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# A quality improvement project to strengthen immunisation practices for high-risk infants in the Chris Hani Baragwanath Academic Hospital neonatal unit, Johannesburg, South Africa

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While premature infants are at increased risk of vaccine-preventable infections, delays in their vaccination are often encountered. This project aimed to enhance neonatal vaccination. The project was conducted in April 2022 and involved routine monitoring, catch-up vaccinations, staff and caregiver education, and vaccine system improvements. Use of the Road to Health book (RTHB) was also promoted. The most notable improvement was in birth oral polio vaccine (OPV) (2% to 69%), facilitated by enhanced provincial stock procurement. Substantial improvement was found at 6 weeks (from 2% to 24%), but gains at 10 and 14 weeks were limited as a result of suspected confounding factors resulting in vaccine deferral. RTHB issuance improved from 45% to 73%. In conclusion, a progressive improvement in vaccine administration was found, while addressing false contraindications and delays. A standardised neonatal unit procedure was established, including provincial OPV procurement. However, challenges remain in an overburdened and understaffed unit, and require systematic engagement beyond vaccination.

Premature infants are at increased risk of vaccine-preventable infections, with vaccination often delayed. Limited evidence supports early immunisation without correction for gestational age, but data and evidence on vaccine efficacy and long-term protection are scarce.<sup>[1,2]</sup> The vulnerability of premature infants is influenced by both humoral and cellular immunological factors, as well as passive transfer of maternal antibodies, which usually occurs after 34 weeks' gestation. Bronchopulmonary dysplasia further increases the risk of pulmonary infections.<sup>[3]</sup> Vaccination programmes prioritise infants and children owing to the significant burden of disease, with ~17 000 under-5 vaccine-preventable deaths daily.<sup>[4]</sup>

Assessing vaccine safety in preterm infants is challenging owing to the increased frequency of adverse events linked to prematurity. The risk of adverse events following immunisation cannot be predicted by gestational age, birthweight or age at immunisation, but rather by the clinical condition affecting cardiorespiratory stability at the time of vaccine administration.<sup>[1]</sup> Infants with pre-existing cardiorespiratory symptoms are thought to have a 5- to 8-fold increase in adverse side-effects after immunisation.<sup>[5]</sup> Various studies suggest that adverse events have limited clinical significance and should not affect the decision to vaccinate, but monitoring is advised after vaccination.<sup>[6,7]</sup>

Vaccination of preterm infants is often delayed owing to lack of knowledge about safety and effectiveness among healthcare workers and parents. Providing parents with information during the hospitalisation is critical in enhancing their understanding of the vaccination process and the importance thereof.<sup>[5]</sup> Vaccine dosages should not be reduced or divided for preterm infants. Despite decreased immune responses observed in some studies,

most patients develop sufficient vaccine-induced immunity. The anterolateral thigh is the preferred site for intramuscular vaccines, and needle length should be determined by the available muscle mass.<sup>[8]</sup> Successfully introducing an immunisation programme for preterm infants in a developing country is attainable, but support and co-operation from all key contributors are needed to enhance the programme's effectiveness.<sup>[3]</sup> The objectives of the present study were to enhance vaccine uptake at Chris Hani Baragwanath Academic Hospital, a tertiary hospital in Gauteng Province, South Africa, focusing on premature and high-risk infants. Several strategies were employed. Firstly, early identification of eligible patients prioritised administering vaccinations at chronological age (Table 1). Secondly, a catch-up system promptly addressed any missed vaccinations. Additionally, comprehensive education initiatives targeted nursing staff, medical doctors and caregivers, to improve vaccination knowledge and awareness. Lastly, an efficient approach to documenting vaccine administration was adopted, using the Road to Health book (RTHB) as a reminder and documentation tool. The aim of implementing these measures was to increase vaccine uptake, safeguarding the health and wellbeing of vulnerable neonatal populations.

## Methods

Infants who were still admitted in the neonatal wards at 5 weeks of age were included in the analysis and intervention plan. Data on gestational age, birthweight, admission area, vaccination status and the presence of an RTHB were collected. Information was obtained from files, medication charts and caregiver interviews. The data were collected in three phases: pre-intervention, immediately after intervention, and once more after a period of 4 months.

The implementation plan focused on effective vaccination practices. Eligible patients without contraindications were identified by doctors. Absolute contraindications included patients receiving antibiotics for suspected or proven sepsis, inotropic requirements, ongoing neurological deficits or uncontrolled seizures, recurrent apnoeas, high oxygen demands, increased work of breathing, or not tolerating feeds. In these situations, vaccinations would be postponed until the patient was deemed clinically stable.

Training and education improved staff and caregiver understanding through presentations and informative posters. Individualised catch-up schedules were created, and contraindications were outlined in a standard operating procedure. Daily electronic reminders maintained vaccination plans, and catch-up schedules were shared on various platforms. Issuing of RTHBs was also promoted. This

comprehensive approach aimed to ensure timely and proper vaccination for all eligible infants.

**Results**

The analysis included all patients in the neonatal unit, considering various weight categories and gestational ages across different admission areas, as detailed in Table 2. Increased vaccine uptake was achieved through various measures, including emphasising vaccine importance, prompt administration during admission, and implementation of catch-up schedules. The standard operating procedure and clear contraindications boosted staff confidence in prescribing and administering immunisations. RTHB issuance increased, ensuring proper vaccination records and empowering caregivers. It is worth noting that RTHB issuance is not yet 100%, as they would only be provided after the first vaccination is given, including patients in the neonatal intensive care unit (NICU). Fortunately, no shortages of RTHBs were noted. Improvements in oral polio vaccine (OPV) availability contributed to progress in birth vaccine administration (Table 3). Significant improvements were seen at 6 weeks, with less noticeable progress at 10 and 14 weeks, possibly owing to factors such as nosocomial sepsis and ongoing need for antibiotic therapy.

**Discussion**

Adherence to vaccinating high-risk infants per the routine schedule is often suboptimal. Despite their increased infection risk, delays are common. Although preterm infants may experience increased

**Table 1. Vaccination schedule for South Africa until 6 months of age<sup>[9]</sup>**

Age of child	Vaccines
At birth	OPV (0), BCG
6 weeks	DTaP-IPV-Hib-HBV (1), PCV (1), RV (1), OPV (1)
10 weeks	DTaP-IPV-Hib-HBV (2)
14 weeks	DTaP-IPV-Hib-HBV (3), PCV (2), RV (2)

OPV = oral polio vaccine; BCG = bacillus Calmette-Guérin; DTaP-IPV-Hib-HBV = diphtheria, tetanus, acellular pertussis, inactivated polio vaccine, *Haemophilus influenzae* type b combined; PCV = pneumococcal conjugated vaccine; RV = rotavirus vaccine.

**Table 2. Patient demographics**

	Before intervention, n (%) <sup>*</sup>	Immediately after intervention, n (%) <sup>*</sup>	4 months after intervention, n (%) <sup>*</sup>
Patients aged >5 weeks, N	53	56	54
Neonatal areas assessed			
NICU	10 (19)	9 (16)	5 (9)
TICU	18 (34)	13 (23)	12 (22)
Ward 66	14 (26)	20 (36)	21 (39)
Ward 40	11 (21)	14 (25)	16 (30)
Birthweight (g)			
<999	9 (17)	13 (23)	12 (22)
1 000 - 1 499	22 (42)	23 (41)	26 (48)
1 500 - 2 499	15 (28)	14 (25)	10 (19)
≥2 500	7 (13)	6 (11)	6 (11)

NICU = neonatal intensive care unit; TICU = transitional/high-care unit; Ward 66 = low-care neonatal ward; Ward 40 = low-care and kangaroo mother care unit. <sup>\*</sup>Except where otherwise indicated.

**Table 3. Vaccine administration at various time points**

	Before intervention, n (%) <sup>*</sup>	Immediately after intervention, n (%) <sup>*</sup>	4 months after intervention, n (%) <sup>*</sup>
Patients aged >5 weeks, N	53	56	54
Birth vaccines			
BCG	22 (42)	37 (66)	39 (72)
OPV (0)	1 (2)	1 (2)	37 (69)
6 weeks	1 (2)	9 (16)	13 (24)
10 weeks	0	3 (5)	2 (4)
14 weeks	0	0	1 (2)
RTHB issued	24 (45)	35 (63)	39 (72)

BCG = bacillus Calmette-Guérin; OPV = oral polio vaccine; RTHB = Road to Health book. <sup>\*</sup>Except where otherwise indicated.

cardiorespiratory symptoms after vaccination, these symptoms are typically self-limiting, requiring only monitoring. Improved knowledge and awareness among healthcare workers and staff was vital in this quality improvement project, addressing initial limited understanding of vaccine safety and efficacy for preterm and high-risk infants.

Health promotion strategies should prioritise including this population in vaccination efforts. To prevent inappropriate delays, regular training and education are essential. Thorough discharge planning ensures seamless service transfer and minimises vaccination delays. Achieving and sustaining a preterm vaccination programme in a resource-limited setting is crucially important, given the significant benefits of vaccinating at chronological age. Neonatal units in developing countries should explore adopting similar guidelines.

The project had several limitations. Firstly, ongoing vaccine fridge repairs affected the smooth execution of the project, as there was no dedicated fridge for proper storage. Secondly, a national shortage of OPV posed a challenge. Additionally, most areas in the unit were overburdened and understaffed, which affected the vaccination process, as staff perceived it as additional workload. Furthermore, the analysis included all patients in the NICU, even those with clear contraindications to vaccinations, potentially skewing results and limiting generalisability.

## Conclusion

The primary goal of this study was to enhance vaccine coverage and minimise missed opportunities through heightened awareness. Initial results were promising, underscoring the need for ongoing efforts in the neonatal unit. While achieving 100% coverage may be challenging, the focus remains on continuous improvement.

**Declaration.** The research for this study was done as part of LB's community paediatrics rotation at the University of the Witwatersrand and in partial fulfilment of the requirements for the paediatrics and child health registrar training programme.

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**Author contributions.** LB: conceptualised the research, data collection and analysis, and preparation of the manuscript. FN, HS and TR: conceptualised the research, and reviewed the data, the analysis and the manuscript.

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# Organophosphate poisoning and outcomes in pregnant women at Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa

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Organophosphate poisoning (OPP) is of public health importance because it poses a significant health risk. The objective of this study was to investigate the sociodemographic characteristics, clinical features, and maternal, fetal and early neonatal outcomes of OPP in pregnancy. We retrospectively reviewed 30 medical records of pregnant women who presented with OPP. Descriptive analysis used measures of central tendency, frequencies and percentages. The majority of the women were booked, were HIV negative, and had toxidrome features on presentation. The maternal case fatality rate was 10.0%, and half of the patients required ventilation. There were 43.3% live births, 13.3% miscarriages and 43.3% stillbirths. Factors associated with poor maternal outcomes were low acetylcholinesterase levels and a high atropine loading dose on admission. Poor fetal outcomes were associated with maternal ventilation, maternal Glasgow Coma Score  $\leq 14$ , hospital stay  $>1$  week, and maternal pH  $\leq 7.35$ . OPP in pregnancy is associated with morbidity and mortality.

Global trends have shown that pesticide poisoning, including organophosphate poisoning (OPP), is a significant problem in low- and middle-income countries (LMICs) compared with high-income countries.<sup>[1]</sup> Pesticide exposure causes ~1 million unintentional and 2 million suicidal poisonings worldwide, leading to ~200 000 deaths per year{Adhikari, 2011 #4;Organophosphate poisoning at Chris Hani Baragwanath Academic Hospital 2012 - 2015 J Bruins, #73;Cebekhulu, 2018 #2}.<sup>[1,2]</sup> OPP in spheres of domestic and farming use, as well as the use of organophosphates (OPs) in instances of self-harm, have been noted to be on the rise in recent years in LMICs such as South Africa (SA).<sup>[1,2]</sup> Two studies from Western Cape Province in SA demonstrated a 40% rise in the incidence of OPP in the region from 2001 to 2005, with suicide the main reason for ingestion, and reported a fatality rate of 3.4%.<sup>[3]</sup>

OPP leads to accumulation of acetylcholine, causing overstimulation of muscarinic and nicotinic receptors.<sup>[4]</sup> The clinical muscarinic receptor effects include vomiting, lacrimation, urination, salivation, diarrhoea, miosis, bradycardia and bronchospasm.<sup>[4-6]</sup> Overstimulation of nicotinic receptors results in muscle paralysis and fasciculations, hypertension, hypoglycaemia, convulsions, respiratory distress, circulatory failure and altered Glasgow Coma Score (GCS).<sup>[5,6]</sup> The diagnosis of OPP is made by confirmed OP exposure. Studies suggest that transfer of OPs from a pregnant woman to the fetus via the placenta is probable, as pesticides have been detected in amniotic fluid, umbilical cord blood, meconium and infant urine.<sup>[5-8]</sup> Exposure to OPs can be confirmed by measurement of butyrylcholinesterase and acetylcholinesterase (AChE) activity in red blood cells and plasma.<sup>[8,9]</sup> The mainstay of treatment in OPP is atropine, which blocks the action of acetylcholine at the muscarinic receptors.<sup>[4,6,9,10]</sup> The present study aimed to address the knowledge gap in OPP by investigating the sociodemographic characteristics and maternal and pregnancy outcomes of OPP in pregnancy at Chris

Hani Baragwanath Academic Hospital (CHBAH), a tertiary hospital affiliated to the University of the Witwatersrand, Johannesburg, SA.

## Methods

This was a retrospective, descriptive study of pregnant women who presented at CHBAH with a clinical diagnosis of OPP from 1 January 2017 to 31 December 2019. Probable cases were suspected OPP with suggestive clinical toxidrome features, while definite cases had a confirmed history of OPP ingestion with clinical features and reduced AChE levels. Women with multiple chemical exposures or drug ingestion and incomplete records were excluded from the study. Details of pregnant women admitted for OPP were retrieved from registers in the high-care unit and the intensive care unit (ICU), and from maternity admissions. Medical records were accessed from the hospital records department. The National Health Laboratory Service (NHLS) provided data on all female patients who had AChE levels tested at CHBAH during the study period, and pregnant women were identified.

The de-identified information collected from medical records using a data collection tool included sociodemographic factors, circumstances of OPP exposure, examination findings on presentation, and the worst readings during admission. Information was also obtained from the paramedics' charts used when transporting patients to hospital. The amount and duration of atropine administration and results of the investigations done were obtained from the patients' files. Maternal outcomes captured included ventilation requirements, duration of ventilation and length of hospital stay, mode of delivery, and discharge status. Fetal and early neonatal outcomes included miscarriages, live births, stillbirths, birthweight, Apgar scores, malformations, duration of hospital stay and discharge status. The de-identified information recorded on the data sheet was entered into the REDCap (Research Electronic Data Capture) data management system (version 4.8.6) and exported

into Stata version 15 (StataCorp, USA) for analysis. Categorical variables were summarised by frequency and percentage tabulations. Continuous variables were assessed for normality using the Shapiro-Wilk test and, where applicable, data were summarised using means and standard deviations or medians with interquartile ranges (IQRs) and ranges. Factors associated with outcomes were evaluated using Fisher's exact test, and *p*-values <0.05 were considered significant.

### Ethical and regulatory approval

The study was approved by the University of Witwatersrand's Human Research Ethics Committee (ref. no. M200335), and permission was also obtained from the NHLS and CHBAH management.

### Results

A total of 62 patients were identified as having OPP. These included 43 patients from the admission registers in the maternity section at CHBAH and 19 from the NHLS database. Forty-six files were retrieved from the records department, and 16 were missing owing to the manual filing system. Of the 46 files retrieved, a total of 30 met the study criteria and were included in the analysis (Table 1).

Of the women with OPP, 17.9% had hypovolaemic shock. The median (IQR) GCS on presentation was 14 (11 - 15, range 3 - 15), while the median worst GCS during the hospital stay was 12 (8 - 14, range 3 - 15). All 30 patients presented with an increase in respiratory secretions on admission, and 96.4% (*n*=27/28 files from which the variable was captured) had pinpoint pupils, 92.6% (*n*=25/27) salivation, 54.2% (*n*=13/24) fasciculations, and 43.5% (*n*=10/23) diarrhoea. Fifteen (51.7%; 15/29) of the women with OPP had live fetuses on admission, while 14 (48.3%) had confirmed intrauterine deaths. Five (38.5%) of the 13 patients who had a cardiotocogram had pathological (category III) traces, 4 traces (30.8%) were normal (category I), and 8 traces (30.8%) were suspicious (category II).

Most patients (81.2%) showed a general picture of metabolic acidosis, as shown by a median pH <7.35, base excess >2.0, and lactate >2.0. The maternal fatality rate was 10.0% (*n*=3). The median (IQR) loading dose of atropine was 9 (6.0 - 14.0, range 3 - 60) mg, while the median duration of atropine infusion was 2 (1 - 3, range 1 - 7) days. Ventilation was required in 15 (50.0%) of the admitted patients, with a median duration of 4 (1 - 3, range 1 - 29) days. The indications for ventilation were as per high-care unit or intensive care unit protocol, which includes metabolic acidosis, respiratory failure and low GCS. The median duration of hospital stay was 6.5 (4 - 10, range 3 - 45) days. The fetal outcomes of the pregnant women with OPP are shown in Table 2. All the women had miscarried or delivered by the time they were discharged or died. Admission to the neonatal ICU was based on extreme prematurity or severe respiratory distress.

Fetal mortality was significantly associated with unbooked status (*p*=0.01), worst maternal pH ≤7.35 (*p*=0.02), maternal ventilation (*p*=0.01), maternal length of hospital stay >6.5 days (*p*=0.02), and maternal GCS ≤14 (*p*=0.05), as shown in Table 3. Factors associated with poor maternal outcomes were low acetylcholinesterase levels and a high atropine loading dose on admission.

### Discussion

Most OPP cases in our study were a result of intentional ingestion, and these tend to be suicidal or parasuicidal, a termination of pregnancy attempt, or intentional poisoning by another individual.<sup>[1,3,10]</sup> In our study the most common clinical effects of OPP were muscarinic, which is consistent with previous studies that showed a predominance of muscarinic effects over nicotinic effects.<sup>[6,10]</sup> Clinicians should be on the lookout for these features of muscarinic and nicotinic toxicity and

**Table 1. Baseline characteristics of the pregnant women with organophosphate poisoning (N=30)**

Description	<i>n</i> (%)*
Age (years)	
<18	4 (13.3)
18 - 35	25 (83.3)
>35	1 (3.3)
Marital status	
Single	26 (86.7)
Married	4 (13.3)
Employment status	
Employed	8 (26.7)
Unemployed	22 (73.3)
Ward of admission	
High-care unit	26 (86.7)
Intensive care unit	4 (13.3)
Parity, median (IQR, range)	1 (0 - 1, 0 - 3)
Gravidity, median (IQR, range)	2 (1 - 2, 1 - 4)
Booking status	
Booked	21 (70.0)
Unbooked	9 (30.0)
Gestational age (weeks), median (IQR, range)	21 (18 - 24, 14 - 37)
Booking bloods	
HIV positive	2 (6.7)
Rhesus negative	1 (3.3)
Hb (g/dL), median (IQR, range)	10.4 (10.1 - 12.1, 9.0 - 13.4)
Exposure to organophosphate	
Intentional	24 (80.0)
Accidental	1 (3.3)
Not stated	5 (16.7)

IQR = interquartile range; Hb = haemoglobin.

\*Except where otherwise indicated.

be quick to institute management without waiting for laboratory AChE confirmation. An altered maternal GCS (≤14) occurred in 81.5% of patients in this study (*n*=22/27). The literature has shown that a low GCS indicates poor prognosis, as it is associated with higher amounts of OP ingestion, respiratory depression, and other organ failures.<sup>[4,9,10]</sup>

The overall results of the blood gas tests showed that most of the patients in this study had some metabolic acidosis, which is in keeping with other findings in the literature.<sup>[1,6,7]</sup> There were poor pregnancy outcomes in this study, with 13 women (43.3%) delivering live babies, comparable to published studies that have reported high fetal losses.<sup>[3,5,8,9]</sup> According to the literature, the negative effects of atropine on the fetus include tachycardia and reduced variability of heart rate.<sup>[5,7,9]</sup> Clinicians should be aware that atropine may make it difficult to interpret the cardiotocograph, leading to an increased caesarean section rate.

The high maternal fatality rate of 10.0% is comparable to studies in the literature. Reasons suggested for high fatality rates include variation in the toxicity of the OP consumed, the lack of readily available antidotes, long distances between hospitals, and overstretched staff and resources.<sup>[3,4,10]</sup> Our findings of poor fetal outcomes are also in keeping with the literature, with reports of spontaneous abortions due to possible stimulation of uterine muscle and intrauterine fetal death from maternal metabolic acidosis as common outcomes among pregnant women with OPP.<sup>[5,9,10]</sup>

**Table 2. Fetal outcomes in cases of maternal organophosphate poisoning (N=30)**

Description	n (%) <sup>*</sup>
Delivery outcome	
Miscarriage	4 (13.3)
Live birth	13 (43.3)
Stillbirth	13 (43.3)
Stillborn status (n <sup>‡</sup> =13)	
Macerated stillbirth	5 (38.5)
Fresh stillbirth	8 (61.5)
Birthweight (g), median (IQR, range) (n=26)	1 815 (1 100 - 2 575, 325 - 3 905)
Apgar score, median (IQR, range) (n <sup>‡</sup> =13)	
1 minutes	6 (5 - 8, 2 - 9)
5 minutes	9 (7 - 10, 6 - 10)
Admission to NICU (n <sup>‡</sup> =13)	6 (46.2)
Hospital stay (days), median (IQR, range) (n <sup>‡</sup> =13)	2 (1 - 3, 0 - 10)
Discharge status	
Alive	11 (36.7)
Fetal loss	17 (56.7)
Early neonatal death	2 (6.7)

n<sup>‡</sup>=number of files from which variable was captured; IQR = interquartile range; NICU = neonatal intensive care unit.

