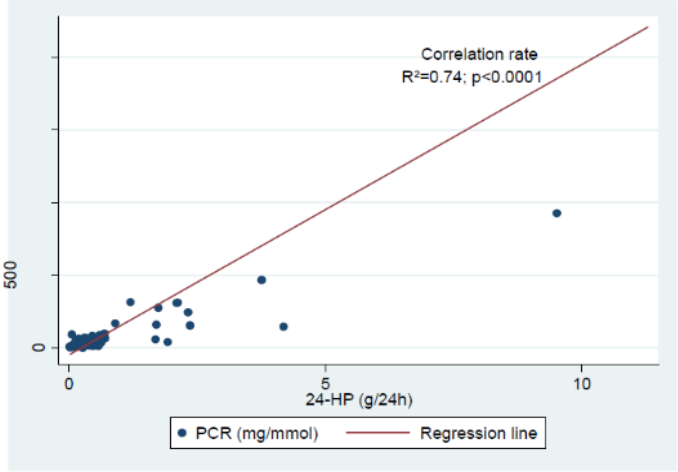

Figure 1: Correlation between the protein-to-creatinine ratio (PCR) and 24-h proteinuria (24HP).

The correlation between the PCR values and 24-hour urine protein values is shown in Figure 1. There was a significant relationship between the PCR and the 24HP, with a correlation rate of r=0.74, P<0.001.

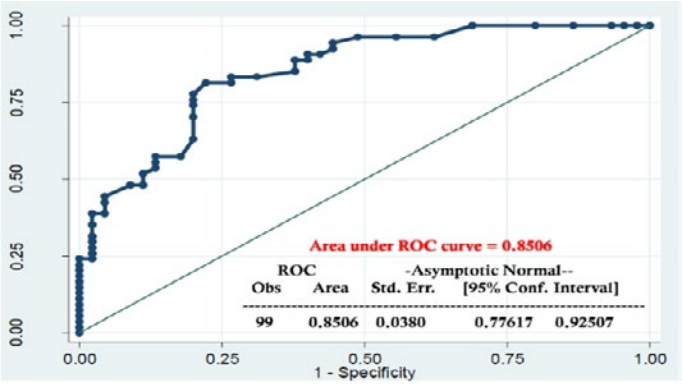

Figure 1: ROC curve.

The area under the ROC curve (Figure 2) was 0.8506. The optimal PCR cut-off (Table 2) found was 30mg/mmol (sensitivity=81.45%, specificity=77.7 8%). The PPV was 81,48 % and the NPV was 77,78 %. The LR+ was 3.67 and LR- was 0.24.

Discussion

The aim of the present study was to evaluate the accuracy of the urine spot protein: creatinine ratio for diagnosis or exclusion of significant proteinuria in preeclampsia by correlating it with quantitative 24-hour urine protein excretion, and also to assess if urine spot protein: creatinine ratio can be used in our setting as an alternative test to a quantitative 24-hour urine protein excretion for diagnosis of significant proteinuria in preeclampsia.

This will reduce the waiting time until the diagnosis, the duration of the patient's stay in hospital, prevent complications associated with preeclampsia, and shorten the diagnosis-treatment interval.

The findings of this study suggest that PCR might be a good alternative diagnostic test for significant proteinuria in preeclampsia because of its high correlation rate (r=0.74, P<0.001.) with 24-hour urine protein and because it had an area under curve of 0.8506. PCR has other benefits in that it is cheap, non-invasive, easy, and faster to do compared to traditional 24-hour urine protein collection. The findings are in agreement with other studies.[12-17]

According to the analysis of the ROC curve, the optimal PCR for the detection of urine protein excretion of 300 mg/day was identified as 0.45 mg/mg, with a sensitivity and specificity of 74,4% and 94,2%, respectively. The cut-off in our study can only exclude the presence of significant proteinuria.[12-17] However, we found that PCR is more sensitive and more specific for the detection of proteinuria >1 g/day.

The urinary spot protein: creatinine ratio on a mid-day sample was investigated in many studies as an alternative diagnostic test to traditional quantitative 24-hour protein excretion, with the cut-off value of 0.03mg/dL being found to correlate well with 24-hour urine collection for quantitating urinary protein loss.

The evidence is, however, conflicting as other studies have concluded that it is not a proper diagnostic test, because of poor sensitivity and specificity. Wheeler et al.[10] reported that PCR was 100% sensitive and specific to detect the proteinuria >5 g/day in preeclamptic women. However, their study group for the assessment of proteinuria >5 g/day was too small.

Bethert et al.[5] evaluated the accuracy of the PCR as a diagnostic test to affirm the presence of significant proteinuria in preeclampsia.

With 148 patients, this study demonstrated a high correlation rate (r=0.80, P<0.001). The area under curve was 0.92, the optimal cut-off was 56.9 mg/mmol (sensitivity=79.3%, specificity=91.5%), the PPV was 97,1% and the NPV was 55,1%. The LR+ was 9.3 and the LR- was 0.23. Nahid et al. (2008) evaluated a comparison of spot urine protein-creatinine ratio with 24-hour urine protein excretion in women with preeclampsia at Imam Khomeini Hospital in Ahwaz, Iran – a tertiary care centre – between March 2006 and September 2007.[18]

This was a prospective study, consisting of 81 patients. A strong correlation between the spot P/C ratio and 24-hour urine protein excretion was observed (r = 0.84; P < .001). The optimal spot P/C ratio cut-off point was 0.20 for 300 mg/24 h of protein excretion, with a sensitivity (91,2%), specificity (87,8), positive predictive value (94,4%), and negative predictive value (96,6%). Sami et

Table 1. Sensitivity, specificity, classified, LR+, LR-, PPV, and NPV for different cut-offs

Cut-off (mg/mmol)	Sensitivity (%)	Specificity (%)	Correctly classified	LR+	LR-	PPV (%)	NPV (%)
30	81.48	77.78	79.80	3.67	0.24	81.48	77.78
35	75.93	80.00	77.78	3.79	0.30	82.00	73.47
40	57.41	82.22	68.69	3.22	0.52	79.49	61.67
45	51.85	88.89	68.69	4.67	0.54	84.85	60.10
50	48.15	88.89	66.67	4.33	0.58	83.87	58.82
56	44.44	95.56	67.68	10.00	0.58	92.31	58.90

LR+: positive likelihood ratio; LR-: Negative likelihood ratio; PPV: Positive predictive value; NPV: Negative predictive value

al. (2016) also evaluated the diagnostic accuracy of spot urinary protein/creatinine ratio for proteinuria in pregnancy-induced hypertension at Lal Ded Hospital, Srinagar, India.[19]

This prospective study consisted of 100 participants. The study demonstrated a strong correlation between the spot urinary protein-creatinine ratio and 24-hour urine protein excretion (r=0.824; P<0.001). The optimal spot P/C ratio cut-off point was 0.33 for 300 mg/24 hours of protein excretion, with sensitivity and specificity of 82,8% and 76,1%, respectively. Positive and negative predictive values were 58,8% and 91,5%.

We are not aware of any study of this nature done in Africa.

Many obstetric centres started using PCR to diagnose the significant proteinuria in preeclampsia with a cut-off of 30mg/mmol. The American College of Obstetricians and Gynecologists (ACOG) consider PCR to be positive when it is 0.3 mg/dL or higher, and the Royal College of Obstetricians and Gynaecologists (RCOG) consider it positive when it is more than 0.3 mg/dL.[20,21]

Our study excluded patients with the highest risk of preeclampsia, e.g., diabetes mellitus, chronic kidney disease, and urinary tract infections. This could make it a good representation of the general population. PCR must be considered as an alternative diagnostic tool, especially in low-resource countries in order to attempt to reduce the financial burden on the health-care system.

Conclusion

Random urine spot protein creatinine ratio is a good alternative diagnostic test for significant proteinuria in preeclampsia because of its high correlation rate (r=0.74, P<0.001.) with 24-hour urine protein. PCR can be considered as an alternative diagnostic test for patients admitted with a poor clinical status of protein quantification in preeclampsia work-up. The spot PCR can be of value in reducing the current delay in diagnosing and initiating treatment for patients with preeclampsia presenting at primary care levels. This could be one of the ways forward, especially for low-resource countries at primary health-care level, which could scale up existing community-based delivery platforms for screening and delivering intervention strategies in order to reduce the morbidity and mortality of hypertensive disease during pregnancy.

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Conflict Of Interest

None

Funding

None

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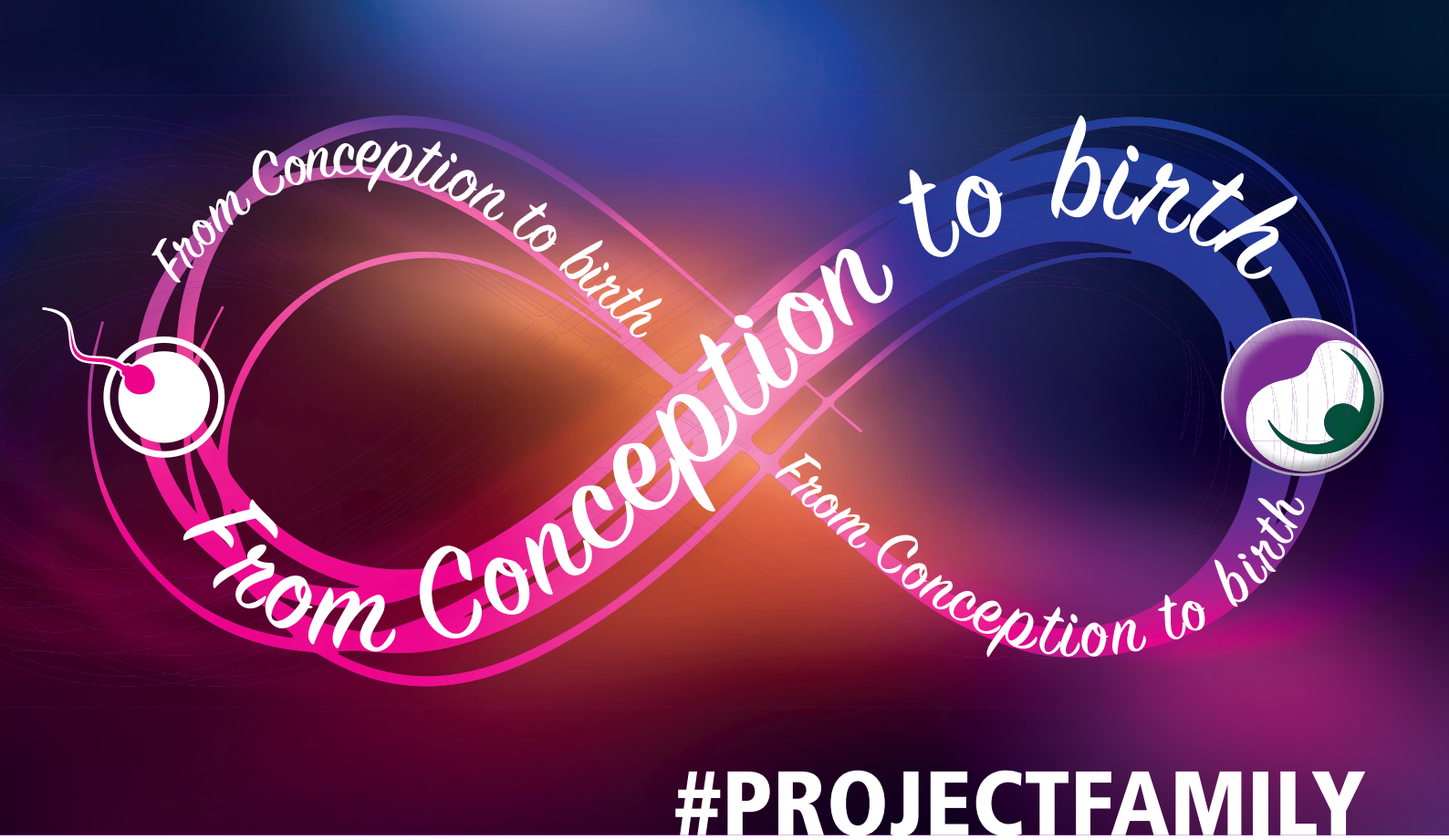

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BIRTH STORIES

Post-partum haemorrhage (PPH), or excessive bleeding after childbirth, is the leading direct cause of maternal mortality.[2] The vast majority of maternal deaths occur in low and lower-middle income countries,[3] where women often do not have access to prenatal care, skilled birth attendants or quality treatments.

