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Short term perinatal and obstetrics outcomes in singleton pregnancies with Oligohydramnios: a prospective study

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Short term perinatal and obstetric outcomes in singleton pregnancies with oligohydramnios:

a prospective study



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This research report is submitted in partial fulfilment for the degree of Master of Medicine in Obstetrics and Gynaecology

Table of contents

	Page
Declaration	ii
Abstract	iii
Dedication	v
Acknowledgments	vi
List of abbreviations	vii
List of tables	viii
Chapter 1. Research protocol and extended literature review	1
Chapter 2. Submissible article	24
Appendix A: Data collection sheet	48
Appendix B: Information sheet	50
Appendix C: Consent form	51
Appendix D: Hospital Chief Executive Officer approval	52
Appendix E: HOD approval	53
Appendix F: Human research ethics committee approval	54
Appendix G: Turnitin report	56

Declaration

I, Dr Lefihlile Ally Morudu, declare that this dissertation is my own work and it is being submitted in partial fulfilment for the degree of Master of Medicine in Obstetrics and Gynaecology at the University of Witwatersrand, Johannesburg.

This work has not been submitted before for any degree or examination at this institution or other universities.

Signed: 

Date: 21/06/2021

Abstract

Background

Oligohydramnios is best defined as an amniotic fluid volume <5th centile expected for a certain gestational age. It is a common complication that affects from 0.8-5.5% of pregnancies and 12% of pregnancies that go beyond 41 weeks.

Objectives

The objectives of this study were to describe the perinatal and obstetric outcomes as well as fetal and maternal co-morbidities in singleton pregnancies diagnosed with oligohydramnios, in a South African setting.

Methods

This was a prospective longitudinal observational study conducted at the Chris Hani Baragwanath Academic Hospital's fetal medicine and obstetric unit. Women were recruited over a period of six months following ultrasound diagnosis of oligohydramnios (amniotic fluid index <5th centile for gestational age). Sixty-one files were retrievable for analysis and descriptive statistical analysis was used.

Results

The caesarean section rate for the study population was 59.0%, with 72.2% of caesarean sections performed for fetal distress. Among the 35 women with co-morbid conditions, 23 (65.7%) had hypertensive disorders of pregnancy. The low birth weight proportion was 62.3% and a majority of the neonates were born at <38 weeks of gestation (54.1%), with 16.3% of the fetuses having intrauterine growth restriction. Overall, 49.1% showed evidence of fetal distress, 20.4% had low Apgar scores and

8.2% had meconium-stained amniotic fluid. Thirteen live-born neonates (24.1%) required resuscitation and 35.2% were admitted to the neonatal intensive care unit.

Conclusion

Oligohydramnios is associated with a high risk of caesarean section due to fetal distress. There is also an association with maternal hypertensive disorders. Patients with oligohydramnios should be managed with intensive antepartum and intrapartum surveillance to improve the perinatal outcomes.

Dedication

This project is dedicated to my father and high school science teacher Mr Sealalo Samuel Morudu, who sadly departed on the 18th of July 2018, shortly after I commenced this project.

"May his soul continue to rest in eternal peace."

My second dedication goes to Prof Shisana Baloyi, Academic Head of Obstetrics and Gynecology, University of the Free State.

He identified me while I was working in the maternity unit of the FH Odendaal Hospital in the Limpopo province while he was the provincial head of obstetrics.

He encouraged me to write the diploma in obstetrics and to pursue the obstetrics and gynecology speciality.

"For that I salute him."

Acknowledgements

My appreciation is directed to my supervisor Dr Jayshree Jeebodh and co-supervisor Dr Nadiya Frank for their inspiration, motivation, support and guidance on this research project.

I would like to thank the almighty God for giving me the knowledge, power and strength to make it possible to achieve this great work.

