Review of the contemporary use of transvaginal cervical cerclage for the prevention of preterm birth at Tygerberg Hospital

by Doris Kayambo

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Supervisor: Dr. J.L van der Merwe

Co-supervisor: Prof D.R Hall

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Declaration

By submitting this thesis electronically, I declare that the entirety of the work contained therein is my own original work, that I am the authorship owner thereof (unless to the extent explicitly otherwise stated) and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

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Abstract

Aim: The main aim of this study was to review the contemporary use of transvaginal cervical cerclage.

Methods: This retrospective observational study was done at Tygerberg Academic Hospital (TBH), a secondary and tertiary referral centre in the Western Cape Province. It included all pregnancies in whom a transvaginal cervical cerclage was placed from 1 Jan 2009 to 31 Dec 2014. Cervical cerclage was deemed successful if pregnancy was carried beyond 28 weeks of gestation.

Results: 140 transvaginal cerclages were identified for analysis, which consisted of 80 history indicated (HI), 51 ultrasound indicated (UI) and 9 clinical indicated (CI) cerclages. An overall success rate of 74.3% was noted, with individual success rates of 81.3% and 76.5% in the HI and UI groups respectively. All CI cerclages delivered before 28 weeks. The overall live born rate after 24 weeks gestation was 78.6%; 85.0% in the HI group, 76.5% in the UI group and 22.2% in the CI group. The preterm birth (PTB) rate <34 weeks was 42.6% and 33.3% in the HI and UI groups. Cerclage related complications, specifically perioperative rupture of membranes (1.4%), cervical tears (2.1%) and suture displacement (5.0%) were infrequently seen, while preterm rupture of membranes at any gestation was encountered in 22.1% of all cases.

Conclusion: Cervical cerclage remains one of the key preventative measures in prevention of PTB especially in high risk populations. Our data highlights the diversity of patients at risk of PTB and the complexities involved in their care. This study sheds light on the need for correct identification of suitable women for cervical cerclage insertion in a developing country setting.

Opsomming

Doel: Die hoofdoel van hierdie studie was om die kontemporêre gebruik van transvaginale servikale steek te hersien.

Metodes: Hierdie retrospektiewe waarnemingstudie is by Tygerberg Akademiese Hospitaal (TBH), 'n sekondêre en tersiêre verwysingsentrum in die Wes-Kaapprovinsie, gedoen. Alle swangerskappe is ingesluit in wie 'n transvaginale servikale steek van 1 Januarie 2009 tot 31 Desember 2014 geplaas was. ’n Servikale steek is as suksesvol beskou as die swangerskap verby 28 weke volhou.

Resultate: 140 transvaginale steke is geïdentifiseer vir analise, wat saamgestel is uit 80 geskiedenis aangeduide (HI), 51 ultraklank aangeduide (UI) en 9 klinies aangeduide (CI) steke. Die algehele sukseskoers van 74.3% was waargeneem, met individuele sukseskoerse van onderskeidelik 81,3% en 76,5% in die HI- en UI-groepe. Al die CI steke is voor 28 weke verlos. Die algehele lewendige geboortekoers, na 24 weke, was 78,6%, 85,0% in die HI-groep, 76,5% in die UI-groep en 22,2% in die CI-groep. Die voortydige kraam (PTB)-koers <34 weke, was 42,6% en 33,3% in die HI- en UI-groepe. Steek-verwante komplikasies, spesifiek peri-operatiewe ruptuur van membrane (1.4%), servikale skeure (2.1%) en steek verplasing (5.0%) was selde gesien terwyl premature ruptuur van membrane by enige swangerskapsduur voorkom in 22.1% van alle gevalle.

Gevolgtrekking: Servikale steke bly een van die belangrikste voorkomende maatreëls in die voorkoming van PTB, veral in hoërisiko-bevolkings. Ons data beklemtoon die omvang van pasiënte wat ’n risiko het vir PTB en die kompleksiteite wat by hul sorg betrokke is. Hierdie studie beklemtoon die behoefte aan korrekte identifisering van geskikte vroue vir servikale steke in 'n ontwikkelende land omgewing.

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Dedications

I dedicate this Dissertation to my late grandfather Mr Horace Chakulenga Phiri, who will always be my inspiration. Rest in peace Achaku.

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List of Abbreviations

BMI -	Body mass index
CI -	Clinical indicated cerclage
DES -	Diethylstilboestrol
ENND-	Early neonatal death
FGR-	Fetal growth restriction
FSB-	Fresh still born
GA-	Gestational age
HI -	History indicated cerclage
HIV -	Human Immunodeficiency Virus
HAART -	Highly Active Antiretroviral Treatment
IAI-	Intra amniotic infection
IUGR-	Intrauterine growth restriction
IQRs -	Interquartile ranges
UI -	Ultrasound indicated cerclage
kg/m^2-	Kilogram per square meter
LLETZ -	Large loop excision of the transformation zone
MTL-	Midtrimester loss
NICU-	Neonatal intensive care unit
NT -	Nuchal translucency
PI-	Principle Investigator
PMTCT -	Prevention of mother to child transmission
PPROM -	Preterm prelabour rupture of membranes
PTB -	Preterm birth
RCT -	Randomised control trial
RR-	Relative risk
SD-	Standard deviation
TAC-	Transabdominal cerclage
TBH -	Tygerberg Hospital
T1 -	First trimester
T2 -	Second trimester
TVUCL-	Transvaginal ultrasound cervical length
vs-	versus
w-	weeks

Chapter 1: Introduction

1.1 Background

Preterm birth (PTB) is estimated to be responsible for 35% of the world's 3.1 million annual neonatal deaths[1]. Complications of PTB are now the second most common cause of death after pneumonia in children under 5 years of age.[1] Furthermore, PTB results in both immediate and long term morbidity in the neonate and child.[2] Consequently leading to huge socio-economic burdens and continued psychosocial and emotional stress on families.[3]

Prevention and treatment strategies of PTB have been rather ineffective and disappointing. However, one specific aspect of the preterm birth spectrum that has a known surgical intervention is cervical incompetence or cervical insufficiency as it is sometimes known.[4] Cervical incompetence is defined as the painless dilation of the cervix during the second trimester of pregnancy leading to spontaneous PTB (or late miscarriage) of a live and otherwise healthy foetus. Cervical incompetence affects 0.1 – 2.0% of the global obstetric population and 8% of women with recurrent 2nd trimester losses.[4] In developing countries it accounts for up to 15 - 20% of pregnancy losses.[5] The mainstay of treatment for cervical incompetence is a timely surgical intervention, which involves the placement of a surgical suture around the cervix to prevent miscarriage or PTB.

The rates of cervical cerclage placement vary from country to country, with some authors reporting that the procedure is more commonly performed in developing than developed countries.[5] Meta-analyses and systemic reviews on cervical cerclage have certainly differed on the effectiveness and benefits of this procedure. Data from African-based studies are limited and documented outcomes, especially of history-indicated cervical cerclage still need further support.[6]

1.2 Problem Statement

Cervical cerclage efficacy and safety has remained controversial. Multiple studies and systemic reviews have been done but with minimal involvement of African countries. Therefore, current and good quality data on cervical cerclage insertions and outcomes are lacking from South Africa and Africa in particular.

The aim of this study was to review the contemporary use of transvaginal cervical cerclage at Tygerberg Academic Hospital (TBH), which serves as a large secondary and tertiary referral centre in Cape Town, Western Cape Province, South Africa. Ultimately to compare patient selection, management and outcomes to international literature, with the hope of improving the provision of evidence-based cervical cerclage in the local population. These results could then be extrapolated to other similar African settings.

Chapter 2: Literature Review

2.1 Context of preterm birth

The cervix plays a critical role in a successful pregnancy. Broadly speaking the cervix helps contain the pregnancy within the uterus until the end of gestation. Thereafter it must undergo significant changes that allow the safe delivery of the baby during labour. The inability to perform the first function can result in a late miscarriage or PTB.[7]

PTB, defined as delivery of a fetus before 37 weeks of pregnancy, occurs in 9.6% pregnancies according to the World Health Organisation's 2005 report. This translated into approximately 13 million preterm births worldwide, with Africa and Asia accounting for over three quarters of these births.[8] The importance of PTB is that it contributes to up to 14.1% of perinatal mortality worldwide.[2] Those premature babies that survive are at risk of developing spastic cerebral palsy, cognitive, behavioural, attention and socialisation defects, chronic lung disease, vision disturbance and hearing loss.[9] Such impediments result in multiple hospital visits and admissions with significant psychosocial and emotional consequences that impact the individual and their families. Such consequences have both short and long-term health service cost implications.

Despite the mortality, morbidity and psychosocial impact of PTB, preterm labour has remained a poorly understood and complicated syndrome. PTB may either be spontaneous or iatrogenic when a woman is electively delivered. Spontaneous PTB can be as a result of maternal or fetal causes or a combination of them both. However, in the majority of spontaneous cases the cause is unknown or idiopathic. Maternal conditions that may lead to PTB include hypertensive disorders, autoimmune conditions like systemic lupus, diabetes mellitus, smoking, as well as maternal infections such as malaria, urinary tract infections, or intrauterine infections. Furthermore, uterine anomalies, cervical incompetence, polyhydraminos, immunological factors may also play a role while fetal anomalies itself can play a role in preterm labour and birth.

As noted in the wide range of the above causative elements many factors are known to influence the dynamic structure and function of the cervix. These factors may differ between patients as well as different pregnancies of the same patient. This complex and poorly understood pathophysiology has made the identification and formulation of effective prevention strategies difficult. However, there is one component with a known preventive strategy that has been identified within the complex spectrum of preterm labour, namely cervical incompetence also known as cervical insufficiency.

2.2 Cervical incompetence

The term cervical incompetence was first described as early as 1865 in the Lancet. However, it was only in the 1955 when Shirodkar described the interval repair of anatomical cervical defects associated with the obstetric history of recurrent spontaneous mid-trimester births that the concept was widely accepted.[10]

Cervical incompetence is a clinical diagnosis, and is mostly made retrospectively. Its definition varies but there are two widely accepted definitions. The first one defines cervical incompetence as the inability of the uterus to retain a pregnancy in the absence of signs and symptoms of clinical contractions or labour or both in the second trimester of pregnancy.[11] The second definition involves both clinical and physical components, namely “the painless dilatation of the cervix resulting in rupture of membranes and mid-trimester miscarriage (12 - 24 weeks) and the passage without resistance, of size 9 Hegar dilators (9mm), through the cervix in the non-pregnant state.[12] The latter finding is no longer regarded as reliable. Although an ultrasound finding of a short cervical length in the second trimester of pregnancy can be used as a tool to aid in the diagnosis of cervical incompetence in some cases, this is not an acceptable sole criterion for the definition. Therefore, the diagnosis of cervical incompetence comprises a historical component, namely the history of a painless cervical dilatation with preterm mid-trimester loss or preterm delivery, and/or the combination of physical findings of cervical shortening and dilatation during digital cervical examinations, and/or findings of a short cervix during mid-

trimester sonography in women with the relevant history of spontaneous PTB or a combination of all three.