<sup>\*</sup>Except where otherwise indicated.

**Table 3. Factors associated with poor maternal, fetal and early neonatal outcomes**

Variable	Maternal outcomes			p-value (Fisher's exact test)
	Total, n (%) <sup>†</sup>	Alive, n (%) <sup>†</sup>	Dead, n (%) <sup>†</sup>	
Atropine dose (mg), n	26	23	3	0.04 <sup>*</sup>
≤9	16 (61.5)	16 (69.5)	0	
>9	10 (38.5)	7 (30.5)	3 (100)	
	Fetal and early neonatal outcomes			
	Total, n (%) <sup>†</sup>	Alive, n (%) <sup>†</sup>	Fetal loss/END, n (%) <sup>†</sup>	
Booking status, n	29	11	18	0.01 <sup>*</sup>
Booked	21 (72.4)	11 (100)	10 (55.6)	
Unbooked	8 (27.6)	0	8 (44.4)	
Maternal worst pH, n	26	10	16	0.02 <sup>*</sup>
≤7.35	20 (76.9)	5 (50.0)	15 (93.8)	
>7.35	6 (23.1)	5 (50.0)	1 (6.2)	
Maternal ventilation, n	29	11	18	0.02 <sup>*</sup>
Yes	15 (51.7)	2 (18.2)	13 (72.2)	
No	14 (48.3)	9 (81.8)	5 (27.8)	
Maternal length of stay (days), n	29	11	18	0.02 <sup>*</sup>
<6.5	15 (51.7)	9 (81.8)	6 (33.3)	
>6.5	14 (48.3)	2 (18.2)	12 (66.7)	
Maternal GCS, n	27	10	17	0.05 <sup>*</sup>
≤14	22 (81.5)	6 (60.0)	16 (94.1)	
>14	5 (18.5)	4 (40.0)	1 (5.9)	

END = early neonatal death; GCS = Glasgow Coma Score.

<sup>\*</sup>Significant (p<0.05).

<sup>†</sup>Except where otherwise indicated.

## Conclusion

OPP in pregnancy is associated with significant morbidity and mortality in pregnant women, fetuses, and infants in the early neonatal period. Nurses and primary care doctors at community health clinics, and healthcare workers at hospitals, must be trained in the early recognition and management of OPP. Clinicians should also utilise mental health screening tools in maternity case records,

and protocols should be put in place to guide the management of OPP in pregnant women. Early referral for psychosocial support is of fundamental importance in preventing OPP.

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**Conflicts of interest.** None.

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# Individual and population correlates of syphilis screening among pregnant South African women aged 15 - 49 years in 2017

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Based on 2016 global estimates reported by the World Health Organization, syphilis is thought to infect 2 million pregnant women annually worldwide, with 5 million occurrences of negative pregnancy outcomes. We report on a survey-weighted secondary analysis of data collected in the 2017 South African National Antenatal HIV Sentinel Survey of 32 716 pregnant women who attended antenatal care in 1 585 public health facilities. The overall syphilis screening coverage for pregnant women in 2017 was 96.7% (95% confidence interval (CI) 96.12 - 97.20). In a multivariable model, the factor significantly associated with women not being screened for syphilis during pregnancy was attending only the first antenatal visit. The odds (adjusted odds ratio 1.82; 95% CI 1.38 - 2.39) of not being screened increased with attending only the first antenatal visit. Poor maternal syphilis screening coverage for pregnant women in their first antenatal visit in the present study demonstrates the importance of follow-up in antenatal care and screening.

Syphilis in pregnancy is known as maternal syphilis. Maternal syphilis can be transmitted to the fetus from an infected pregnant woman during the pregnancy via the placenta and during birth through the infant's contact with active syphilis lesions in the birth canal.<sup>[1]</sup> Pregnant women who are in the early stages of infection with syphilis have a high probability of transmission.<sup>[1]</sup> Untreated maternal syphilis can cause spontaneous miscarriage, stillbirth, early neonatal death, intrauterine growth restriction and perinatal death.<sup>[1]</sup> Syphilis also has consequences for infants who are born infected. These infants may develop skin rashes, severe anaemia, an enlarged liver and spleen, jaundice, nerve issues that may result in blindness or hearing impairment, meningitis, and bone damage.<sup>[2]</sup>

According to World Health Organization (WHO) 2016 global estimates, syphilis is thought to infect 2 million pregnant women annually worldwide, with 5 million occurrences of negative pregnancy outcomes.<sup>[3]</sup> The 2021 WHO priority goal is to reduce the incidence of maternal syphilis by 90% globally, aiming for a decrease in syphilis transmission from pregnant women to unborn babies through the implementation of early diagnosis of syphilis with screening and early initiation of treatment for pregnant women, and reducing the incidence of congenital syphilis to <50 infections per 100 000 live infant births.<sup>[4]</sup> To estimate and monitor the prevalence of HIV and syphilis, South Africa (SA) has conducted annual antenatal HIV sentinel surveys from 1990 to 2015, and biennial surveys from 2015 to date.<sup>[5]</sup>

Studies in Africa showed that there was poor maternal syphilis screening coverage in rural areas compared with urban areas.<sup>[4]</sup> Challenges faced by rural areas in Africa are related to poor infrastructure, poor access to healthcare facilities, poor programme activity integration, and lack of patient information on syphilis screening and treatment history, which lead to poor routine syphilis

screening, treatment and follow-up care.<sup>[6]</sup> According to most of the literature reviewed, lack of or poor routine syphilis screening during antenatal care has negative and adverse effects on pregnant women.<sup>[7]</sup> In a study conducted in Rwanda, aiming to determine trends of syphilis over time, it was discovered that poor access to public healthcare, poor infrastructure, and shortages of healthcare personnel and diagnostic tools were the main factors that led to poor syphilis screening of pregnant women.<sup>[7]</sup>

The present study aimed to assess and determine the geospatial distribution of maternal syphilis screening coverage in SA in 2017, and to determine individual and population-level factors associated with not being screened for syphilis in pregnancy in SA in 2017.

## Methods

Data from the 2017 Antenatal HIV Sentinel Survey (ANCHSS) were used in this study as a secondary data analysis. The primary study involved data collection on HIV and syphilis prevalence among all pregnant women aged 15 - 49 years attending public facilities for any antenatal care service during their current pregnancy in SA.<sup>[5]</sup> The ANCHSS was conducted from 1 October through to the second week of November 2017. The survey involved a brief interview, a review of medical records, and collection of blood samples by regular antenatal care nurses. The demographic data gathered were age, race, education level, marital status, gravidity, parity, type of antenatal visit, and gestational age.

In the present study, descriptive statistics were used to describe the enrolled pregnant women. Medians and interquartile ranges (IQRs) were used to present characteristics for continuous variables, while frequencies were used to report characteristics for categorical variables. Pearson's  $\chi^2$  test was performed for associations between different categorical variables and syphilis screening.

The geographical distribution of syphilis screening among participants based on their district and province of enrolment was analysed using ArcGIS 10.5.1 (Esri, USA) to generate thematic maps. Raster spatial data were used to create shape files and maps. A multivariable logistic regression model using predictor variables selected from univariate logistic regression was used. All analyses were weighted using survey weights.

**Results**

The overall median (IQR) age of the study participants was 26 (22 - 31) years; 45.8% of the participants were aged 25 - 34 years, and 86.7% were black Africans. The majority had completed secondary education (74.6%), were single (70.3%), lived in an urban area (64.8%), and were HIV negative (68.6%). The median age of pregnant women who were not screened for syphilis was 26 (22 - 30) years, 45.2% were aged 25 - 34 years, 85.1% were black Africans, 74.2% had secondary education, and 71.1% were single. In terms of prenatal characteristics, most of the women who were not screened had parity of  $\geq 1$  (62.9%) and gravidity of  $>1$  (67.4%) (Table 1). Figures for those who were screened were very similar at 63.0% and 66.9%, respectively. Interestingly, of those who were screened, 61.1% were attending a follow-up antenatal clinic visit, while 53.5% of those who were not screened were attending their first antenatal clinic visit (Table 1).

According to the findings of the present study, maternal syphilis screening coverage in SA in 2017 was 96.7% (95% confidence interval (CI) 96.12 - 97.20). However, this study only analysed participants who had data on syphilis screening during the 2017 HIV Sentinel Survey, i.e. only 25 188 of the participants were screened out of 26 039 participants who had data on syphilis screening outcome. Furthermore, all the nine provinces achieved maternal syphilis screening coverage  $>90\%$ , with only North West Province not reaching the global target for elimination of mother-to-child transmission of syphilis of 95% at the lowest maternal syphilis screening coverage of 93% (95% CI 81.70 - 97.53) (Fig. 1). In this study, the odds of not being screened for syphilis were higher among pregnant women who attended only their first visit for antenatal care at enrolment and lived in Gauteng, Eastern Cape, Mpumalanga, Limpopo, North West, Northern Cape or Western Cape provinces, compared with those who lived in KwaZulu-Natal Province (Table 2).

**Discussion**

Intensifying point-of-care syphilis screening during pregnancy, early diagnosis, and treatment of positive pregnant women are important in reducing maternal syphilis and its detrimental effects on pregnancy outcome. It is important to note that there needs to be improvement in the coverage of antenatal care services in hospitals and primary healthcare facilities, which should include syphilis screening and testing during pregnancy, treatment of pregnant women who

**Table 1. Antenatal characteristics of the pregnant women obtained during antenatal clinic visits according to syphilis screening status**

Variable	Screened for syphilis (n=25 188; 96.7%)			Not screened for syphilis (n=851; 3.3%)			Total (N=26 039)			p-value (χ <sup>2</sup> test)
	n	Weighted (%)	95% CI	n	Weighted (%)	95% CI	n	Weighted (%)	95% CI	
Parity										0.520
0	9 276	36.3	35.7 - 36.8	301	36.1	33.4 - 38.9	9 577	36.3	35.7 - 36.8	
$\geq 1$	15 732	63.0	62.5 - 63.6	541	62.9	60.3 - 65.4	16 273	63.0	62.5 - 63.6	
Missing	180	0.7	0.6 - 0.8	9	1.0	0.5 - 1.9	189	0.7	0.6 - 0.9	
Gravidity										0.891
1	8 367	32.6	32.1 - 33.2	267	32.1	29.7 - 34.7	8 634	32.6	32.1 - 33.1	
$>1$	16 695	66.9	66.4 - 67.4	579	67.4	64.8 - 69.8	17 274	66.9	66.4 - 67.4	
Missing	126	0.5	0.4 - 0.6	5	0.5	0.2 - 1.2	131	0.5	0.4 - 0.6	
Type of antenatal visit										$<0.001$
First	9 125	38.3	37.3 - 39.3	468	53.5	48 - 58.9	9 593	38.8	37.9 - 39.8	
Follow-up	15 916	61.1	60.1 - 62.1	379	46.2	40.7 - 51.6	16 295	60.6	59.7 - 61.6	
Missing	147	0.6	0.5 - 0.7	4	0.3	0.2 - 0.8	151	0.6	0.5 - 0.7	
Gestational age										$<0.001$
First trimester: 1 - 13 weeks	3 695	14.9	14.4 - 15.4	163	18.6	16.2 - 21.3	3 858	15.0	14.6 - 15.5	
Second trimester: 14 - 27 weeks	10 703	42.7	42.1 - 43.3	361	41.6	38.9 - 44.4	11 064	42.7	42.1 - 43.3	
Third trimester: 28 - 43 weeks	9 959	39.1	38.4 - 39.8	280	34.3	30.8 - 38.1	10 239	39.0	38.3 - 39.6	
Missing	831	3.3	3 - 3.5	47	5.4	4.1 - 7.2	878	3.3	3.1 - 3.6	
HIV and ART status										0.006
Negative	17 014	68.6	67.9 - 69.2	607	70.7	68 - 73.3	17 621	68.6	68 - 69.3	
Positive - on ART	6 771	25.7	25.1 - 26.4	183	21.9	19.3 - 24.7	6 954	25.6	24.9 - 26.2	
Positive - not started ART/unknown	1 403	5.7	5.5 - 6.0	61	7.4	5.9 - 9.3	1 464	5.8	5.5 - 6.1	

**Table 2. Factors associated with not being screened for syphilis among pregnant women in the 2017 survey**

Characteristic	Weighted % of screening coverage	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age of woman (years)					
15 - 24	3.4	1		1	
25 - 35	3.3	0.96 (0.85 - 1.08)	0.504	0.95 (0.82 - 1.10)	0.511
≥35	3.1	0.92 (0.76 - 1.12)	0.432	0.87 (0.70 - 1.08)	0.210
Race					
Non-black African	3.9	1		1	
Black African	3.2	0.84 (0.59 - 1.19)	0.319	0.94 (0.70 - 1.26)	0.675
Level of education					
None to primary education	3.1	1		1	
Secondary education	3.3	1.07 (0.79 - 1.44)	0.673	1.15 (0.85 - 1.54)	0.358
Tertiary education	3.8	1.25 (0.83 - 1.88)	0.292	1.42 (0.97 - 2.09)	0.073
Marital status					
Single	3.3	1		1	
Married/living with partner	3.2	0.94 (0.76 - 1.16)	0.562	0.86 (0.70 - 1.07)	0.184
Divorced/widowed/separated	5.9	1.80 (0.92 - 3.54)	0.086	1.94 (0.97 - 3.85)	0.060
Province					
Eastern Cape	3.7	2.37 (1.35 - 4.13)	0.002	2.40 (1.36 - 4.24)	0.003
Free State	2.2	1.38 (0.67 - 2.86)	0.380	1.43 (0.68 - 3.00)	0.348
Gauteng	3.6	2.33 (1.25 - 4.36)	0.008	2.49 (1.28 - 4.84)	0.007
KwaZulu-Natal	1.6	1		1	
Limpopo	4.1	2.64 (1.49 - 4.66)	0.001	2.62 (1.47 - 4.68)	0.001
Mpumalanga	3.5	2.23 (1.15 - 4.31)	0.018	2.34 (1.20 - 4.51)	0.012
North West	7.0	4.69 (1.4 - 15.39)	0.011	5.56 (1.65 - 18.69)	0.006
Northern Cape	3.1	2.02 (0.92 - 4.40)	0.079	2.33 (1.04 - 5.26)	0.041
Western Cape	4.7	3.08 (1.67 - 5.66)	<0.001	3.51 (1.88 - 6.55)	<0.001
Location					
Rural	3.5	1.88 (0.87 - 4.08)	0.110	2.02 (0.86 - 4.75)	0.108
Urban	3.4	1.81 (0.83 - 3.94)	0.136	1.67 (0.74 - 3.75)	0.219
Peri-urban	1.9	1		1	
Gravidity					
1	3.3	1		1	
>1	3.3	1.02 (0.91 - 1.15)	0.695	1.29 (0.98 - 1.69)	0.070
Parity					
0	3.3	1		1	
≥1	3.3	1.00 (0.89 - 1.13)	0.966	0.82 (0.63 - 1.07)	0.146
Type of antenatal visit					
Follow-up	2.5	1		1	
First	4.6	1.85 (1.47 - 2.32)	<0.001	1.81 (1.38 - 2.38)	<0.001
Gestational age					
First trimester: 1 - 13 weeks	4.1	1		1	
Second trimester: 14 - 27 weeks	3.2	0.78 (0.67 - 0.91)	0.002	0.96 (0.83 - 1.12)	0.601
Third trimester: 28 - 43 weeks	2.9	0.70 (0.56 - 0.88)	0.002	1.12 (0.91 - 1.38)	0.278
HIV and ART status					
Negative	3.4	1		1	
Positive – on ART	2.8	0.82 (0.70 - 0.97)	0.017	1.03 (0.88 - 1.21)	0.725
Positive – not started ART/unknown	4.2	1.26 (0.98 - 1.61)	0.068	1.13 (0.89 - 1.43)	0.327

OR = odds ratio; CI = confidence interval; ART = antiretroviral therapy.

are positive, and re-screening of those who initially tested negative. A 2019 study concurs with our findings; it was recommended that improving maternal syphilis point-of-care screening could reduce the turnaround time for results and improve rapid response to positive results by healthcare practitioners.<sup>[8]</sup>

The present study showed that there were differences between provinces and districts in the percentages of pregnant women who underwent syphilis screening. The discrepancies between provincial and district maternal syphilis coverage could be attributed to the provinces' different levels of resources, particularly in terms of

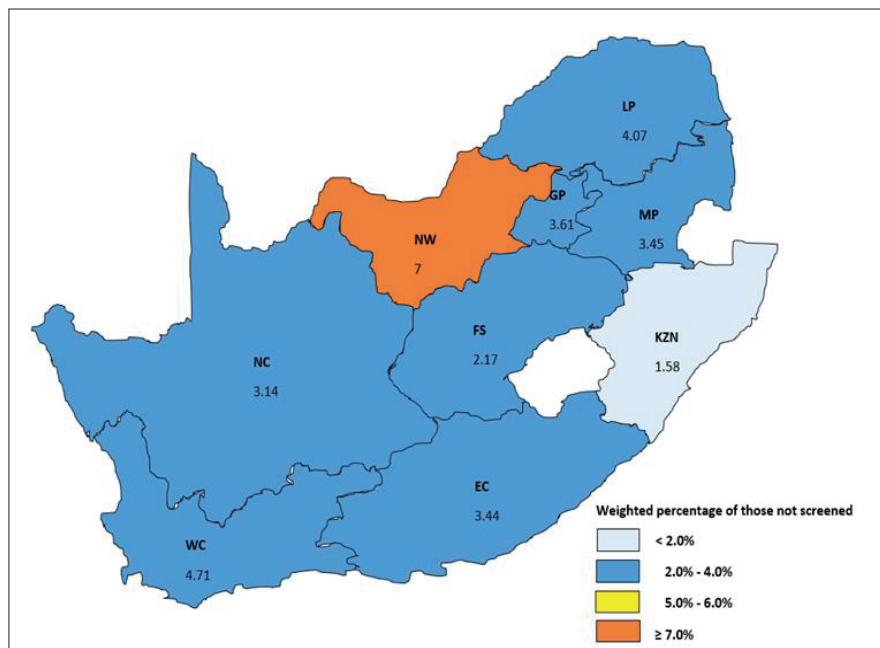


Fig. 1. Mapping of maternal syphilis coverage by province in the 2017 South African National Antenatal HIV Sentinel Survey. (LP = Limpopo Province; KZN = KwaZulu-Natal; EC = Eastern Cape; WC = Western Cape; NC = Northern Cape; NW = North West; FS = Free State; GP = Gauteng Province.)

lack of medical professionals, differences in health facilities such as poor health facility infrastructure, and limited health resources. Findings were similar in another study,<sup>[9]</sup> which showed that access to obstetric services was not evenly distributed throughout SA. The socioeconomic groups and geographical regions with the greatest disparities in access to treatment were noted.<sup>[9]</sup>

The present study revealed an association between attending only the first antenatal care visit and not being screened for syphilis. This finding points to an opportunity lost to reduce the negative effects of maternal syphilis, and the importance of follow-up antenatal care visits for prompt management of problems that arise in pregnancy. Inadequate syphilis screening at the initial antenatal visit may be associated with the pregnant woman's delay in seeking antenatal care, the woman being unaware of syphilis screening and not asking for it to be done if the healthcare practitioner does not offer it, lack of health education about syphilis screening for patients and communities, shortages of syphilis test kits, inadequate laboratory services, shortages of drugs for treatment, and poor reporting or recording by healthcare practitioners.

The study has certain limitations, as the data analysed on maternal syphilis

screening coverage and factors associated with not being screened dated from a 2017 survey, 5 years before the time of writing. It is acknowledged that the situation with regard to maternal syphilis in SA may have changed, either for the worse or for the better, given the emergence of the COVID-19 pandemic in 2020. Furthermore, the study was limited to only one maternal syphilis screening and did not assess re-screening for syphilis at 32 - 34 weeks' gestation in women who had previously screened negative. The study also has the limitation of not addressing all the 95-95-95 syphilis targets.

## Conclusion

The 2017 HIV seroprevalence survey showed 96.7% maternal syphilis screening coverage in SA. Attending only the first antenatal visit was the only factor significantly associated with not being screened for syphilis. The study indicates that further studies on maternal syphilis screening coverage and factors associated with not being screened for syphilis in pregnancy are necessary. We also recommend qualitative studies on pregnant women and healthcare providers to understand barriers to syphilis screening from the perspective of both patient and healthcare provider.

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# An audit of maternal deaths from tuberculosis in eThekweni District: 2020 - 2022

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Tuberculosis (TB) is the main cause of maternal deaths in non-pregnancy-related infections. We audited maternal deaths with a TB diagnosis in the eThekweni District for the triennium of 2020 - 2022. Among the 23 recorded deaths, only 47.8% ( $n=11$ ) were booked, 87% ( $n=20$ ) were HIV positive and 65.2% ( $n=15$ ) were diagnosed with disseminated TB. Sensitivity was only known for 15 women. The most common symptom was shortness of breath. Modifiable factors were found in 69.6% ( $n=16$ ) of the cases, with the main factors being delayed investigation for TB, unchecked persistent tachycardia and failure to recognise a sick patient. In addition, almost all the booked women did not receive a routine GeneXpert test or TB preventative therapy.