List of abbreviations

AFI	Amniotic fluid index
AFV	Amniotic fluid volume
CHBAH	Chris Hani Baragwanath Academic Hospital
FAC	Fetal assessment centre
IUGR	Intrauterine growth restriction
MSAF	Meconium-stained amniotic fluid
MTOP	Medical termination of pregnancy
NICU	Neonatal intensive care unit
SDP	Single deepest pocket

List of Tables

	Page
Table 1.1: Amniotic fluid volume levels per gestational age	3
Table 2.1: Obstetric outcomes	32
Table 2.2: Perinatal outcomes	33
Table 2.3: Indications for caesarean sections	35
Table 2.4: Maternal co-morbidities	36
Table 2.5: Relationship between maternal co-morbidities and Fetal distress	37
Table 2.6: Relationship between maternal co-morbidities and Low Apgar scores	37

Chapter 1. Research protocol and extended literature review

Introduction

Oligohydramnios is a common complication in pregnancy, in which the measurement of the amniotic fluid volume (AFV) is less than expected for a certain gestational age.[1] This is, by definition, an amniotic fluid index (AFI) <5 cm or a single deepest pool (SDP) <2 cm.[2] Oligohydramnios is more common in the third trimester but can occur at any time during pregnancy. It complicates from 2-5% of all pregnancies, and 12% of pregnancies that go beyond 41 weeks.[2]

Amniotic fluid formation and regulation

The amniotic sac develops from a fluid-filled extracoelomic cavity that is identifiable at the time of implantation. AFV increases more rapidly during embryogenesis in comparison with the embryonic size. The water constituting the amniotic fluid is initially derived from maternal plasma by diffusion through the fetal membranes, mediated by hydrostatic and osmotic pressures. Water and solutes from the maternal plasma reach the amniotic fluid through the placenta and the fetus once the placenta and fetal vessels have developed. By the 12th week the AFV is about 25 mL and this increases to about 400 mL by the 20th week.[3]

There is rapid bi-directional fluid diffusion between the fetus and the amniotic fluid through the non-keratinized fetal skin, umbilical cord, placenta and amnion surfaces, which are freely permeable to water and solute.[4] Once the fetal skin is fully keratinized, AFV is determined by other factors that constitute the amniotic fluid circulation.

Amniotic fluid originates mainly from fetal urine production once the fetal urinary system is formed, from around 8-11 weeks of gestation. AFV production is equivalent to 300 mL/kg fetal weight/day or 600-1200 mL/day near term.[4] Secretions of oral, nasal, tracheal and lung fluids add about 60-100 mL/kg fetal weight/day, and fetal breathing movements contribute to the efflux of lung fluids into the amniotic fluid.[4] The removal of amniotic fluid is predominantly achieved by fetal swallowing, which is estimated at 200-250 mL/kg fetal weight/day.

The transmembranous pathway refers to the movement of amniotic fluid through the fetal membranes into the maternal circulation through the uterine decidua.[3] The amount of fluid passing through this pathway is estimated at 200-500 mL/day. However, the transmembranous pathway does not significantly affect the AFV.[3]

The regulatory dynamics of amniotic fluid are complex and in constant flux, with the entire volume turning over on a daily basis.[5] Fetal swallowing, respiratory tract absorption, diffusion through the membranes and urine voiding are some of the mechanisms that play a role. The amniotic fluid volume increases with increasing gestational age but then decreases towards term, from 100 mL at 16 weeks, peaking at 1000 mL at 28 weeks and then decreasing to about 800 mL at 40 weeks (Table 1.1). Failure of these mechanisms may lead to either oligohydramnios, which is a low volume of amniotic fluid, or polyhydramnios which is a high volume of amniotic fluid.[4]

Table 1.1: Amniotic fluid volume levels per gestational age

Gestational age (weeks)	Fetus (g)	Amniotic fluid (mL)	Placental weight (g)
16	100	200	100
28	1000	1000	200
36	2500	900	400
40	3300	800	500