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FERRING PHARMACEUTICALS

Factors affecting VBAC success at a Tertiary Level Hospital in Pretoria, South Africa

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Abstract
There is growing concern about rising global caesarean delivery (CD) rates. One of the strategies to overcome this problem is to reduce primary caesarean section. A trial of labour following a previous CD is another option that may be explored.
Aim
The aim of the study was to determine the success rate and risk factors for women attempting vaginal birth after a prior caesarean delivery (VBAC).
Methods
This was a retrospective analysis from 2013-2018 of women attempting a vaginal birth after caesarean section at a tertiary level hospital in Pretoria, South Africa.
Results
The VBAC success rate was 36%. Factors that were associated with a successful VBAC were a third pregnancy, previous successful VBAC (61%), presentation in the active phase of labour and a neonatal birthweight of less than 3kg.
Conclusion
Pregnant women with a CD in a prior pregnancy should be appropriately counselled regarding delivery options. Risks and benefits of elective repeat caesarean delivery versus trial of labour should be clearly explained to expectant mothers.

Introduction
There is a global concern regarding the increasing rate of caesarean deliveries (CDs). While a CD may be a lifesaving procedure, it may be performed unnecessarily with no additional benefit. The World Health Organisation (WHO) states that there is no improvement in maternal and neonatal mortality if CD rates are in excess of 10-15% per region.[1] The CD rate in South Africa is presently 25% and this rate varies in different regions and institutions in the country.[2] In some regions the CD rate can be as low as 8% but in other institutions like Steve Biko Academic Hospital (SBAH) the rate is 53%. Caesarean delivery rates in tertiary institutions are generally higher than that of district level hospitals. While the reasons for the rise in CD are many and complex one of the reasons that has contributed to the increasing rate is the dictum "once a caesarean, always a caesarean".[3] This may lead to many repeat CDs being performed. With the increase in CD rates there is also an increase in the complications associated with repeat CD. These include, abnormal placentation disorders such as the placenta accreta spectrum disorders and placenta praevia. Women who have had a CD have an increased risk of unexplained stillbirth. [3] In low resource settings, CD is associated with high morbidity and mortality. Women who undergo a CD in South Africa are three times more likely to die than those who deliver vaginally.[2]

A study performed at Chris Hani Baragwanath Academic Hospital in Johannesburg, South Africa found that a previous CD was the third most frequent reason for CD, contributing 23% of all CDs.[4] A case series published in 2018 evaluating global trends for CD reported that countries such as Brazil and China had CD rates of 55.6% and 45.7% respectively.[5] Caesarean section rates for women classified as group 5 under the Robson classification system (group 5 = women with a previous uterine scar, who begin labour at or after 37 weeks gestation with a singleton cephalic presentation) contribute 32.7% in Brazil and 33.9% in China. This category, along with other strategies to reduce the CD rate, should be studied further.[5]

In the 1970's researchers began to collect data on trial of labour after prior CD. Some studies have reported success rates of up to 67% but rates vary in different parts of the world. The Royal College of Obstetricians and Gynaecologist (RCOG) quote figures as high as 85-90% success for VBAC.[6] A study conducted at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) evaluated the mode of delivery and outcomes of women with a single previous CD. The authors found that 63% of women with a single previous caesarean scar chose to attempt VBAC. The VBAC success rate in this study was 35%.[7]

The aim of the study was to determine the success rate and risk factors for women attempting vaginal delivery after a prior caesarean delivery.

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Methods

This was a retrospective analysis of women with one previous caesarean delivery attempting vaginal birth in the current pregnancy. Delivery information was obtained for women who delivered at SBAH from 2013-2018. SBAH is a tertiary referral hospital and is the only hospital performing VBAC in the central and eastern parts of the Tshwane District. Women with a CD in a prior pregnancy are counselled at their local ante-natal clinic or district level hospital about the risks and benefits of vaginal delivery versus elective CD. Women with the following clinical characteristics are advised not to attempt vaginal delivery: more than one previous CD, known previous classical uterine incision, prior uterine rupture, multiple gestations, previous uterine surgery in the upper segment of the uterus and those in whom vaginal delivery is contraindicated, eg placenta praevia. The level of healthcare worker providing the counselling ranges from a midwife to specialist. Women choosing to attempt vaginal delivery are requested to present to SBAH when in labour. Progress of labour is monitored using a partogram and surgeons, anaesthetists and theatre staff are available on site should an emergency CD be required.

Data were collected from the daily delivery record sheets that are completed for all women delivering at SBAH. Additional information was obtained from patient case notes and the maternity register.

Descriptive statistics in the form of means and standard deviations in the case of continuous data and frequencies and percentages in the case of categorical data were calculated. The sample size was calculated using the nQuery version 8.2.1.0, based on the suspect that 75% of women who attempt VBAC fail, and deliver by emergency caesarean section, with an accuracy within 0.05 (5%) with a 95% confidence. Ethical approval was obtained from the University of Pretoria Research Ethics Committee (ref: 270/2019)

Results

Two hundred and eighty nine maternal case notes were analysed for the study period from 1 January 2013 to 31 December 2018. The baseline characteristics of the study population are shown in Table 1.

One hundred and three women (36%) attempting a trial of labour had a successful vaginal birth. One hundred and one women who delivered vaginally had one prior CD while there were 2 women with 2 prior CDs. Both women with 2 prior CDs presented in advanced stages of labour and delivered vaginally before surgery could be arranged. Reasons for failed VBAC included: poor progress of labour (n=138, 74.2%), fetal distress (n=24, 12.9%), cephalo-pelvic disproportion (n=15, 8.1%) and 5 women (2.7%) later declined continuation of a trial of labour. Ninety-five percent (n=275) of women in the study population had no complications. There were 9 (3.1%) cases of postpartum hemorrhage, 5 in those who had a successful VBAC (4.8%) and 4 (2.1%) in the failed VBAC group. Two (0.7%) women required blood transfusions: one in the failed VBAC group and 1 in the successful VBAC group. There were no maternal deaths.

The mean neonatal birth weight was 2964g in the successful VBAC group, compared to an average of 3248g in the failed VBAC group. Four neonates (3.9%) in the successful VBAC group were born with a 5-minute Apgar score of < 7 compared to 7 neonates (3.8%) in the failed VBAC group (p = 0.91). Fifteen (5.2%) neonates required admission to the neonatal intensive care unit, 4 (3.9%) in the VBAC group and 11 (5.9%) in the failed VBAC group.

Table 1. Clinical characteristics of women admitted for trial of labour after caesarean section

Age (years)	
Mean(SD)	29.3 (4.7)
Obstetric History	
Parity, median (IQR)	1 (1-2)
Gravidity, median (IQR)	2 (2-3)
Race, n (%)	
Black	257 (88,9)
White	15 (5,2)
Indian	9 (3,1)
Colored	4 (1,4)
Not classified	4 (1,4)
Antenatal booking, n (%)	**279 (96.5)**
Number of previous caesarean deliveries	**n** (%)
1	285 (98.6)
2	4 (1.4)
Cervical dilatation on admission (cm)	**n,** (%)
1-3	178 (61.6)
4-7	71 (24.6)
8-10	40 (13.84)
Previous VBAC, n (%)	**33 (11.4)**
Previous vaginal delivery (unscarred uterus), n (%)	**69 (23.9)**
Indication for the primary caesarean delivery	**n** (%)
Fetal distress	148 (51.1)
Labor dystocia	78 (27)
Malpresentation	16 (5.5)
Failed induction of labor	15 (5.1)
Other /not recorded	32 (11.0)
Maternal weight, mean (SD)	**74.1 (11.4)**
HIV status	**n,** (%)
Positive	49 (17.0)
Negative	234 (81.0)
Unknown	6 (2.1)
Maternal co-morbidities	**n,** (%)
None	264 (91.4)
Hypertension	21 (7.3)
Diabetes	2 (0.7)
Asthma	2 (0.7)

Abbreviations: IQR; interquatile range, SD; standard deviation, VBAC; vaginal birth after caesarean section

Discussion

The VBAC success rate of 36% at our institution was significantly lower than rates reported in developed countries. The RCOG Green Top Guideline advises that women be counseled that the chance of the successful VBAC is approximately 70% but lower success rates have been reported for women of African ancestry.[6,8] Wu et al. reported a success rate of 54% for women from African regions.[9] Van Bogaert and van der Walt reported success rates of 42% and 54% respectively.[8,10]Both studies were carried out in South African hospitals with a similar population to our study participants. Factors that were associated with a successful VBAC in our study were a third pregnancy, previous successful VBAC (61% success rate), presentation in the active phase of labor, neonatal birthweight of less than 3kg. These findings were similar to findings by Wu et al, who reported that previous VBAC, previous vaginal delivery and Bishop score were associated with a significant likelihood of successful VBAC.[9] The average gravidity of the patients who had a successful VBAC was 3 and those who failed to achieve VBAC was 2, supporting the evidence that higher parity improves chances for a successful VBAC. Our study population in general had a low parity

Table 2 Factors associated with a successful vaginal birth after caesarean section.

Characteristics	Successful VBAC (n=103)	Failed VBAC (n=186)	p-value
Age, mean (SD)	29.0 (4.5)	29.5 (4.7)	0.43
Gravidity, mean (IQR)	3 (2-3)	2 (2-3)	**0.04**
Parity, mean (IQR)	1 (1-2)	1 (1-2)	0.08
Ante-natal care attendance, n (%)	102 (95.3)	179 (98.8)	0.07
Race, n(% of population)			
Black	92 (35.8)	165 (64.2)	
White	5(33.3)	10 (66.7)	
Indian	5 (55.6)	4 (44.4)	
Coloured/mixed race	4 (50.0)	4 (50.0)	
Previous successful VBAC, n (%)	19/31 (61,3)	12/31 (38,7)	**0.002**
Previous vaginal delivery n (%)	21 /62(33,9)	41/62 (66,1)	0.16
Maternal weight, mean (SD)	74.1 (11.7)	74.1 (10.9)	0.98
Cervical dilatation (cm) on admission			
1-3, n (%)	42 (39.3)	136 (73.1)	
4-7, n (%)	38 (37.4)	29 (15.6)	< **0.01**
8-10, n (%)	23 (23.3)	21 (11.2)	< **0.01**
Outcomes			
Reasons for failed VBAC			
Foetal distress		24 (12.9)	
Poor progress		138 (74.2)	
CPD		15 (8.2)	
Decline VBAC		5 (2.4)	
Not indicated		4 (2.2)	
Post partum hemorrhage, n (%)	5 (4.8)	4 (2.1)	0.37
Birth weight (g), mean (SD)	2964 (474.2)	3248 (409.9)	<**0.01**
10 minute Apgar score < 7, n (%)	4 (3.9)	7 (3.8)	0.91
NICU admission, n (%)	4 (3.9)	11 (5.9)	0.78

with mean of 1 in both groups. A previous vaginal delivery did not improve the chance of VBAC success in our study.

Seventy six percent of patients admitted in the latent phase of labour had a failed VBAC, compared to 43% those who were admitted active phase and 47% of those admitted in advanced labour. Presentation to the labour ward in advanced labour was associated with a 52% success rate. This rate is modest compared to the 60-80% success rate quoted by first world countries.[7] The admission Bishop score should be one of the factors considered during admission to predict the likelihood of a successful VBAC.

Several studies have found an association between the primary indication for the previous CD and the success rate of VBAC. The American College of Obstetrics and Gynecology Practice Bulletin 205 states that women with a prior CD for arrested labour are less likely to achieve a VBAC than those who have a CD for a non-recurring indication such as breech presentation.[3] Previous vaginal delivery and/or previous successful VBAC are also associated with higher VBAC success rates. Ten percent of study participants in our study had a previous successful VBAC while 21% had delivered vaginally previously. Of those with a previous VBAC, 61% (p=0.002) had a successful VBAC and 34% (p=0.16) of the patients with a previous vaginal delivery had a successful VBAC.

Complications of VBAC

The complication rate in our study was low. No woman attempting VBAC was admitted to the intensive care unit and there were no cases of uterine rupture. There was no significant difference in the rates of postpartum hemorrhage and only 2 women received a blood transfusion post- delivery (0.1%). Neonatal outcomes were also comparable between the 2 groups. Adverse outcomes were measured in terms of 10-minute Apgar score and Neonatal Intensive Care Unit (NICU) admission. Ten-minute APGAR scores of less than 7 were present in 3.74% of the successful VBAC group and 3.84% in the failed VBAC group. There was no significant difference in NICU admission between the 2 groups. The low complication rate observed in our study is most likely due with the strict VBAC protocol that was followed. All women admitted for trial of labour were admitted to delivery room where a drip and catheter were inserted. Labour progress was plotted on a partogram. If labour did not progress adequately, women were offered a CD and this was performed within an hour after the decision was made.

The time interval between the prior CD is important. Henler and Bujod found a significantly higher risk of uterine rupture for women who had had a CD in the preceding 24 months.[11] The risk of uterine rupture was 4.8% for those with a CD less than 12 months prior, 2.7% between 12-24 months and 0.9 % for those who attempted VBAC after 25 months.[11]This is important in counseling and policy making with regards to patient selection as suitable candidates for VBAC.