Maternal deaths attributed to non-pregnancy-related infections (NPRI) have been decreasing. The Saving Mothers Report<sup>[1]</sup> for the triennium spanning 2017 - 2019 showed a substantial reduction in maternal deaths, amounting to 21.3%, compared with the previous report. However, NPRI was the leading cause of maternal deaths overall and was the most common cause of maternal deaths in six provinces. Tuberculosis (TB) was the main cause of death in the NPRI category. A marginal decline of 7.3% was observed in TB-related deaths when compared with the 2014 - 2016 period.<sup>[2]</sup> TB was also the leading cause of death in the eThekweni District, KwaZulu-Natal Province, during the 2017 - 2019 period, accounting for 29 cases of maternal deaths attributed to TB.

The World Health Organization (WHO) recommends that systematic screening for active TB should be considered for pregnant women as part of antenatal care (ANC). In South Africa (SA), the WHO 4 symptom screen has been part of Basic Antenatal Care Plus (BANC+). Any one of the four symptoms—cough, fever, weight loss or night sweats—may indicate TB and should prompt a TB evaluation. The recent evidence from the *WHO 2021 guidelines for TB*<sup>[3]</sup> outlined its poor sensitivity. Due to the poor sensitivity of the symptom screening tool for HIV-positive pregnant women, the 2019 Prevention of mother to child transmission (PMTCT)<sup>[4]</sup> guidelines recommended a routine GeneXpert (GXP) for all pregnant women who are HIV-positive at the first ANC visit.

TB preventative therapy (TPT) was also recommended for all HIV-positive women for whom TB was excluded. Most people with latent TB will not develop active TB, however, for those who are at high risk, TPT can significantly reduce their risk of developing active disease. SA has also introduced the use of lateral flow urine lipoarabinomannan (LF-LAM) assay for the diagnosis of active TB in people living with HIV.<sup>[5]</sup> In 2021 (circular 2021/06/29/EDP/01), dolutegravir (DTG) was introduced into the treatment regimen for pregnant women. Following a comprehensive review of the evidence, the *National Essential Medicines List Committee* concluded that, in comparison with efavirenz, the benefits of DTG outweighed the risks and recommended it as part of the preferred first-line ART for all adults and adolescents, including pregnant women and women of childbearing potential. Despite all these policies and guidelines in place, maternal deaths from TB persist. TB is largely curable and preventable. The main aims of the audit, therefore, were to determine the modifiable factors present, including compliance with the guidelines, and to determine TB characteristics.

## Methods

All maternal deaths in the eThekweni District are reported to the district clinical specialist team obstetrician. All instances of maternal deaths related to TB from 2020 - 2022 were analysed and the data were collected using a data sheet.

## Results

In total, 23 maternal deaths were determined to be attributed to TB. Eleven (47.8%) women were booked. Four women had a previous TB diagnosis. Most ( $n=14$ ; 60.9%) women died without giving birth. Of the 23 women, 20 (87%) were HIV positive. Details of the HIV-positive patients' deaths are presented in Table 1.

Among HIV-negative women, two died. Both women were not booked. Case 1 presented with clinical features indicative of a ruptured ectopic pregnancy and she died within 2 hours of arrival. The diagnosis of TB was made on a post-mortem examination. In case 2, the patient presented with symptoms of a respiratory tract infection. However, there was a 10-day delay in obtaining the GXP result and conducting testing for multi-drug resistant (MDR) TB. Although MDR TB treatment was initiated in the intensive care unit (ICU), she died the following day.

Tables 2 and 3 outline the details of TB and presenting symptoms, respectively. In 15 (65.2%) cases, the diagnosis was disseminated TB. The sensitivity was only determined in eight cases. In 12 (52.2%) cases, the diagnosis was made based on clinical assessment and chest x-ray findings. GXP, LF-LAM and lumbar puncture were the diagnostic tests in 10 (43.5%), eight (34.8%) and one case, respectively. In one case, the diagnosis was confirmed through echocardiography. Twelve (52.2%) women presented with chest signs.

TB treatment was initiated in 17 patients. Among the 23 cases of maternal deaths, 13 (56.5%) patients died within 5 days or less of commencing treatment and six died within 1 day of commencement of treatment.

In 16 (69.6%) cases, modifiable factors were present, all of which involved a delay in investigating or checking for TB results. Persistent tachycardia was not managed in 15 (65.2%) cases. In eight cases (34.8%), there was a failure to recognise the sick patient. In three cases, there was a delay in commencing treatment after the diagnosis. Weight loss was not managed in two patients. Ten of the 11 booked patients did not receive consistent TB screening, only two of the 11 had a routine GXP at the first visit and none were offered TPT.

**Table 1. HIV-related deaths (n = 20)**

Variable	n, %
Booked	11 (47.8%)
CD4 count tests performed	20 (100%)
CD4 <200 cells/mm <sup>3</sup>	15 (75%)
CD4 <100 cell/mm <sup>3</sup>	13 (65%)
VL tests performed	11(55%)
VL = LDL (LDL)	3 (15%)
Previous TB	4 (20%)
On ART before pregnancy	4 (20%)
ART commenced during pregnancy	7(35%)

VL = viral load; LDL = lower than detectable level; TB = tuberculosis; ART = antiretroviral treatment.

**Table 2. Details of tuberculosis**

Variables	n
Disseminated TB	15
Extrapulmonary TB	3
Pulmonary TB	5
Rifampicin-sensitive TB	7
MDR TB	1
Unknown sensitivity	15

TB = tuberculosis; MDR = multidrug resistant.

**Table 3: Presenting symptoms**

Symptom	n
Shortness of breath	15
Cough	12
Malaise	6
Night sweats	5
Fever	4
Loss of weight	4
Chest pain	4
Photophobia	1
Haemoptysis	1
Headache	1
Diarrhoea	1

## Discussion

There was a 20% improvement in the number of TB deaths in the 2017 – 2019 period. This observation could be due to the partial implementation of the PMTCT guidelines. It is not possible, however, to exclude missed cases because of the Covid-19 pandemic.

Many of these women were sick, immunocompromised and treatment defaulters when they accessed the maternity care services. Despite this, there were many opportunities to screen, diagnose and commence early treatment. In 16 (69.6%) cases, modifiable factors were identified.

The PMTCT guideline recommendations were not followed. Only two patients had the routine GXP, and neither were offered TPT. This could be partially attributed to the initial focus of the guidelines ‘training’ on nurses.

Another main problem identified was the difficulty in identifying the sick patient and responding appropriately. Persistent tachycardia was unnoticed, or its significance was not appreciated. The root causes likely stem from a combination of factors, including lack of knowledge, incomplete clinical assessments, lack of supervision and systemic issues.

Healthcare workers in maternity care need to have a heightened level of suspicion for TB. They should be aware of the poor sensitivity of the symptom screening tool and the difficulties in making a diagnosis in immunocompromised patients. The commonest symptom was shortness of breath, which is not on the WHO 4 symptom screen. In many cases of active TB, the results of the symptom screening would appear normal. Healthcare workers in maternity care should be familiar with the different diagnostic tests for TB and the TB diagnostic algorithm.

## Conclusion

To mitigate maternal deaths resulting from TB during pregnancy, improvements must be made in HIV care and the detection of TB beyond the pregnancy context. Further, more can be done by maternity care providers to prevent, diagnose and treat TB when at-risk women access maternity care services. Widespread application of the PMTCT guidelines is a starting point.

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# Quality of breastmilk produced by mothers of preterm infants and the infants' short-term outcomes at two tertiary hospitals in Bloemfontein, South Africa

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Breastfeeding is widely acknowledged to enhance infant survival, health and overall development. This study aimed to investigate the quality of breastmilk produced by mothers of infants weighing <1 500 g, focusing on short-term outcomes. We evaluated the macronutrient composition, specifically protein and triglycerides, total calcium, and energy levels in breastmilk from mothers who had delivered preterm infants. There was a significant reduction over the first 2 weeks after birth in the mean (standard deviation) protein and energy content of breastmilk, from 2.9 (1.6) to 1.8 (1.1) g/dL ( $p<0.001$ ) and 116.1 (65.0) to 73.5 (42.0) kcal/dL ( $p<0.001$ ), respectively. There was a significant increase in mean calcium from 5.8 (1.7) to 6.3 (2.0) mmol/L ( $p=0.002$ ) over the 2 weeks. There were no statistically significant changes in triglycerides ( $p=0.176$ ). There was significant weight gain velocity. These findings highlight the importance of fortifying breastmilk with energy (calories) and protein to optimise the growth of preterm infants.

Human milk is the gold standard for neonatal nutrition, especially for very low-birthweight (VLBW) infants, whose nutritional demands exceed those of term neonates.<sup>[1,2]</sup> Despite its virtues, however, human milk alone cannot fully meet the elevated requirements of preterm infants, potentially impeding their optimal growth, a critical factor for long-term neurodevelopment and overall health.<sup>[1,3]</sup> The nutritional composition of human milk is intricate and is influenced by variables such as lactation stage, milk type (mother's own milk or donor human milk) and maternal diet. In low- and middle-income countries (LMICs), outdated data underscore deficiencies in breastmilk protein, energy and minerals that hinder targeted growth for preterm infants.<sup>[3,4]</sup>

In LMICs, a pervasive challenge stems from suboptimal nutritional status of women during their childbearing years, often indicative of poverty. Global initiatives, notably the 2030 Sustainable Development Goal 2, underscore the urgency of eradicating worldwide hunger, emphasising the critical role of adequate maternal nutrition. Essential tools for antenatal nutritional assessment, including mid-upper arm circumference (MUAC) and body mass index (BMI), are outlined in the 2017 Basic Antenatal Care (BANC-Plus) guidelines.<sup>[5]</sup>

Existing fortification practices, primarily based on high-income country guidelines, may not be universally applicable. Integrating antenatal and postnatal supplementation into healthcare protocols is therefore imperative, especially considering the differing maternal nutritional status in LMICs. Optimal maternal nutrition and supplementation during the antenatal period are vital for the mother and ensure the provision of high-quality breastmilk to the newborn infant. This study assessed the quality of breastmilk produced by mothers of preterm infants, emphasising the need for tailored nutritional interventions encompassing the antenatal and postnatal phases.<sup>[6,7]</sup>

## Methods

The study employed a prospective, descriptive approach, evaluating the macronutrient composition (specifically protein and triglycerides), total calcium, and energy levels in breastmilk from mothers who had delivered infants weighing <1 500 g at two tertiary hospitals in Bloemfontein, South Africa. Ethical approval for the study was obtained from the University of the Free State (UFS)'s Health Sciences Research Ethics Committee (ref. no. UFS-HSD2021/0174/2610), and participants were carefully selected based on the following inclusion criteria: exclusive breastfeeding; infant weighing <1 500 g; and infant referred within 48 hours from a peripheral health facility or born at Universitas Academic Hospital or Pelonomi Tertiary Hospital.

Two breastmilk specimens (~2 - 3 mL of hindmilk) were collected from each mother in dedicated specimen bottles during the postpartum period, on days 2 - 3 (week 1) and days 12 - 14 (week 2) of postnatal age. The breastmilk specimens were collected between 09h00 and 12h00 and transferred on ice to the laboratory for analysis on a Roche Cobas analytical system (Cobas Integra 400 Plus/Cobas c 311, Cobas c 501/502; Roche Diagnostics Corp., USA) at the Universitas Hospital National Health Laboratory Service (NHLS) Chemical Pathology Division.

Calories were measured using a calorimetric test. A colorimetric assay test was used to analyse the total protein, and an enzymatic colorimetric test to analyse the triglyceride content. The calcium concentration was determined by assessing the change in absorbance directly proportional to the calcium concentration and was measured photometrically. The study infants' weekly weight and head circumference were plotted on a Fenton growth chart. The UFS Department of Biostatistics analysed the data using SAS 9.4 statistical analysis software (SAS Institute, USA). Patients who did not have

milk collected or tested at both periods were excluded from the comparisons. Comparisons between the two weeks were performed using paired *t*-tests for normally distributed variables and Wilcoxon signed-rank tests for non-parametric variables. Differences with a *p*-value <0.05 were considered statistically significant.

## Results

Of 82 eligible mothers enrolled in the study, 12 did not have specimens collected for week 2 and were therefore not included in the paired analysis. The study shed light on maternal nutritional status (Table 1), emphasising the prevalence of undernourished mothers ( $n=14/82$ ), of whom 11 (79%) had received antenatal care. Although none of these 11 undernourished mothers received no antenatal supplementation, antenatal care attendance did not translate to adequate nutritional support in this subgroup, highlighting critical gaps in existing healthcare practices.

A total mean weight gain of 507.5 g (range 410.0 - 678.5) was achieved over a mean period of 38 days (average length of stay), with a statistically significant weight gain velocity of 13.4 g/d.

Key findings were that there were changes in human milk composition from the first 2 - 3 days of life to the 2nd week of life (Table 2), notably a decline in total protein ( $p<0.001$ ) and energy ( $p<0.001$ ) and an increase in calcium ( $p=0.002$ ), but that there was no significant change in triglycerides ( $p=0.176$ ).

## Discussion

Our study showed that over the first 2 weeks of postnatal life there were reductions in protein and energy content and increased triglyceride levels in breastmilk from mothers who delivered preterm. Comparing our results with the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) (2022) standards, our findings align with their ranges except for calories at days 2 - 3, which were notably higher in our study.<sup>[8]</sup> This variation corresponds with the findings of Gidrewicz and Fenton's<sup>[3]</sup> systematic review, which indicated a reduction in protein and energy over time in preterm human milk. Furthermore, research conducted in Germany by Bauer and Gerss in 2011, in conjunction with the ESPGHAN Committee on Nutrition, 2022,<sup>[8]</sup> highlighted the rapid decline in protein content with progressing lactation weeks. According to these findings, it is recommended that very preterm infants, particularly during the first 2 weeks of life, should receive a minimum of 3.5 - 4.5 g protein/kg/d.<sup>[8]</sup> Studies examining the triglyceride/fat composition of human milk, including the Gidrewicz and Fenton<sup>[3]</sup> review, indicate an increase over time in preterm human milk, with a notable 50% increase in fat content.<sup>[3]</sup>

Additionally, our study revealed slightly higher calcium levels in week 2 breastmilk specimens compared with days 2 - 3. This finding is not aligned with existing research indicating an initial calcium concentration of ~7.0 mmol/L in preterm human milk, which decreases during lactation.<sup>[3,8,9]</sup> Maternal nutrition and eating habits during lactation are of pivotal importance yet often suboptimal, especially in low-resource settings. Our study revealed a concerning 17% ( $n=14/82$ ) prevalence of undernourished mothers (MUAC <23 cm); 11/14 women in this subgroup (79%) attended antenatal care at primary healthcare level, but did not receive sufficient essential food supplementation. Surprisingly, maternal BMI and MUAC did not affect human milk composition, suggesting complex underlying factors.<sup>[1,2,10]</sup> Considering the initial weight loss experienced by preterm infants in the first 14 - 21 days, fortifying human milk becomes imperative. In our study, bovine-derived multinutrient fortification commenced at 150 mL/kg/d, aligning with similar studies suggesting that fortification can start as low as 100 mL/kg/d.

**Table 1. Baseline characteristics of mothers and infants**

Variable	<i>n</i> (%) <sup>*</sup>
Mothers ( <i>N</i> =82)	
Age (years)	
<18	5 (6.1)
19 - 34	59 (71.95)
>35	18 (21.95)
Comorbidities	
Hypertension	16 (19.5)
Asthma	2 (2.4)
Epilepsy	2 (2.4)
Other (depression)	2 (2.4)
BMI (kg/m <sup>2</sup> ), mean (range)	27.15 (23.2 - 32.7) <sup>*</sup>
MUAC (cm)	
<23	14 (17.1)
23 - 33	53 (64.6)
>33	15 (18.3)
Primigravida	22 (26.8)
Antenatal care	
Attendance	67 (81.7)
No attendance	15 (18.3)
No antenatal food supplementation received	0
Previous breastfeeding experience	60 (73.2)
Antenatal breastfeeding education	44 (53.7)
Caesarean section	41 (50.0)
Infants ( <i>N</i> =82)	
Gestational age (weeks)	
<30	40 (48.7)
30 - 32	30 (36.59)
>32	12 (14.63)
Birthweight (g), mean (range)	1 240 (1 060 - 1 370)
Small for gestational age	27 (32.9)
Fortification	67 (81.7)
Days of life full feeds achieved, mean (range)	9 (7 - 12)
Length of stay (days), mean (range)	38 (28 - 46)
Weight gain velocity (g), over mean of 38 days, mean (range)	507.5 (410.0 - 678.5) ( $p<0.001$ ; $\chi^2$ test)

BMI = body mass index; IQR = interquartile range; MUAC = mid-upper arm circumference.

<sup>\*</sup>Except where otherwise indicated.

These fortifiers typically provide ~1 - 1.1 g additional protein per dL, crucial for enhancing weight gain. Notably, Kashyap and Heird's<sup>[10]</sup> study underscored the positive impact of protein supplementation, indicating that adding 1 g/kg of protein to a human milk diet increased weight gain significantly. Following ESPGHAN committee guidelines and corroborated by previous studies, our findings emphasise the critical importance of fortification to meet the recommended requirement of 15 - 20 mg/kg/d for adequate weight gain in preterm infants.<sup>[3,8]</sup> These insights underscore the significance of tailored nutritional interventions to optimise the growth and development of these infants, especially in resource-challenged environments.

## Study limitations

- The BMI/MUAC of the lactating mothers was used as a proxy to determine maternal nutritional status.

**Table 2. Protein, triglyceride, energy and calcium composition of human milk from mothers of preterm infants in the first 2 weeks of lactation**

Variable	Day 2 - 3 postnatal age (N=70), mean (SD)	Day 12 - 14 postnatal age (N=70), mean (SD)	Mean difference (95% CI)	p-value
Protein (g/dL)	2.9 (1.6)	1.8 (1.1)	9.6 (4.9 - 14.3)	<0.001
Triglycerides (g/dL)	4.0 (4.7)	4.6 (4.7)	-0.6 (-2.0 - 0.8)	0.176
Calories (kcal/dL)	116.1 (65.0)	73.5 (42.0)	38.5 (19.6 - 57.4)	<0.001
Calcium (mmol/L)	5.8 (1.7)	6.3 (2.0)	-0.7 (-1.1 - -0.2)	0.002

SD = standard deviation; CI = confidence interval.

- The NHLS does not routinely test human milk, so the machine must be standardised.
- The carbohydrate level of human milk was not included in the study.

### Recommendations

- Food supplementation for mothers during the antenatal and lactating periods to optimise their nutritional status, especially those who are underweight.
- Early antenatal booking, with iron, folic acid and calcium supplementation started as soon as possible, early evaluation to detect inadequate nutrition, and timeous referral to the dietician for intervention.
- Promote exclusive breastfeeding practices to pregnant women and support them in achieving these, because of the benefits and cost-effectiveness of human milk.
- Implement strategies to sustain human milk volume, especially promoting kangaroo mother care/skin-to-skin practices that improve milk production and assist bonding between mother and infant.
- Fortification of human milk to meet requirements by improving protein and energy composition to improve growth outcomes of preterm and VLBW infants could decrease hospital stays.
- Standardisation of a nutrition protocol for premature infants in our setting would assist in reducing costs and supporting low-income mothers.
- A longitudinal meta-analysis in our setting would contribute to the minimal studies available in LMICs.

### Conclusion

This study demonstrated a decline in protein and energy content in breastmilk from mothers delivering infants weighing <1 500 g, with increased triglyceride levels, over the first 2 weeks after birth. These changes were unaffected by maternal and neonatal factors. Considering these findings, promoting the fortification of breastmilk is essential to support adequate growth in preterm infants, emphasising the vital role of tailored nutritional interventions in neonatal care.

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**Author contributions.** AJ: principal researcher, study conceptualisation and design, data collection, analysis and interpretation of results, manuscript writing and editing. TBM: supervision of study concept and design, critical revision of clinical content and interpretation of results. TCvR: analysis of biostatistics data. CJM: laboratory analysis of breastmilk specimens. Final approval of the version to be published: all authors.

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# Risk factors for intraventricular haemorrhage in very low-birthweight infants at Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa

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Intraventricular hemorrhage (IVH) is the commonest form of bleeding in the central nervous system in premature neonates. Risk factors are multifactorial and related to events that may occur *in utero*, peripartum and postnatally. In a retrospective descriptive study, a total of 1 590 very low-birthweight infants (<1 500 g) were admitted to a neonatal unit over a 2-year period, and 529 who had cranial ultrasound scans were studied. Infants with IVH were cases and those without IVH were controls. Thirty-three percent ( $n=176$ ) had IVH, which was severe (grades 3 and 4) in 43.8% ( $n=77$ ). Apgar score <6 at 5 minutes, intubation and meningitis were associated with IVH. Cases had a higher likelihood than controls of post-haemorrhagic hydrocephalus and death. On multivariate analysis, risk factors for IVH were low Apgar score at 5 minutes, intubation and meningitis.