Amniotic fluid functions

Amniotic fluid provides a protective and supportive environment for the developing fetus. It cushions against trauma, allows for fetal movements, aids the development of the fetal limbs and lungs, and prevents compression of the umbilical cord.[3] Amniotic fluid also plays a defensive role as part of the innate immune system. Substances such as a-defensins, lactoferrin, lysozyme, bactericidal/permeability-increasing protein, calprotectin, secretory leukocyte protease inhibitors, psoriasin and a cathelicidin, which have been shown to have significant antimicrobial properties, have been found in the amniotic fluid and vernix. These potent antimicrobials show a broad spectrum of activity against bacteria, fungi, protozoa and viruses.[3] Amniotic fluid contains carbohydrates, proteins and peptides, lipids, lactate, pyruvate, electrolytes, enzymes and hormones, indicating potential nutritive functions. Other substances, found in both human breast milk and amniotic fluid at high levels, are epidermal growth factor (EGF), transforming growth factor alpha (TGF-A), transforming growth factor beta-1 (TGF-B1), insulin-like growth factor 1 (IGF-1), erythropoietin (EPO) and granulocyte colony-stimulating factor (G-CSF).[3]

Amniocentesis and amniotic fluid analysis can be used to diagnose fetal chromosomal anomalies by karyotyping or polymerase chain reaction techniques. Amniotic fluid can also be used to assess fetal lung maturity by determining the lecithin/sphingomyelin ratio and/or the presence of phosphatidyl glycerol, and most recently by the assessment of lamellar body counts. The surfactant to albumin ratio and electrical conductivity of amniotic fluid have been suggested as potentially superior methods of evaluation of fetal lung maturity.[3]

Amniotic fluid volume evaluation

AFV is assessed mainly by ultrasonography, and multiple methods are available.[6,7] AFV can be assessed non-invasively by the amniotic fluid index (AFI), or by the single deepest pocket (SDP) technique. AFI estimates the AFV by first dividing the uterus into four quadrants using an imaginary line drawn transversely through the umbilicus and longitudinally along the linea nigra. Then, the sum of vertical measurements in cm of the deepest fluid pockets in each of the four quadrants (devoid of fetal parts or umbilical cord) gives the AFI.[8,9] AFI estimation is a method that is reasonably objective and reproducible.[8] Single deepest pocket (SDP) estimation is a single measurement of the deepest vertical pocket (devoid of fetal parts or umbilical cord) anywhere in the uterus.[10] There is no clear consensus in the literature as to which of the two methods is superior. The AFI has been recommended for use as a 'gold standard' because it is claimed to be more reproducible.[8] However, a multicentre, open-label randomized controlled trial (the SAFE trial) compared use of AFI and SDP, and concluded that the AFI method increased the rates of diagnosis of oligohydramnios and labour inductions without improving perinatal outcomes, therefore making SDP the more favorable method in low-risk pregnancies.[11] A Cochrane systematic review and meta-analysis also found that AFI increased the diagnosis of oligohydramnios and the rate of induction of labour without improvements in perinatal outcomes.[12]

Other described methods in the literature include dye dilution techniques, which can be time-consuming and invasive, where the AFV is measured indirectly or directly at amniocentesis or caesarean delivery respectively.[5,6] A somewhat subjective ultrasonographic assessment, which is described as visual interpretation without measurements (although how frequently it is used is uncertain), is the two-diameter pocket technique. This technique is no longer widely used as it gives a poorer prediction of abnormal AFV than the AFI.[7] Lastly, there is colour-Doppler sonography, which is however unhelpful as it appears to overdiagnose oligohydramnios.[7] Hughes et al studied these methods and concluded that the dye-determined AFV correlated well with ultrasonographic estimates for normal AFVs, but poorly for oligohydramnios and polyhydramnios. Overall, it appears from available evidence that the SDP technique should be the non-invasive measurement of choice for AFV estimation.