There are two main theories that identify the pathophysiology of cervical incompetence in preterm labour. The first theory is that cervical incompetence results in the loss or compromise of the mucus plug resulting in the ascending of vaginal infection that can result in PTB.[13] The second proposed model suggests that cervical incompetence is a continuum that is a consequence of premature cervical ripening (in absence of clinical labour) caused by one or more underlying factors including infection, local inflammation, hormonal effects, or genetic predisposition. These factors may be superimposed on a cervix with compromised mechanical integrity, and by means of the inflammatory cascade may also present as part of the preterm labour syndrome.[14] Epidemiological and historical factors have been identified for cervical incompetence. These include prior cervical surgery such as cone biopsy, large loop excision of the transformation zone, trachelectomy, in utero exposure to diethylstilboestrol (DES), prior induced or spontaneous first- and second-trimester miscarriages (including dilatation and instrumentation of the cervix), uterine anomalies, multiple gestations and prior spontaneous PTBs.

The incidence of cervical incompetence is approximately 1 - 2% of the global obstetric population and 8% of women with recurrent second trimester losses.[4] The incidence differs in different countries and even in different hospitals within the same country due to population and ethnic differences, variable diagnostic criteria, and reporting bias. However, although certain authors state that the incidence of cervical incompetence is much higher in women of African origin and in developing African countries[5], the actual figures remain largely unknown due to poor documentation, differences in diagnostic criteria and scarce research in these countries.

2.3 Evidence for cervical cerclage

The mainstay of treatment for cervical incompetence is a surgical procedure, namely cervical cerclage. This entails the placement of a surgical suture around the cervix as close as possible to the level of the internal cervical os. The

procedure is performed at a gestational age of 14 - 24 weeks gestational age (GA) via either a transvaginal or transabdominal route. The ideal timing varies according to the specific type of procedure and in some cases, is even considered prenatally. It is believed that the cervical cerclage helps to prevent the loss of the cervical mucus plug, which prevents the ascension of microorganisms in the cervical canal in addition to providing mechanical support. The suture is usually removed at 37 weeks of gestation in the absence of contraindications. However, in some cases it is left in-situ when a caesarean delivery is performed and the cerclage (typically of the transabdominal type) is retained for the next pregnancy.

The original method described in 1955 by Shirodkar was an interval repair of anatomical cervical defects associated with the obstetric history of recurrent spontaneous mid-trimester birth that was a particularly invasive vaginal procedure.[10] Another widely accepted and less invasive procedure was described by McDonald in 1957.[15] These two procedures have not been compared directly and because the latter procedure is less invasive and vaginal delivery more easily accomplished, it is currently the more favoured method.[16] There are three main indications for the placement of a cervical cerclage namely, history indicated (HI), ultrasound indicated (UI) and rescue or clinical indicated (CI) cerclage.

2.3.1. *History indicated cerclage*

HI cerclage is usually offered to a woman with three consecutive second trimester losses that have a typical history of cervical incompetence, namely spontaneous painless fast miscarriage in absence of labour or other known causes.[17] The final report of the Royal College of Obstetricians and Gynaecologists multicentre randomised trial of cervical cerclage also showed benefit in “women with a history of three or more spontaneous preterm births.”[17] It is important to rule out other causes of PTB or second trimester loss, through a detailed history and physical examination prior to offering a history indicated cervical cerclage.

HI cervical cerclage is ideally placed electively at 13 - 14 weeks of gestation. There are no recent randomised controlled clinical trials that have reported the efficacy of HI cerclage. The three main trials that have reported on the effectiveness of this procedure are now regarded as “older” studies. The largest trial on HI cervical cerclage was the MRC/RCOG Working Party on Cervical Cerclage. This study recruited women at risk of preterm delivery from multiple international centres based on their history but whose obstetricians were unsure of the diagnosis of cervical incompetence. A total of 1292 women were randomised to either receive a cervical cerclage or not. In this trial, cerclage was regarded as successful if the pregnancy reached 33 weeks’ gestation. Results showed fewer deliveries before 33 weeks in the cerclage group (83 of 647) 15%, compared to the control group 32%, (RR 0.46 95% CI 0.22-0.98). However, further statistical analysis revealed that the results were mainly influenced by a subset of 107 women who had a history of three or more second trimester losses. Removal of this subset nullified the difference between the two groups. This data thus supports the use of cervical cerclage in women with a history of three consecutive second trimester losses.

The other 2 trials showed no significant benefit with the use of cervical cerclage based on history alone.[18,19] In both studies women with moderate and high risk (30%) of having a late miscarriage or preterm delivery were randomly allocated to cerclage insertion. The results showed no difference gestational age of delivery or survival. Although the cerclage group had multiple hospital admissions and prolonged hospital stay with an increase in tocolytic drug use, puerperal sepsis, caesarean section and ultimately preterm deliveries in the cerclage group. Though this was not statistically significant as numbers were small.

Overall the evidence for HI cerclage is less robust than that currently available for UI cerclage procedures.

2.3.2. *Ultrasound indicated cerclage*

Cervical screening using transvaginal ultrasound for the prediction of preterm labour in women with a positive history has become a safe gold standard. This accolade presupposes that it is performed correctly.[20] Evidence to support the use of transvaginal ultrasound to predict preterm labour risk in these women was provided in the blinded observational study by Owen et al., in 2001.[21] This study found that women with a previous spontaneous PTB <32 weeks, with cervical lengths <25mm in the current singleton pregnancy had a relative risk of spontaneous PTB before 35 weeks of 4.5 (95% CI 2.7-7.6). This threshold of <25 mm had a sensitivity of 69%, specificity of 80% and positive predictive value of PTB of 55%. It is now widely accepted that cervical length assessment in this group of women can be used as a surrogate of cervical incompetence at appropriate gestations. On the other hand, in low risk women without a prior history of PTB where an incidental finding of a short cervix (<25mm) at 16 - 23 week scan was noted only 17% ended up with a PTB <32 weeks.[17] The use of cervical cerclage in this group had no effect on the reduction of PTB.[17] It has been shown that a short cervix <15mm does predict a high risk of PTB but it means screening over 100 women to find 1 case in a low risk population.[22] Therefore, in low risk groups, transvaginal cervical ultrasound assessment is still not regarded as an effective screening tool. In addition, funnelling of the cervix does not predict or add to the prediction of PTB.[23]

A recent meta-analysis on UI cervical cerclage involved five randomised, controlled trials incorporating over 500 women. UI cerclage achieved a decrease in the rate of PTB by 30% and composite perinatal morbidity and mortality by 36% compared with the non-cerclage group. There also a decrease in previable PTB <24 weeks and perinatal mortality.[24] In another meta-analysis of trials using individual patient–level data, with the incidental finding of a short cervix of <25 mm between 16 and 24 weeks of gestation without prior history of PTB, cervical cerclage placement did not decrease the rate of PTB.[25,26] In addition, in women with other risk factors for PTB, such as cone biopsy, DES exposure, dilation and curettage, who were randomised to cerclage vs no cerclage after cervical screening and findings of cervical length of <25 mm,

cerclage placement did not show a decrease in PTB.[27] Therefore, ultrasound indicated cerclage is reserved for cases with a cervical measurement of <25mm, with or without funnelling, before a gestational age of 24 weeks in women who are undergoing cervical length screening due to a prior history of spontaneous PTB between 16 - 24 weeks gestation. This group may also be a target for progesterone therapy which will be briefly discussed later.

2.3.3. *Clinically indicated (emergency, rescue) cerclage*

Clinically or physical examination indicated cerclage is the placement of cervical cerclage in women in the second trimester who present with cervical dilatation in absence of labour, and placental abruption. Although controversial, when inserted in correctly selected cases the overviews show greater benefit than harm. To date there is only one randomised controlled trial for this indication, but it was small with a total of 27 women including seven sets of twins.[28]

There has been a recent systematic review and meta-analysis of CI cerclage that included ten studies (aforementioned one small randomised control trial, two prospective cohorts and seven retrospective groups).[28] This analysis studied women between 14 - 27 weeks' gestation with a minimum cervical dilatation of 0.5cm. It included a total of 757 women. The primary outcome of neonatal survival was higher in the cerclage group vs control group. There was a significant prolongation of pregnancy (mean difference 34 days), and a greater gestational age at delivery (mean difference 32 days), with reduced PTB between 24 - 28 weeks (8% compared to 37%) and PTB less than 34 weeks of gestation (50% compared to 82%). However, there was no difference in PTB under 24 weeks. It must be appreciated that the studies included in this systematic review were limited in size and had variable quality and study design. Overall there is weak positive evidence that CI cerclage is effective in reduction of PTB. Therefore, large well designed randomised trials, providing good quality evidence are still required.

Of concern is that CI cerclage may prolong pregnancy only to advance previable pregnancies to extremely preterm deliveries with their high rates of

complications of prematurity. However, these women usually enter pregnancy with high risks for PTB and clinicians will work hard to simply achieve the threshold of viability. There may be clinician bias in the decision whether to place a cerclage based on the clinician's own interpretation of the possible success of that cerclage. In the analysis by Ehsanipoor et al., several risk factors were identified that influenced the outcome of CI cervical cerclage, namely cervical dilatation, membrane prolapse, obstetric history, evidence of infection.[28]

2.4 Cerclage under special circumstances

2.4.1. *Transabdominal cerclage*

This cerclage is placed in women with poor obstetric history where transvaginal cerclage has failed, the cervix is very short (e.g. after recurrent cone biopsies) or has significant damage such as deep tears. Transabdominal cerclage involves the insertion of the cerclage internally at the upper level of the cervical canal. The procedure may be performed openly or laparoscopically. The timing in open surgery is usually restricted to a gestation window from 12 - 14 weeks (thereby allowing for spontaneous first trimester miscarriage) but laparoscopic procedures are often performed prior to pregnancy. The success rates in reported case series are very high (85 - 90%).[29] However, the morbidity (especially haemorrhage) associated with this procedure needs to be carefully considered.

2.4.2. *Cerclage in multiple gestation*

Twin gestations have a higher risk of PTB compared to singleton pregnancy. However, unlike singleton pregnancy the use of cervical cerclage in an asymptomatic twin pregnancy with a short cervix < 25mm before 24 weeks does not prevent PTB and may increase the risk for harm. This position is supported by the recent Cochrane review[30] and another large meta-analysis[25]. These reviews showed associated worse neonatal outcomes with delivery up to four weeks earlier compared to controls. However, these outcomes were not adjusted for confounders of demographic characteristics, risk factors and

indication for cervical cerclage. This prompted a recent meta-analysis where the outcomes were adjusted for such confounding variables and results were reported using a random effects model.[31] These results showed no benefit or harm from cervical cerclage compared to controls, with the rate of very low birth weight and respiratory distress syndrome being higher in the cerclage group compared to the control group with borderline significance.

In conclusion, there is currently no role in the use of cervical cerclage in asymptomatic twins with short cervix <25 mm on transvaginal ultrasound.

2.4.3. *Cerclage and PPROM*

Insertion of cervical cerclage with preterm prelabour rupture of membranes (PPROM) is not recommended. Additionally, there is insufficient evidence for the removal of cervical cerclage upon immediate diagnosis of PPROM or even within 24 hours after administration of steroids. Although it has been shown that retention of cervical cerclage for more than 24 hours after PPROM has been shown to prolong pregnancy there is also an increased risk of infection for both the mother and neonate.[32] Individualisation of specific case circumstances should be applied, but cerclage removal is generally recommended either immediately after diagnosis or following the administration of corticosteroids (i.e. after about 48 hours).