Intraventricular haemorrhage (IVH) is a subependymal germinal matrix haemorrhage, intraventricular haemorrhage, or IVH and parenchymal haemorrhage.<sup>[1]</sup> It is the commonest form of bleeding in the central nervous system in premature neonates.<sup>[2]</sup>

The most commonly used classification of IVH is that of Papile *et al.*,<sup>[1]</sup> who described four grades of IVH: grade 1 is bleeding confined to the germinal matrix, grade 2 is IVH without ventricular dilation, grade 3 is IVH with ventricular dilation, and in grade 4 there is additional bleeding in the brain parenchyma.<sup>[1]</sup> Mild bleeds, classified as grades 1 and 2, usually resolve; grades 3 and 4 are severe and associated with adverse outcomes.<sup>[1]</sup>

The risk factors for IVH are multifactorial and the pathogenesis is attributed to the germinal matrix fragility and impaired cerebral autoregulation due to immaturity in preterm neonates. Factors associated with decreased IVH rates are antenatal steroids, hypertension in pregnancy, and administration of magnesium sulphate ( $MgSO_4$ ).<sup>[3]</sup> The aim of the present study was to describe the characteristics, risk factors, morbidity, mortality and outcome of very low-birthweight (VLBW) neonates with IVH.

## Methods

This was a retrospective, descriptive study in the neonatal unit at Chris Hani Baragwanath Academic Hospital (CHBAH), Johannesburg, South Africa. The unit captures all admitted patients on a REDCap (Research Electronic Data Capture) database.<sup>[4]</sup> The study population included all VLBW premature infants (<1 500 g) who were admitted between January 2017 and December 2018 and had cranial ultrasound scans during their admission. According to the neonatal protocol at CHBAH, all VLBW infants have cranial ultrasound screening during the first 7 days after birth, at 14 days and at 28 days. The reasons for the cranial ultrasound scans in this study population were probably unit protocol or other reasons that were not explored in the study.

Infants excluded from the study were those with severe malformations, cranial ultrasound abnormalities other than IVH, and incomplete data. IVH was classified according to the Papile classification.

Maternal demographic data, neonatal characteristics and outcome variables were extracted for each infant from the REDCap database. The infants were then assigned to cases (those with IVH) and controls (those without IVH).

## Ethics considerations

The Human Research Ethics Committee at the University of the Witwatersrand approved the study (ref. no. M190739) and the neonatal REDCap database (ref. no. M115196).

## Statistical analysis

Data were analysed using Stata version 15.1 (StataCorp, USA). Continuous demographic data were summarised and analysed using medians and interquartile ranges, where appropriate, and then grouped into categories. Pearson's  $\chi^2$  tests and Student's *t*-tests were used to assess associations between outcome variables and demographic and clinical characteristics. A multivariable logistic regression model of the outcome variables was constructed to control for confounders and identify independent predictors. Associations with these predictors are reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs) and *p*-values. A *p*-value <0.05 was considered statistically significant.

## Results

Five hundred and twenty-nine of the 1 590 VLBW infants who were admitted met the study criteria and were included in the study cohort. One hundred and seventy-six infants (33.3%) had IVH (cases). Of the 176 who had IVH, 56.3% had mild IVH (grades 1 and 2) and 43.7% had severe IVH (grades 3 and 4) (Fig. 1).

**Table 1. Characteristics of the study population**

	Total (N=529), n (%) <sup>*</sup>	Cases, IVH (n=176; 33.3%), n (%) <sup>*</sup>	Controls, no IVH (n=353; 66.7%), n (%) <sup>*</sup>	p-value
Maternal age (years), mean (SD)	27.5 (7.3)	27.1 (7.8)	27.7 (7.1)	0.405
Maternal age (years)				0.343
<20	60 (11.3)	18 (10.2)	42 (11.9)	
20 - 40	447 (84.5)	148 (84.1)	299 (84.7)	
>40	16.3 (3.0)	6 (3.4)	10 (2.8)	
Undocumented	6 (1.1)	4 (2.3)	2 (0.6)	
Maternal parity, median (SD)	2 (1 - 3)	2 (1 - 3)	1 (1 - 2)	0.002
Maternal parity				0.033
0 - 1	243 (45.9)	93 (52.8)	152 (43.1)	
>2	286 (54.1)	83 (47.2)	201 (56.9)	
Maternal comorbidities				
Hypertension	105 (21.0)	17 (9.7)	88 (24.9)	<0.001
Diabetes mellitus	4 (0.8)	2 (1.1)	2 (0.6)	0.603
Antenatal steroids	196 (37.1)	53 (30.1)	143 (40.5)	0.020
MgSO <sub>4</sub>	47 (8.9)	5 (2.8)	42 (11.9)	<0.001
Place of birth				0.317
Inborn	469 (88.7)	153 (87.4)	316 (89.5)	
Outborn	56 (11.3)	22 (12.6)	34 (9.7)	
Mode of delivery				0.007
Vaginal	212 (40.0)	81 (46.0)	131 (37.1)	
Caesarean	292 (55.2)	82 (46.6)	210 (59.5)	
Undocumented	25 (4.7)	13 (7.4)	12 (3.4)	
Gestational age (weeks), mean (SD)	29.4 (2.6)	29.9 (2.7)	28.4 (2.3)	<0.001
Gestational age (weeks)				<0.001
<30	264 (49.9)	115 (65.3)	149 (42.2)	
≥30	258 (49.4)	58 (33.5)	200 (57.3)	
Birthweight (g), mean (SD)	1 156 (209)	1 077 (200)	1 195 (203)	<0.001
Birthweight (g)				<0.001
<1 000	121 (22.9)	62 (36.9)	59 (15.9)	
1 000 - 1 500	408 (77.1)	114 (64.8)	294 (83.3)	
Sex				0.018
Male	262 (49.5)	100 (56.8)	162 (45.9)	
Female	267 (50.5)	76 (43.2)	191 (54.1)	
Resuscitation	313 (59.2)	102 (58.0)	211 (59.8)	0.708
Bag-mask ventilation	183 (34.6)	55 (31.3)	128 (36.2)	0.286
CPR	17 (3.2)	8 (4.5)	9 (2.5)	0.294
Intubation	16 (3.0)	12 (3.4)	4 (1.1)	0.001
Adrenaline	5 (0.009)	3 (0.017)	2 (0.0057)	0.339
Apgar at 1 min, median (IQR)	7 (5 - 8)	5 (2 - 8)	7 (5 - 8)	<0.001
Apgar <6 at 1 min	181 (34.2)	107 (60.8)	134 (38.0)	<0.001
Apgar at 5 min, median (IQR)	9 (7 - 10)	8 (5 - 9)	9 (8 - 10)	<0.001
Apgar <6 at 5 min	61 (11.5)	58 (33)	31 (8.8)	<0.001
nCPAP	321 (60.7)	109 (61.9)	212 (60.1)	0.706
IPPV	132 (25.0)	67 (38.1)	65 (18.4)	<0.001
Surfactant	164 (31.5)	74 (42.0)	90 (26.0)	<0.001
Hypotension	77 (14.6)	45 (25.6)	32 (9.1)	<0.001
Inotropic support	66 (12.5)	40 (22.7)	26 (7.4)	<0.001
Sepsis	203 (38.8)	117 (66.5)	86 (24.4)	<0.001
Meningitis	162 (30.6)	143 (81.3)	19 (5.4)	<0.001
Seizures	31 (5.9)	26 (14.8)	5 (1.4)	<0.001
PHHC	12 (2.3)	11 (6.3)	1 (0.3)	<0.001
Discharge	392 (74.0)	82 (46.6)	310 (87.8)	<0.001
Death	134 (25.3)	92 (52.3)	42 (11.9)	<0.001

SD = standard deviation; IVH = intraventricular haemorrhage; MgSO<sub>4</sub> = magnesium sulphate; CPR = cardiopulmonary resuscitation; IQR = interquartile range; nCPAP = nasal continuous positive-pressure ventilation; IPPV = intermittent positive-pressure ventilation; PHHC = post-haemorrhagic hydrocephalus.

<sup>\*</sup>Except where otherwise indicated.

**Table 2. Multivariate logistic regression analysis of characteristics associated with IVH**

Variable	IVH		
	aOR	95% CI	p-value
Maternal parity			
0 - 1	Ref.	-	-
>2	0.801	0.380 - 1.689	0.560
Maternal hypertension	0.370	0.128 - 1.072	0.067
Antenatal steroids	0.936	0.434 - 2.018	0.866
MgSO <sub>4</sub>	0.159	0.024 - 1.050	0.056*
Mode of delivery			
Vaginal	Ref.	-	-
Caesarean	1.306	0.472 - 3.618	0.607
Undocumented	1.658	0.122 - 22.605	0.704
Gestational age (weeks)			
<30	Ref.	-	-
≥30	0.911	0.763 - 1.087	0.302
Birthweight (g)			
<1 000	Ref.	-	-
1 000 - 1 500	0.999	0.997 - 1.001	0.303
Sex			
Male	Ref.	-	-
Female	0.575	0.277 - 1.194	0.138
Intubation	8.822	1.379 - 56.414	0.021*
Apgar <6 at 1 min	0.710	0.304 - 1.661	0.430
Apgar <6 at 5 min	8.174	2.540 - 26.301	<0.001*
IPPV	0.845	0.332 - 2.155	0.725
Surfactant	1.548	0.719 - 3.332	0.264
Hypotension	0.314	0.027 - 3.582	0.351
Sepsis	0.5561	0.224 - 1.382	0.207
Meningitis	104.921	40.103 - 274.502	<0.001*
Seizures	2.094	0.401 - 10.949	0.381
PHHC	20.245	1.210 - 338.835	0.036*
Outcome			
Discharged	Ref.	-	-
Died	3.703	1.499 - 9.145	0.005*

IVH = intraventricular haemorrhage; aOR = adjusted odds ratio; CI = confidence interval; MgSO<sub>4</sub> = magnesium sulphate; IPPV = intermittent positive-pressure ventilation; PHHC = post-haemorrhagic hydrocephalus.

\*Significant ( $p < 0.05$ ). Logistic regression with all variables with a  $p$ -value  $< 0.1$  included. All logistic regression analyses were performed at 95% CI.

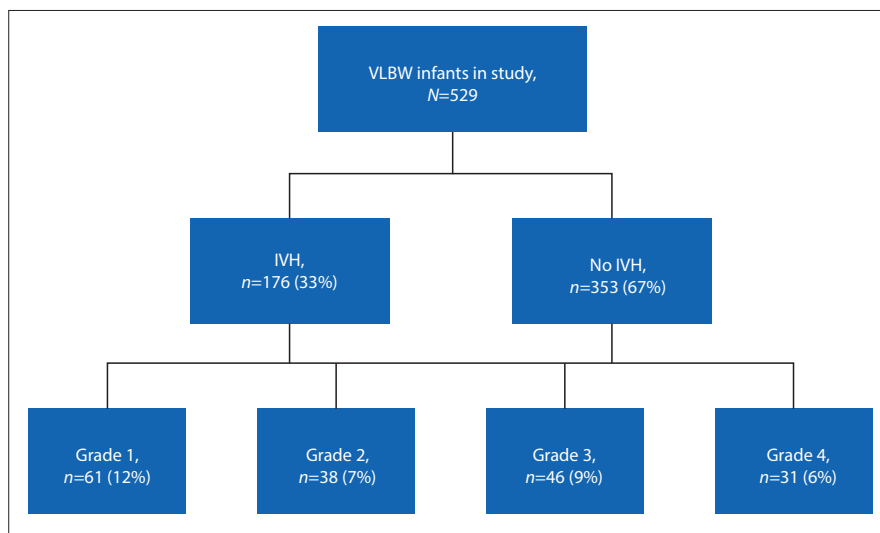


Fig. 1. Consort diagram of neonates with IVH. (IVH = intraventricular haemorrhage; VLBW = very low-birthweight.)

The majority of the mothers were between 20 and 40 years of age. Mothers in the control group had higher parity than the cases (56.9% v. 47.2%  $> 2$ ;  $p = 0.033$ ), and more mothers in the control group had hypertension (24.7% v. 9.7%;  $p < 0.001$ ) and received antenatal steroids ( $p = 0.020$ ) and MgSO<sub>4</sub> ( $p < 0.001$ ) (Table 1).

Infants with IVH had lower gestational age (28 weeks v. 30 weeks;  $p < 0.001$ ) and lower birthweight (1 077 g v. 1 195 g;  $p < 0.001$ ) than the controls. Seventy-seven percent of neonates in the study population weighed 1 000 - 1 500 g, but more cases were observed in the group weighing  $< 1$  000 g (36.9% v. 15.9%;  $p < 0.001$ ). More males than females had IVH (56.8% v. 45.9%;  $p = 0.018$ ) (Table 1).

There were no differences between the groups with regard to need for resuscitation, but cases had a higher intubation rate than

controls (3.4% v. 1.1%;  $p=0.001$ ). The median Apgar score at 1 minute (5 v. 7;  $p<0.001$ ) and 5 minutes (8 v. 9;  $p<0.001$ ) was lower in the cases. There was no difference in the use of nasal continuous positive-pressure ventilation between the groups ( $p=0.706$ ). More cases than controls were ventilated ( $p<0.001$ ), received surfactant ( $p<0.001$ ), had hypotension ( $p<0.001$ ) and required inotropes ( $p<0.001$ ), and a higher proportion of cases had sepsis (66.5% v. 24.4%;  $p<0.001$ ) and meningitis (81.3% v. 5.4%;  $p<0.001$ ).

Twenty-six (14.8%) of the 176 neonates with IVH had seizures ( $p<0.001$ ). Eleven (91.6%) of the 12 neonates who developed post-haemorrhagic hydrocephalus (PHHC) had IVH ( $p<0.001$ ). A higher proportion of controls than cases were discharged (87.8% v. 46.6%;  $p<0.001$ ), and mortality was higher among the cases (52.3% v. 11.9%;  $p<0.001$ ).

On univariate analysis, risk factors for IVH were higher parity ( $p=0.002$ ), normal vaginal delivery ( $p<0.007$ ), birthweight  $<1\ 000\ g$  ( $p<0.001$ ), gestational age  $<30$  weeks ( $p<0.001$ ), being male ( $p=0.018$ ), intubation ( $p<0.001$ ), having an Apgar score  $<6$  at 5 minutes ( $p<0.001$ ), receiving IPPV ( $p<0.001$ ) and surfactant ( $p<0.001$ ), being hypotensive ( $p<0.001$ ) and requiring inotropic support ( $p<0.001$ ), and having sepsis ( $p<0.001$ ) and meningitis ( $p<0.001$ ). Protective factors were receiving antenatal steroids ( $p=0.020$ ) and  $MgSO_4$  ( $p<0.001$ ). On multivariate analysis, neonates with an Apgar score  $<6$  at 5 minutes (aOR 8.174; 95% CI 2.54 - 26.30) and those who were intubated (aOR 8.822; 95% CI 1.38 - 56.41) or had meningitis (aOR 104.921; 95% CI 40.10 - 274.50) were more likely to have IVH. Infants with IVH had a 20-fold increased chance of having PHHC (aOR 20.255; 95% CI 1.21 - 338.84) and a higher likelihood of mortality (aOR 3.703; 95% CI 1.50 - 9.15) (Table 2).

## Discussion

The present study revealed significant risk factors for IVH on multivariate analysis. A low Apgar score of  $<6$  at 5 minutes was identified as a risk factor, with an 8-fold increase in IVH. Consistent with our study, low Apgar scores and perinatal asphyxia have been reported as risk factors for IVH and severe forms of IVH.<sup>[5]</sup> In a preterm baby, the germinal matrix has fragile microvasculature, making it vulnerable to postnatal events.<sup>[6]</sup> Cerebral blood flow is pressure passive, so events that lead to a fluctuation in cerebral blood flow increase the risk of IVH. Resuscitation, intubation, mechanical ventilation, administration of surfactant, hypotension and the use of inotropes are some events that may affect cerebral blood flow.<sup>[5]</sup>

Another risk factor for IVH identified in this study was intubation. We found an almost 9-fold increased risk of IVH for VLBW neonates who required intubation. Multiple intubation attempts in the delivery room have been shown to increase the risk of IVH in VLBW neonates.<sup>[7]</sup> In another study, reduction in delivery room intubation was shown to be associated with a decrease in severe IVH.<sup>[8]</sup> The timing of intubation was not explored in the present study. Another risk factor identified in this study was meningitis. The unit has a high sepsis rate, and infants could have contracted meningitis after IVH.

Our results showed an association of severe IVH with PHHC, which is consistent with other studies.<sup>[1,9]</sup> The odds of death were 3.7 times higher in infants with IVH in our study. Other studies have observed higher mortality rates in infants with severe forms of IVH.<sup>[10]</sup> The high mortality rate in infants with IVH could also have been caused by other comorbid conditions during the neonatal course.

Sepsis is still a serious concern, with meningitis identified as a risk factor for late IVH and associated with mortality. Infection control measures must be reinforced to prevent late IVH.

The retrospective study design was a limitation of the present study, as incomplete and missing information on the database affected the cohort dataset. More than 50% of patients had no cranial ultrasound results documented. Lack of human resources limited cranial ultrasound screening and documentation of the findings on the database. Some infants may have died before a cranial ultrasound scan was performed. The timing of the scan was not documented, and cases could therefore not be stratified to early or late IVH.

## Conclusion and recommendations

The significant risk factors for IVH were a low Apgar score of  $<6$  at 5 minutes, intubation and meningitis. Further studies to identify pharmacological neuroprotective agents that may be administered prenatally and postnatally may prove beneficial. Long-term follow-up of neonates with all grades of IVH is warranted in our study cohort and in future studies.

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**Author contributions.** KM, NN and FLN conceptualised the study, KM wrote the first draft of the manuscript, KM, NN and FLN reviewed the manuscript, and all authors approved the final version for submission.

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**Conflicts of interest.** None.

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# Harnessing technology to improve perinatal outcomes and digitalise intrapartum care: Use of the IntelliSpace Perinatal clinical information system at Cecilia Makiwane Hospital, Eastern Cape Province, South Africa

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The Health Professions Council of South Africa (HPCSA) requires that records of minors must be kept until their 21st birthday. Medicolegal claims in Eastern Cape (EC) Province, South Africa, were ZAR39 billion in 2022. Contributory factors were identified as poor intrapartum care and missing information, especially unavailability of cardiotocograph (CTG) traces and clinical notes. To mitigate against this, the EC government procured a clinical information system (CIS) from Philips Healthcare, the IntelliSpace Perinatal (ISP), which stores intrapartum notes and CTG traces. Hospital champions monitor the use of this CIS. A Philips Clinical Application Specialist reviewed the use of the ISP in 2022 at Cecilia Makiwane Hospital in EC. Data analysis showed that 70% of patient notes were on the ISP, and CTG traces were available for 85% of patients admitted to the labour ward and 100% of those at the antenatal clinic. Use of the Philips ISP has the potential to improve documentation and perinatal care. Digitising records will enable the province to retain records for 21 years, as required by the HPCSA.

Record-keeping is an essential requirement in the healthcare environment. In alignment with the Health Professions Council of South Africa (HPCSA)'s Guidelines for Good Practice in the Health Professions, medical records of minors must be kept until their 21st birthday.<sup>[1]</sup>

As healthcare providers, we need to move from a mindset of compliance for the sake of compliance to a new mindset of continuous improvement to improve patient outcomes and our joy in our work. We need to strengthen the systems, processes and environments that help to sustain improvement and the quality of services. There is high staff turnover in maternity facilities for various reasons, with most institutions' staffing levels not meeting norms, and there is a lack of mentors in the teams. This situation creates new challenges of doctor and nurse burnout, talent scarcity, less patient focus and poor decision-making. There is not enough time to ensure that all required monitoring is done according to protocol, resulting in high litigation rates.

Factors contributing to the rise in litigation include poor intrapartum care as well as missing records, both cardiotocograph (CTG) traces and clinical notes. The leading cause of death for newborns weighing >2 500 g is intrapartum asphyxia and birth trauma, with the main avoidable factor being fetal distress not detected intrapartum. Poor progress in labour with the partogram not used correctly and poor progress in labour with the partogram interpreted incorrectly are additional avoidable factors. Missing records is another challenge cited by medicolegal teams, as is fading quality of CTG traces. The impact of medicolegal claims from cerebral palsy threatens the vision of the government to provide health for all citizens. Medicolegal claims in Eastern Cape (EC) Province were ZAR39 billion in 2022. As part of mitigating strategy, the province procured a clinical information system (CIS) from Philips Healthcare, the IntelliSpace Perinatal (ISP).

The EC Department of Health has embarked on rolling out an obstetrics CIS in specific hospitals in the province. It was envisaged that use of the Philips ISP would provide the following key outcomes: improved clinical workflow, improvement in electronic record-keeping and auditing (in accordance with the HPCSA Guidelines), improved care-team collaboration and mitigation for the shortage of clinicians, medicolegal risk mitigation, standard-based practice, and advanced maternal and fetal monitoring.<sup>[2]</sup>

The system stores all CTG traces and allows for digitising of medical notes including partograms, and storage in the cloud. It has a built-in system for computerised interpretation of CTG non-stress tests (NSTs). It also has an alarm system to alert healthcare providers to abnormalities detected, thus potentially reducing the incidence of hypoxic ischaemic encephalopathy (HIE).

The ISP is currently implemented at the following hospitals: Frere Hospital (January 2020), Butterworth Hospital (November 2021), Cecilia Makiwane Hospital (CMH) (November 2021), Frontier Hospital (November 2021), Mthatha General Hospital (March 2022), and St Elizabeth's Hospital (May 2022).

## Methods

The CMH maternity department is one of five maternity sites at the hospital with the ISP, and 95% of midwives and doctors in the obstetrics department have been trained on the workflow, which includes daily checking of the system to monitor whether notes are accurately entered and patients appropriately disposed (Table 1). All new doctors and midwives are trained on the ISP, including the interns rotating through the department every 3 months. They are provided with log-in details by the hospital champions who monitor the use of the system.