Counseling for VBAC

Counseling a woman about the benefits and risks associated with ERCD and VBAC is important and should be undertaken as early as

possible in the pregnancy. This will give the patient time to make an informed choice. It also allows the woman to have the opportunity to discuss, throughout the pregnancy, concerns and questions regarding the delivery. The health care provider should be able to give non-directive counseling and should have the necessary skills and knowledge about the different delivery options.

Nilsson et al conducted a study on views of women in countries with low VBAC rates.[12] The findings were that different caregivers have different views on VBAC. The differing views made decision-making difficult for women and counseling was framed by the attitudes and beliefs of the attending practitioner.[12] Counselling regarding mode of delivery in our study was performed by the attending registrar on call (91%), referring medical officer (3.5%) or midwife (4.8%).

Cost effectiveness of VBAC.

Failed VBAC is associated with both monetary and non-monetary costs including emotional and physical complications for the patient. Factors such as lengthier hospital stay and physical complications such as uterine rupture, post-partum hemorrhage, maternal sepsis and poorer neonatal outcomes have been reported.[3] Although the overall complication rate in our study was low, the average hospital stay for women who had a failed VBAC was increased by 1-2 days compared to women admitted for elective CD. The cost effectiveness of VBAC depends on the likelihood of successful trial of labour and the risk of complications. Gilbert et al found that TOLAC was only cost effective when the VBAC success rate was more than 46%.[13] Paré et al found that for a woman with a single prior CD planning one future pregnancy, an ERCD was preferred since it resulted in fewer hysterectomies.[15] In contrast, if several future pregnancies were desired TOLAC was preferred due to the overall reduction in cases of hysterectomy and placenta accreta.[14] This should be taken into consideration in our setting where resources are limited and staff and bed shortages are a constant problem. In addition, TOLAC was still more cost effective than ERCD in low risk women with a high likelihood of successful VBAC. Long-term effects of multiple repeat CD and the impact on future pregnancy complications must be considered. The review lists the conditions under which ERCD is more cost effective than TOLAC, "these include a low likelihood of high likelihood of TOLAC success, high likelihood uterine rupture and a high cost of TOLAC relative to ERCD and high likelihood of disutility resultant from stress urinary incontinence after VBAC."[15]

Other non-monetary considerations which are difficult to predict are the risks of increasing complications with higher numbers of CD. Often women find this difficult to understand as it is related to potential risk in a future pregnancy that they may have not considered yet. There may also be emotional distress to women who feel their reproductive choice of family size is limited if they deliver by CD. Women who achieve a successful VBAC are often very satisfied with the outcome as there is a sense of accomplishment that comes with the ability to deliver vaginally. Often both the women and physicians do not like the unpredictability of awaiting labor, while ERCD is timed for both the convenience of the doctor and patient.[3]

Strength and Limitations

The strength of this study is that all the deliveries were managed according to a strict protocol in the labor ward and this is an accurate indication of the success rate under optimal conditions in a tertiary center. A limitation of the study was that this was a single center retrospective study and some cases could have been missed. Study numbers of White, Indian and Coloured populations were low and do not necessarily reflect the true status in these groups.

Conclusion

The success rate of VBAC in our institution was 37%, which is comparable to other South African public health institutions. Although the short-term maternal and neonatal complication rates were low, the low likelihood of successful VBAC makes one consider the feasibility of encouraging women in our setting for TOLAC. The results of this study may assist with the development a VBAC success prediction model in our institution.

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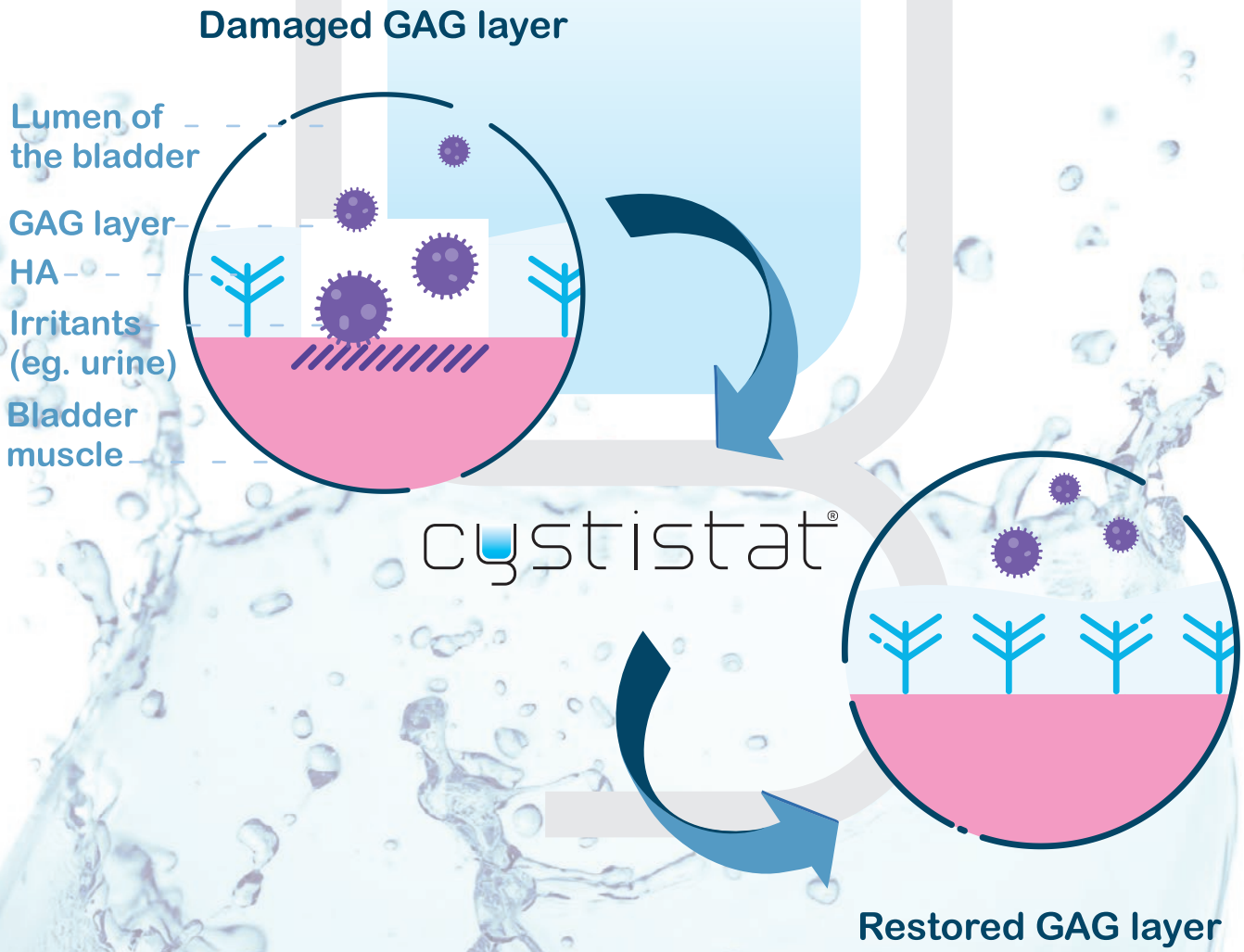

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Knowledge about human papilloma virus (HPV) disease and vaccination among primary health care nurses at Nelson Mandela Bay clinics

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Abstract
Background: Primary prevention of cervical cancer is recommended by prophylactic HPV vaccine administration to girls before sexual debut. Vaccination coverage can be increased by nurses' counselling and recommendations to parents.
Objectives: Our aim was to investigate the knowledge of nurses working in primary health care clinics in the Nelson Mandela Bay (NMB) area, Port Elizabeth, on HPV disease and vaccine. We also explored the attitudes and perceptions of the nurses on HPV vaccine.
Methods: We conducted a cross-sectional descriptive study by means of self-administered questionnaires, completed anonymously by nurses in primary health care clinics in NMB. Data were collected on participants' demographics, knowledge of HPV infection and – vaccine as well as their attitude and perception regarding the HPV vaccine.
Results: The mean age of participating nurses was 46.9 years, and about 75% had more than five years' work experience. Knowledge on HPV transmission and its prevention was good, but was lacking on HPV vaccine and vaccination. Respondents showed a positive attitude and perception towards the HPV vaccine.
Conclusion: Our study showed that the nurses at Nelson Mandela Bay clinics have limited knowledge about HPV and had poor knowledge about the HPV vaccine itself and to whom and when to administer it.

Background

Cervical cancer is a major global health problem and in 2018 ranked as the fourth most frequent cancer in women, with about 570 000 new cases and accounting for 7.5% of all female cancer deaths.[1] Globally, it was estimated that more than 311 000 women died from cervical cancer in the same year[1], of which 85% deaths occurred in less developed regions.

Human papillomavirus (HPV) infection is the most important etiological factor in cervical cancer.[2] Primary prevention of the disease is recommended by prophylactic HPV vaccine administration.[3] The ideal time for vaccination is before sexual debut, with the recommended age of 9 – 14 years.[3,4] Vaccination coverage is considered adequate when immunisations with the second dose reach 80% in the target populations.[5] In South Africa, the coverage on implementation of the school-based HPV immunisation program in 2014 was fair (85%), but has decreased with 21 – 26% between the first and second doses in 2014 and 2016 respectively, which is suboptimal.[6] Demonstration pilot studies have demonstrated that high coverage is possible[7-9] and it shows that there is room for improvement of coverage in South Africa if certain factors can be addressed.

Vaccine uptake is clearly dependent on parental decisions for their children. Increased effectiveness of immunisation programs can be achieved by overcoming communication challenges such as explaining, consenting and managing conflicts between parents and their children with respect to vaccination decisions.[10] Recommendations by health care providers can highly influence parental decisions. Primary health care nurses working in clinics are the first contact to patients and most of the counselling is done by them. These nurses are crucial to achieving high vaccine uptake, but to be effective in this regard, they must be knowledgeable about HPV infection as well as the HPV vaccine so that they can communicate confidently. A questionnaire-based study of 602 Nigerian healthcare professionals concluded that, while they had good knowledge of HPV infections, their awareness of the HPV vaccine was low.[11] Nurses in particular had the lowest level of knowledge about the HPV vaccine, or even its existence. A quantitative study conducted in a South African hospital, using self-administered questionnaires to nurses, showed that the majority of the nurses lacked understanding of HPV infections and vaccinations, but were yet willing to recommend vaccinations to patients.[12]

Our aim was to investigate the knowledge of nurses working in

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primary health care clinics in the Nelson Mandela Bay (NMB) area, Port Elizabeth, on HPV disease and vaccine. We also explored the attitudes and perceptions of the nurses on HPV vaccine.

Methods

We conducted a cross-sectional descriptive study, using convenience sampling. Our survey was carried out from 9 – 20 December 2019 by means of self-administered questionnaires completed anonymously by nurses in 23 primary health care clinics in NMB, Port Elizabeth, South Africa. Approval for the study was granted by the Health Research Ethics Committee at Walter Sisulu University (HRCCC no. 065/2019), the Eastern Cape Health Research Committee (EC_201910_004) and the clinical governance manager of NMB health district.

The target population was nurses working in NMB primary health care clinics, including professional nurses (PNs), enrolled/staff nurses (ENs) and enrolled nursing assistants (ENAs), who met the inclusion criteria. Participants had to work permanently in primary health care clinics, with current registration at the South African Nursing Council and had work experience at the clinic of at least three years. Managers and community service nurse practitioners were not eligible to participate in the study.

The data collection instrument was a self-administered questionnaire, consisting of four sections. Section A related to participants' demographic information, Section B measured the participants knowledge on the HPV vaccine and comprised true or false questions, Section C sought to measure the participants attitudes towards the HPV vaccine and comprised closed/ended questions, Section D measured the perceptions of nurses regarding the HPV vaccine and contained 4-likert scale type of questions ranging from strongly agree to disagree. The questionnaire was developed and adapted for local use from similar global surveys and was reviewed by the study supervisor and an expert panel of quantitative researchers for validity. Our pilot study revealed no methodological flaws and these findings were added in the main findings.

Data collection was preceded by addressing the nurses at the particular clinic to inform them of the study, and those willing to participate each received an informed consent form and a questionnaire. Nurses completed the questionnaires at their own time so that service delivery would not be disrupted. Confidentiality was ensured by placing the consent forms into a separate box from the anonymously completed questionnaires.

Data were captured on a Microsoft Excel® (version 2016) spreadsheet and were analysed using the software package IBM SPSS version 25 program, with assistance from a biostatistician.

Results

One hundred and sixty questionnaires were distributed, of which 110 were completed and returned, resulting in a response rate of 68.8%. Demographic data showed the mean age of participants was 46.9 years (27 – 65 years; SD±9.37 years), and 102 (92.7%) were female. Ninety (81.8%) participants were African, 16 (14.5%) were Coloured and 4 (3.6%) were White. Most of the respondents, 79 (71.8%) were professional nurses, 22 (20.0%) enrolled/staff nurses and 9 (8.2%) were enrolled nursing assistants.