2.4.4. *Cervical Cerclage in African countries*

The prevalence of cervical incompetence in African populations remains unknown. The PRAM study showed a prevalence of cervical incompetence of 5.3% in black Hispanics and 4.1% in American Whites.[33] Another study reported the incidence of PTB to be higher in women of African origin living in America[34]. However, these results cannot be extrapolated to African countries as demographic, behavioural and environmental factors are certainly different. Although it can be speculated that the rate of cervical incompetence is higher in African countries there are no robust data to support this.

Very few studies have been done exclusively in African countries, with most studies involving African countries as part of international multicentre trials.[17 35] Studies performed exclusively in single African locations have taken the form of retrospective audits on the use of cervical cerclage in single units with small numbers.[5,36] An example of the above is a retrospective observational study of 199 patients performed in Kenya.[5] Most women in this study received a HI cervical cerclage for cervical incompetence and the majority (66%) did not have any ultrasound examination. Of the 34% that had an ultrasound scan, only 7.8% received a transvaginal ultrasound cervical length assessment. This reflects one of the challenges faced by developing African countries.

Two studies on cervical cerclage have been performed in South Africa.[19,17] One which is now more than 30 years old, was a randomised controlled trial for HI cerclage which was performed exclusively in this country[19]. The other was part of a multinational study.[17]

Contextually, the majority of the women included in African studies were of low economic status. These women often suffered more than the required number of pregnancy losses before a diagnosis of cervical incompetence is made, due to poorly functioning health care systems and under reporting by patients. In addition, low socio-economic status is associated with high risk infection profiles. This concurs with other studies in that low social and economic status seem to be stronger determinants of poor pregnancy outcome than actual ethnicity.[37] In addition, few women (8%) who received cervical cerclage underwent gold standard, transvaginal ultrasound cervical assessment.[5] This means that too few high-risk women receive appropriate screening for cervical incompetence. It is concerning that in these studies the majority of women who underwent “history indicated cerclage” did not have a complete work up to rule out other causes of second trimester losses. This could be attributed to poor clinical skills, record keeping and the lack of available, appropriate diagnostic equipment.

Alternative PTB prevention strategies such as progesterone are not available in most public hospitals in African countries due to financial constraints. Overall

the diagnosis and management of cervical incompetence in African countries is negatively influenced by the financial situation and poor health systems.

2.5 Other interventions for the prevention of PTB

Progesterone - There is good evidence for use of progesterone beginning at 16-20 weeks until 36 weeks, in women with previous PTB[38]. Vaginal progesterone suppositories have been shown to reduce PTB and perinatal morbidity and mortality.[39] There is weak evidence for the use of progesterone in women with no prior history of PTB with a short cervix <20mm at < 24 weeks identified during transvaginal ultrasound. Progesterone is not clearly effective in twin gestations, preterm labour or PPROM.[40]

Cervical pessary - Cervical pessaries have been compared to cervical cerclage with favourable effect in small studies[41], but this benefit has seemed elusive in larger one[42].

Bed rest - Currently there is no evidence that bed rest is beneficial for this condition.[43]

2.6 Conclusion

From this literature review it is clear that the strongest evidence is for UI cerclage in women with prior spontaneous PTB. On the other hand, evidence for cervical cerclage placement purely on past obstetric history is less robust with effectiveness seen only in a subset of women with three or more consecutive PTBs or second trimester losses. Finally, there is weak positive evidence that CI cerclage is effective in reduction of PTB. Although the use for vaginal progesterone is emerging to be just as effective as cervical cerclage insertion in women with previous preterm birth[33], its lack of availability in developing countries makes it a limited option.

Chapter 3: Methods

3.3 Research Design

3.3.1. *Type of study*

This was a retrospective observational study

3.3.2. *Study setting*

Tygerberg Academic Hospital (TBH), a secondary and tertiary referral centre in the Western Cape Province responsible for the Metro East region of Cape Town and designated rural areas. Tygerberg Hospital is a tertiary hospital located in Parow, Cape Town. The hospital is the largest hospital in the Western Cape and the second largest hospital in South Africa. It acts as a teaching hospital in conjunction with the University of Stellenbosch's Health Sciences Faculty, serving the Metro East region of Cape Town. It has a catchment population of over 2.6 million.

3.3.3. *Study Subjects*

We included all pregnancies in whom a transvaginal cervical cerclage was placed from 1 Jan 2009 to 31 Dec 2014. Patients were identified from the obstetrics theatre lists. Women who have had a transvaginal cervical cerclage inserted outside Tygerberg hospital but delivered at this institution were excluded.

3.4 Data collection

The principal investigator (PI) extracted data from the files to complete a coded data sheet (Appendix 1) reflecting no patient identifiable information. This data was loaded onto a Microsoft Excel database in strictly anonymous fashion.

3.5 Outcome measures

3.5.1. *Primary outcome measures*

- Gestational age at delivery (delivery before 28 and 34 weeks of gestation)

- Live born rate defined as number of deliveries that result in a live neonate at time of discharge.

3.5.2. *Secondary outcomes*

- Cerclage specific outcomes: indication and incidence of cervical cerclage placement, cerclage interval duration and cerclage specific complications.
- Maternal morbidity outcomes: miscarriage (defined as pregnancy loss before 24 weeks of gestation), preterm labour (defined as regular uterine contractions resulting in cervical changes before 37 weeks of pregnancy), preterm rupture of membranes (defined as rupture of membranes before 37 weeks of pregnancy), mode of delivery.
- Neonatal morbidity outcomes – birth weight (weight below 2000g and below 1500g), duration of neonatal hospital stay, composite neonatal morbidity score (including FSB, ENND, 5min APGAR <7, admission to NICU).

3.6 Ethics

The protocol was submitted for local ethical review and was approved by the Health Research Ethics Committee of Stellenbosch University (S14/09/179) to conduct this anonymised audit.

3.7 Data analysis and statistical methods

Data was collected and analysed in Statistic version 12 (2014). For descriptive statistics, first data was checked for normality of distribution using a Kolmogorov-Smirnov test. Continuous variables were expressed as means and standard deviations if normally distributed and medians and interquartile ranges (IQRs) if the data was non-normally distributed. For ordinal variables medians and interquartile ranges (IQRs) if data are non-normally distributed. For nominal variables, data was presented using frequency distributions with graphical presentation will be by means of bar charts and 95% confidence for binary proportions were presented.

A multivariate linear regression analysis was used to define the cerclage interval relationship between the groups and defined co-variables (age, BMI, gravidity, parity, previous obstetric history, cervical assessment, case assessment, gestational age at insertion, primary surgeon and suture material used). A 5% significance level will be applied throughout for all analyses.

Chapter 4: Results

4.1 Baseline population characteristics

A total of 154 transvaginal cerclages were identified from the Tygerberg Hospital surgical records from the period of January 2009 to December 2014. Fourteen cases were excluded due to missing clinical records. Another 22 records were incomplete but they were still included in the final analysis of the remaining 140 cases. A total of 80 history indicated (HI), 51 ultrasound indicated (UI) and 9 clinical examination indicated (CI) transvaginal cerclages were analysed.

The baseline population characteristics are depicted in **Table 1**. Social drug use was common in this population with 28.6% (40/140) admitting to smoking, 20% (28/140) to alcohol use, and 1.4% (2/140) to methamphetamine use. The women in the CI group were older, more obese and had a higher incidence of smoking making it a particularly high-risk group.

Table 1: Patient demographic data

	History Indicated N=80	Ultrasound Indicated N=51	Clinical Indicated N=9	All N=140
Age (years)*	30±6	31±5	32±5	30±5
Gravidity #	5 (1-7)	5 (1-8)	5 (1-9)	5 (1-9)
Parity #	1 (0-5)	2 (0-6)	0 (0-3)	1 (1-6)
BMI ≥ 30 kg/m^2 ‡	28 (35.0%)	6 (11.8%)	6 (66.7%)	40 (28.6%)
Syphilis – positive Rapid Plasma Reagin test ‡	5 (6.3%)	3 (5.9%)	-	8 (5.7%)
HIV Positive on PMTCT ‡	5 (6.3%)	2 (3.9%)	1 (11.1%)	8 (5.7%)
HIV Positive on HAART ‡	4 (5.0%)	3 (5.9%)	-	7 (5.0%)
Smoking ‡	21 (26.3%)	15 (29.4%)	4 (44. 4%)	40 (28.6%)

* Mean ± SD; # Median (Range); ‡ n (%)

BMI - body mass index; HIV - Human Immunodeficiency Virus; HAART - Highly Active Antiretroviral Treatment; PMTCT - Prevention Mother to Child Transmission

4.2 Medical and surgical history

The study population medical history profile mimics that of a high-risk group with 1 in 4 women having a pre-existing medical disorder, specifically hypertension (12.1%) and diabetes mellitus (4.3%).

A history of Large Loop Excision of the Transformation Zone (LLETZ) was noted in 5.8% of the patients. One case belonging to the HI group, a deep cervical tear was noted at time of cerclage placement. She had a history of three second trimester losses intermixed with 2 preterm deliveries and in this index pregnancy she unfortunately miscarried at 21w. She was offered a TAC in her next pregnancy.

The past medical and surgical history is depicted in **Table 2**.

Table 2: Medical and surgical history

	History Indicated N=80	Ultrasound Indicated N=51	Clinical Indicated N=9	All N=140
Medical History				
Hypertension	8 (10.0%)	8 (15.7%)	1 (11.1%)	17 (12.1%)
Diabetes	5 (6.3%)	1 (2.0%)	-	6 (4.3%)
Asthma	3 (3.8%)	2 (3.9%)	1 (11.1%)	6 (4.3%)
Other chronic medical conditions*	1 (1.3%)	5 (9.8%)	1 (11.1%)	7 (5.0%)
Surgical history				
Previous caesarean deliveries	9 (11.3%)	6 (11.8%)	1 (11%)	16 (11.4%)
Gynaecological surgery	-	3 (5.9%)	-	3 (2.1%)
Large Loop Excision of the Transformation Zone	4 (5.0%)	3 (5.9%)	-	8 (5.7%)

Data presented as n (%)

*other medical conditions included: chronic cystitis, pneumonia, pyelonephritis

4.3 Obstetric history

Reviewing the past obstetric history of this cohort, it was noted that 2.9% (4/140) had a previous hypertensive disorder in pregnancy with 1.4% (2/140)

having a pregnancy complicated by a placenta abruption. In 3.6% (5/140) of the cases a uterine curettage post miscarriage was done. The past obstetric history concerning miscarriages and PTB are captured in **Table 3**. Of those with T2 miscarriages, 17.8% (21/118) were deemed to have clear history of a fast and painless miscarriage. Out of the 39 patients who had one previously placed cervical cerclage, 71.8% were successful. In the 18 cases with more than one prior cervical cerclages placement, 66.7% of these were successful.