CMH was the first hospital to digitise caesarean section (CS) case notes and Apgar scores. There has been quick progress from admission

**Table 1. Training conducted at Cecilia Makiwane Hospital**

Activity	Number of hours	Number of days	Number trained	Dates
Super-user, end-user and physician training	32	4	81	22 - 25 November 2021
Go-live support, configuration	8	2	n/a	25 - 26 November 2021
Refresher training for midwives, frontliners and doctors	18	3	60	21, 22, 23 February 2022
Advanced fetal monitoring with ISP	15	3	58	25, 26, 27 October 2022
Totals	73	12	199	

ISP = Philips IntelliSpace Perinatal.

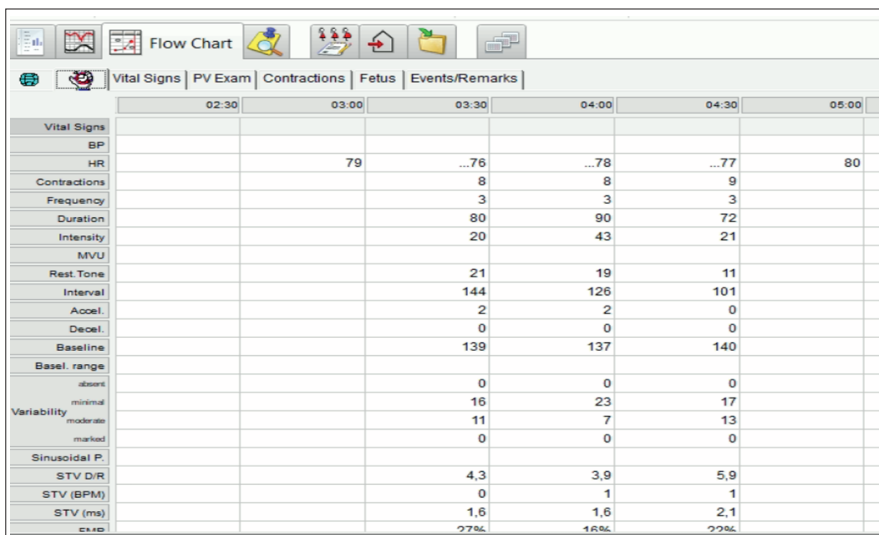


Fig. 1. Example of a maternal and fetal monitoring analysis cardiotocograph trace report.

and discharge to digitising of intrapartum care notes and recently partograms and vital signs. The digital partogram will improve visualisation of the progress of labour and allow direct comparison with the CTG and maternal observations. All near-miss cases are discussed at perinatal mortality meetings. The champions check completeness of information in the ISP and encourage staff to complete the K2 perinatal training programme to improve knowledge, intrapartum CTG management and outcomes.

**Clinical decision support with the Dawes-Redman NST**

The NST is a prenatal method used to assess fetal wellbeing. It is an additional level of advanced fetal monitoring and evidence should there be a case of litigation. It can be used as a teaching tool for less experienced midwives and clinicians.<sup>[2]</sup> The NST can be printed out and attached to the paper medical records or uploaded to Hospital Management System HMS2, our patient administration system, once the integration is complete. The system will analyse the variables in an intrapartum CTG; however, the clinician looking at patient risk factors, maternal condition and progress of labour

must classify the CTG as normal, suspicious or pathological and complete the patient management steps.

Advanced maternal and fetal monitoring enables the automatic charting of key clinical data in the ISP, providing clinicians with more in-depth clinical insight into fetal and maternal wellbeing, and assisting with improved health outcomes.<sup>[3]</sup>

These parameters are presented as a report (Fig. 1) which also includes detailed clinical data relating to the quality of maternal contractions and fetal observations. The data allow clinical staff to adhere to the guidelines for the interpretation of CTGs, identifying abnormal CTGs and the clinical management thereof, to improve fetal and maternal outcomes.

A Philips Clinical Applications Specialist reviewed the use of the ISP on 13 September 2022. In this article we report on use of the ISP at CMH.

**Results**

The data analysis showed that 70% of patients in the labour ward had been registered electronically on the ISP system. Once patients are registered, those eligible for fetal monitoring will have a CTG done. A CTG trace was available for 85% of patients

in the labour ward and 100% in the antenatal clinic.

A survey was conducted among healthcare workers using a questionnaire. The analysis was conducted to examine use of the ISP by healthcare workers at Frere, CMH and Butterworth hospitals in EC, looking at healthcare workers' perceptions of the ISP, their confidence with using it, and usage and challenges.

Findings from the survey were that installation of the system improved record-keeping and enabled users to compare traces, and that archiving of records was valuable. CMH has started using NSTs and digitising Apgar scores and delivery notes. The staff have embraced the project and are keen on digitalisation, although entries are duplicated on the maternity case record for now. ISP challenges include network stability – the system drops out during loadshedding, during which records are stored and uploaded to cloud later. Capturing of vital signs and labour progress will be done manually until Avalon 3 machines are procured. A few doctors and midwives are not completing the discharge documents despite training and not closing pregnancies, leaving the system overpopulated. Daily reminders for all to appropriately document, discharge and close pregnancies are provided by the champions.

**Discussion**

EC is in the process of installing Hospital Management System HMS2. Activation of the integration between HMS2 and the ISP will assist in solving challenges with admission, transfer and discharge. Software provides digital storage of CTGs when there is no CTG paper.

CTGs can be downloaded and printed. CTG traces can be reviewed remotely by the registrar on call or by a consultant. To aid implementation, information and digital health technology need to be an integral part of healthcare worker training.

**Conclusion**

Use of the Philips ISP has the potential to assist and improve perinatal care.<sup>[4]</sup> It has an

alarm system to alert healthcare providers, reducing the incidence of HIE and hence potential litigation. Delivery documents with completed Apgar scores and surgical notes at CS are entered on the system. This enables integrity of patient data and improved record-keeping. Documentation of key clinical data supports medicolegal cases with access to the patient's clinical data, allows for remote consultation, and aids Perinatal Problem Identification Programme information support during perinatal meeting discussions, which informs national recommendations for improving care.<sup>[5]</sup> Digitising the intrapartum care records will enable EC to meet the HPCSA guideline to retain records for 21 years.

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# A web-based perinatal training programme to bridge the cardiotocograph and maternity training gap crisis caused by COVID-19 restrictions on meetings in Eastern Cape Province, South Africa

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Training in fetal heart rate monitoring interpretation has long been recognised as a way to reduce the exorbitant cost of claims arising from adverse intrapartum outcomes in South Africa. Unable to offer training in person during COVID-19 restrictions in 2020 - 2022, we procured the K2MS Perinatal Training Programme (K2 PTP), an interactive web-based perinatal training programme that provides online cardiotocography training. A clinical officer was designated as administrator of the programme, and supervised and monitored the progress of the training. Built into the system is a competency assessment centre. It was made mandatory for all interns working in obstetrics to participate in the training. Seventy-one percent of interns and 60% of registrars completed the course. Completion rates ranged from 33% to 60% in most facilities. Approximately 80% of participants found that the content enhanced their skill and improved clinical care. The K2 PTP appears to be a useful and acceptable training tool, and it should be included as mandatory cardiotocography training in addition to the Essential Steps in the Management of Obstetric Emergencies training programme.

To reduce the exorbitant cost of claims arising from adverse intrapartum outcomes in South Africa (SA), the importance of training and use of e-learning in fetal heart rate monitoring interpretation, as in Australia,<sup>[1]</sup> has long been recognised. Various factors contributed to the occurrence of adverse events that resulted in 203 malpractice claims having to be paid out over 11 years (2006 - 2016) in the public healthcare sectors of Gauteng and Eastern Cape provinces. These factors included failure to implement guidelines/protocols in 91.6% of cases, clinical signs not responded to in 76.8%, and system failure in 12.3%. It was reported that of 154 patients who required fetal heart rate monitoring, only 10 (4.9%) were monitored completely, and 143 (70.4%) were monitored incompletely.<sup>[2]</sup>

The SA National Committee on Confidential Enquiries into Maternal Deaths recommendations for the 2017 - 2019 triennium<sup>[3]</sup> include that provinces ensure that there is training in Essential Steps in Management of Obstetric Emergencies (ESMOE) for all new staff and 2-yearly updates for existing staff, and that emergency obstetric simulation testing drills and exercises are done every month in maternity facilities. Every hospital and community health centre should have at least one on-site trainer able to run the relevant ESMOE modules and drills.<sup>[4]</sup> Many avoidable causes of intrapartum asphyxia are related to problems with monitoring, according to the Saving Babies report for 2014 - 2016.<sup>[5]</sup> ESMOE has one module on the cardiotocograph (CTG), which is considered to be inadequate to provide sufficient knowledge and competency. Individual competency evaluation is not done after ESMOE modules. Saturation training has proved to be effective in ESMOE training in Amathole (unpublished). However, during 2020 - 2022 we were unable to implement the recommended ESMOE training because of COVID-19 restrictions on venues. We also had high staff turnover of trained maternity personnel and new nurses placed in maternity. Training during this time was conducted successfully online and via the National Department of Health Knowledge Hub. We report on the uptake and acceptability of a web-based interactive CTG training

programme in the Amathole and Buffalo City districts, Eastern Cape Province, SA.

## Methods

The Eastern Cape government procured the K2MS Perinatal Training Programme (K2 PTP) (K2 Medical Systems Ltd, UK), an interactive web-based perinatal training programme that provides online CTG training, for central, regional and district hospitals. Doctors and midwives working in different facilities were registered into the programme. The K2 PTP is the largest provider of online CTG training in the UK and the only provider to offer National Institute for Health and Care Excellence (NICE), FIGO and Physiological guidelines.<sup>[3]</sup> The K2 PTP is used in over 90% of UK hospitals as well as at Tygerberg Hospital in Cape Town, SA. It was procured by Eastern Cape after a free pilot of 3 months with participants using their own devices and data. It has 16 chapters, covering training on the CTG, the antenatal and intrapartum periods, fetal physiology, errors, limitations of CTG, intrapartum intermittent auscultation, fetal blood sampling, and cord blood gases. The maternal crisis modules cover uterine rupture, postpartum haemorrhage, maternal collapse, antepartum haemorrhage, pre-eclampsia, COVID-19, and obstetric emergencies.

Once the programme is installed, a clinical officer is designated as an administrator who has the responsibility of supervising and monitoring the progress and performance of all the staff members. Built into the system is an assessment centre comprising a competency assessment tool and a training simulator. We made it mandatory for interns to complete the course within their 3-month rotation.

A computer and technology equipment audit showed that fewer than 10% of maternity departments have laptops or connectivity, so participants used their own data and devices initially. We also scheduled topics for group learning sessions. To facilitate saturation to implement K2 perinatal training, we provided one to three tablets

**Table 1. Completion rates for K2 PTP modules in Amathole and Buffalo City districts by February 2023**

Healthcare facilities with access to the K2 PTP course	Total registered users, N	Registered users who completed the course, n	% completion
Adelaide Hospital	13	8	61.6
Butterworth Hospital	60	35	58.3
Madwaleni Hospital	23	9	39.1
Nompumelelo Hospital	15	5	33.3
Idutywa CHC	15	3	20.0
Stutterheim Hospital	24	11	45.8
Victoria Hospital	26	9	34.6
Frere Hospital	41	14	34.1
Cecilia Makiwane Hospital	55	12	21.8
Bisho Hospital	28	2	7.1
Dimbaza MOU	18	12	66.7
Duncan Village Day Hospital MOU	8	3	37.5
Empilweni Gompo MOU	15	2	13.3
Nontyatyambo MOU	13	5	38.5
Interns registered as group	21	15	71.4
Total	375	145	38.7

K2 PTP = K2MS Perinatal Training Programme; CHC = community health centre; MOU = midwife obstetric unit.

**Table 2. User feedback for the intrapartum care chapter of the K2 PTP**

Question	Users scoring 4 (excellent), %	Users scoring 3, %	Users scoring 2, %	Users scoring 1, %
The chapter reinforces my knowledge of the physiology behind both normal and abnormal characteristics of the fetal CTG	66.8	16.6	0	16.6
The chapter underpins my knowledge to classify a CTG according to the guidelines	75.0	25.0	0	0
The learning objectives for the cardiotocography chapter were fulfilled	75.0	25.0	0	0
The graphics were conducive to learning	91.0	9.0	0	0
The design is flexible for moving at individual pace	83.4	16.6	0	0
Usefulness of content to clinical practice	83.4	16.6	0	0

K2 PTP = K2MS Perinatal Training Programme; CTG = cardiotocograph.

per facility in Amathole and used a hospital computer lab in Buffalo City district.

## Results

At the time of accessing the results in February 2023, ~67% of users had accessed the modules, with 39% of users who completed training and ~32% in progress in the Amathole and Buffalo City districts.

Seventy-one percent of interns (Table 1) and 3 of 5 registrars completed the course. Amathole and Buffalo City registered 375 users who could access the course, with 145 registered users completing it. The average per facility was ~35%, ranging from 33% to 60% percent in most facilities.

Challenges cited included unstable networks in computer labs as well data access. Worsening load shedding had a negative impact. Computers are in the process of being installed in most maternity units for the patient administration system, which it is anticipated will improve the situation. Rural facilities often experienced connectivity and unstable electricity challenges with load shedding. A feedback questionnaire was conducted for each module, and ~80% of participants found that the content enhanced their skill and improved clinical care. The questions included 'The chapter reinforces my knowledge of the physiology

behind both normal and abnormal characteristics of the fetal CTG; and 'The chapter underpins my knowledge to classify a CTG according to the guidelines.' The questions and responses are outlined in Table 2, sourced from a K2 PTP detailed automated report on a sample of users in the pilot. The course was easy to do and was bookmarked.

## Discussion

In order to make on-line training a success, Eastern Cape needs to invest in solid and robust IT network and infrastructure. Computers or tablets with sufficient hardware capability and with data, and training rooms in hospitals, are planned for the 2024/25 financial year. Strong on-site leadership to support ongoing training and change management needs to be built into the organisational culture. Making mandatory training completion part of performance management, as well as providing protected time for training, yielded success in facilities where it was implemented. Managers need to ensure that training is compulsory for new employees during their induction, and competency needs to be evaluated by team leaders. Similar training and implementation of a care bundle have had a positive impact on reducing stillbirths in the UK.<sup>[6]</sup> It was too early for us to evaluate the impact of our training on maternal and fetal

outcomes and staff satisfaction. The Perinatal Problem Identification Programme will be used to see whether reductions in perinatal deaths and a reduced contribution of incorrect management of the CTG to medical avoidable factors were achieved after introduction of the K2 PTP.

## Conclusion

The web-based K2 perinatal training has the potential to complement but not replace ESMOE. The K2 PTP has many strengths and can focus on CTG training and competency owing to its complex web design and interactive nature. It is endorsed by the Royal College of Obstetricians and Gynaecologists and the South African Society of Obstetricians and Gynaecologists, and is approved for 17 CPD points in SA. It can be implemented in all facilities that train interns, as demonstrated by a 71% completion rate for interns in this pilot. Completing the K2 PTP should be mandatory for registrars also. Registration costs less than ZAR1 000 per year per user. Offline group-learning K2 CTG training is available with a CTG bank and case scenario to subscribed facilities. Online learning can be effective and needs to be expanded.

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# Analysis of histopathological features of placental tissue from COVID-19-infected mothers at a resource-limited South African tertiary hospital

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The spectrum of placental findings in maternal SARS-CoV-2 infection remains unclear. We present the results of a comprehensive study of histological placental findings among pregnant women with COVID-19. We retrospectively analysed histopathological findings and maternal and neonatal medical records of 39 women infected with COVID-19. Using the Amsterdam consensus classification system, 40 placental pathology slides were reviewed (there was one set of dichorionic twins). Thirty-five placenta formalin-fixed paraffin-embedded tissues were tested for SARS-CoV-2 using the reverse transcriptase polymerase chain reaction (RT-PCR) test. The most common placental pathological lesions were maternal vascular malperfusion ( $n=18/40$ ; 45.0%) and acute chorioamnionitis with a maternal response ( $n=15/40$ ; 37.5%). Notably, chorangiosis was seen in 6/40 (15.0%), 4/40 (10.0%) had chronic histiocytic intervillitis, and fetal vascular malperfusion was seen in 4/40 (10.0%). Twelve of 35 placenta specimens (34.3%) tested RT-PCR-positive for SARS-CoV-2. In conclusion, there is a heterogeneous COVID-related spectrum of placental morphological changes, commonly reported in COVID-19, suggestive of vertical SARS-CoV-2 transmission. Collaborative multidisciplinary studies are needed to determine the transplacental transmissibility.

SARS-CoV-2, the virus that causes COVID-19, had claimed over 6 million lives globally by April 2022 and can cause severe disease in pregnancy.<sup>[1]</sup> However, the effects of SARS-CoV-2 infection on the placenta and the risk of vertical transmission remain unknown.

The placenta plays a very important protective role in defending the fetus against infection.<sup>[2]</sup> Examination of the placenta after birth can potentially offer some explanations for adverse pregnancy outcomes,<sup>[3]</sup> including those seen in pregnancies affected by COVID-19. To date, studies have observed a heterogeneous spectrum of COVID-related placental morphological changes,<sup>[2]</sup> including hypoxia, maternal vascular malperfusion (MVM), fetal vascular malperfusion (FVM) and inflammatory lesions.<sup>[4]</sup> Parabasal calcification, chorangiosis, diffuse villous oedema and chronic histiocytic intervillitis (CHI) have been also reported.<sup>[5]</sup>

We studied the spectrum of histological placental findings in COVID-19, and used a two-fold approach, examining both transplacental and neonatal transmission, to establish the presence of vertical transmission in an HIV-affected population living in South Africa (SA).<sup>[6]</sup>

## Methods

### Case selection

In a retrospective cohort study, all births to women who were positive for SARS-CoV-2 during pregnancy were screened for eligibility between June 2020 and June 2021 at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), a tertiary academic hospital in Johannesburg, SA. All available placental slides were re-examined, and the placental morphological features were analysed using the Amsterdam consensus classification system.<sup>[7]</sup>

### Detection of SARS-CoV-2 in placental tissue

Formalin-fixed paraffin-embedded tissue from 35 participants was tested for SARS-CoV-2 using the TaqPath COVID-19 CE-IVD reverse transcriptase polymerase chain reaction (RT-PCR) kit (Thermo Fisher Scientific, USA). Gene amplification was performed by the Applied Biosystems 7500 Fast Dx (Thermo Fisher Scientific, USA), targeting the *N2*, *ORF1ab* and *S* genes.

### Statistical analysis

Data analysis was performed using Stata 16.1 software (StataCorp, USA). The Anderson-Darling normality test was used to analyse the distribution of each continuous variable, with  $p \leq 0.05$  considered not normally distributed. Summary statistics were used to describe frequencies and percentages of categorical variables, and means with standard deviations for normally distributed variables or medians with interquartile ranges (IQRs) for non-normally distributed variables.

### Ethical considerations

Ethical approval was received from the University of the Witwatersrand Human Research Ethics Committee (ref. no. M180909). Additional approval was sought from the CEO of CMJAH, the Department of Anatomical Pathology, the Department of Paediatrics and Child Health, and the Department of Obstetrics and Gynaecology.

## Results

### Demographics and obstetrics clinical data

Thirty-nine women met the study inclusion criteria. Clinical data were available for all (Table 1). The mean age was 31 years, and most

patients had received antenatal care ( $n=33/39$ ; 84.6%). A third of the patients were HIV positive ( $n=14/39$ ; 35.8%). Eighteen pregnancies (46.1%) were complicated by a comorbidity. Only 5/39 patients (12.8%) presented with COVID-19 symptoms, of whom 2 (40.0%) had mild disease and 3 (60.0%) had moderate disease. One patient (1/39, 2.6%) required intensive care unit admission.

Overall, 12/35 placenta specimens (34.3%) tested positive for SARS-CoV-2.

**Neonatal clinical data**

Of 40 infants born to 39 women, 19 (47.5%) were admitted to the neonatal unit. The median (IQR) birthweight was 2 060 (1 740) g (Table 1). Table 2 describes the clinical characteristics of neonates born to COVID-19-positive women.

**Placental histological findings**

The most common pattern of placental injury was acute chorioamnionitis with a fetal response, observed in 19/40 (47.5%), while acute chorioamnionitis with a maternal response occurred in 15/40 (37.5%). MVM was observed in 18/40 cases (45.0%). CHI lesions were detected in only 4/40 cases (10.0%). Chorangiosis was seen in 6/40 (15.0%) and FVM in 4/40 (10.0%) (Table 3).

**Table 1. Demographic data for and medical disease present in pregnant women with COVID-19 (N=39)**

Characteristic	n (%)*
Race	
White	1 (2.6)
Black	37 (97.4)
Age (years), mean (SD)	31.1 (6.3)
Antenatal care	
Yes	33 (84.6)
No	6 (15.4)
Comorbidities <sup>†</sup>	18 (46.1)
Hypertension	17 (43.6)
Chronic hypertension	2 (5.1)
Pre-eclampsia	9 (23.1)
Severe pre-eclampsia	6 (15.0)
Diabetes mellitus	2 (5.0)
Tuberculosis	1 (2.6)
HIV positive	14 (35.8)
Antiretroviral treatment	13/14 (92.8)
Symptomatic for COVID-19	5 (12.8)
Severity of COVID-19 symptoms	
Mild	2/5 (40.0)
Moderate	3/5 (60.0)
Severe	0
ICU admission	1 (2.6)
Maternal death	0
Birth details (N=40)	
Gestational age (weeks), mean (SD)	32.5 (8.0)
Fetal weight (g), mean (SD)	2 060 (1 740)
Fetal losses	9 (23.1)
Miscarriage	1/9 (11.1)
Fresh stillbirth	1/9 (11.1)
Macerated stillbirth	7/9 (77.8)

SD = standard deviation; ICU = intensive care unit.  
\*Except where otherwise indicated.  
<sup>†</sup>Some patients had more than one comorbidity.