Regarding working experience as nurse, 26 (23.6%) had 3 – 5 years work experience, 21 (19.1%) reported 6 – 10 years experience, 28 (25.5%) had 11 – 20 years work experience, 28 (25.5%) had 21 – 30 years work experience and 10 (9.1%) had more than 30 years work experience. The majority of participants (> 75%) had more than 5 years work experience.

The second section in the questionnaire comprised twelve items which measured the knowledge of the participants about HPV and HPV vaccine. True or false statement were used to test how knowledgeable the respondents were on the subject, with the results displayed in Table 1.

Table 1. Responses of participants to statements on knowledge about HPV and HPV vaccine

Statement	Responses (%)	
	True	False
1. Human papillomavirus (HPV) is an extremely common worldwide virus	93.64	6.36
2. There are 4 types of HPV	45.45	54.55
3. HPV is mainly transmitted through sexual contact	76.36	23.64
4. Condoms are not protective of HPV infection	36.36	63.64
5. High-risk types of HPV causes cancer	93.64	6.36
6. Cervical cancer is the only cancer caused by HPV	49.09	50.91
7. HPV is a live attenuated vaccine	79.09	20.91
8. HPV is administered as oral drops	13.64	86.36
9. HPV vaccine is given as once off dose	50.00	50.00
10. HPV vaccine is given to both boys and girls	29.09	70.91
11. HPV vaccines is given for primary prevention of cancer of the cervix	90.91	9.09
12. HPV is given to 9-year old girls only	32.73	67.27

Table 2. Responses of participants to questions testing their attitudes towards the HPV vaccine.

Question	Responses (%)	
	Yes	No
1. Do you think it is necessary that HPV vaccine should be included in the immunisation program?	99.1	0.9
2. Would you advise your own child / family to receive HPV vaccine?	97.3	2.7
3. Do you think HPV vaccine is a safe drug to give?	98.1	1.8
4. Are you willing to administer HPV vaccine if available in your clinic?	97.3	2.7
5. Do you think HPV vaccination will eventually eradicate cervical cancer?	90.0	10.0

The third section in the questionnaire tested the participants' attitude towards the HPV vaccine. Five closed end questions required either a 'yes' or 'no' response as shown in Table 2.

The fourth section in the questionnaire collected data on nurses' perception on HPV vaccination, by using 4-point Likert-scale type statements. The possible responses ranged from A to D, with A = "Strongly agree", B = "Agree", C = "Strongly disagree" and D = "Disagree". The data collection from this section is displayed in Table 3.

Discussion

The majority of our respondents knew that HPV is common worldwide (93.6%), it is mainly a sexually transmitted disease

Table 3. Responses of participants to questions testing their perceptions about the HPV vaccine.

Statement	Responses (%)			
	A. Strongly agree	B. Agree	C. Strongly disagree	D. Disagree
1. 9 to 12-year-old girls should be informed about HPV vaccination	74.55	23.64	0.91	0.91
2. 9 to 12-year-old girls should be informed about HPV transmissionn	71.82	26.36	1.82	0
3. Parents should be informed about HPV vaccine	89.09	10.91	0	0
4. Parents should be informed about other methods to prevent HPV transmission	82.73	16.6	0.91	0
5. Providing information about HPV vaccination is different as compared to other vaccinations	40.00	30.91	8.18	20.91
6. Boys should be offered the HPV vaccination	31.82	24.55	6.36	37.27
7. Cultural background will influence the uptake of the HPV vaccine	30.00	45.5	5.45	19.09
8. Parents should give consent for HPV vaccine	51.82	37.27	1.82	9.09
9. If the parent and child have different opinions, the child's decision should take preference	35.45	36.36	6.36	21.82
10. The child's social background has an influence on whether he/she is vaccinating	30.00	40.00	12.73	17.27

(76.4%), condoms are protective of HPV infection (63.6%) and the high-risk HPV types cause cancer (93.6%). Only 54.5% of the participants knew that there are more than 4 types of HPV and 50.9% of the participants knew that cervical cancer is not the only cancer caused by HPV. These results clearly show that the participants' knowledge is limited to HPV transmission and prevention thereof, which implies that a significant number of participants will have challenges in counselling about HPV and its consequences, and would therefore avoid recommending HPV vaccination to patients.

Results on assessment of nurses' knowledge on the HPV vaccine and vaccination **show that their** knowledge is lacking on HPV vaccine: 79.1% thought it is a live attenuated virus, half of the participants thought it was given as a once off dose, 70.9% did not know that it can be given to both boys and girls and 67.3% thought it is given to 9-year old girls only. The majority (90.9%) of participants knew that the HPV vaccine was for primary prevention of cervical cancer, which links to the belief that the vaccine it is only meant for girls.

Our results are in line with research studies done in developing countries, including African countries that showed that health workers had poor knowledge on HPV vaccination, causing in a barrier to promotion of the vaccine during healthcare visits.[13] In an HPV vaccination project in KwaZulu-Natal, it was demonstrated that acceptance of the vaccination program by key stakeholders was necessary and in order to achieve this, training and education of these stakeholders were done.[7] The Centers for Disease Control and Prevention highlighted that education of the parents needs to be addressed as many parents don't understand the need for the vaccine and have concerns over its safety.[14]

More than 90% of our participants showed a positive attitude towards the HPV vaccine. They felt it was necessary for the vaccine to be included in the immunisation program, were willing to administer the vaccine, and were willing to advise their children or family members to receive the vaccine. This finding is congruent to a Swedish school nurse study, where school nurses felt competent to administer the HPV vaccine even though they did not have adequate knowledge about it, because they were previously involved in other immunisation programs.[15] Our participants also believed that it is a safe drug and it will eventually eradicate cervical cancer, an important finding as it further emphasizes the willingness to promote and administer the vaccine. In a study on Zambian health professionals' feedback on HPV vaccination rollout, their attitudes were shown to be influenced by factors beyond medical knowledge, like misconceptions and myths surrounding the vaccine, which in turn translated into a fear of the HPV vaccine by the community. Some of these misconceptions were that the vaccine causes infertility and illness, such as cervical cancer itself.[13] The positive attitude of our participants showed a willingness to learn about HPV and – vaccination, which can result in clear communication with parents, hence improving parental knowledge and therefore increased uptake of the vaccine by children.[8] Communication with the parents about HPV vaccination, also offered an opportunity to link primary and secondary prevention in a mother-daughter program and increased screening for cervical cancer by the mothers and female guardians.[16]

Results on participants' perceptions on HPV vaccination showed about 71% felt that 9 to 12-year-old girls should be informed about HPV transmission and vaccination. This indicated that although HPV is a sexually transmitted infection, there was no barrier to counselling and offering the vaccine, despite the fact that many felt that giving information about this vaccination will be different from other immunizations. More than 82% of the participants agreed that parents should be informed about HPV vaccination and prevention of transmission. In a KwaZulu-Natal HPV vaccination demonstration project, it was shown that intense communication with the parents prior to vaccination to address questions and concerns led to high uptake.[14] Over 40% of our respondents agreed that cultural backgrounds will influence the uptake of the vaccine and that a child's social background has an influence on whether he/she is vaccinated or not; this is a worrying fact resulting to some children not being vaccinated because of their cultural and social backgrounds and thereby exposing them to cervical cancer. The results of our study is similar to a Zambian study where health workers highlighted a need for specific cultural barriers to be addressed before HPV vaccine rollout as Zambian women rely on male or elders' permission to vaccinate their children.[13] The majority of our respondents felt that parents should consent for HPV vaccination and if opinions between a child and a parent differ, the child's decision should take preference. This will apply for children 12 years and older who are legally permitted to consent as per The Child Act 38 of 2005.[14] Many of participants (43.7%) disagreed that boys should be offered vaccination, which supported their belief that the virus causes only cervical cancer. Swedish school nurses felt

it was unfair to exclude boys from the HPV vaccination program as they can be carriers of the virus.[10] Health workers' perceptions can influence their administration of the HPV vaccine, for example, interviews with fifteen health professionals in exploring their views on cervical cancer screening concluded that professionals' perceptions of screening barriers influenced their management goals, practices and decisions surrounding how best to deal with cervical cancer.[17]

A limitations to our study is the fact that these research results are specific to nurses working in Nelson Mandela Bay, and the results cannot be generalized. Due to the simplicity of the questionnaire, some of the questions used to test knowledge have ambiguous answers.

Conclusion

Our study showed that the nurses at Nelson Mandela Bay clinics have limited knowledge about HPV and had poor knowledge about the HPV vaccine itself and to whom and when to administer it. The majority showed positive attitudes on administration of the HPV vaccine at the clinics. The nurses also perceived social and cultural backgrounds as barrier to the vaccine uptake. More should be done to empower our health care professionals regarding vaccines including the HPV vaccine which is important in the fight against cervical cancer.

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Tubal Ectopic Pregnancy 4 years after hysterectomy: a case report

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Abstract
Background:
Ectopic pregnancy after hysterectomy is a rare event. To date there are 73 definitive cases of post-hysterectomy ectopic pregnancy. The first case was reported by Wendler in 1895.

Case:
A 31 year old P2G4 (one miscarriage) presented with a history of severe lower abdominal pain of three days duration. She previously had a subtotal hysterectomy four years prior her current presentation for a septic miscarriage with multiple organ dysfunction.
She had a background history of being HIV reactive on antiretroviral therapy initiated two days before her presentation. Her CD4 count was 54 cells/uL, negative cryptococcal latex test. She was first diagnosed with HIV in 2015, however had not been on antiretroviral therapy since then.
On clinical examination she was hemodynamically stable, normal blood pressure and pulse, afebrile and no stigmata of AIDS. She had an acute abdomen and on pelvic examination a cervical stump was palpable with no blood from the cervical os. Her haemoglobin was 13.4g/dl. Urine pregnancy test was positive. Her quantitative beta-HCG of 3979 IU/L.
Pelvic ultrasound showed fluid collection in the pelvis, no definite masses seen, no uterus seen and ovaries could also not be visualised.
Abdominal ultrasound did not show any abnormalities in the rest of the abdomen.
The patient was counselled for surgery. Preparation with multidisciplinary consultation was done.
Intraoperatively, 100ml haemoperitoneum was found. There were dense pelvic adhesions. Adhesiolysis was done and a bleeding right fallopian tube ampullary pregnancy was found. The right ovary was grossly normal. The contralateral adnexa could not be identified. A right salpingectomy was done. Total blood loss was 100ml.
She recovered well post operatively and was discharged three days later to continue her antiretroviral therapy.

Discussion:
A rare case of tubal ectopic pregnancy after hysterectomy is presented.
Access to the peritoneal cavity and fallopian tube through the cervical canal, we postulated as the mechanism in this case.
Ectopic pregnancies after hysterectomy are classified into early and late. The former being associated with a pregnancy (or viable gametes) that was present at the time of hysterectomy. These present soon after the hysterectomy. The latter present long after the hysterectomy.
Conception can occur after hysterectomy through access via a prolapsed fallopian tube, a fistula or defect in the vault. Cervical stump pregnancy is also described. Surgical intervention is the most common intervention described amongst the case reports.

Conclusion:
Pregnancy after a hysterectomy is a rare possibility with possible adverse outcomes. Clinicians must have a strong index of suspicion for a possible ectopic pregnancy in patients that present with abdominal pain after hysterectomy.

Background

Ectopic pregnancy after hysterectomy is a rare event. To date there are 73 definitive cases of post-hysterectomy ectopic pregnancy. The first case was reported by Wendler in 1895.[1]

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The 73rd case which was a cervical stump ectopic pregnancy was reported in Ethiopia by Ahmed et al in 2019.[2]

Case presentation

A 31 year old P2G4 (one miscarriage) presented with a history of severe lower abdominal pain of three days duration. She presented to a local primary health clinic and did not disclose the history of having had a subtotal hysterectomy four years prior her current presentation. The hysterectomy was done for a septic miscarriage with multiple organ dysfunction.

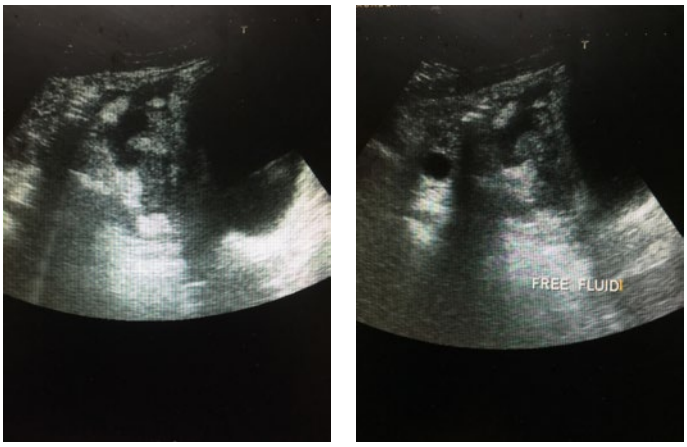

Figure 1: Ultrasound images showing the bladder on the right side of the images and clots on the left of the images. No uterus visible.