Table 3: Miscarriage, preterm birth and cervical cerclage history

	History Indicated N=80	Ultrasound Indicated N=51	Clinical Indicated N=9	All N=140
TI miscarriage (<13w0d)				
· **Once**	20 (25.0%)	16 (31,4%)	-	36 (25.7%)
· **Twice**	6 (7.5%)	2 (3.9%)	2 (22.2%)	10 (7.1%)
· **≥ 3**	2 (2.5%)	3 (5.9%)	2 (22.2%)	7 (5.0%)
T2 miscarriage (13w0d -23w6d)				
· **Once**	8 (10.0%)	15 (29.4%)	-	23 (16.4%)
· **Twice**	31 (38.8%)	17 (33.3%	2 (22.2%)	50 (35.7%)
· **≥ 3**	33 (41.3%)	9 (17.6%)	3 (33.3%)	45 (32.1%)
· **Spontaneous, painless ≥2**	30 (37.5%)	12 (23.5%)	1 (11.1%)	43 (30.7%)
· **Spontaneous, painless ≥3**	16 (20.0%)	4 (7.8%)	1 (11.1%)	21 (15.0%)
Preterm birth 24w0d-27w6d	26 (32.5%)	19 (37.3%)	3 (33.3%)	48 (34.3%)
Preterm birth 28w0d-33w6d	17 (21.3%)	16 (31.4%)	2 (22.2%)	35 (25.0%)
Preterm birth 34w0d-36w6d	7 (8.8%)	2 (3.9%)	-	9 (6.4%)
Previous cerclage				
· **1**	27 (33.8%)	10 (19.6%)	2 (22, 2%)	39 (27.9%)
· **≥2**	10 (12.5%)	7 (13.7%)	1 (11.1%)	18 (12.9%)
Success				
· **1**	19 /27 (70%)	8 /10 (80%)	1/2 (50.0%)	28/39 (71.8%)
· **≥2**	8/10(80%)	4/7 (57%)	-	12/18 (66.7%)

Data presented as n (%)

4.4 Indication and placement of cervical cerclages

During selection of the cases just over half of the women 57.1% (80/140) had a Nuchal Translucency (NT) screening scan. 2 screened high risk due to an NT measurement above the P95, one belonging to the HI and one to the UI group.

Both opted for no further invasive testing and had normal structural review ultrasounds at 20 weeks, both babies were phenotypically normal at birth.

Of the 87.1% (122/140) who had a mid-trimester anomaly scan, 7 screened high risk (2 in HI group, 4 UI group, 1 CI group). This was due to soft markers in 6 cases, 5 delivered phenotypical normal babies and in one case the outcome is unknown. The seventh case had a HI cerclage placed at 14 weeks, invasive testing was performed due to multiple major structural anomalies detected at 19 weeks gestation. Karyotyping in this case revealed T18 and a termination of pregnancy was subsequently performed.

Almost all cases 96.4% (135/140) had midstream urine sent for microscopy and culture, wherein 15.7% (22/140) had a positive culture and were treated, 13 from the HI group, 8 from the UI and 1 from the CI group.

Sonographic and clinical evaluation of the cervices is depicted in **Table 4**.

Table 4: Cervical screening parameters

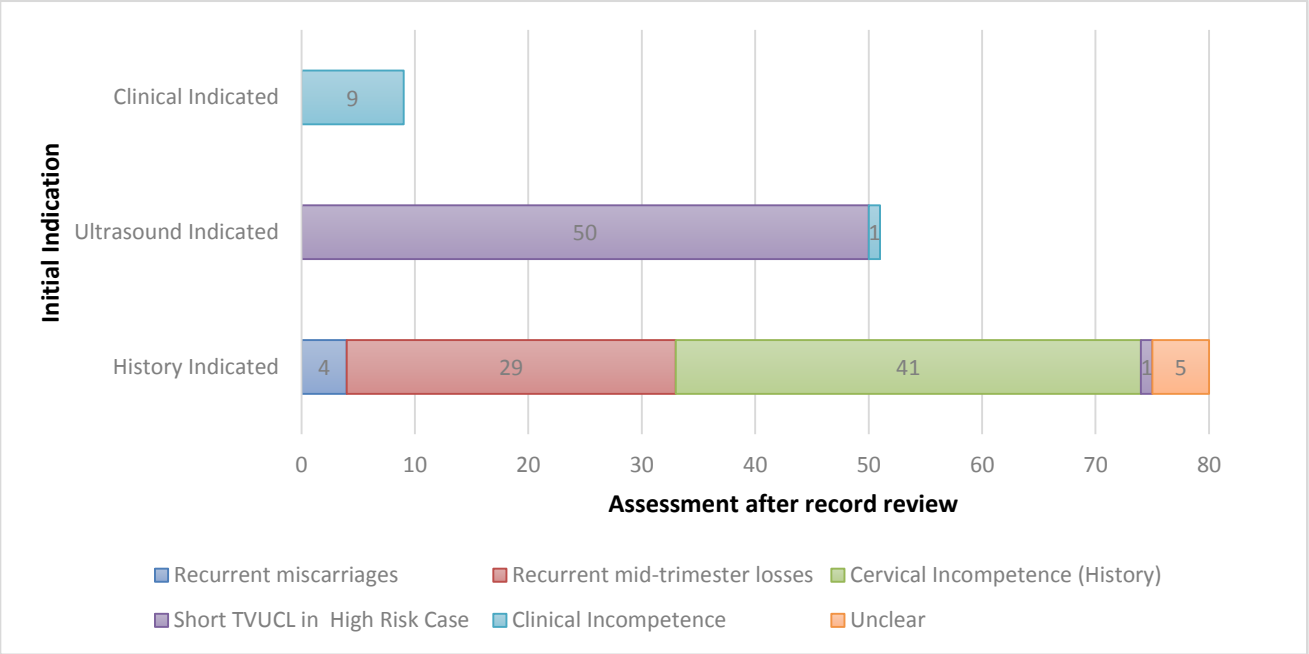
	History Indicated N=80	Ultrasound Indicated N=51	Clinical Indicated N=9	Total N=140
TVU Cervical length (mm) #	25 (10-45)	15 (3-25)	7 (0-38)	15 (0-45)
Cervical tear/trauma on clinical assessment	12 (15.0%)	7 (13.7%)	-	19 (13%)
Cervical portio on clinical assessment (mm) #	15 (0-41)	15 (0-25)	8 (0-15)	15 (0-41)
Cervical dilatation on clinical assessment (mm) #	-	0 (0-25)	20 (10-25)	0 (0-25)
Bacterial vaginosis	2 (2.5%)	5 (9.8%)	-	7 (5.0%)
Trichomonas vaginalis	4 (5.0%)	-	-	4 (2.9%)
Candidiasis	6 (7.5%)	1 (2.0%)	-	7 (5.0%)

*# Median (Range) or n (%)
TVU – transvaginal ultrasound

The indications by the attending doctor and final indications for the cervical cerclage insertion after reviewing all the medical records are depicted in **Figure 1**.

In the HI group, where women were selected purely based upon their past obstetric history, 51.3% (41/80) of the cases had a classical history of cervical insufficiency. All the UI cerclages insertions were based upon a shortening cervical length (25mm or less) on serial transvaginal ultrasonography. One case in this group progressed to clinically dilatation by the time the cerclage was being placed. In this case, there was a discrepancy between cervical length at screening which was 25mm with a closed cervical os and the intraoperative clinical findings of clear cervical dilatation of 25mm. Of note there was a 5-day interval from the initial screening to placement due to the unavailability of theatre lists, yet she delivered at term after elective cerclage removal at 37w.

Figure 1: Case assessment and final indication



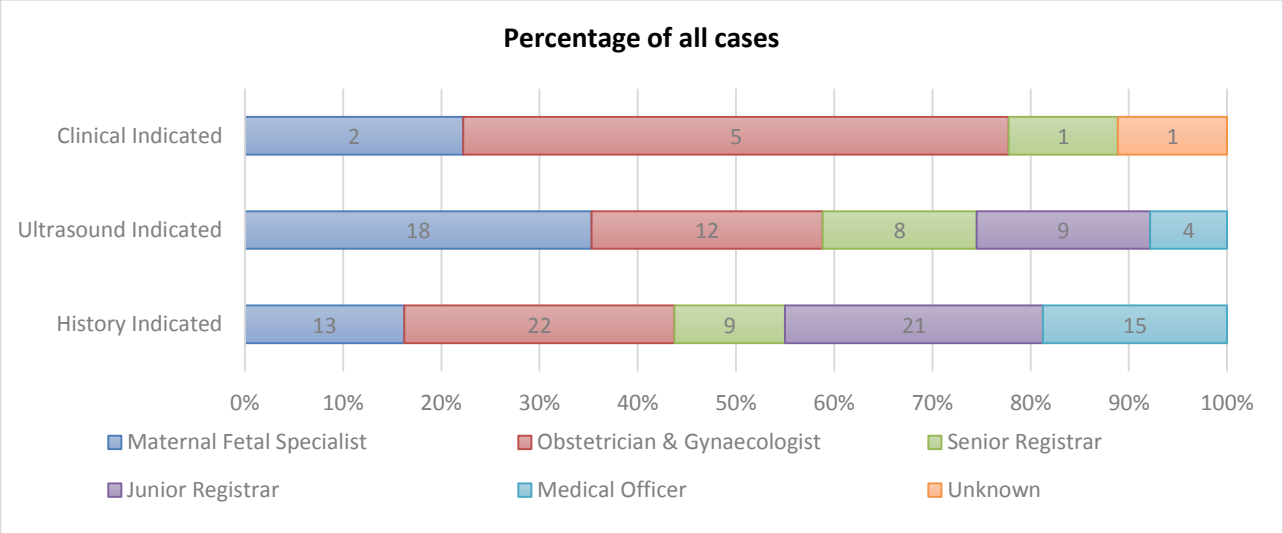
*Recurrent miscarriages – repetitive (not necessary consecutive) first trimester miscarriages; Recurrent (not necessary consecutive) mid-trimester losses – GA 13w0d – 23w6d; Cervical incompetence – consecutive recurrent spontaneous painless mid trimester losses 3; TVUCL – transvaginal ultrasound cervical length less than 25mm; Clinical incompetence – clinical painless cervical dilatation

As part of preoperative management, the majority of the patients received antibiotics [77.5% (62/80) in the HI group, 82.4% (42/51) in the UI group and 66.7% (6/9) in the CI], of which intravenous antibiotics were given to 43.8% (35/80), 56.9% (29/51) and 66.7% (6/9) in the HI, UI and CI cases respectively.

Additionally, perioperative indomethacin was given to 90.0% (72/80) of the HI, in 86.3% (44/51) of the UI and in 66.7% (6/9) of the CI cases.

All cerclages were placed under spinal anaesthesia except for 2.5% (2/81) of HI and 2.0% (1/51) of the UI cases. In these three cases, general anaesthesia was administered after numerous failed spinal attempts. Unfortunately, the anaesthetic notes on these 3 cases were not clear and no definitive reason for the inability to place a spinal anaesthesia was given. The primary surgeon involved in placing the cerclage is depicted in **Figure 2.**

Figure 2: Primary surgeon involved



Numbers of cases in each group depicted as a percentage stacked bar chart.
*Maternal-Fetal specialist – subspecialty of Obstetrics; Obstetrician and Gynaecologist – qualified specialist; Senior registrar – year 3 and 4 residency in Obstetrics and Gynaecology; Junior registrar – year 1 and 2 residency in Obstetrics and Gynaecology; Medical officer - qualified medical doctor working in Obstetrics and Gynaecology department

The median duration of surgery time was 19 minutes (5 – 65 minutes) and did not differ significantly between the groups (HI 15 minutes (5 – 65 minutes), UI 17 minutes (10 – 45 minutes), CI 20 minutes (10 – 35 minutes).