Classification of amniotic fluid volume

Phelan et al have classified AFVs using the AFI method, where an AFI <5 cm is classified as oligohydramnios, 5-20 cm is normal, and >20 cm is classified as polyhydramnios.[5] When using the SDP method, AFV is classified by the depth of the deepest visible pool, where <1 cm is severe oligohydramnios, 1-2 cm is mild oligohydramnios, 2-8 cm is normal, 8-12 cm is mild polyhydramnios, 12-16 cm is moderate polyhydramnios, and >16 cm is severe polyhydramnios.[7]

Multiple other definitions of what constitutes an abnormal AFV can be found in the literature. Oligohydramnios, or low AFV, has been described as a total AFV <200 mL, total AFV <500 mL, AFV <5th centile for gestational age, SDP <2 cm, or an AFV that appears subjectively low. Shank et al concluded that oligohydramnios is best defined as an AFI <5th centile, as it may better predict fetuses at risk for adverse perinatal outcomes as compared with an AFI <5

cm.[13] Polyhydramnios, or an increased AFV, has been variously defined as a total volume >2000 mL, an AFV >95th centile for gestational age, an SDP >8 cm, an AFI >24 cm or >25 cm, or an AFV that appears subjectively increased.[5,7]

Oligohydramnios

From the above discussion, oligohydramnios is best considered as a reduced AFV <5th centile for gestational age. It complicates about 0.8-5.5% of pregnancies and up to 12% of pregnancies that go beyond 41 weeks of gestation and is more commonly observed in the third trimester.[2,14] There are two gestational age peaks in the incidence of oligohydramnios, from 13-21 weeks and from 34-42 weeks.[14]

Aetiology of oligohydramnios

Most frequently, rupture of membranes, or a decrease in fetal urine production or excretion leads to oligohydramnios. The most common cause of oligohydramnios is rupture of the membranes. Other causes include congenital fetal abnormality, intrauterine growth restriction (IUGR) with a decrease in urine production, poor maternal hydration, and postdates pregnancy.[15]

Premature rupture of membranes (rupture before onset of labour) complicates approximately 8% of pregnancies. About 3% of pregnancies are complicated by preterm premature rupture of membranes,[15] and this may occur as a result of various mechanisms, for example as physiologic weakening of the membranes associated with apoptosis, enhanced by a cytokine cascade initiated by ascending genital tract infection. Other mechanisms include protease production and dissolution of extracellular matrix, and placental abruption with decidual thrombin expression triggering thrombin-thrombin receptor interactions.[15]

Nicolaides et al concluded in their study that there was an association between oligohydramnios and IUGR and maternal disease, including maternal hypertension.[16] Impaired placental function, in addition to hypoxia, contributes to oligohydramnios.[16] In growth-restricted fetuses, secondary to hypoxaemia-induced redistribution of fetal cardiac output, there is shunting of fetal blood from the kidneys to vital organs, leading to oliguria or anuria and therefore oligohydramnios.[16-19]

Fetal abnormalities contribute up to 50% of cases of decreased AFV observed in the second trimester. Major or lethal malformations generally cause severe oligohydramnios because of fetal anuria.[15] Examples are congenital absence of functional renal tissue and obstructive uropathy, respectively preventing formation of urine, and entry of urine into the amniotic sac. Fetal urinary tract malformations include bilateral renal agenesis, ureteral atresia, posterior urethral valves, bilateral ureterojunction obstruction, bilateral multicystic dysplastic kidneys, and infantile polycystic kidney disease.[16-19]

In post-term fetuses, decreased efficiency of placental function has been proposed to cause a decrease in urine production, but has not been confirmed histologically. However, a decrease in fetal renal blood flow and urine production has been demonstrated in pregnancies beyond 42 weeks' gestation.[16-19]