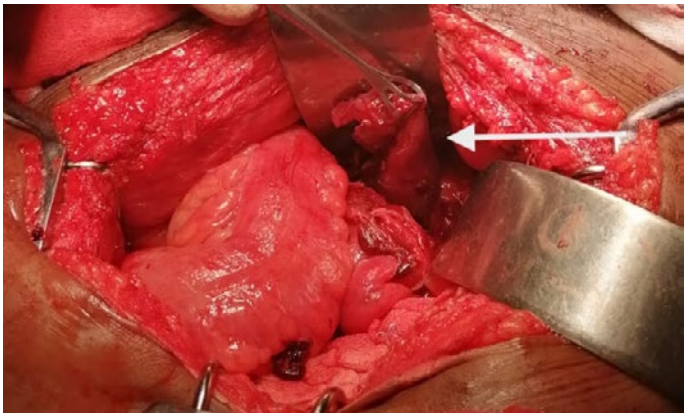

Figure 2: Right fallopian tube after adhesiolysis

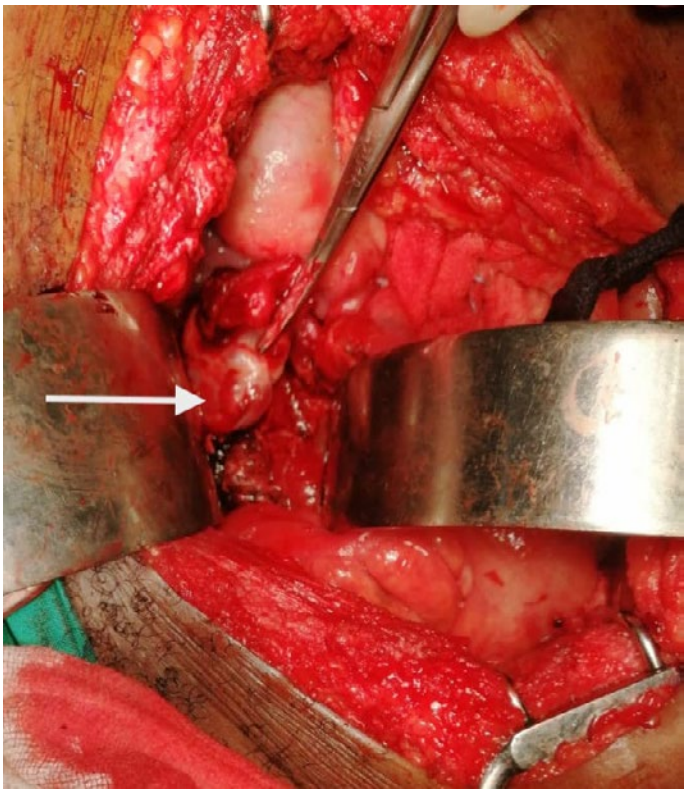

Figure 3: Right ovary after salpingectomy

A urine pregnancy test was done at the clinic and it confirmed a pregnancy. She was then sent to our centre for suspected ectopic pregnancy.

She had a background history of HIV infection on antiretroviral therapy initiated two days before her presentation. Her CD4 count was 54 cells/uL, negative cryptococcal latex test. She was diagnosed with HIV in 2015, however had not been on antiretroviral therapy since then.

On clinical examination she was hemodynamically stable, normal blood pressure and pulse, afebrile and no stigmata of AIDS. She had an acute abdomen and on pelvic examination a cervical stump was palpable with no blood from the cervical os. Her haemoglobin was 13.4g/dl. Urine pregnancy test was positive. Her quantitative beta-HCG was 3979 IU/L.

A pelvic ultrasound showed fluid collection in the pelvis, no definite masses seen, no uterus seen and ovaries could also not be visualised.

Abdominal ultrasound did not show any abnormalities in the rest of the abdomen.

An assessment of ectopic pregnancy post hysterectomy was made.

The patient was counselled for surgery. Preparation with multidisciplinary consultation was done.

Intraoperatively, 100ml haemoperitoneum was found. There were dense pelvic adhesions involving the bladder, bowel and adnexae. No macroscopic fistulous tract was observed. Adhesiolysis was performed and a bleeding right ampullary ectopic pregnancy was found. The right ovary was grossly normal. The contralateral adnexa could not be identified. A right salpingectomy was done. Total blood loss was 100ml.

She recovered well post operatively and was discharged three days later to continue her antiretroviral therapy.

The histopathology examination confirmed a tubal pregnancy.

Discussion

Pregnancy after hysterectomy is a very rare occurrence. We postulate that there may have been a fistulous tract allowing passage of spermatozoa into the peritoneal cavity.

Post hysterectomy ectopic pregnancies occur either early after a hysterectomy or many years later.[3]

Early post hysterectomy ectopic pregnancy occur if there is a luteal phase pregnancy at the time of hysterectomy.[3] The fertilised ovum is in transit to the uterus. The other possibility is the presence of spermatozoa in the fallopian tube when the hysterectomy is performed. Diagnosis in this case may be delayed by the pursuit of other likely causes of pain post hysterectomy such as vaginal cuff infection, pelvic hematoma etc.

It is therefore recommended that a hysterectomy be performed in the pre-ovulatory phase or after effective contraception.[2]

Late occurring post hysterectomy ectopic pregnancy occur as a result of a fistulous communication between the vagina and the peritoneum.

50% of these follow vaginal hysterectomy.[3,11] This may be due to proximity of the fallopian tube to the vaginal cuff at closure of the vaginal vault.

15% (11/72) of the hysterectomies in a review by Fylstra were subtotal hysterectomies.[3] There can be direct communication between the cervical canal and peritoneum through a fistulous tract.

The fistulous tract can be macroscopic or microscopic. Sobczyk reported a surgically created and later cauterised fistulous tract.[4] Babikian describes a macroscopic tract, pin hole sized between the cervix and peritoneal cavity which was observed at laparotomy for a post hysterectomy ectopic pregnancy.[5]

The commonest presenting complaint is abdominal pain.[2-9]

Due to the history of hysterectomy, the diagnosis of a pregnancy is often not expected and is made after several biochemical tests, imaging techniques, at surgery or even at histopathological examination.

Surgery is the most common intervention amongst the case reports.[2-9] The various approaches include one or more of the following: salpingectomy, adnexectomy and trachelectomy (in cases

of previous subtotal hysterectomy).

In sealing off the fistulous tract cauterisation and the use of an omental patch has been described in some case reports.[4,5]

McCool reported successful management of a post hysterectomy ectopic pregnancy with single dose methotrexate.[9] The pregnancy was diagnosed early and the patient was clinically stable and a candidate for conservative management.

Morbidity and mortality is high due to delayed diagnosis. A systematic review in 2017 (57 cases at the time) found that 51% of patients had considerable blood loss, with 30% requiring blood transfusion.[3]

In this review there was one case of maternal death of a patient who required repeat blood transfusions and subsequently demised from sepsis.

To prevent pregnancy after hysterectomy, it is recommended that elective hysterectomy be performed in the pre-ovulatory phase of the menstrual cycle. Contraception before hysterectomy is also recommended.

Opportunistic salpingectomy at the time of hysterectomy is currently recommended to reduce the risk of ovarian cancer.[12] This possibly has an added benefit of reducing the risk of pregnancy after hysterectomy. More data is needed to confirm this.

Conclusion

Ectopic pregnancy after hysterectomy is rare but carries a high morbidity and mortality risk.

To prevent this, elective hysterectomy must be considered in the pre-ovulatory phase of the menstrual cycle and with effective contraception onboard. Clinicians must have a high index of suspicion for this condition in patients who present with pain after hysterectomy.

Authors Declaration:

We declare that this material is original and has not been previously published and has not been currently submitted elsewhere for publication.

Conflict of interest

We declare that there is no conflict of interest.

Consent for publication

A written consent for the publication of this article and clinical images was obtained from the patient.

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We wish to thank the patient and staff at Steve Biko Academic Hospital who were involved in the management of this case.

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CASE REPORT
O&G Forum 2021; 31: 26 - 27

Three cases of heterotopic pregnancy at a tertiary hospital in Port Elizabeth, South Africa

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Abstract
Heterotopic pregnancy is defined as the coexistence of intrauterine and extra uterine pregnancy. A high index of suspicion is needed for early and timely diagnosis and intervention. Clinicians should remain alert to the possibility of heterotopic pregnancy even when an intrauterine pregnancy is confirmed. Management options for heterotopic pregnancy includes expectant management, surgical intervention, medical management as well as transabdominal sonographic guided aspiration of the ectopic gestational embryo.
With early diagnosis and treatment, 70% of the intrauterine pregnancies will reach viability

Key words:
Heterotopic pregnancy, salpingectomy, haemoperitonium, transvaginal ultrasound, laparoscopy, laparotomy.

Introduction
Heterotopic pregnancy (HP) refers to the simultaneous existence of multiple pregnancies, usually an extra-uterine (ectopic pregnancy) and intrauterine pregnancy. The incidence of spontaneous HP in the general population is estimated at 1/7 963 to 1/30 000, but much higher, at 1%, with modern interventions like assisted reproduction therapy.[1]

HP can be a potential life-threatening condition, and early diagnosis is often missed since the presence of an intrauterine pregnancy distracts attention from signs or symptoms of a parallel pregnancy.[2,3] Patients commonly present with complaints of abdominal pain,[1,2] clinical signs of rupture and intra peritoneal hemorrhage. In any patient with intra uterine pregnancy, presenting with increasing abdominal pain and / or bleeding, a differential diagnosis of HP should also be considered. Management of HP includes a surgical approach,[1,4] with a reported abortion rate of about 15% of the intra uterine fetus after surgical management.[3]

We describe three cases of spontaneous heterotopic pregnancy, where the intra uterine pregnancy continued after surgical management and the patients delivered live healthy infants.

Case report 1
A 21-year-old female, primigravida, at 7 weeks 4 days' gestation, presented at the local clinic with high blood pressure (BP) of 147/87 mm Hg and anaemia (hemoglobin, Hb, level 5.8 g/dl). She had no knowledge of having hypertensive illness before, tested rhesus positive, and negative for syphilis and HIV. A positive family history of hypertension was reported, with no other risk factors. She was put on alpha methyldopa at the clinic and referred to hospital immediately. On arrival at the hospital her BP was 125/63 mm Hg with a pulse of 108 beats per minute (bpm). There were no complaints of lower abdominal pain or vaginal bleeding. She was noted to be pale with a ward Hb level of 6 g/dl, the chest was clinically clear, abdomen soft with no palpable masses. On speculum examination there was no vaginal bleeding and the cervical os was closed. There was no adnexal or cervical motion tenderness.

An ultrasound examination revealed a live singleton intra uterine pregnancy at 8 weeks 6 days and what appeared to be a left sided adnexal mass with a bagel sign and free fluid in the pouch of Douglas. A laparotomy was performed and a ruptured ectopic pregnancy with approximately 1 000 ml of haemoperitonium was found on the left side. A salpingectomy was done and histology confirmed an ectopic pregnancy. The patient received two units of packed cells with a litre of crystalloid solution as part of her initial resuscitation. On day two post laparotomy a transvaginal ultrasound (TVUS) revealed a singleton live intra uterine pregnancy. The patient recovered well post laparotomy and was subsequently discharged on day four on alpha methyldopa 500 mg per os three times per day for hypertension, iron and folic acid, and she was to be followed up for her antenatal care.

At 11 weeks 6 days she had a nuchal translucency and at 20 weeks an anomaly scan; both were normal. She continued with her follow up and at 36 weeks she presented at labour ward emergency care after an eclamptic fit at home. The patient was resuscitated and convulsions controlled, labetalol was given for BP control and magnesium sulphate to prevent further convulsions. On assessing the cervix, the Bishop score was unfavorable for induction of labour and she was offered delivery via caesarian section. A live female infant at 2,4 kg was delivered with Apgar scores of 8/10 and 10/10. Post-operative recovery was uneventful and mother and baby were discharged on day four post-delivery in good condition.

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Case Report 2

A 33-year-old female, gravida 5, para 4, was referred to our unit by her local hospital with suspicion of an ectopic pregnancy. She had history of one day's lower abdominal pain, with no vaginal bleeding or other associated symptoms. She was HIV positive, on antiretroviral treatment for the previous seven years, virally suppressed, with no other comorbidities. She had a previous caesarean section 11 years ago for failed induction of labour due to pre-eclampsia, followed by three successful vaginal births at term.