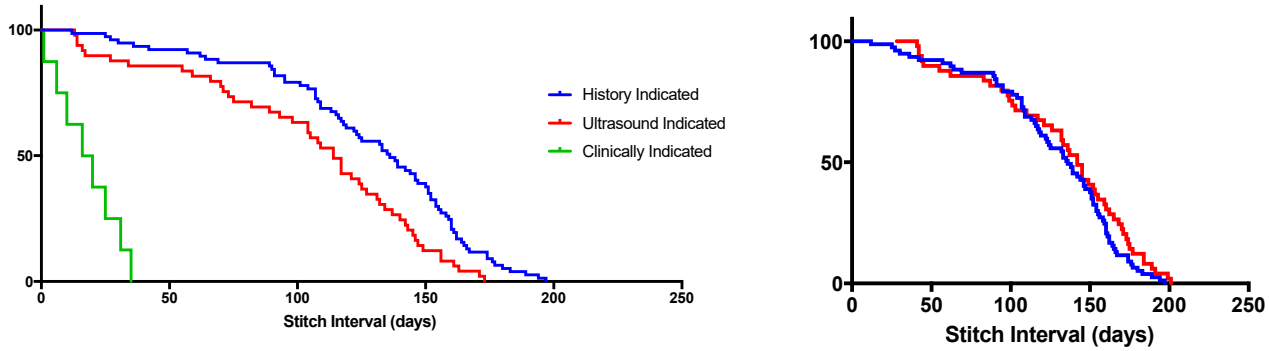
Hospital stay duration was similar between the groups with almost all women being discharged by day 2 postoperative. The median hospital stay was one day

(0 - 5 days) in the HI, one day (0 - 5 days) in the UI and one day (1 - 17 days) in the CI group. In the HI group one women remained in hospital for 5 days due to persistent mild vaginal bleeding but was discharged subsequently. Similarly, one women in the UI group had a very challenging cerclage placement at 14 weeks. It was complicated by vaginal bleeding and rupture of membranes and she stayed in hospital for 5 days. The suture was left in place and she ultimately delivered at 29 weeks. The longest hospital stays of 17 days belongs to a woman in the CI group. She was hospitalised for a total of 17 days due to persistent per vaginal bleeding after cerclage placement at 23 weeks, followed by rupture of membranes on the 4th postoperative day. She remained in hospital and the cerclage was only removed at 25w3d after the onset of mild contractions. In this case the patient chose to be expectantly managed, remained in hospital ultimately delivering spontaneously at 26w.

4.5 Cerclage specific and antenatal outcomes

The median gestational age of cervical cerclage insertion was 108 days (57-151), 136 days (96-161) and 145 days (100-166) respectively for HI, UI and CI groups. While the median gestation of removal was 237 (112-279), 246 (112-274) and 164 (101-183) days respectively. The stich intervals of each group are depicted in a survival plot in **Figure 3a**. This is not seen as a true comparison between the groups since the gestational age at insertion plays a key role in interpretation of the cerclage interval. Therefore, in **Figure 3b** the cerclage interval is depicted with the true GA depicted on the x axis. The median stitch intervals per group were 134 (25-197), 114 (13-173) and 16 (10-35) days respectively for the HI, UI and CI groups. To define which antenatal and surgical variables are most predictive of the cerclage success i.e. cerclage interval, a univariate general linear regression model was performed and only the GA at insertion proven to be predictive. Consequently, if the cerclage interval is corrected for the GA at insertion then there is no difference in the cerclage interval between the HI and UI groups and a trend toward better outcomes in the UI group.

Figure 3: Cerclage interval as survival analysis plot.



*A-survival analysis of cerclage interval between the groups; B-survival analysis between the HI and UI groups weighted for gestational age of insertion.

Another key factor in the success of a cerclage is the incidence of cerclage related complications and this is depicted with the antenatal obstetric outcomes in **Table 5**. Intraoperative complications were infrequently seen but in roughly 3% of cases a direct cervical tear was caused or the membranes ruptured during the cerclage placement. Both cases in which a cervical tear occurred in the HI group delivered a live born babies before 34 weeks GA, while ONR case in the UI group miscarried at 20 weeks. Vaginal bleeding after cerclage placement prior to discharge was seen in 3.6% of all women, which was mostly mild and all were self-limiting. The main cerclage complication after hospital discharge was rupture of membranes, at any gestation before 37 weeks, and was noted in 22.1% of the cases. Spontaneous cervical cerclage suture displacement was also seen in 5.0% of cases during subsequent antenatal care. Displacement in the HI group occurred in three cases, with two cases having a portio vaginalis of 10mm, both delivered live babies at 29 and 31 weeks GA. The last case in the HI group had a portio of 15mm but with two old lateral cervical tears and she delivered a live born at 27w4d. In the UI group, two cases had no visible portio vaginalis and had difficult cerclage placement, they both miscarried at 16 and 23 weeks. The last case in the UI group had a portio of 10mm and an uncomplicated placement with a live born delivery at 31w.

Table 5: Cerclage and antenatal outcomes

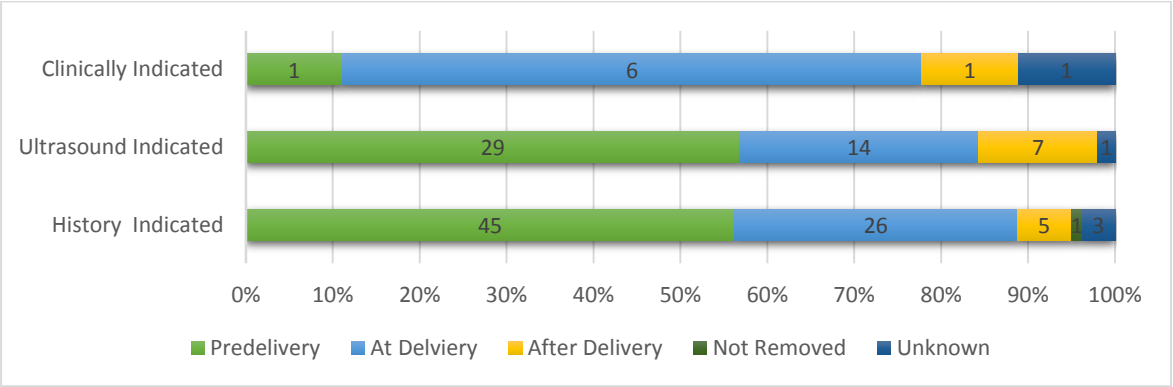
	History Indicated N=80	Ultrasound Indicated N=51	Clinical Indicated N=9	All N=140
Immediate surgical complications (before discharge) (n %)				
Tear	2 (2.5%)	1 (1.9%)	-	3 (2.1%)
Inability to place	-	1 (1.9%)	-	1 (0.7%)
Per vaginal bleeding	2 (2.5%)	2 (3.9%)	1 (11.1%)	5 (3.6%)
Rupture of membranes (within 72 hours of placement)	0	1 (1.9%)	1 (11.1%)	2 (1.4%)
Cerclage complications (after discharge) (n%)				
Displacement	3 (3.8%)	3 (5.9%)	1 (11.1%)	7 (5.0%)
Rupture of membranes (at any gestation)	16 (20.0%)	12 (23.5%)	3 (33.3%)	31 (22.1%)
Antenatal complications after 24w (n%)				
Preterm labour	31 (38.8%)	13 (25.5%)	4 (44.0%)	48 (34.3%)
PPROM	10 (12.5%)	7 (13.7%)	1 (11.1%)	18 (12.9%)
Antepartum haemorrhage	-	2 (3.9 %)	1 (11.1%)	3 (2.1%)
Gestational hypertension	3 (3.8 %)	2 (3.9 %)	-	5 (3.6 %)
Preeclampsia	4 (5.0%)	5 (9.8%)	-	9 (6.4 %)
Gestational diabetes	6 (7.5 %)	3 (5.9 %)	-	9 (6.4%)

*Displacement - defined as cerclage suture slip from its original insertion around the cervical os or not in its place at follow up

There were a total of 63, 36 and 8 antenatal admissions events for the HI, UI and CI groups respectively. This was mostly for preterm labour episodes occurring in 34.3% of all cases. This lead to antenatal tocolysis being given to 23.8% (19/80), 19.6% (10/51) and 44.4% (4/9) of the HI, UI and CI groups respectively. Antenatal corticosteroids were given to 35% (28/80), 35.3% (18/51) and 33.3% (3/9) of the HI, UI and CI groups respectively. Beyond the anticipated but remarkably common preterm labour and PPROM, gestational hypertensive disorders were seen in 10.0%. No cases of IUGR/ FGR were detected antenatally in this cohort. Preeclampsia was seen in 2 cases <34 weeks gestation, one from the HI group and the other from the UI group respectively.

The cervical cerclages was removed at a median gestation age of 237 (112-279), 246 (112-274) and 164 (101-183) days respectively for the HI, UI and CI groups. The timing of the removal is depicted in **Figure 4**.

Figure 4: Timing of cervical cerclage removal



*Numbers per time point of cerclage removal for each group depicted as a percentage stacked bar chart.

4.1 Delivery outcomes:

The median gestation age at delivery was 248 (112-295), 254 (112-288) and 164 (101-183) days respectively for the HI, UI and CI groups. The delivery outcomes are depicted in **Table 6**. Labour occurred spontaneously in 79.3% (111/140) of all cases. However, in 4.3% (6/140) a prelabour caesarean delivery was indicated. Indications being hypertensive disorders of pregnancy (n=2), fetal malposition (n=2), failed induction of labour (n=2).In addition 10.0% (14/140) of cases an induction was required for hypertensive disorders of pregnancy (n=7), gestational diabetes (n=2), PPROM (n=2), post term (n=1) and unknown indication in two cases.

One case in the CI cerclages was delivered by Caesarean Section due to fetal distress after preterm rupture of membranes at a gestation of 25w6d.

Table 6: Delivery outcomes

	History Indicated N=80	Ultrasound Indicated N=51	Clinical Indicated N=9	All N=140
Gestational age of Delivery (n %)				
· **Unknown**	3 (3.8%)	2 (3.9%)	1 (11.1%)	6 (4.3%)
· **<24w**	9 (11,3%)	7 (13,7%)	4 (44.4%)	20 (14.3%)
· **24-27w6d**	3 (3.8%)	3 (5.9%)	4 (44.4%)	10 (7.1%)
· **28-33w6d**	22 (27.5%)	7 (13.7%)	-	29 (20.7%)
· **34w-36w6d**	9 (11.3%)	11 (21.6%)	-	20 (14.3 %)
· **37+w**	34 (42.5%)	21 (41.2%)	-	55 (39.3%)
Mode of delivery (n %)				
· **Unknown**	6 (7.5%)	2 (3.9%)	1 (11.1%)	9 (6.4%)
· **Caesarean Section (total)**	18 (22.5%)	14 (27.5%)	1 (11.1%)	33 (23.6%)
· **Caesarean Section (elective)**	4/18 (22%)	2/14 (14%)	-	6/33 (18%)
· **Vaginal delivery**	56 (70.0%)	35 (68.6%)	7 (77.8 %)	98 (70.0%)

4.2 Neonatal outcomes

The overall median delivery gestation was 240 (101-295) days. Each group had one neonatal death related to extreme prematurity complications after a spontaneous vaginal delivery before 28 weeks gestation. Overall still born rate for deliveries after 24 weeks gestation was 2.9%. These were related to a single case of abruption placentae at 29 weeks' GA in the UI group, and three cases of ROM at the limits of viability (24w1, 24w3 and 26w1).