Maternal causes of oligohydramnios include poor hydration, hypertensive disorders including preeclampsia, pre-existing or gestational diabetes and chronic hypoxia. Alterations in maternal hydration may lead to changes in the net movement of fluid into or out of the fetus and this in turn affects fetal urine production and hence AFV.[18] The use of medications like non-steroidal anti-inflammatory drugs and angiotensin-converting enzyme inhibitors has also been

implicated. Placental causes include abruptio placenta and twin-to-twin transfusion syndrome (in monochorionic twins), while many cases of oligohydramnios are idiopathic.[18]

Clinical features and complications

Clinical features of oligohydramnios are easily palpable fetal parts, fetal malpresentation and small-for-gestational-age uterine symphysis-fundal height. In 2011, Buchmann et al. conducted a study at Chris Hani Baragwanath Academic Hospital, looking at clinical abdominal palpation for predicting oligohydramnios in suspected prolonged pregnancy. They concluded that a fetal head which is ballotable on abdominal palpation may have value in excluding oligohydramnios where ultrasonography is not available.[20]

Complications of oligohydramnios include umbilical cord compression leading to fetal distress, fetal musculoskeletal abnormalities like facial distortion and clubfoot, pulmonary hypoplasia, IUGR, and amnion nodosum, which is the presence of nodules on the surface of the amnion.[4] A reduction in AFV is also associated with findings of non-reassuring fetal heart rate and meconium-stained amniotic fluid (MSAF), requiring interventions such as induction of labour, instrumental delivery and caesarean section, which may result in perinatal and maternal morbidity.[17]

Management of oligohydramnios

Management of oligohydramnios depends on the gestational age at which the diagnosis is made. Transfer of the patient to a referral centre for expert ultrasound assessment and a planned delivery in a hospital setting is recommended, due to the associated obstetric and perinatal complications.[21] Before term, expectant management is often the most appropriate course of action. This depends on both the maternal and fetal condition as well as the cause of

oligohydramnios. Ongoing fetal surveillance including fetal growth tracking, Doppler studies and serial monitoring of the AFV is necessary. During labour, continuous fetal heart rate monitoring has been advocated for all pregnancies complicated by oligohydramnios.[22,23]

When the diagnosis is made at term, delivery is often the most appropriate management plan. If the fetal heart rate is reassuring, the decision to deliver is based on gestational age, maternal and fetal well-being, past obstetric history and favourability of the cervix.[22,23] Improving maternal hydration status with hydration therapy has been shown to significantly increase the quantity of the AFV where there is no identifiable cause of the oligohydramnios.[18]

Other modalities have been described in the management of oligohydramnios, especially in the preterm period. These methods are aimed at prolonging gestation and therefore reducing the neonatal complications of prematurity.[14] Amnioinfusion involves the infusion of isotonic solutions like normal saline or Ringer's lactate into the amniotic cavity either transabdominally or transcervically. The amniopatch makes use of an infusion of a solution containing platelets and cryoprecipitate, and this may be useful in cases of iatrogenic prelabour premature rupture of membranes.[14] The use of vesico-amniotic shunts involves the shunting of urine from the fetal bladder into the amniotic cavity, and this procedure is used in cases of obstructive uropathy.[14] Other procedures include in-situ cerclage and intra/trans-cervical instillation of coagulation factor with or without a cerclage, the latter using a catheter or fetoscopy. Of some interest is fetoscopic closure of the membrane defect (amniograft), or fixation of the defect with a transcervical double balloon catheter or gelatin sponge. However, these interventions have not gained ground in clinical practice and there are insufficient data establishing their efficacy in the prevention of pulmonary hypoplasia or delaying delivery.[14,24,25]