On arrival her BP was 109/74 mm Hg, pulse 79 bpm, Hb 12.3 g/dl and her urine pregnancy test was positive. The abdomen was soft, with lower abdominal tenderness and localized peritonitis in the left iliac fossa. Vaginal examination showed no bleeding, but marked cervical excitation tenderness as well as tenderness of the left adnexa. No obvious adnexal mass was palpable. TVUS revealed an intrauterine gestational sac measuring 6 weeks 2 days, as well as an extra uterine gestational sac with a doughnut sign in the left adnexa. There was also free fluid in the pouch of Douglas. During laparotomy 100 ml haemoperitoneum and a ruptured left sided tubal ectopic was found. A left sided salpingectomy was performed and histology confirmed the diagnosis of an ectopic pregnancy.

Recovery was uneventful and the patient was discharged on the third postoperative day. She continued follow-up in our unit, with a normal nuchal translucency measurement at 12 weeks and a normal fetal anomaly scan at 20 weeks. The pregnancy continued uneventfully and she had a successful vaginal birth after cesarean (VBAC) of a 3 800 g healthy male infant at 40 weeks 3 days. Both mother and baby were discharged on the first day post-partum.

Case Report 3

A 36yr old G3P2 unbooked patient, unsure of last menstrual period, presented to our unit with intermittent lower abdominal pain that was gradually worsening. She had no vaginal bleeding or discharge. Her pregnancy test was positive. On clinical examination she had a BP of 138/27 and pulse of 74 with an Hb was 10.4g/dl. Her abdomen was soft, tenderness but no peritonitis. On vaginal examination she had no cervical excitation tenderness or bleeding and no obvious palpable mass. TVS confirmed a heterotopic pregnancy with a live intra-uterine pregnancy of 7w1d, and an extra uterine gestational sac measuring 2.3cm. The patient was taken for a laparotomy and salpingectomy of the left fallopian tube was done for a ruptured fimbrial ectopic. Findings were confirmed on histology. Postoperative recovery was uneventful and she was discharged on the third postoperative day after the fetal heart of the intrauterine pregnancy was confirmed. The patient continued antenatal care in our unit. At 41w gestation she went into spontaneous labour and delivered a 3320g healthy female baby**.**

Discussion

Heterotopic pregnancy is defined as the co-existence of an intrauterine and an ectopic pregnancy.[1] Increased incidence of heterotopic pregnancy(HP) is usually associated in cases where assisted reproductive techniques are used, but none of our existing cases had a history of this procedure. Heterotopic pregnancy is a serious emergency that is potentially life threatening for the woman and her intrauterine pregnancy. ALL three patients presented with vague abdominal and pelvic signs. Ultrasonographic evaluation is the gold standard for the diagnosis, with finding of a second gestational sac or a complex adnexal mass in addition to the intrauterine pregnancy. The detection rate of heterotopic pregnancy with transvaginal ultrasound varies from 41% to 84%.[5] The intrauterine and ectopic pregnancies were visualized via TVUS in all our cases, all of which had ruptured ectopic pregnancies at time of diagnosis. The absence of typical symptoms and signs of ectopic pregnancy could lead to difficulty and delay in diagnosis, especially where a viable intra-uterine pregnancy is visualized on TVUS. When intrauterine gestation has already been diagnosed, HP is even more commonly missed. Tal et al reports that 90% of cases are diagnosed between 5 – 10 weeks' gestation and 10% in the 11th week,[4] although there are reports of HP being diagnosed at later gestation.[1,6] βHCG is of little significance in diagnosing HP because the developing intrauterine pregnancy that makes it difficult to interpret the results. The differential diagnosis of heterotopic pregnancy includes adnexal torsion, haemorrhagic corpus luteum, ovarian cyst, tubo-ovarian abscess and appendicitis.

The aim of management in heterotopic pregnancy is to remove the extra uterine pregnancy completely with minimal interference to the intrauterine pregnancy. This includes surgical intervention, medical management and transabdominal sonographic guided aspiration of the ectopic gestational embryo.[3] In cases where the ectopic pregnancy has ruptured the management should be surgical. Laparoscopy is the gold standard of surgical intervention in patients with heterotopic pregnancy. Laparoscopy is safe, results in less bleeding, less manipulation of the uterus and less hospital stay. Where laparoscopy is not available, laparotomy is acceptable alternative. All our cases underwent laparotomy, with favorable outcomes.

Where medical management is considered, methotrexate is contraindicated due to its potential teratogenic effect on the adjacent intrauterine pregnancy. Injection of the ectopic embryo with potassium chloride or hyperosmolar glucose, followed by transabdominal sonographic guided aspiration is considered a minimally invasive and effective management option.[3] This procedure requires a skilled and trained person. The patient also needs to be dedicated and reliable for close follow up care. In our setting with limited resources and skill this procedure is not encouraged. Surgeons operating on these patients must bear in mind the possibility of HP and the uterus must be handled with care. With early diagnosis and treatment, 70% of the intrauterine pregnancies will reach viability.[7]

Conclusion

Clinicians should remain alert to the possibility of HP even when an intrauterine pregnancy is confirmed via TVUS, due to the atypical presentation of patients with HP. A high index of suspicion is needed for early and timely diagnosis and intervention. Routine inspection of the adnexa should form part of first trimester scanning. A patient who presents with lower abdominal pain, anemia or hypovolemic shock in the presence of a visible intrauterine pregnancy on TVUS could be predictive of HP. The choice of management depends on the clinical status of the patient, available resources and expertise. Timely diagnosis and intervention result in favorable obstetric outcome**.**

Author contributions.

All authors contributed equally to writing and review of the manuscript.

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Conflict of interests. None

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CASE REPORT
O&G Forum 2021; 31: 28 - 30

Amniotic Band Destruction Syndrome causing Umbilical cord strangulation in a pregnancy with diabetes: a case report

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Abstract
Amniotic band destruction syndrome is rare. It is a constellation of major and minor abnormalities, which arises from lacerated amniotic band. The amniotic band syndrome involving umbilical cord constriction is even rare. We describe a case of umbilical cord constriction resulting in fetal demise and limb defects in second trimester.

Key words
Amniotic band syndrome, Fetal malformation, Umbilical cord constriction band, Second trimester fetal death, Limb malformation

Introduction
An umbilical cord strangulation by an amniotic band is a rare complication. It is usually associated with other manifestations of amniotic band syndrome (ABS). ABS is found in approximately 1 in 1,200 to 15,000 live births. It occurs due to laceration in the amniotic membrane, although exact etiology and pathology are unknown. The lacerated amniotic band has adhesive property and encircles floating fetal parts resulting in improper histogenesis and fibrosis, necrosis, malformations. The time of gestation and the system involved decides the degree of deformity.[1]

Here, we describe a case of umbilical cord strangulation and bilateral lower limb deformity diagnosed at 16 weeks, which resulted in pregnancy loss in the early second trimester.

Case report
36-year elderly, gravidae 2, abortion 1, presented at 5+ weeks of gestational age (GA). It was a spontaneous pregnancy of a non-consanguineous marriage. She underwent Medical termination of pregnancy 9 months back in view of blighted ovum (8 weeks of GA). She was diagnosed to have diabetes and managed by medical nutritional therapy. Her BMI was normal (22kg/m^2).

The present pregnancy report suggested glycosylated hemoglobin (HbA_1C) of 6% with abnormal 75-gram GTT (127/247/180 g/dl). Her other investigations and ultrasound (7 weeks) were normal. She was started on oral hypoglycemic agent and lifestyle modification, and added with insulin at 9 weeks. Her sugars were controlled on intermediate acting insulin (Mixtard), 10 units in the morning and the evening, along with metformin 1 gram twice a day. Her early anomaly scan at 12 weeks of gestation didn't show any apparent anomaly except echogenic string between two legs. Her dual marker test suggested a low risk for aneuploidy (NT of 1.8mm). She was explained about invasive testing/noninvasive prenatal testing (NIPT) because of advanced maternal age, she refused the testing. Her PAPP-A and B-HCG levels were 1.08 MoM and 0.68 MoM (normal). After a month (16 weeks), she reported in view of lower limb evaluation and diagnosed to have intrauterine fetal demise. She underwent medical termination of pregnancy and macerated hydropic fetus was aborted. The fetal examination suggested 12.5 cm length, head circumference of 8.5cm and foot length of 1.3 suggested 14-15 weeks of gestation. The fetus had a constriction band in the left hand, leading to complex syndactyly. There was an amniotic band of about 2.5 cm between lower limbs, entangling right foot and left ankle, involving the umbilical cord about 4 cm from fetal umbilicus. The amputation of two digits of right-foot was noted. The constriction band around the umbilical cord had resulted in the proximal dilation of vessels and edema. Marked edema was present in left-foot distal to ankle constriction (Figure 1). The rest of external examination (skull, palate, chest and abdominal wall, external genitalia) and Internal examination were unremarkable. Fetal radiograph suggested similar findings. Parental karyotype was normal. Placenta found to be denuded of amniotic membrane on fetal aspect measuring 3cm in length.

Discussion
ABDS results from the rupture of the amniotic membrane. It is a rare condition with an incidence of 1:1,200 to 1:15,000 livebirths.[2,3] The incidence is higher in the specimens of missed abortion and intrauterine death (178-191/10,000 cases).[4,5] The involvement of

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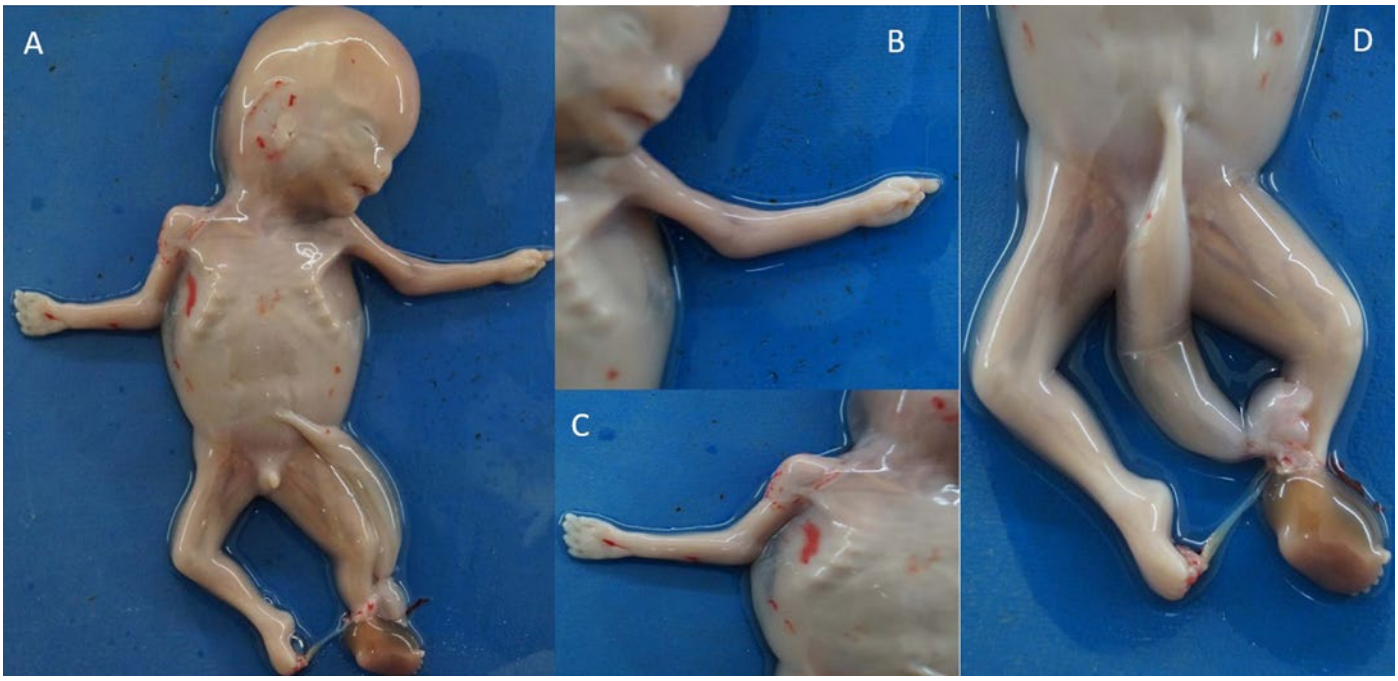

Figure 1: The fetus with multiple constriction bands. A) Amniotic band between lower extremities entangling right foot and left ankle and umbilical cord. B) Amputated digits of left hand C) Normal right upper limb D) An Umbilical cord constriction and left foot edema

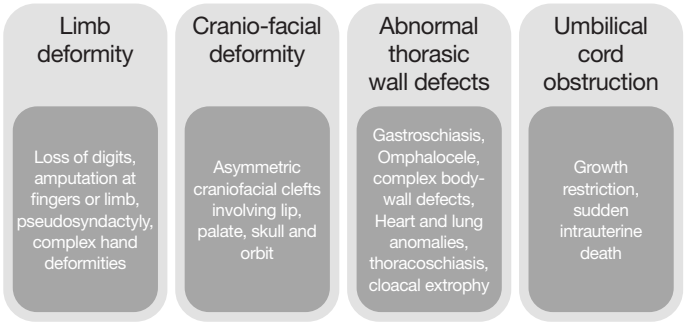

Figure 2: Spectrum of Amniotic band destruction sequence

the umbilical cord occurs in 10% of ABS. There are two types of ABS – lethal and nonlethal. The non-lethal type is life compatible, and malformations have mild to severe spectrum. Severe cases are associated with large cutaneous and visceral abnormalities. The lethal cases result from large defects involving vital organs and strangulation of umbilical cord.[6]

Theory of pathogenesis of Amniotic bands

There are five hypothetical models for the genesis of ABSD, namely intrinsic, extrinsic, disorganization, vascular disruption, and primary ectodermal failure model[2]body wall, and limb anomalies that may be associated with fetalplacental fibrous bands. Its prevalence has been reported to range from 0.19 to 8.1 per 10 000 births. Different theories have attempted to explain the etiology of amniotic band sequence; however, none has individually been able to support each and every defect observed, so it has been considered to be a multifactorial condition. The (pre- and post-natal).[6] The intrinsic disruption of embryonic disc early in the gestation leads to mesodermal strings and congenital abnormalities; here, the amniotic band is a result rather than a cause. This intrinsic theory is not accepted by many. The most accepted theory is an extrinsic theory wherein the amniotic membrane's inflammatory damage and rupture lead to the entanglement of fetal part and umbilical cord by the amniotic band, resulting in a spectrum of malformation. Either intrinsic or extrinsic theory can't explain the defects like cleft lip, polydactyly, imperforated anus and septo-optic dysplasia. The disorganization gene theory can explain such an anomaly. The theory of ectodermal dysplasia explains body wall complex defects involving the trunk and chest wall. Vascular accidents can result in embryonic damage and abnormal morphogenesis of affected structures. In fact, not a single theory can explain all the types of abnormalities.