Furthermore, there was a fetal loss rate before 24 weeks gestation of 14.3% (20/140) resulting in a total perinatal loss rate of 19.3% (27/140).

Table 7: Neonatal outcomes:

	History Indicated N=80	Ultrasound Indicated N=51	Clinical Indicated N=9	All N=140
Unknown	3 (3.8%)	2 (3.9%)	1 (11.1%)	6 (4.3%)
Delivery gestation (days)	248 (112-295)	254 (112-288)	164 (101-183)	240 (101-295)
Live born#	68 (85.0%)	39 (76.5%)	3 (22.2%)	110 (78.6%)
Fresh Stillbirth#	0	3 (5.9%)	1 (11.1%)	4 (2.9%)
Early neonatal death#	1 (1.3%)	1 (2.0%)	1 (11.1%)	3 (2.1%)
Birth weight (g)#	2500 (720-4610)	2535 (600-4080)	710 (630-800)	2460 (630-4610)
5min Apgar	9 (0-10)	9 (0-10)	0 (0-9)	9 (0-10)

* Data displayed as median (range) or n (%); # For GA ≥ 24w0d

Chapter 5: Conclusion

5.1 Summary of Finding

In this moderately sized retrospective review of transvaginal cervical cerclage insertion 80 HI, 51 UI and 9 CI cerclages were identified over a period of 5 years. An overall success rate (i.e. delivery after 28 weeks of gestation) was 781.3% in the HI and 76.5% in the UI groups respectively. Regrettably all CI cerclages delivered before 28 weeks. Cervical cerclage insertion lead to an overall live born rate after 24 weeks gestation of 78.6%, once again better trends being seen in the HI group (85.0%) than the UI group (76.5%). The low live born rate in the CI group (22.2%) is mostly related to the extreme preterm delivery gestational age.

More sombrely cerclage related complications were frequently encountered especially displacement of cervical cerclage (5.0%) and rupture of membranes after discharge of the patient (22.1%). Moreover, the high rates of PTB of 56.4% (before 37 weeks) and 42.1% (before 34 weeks) were difficult to interpret due to the high-risk profile of this cohort.

5.2 General Discussion

Publications on cervical cerclages are rarely uniform in reporting outcomes. This makes it particularly difficult to directly compare the outcomes between data sets. Most studies report on a PTB rate before 34 weeks[44] or 37 weeks gestation[45,18] . Live born rates were also not consistently reported in all trials. In some trials stillbirth and miscarriages were subtracted from the total number randomised to the cerclage group to extrapolate live birth rates. In addition, most studies do not report on fetal loss alone but rather as a composite perinatal outcome.

The best comparative evidence for PTB rates for HI is from an old study carried out in South Africa by Rush et al.,[19] where a total of 194 high risk women were enrolled, randomised to cerclage vs. standard care. The cerclage group had a high PTB rate less than 37 weeks of 34% which was higher than the control group of 32%. The first published multicentre study of 506 women at moderate risk of PTB (based upon a scoring chart), were randomly allocated to either cervical cerclage insertion or standard care.[18] Herein the PTB rate, less than 37 weeks, was merely 6.7% and similar to the 5.5% in their control group. While the only RCT on HI

cerclage, was composed of 1292 women whom were randomised to cerclage insertion or standard care only if the obstetrician was uncertain of cervical cerclage insertion.[17] This RCT reported PTB rates <37 weeks of 26% and <34 weeks of 13% in the cerclage group, and PTB rates <37 weeks of 30% and < 34 weeks of 18 % in the standard care group. Our study reported a much higher PTB rates in the HI group; < 37 weeks of 54 %, < 34 weeks of 43% and 15% for < 28 weeks GA. This contrast may be due to the high-risk profile of our cohort influenced by a high smoking prevalence, older maternal age, one in four women having pre-existing medical disorders and the previous obstetric history. Furthermore, our study had a mixed miscarriage profile for the HI cerclage group, with only 51% having a typical history of cervical incompetence. This may have influenced our PTB rates as reported in the RCOG study where the effect of cervical cerclage was only seen in a subset of women with three or more second trimester pregnancy losses.

The ultimate aim of cervical cerclage insertion is to reduce perinatal mortality and morbidity from prematurity through reduction of PTB. This is best reflected in the reported live birth and perinatal loss rates. Literature identified for live birth and perinatal loss rates for HI cerclages are limited to only 2 trials. Both these studies reported a live born rate of approximately 93% and a perinatal loss rate of 9%.[17,19] In comparison, the slightly lower live born rates reported in our study of 85% in the HI group, might primarily be attributed to the higher early pregnancy loss and PPROM rates. This is again a clear reflection of the high-risk profile and multiple comorbidities observed in this cohort.

For UI cerclages, the first evidence comes from a small study by Althuisius [44] in which 35 women with risk factors for cervical incompetence and a TVUCL of < 25mm were randomised to cervical cerclage insertion or bed rest. In this study cerclage insertion group, there were no PTB before 28 weeks of gestation, and the PTB rate before 37 weeks GA was 21%. While in the bedrest group the PTB rate before 28 weeks was 19% and the PTB rate before 37 weeks GA was 63%. A subsequent study targeting high risk women by Berghella et al.,[27] randomised 61 women to a cervical cerclage or bed rest when the TVUCL was less than 25mm. Here the reported PTB rates for < 37 weeks GA and <34 weeks GA were 52% and

42% respectively in the cerclage group. On the other hand the PTB rate in the bed rest group for <37 weeks and < 34 weeks GA were 64% and 50% respectively. However these findings should be treated with caution as this final study population was a combination low risk and high-risk women including twins.[27] The largest RCT study targeting high risk women with TVUCL screening was done by Owen et al.[46] In this multicentre trial 302 women were randomized to a cervical cerclage insertion or standard care after they had a TVUCL < 25mm. Here the reported PTB rates before 37 and 34 weeks' GA were 45% and 28% respectively in the cervical cerclage group. While in the standard care group the PTB rates <37 weeks and <34 weeks GA were 59% and 37 %. Interestingly, the multicentre RCT reported by TO et al.,[22] targeting all women at routine screening with a TVUCL of 15mm or less, reported a lower PTB rate before 33 weeks' GA of 26% in the cervical cerclage group and 37% in the control group. Our data reflects the trend of a high-risk population as in the publication of Owen et al., with our reported PTB rate before 37, 34 and 28 weeks' GA of 55%, 33% and 20% respectively in the UI group. This is expected as our women in the UI group only qualified for serial TVUCL if they had a high risk obstetric history of PTB in combination with a TVUCL <25mm. These trends, although slightly higher, are comparable and also in keeping with another meta-analysis by Berghella et al.,[24]. In this met analysis the PTB rate before 35 weeks GA was 28% in the cerclage group compared with 41 % in the no cerclage group.

The reported live birth rates of UI cerclages, from the above mentioned international studies in developed countries, range from 88-100%,[44,22] which are higher compared to our study results of 77% in the UI group. This could be explained by the heterogeneity of the so called high risk profile inclusion criteria for TVUCL screening in the international studies. These included a spectrum of high-risk profile patients with previous cold knife conisations, diethylstilbestrol exposure, to women with repeated PPROM history. On the other hand our study case selection for UI was based primarily on a history of preterm birth or MTL and shortening midtrimester cervix of <25mm. In addition, our study profile is clearly that of a high-risk group due to a complexity of variables including maternal comorbid as well as pregnancy related factors.

When reflecting on the PTB rate comparison between the HI and UI groups in our study, outcomes at first appear to be similar, PTB rate before 37 weeks' GA was around 54% in both groups. However, a difference is noted in the PTB rates specifically before 34 weeks' GA with higher rates in the HI group (43% in HI and 33% in UI group). This difference before 34 weeks GA could be explained by the obstetrical risk profile in the HI group which was much 'worse' with higher incidences of recurrent T2 miscarriages. A paradoxical trend of a higher rate for PTB rate before 28 weeks' GA was seen in the UI group (15% in HI group and 20% in UI group) but the numbers were small and very difficult to interpret whether this trend reflects any clinical importance.

The previously mentioned meta-analysis by Berghella et al.,[45] also noted similar PTB rates with no clear differences in deliveries before 37weeks GA (31% in both HI and UI cerclage groups) but a higher rate of PTB before 34 weeks' GA in HI cerclages (23% in HI vs. 17% in UI cerclages). As a result of these findings, Berghella concluded that those women with a singleton pregnancy and previous history of PTB can safely be monitored with serial transvaginal ultrasound, and a cervical cerclage inserted in the women with a shortening cervix compared to policy of routine HI cerclage. When reflecting on PTB rates <34 weeks' GA our study supports this conclusion. However not all centres may have the manpower, skill and equipment to carry this out especially in a developing country. Nevertheless, when reflecting on the higher live birth rates in the HI group, targeted screening with appropriate history taking will remain a corner stone for HI indicated cerclages to reduce the morbidity and mortality associated with PTB in a resource restricted country.

As for CI cerclages, a recent systemic review and meta-analysis included 10 studies of which only one was a RCT and reported a PTB rate in the cerclage group of 50% and 8% before 34 and 28 weeks' respectively.[47] Although it was stated that the quality of the included studies was limited, this remains the best data to date. In our study, all CI cerclages delivered before 28 weeks' gestation. Unfortunately, we do not have placenta histology which may have assisted in determining the causes of PTB in some of the cases. The findings do emphasise that CI cerclage should only be considered in carefully and appropriately selected patients. Even if multiple risk factors can be identified in our CI group the numbers were too limited

to draw any firm conclusions. There is a need to diligently assess the outcomes of CI cerclages in specifically resource restricted settings and critically evaluate all cases that qualify for CI cerclage.

Fetal and neonatal outcomes for CI cerclage are inconsistently reported in literature.[48] The systematic review mentioned earlier reported a neonatal survival of 71%,[47] with individual studies reported an average neonatal survival rate of about 60%.[49,50] The low live born outcome of 22% in our study is explained by the high miscarriage rate and extreme premature GA at delivery.

Overall, in our study the spontaneous vaginal delivery rate (77%) and caesarean section (23%) rate were in keeping with published data on cervical cerclage outcomes.[60] The latest Cochrane review on cervical cerclage for prevention of pregnancy loss in women reported an overall caesarean section rate of 18%, with specific rates of 14% and 28% reported for HI and UI groups.[51] [52] Our study's 23% caesarean section rate is also comparable with the South African national and local provincial caesarean rate of about 25%.[53] While the Cochrane collaboration review stated that Caesarean section rates are higher after cervical cerclage insertion, the background risk profile of the population should be taken into consideration. Lastly, 14.3% (20/140) of the deliveries in our study were either induced or underwent pre-labour caesarean section. This highlights the high rate of pregnancy related complications in this cohort, which has directly influenced the lower spontaneous vaginal delivery rate.