**Discussion**

This retrospective study describes the spectrum of placental histological findings in women with documented COVID-19, 35.8% of whom were also HIV infected. There are few studies on the effects of COVID-19 in low- and middle-income countries.<sup>[8]</sup> The reasons underpinning the transmission dynamics of SARS-CoV-2 remain unclear.

In the present study, most neonates born to women with SARS-CoV-2 in pregnancy were asymptomatic or mildly symptomatic and had good outcomes with a low mortality rate, similar to what has been reported in previous systematic reviews.<sup>[9]</sup> Only one neonate tested SARS-CoV-2 PCR positive on day 3 of life. Three neonates died; all tested negative for SARS-CoV-2 by nasopharyngeal swab

**Table 2. Clinical characteristics of neonates born to COVID-19-infected mothers admitted to a neonatal unit (N=19)**

Characteristic	n (%)
Need for resuscitation in the delivery room	
Nasal prong oxygen	7 (36.8)
Bag mask ventilation	3 (15.8)
Intubation	1 (5.3)
COVID-19 PCR swab result positive	1 (5.3)
Neonatal complications*	
Fever (>37.5°C)	7 (36.8)
Respiratory distress	14 (73.7)
Feeding abnormalities	1 (5.3)
Asymptomatic	3 (15.8)
Neonatal outcome	
Discharged	16 (84.2)
Died	3 (15.8)

PCR = polymerase chain reaction.  
\*Some neonates had more than one complication.

**Table 3. Placental pathology (N=40) in COVID-19-infected mothers according to the Amsterdam classification<sup>[7]</sup>**

Characteristic*	n (%)
Major placental injuries	
Acute chorioamnionitis, maternal	15 (37.5)
Acute chorioamnionitis, fetal	19 (47.5)
Fetal vascular malperfusion	4 (10.0)
Maternal vascular malperfusion	18 (45.0)
Villitis of unknown aetiology	2 (5.0)
Other histological features	
Distal villous hypoplasia	21 (52.5)
Increased intervillous fibrin	25 (62.5)
Infectious villitis	0
Abruptio	2 (5.0)
Delayed villous maturation	2 (5.0)
Maternal floor infarction	2 (5.0)
Massive perivillous fibrin deposition	2 (5.0)
Meconium-associated vascular necrosis	14 (35.0)
Placental insufficiency	2 (5.0)
Fetal compromise	11 (27.5)
Chorangiosis	6 (15.0)
Chronic histiocytic intervillitis	4 (10.0)
Chronic deciduitis	2 (5.0)

\*Some placentas had more than one pathology.

PCR, and placental pathology was also negative, suggesting that their deaths were unrelated to COVID-19 infection.

Only 1/35 cases (2.9%) had confirmed placental and neonatal SARS-CoV-2 infection, further suggesting that vertical transmission is rare, even in populations with a high HIV prevalence (35.8% in our cohort).

The present study showed no definite correlation between maternal/neonatal symptoms, the severity of maternal illness, and placental findings, corresponding with work by Tolu *et al.*<sup>[10]</sup> Consistent with the literature, we also found that the transmission rate was low (2.5% of total neonates ( $n=1/40$ )).<sup>[9]</sup>

Strengths of the study were the multidisciplinary analysis of the COVID-19 infections and a relatively large sample size, including both preterm and term deliveries and pregnant women who were HIV positive. In addition, SARS-CoV-2 infection of the placenta was confirmed using RT-PCR testing, which has higher specificity than immunohistochemistry, leading to fewer false-positive results.

Study limitations were incomplete access to clinical records owing to the retrospective nature of the study, and lack of antibody testing of neonates to confirm the route of vertical transmission. In addition, owing to system-wide resource constraints, not all placentas of pregnant women testing positive for SARS-CoV-2 underwent histological assessment.

## Conclusion

Placental examination plays a pivotal role in understanding the COVID-19 disease trajectory. We confirm the presence of COVID-19-related placental patterns and hypothesise the presence of vertical transplacental transmission. Long-term follow-up of neonates to rule out potential teratogenic complications secondary to SARS-CoV-2 is recommended. The behaviour of SARS-CoV-2 in pregnancy remains unclear. Collaborative multidisciplinary studies should determine the transplacental transmissibility and optimal management of COVID-19 in pregnancy.

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**Author contributions.** NZM and SB conceptualised the study and led the project. PM led the placental testing and statistical analysis. TR and PN assisted with maternal and neonatal data capturing. All authors assisted with the development and finalisation of the final version of the manuscript.

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# Review of seizure management and short-term outcomes in cooled babies with neonatal encephalopathy with suspected intrapartum hypoxia and seizures

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Seizures and neonatal encephalopathy (NE) following intrapartum hypoxia-ischaemia (NESHIE) are often sub-clinical, and there is a lack of consensus on their management. A suppressed 48-hour amplitude-integrated electroencephalography (aEEG) is associated with a poor outcome. We retrospectively reviewed data from a cohort of babies with moderate to severe NESHIE treated with therapeutic hypothermia. We aimed to determine the proportion of babies with aEEG-confirmed seizures treated with second and third-line anti-seizure agents and determine the association between seizures, management and outcome. Forty neonates were included. Of those, 25 had electrical seizures and three of them died. Second or third-line anti-seizure agents were required by 71% of the treated babies. Poor outcome, defined as a suppressed 48-hour aEEG or death, did not occur in babies who only required phenobarbitone. The risk was not significantly increased with the addition of midazolam and was most frequent when third-line or further agents were used (OR 30.3, 95% CI 12.1 - 1467.3,  $p=0.002$ ).

Neonatal encephalopathy (NE) with suspected intrapartum hypoxic-ischaemic encephalopathy (NESHIE) is clinically diagnosed based on the presence of NE co-occurring with abnormal acid-base status at birth and/or low Apgar scores, particularly when associated with acute peripartum hypoxic events.<sup>[1]</sup> Therapeutic hypothermia is recommended for NESHIE in tertiary settings<sup>[2]</sup> and is the standard of care at the Grootte Schuur Hospital (GSH) neonatal unit. Seizures commonly occur with NESHIE, with the majority being sub-clinical. Globally, there is a lack of consensus on seizure management and diagnosis.<sup>[3]</sup>

Amplitude-integrated electroencephalography (aEEG), a bedside tool for seizure detection and monitoring, is recommended to guide the appropriate use of anti-seizure medication. A suppressed 48-hour aEEG background pattern is associated with poor neurodevelopmental outcomes in cooled babies.<sup>[4]</sup>

The primary objective was to determine the proportion of babies who required second and third-line anti-seizure agents after phenobarbitone within a cohort of cooled babies admitted to the GSH neonatal unit with moderate to severe NESHIE. The secondary objectives were: i) to determine if electrographic seizures were associated with a suppressed 48-hour aEEG or death and ii) to determine if treatment with second and third-line anti-seizure agents was associated with a poor outcome, defined as a suppressed 48-hour aEEG or death.

## Methods

The study was a retrospective descriptive review of observational data prospectively collected at GSH as part of an existing multi-centre study. Approval was obtained from the University of Cape Town Human Research Ethics Committee (number: 102/2022). A subset of data was extracted over a 2-year period, from July 2019 to July 2021, which was the period with the most complete data at the time of the first analysis.

## Definitions

Seizures were defined as recurrent or prolonged (>3 minutes) electrographic repetitive evolving stereotypic waveforms, with or without clinical signs.<sup>[3]</sup> Persistent seizures were defined as electrographic seizures requiring treatment beyond first line.<sup>[3]</sup>

Suppressed aEEG background patterns included any of the following patterns: burst-suppression, continuous low voltage or flat-trace.<sup>[4]</sup>

## GSH protocol for seizures

First-line agent: Phenobarbitone 20 mg/kg intravenous (IV), repeated once if seizures persist.

Second-line agent: Midazolam 0.05 mg/kg IV followed by 0.15 mg/kg/hour if seizures persist. Increase by 0.05 mg/kg/hour every 15 minutes to a maximum dose of 0.25 mg/kg/hour.

Third-line agent: Lignocaine infused in three decreasing doses over 27.5 hours.

Fourth-line agent: Pyridoxine 50 mg IV or orally, repeat once if seizures persist.

Fifth-line agent: Levetiracetam 30 - 50 mg/kg/dose orally as a loading dose, then 10 - 30 mg/kg/dose orally 12-hourly. Start low and increase by 10 mg/kg/dose over 30 minutes until seizures stop or the maximum dose is reached.

## Inclusion criteria

Babies admitted to the GSH neonatal unit who met criteria as specified in all three categories A, B and C in Table 1, were considered for therapeutic hypothermia and study inclusion.

## Exclusion criteria

Babies with the following conditions were excluded:

- Unstable and not responding to standard treatment
- Severe persistent pulmonary hypertension of the newborn (PPHN)

- Severe hypotension
- Uncontrolled bleeding
- Congenital infections
- Congenital or chromosomal anomalies
- Moribund
- Asystole for >10 minutes

## Results

Seventy-three babies were screened. Of those, 41 were recruited and one mother withdrew consent. Ultimately, 40 babies were included, 25 of whom had aEEG-confirmed seizures. Three babies from the seizure group died, all after the fourth day of life. There were no deaths in the group without seizures.

Baseline characteristics are shown in Table 2. The babies in the non-seizure group had significantly higher birthweights and were predominantly male ( $p<0.04$ ).

The features of intrapartum hypoxia are shown in Table 3. A sentinel event did not increase the odds of having seizures (odds ratio (OR) 1.3, 95% confidence interval (CI) 0.36 - 4.78,  $p=0.69$ ).

## Seizures and anti-seizure medication

Twenty-five babies had electrical seizures, none of whom had clinically observable seizures. One baby had no indication for treatment, was not

treated with anti-seizure medication and seizures did not recur. Seven (29%) of the 24 treated babies received first-line management only. Nine (38%) babies required phenobarbitone and midazolam only, while eight (33%) required a third-line agent or more for seizure termination. All three babies who died required second-line treatment or higher.

## Seizures and poor outcome

Poor outcome, defined as a suppressed 48-hour aEEG or death was more frequent in babies with seizures; 48% compared to 7%. The odds of poor outcome were increased 13-fold with electrical seizures (OR 13, 95% CI 1.47 - 113.8,  $p=0.01$ ). However, none of the babies who only required phenobarbitone had a poor outcome and the addition of midazolam alone did not significantly increase the chances of a poor outcome. The odds of a poor outcome were significantly higher when third- and fourth-line agents were required compared to phenobarbitone and midazolam alone (OR 21, 95% CI 1.94 - 227.2,  $p=0.006$ ).

## Discussion

Most babies achieved complete seizure cessation in response to first and second-line anti-seizure medication and response was associated with survival and a non-suppressed 48-hour aEEG. These findings validate the stepwise approach for seizure management at GSH and

**Table 1. Inclusion criteria**

Category	Inclusion criteria
<b>Category A</b> All the following must be present	<ul style="list-style-type: none"> <li>• Gestational age <math>\geq 36</math> weeks AND</li> <li>• Birth weight <math>\geq 1800</math> g AND</li> <li>• Able to commence cooling by 6 hours of age</li> </ul>
<b>Category B</b> At least one of the following must be present	<ul style="list-style-type: none"> <li>• Worse gas within the first hour of life: pH <math>\leq 7</math> or Base deficit <math>\geq -16</math> OR</li> <li>• Worse gas within the first hour of life: pH <math>\leq 7.15</math> or Base deficit <math>\geq -10</math> and history of sentinel event OR</li> <li>• Need for positive pressure ventilation at 10 minutes of life OR</li> <li>• 5-minute APGAR score <math>&lt; 7</math> (only if no early gas)</li> </ul>
<b>Category C</b> Both must be present	<ul style="list-style-type: none"> <li>• Signs of moderate or severe encephalopathy AND</li> <li>• Abnormal aEEG (mandatory for cooling at GSH)</li> </ul>

aEEG = amplitude-integrated electroencephalography; GSH = Groote Schuur Hospital.

**Table 2: Baseline characteristics**

	Cohort (N=40)	Seizures (n=25)	No seizures (n=15)	p-value
Birthweight (g), mean (SD)	3 014 (435)	2 907 (404)	3 192 (440)	0.04*
Gestational age (weeks), mean (SD)	38.5 (1.8)	38.4 (1.6)	38.7 (2.1)	0.6
Caesarean section, n/N (%)	13/40 (33%)	8/25 (32%)	5/15 (33%)	0.93
Male, n/N (%)	26/40 (65%)	12/25 (48%)	14/15 (95%)	0.04*

\* $p<0.05$

SD = standard deviation.

**Table 3. Features of intrapartum hypoxia**

	Cohort (N=40)	Seizures (n=25)	No Seizures (n=15)	p-value
pH, <sup>†</sup> mean (SD)	7.02 (0.16)	7.0 (0.18)	7.04 (0.15)	0.6
Base deficit, <sup>†</sup> mean (SD)	15.1 (4.9)	15.9 (5.3)	13.9 (4.1)	0.3
5-minute APGAR score, median (range)	5 (1 - 7)	5 (1 - 7)	5 (1 - 7)	0.08
Sentinel events, n/N (%)	23/40 (58%)	15/25 (38%)	8/15 (53%)	0.68

SD = Standard deviation.

<sup>†</sup>Worst gas within the first hour of life

the use of aEEG for seizure detection and prognostication to assist with management and resource allocation for cooled neonates. The study findings provide further support to the accumulating data showing associations between a high electrographic seizure burden, persistent seizures in cooled babies with moderate to severe NESHIE and an abnormal outcome.<sup>[3]</sup> Further research, particularly in the SA setting, should be conducted with a larger sample size and include the most severely affected babies.

### Limitations and strengths

The major study limitations were: i) the small sample size without multivariate analysis and ii) the exclusion of the most severely affected babies due to consent refusal or death before recruitment. The main study strength was the use of prospectively collected data in a neonatal unit with well-established management protocols and experience with the use of aEEG.

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**Conflicts of interest.** None.

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# Correlation of procalcitonin levels and the quick Sequential Organ Failure Assessment score in obstetric patients admitted to labour ward high care

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Early identification of sepsis in pregnancy is challenging, and there is a need to validate early warning scores and biomarkers that could potentially be used to detect sepsis. To correlate procalcitonin (PCT) levels and the quick Sequential Organ Failure Assessment (qSOFA) score in high-risk obstetric patients, we conducted a prospective study of 100 high-risk obstetric patients. We determined their qSOFA scores and PCT levels. Statistical analyses were conducted using R software, version 4.00 (R Foundation for Statistical Computing, Austria, [www.R-project.org](http://www.R-project.org)). A significant ( $p < 0.001$ ) positive correlation was found between PCT and qSOFA scores. PCT levels  $< 0.5$  ng/mL correlated significantly with a qSOFA score of 0. Our data indicate the potential usefulness of the qSOFA score to predict PCT levels in the obstetric population studied. Further large-scale randomised studies are needed to validate the use of qSOFA and PCT in the obstetric population.

According to the latest report from the National Committee on Confidential Enquiries into Maternal Deaths of South Africa (SA), non-pregnancy-related infections were the leading cause of maternal deaths from 2017 to 2019.<sup>[1]</sup> A large majority of these deaths could have been prevented.<sup>[2]</sup>

The bedside quick Sequential Organ Failure Assessment (qSOFA) score can be used to rapidly identify patients with suspected infection.<sup>[3]</sup> The clinical parameters include any alteration in mental status, systolic blood pressure  $\leq 100$  mmHg, and respiratory rate  $\geq 22$  breaths per minute.<sup>[3]</sup> The appeal of the qSOFA score is that it can be applied quickly and repeatedly.<sup>[3]</sup> A score of  $\geq 2$  on the qSOFA should prompt additional investigation of organ dysfunction, initiation or escalation of interventions, referral to a higher level of care, and more intensive monitoring.<sup>[3]</sup> The Society for Maternal-Fetal Medicine published a consult series on sepsis, in which it was stressed that the qSOFA score does not define sepsis.<sup>[4]</sup> Instead, it should be used as a rapid tool to identify high-risk patients who are prone to develop severe complications.<sup>[4]</sup> The qSOFA score has not been evaluated in pregnancy, and the physiological changes that occur during pregnancy may cause false-positive results.<sup>[4]</sup> At the time of writing, no study investigating use of the qSOFA score in obstetric patients had been published.

Biomarkers of infectious disease such as procalcitonin (PCT) and C-reactive protein have been proven to detect infection and predict mortality from sepsis accurately.<sup>[5]</sup> PCT is a prohormone in the serum.<sup>[6]</sup> A study from Finland concluded that although reference ranges for PCT had not yet been established in the pregnant population, it was likely to be a useful biomarker to distinguish infection from inflammation in obstetric patients.<sup>[6]</sup> Quantitative estimation of PCT, particularly the change in PCT values over time, is useful to diagnose bacterial infection and guide antibiotic management.<sup>[6]</sup>

Paccolat *et al.*<sup>[7]</sup> tried to establish 'normal' PCT values in pregnant women during the third trimester, at delivery and up to 10 days after delivery. They included 60 women, and proposed that a PCT level  $< 0.25$   $\mu$ L could be used to rule out bacterial infection. In another study, the authors cautioned that other pathologies, such as pre-eclampsia (PET), eclampsia, premature rupture of membranes, and liver, lung and thyroid malignancies, can elevate PCT levels in pregnant patients.<sup>[8]</sup>

## Methods

This was a prospective study to correlate PCT levels and qSOFA scores in high-risk obstetric patients admitted to labour ward high care at a tertiary facility in Johannesburg, SA. Ethics clearance was obtained from the Human Research Ethics Committee of the University of the Witwatersrand (ref. no. M191151). The study was conducted from 1 July to 31 August 2020. Written consent was obtained from all the patients, and baseline demographic data and details on the condition that necessitated their admission to high care were captured. We used the provisional high-care admission diagnosis for this study. We chose to collect our data upon the patient's admission to high care, to obtain baseline vital signs and scores before significant interventions could occur that would potentially alter qSOFA scores and PCT.

We calculated the qSOFA score upon admission to labour ward high care using the patients' standard vital signs and drew 2 mL of blood to measure their PCT levels. Blood was put into ethylenediaminetetraacetic acid (EDTA) tubes. Serum was separated immediately by the principal investigator (MS) using a centrifuge. EDTA tubes were spun at 15 000 revolutions per minute for 5 minutes. PCT levels were measured immediately using the patients' serum and a rapid PCT assay, and an Edan 3TC point-of-care machine, a bedside tool sponsored by Biocom Biotech (SA). The sample size was determined

by Biocom Biotech's generous donation of 100 rapid PCT assays. Statistical analyses were conducted using R software, version 4.00 (R Foundation for Statistical Computing, Austria, www.R-project.org). The dataset did not meet the assumptions of normality (Shapiro-Wilk test), and non-parametric statistical analyses were used. Tests were two-tailed, and model significance was set at 0.05. Data are reported descriptively as counts for categorical data and means with standard deviations (SDs) for continuous data. Spearman's rank test was used to analyse the association between the qSOFA score and the PCT level. Pearson's  $\chi^2$  tests (with Yates's correction) were used to analyse the association between PCT and women who had a normal vaginal delivery (NVD), those who had a surgical intervention, and those with PET.

**Results**

The clinical characteristics of the 100 patients studied are summarised in Table 1. Continuous variables are shown as means with SDs. For categorical values, counts are shown. Statistics are comparisons only for categorical variables, which all deviated significantly from chance.

For statistical analysis, we grouped PCT levels into three categories, to correlate a continuous variable (PCT) with a categorical variable (qSOFA score). PCT levels <0.5 ng/mL were designated as 0, 0.51 - 1.00 ng/mL as 1, and >1.00 ng/mL as 2. These levels correlate with bacterial infection being unlikely (0), possible bacterial infection (1) and bacterial infection being likely (2), as is already established in the normal adult population. The Spearman regression between qSOFA and PCT scores was significantly positively correlated (Fig. 1), generating a Spearman's rho of 1. We found that PCT levels <0.5 ng/mL correlated significantly with a qSOFA score of 0. Most of the patients scored 0 for both qSOFA and PCT, and few women scored 1 and 2 for both qSOFA and PCT (Fig. 1).

In addition to our primary aim of correlating PCT and qSOFA scores, we found additional significant results when we analysed associations with NVD, PET and surgical intervention.

The association between PCT scores and NVD did not deviate significantly from chance (Table 2). Most patients had a PCT score of 0, regardless of whether they did or did not have an NVD. The association between PCT scores and PET differed significantly from chance. Significantly more patients who did have PET than those who did not had PCT scores of 0. Most women with a PCT score of 0 did not have a surgical intervention such as a re-look laparotomy or evacuation of the uterus. Confounding factors necessitating surgical intervention to control bleeding,

or laparotomy for source control of suspected sepsis, need to be considered when interpreting these data.