Predisposing factors

There are multiple predisposing factors, for example smoking, young primi, first and second degree relative having had fetal ABSD, firstborn fetuses, low socio-economic class, previous abortion, acute illness, medications (misoprostol, aspirin. aceta-aminophen), alcohol, cocaine, diabetes etc.[7] Iatrogenic ABSD occurs following prenatal procedures like chorionic villi sampling, amniocentesis, amnio-reduction, cordocentesis and fetoscopic procedures.[8]

Involvement of body systems

Figure 2 depicts the frequently affected body systems. The umbilical cord is the second most commonly affected structure after limbs/appendages. An umbilical cord freely moves in amniotic fluid and contracts the torn membrane during movements. The attachment of fetal membranes to body parts leads to the growth abnormality of the involved structure. It can result in asymmetry, constriction band and amputation of limbs/digits and constriction/strangulation of the umbilical cord as depicted in Figure 1. The defect can be isolated or in combination. The limb anomalies can be further divided into five different stages.[9] This classification is essential for in utero conservative or operative management. Amniotic band sequence doesn't follow the rules of development and hence, there can be bizarre anomalies. In our case, the cause of amnion tearing may be accidental but overt diabetes and previous first trimester medical termination of pregnancy can be a predisposing factor. An umbilical cord, lifeline of a fetus, if encircled by an amniotic band, leads to the obstruction of umbilical vessels and fetal demise in most of the cases.

Prenatal diagnosis

The 2D Ultrasound is widely used for detecting anomalies and amniotic band. The amniotic band is diagnosed as a thin echogenic string in amniotic fluid, arising from uterine wall and reaching to apparently normal fetal part/to abnormal looking fetal part on

ultrasound. The types of ABS described on scan are amniotic net type, dividing amnion, amniotic connection and baby in the envelope.[10] Our patient had amniotic net type, where amniotic band are free floating or attached to fetal parts leading to atypical limb anomalies (commonly) with or without other body part malformations. The band can be identified at finger, toes, or at any joint as constriction band. Secondary edema distal to band is often noticed. In an extreme case, auto-amputation of fingers and limb can be seen. Doppler interrogation of vessel helps in identification of partial or complete obstruction if present. Experience and expertise are necessary for the early and correct identification of anomalies. For the 1st trimester diagnosis, a transvaginal scan is of great help as it delineates the amniotic band with better resolution. 3D/4D ultrasound helps in realization of spatial relationship between the amniotic bands and fetus. it is supplementary to 2D Ultrasound. Patient counselling and management becomes precise with adjuvant modalities like 3D and MRI. The MRI defines the depth of a constriction band and vascular status and usually it is advised before surgical management.[11]

Prognosis

Earlier the time of insult, the more severe would be the sequence of malformation. A milder variety of ABDS has better a prognosis. Severe disease state may need multiple corrective procedures.

Treatment

Most of the literature regarding the release of the band in umbilical cord and in limbs have been described after anomaly scan. We had fetal demise very early in gestation, this gestation is amenable to fetoscopic surgery as positive impact is quationable[12] surgical technique, and postoperative follow-up. In our population and the literature, the majority of the children acquired a functional limb (75%. For non-lethal cases, intra-uterine and/or extra-uterine procedures can be planned and the severity of pathology decides for the timing of intervention. In the intra-uterine life, surgical release of amniotic band by fetoscopic approach is feasible for limb constriction and umbilical cord bands.[13,14] Lysis of the amniotic band is advised by either laser, photocoagulation, cautery, or mechanical modality to prevent strangulation of umbilical cord and limb gangrene/amputation. Any non-lethal anomaly correction in utero requires agreement from fetal medicine specialists, patents and other concern teams like orthopaedic/paediatric surgeons.

Genetic counselling

It is considered as a sporadic event and risk of recurrence is similar to general population. However, few familial incidences increase the risk of recurrence.

Conclusion

An amniotic band syndrome is a definite entity resulting in various degrees of fetal malformations. Transvaginal ultrasound helps in diagnosing as it is more sensitive than an abdominal scan in first trimester. It can result in fetal death hence; this condition should be kept in mind while evaluating a case of sudden intrauterine fetal death. Timely intervention is the key for salvage of pregnancy.

Key message

Amniotic band is rare entity and hard to diagnose in the first trimester. Vaginal ultrasound is vital for identification in 1st trimester.

When a limb defect or body wall complex defect is found, it should raise a suspicion of ABSD.

Restriction of fetal movements and fixed fetal movement is another clue for an underlying amniotic band.

Overt diabetes is a risk factor as it causes vascular damage leading to abnormal embryo development/rupture of amniotic membrane and its consequences.

An umbilical cord strangulation due to entanglement of the cord by an amniotic band can result in sudden intrauterine death.[15]

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Marketing novel devices in medicine with reference to gynaecological innovations: Ethical dimensions

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Abstract
New scientific and technological discoveries in all spheres of Medicine continuously challenge the boundaries of healthcare. To this end, the discipline is considered progressive and accomplished. The birth of this heavily professionalized discipline has leveraged the potential for the healthcare industry to innovate, regulate and disseminate proprietary products with relative ease. The rise and fall of four novel gynaecological devices represent excellent examples of ethical dilemmas in clinical medicine. This paper aims to deconstruct the power versus knowledge conflict, and suggest that reappraisal and recourse to Aristotelian virtue ethics will assist in shifting the decisional power balance primarily towards the physician.

1. Introduction: Medicine, a dynamic discipline?

1.1. Evolution of medicine- a necessary endeavour

The twentieth century has witnessed advances in medicine introducing extraordinary challenges to physicians, patients and the healthcare industry (HCI). The rationale for the introduction of 'new and improved' drugs, medical devices or technology is to optimize human life qualitatively and quantitatively by improving all health-related domains.[1,2,3] Conferring benefit without harm is fundamental for the physician and improved health with reduced suffering is an important expectation of the patient. Thus, medicine is a necessary endeavour that continuously expands, challenging the boundaries of science and ethics. Simplistic devices (tongue depressors, stethoscopes) were readily incorporated in clinical medicine. The introduction of penicillin heralded a revolution in the treatment of common and serious infections. Yet medical devices such as implants, surgical instruments, and medical equipment have ignited controversy amongst the HCI, regulatory authorities, physicians and patients due to concerns of efficacy and safety. Litigation, regulatory alerts/notifications, manufacturer recalls and ultimately the banning of medical devices signify the extent of these controversies. Examples of such medical devices include metal-on-metal hip implants, pacemakers, heart pump controllers, anaesthetic delivery systems and gynaecological devices. (www.fda.gov). Innovations like the Dalkon Shield intrauterine device (IUD), laparoscopic power morcellators (PMs), transvaginal mesh (TVM) implants for pelvic organ prolapse (POP), and the Essure™ PBC (permanent birth control) system have entered the market with great initial enthusiasm, only to exit after safety concerns, litigation and eventual banning. Is this disruptive innovation? Philosophically this conundrum demonstrates the power of the HCI over both physicians and society, or an imbalance of the 'power and knowledge' relationship between the HCI, physicians and patients? In the context of deconstructing the introduction of novel devices in medicine, the words of French philosopher, Michel Foucault, ring true:

'*People know what they do; frequently know why they do what they do; but what they don't know is what they do does.*' [4]

This paper relates to gynaecological medical devices that have raised global safety concerns.

1.2. The HCI: Power to discover and deliver:

The HCI is the largest and fastest growing industry globally. The development of modern medicine in the nineteenth century set the scene for intense healthcare innovation i.e. development and application of beneficial novel devices. The success of the HCI lies in the conceptual framework of product development, followed by implementation: marketing and delivery to various stakeholders.[5] This includes physicians, the knowledgeable gatekeepers to health who are ideally positioned to disseminate innovation to society. The powerful HCI is ideally positioned to discover, develop and deliver novel products. The purpose of their marketing strategies is to align physician behaviour to desired objectives. Common strategies include:

- involvement and commercial support of medical education programs such as continuing medical education (CME)[6]
- pharmaceutical and academic 'detailing' to physicians[7]

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- promotion of off-label use of drugs and devices
- outsourcing clinical research to private entities such as contract research organizations (CROs)
- enticements and gift offering to physicians
- direct-to-consumer marketing

These strategies are relevant because they may influence prescribing behaviour (number of prescriptions and motivations for addition to hospital formularies) and impact on patients' health. Thus, remotely 'controlled' by the HCI, physicians are the effective ultimate purveyors of power to implement utilization objectives. How are these modes of persuasion achieved?

1.2.1. Visitation by carefully selected sale representatives ('reps') to detail products through three mechanisms: pharmaceutical detailing (aimed to educate the physician); academic detailing (physicians educate other physicians) and e-detailing (building networking platforms).

1.2.2. Involvement in CMEs and industry-sponsored research to introduce and promote novel medical devices. Academic discussions coupled with product information subtly shifts marketing to a new level. Arrays of print materials and logo embossed stationary are made available to reinforce the 'reminder effect'.

1.2.3. Shaping medical opinions via identification of key opinion leaders (KOLs) is a vital marketing strategy. KOLs are "physicians who influence their peers' medical practice, including but not limited to prescribing behaviour" (www.pharma-mkting.com/glossary/keyopinionleader). They are skilfully selected (high academic credentials; usually academically employed; experienced researchers; members of respective professional societies/organizations).[8] Ghostwriting and guest authorship are other effective strategies to shape and control research outcomes and is the core business of some companies.[9]

1.3. Does it change practice?

The majority of studies are affirmative. Both small and elaborate enticements such as free lunch, dinners, pens and free luxurious getaways have the power to influence prescription in favour of promoted products.[10,11] The acceptance of samples may be equally effective. More scripts are written in favour of the sample supplied compared to those not advertised or the preferred drug choice.[12,13,14] This practice illustrates the power of hidden bias that is introduced by accepting samples, conceptually another form of gifting. In South Africa, only gifts with low intrinsic value are permitted for distribution (www.marketingcode.co.za) while the United Kingdom General Medical Council (GMC) suggest that doctors may accept unsolicited gifts from patients after careful consideration of several potential implications such as impact on professional decision making apart from others (www.gmc-uk.org). "Gifts are a symbolic representation of power and relationships. Their moral implications lie in the innate power of the act, inevitably creating a sense of debt and pressure to appropriately reciprocate".[15,16]

Gifts represent a more direct and measureable outcome for altering prescription behaviour, meetings with 'reps', CMEs, R&D, KOLs and ghostwriting/guest authorships are more subtle ways laden with power to influence. Thus, there is a need to regulate this relationship to ensure patient safety is considered and prioritized across all platforms.