5.3 Population risk profiles

It is well established that a detailed history, physical assessment and TVUCL scan are the corner stones for the appropriate management of patients with potential cervical incompetence. The risk profile of a patient can be altered due to countless factors that in turn can influence the outcome. As in this cohort there have been several observations on differences in patient demographic profile between developing and developed countries.[7] These differences have been attributed to ethnic variations, social factors such as poverty, behavioural patterns, early sexual debut and intrinsic biological factors.[7] The majority of our study population are of a

low socioeconomic status that could explain some issues surrounding difficulty in health care access, health education as well as the high recreational drug use.

Another major comorbidity of our time, obesity, was common in our study (29%). Farinelli et al., clearly noted an association between increasing BMI and earlier GA at delivery in women undergoing UI cervical cerclage insertion.[54] However, this result was driven by several women with a BMI >47 kg/m^2 and overall obesity had no significant effect on the gestational age of delivery in the cervical group. A subsequent systematic review on this topic, concluded that obesity did not affect the gestational age of delivery in women with cervical cerclage but due to small numbers and methodological heterogeneity no firm deduction could be made. [55] In our cohort BMI definitely added to the risk profile of the groups but was not independently associated with a difference in stitch interval or cerclage success.

Several maternal risk factors are known to be associated with recurrent pregnancy losses and PTB. These include smoking, maternal infections, hypertensive and autoimmune disorders among others.[7] The high South African national and local provincial smoking prevalence of 18% and 32% respectively are reflected in our cohort.[56] This is similar to an American publication[57] but significantly higher than other publications from Africa[5]. This high smoking prevalence maybe a significant confounding factor in our reported outcomes as smoking is a known risk factor for PTB.[58] South Africa is also known to have one of the highest prevalence of hypertension in the world and chronic hypertension is a well-known risk factor for preterm delivery.[59,60] Unfortunately, this is not well reported in other cervical cerclage studies and therefore we cannot comment on the differences of chronic comorbidities between cervical cerclage studies. Yet, the overall incidence of chronic hypertension of this cohort (12%) must have played a role in the perinatal outcomes.

Therefore, the presence of each or a combination of the above risk factors already places the patient at high risk of PTB and could have significantly influenced our study PTB outcomes. Hence pre-pregnancy counselling and management of these risk factors in any population setting is of paramount importance to improve any obstetric outcome.

5.4 Cases selection and management

Although it was clear that the background history from our study was filled with multiple pregnancy losses and PTB, it was extremely difficult to obtain a clear history and to establish the exact order of events. As in our study where after record review only 51% of our HI cerclages were deemed to have a classic history of cervical insufficiency. This could potentially have resulted in unnecessary interventions and potential harm in the those who had an unnecessary HI cerclage insertion as stated by Althuisius.[44] It is therefore crucial that a detailed history is obtained during the screening process, especially for HI cerclages. This can be facilitated by clear documentation and proper discharge notification with adequate patient education after a poor obstetrical outcome. In cases where there is an unclear miscarriage profile or PTB history, close follow up with serial transvaginal ultrasound could be advocated.[45]

The importance of a thorough structural fetal assessment through a dedicated ultrasound service cannot be overstated. Many developed countries have routine services that reaches all women and ensures accurate gestational age determination and early structural abnormality identification. Unfortunately, many developing countries lack basic ultrasound facilities as reflected in the Kenyan study where the majority of women (66%) had no ultrasound examination beforehand.[5] This makes it difficult to identify high risk patients and institute early management. Even in our cohort a fetus with T18 was noted only at the routine T2 scan after a HI cerclage was already inserted at 14w. This could have been potentially been picked up with a policy of routine first trimester screening.[61]

In our cohort, UI cerclages were only placed in high-risk women with previous spontaneous PTB and MTL, in combination with shortening midtrimester cervical length as in the study of Owen et al.[21] This selective high-risk profile screening program is preferred to universal cervical length screening program as demonstrated in the study done by Shinker et al. In this study universal cervical length screening programs in low risk women lead to an increase in antenatal interventions, increase cost and no reduction in PTB rates.[62] Despite initial positive evidence for an universal screening program[63] follow up studies show less robust

evidence for it use[62 64] and reduced acceptability by clients[65].

Unlike the heterogeneity of the HI cerclage group the UI group had a good case selection, appropriate TVUS and timely cervical cerclage insertion. However, there are challenges faced with implementation of a good cervical length screening program in resource restricted settings. A crucial influencing factor is the skill of the ultrasonographer and the process of quality control. This has impact on the quality and reproducibility of any cervical length assessment.[66] Boelig et al.,[66] reported up to 15% of qualified trained sonographers failed to produce reproducible cervical length assessment images. Furthermore, patient's acceptability for TVUS is also a challenging factor, as observed by Ghartey et al.,[65] where multigravida, African American, smoking, obese and older women were more likely to decline TVUCL. This patient profile is similar to our cohort however there is a need for local and African based studies to identify patient related limiting factors to TVUCL screening. Another major factor is the cost and availability of ultrasonography as reported in the previously mentioned Kenyan study where only 34% had an ultrasound scan for cervical length assessment, and 7.8% received a transvaginal ultrasound.[5]

As for CI cerclages, the biggest challenge lies within selecting the most appropriate candidates. Our data is limited in numbers but already from this small series the complexity of how they present can be appreciated. A great concern, especially in this group, is missing those with an established amniotic fluid microbial invasion. This is supported by evidence from a study where Romero et al., in which amniotic fluid microbial invasion was identified in >50% of women with acute cervical insufficiency and cervical dilatation of >2 cm.[67] This invasion can lead to subclinical intraamniotic infection (IAI) and has been reported in up to a third of patients being screened for CI cerclage.[68,69] However, there is currently no consensus on routine amniocentesis use, and the safety and efficacy of amniocentesis prior to citing a CI cerclage. In this cohort, no amniocentesis was performed to rule out infection beforehand and it could be debated whether this would have resulted in better case selection. However, there is strong enough evidence to perform an amniocentesis in cases with already suspected subclinical IAI prior to placement of an CI cerclage.[70]

Different strategies have been used and reported with regards to perioperative tocolysis antibiotics use. Generally, their use is not uniformly reported and therefore there are no current standardised regimes that can be reviewed. For women undergoing HI cerclage, when the cervix is not short or dilated, the use of prophylactic antibiotics is not indicated.[71] The same can be advised for women undergoing UI cerclages. Although four RCTs have reported on the use of perioperative antibiotics in UI cerclages, due to the study structures no separate assessment on efficacy of such an intervention was done.[46,44,22] Only in one secondary analysis of a multicentre trial was antibiotic use associated with a prolonged gestation but this was not superior to the no treatment arm nor was there a finding of any one specific antibiotic regime superior to another.[72]
Therefore, currently for both HI and UI cerclages routine prophylactic antibiotics are not endorsed.[11] For women undergoing CI cerclage the role of perioperative antibiotics is unclear and definitely dependant on the risk profile of the women. Several trials have used prophylactic antibiotic regimes for extended periods but no separate analysis evaluated the efficacy of such co-management strategies.[73,74,50] Another small retrospective and poorly controlled study has suggested benefit of antibiotics but the evidence is insufficient to make such a recommendation.[75] In our cohort, a uniform regimen of prophylactic perioperative antibiotics was used in the majority of cases. However, as with PTB prevention in asymptomatic women antibiotics should best not be used as benefit appears limited and a real possibility of harm with unscrupulous use does exist.[76]

As with perioperative antibiotic use, evidence for use of tocolytic agents is also limited especially in asymptomatic women undergoing HI cerclage. For women undergoing UI cerclage, one retrospective study reported no difference with the use of perioperative indomethacin.[77] Once again, the same conclusion was made in a retrospective study evaluating the role of indomethacin in CI cerclages.[78] Therefore, as for antibiotics, perioperative tocolysis is not currently endorsed due to the lack of prospective data and retrospective data indicating no significant benefit.[11] Lastly, although neither of the above strategies has been proven efficacious on their own, their combined use has been recently reported in a RCT[79].The the combined use of broad spectrum antibiotics and indomethacin in this RCT lead to a longer gestational latency, but no difference in the GA at delivery

or neonatal outcomes in CI cerclages. In our cohort, close to 80-90% of all cases received both perioperative antibiotics and indomethacin and this practice needs to be re-evaluated. In addition the use of routine preoperative cervical cultures has not been shown to be beneficial in women undergoing cerclage either.[70]

5.5 Minimizing the procedure related costs and complications

Current practices are moving towards adopting UI cerclage policies and away from HI cerclage, as evidence for its use is more robust, and points towards better outcomes.[25] Evidence has also shown that women with a singleton pregnancy and previous history of PTB can safely be monitored with serial transvaginal ultrasound, with cervical cerclage inserted only in the women with shortening cervix compared to policy of routine HI cerclage.[11] This may then avoid over half of unnecessary HI cerclage insertions reducing long term costs, operative risks and complications. In our study, HI and UI cerclages had similar success rates of 81% and 76%, but in the UI group there were less deliveries before 34 weeks' gestation (43 vs. 33%). In view of the above evidence presented and our study results, it can safely be concluded that a trend towards UI cerclage rather than HI cerclage insertion has the potential to yield better pregnancy outcomes. The increase use of TVUCL brings in the debate of universal cervical length screening of all pregnant women versus targeted high risk cervical length screening. Universal cervical length screening was initially recommended as a strategy to reduce PTB, through which patients with shortening cervical length are offered intervention of progesterone or cervical cerclage insertion[80]. This has brought in the issue of cost effectiveness. Although a RCT by Werner et al., in 2011[81] initially conclude that universal screening was cost effective the specific efficacy of such an approach remains debatable.[82] It would require screening 100,000 women to prevent 10 neonatal deaths. Resulting in unnecessary procedures and interventions, anxiety and stress to the clients.[83] Therefore, high risk TVUCL remains the best option, and there is robust evidence for it as discussed previously. It is of paramount importance that TVUCL are done with proper TVU technique with continuing quality assurance, single targeted screening gestation between 18 – 24 weeks and a cut off for intervention when TVUCL equal to or less than 25mm.[80] In absence of these prerequisites the efficacy and cost effectiveness of this intervention is nullified.

Despite the evidence for UI cerclage the cost of ultrasound scan equipment, infrastructure, training of medical personnel, ineffective referral system may make implementation difficult in a developing country setting. This is especially challenging where provision of basic primary health care is already a problem. One possible feasible solution is setting up appropriate referral systems with expertise centres that could reduce the overall cost.

The primary surgeon involved in placement of cerclage was mainly a qualified obstetrician. On the contrary other reports from developing countries such as Nigeria, the majority of the cerclages were placed by a senior registrar.[48] There is a distinct advantage of having senior and especially skilled personnel to perform these procedures. This ensures the transfer of skill and correct placement of cervical cerclages with reduction of intraoperative and perioperative complications. Therefore, providing this skill in a reference centre will be more beneficial to the outcome, promote and retain specialised skills in the area and provide adequate data for research purposes.