**Discussion**

A significant positive correlation was found ( $p < 0.001$ ), with all patients in the study scoring in the same category for PCT and qSOFA score. The strengths of the data can be used to encourage the use of an early warning score such as the qSOFA at the bedside, to rapidly identify patients at risk of poor outcomes. Our data contribute to the effort to establish reference ranges for PCT levels and to validate the use of the qSOFA score in obstetric patients. We

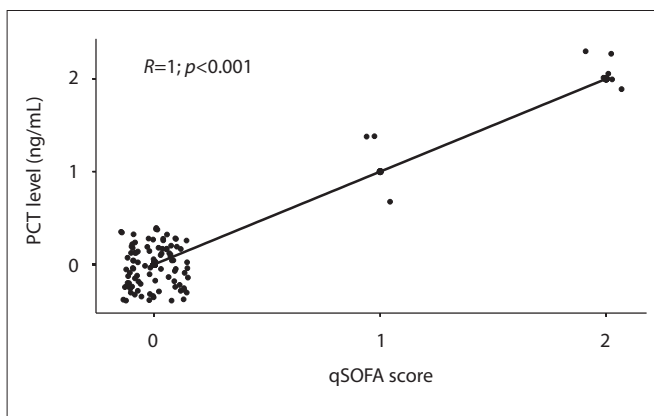
**Table 1. Clinical parameters of women admitted to labour ward high care at a tertiary facility (N=100)**

Variable	Values*
Respiratory rate (breaths per minute)	19.88 (2.48)
Non-invasive systolic blood pressure (mmHg)	135.09 (24.57)
GCS (score out of possible 15)	All scored 15
Age (years)	28.98 (6.40)
Parity (number)	1.63 (1.41)
Gravidity (number)	2.54 (1.31)
HIV status	
Positive	25
Negative	75
CD4 cells/ $\mu$ L (if HIV positive)	372.71 (253.83)
VL copies/mL (if HIV positive)	66 144 <sup>†</sup> (118 559.49)
Still pregnant at the time of the PCT test	
Yes	64
No	36
Gestational age currently or at delivery (in weeks)	34.94 (4.53)
Diabetes	
Yes	9
No	91
Did the patient have an NVD	
Yes	22
No	78
Did the patient have an assisted delivery	
Yes	2
No	98
Did the patient have a surgical intervention	
Yes	14
No	86
Known source of sepsis	
Yes	9
No	91
Did the patient have PET	
Yes	60
No	40
COVID-19 suspected/confirmed	
Yes	5
No	95

GCS = Glasgow Coma Score; VL = viral load; PCT = procalcitonin; NVD = normal vaginal delivery; PET = pre-eclampsia.

\*Mean (standard deviation) for continuous variables, counts for categorical variables.

<sup>†</sup>Most patients on treatment for HIV had viral loads lower than the detectable limit. The mean is not representative because 2 patients had virological failure and therefore very high viral loads.



**Fig. 1. Association between qSOFA scores and PCT levels in women admitted to labour ward high care. The Spearman regression and statistical output are presented. (qSOFA = quick Sequential Organ Failure Assessment; PCT = procalcitonin.)**

**Table 2. Proportions of women admitted to labour ward high care who did and did not have normal vaginal delivery, surgical intervention and PET, in relation to PCT score categories (N=100)**

Variable	PCT, n (%)			Statistics
	0	1	2	
NVD				$\chi^2=4.62$ ; df=2; p=0.099
No	73 (93.6)	1 (1.3)	4 (5.1)	
Yes	18 (81.0)	2 (9.5)	2 (9.5)	
Surgical intervention				$\chi^2=6.85$ ; df=2; p=0.034
No	81 (94.2)	1 (1.2)	4 (4.6)	
Yes	10 (71.4)	2 (14.3)	2 (14.3)	
PET				$\chi^2=6.81$ ; df=2; p=0.033
No	33 (82.5)	3 (7.5)	4 (10.0)	
Yes	58 (96.7)	0	2 (3.3)	

PCT = procalcitonin; PET = pre-eclampsia; NVD = normal vaginal delivery.

found that PCT levels <0.5 ng/mL correlated significantly with a qSOFA score of 0.

The results show that NVD does not appear to alter PCT, which adds to the existing pool of data on what 'normal' PCT values are in postpartum women. Importantly, we also found that PET did not significantly elevate PCT levels in pregnant patients, as previously reported by Agarwal *et al.*<sup>[8]</sup> and other authors.<sup>[6]</sup> This is especially important in the SA context, as PET is very common and is a major cause of maternal mortality.<sup>[11]</sup>

A limitation of this study was that there was no allocation of case and control patients, as their final diagnosis was not clearly established on admission to high care, at the time of data collection. We did not follow up their final outcomes if they scored 0 for both PCT and qSOFA. Another limitation is that only 9% of the patients in the study scored >0 for both PCT and qSOFA. We followed up the outcomes of these patients, and bacterial sepsis was confirmed in most of them. The most common causes were lower respiratory tract infections and urosepsis. The uterus was confirmed as the source of sepsis at laparotomy in two of the patients. Severe COVID-19 disease was confirmed in one patient.

## Conclusion

The data indicate the potential usefulness of the qSOFA score to predict PCT levels in the obstetric population studied. The score may be especially useful outside the intensive care unit setting, such as in primary healthcare clinics and district hospitals where PCT testing may not be available. We stress that neither the qSOFA score nor PCT levels are meant to be used in isolation, but rather that clinicians can utilise these tests in the obstetric population when sepsis is suspected. We recommend further randomised large-scale studies to validate the use of the qSOFA score in obstetric populations across the continents.

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**Author contributions.** SB conceptualised the project and finalised sponsorship. MS, as primary investigator, collected and analysed data. MS, SB, GR and NF all contributed to the interpretation of the study findings.

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**Conflicts of interest.** None. The authors have no affiliation to Biocom Biotech.

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# Intact neurological survival after emergency caesarean delivery for pathological fetal heart rate tracings at term: is it time to rethink ‘fetal distress’ interpretation on cardiotocography in South African cerebral palsy lawsuits?

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This descriptive study aimed to critically review cardiotocographic (CTG) tracings that informed the decision for an urgent caesarean delivery (CD) in cases resulting in favourable neonatal outcomes. This observational cross-sectional study used data extracted from medical records at Tygerberg Academic Hospital. The mean duration from the decision to perform a CD of the baby was 113 minutes. Additionally, the mean time lapse from the removal of the CTG from the patient (or the last CTG available for review in the folder) to the start of surgery was 46 minutes. The mean duration of abnormal tracings (from diagnosis to recovery or the last CTG taken if there was ongoing abnormal CTG) was 72 (range 30 - 355) minutes. This audit showed that in most babies with pathological CTG tracings, neither prolonged periods of abnormal tracing nor delays in delivery necessarily lead to an adverse outcome.

Approximately 3 500 caesarean deliveries (CD) are performed at Tygerberg Academic Hospital (TAH) each year. Of these, 63% are emergencies, involving decisions for urgent delivery made during the intrapartum period. Most of these emergency CDs are performed based on pathological cardiotocographic (CTG) tracings, commonly called ‘fetal distress’. Among those, only a small number of neonates have poor outcomes or require admission to neonatal care. Electronic fetal monitoring (EFM) has become the most performed obstetric procedure in the world, being employed in more than 85% of deliveries across both low and high-risk pregnancies.<sup>[1]</sup> Although initially designed to reduce the incidence of cerebral palsy (CP), mental retardation and perinatal mortality, EFM was quickly incorporated into widespread use without any randomised trials and with very little supporting evidence for its efficacy and reliability.<sup>[2]</sup>

Fetal heart rate (FHR) patterns associated with fetal asphyxia include absent and minimal baseline variability, which is the most specific but only identified in 17% of cases of asphyxia, along with late and prolonged decelerations. The fallibility, varied interpretation and poor sensitivity of EFM contribute to an increase in the number of operative vaginal deliveries, fewer spontaneous vaginal births and more CDs for abnormal FHR patterns or suspected acidosis.<sup>[3,4]</sup> The exact etiopathology of CP is difficult to establish in most cases, especially regarding timing. However, it has been largely established that only 10 - 20% of cases can be linked to intrapartum events. Therefore, taking action based on suggestive findings from EFM would only prevent that same proportion. CP is likely predominantly caused by prenatal factors, making it not preventable through responses to intrapartum FHR patterns.<sup>[5]</sup> Also, it is important to note that babies that are encephalopathic at birth do not necessarily result in children affected by CP.<sup>[6]</sup> Hypoxic insults to the fetus may manifest as chronic events, such as placental insufficiency, infection, genetic abnormalities or exposure to toxins. Alternatively, they may occur acutely or sub-acutely, influenced by a combination of various factors.

When interpreting the CTG trace, it is important to consider risk factors, such as prolonged spontaneous rupture of membranes (SROM), prematurity, intrauterine growth restriction (IUGR), infection or the presence of meconium-stained liquor, the use of oxytocin for failure to progress in labour and the presence of a uterine scar. In addition, a critical analysis of the CTG trace needs to be made to differentiate between a fetus that is compensating well with the ongoing stress of labour from one that is unable to compensate or has begun the process of decompensation.<sup>[7]</sup> In South Africa (SA), as in the rest of the world, ‘failure to diagnose and treat fetal asphyxia’ is the most common claim in obstetrical malpractice litigation.<sup>[8]</sup>

The characteristics of fetal monitoring in term infants with moderate to severe neonatal encephalopathy after birth at TAH were recently described by Adams *et al.*<sup>[9]</sup> The main avoidable factors were a delay in access to the theatre (waiting time on average 1 hour and 40 minutes from decision to incision) and failure to recognise or react to abnormal CTG tracings in 36% of cases. The purpose of this current study was to scrutinise term CDs indicated by severe fetal compromise on CTG, but where the pattern was recognised in time and the outcome was normal (5-minute Apgar score >5 and uneventful neonatal course with discharge to the mother after birth).

## Methods

This was an observational cross-sectional study using data from the labour ward theatre register and clinical data from patient folders.

## Setting and study population

All women >36 weeks gestation who delivered by emergency caesarean section (CS) between 1 January and 31st August 2019, with the indication for ‘fetal distress’ or ‘pathological CTG’ and had normal neonatal outcomes were included.

## Results

Three hundred and fifty folders (identified from the theatre register as 'CS for fetal distress' were reviewed to obtain 100 consecutive cases that met the inclusion criteria. Data were available for all 100 women. Gestational age was calculated using early ultrasound (<24 weeks) where available. Eighty percent of women booked early enough to have accurate gestational age available. All patients were referred for high-risk management during the antenatal or intrapartum period. The most frequent reason for referral to the labour ward was late-onset pre-eclampsia (49 cases). Planned induction of labour was primarily conducted for gestational diabetes (24 cases) or a previous fetal death or adverse outcome (18 cases).

Labour was induced in 55 cases. A combination of prostaglandin (oral misoprostol) and/or mechanical (catheter bulb) was used.

CTG tracings indicating a diagnosis of fetal distress were reviewed by both authors and cross-referenced with the clinical notes in the folder. There was unanimous agreement that the CTG was pathological according to the NICE 2017 guidelines, amended in 2022, in all cases. Tracings were described at two time points: 1) at the first diagnosis of pathological changes, encompassing the period during and after intrapartum resuscitation until the decision for CS was made and 2) during the last 30 minutes before removal of the CTG to take the patient to the theatre.

For 28 women, pathological changes were documented before the onset of labour. Diagnosis during the latent stage of labour was established in 40 cases, while 27 women were already in active labour when CTG changes were diagnosed. The remaining five cases were detected during the second stage of labour. Of those, only two had a simultaneous diagnosis of cephalopelvic disproportion.

Evidence of intrapartum resuscitation was documented in 71 cases. In an additional 20 women, the diagnosis was made before the onset of labour and intrapartum resuscitation was not deemed necessary by the managing clinicians.

The contraction pattern, using only an external transducer, was normal in 35 CTGs at the time of diagnosis, despite the presence of other pathological changes. For 30 women, contractions were noted as normal in the folder, but the tocographic tracing was difficult to evaluate owing to the poor tracing of the contraction pattern. Among the remaining 14 women who

were in labour at the time of diagnosis, the contraction pattern was abnormal. Hypertonus contractions (lasting >2 minutes) were present in 10 women and tachysystole (more than 5 contractions per 10 minutes) were observed in four women. Twelve of the 14 (85%) women received intrapartum resuscitation. Eighty percent of women still had pathological changes on the CTG at the time of transport to the theatre. It took on average 113 minutes to deliver a baby after the diagnosis of fetal distress and the decision to deliver urgently was made. This could take as long as 430 minutes.

Three examples of abnormal tracings are shown in Figs. 1 - 3.

### Fetal outcome

For the entire cohort of 100 women, the median 1- and 5-minute APGAR scores were 8 and 9, respectively and all infants were discharged to their mothers. The 10-minute APGAR score was 10 for 93 babies, nine for six babies and one baby had a 10-minute score of 7. None of the babies required more than the routine resuscitative care provided during CS birth. No subsequent hospital admissions were made in the first six weeks after discharge. The incidence of small-for-

gestational-age (SGA) babies was higher than expected (19% <10<sup>th</sup> centile). Of the 19 SGA babies, 73% (14/19) had confirmation of gestational age by early ultrasound.

## Discussion

This study aimed to describe the CTG patterns in CDs conducted owing to fetal compromise during labour, despite resulting in a completely normal neonatal outcome. All the women were referred owing to an underlying obstetric complication, primarily late-onset pre-eclampsia or gestational diabetes. A fifth of the babies were also smaller than expected for their gestational age, indicating possible additional fetal compromise such as intra-uterine growth restriction.

The most likely explanations are false-positive patterns, where there is no insult to the fetus, but the CTG pattern appears abnormal. Alternatively, there could have been genuine fetal distress but that intrapartum resuscitation and a quick delivery prevented hypoxic brain injury. To minimise possible false-positive patterns, two independent researchers used the internationally accepted classification system (NICE) to describe the changes.

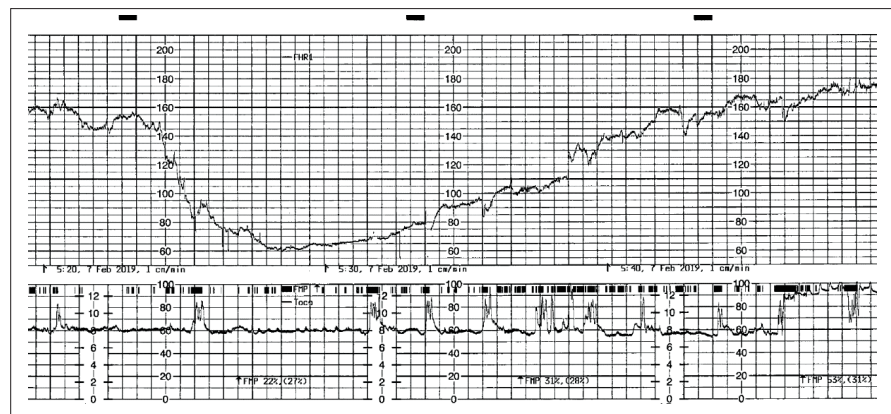


Fig. 1. Prolonged bradycardia (a single prolonged deceleration lasting 3 minutes or not)

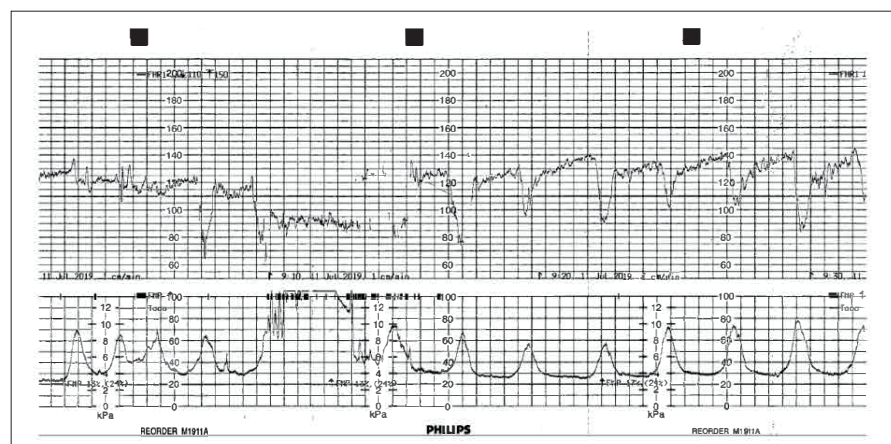


Fig. 2. Repetitive variable decelerations with concerning features

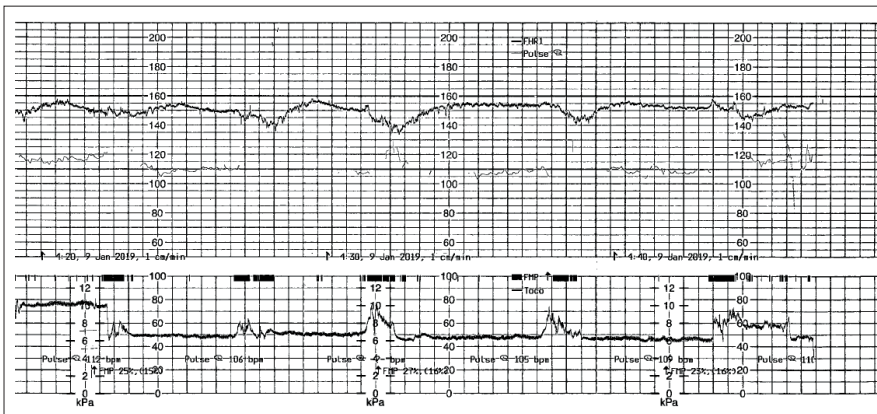


Fig. 3. Variability <5 bpm with repetitive late decelerations (bpm = beats per minutes).

Cases in which pathological changes were dramatically apparent, lasting for at least 30 minutes were chosen. Additionally, to monitor the possible protective effect of successful intrapartum resuscitation and quick delivery, both the decision-to-delivery time and the duration from the last CTG to delivery were calculated.

In a previous study<sup>[9]</sup> from this same hospital, a delay in accessing the theatre after establishing a diagnosis of fetal distress was the main system-related modifiable factor (25/58; 43% of cases delivered by emergency CS). However, the outcome of that study was hypoxic ischaemic encephalopathy (HIE).<sup>[9]</sup> The average decision-to-delivery time in that study was 100 minutes. All the cases in the present study fell under the NICE Category 2 urgency, wherein the recommendation is to perform caesarean birth as soon as possible, typically within 75 minutes of making the decision.<sup>[10]</sup> In contrast, our findings showed that even a delay of almost 2 hours can still lead to a normal outcome, indicating that this should not be the sole modifiable factor quoted when there is an adverse outcome. Category 1 urgency (immediate threat to the life of the mother or baby) was excluded from the study analysis because an acute intrapartum event is a known cause of hypoxic brain injury.

If the delivery delay is not contributing to a negative outcome, it is plausible that timely recognition and resuscitation could be the main reason for a positive outcome. This expectation is typically met when the CTG

completely recovers, and the final minutes or hours of the tracing appear entirely normal. However, in the present study, only 16% of tracings were classified as normal in the last 30 minutes of available tracing and 4% were still suspicious. Despite intrapartum resuscitation, 80% of tracings remained pathological by the time the CTG was removed, and the patient was transported to the theatre. The main difference from the previous audit (HIE outcome) was the non-recognition of abnormal CTG tracings in the HIE cases. In the current study, there was a notable improvement in the recognition and management despite the logistical challenges. While most participants in this audit had underlying maternal or fetal conditions, most entered labour with an initially normal CTG. Also, known cases of prolonged chronic intra-uterine hypoxia (placental insufficiency) were excluded.

## Conclusion

In a public sector hospital in SA, a term baby with pathological CTG tracing will need intrapartum resuscitation and prompt delivery if the abnormal pattern persists. This is because there are currently no alternative measures available to distinguish the hypoxic fetus from one who is still compensating for the normal insults of labour. This study showed that in most babies with pathological CTG tracings, neither prolonged periods of abnormal tracing nor delays in delivery necessarily lead to a negative outcome. In litigation

cases involving term hypoxic brain injury, it is crucial to consider other underlying conditions of both the fetus and mother, not solely focusing on CTG interpretation and management before negligence is inferred.

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# Pathological and non-pathological causes of deaths of infants admitted to a neonatal unit in a public tertiary hospital in South Africa

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It is important that information on causes of death is locally derived, and appropriately categorised for decision-making. The aim of this study was to determine the characteristics and pathological and non-pathological (modifiable) causes of death of infants admitted to the neonatal unit at Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa. There were 567 deaths over a 13-month period, of which 523 (92.2%) had death summaries reviewed. Sixty-five percent of the infants weighed <1 500 g at birth, and 62.3% died within the first week of life. Common underlying causes of death were prematurity (61.0%), intrapartum asphyxia (16.6%) and congenital anomalies (16.3%). The commonest immediate cause was healthcare-associated infections, accounting for 56.5% of prematurity- and 42.3% of congenital anomaly-related deaths. Non-pathological causes were identified to be inadequate implementation of infection prevention and control (IPC) measures, unavailability of neonatal intensive care unit (NICU) beds, and hypothermia. Interventions to reduce neonatal deaths should focus on IPC, increasing NICU beds, and preventing hypothermia in preterm infants.

In South Africa (SA), ~12 000 babies die in the first 28 days of life every year, accounting for about one-third (33.4%) of deaths in children under the age of 5 years.<sup>[1]</sup> Common causes of neonatal deaths have been identified to be prematurity (47.9%), intrapartum-related complications or intrapartum hypoxia (24.3%), infections (11.6%) and congenital abnormalities (8.9%).<sup>[2]</sup> These figures are based on national averages, which often hide huge variations between provinces and healthcare facilities. To reduce neonatal deaths, both pathological and non-pathological causes of death must be identified at country, regional and healthcare facility level, so that areas for prioritisation can be identified at both national and local levels. It is important that information about causes of deaths, especially non-pathological or modifiable causes, is appropriately categorised for decision-making on reducing these causes of deaths. The objectives of this study were to determine characteristics of infants who died during their admission to a neonatal unit based in a public hospital in a relatively low-resource setting, and to determine pathological (underlying and immediate) and non-pathological causes (modifiable factors) of the deaths.