2. Novel devices in Gynaecology:

The term 'novel' is based on the Latin novellus "new, young, fresh," thus necessitating a sense of the thoroughness of testing 'novel devices' prior to human use. The last few decades witnessed the rise and fall of several gynaecological devices, including two contraceptive devices (Dalkon Shield IUD and the Essure™ (PBC) system); laparoscopic PMs and TVM for POP. These devices raised significant scientific, ethical and regulatory issues pertaining to device safety. Women suffered harm, disability and death which resulted in professional, social and regulatory discreditation of these devices. An illustrative brief synopsis of these devices follows:

The Dalkon Shield IUD: Conceptualized and invented by Gynaecologist Dr H.J. Davis in 1968, this was an attractive option against the background of alarming side effects related to oral contraceptives. Though claiming high contraceptive efficacy, the actual pregnancy rate was double that of on-market devices (Lippes loop, intrauterine Copper devices)[17]. The Dalkon Shield was a plastic device attached to a multifilament nylon string. Aggressive marketing resulted in more than four and half million IUDs distributed in eighty countries by 1975. By 1974 increasing reports of infectious morbidity and mortality raised questions about the causal relationship between this IUD and pelvic sepsis. Moreover, efficacy was also questioned and studies showed higher pregnancy rates and risk for pelvic sepsis compared to other IUDs on the market.[17] Litigation began, domestic US sales were halted and unsold product retrieved, while distribution in less-developed countries continued.[18] The company filed for bankruptcy protection in 1985. This contraceptive saga is infamous as the largest tort case in history. It also prompted the ushering of the 1976 Medical Device Amendment Act to regulate medical devices as a regulatory oversight for ensuring patient safety.[19]

The Essure™ PBC was approved by the FDA in 2002 as a permanent form of birth control conditional to a five year approval study report. This metal coil was inserted under hysteroscopic guidance into the fallopian tubes to stimulate tissue growth (fibrosis) thereby occluding tubal patency. Demonstration of tubal occlusion with a hysterosalpingogram three months later was mandatory, as was continued use of a contraceptive of choice during this time. It was marketed as a 'minimally invasive' (office) procedure, and appealing, obviating the need for general anaesthesia.[20] The FDA deemed the device reliable based on two non-randomized prospective single-arm clinical trials that lacked a comparator group. Efficacy data was limited to those women with confirmed occlusion of the fallopian tubes i.e. a skewed cohort.[21] Since 2002, thousands of adverse events have been reported by the FDA relating to safety concerns of the device, including death (www.fda.gov/MedicalDevices/). It remains unclear why the first post-approval study was published only thirteen years after the device approval process. A global recall of this device has begun and the company voluntarily decided to discontinue sales after 31st December 2018 for business reasons.

Laparoscopic PMs: Approximately 600 000 hysterectomies are performed annually in the USA and the laparoscopic approach is becoming more popular.[22] Laparoscopic approach is considered preferable for benign disease and is associated with fewer surgical complications, less blood loss and shortened hospital stay compared to abdominal procedures.[23] A laparoscopic PM is used during a laparoscopic procedure when the uterus is too large to remove via the vagina. A rotating circular blade facilitates removal of large uteri (e.g. with large uterine fibroids). In 2014 the FDA discouraged the use of this device as a result of the potential to disseminate malignant and benign tissue (occult uterine sarcomas and parasitic fibroids). The reported incidence of uterine sarcomas is 0.2%. This cancer is more aggressive than endometrial cancer and is associated with a poor prognosis.[24] This decision was prompted by significant publicity and high profile case of a doctor who developed stage four leiomyosarcoma following LPM assisted laparoscopic removal of a fibroid uterus 2013. Many manufacturers have suspended sales of PMs, and physicians halted their use because of hospital mandates and fear of litigation.[25] Dr X claimed lack of informed consent as regards this risk.

TVM for POP: The first surgical mesh for POP received FDA clearance in 2002, despite its off-label use since 1970's. At the time surgical mesh was classified as a 'class II' device and did not require premarket FDA approval. Its entry into the gynaecology was aimed

at addressing the high recurrence rate associated with POP surgery – approximately one-third.[26] Mesh kits were rigorously marketed via the 510k rule. This implied that the TVM kits demonstrated substantial equivalence to already marketed predicate devices, and thus no clinical trials were required to determine safety and efficacy. In 2008 the FDA released its first public health notification after receiving thousands of complaints related to the use of TVM for POP, followed by a safety communication 2011. Major complaints included life-altering issues such as nerve damage, chronic sinus tract formation, organ perforation, need for reoperation and permanent disability. Globally more than one hundred thousand TVM lawsuits have been filed in federal courts against manufacturers, ending in multi-billion dollar settlements. The litigious atmosphere resulted in banning TVM from the Scottish, Australian and United Kingdom markets since 2017.

In summary, the design flaws, mistakes and questionable actions related to the above devices impact on manufacturers, regulatory authorities, physicians and patients. The four gynaecological devices raised tremendous ethical and scientific controversies globally and included the following points:

- Dalkon Shield: The multifilamentous nature of the Dalkon Shield string was more prone to harbouring vaginal microorganisms than monofilament strings, with resultant morbidity and mortality. Marketing was based on a single, falsely reported efficacy study; no safety studies were performed.
- Essure™ PBC: Safety and efficacy data were based on the limited scientific evidence of a skewed cohort. There was no investigation into the delay in in providing post-approval surveillance data mandated by the original approval.
- LPMs: In view of the potentially lethal consequence of upstaging cancer, a mandatory vigilance on post-use surveillance reporting should have been instituted. This lethal complication must form part of the consent process as illustrated by the case of Dr X.
- TVM for POP: Closer analysis indicates that the 510k process was essentially meant to deal with the influx of medical device approvals and not designed to determine scientific validity. Re-classification of TVM to class III medical devices (i.e. need for safety and efficacy studies) was instated only in the aftermath.

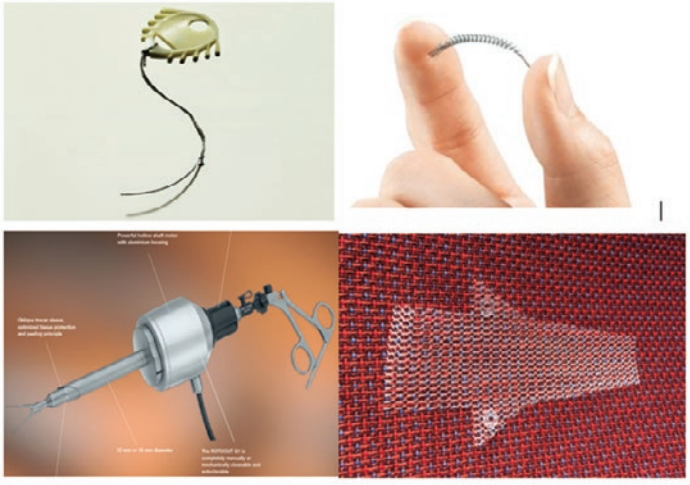

Figure 1. The Dalkon Shield intrauterine device (from http://www.professorwalter.com/2011/08/the-case-that-hung-by-a-thread.html); The EssureTM permanent birth control device (from https://www.nytimes.com/2018/07/20/health/bayer-essure-birth-control.html); A laparoscopic power morcellator used during laparoscopic removal of fibroids (www.baumhedlundlaw.com/defective-medical-device-injuries); Polypropylene mesh used to correct pelvic organ prolapse.

3. Ethical dilemma:

3.1. Nature of the ethical dilemma:

Ethical principles and moral theories have substantial value in guiding moral decision-making. An ethical dilemma requires the additional weighing up of two moral imperatives after considering the evidence.[27] Physicians have fiduciary responsibilities to patients representing a bond of trust: the former implying a standard of care that requires the physician to act in the best interests of the patient, the latter expecting that level of care.

The ethical dilemma in context derives from physicians' fundamental motivation to act in patients' best interests i.e. to provide the benefits of novel treatments while preventing harm, a classical beneficence-non-maleficence dilemma. The authenticity of the informed consent process comes into play in these situations, particularly with respect to serious but 'rare' adverse events.

Even without a formal contract, the fiduciary relationship between the parties implies that physicians wield substantial power over decisions regarding the patient. This knowledge-power-interplay also exists between the HCI, its marketing extensions, and the physician.

Scientific affirmation of medicine and development of innovative devices has resulted in a heavily 'professionalized discipline'. The use of innovative devices by clinicians has challenged the ethical principles of clinical practice. Early adopters of novel devices acquire a false sense of reassurance after regulatory approval and assume that design flaws, adverse events and long-term efficacy and safety were considered prior to approval. Innovation is aimed to benefit society; thus there is a need for all stakeholders to re-examine the introduction of novel devices to society.

5. Conclusion: Time to restore dignity:

The current reality of medicine has been reshaped and redefined by the exponential development of modern medical technological advancements. So much so, that these advances sometimes supersede our ability to fully understand the potential power of a product and therefore formulate the right questions. This represents a sharp departure from traditional medical practice and has introduced new ethical dilemmas involving marketing, profit-sharing, litigation and patient safety.

As it stands, the ultimate use of novel medical devices in the absence of robust scientific data means that current regulatory systems, guidelines and codes of practice represent insufficient control measures to guide physicians when facing new devices. The authors thus propose that the power balance be tipped in favour of the gatekeepers of medicine (i.e. physicians) to relook and reassess our notion of adopting innovation. This may be achieved, firstly by developing a stepwise pathway for medical device approval and use, with incorporation of an ethical component as outlined in figure 2.

Step one commences with the promotion of research integrity with an emphasis on abiding by the classic four principles of biomedical ethics (i.e. respect for autonomy, beneficence, non-maleficence and distributive justice).[27] Application of national regulations and international best practices such as the four principles (honesty, accountability, professionalism and stewardship) and fourteen responsibilities of the Singapore Statement are key to maintaining ethical norms.[28] This in combination with the application of virtue ethics provides a fundamental ethical platform to promote global research integrity.

In the foregoing, several questions have been raised regarding elements of informed consent. Insistence on robust safety data prior to use in patients may have eliminated conflict between beneficence and non-maleficence and allowed physicians to honour prima facie rules and obligations i.e. protecting and defending the rights of others, preventing harm from occurring to others, and removing conditions that will cause harm to others. It is impossible for physicians to meet the ethical demands of autonomy, beneficence, non-maleficence and distributive justice in the absence of robust information. In these circumstances, the four principles which represent the ethical compass of clinical practice may be insufficient to assist and guide physicians when faced with novel products. Hence, we propose a recourse to Aristotelian virtue ethics. The Greek philosopher

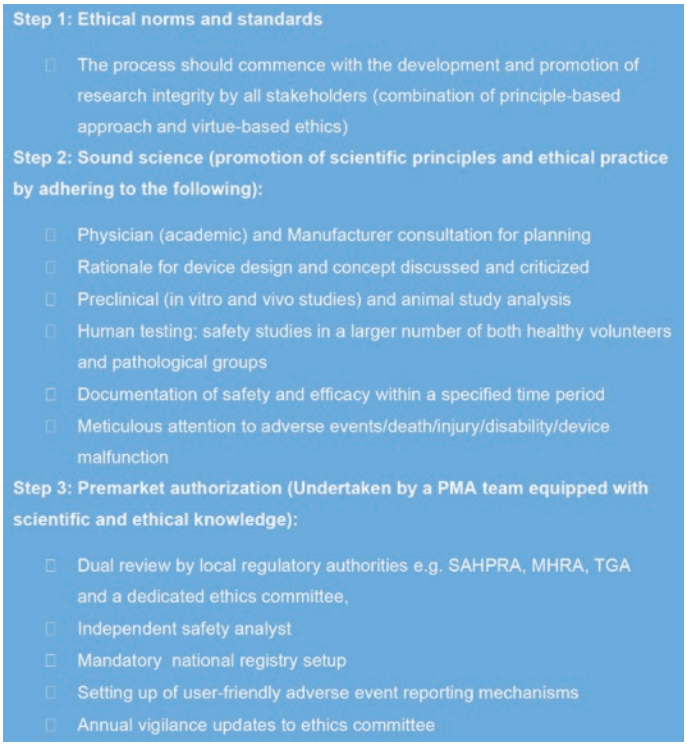

Figure 2. Proposed flow diagram for the process of new medical device evaluation and dissemination. PMA, premarket approval ; SAHPRA, South African Health Products Regulatory Authority; MHRA, The Medicines and Healthcare products Regulatory Agency; TGA, Therapeutic Goods Administration.

(384 BC- 322BC) introduced the idea that moral virtues represent the basis of an ethical life, and are learnt or acquired via practice and habit. Aristotle proposed four cardinal virtues i.e. prudence, temperance, courage and justice while Beauchamp and Childress suggest consideration of five focal virtues for healthcare professionals i.e. compassion, discernment, trustworthiness, integrity and conscientiousness, but in reality the list of applicable moral virtues is endless.[27,29] We believe that virtue ethics may assist the physician in deciding about novel treatments. Both moral (courage, truthfulness, temperance) and intellectual (intelligence, science and theoretical wisdom) virtues are value-laden and underpinned by positive attributes and that in itself is a powerful tool for physicians who conscientiously contemplate the use of novel devices.[28] In addition, country specific regulatory authorities must be coupled with academic physicians who are both scientifically and ethically focussed when considering novel device use. It is within this framework that physicians can once again become the legitimate ultimate purveyors of power.

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