In order to assess the safety and efficacy of cervical cerclage insertion, or any intervention, a thorough understanding of the current management and outcomes are needed. This will direct urgent attention points and future research areas. In our study intraoperative cervical tears (2%), and cerclage displacement (5%) are definitely higher than the reported outcomes.[54] Thorough physical examination during selection criteria and prior to cervical cerclage insertion is critical to plan appropriate surgery and reduce perioperative complications. Women with a very short cervix and especially a short vaginal portia may benefit from transabdominal cerclage rather than transvaginal cerclage insertion reducing the rate of displacement and cervical tears. In addition, an appropriate technique is required which can be achieved through diligent supervision and ensuring sufficient caseloads through dedicated service centres. Though our perioperative complication rate was much higher; a conclusive statement cannot be made and a prospective study may shed more light on this.

PPROM is the most consistently reported complication in cervical cerclage outcomes. Our overall PPROM rate of 22% was in keeping with most reported

studies on either HI or UI cerclages. ACOG reports rates of 0.18-18% [11] and Rush et al 17.7 % [19] for HI. Higher PPROM international rates are seen in the UI group, with ACOG reporting rates between 3-65.2%[53] and Berghella et al [81] reports a rate of 35%. These high rates may be attributed to poor patient selection criteria, for example in some studies any patient with short cervix on TVUS had a cerclage inserted, whether high or low risk. The combination of medical and obstetric conditions as confounding factors could have easily influence the PPROM rate in reported literature as well this cohort. Reduction in PPROM rate would require revision of cerclage techniques and selection of cases.

Higher rates of PPROM, around 20%, are also reported for CI cerclages[84] and our reported 11% might be wrongly interpreted as a low rate. This 'low rate' in our study is mainly because all our patients in CI delivered before 28 weeks' gestation and majority ended up delivering before 24 i.e. being labelled as miscarriages. Most likely PPROM rate in our study was attributed to the predisposition to PTB rather than cervical cerclage insertion itself. Yet the selection of cases strongly influence these rates and several clinical factors have already been identified.[85] Furthermore an initial observation period of 24 hours to ensure the absence of any uterine contractions have shown to improve outcome.[84] Therefore in resource restricted settings a simple observation period with diligent clinical review could lead to better selection and outcomes in CI cerclage.

Other strategies that have been reported on to improve the efficacy of cervical cerclage include the type of suture material and needle, cervical cerclage modified techniques and hospitalisation but no clear benefit of one over another have been shown.[70]

5.6 Limitations of the study

Firstly, the limitation of being a retrospective study must be considered. Notably this study suffered from patient and treatment selection bias. Just under 10% of identified cases could not be analysed due to missing records and another 16% of cases were analysed but did not have complete records. Absence of data on potential confounding factors may have caused a significant observer bias. Another major limitation of this study was the difficulty in collection of neonatal data mainly

because the majority of the maternal case folders were not linked to the neonatal files. Lastly, only a very small CI group was identified due to problematic theatre registrations and therefore this study does not reflect all the CI cases performed.

5.7 Strength of the study

This study provides current data in a real world developing country setting. It is well sized and comparable to other retrospective observational studies from developing countries [86] especially African[5] countries. The true strength of the study is the detailed antenatal clinical review with specific cerclage related complications and categorised delivery outcomes.

5.8 Conclusions and future directions

Cervical cerclage insertion remains a cornerstone in the prevention of PTB especially in high risk populations. In our study both HI and UI cerclages had good success and live born rates, with the outcomes of UI cerclage being comparable to international evidence. Regrettably CI cerclages had poor outcomes but specific variables were difficult to identify due to the complex high-risk nature of this cohort. This study reflects the specific needs of a developing country where the correct identification of eligible women for cerclages are difficult, and that CI cerclages should preferably be done in a clinical research setting.

Appendices

Study Code Nr: **Cerclage Outcome Study -** Confirm that this is a singelton Y/N

Descriptive	Key [Input Form]	[Example]	Input (Capital X for unknown)
EDD (from formal US)	Date [cccc/mm/dd]	[2011.11.11]	
Age	Number [x]	[36]	
G	Number [x]	[2]	
P	Number [x]	[2]	
Prev T1 MC <13w	Number total and number of spont., unknown cause	[x (x)] [2 (1)]	
Prev T2 MC 13-23.6w	Number total and number of spont., unknown cause - LB/FSB	[x (x)] [2 (1)]	
Prev 13-23.6 SFP losses	0 Nil then 1,2,3 etc. [x]	[2]	
Prev PTB 24-27.6w	Number total and number of spont., unknown cause - LB/FSB	[x (x)] [2 (1)]	
Prev PTB 28-33.6w	Number total and number of spont., unknown cause - LB/FSB	[x (x)] [2 (1)]	
Prev PTB 34-36.6w	Number total and number of spont., unknown cause - LB/FSB	[x (x)] [2 (1)]	
Living Children	Number [x]	[2]	
Prev SGA (<2500g)	Number [x]	[2]	
Prev Obs Hx	0 Nil, 1 GHT, 2 PreE, 3 Abruptio, 4 PPROM 5. Severe IUGR,	[0]	
	6 Prolonged 2nd stage, 7 AVD, 8 Prev Curettage, 9 Other		
Medical Hx	0 Nil, 1 CHT, 2 DM, 3 Epilepsy, 4 HIV, 5 Asthma, 6 Other	[0]	
Medication/Other Hx			
Surgical Hx	0 Nil, 1 C-section, 2 Abdominal, 3 Gynae	[0]	
Cervical Surgery	0 Nil, 1 LLETZ/LEEP, 2 CONE, 3 Obs tear, 4 Other	[0]	
Substance use	0 Nil, 1 Smoking, 2 Alcohol, 3 Methamph, 4 Other drug use	[1]	
BMI (kg/m2)	Number [xx,xx]	[31,54]	
Dipsticks	[illegible]	[0]	
RPR	0 Neg, 1 Pos and Rx, 2 Pos and not Rx	[0]	
HIV	0 Neg, 1 Pos on MTCT, 2 Pos on HAART	[0]	
Hb (g/dl) at booking	Number [xx.x]	[11,1]	
MSU	0 No Growth, 1 ASB and Rx, 2 ASB not Rx	[0]	
NT Scan	0 No, 1 Yes, Normal; 2 Yes, High Risk/Fetal Anomaly	[1]	
Anomaly Scan	0 No, 1 Yes, Normal; 2 Yes, High Risk/Fetal Anomaly	[1]	
Prev Cerclage	0 No, 1 McDx1, 2 McD>1, 3 TAC, 4 Shirodkar	[0]	
[illegible]	0 No, 1 Yes x1, 2 Yes x2, 3 Yes x3, 4 Yes x4	[0]	
Cervix Clinical Eval	Portio Vaginalis Shortest (mm)	[15]	
	Old Tears/Trauma 0 No, 1 Yes	[0]	
Wetmount	X Unknown; N Not Done; 0 Normal; 1 BV; 2 Trichomonas; 3 Chronic Cervicitis; 4 Other		
CxL Screening (shortest mm)	X Unknown; N Not done; length in mm	[X or N or 11]	
GA of Shortest CxL (ww.d)	Number [xx.x]	[18.6]	
Cx Dilatation (mm)	X Unknown; N not done, ND not dilated, or dilatation in mm	[X or N or ND or 11]	

Study Code Nr: **Cerclage Outcome Study -** Confirm that this is a singelton Y/N

Assessor's Final Diagnosis	1 Recurrent MC, 2 Recurrent MTL, 3 Cx Incompetence (Hx),		
	4 Short CxL in high risk case (US Indicated); 5 Clinical Incompetence (Rescue Cerclage)		
Date of Cerclage	Date [cccc/mm/dd]	[2011.11.11]	
Gestation of Cerclage (ww.d)	Number [xx.x]	[18.6]	
Procedure indication from file	1 McD Hx Indicated, 2 McD US Indicated, 3 McD Rescue/Emergency, 4 Other	[1]	
Preop or immediate postop Rx	1 Oral Ab, 2 IV Ab, 3 Nifedipine, 4 Indomethacin	[1]	
Surgeon	1 MFM Team, 2 Consultant, 3 Sr Reg, 4 Jr Reg, 5 MO	[1]	
Surgery Time (min)	Number [xxx]	[19]	
Suture Material	X Unknown; 1 Mers. tapercut; 2 Mers. blunt; 3 Mers. Other; 4 Nylon cut; 5 Polypropylene tapercut; 6 Other		
Surgical complications	0 Nil, 1 Cx Tear, 2 Inability to place, 3 PVB, 4 ROM, 5 Other	[0]	
Notes			
Anaesthesia	0 Sedation, 1 Spinal, 2 Epidural, 3 GA	[1]	
Post-op TV US	X Unknown; N Not done; length in mm	[X or N or 11]	
Post op hospital stay (days)	Number [xx]	[1]	
Cerclage Complications (After DC)	0 Nil, 1 Displacement/Slipped, 2 PVB, 3 ROM (any gest), 4 Other	[1]	
	Other		
Antenatal Complications	0 UnCompl, 1 MC, 2 PTL, 3 PPROM, 4 APH, 5 GHT, 6 PreE, 7 GDM, 8 IUGR, 9 Other		
Antenatal Admission Number	0 Nil then 1,2,3 etc. [x]	[2]	
Antenatal Admission Days (total)	Number [xx]	[7]	
Tocolysis (Antenatal)	0 No, 1 Yes (once), 2 Yes (more than once), 3 Yes (note total hours)	[1]	
Tocolysis (Antenatal)	0 Nil, 1 Indomethacin, 2 Nifedipine, 3 Salbutamol		
Antenatal Steroids	0 No, 1 Yes (1 course), 2 Yes (2 Courses), 3 Yes (>2 courses)	[1]	
Suture removal	1 Predelivery, 2 At delivery, 3 After delivery	[2]	
Suture removal gestation (ww.d)	Number [xx.x]	[28.6]	
Date of Delivery	Date [cccc/mm/dd]	[2011.11.11]	
Delivery Gestation (ww.d)	Number [xx.x]	[28.6]	
Labour Onset	1 Spontaneous, 2 Indicated (planned IOL), 3 Indicated (planned CS)	[1]	
Delivery mode	1.Caesarian Section 2.Vaginal Delivery	[2]	
Caesarean Indication			
Gender	1 Male, 2 Female [x]	[1]	
Neonatal Outcome	1. Alive, 2 FSB, 3 MSB, ENND [x]		
Outcome Weight (g)	Number [xxxx]	[1171]	
Outcome APGAR (5min)	Number [xx]	[7]	
Outcome CBG (pH)	Number [x,xx]	[7.19]	
Neonatal Admission to NICU	0 No, 1 Yes [x]	[1]	
Neonatal Complications	0 Nil, 2 Septicaemia, 3 IVH, 4 BPD, 5 NEC	[1]	
Placenta Weight (g)	Number [xxx]	[400]	
Placenta Clinical Description	0 Nil, 1 Infarcts, 2 Abruptio, 3 ChorioAmn [x] [x]	[1]	

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