## Methods

This was a retrospective, descriptive study. All infants who died in the neonatal unit at Chris Hani Baragwanath Academic Hospital (CHBAH) in Johannesburg, SA, from January 2016 to January 2017 were included in the study, irrespective of their postnatal age. The neonatal unit at CHBAH has 185 neonatal beds, including 66 critical care beds (18 in the neonatal intensive care unit (NICU) and 48 in the high-care unit). It is a referral centre for local clinics and for neonates requiring surgical services in southern Johannesburg and North West Province. The NICU admits all infants requiring mechanical ventilation with a birthweight >900 g. It also admits infants from the community who are in paediatric wards and require mechanical ventilation if their current weight is <3 500 g, as the hospital paediatric intensive care unit only admits children weighing

≥3.5 kg. A consultant reviews and summarises all deaths, including patient characteristics, causes of death (underlying and immediate), and avoidable factor/s. In addition, morbidity and mortality meetings are held weekly where pathological and non-pathological causes are allocated to each death reviewed. Death summaries were reviewed for infant data, pathological and non-pathological causes of death. Descriptive analysis was performed. Approval was received from the University of the Witwatersrand Human Research Ethics Committee (ref. no. M180378).

## Results

There were 567 deaths, of which 523 (92.2%) had complete summaries. Sixty-five percent of the infants weighed <1 500 g at birth and 62.3% of the deaths were early neonatal deaths (postnatal age 0 - 6 days at time of death). The leading underlying cause of death was found to be prematurity (61.0%), followed by intrapartum hypoxia (16.6%) (Table 1).

The most common immediate cause of death was nosocomial sepsis, accounting for 56.5% of prematurity- and 42.3% of congenital anomaly-related deaths. Overall, 76.6% of deaths were assessed to have modifiable factors (52.1% probable and 24.5% possible) (Fig. 1).

Modifiable factors were assessed to be related to hypothermia on admission, inadequate implementation of infection prevention and control (IPC) measures, and limited availability of NICU beds (Table 2).

## Discussion

The main findings in this study were that in just over 60% of deaths, prematurity was the underlying cause of death; the most common immediate cause of death was nosocomial sepsis; and the non-pathological causes or modifiable factors were inadequate implementation of IPC measures, inadequate NICU beds, and hypothermia on admission. The proportion of deaths due to prematurity in this study is much higher than the 35% and 48% reported globally<sup>[3]</sup> and in SA at national level.<sup>[2]</sup> The possible explanation for this difference is that the present study was

**Table 1. Characteristics of neonatal deaths and pathological causes**

Characteristic	All deaths (N=523), n (%)	Early neonatal deaths (0 - 6 days) (n=326; 62.3%), n (%)	Late neonatal deaths (≥7 days) (n=197; 37.7%), n (%)
In-hospital births	456 (87.2)	292 (89.6)	164 (83.2)
Died in labour and delivery (triage nursery)	52 (9.9)	52 (16.0)	0
Died in NICU	215 (41.1)	66 (20.2)	149 (75.6)
Died in high care	254 (48.5)	206 (63.2)	48 (24.4)
Died in standard-care nursery/postnatal wards	2 (0.4)	2 (0.6)	0
Birthweight (g)			
<1 000	231 (44.2)	183 (56.1)	48 (24.4)
1 000 - 1 499	108 (20.6)	39 (12.0)	69 (35.0)
1 500 - 1 999	40 (7.7)	16 (4.9)	24 (12.2)
2 000 - 2 499	41 (7.9)	21 (6.4)	20 (10.2)
≥2 500	103 (19.7)	67 (20.6)	36 (18.2)
Gestational age (weeks)			
<26	88 (16.9)	81 (24.8)	7 (3.6)
26 - 29	203 (38.8)	120 (36.8)	83 (42.1)
30 - 33	80 (15.3)	33 (10.1)	47 (23.9)
34 - 36	42 (8.0)	19 (5.8)	23 (11.7)
≥37	110 (21.1)	73 (22.4)	37 (18.8)
Underlying causes of death			
Prematurity	319 (61.0)	202 (63.3)	117 (59.4)
Intrapartum hypoxia	87 (16.6)	77 (23.6)	10 (5.1)
Congenital anomalies	85 (16.3)	26 (8.0)	59 (29.9)
Infection	25 (4.8)	16 (4.9)	9 (4.6)
Other	7 (1.3)	5 (1.5)	2 (1.0)

NICU = neonatal intensive care unit.

**Table 2. Avoidable factors according to underlying causes of deaths**

	All deaths (N=523), n (%)	Prematurity (n=319), n (%)	Intrapartum hypoxia (n=87), n (%)	Congenital anomalies (n=85), n (%)	Infection (n=25), n (%)	Other (n=7), n (%)
Deaths with modifiable factors	402 (76.9)	273 (85.6)	63 (72.4)	53 (62.4)	12 (48.0)	1 (14.3)
Modifiable factors						
Infection control	196 (37.5)	133 (41.7)	8 (9.2)	48 (56.5)	6 (24.0)	1 (14.3)
Limited NICU beds available	121 (23.1)	64 (20.1)	53 (60.9)	1 (1.2)	3 (12.0)	0
Hypothermia on admission	74 (14.1)	69 (21.6)	2 (2.3)	0	3 (12.0)	0
Inadequate monitoring	6 (1.2)	4 (1.2)	0	2 (2.4)	0	0
Surgical procedure related	5 (1.0)	3 (0.9)	0	2 (2.4)	0	0

NICU = neonatal intensive care unit.

conducted in a tertiary centre where high-risk pregnancies are managed and there is likely to be a high proportion of births of preterm infants with intrauterine compromise, whose risk for mortality is exceedingly high. In addition, the limited availability of NICU beds in a setting managing high-risk pregnancies that is also a large referral centre could have contributed to this high proportion of prematurity-related deaths. Limited numbers of NICU beds often result in critically ill neonates with immature lungs being unable to access the respiratory support they require. The recommendation is that there should be 1 NICU bed per 1 000 deliveries.<sup>[4]</sup> The hospital in which the present study was conducted caters for ~35 000 deliveries and should therefore have 35 NICU beds, but it only has 18.

The most common immediate cause of death was healthcare-associated infections (HAIs), which accounted for high proportions

of deaths related to preterm births and congenital abnormalities. This finding is similar to that previously reported from the same hospital by Madhi *et al.*,<sup>[5]</sup> who found that 70.4% of preterm-related deaths were due to HAIs. Inadequate implementation of IPC measures was assessed to be the most common modifiable factor related to deaths in the neonatal unit, and this would explain the most common immediate cause of death being HAIs.

## Conclusion

Most of the infants who died were born preterm. Nosocomial sepsis was the most common immediate cause of death. Efforts to reduce deaths in neonatal units should focus on reducing preterm births, and where this is not possible, antenatal steroids must be administered to all women in preterm labour according to the World Health Organization recommendations.<sup>[6]</sup> Infants who are born

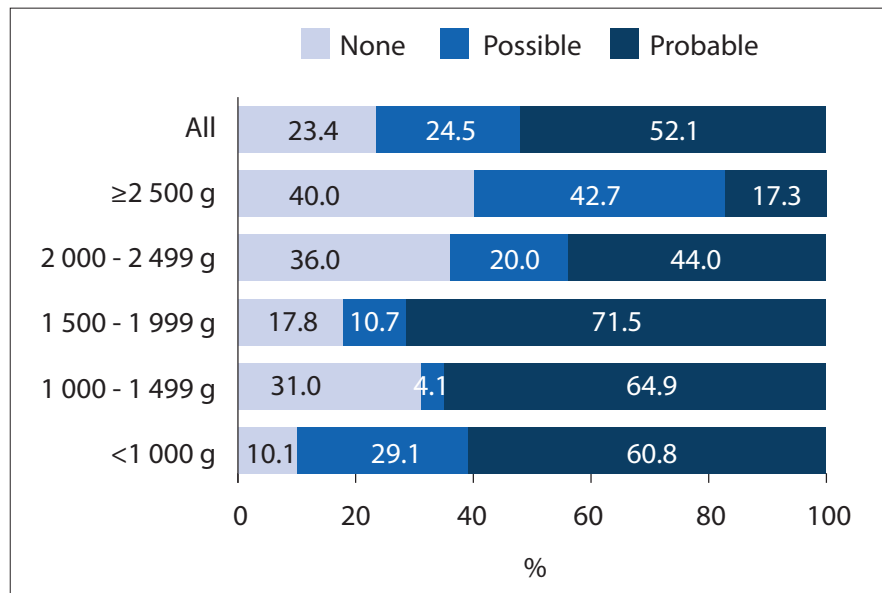


Fig. 1. Proportions of deaths with none, possible or probable modifiable factors.

preterm must receive interventions that have been shown to reduce preterm-related deaths, namely preventing hypothermia, providing caffeine and nasal continuous positive airway pressure in those with respiratory distress syndrome, starting exclusive breastfeeding soon after birth, and nursing the baby in skin-to-skin contact with the mother (kangaroo mother care). IPC measures must be strictly adhered to, including hand hygiene, cleaning and disinfection of the environment and non-critical equipment, and decontamination

and sterilisation of critical equipment or instruments. Access to appropriate healthcare facilities and providing quality care is critical for survival of neonates, especially those born preterm.

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**Conflicts of interest.** None.

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# Experience with Perinatal Problem Identification Programme data over 27 years at Queen Nandi Regional Hospital, KwaZulu-Natal Province, South Africa

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A retrospective analysis of Perinatal Problem Identification Programme (PPIP) data from 1996 to 2022 was done at Queen Nandi Regional Hospital, KwaZulu-Natal Province, South Africa. The following results were found: changes in numbers of deliveries over the years, with an increase in caesarean sections from 20% to 60% when only high-risk patients were accepted for deliveries; a reduction in assisted deliveries; and changes in causes of maternal mortality and stillbirths with HIV treatment and other interventions. The data input improved with 'Hands Up' Mortality and Morbidity Extraction Tool (HUMMET) forms. Everyone at audit meetings to discuss cases could give their opinion during the discussion of the relevant pathology. Poor data input was identified as a problem. In conclusion, ongoing training in PPIP, HUMMET and data capturing is needed, with a dedicated PPIP team.

Lower Umfolozi War Memorial Hospital (LUWMH) in Empangeni, KwaZulu-Natal Province, South Africa (SA), was built and paid for by the war veterans who came back from World War I to Zululand in 1918. It was initially for all races, but when Ngwelezane Hospital was built in the township in the 1970s, only white patients were served. At that stage, one private gynaecologist served the area and most of Zululand. White babies were born at the hospital in a one-bed labour ward. It is estimated that ~30 babies per month were born there.

After the transition to democracy in 1994, there was a period of confusion when the hospital was used by general practitioners as a private facility and only medical aid patients or self-payers used it. There still was only one private gynaecologist. At that stage Ngwelezane Hospital had a consultant, and eventually it was decided to use LUWMH as a 'mother and child' facility because it was underused after other private groups built a facility in Richard's Bay.

In 1996, the Ngwelezane Hospital obstetrics and gynaecology and paediatrics departments moved to LUWMH. The one consultant started using Perinatal Program Identification Programme (PPIP) data. He did it alone, and needed quite some time to work through the files for every stillbirth. When we analysed the data for the present study, we found that he had filled in all the deliveries and stillbirth data but nothing else. The stillbirths were filled with sequential numbers, so the files could be accessed only by the date of birth.

The parity and age of patients were not recorded until October 2014, and the method of delivery was unfortunately not recorded until May 1999. A second gynaecologist was appointed in the early 2000s, but he did not get involved with PPIP. Eventually a new head of department was appointed around 2006. The number of deliveries was stable until 2002 at ~600 per month. During 2004 - 2009 we had up to 1 000 deliveries per month. In 2009 the hospital status was changed from district to regional level. More posts were created for medical officers, specialists and midwives, and the hospital could now take interns. No district hospital was built, so low-risk patients were sent to clinics where midwife obstetric units were established. For urgent referrals, an obstetric ambulance service was created

through co-operation with the District Clinical Specialist Team. Eventually the hospital's name was changed in 2018 to the more appropriate Queen Nandi Regional Hospital. The PPIP data still register under LUWMH.

There was no uniformity in data collection until 2010. For some years PPIP data were not collected or entered owing to low staff numbers, especially during the years with high numbers of deliveries.

## Methods

The head of department developed a 'Hands Up' Mortality and Morbidity Tool (HUMMET) in 2010 because he wanted participation of all staff in the interpretation of the stillbirth data.

Every case was discussed in the audit meetings, and the opinion of the various staff members was asked as an internal quality improvement object. The code for the PPIP was established. The data capturer had an easier time filling in the required information. Unfortunately, the PPIP data on the HUMMET form are mostly not filled in by the doctor, and there is a lot of information on the front

HUMMET - DATA EXTRACTION TOOL	
Institution..... Date..... Maternal Death / FSB / MSB / ENND Apgar <7 @ 5 min / Birth Asphyxia	
"HANDS UP" MORTALITY AND MORBIDITY EXTRACTION TOOL (HUMMET)	
Pt's Names: _____	<b>RISK FACTORS</b>
OPD/In Patient No _____	<b>AVOIDABLE FACTORS</b>
Age: P _____ G _____ RPR _____ Rh _____	<b>SUBSTANDARD CARE/MISSED OPPORTUNITIES</b>
HIV+/- _____ CD4 _____	<b>LEARNING OPPORTUNITIES</b>
<b>SUMMARY ANC</b>	<b>ACTIONS TO BE TAKEN</b>
Booked / Unbooked: Clinic _____	
Hospital: _____	
GA at 1st booking _____ No. of visits _____	
Single / Multiple _____	
Risk factors _____	
<b>LABOUR/DELIVERY</b>	
Admission findings _____	
Progress of Labour _____	
Mode of Delivery _____ Birth _____	
Weight _____	
APGAR 5min _____	

Fig. 1. Hands-Up Mortality and Morbidity Extraction Tool (HUMMET).

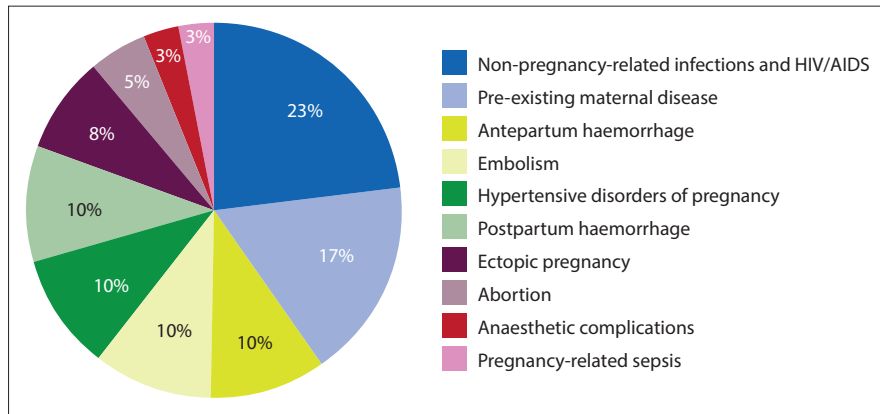


Fig. 2. Maternal deaths from January 2020 to January 2023.

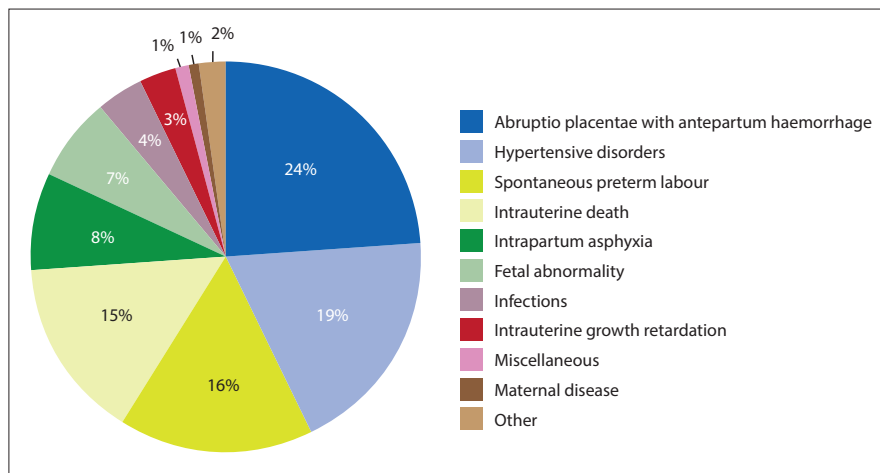


Fig. 3. Stillbirths from January 2011 to January 2023.

page (Fig. 1). The PPIP data capturer has to analyse the information on the front page of the HUMMET form.

### Results

There are no data on maternal deaths between 2004 and 2010 and between 2017 and 2019. The files were sent to the maternal deaths assessors and analysed there, but PPIP is incomplete. There is a large number of cases with unknown method of delivery in the monthly data. We suspect that the labour ward data capturer puts multiple pregnancies down as one method of delivery with two or more babies. We found similar inaccuracies with Wassermann reaction for syphilis and HIV test numbers. PPIP does not accept the numbers unless they correlate. We had to manipulate the negatives to make them accepted. We presume that the positives are correct. HIV results were not captured in the early days, so during the years 1996 to 2009, when the discussion about the disease was at its height, we only had 6% positive results, with 77% unknown. From 2009 to 2020, our patients were 35% positive with 2% unknown. Since then, HIV

positivity is 34.4% with 0.7% unknown. Over the years, methods of delivery at the hospital changed. As all referrals from 16 district hospitals came to Empangeni and no longer to Durban, the caesarean section rate increased from 20% to the current 60%. There has been a reduction in assisted deliveries. Very few forceps deliveries are being done. Vacuum deliveries have come down from up to 35 per month to 5. There are very few vaginal breech deliveries. This is obviously the trend in South Africa, with improved antenatal care and the threat of litigation. Unexpected emergencies are better controlled. Syphilis as a maternal obstetric condition in stillbirths is not listed, despite its being the most common non-pregnancy-related infection causing deaths of babies in our setting. Pulmonary embolus is only listed under obstetric cause of death; it should be listed under final cause too, as there is no 'acute collapse' diagnosis, only acute respiratory failure.

### Maternal death analysis

The causes of maternal mortality have changed over the years, depending on

interventions (Fig. 2). It is difficult to compare them, as the non-reported cases in PPIP maternal mortality make all data inaccurate. The number of maternal deaths from hypertensive disease has decreased. It was the leading obstetric cause of death from 2015 to 2019 at this institution. It is possible that ESMOE (Essential Steps in Managing Obstetric Emergencies) and the RHINO (Rural Health Initiative for Neonates and Obstetrics) project, which focuses on training in the management of hypertension in pregnancy at district and clinic levels, has led to this reduction. Hypertensive disease has been in 5th place for the past 3 years. COVID-19 caused 7 maternal deaths in January 2021. In 2022, 11 of 19 maternal deaths were COVID related (non-pregnancy-related infection). Our HIV/AIDS data are incomplete. The percentage of deaths due to haemorrhage can only be properly established for the past 3 years. We have to rely on the national maternal mortality data to obtain the real numbers.

### Stillbirth analysis

From 1996 to 2000, there was an average of 9 000 deliveries per year with 350 stillbirths (stillbirth rate (SBR) 38.88/1 000). Numbers of deliveries then increased until 2010 to ~11 000 per year with up to 500 stillbirths (SBR 45.54). From 2010 to 2023, numbers of deliveries with available data stabilised again at ~9 000 deliveries per year, with ~500 stillbirths (SBR 55.5) until 2015 and currently ~350 (SBR 38.88). The SBR for regional hospitals in SA as a whole for 2012/13 was 30.2.<sup>[1]</sup>

Analysing recent years, with the knowledge that there are several years of data missing and just to give a general impression, we have found that our biggest challenge is abruptio placentae with antepartum haemorrhage (Fig. 3). In SA's national figures for stillbirths for 2012/13, 'unexplained cause of stillbirth' is listed as the main cause, followed by 'spontaneous preterm labour'.<sup>[1]</sup>

### Avoidable factor analysis

The PPIP data are all similar, even with the missing years. The avoidable factors for the whole period are all listed in the same categories; 48.9% are patient associated, with 'late or no booking', and 34.8% are medical personnel related, with the most common one being no response to hypertension, followed by no response to poor uterine growth. These factors changed in priority in 2016, with no response to poor uterine growth now being the number one avoidable

factor related to medical personnel, followed by no response to hypertension, which we attribute to RHINO training.

### Discussion

Our biggest challenge in terms of stillbirths is abruptio placentae with antepartum haemorrhage. Owing to the wide referral area, numbers are high. The caesarean section rate is high, because only high-risk patients are accepted for deliveries. HIV positivity has not decreased. Hypertension management has improved (RHINO training). With regard to PPIP management, data capturer training must be continuous, both for the labour ward secretary and for the medical person responsible for PPIP data input. The Hummet form should be filled in more completely and the PPIP codes more accurately to make things easier for the data capturer. There must be a dedicated PPIP team who must use PPIP data for presentations. Neonatal deaths data input should be done by a paediatrics team to provide complete statistics.

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