Perinatal and obstetric outcomes

Oligohydramnios has been associated with adverse perinatal outcomes including increased caesarean section rates due to fetal distress, induction of labour, IUGR, Apgar scores <7 at 5 minutes, MSAF, stillbirth, and admission to neonatal intensive care unit (NICU). A systematic review by Khatun et al showed an association between oligohydramnios and IUGR, small for gestational age infant, prolonged labour, caesarean section, fetal distress, MSAF, low Apgar score and NICU admission.[26] Rabie et al conducted a systematic review on oligohydramnios in complicated and uncomplicated pregnancies which included 15 studies, nine of which were in high-risk and six in low-risk patients, including 8067 and 27526 women respectively. They found that uncomplicated pregnancies with oligohydramnios had significantly higher rates of meconium aspiration syndrome (risk ratio 2.83; 95% CI 1.83-5.77), admission to NICU (risk ratio 1.71; 95% CI 1.20-2.42), and caesarean section for fetal distress (risk ratio 2.16; 95% CI 1.64-2.85).[27] Women who had oligohydramnios with a co-morbidity were more likely to have an infant with low birth weight (risk ratio 2.35; 95% CI 1.27-4.34), however the frequencies of 5-min Apgar score <7, NICU admission, MSAF and caesarean section for fetal distress were similar to those with normal AFI.[27]

A prospective study conducted in Gujarat, India, by Jagatia et al, which included 100 women, found that the incidence of oligohydramnios was higher in primigravidas (52%) with an increased operative morbidity (55.7%).[28] The commonest 'cause' of oligohydramnios was idiopathic (52%), followed by known associations such as pregnancy-induced hypertension (25%), which had the highest operative morbidity (60%). Most affected patients had caesarean deliveries for fetal distress, which was either due to umbilical cord compression or IUGR. They also concluded that there was an association between oligohydramnios, IUGR and NICU admission.[28]

A study of 100 women with oligohydramnios from Zagazig University in Egypt revealed that these pregnancies carried a statistically significant increased risk of fetal heart rate decelerations, thick meconium, low Apgar score at 5 minutes, admission to NICU, congenital anomalies and IUGR.[29] They also found that the rate of caesarean section was significantly higher in women with oligohydramnios (42%) vs a control group (20%).

A prospective hospital-based study conducted in Gantur government hospital in India over one year (October 2007 to October 2008) recruited 100 women with oligohydramnios. The results showed a marginal increase of oligohydramnios in unbooked women, a higher incidence of maternal hypertension (52%), a labour induction rate of 48%, and a 75% caesarean section rate in women who had induced labour compared with 42% in those with spontaneous labour.[30] Fetal distress was found to be the dominant indication for caesarean section in the study group at 40%, compared to 10% in a control group. MSAF was found in 36% of the study group compared with 14% in the control group and Apgar scores <7 at 5 minutes were reported in 20% of the study group compared with 4% of the control group. Thirty-four percent of neonates required admission to NICU compared with only 8% of the control group. Six percent of newborns had meconium aspiration syndrome, with none affected among the controls. The incidence of low birth weight babies was 56%.[30]

A retrospective cohort study reported by Melamed et al found that patients with isolated oligohydramnios had a higher rate of preterm deliveries (27% vs 12%) than controls. Most were of iatrogenic origin (90%) and occurred before 34 weeks of gestation. There were higher rates of labour induction (50% vs 10%, $p<0.001$) and caesarean delivery (47% vs 17%, $p<0.001$), principally due to higher rates of breech presentation, failed induction and non-

reassuring fetal heart rate.[31] Another cohort study, conducted by Umber, showed significant differences, where pregnancy with oligohydramnios, compared with controls, was associated with increased chances of induction of labour (41% vs 22%), non-reassuring fetal heart rate (5% vs 3%), decelerations of the fetal heart rate (48% vs 39%), caesarean delivery for fetal distress (32% vs 23%), Apgar scores <6 at 1 minute (8% vs 1%), Apgar scores <7 at 5 minutes (6% vs 0.6%), neonatal resuscitation (3.4% vs 0.8%) and admission to NICU (7% vs 2%).[32]

Ghimire et al. conducted a prospective hospital-based study in Nepal, looking at pregnancy outcomes in cases with oligohydramnios after 28 weeks. They found that 85% of affected women had operative deliveries, 16% (vs 5% in controls) had labour induced, and fetal distress was the second commonest indication for caesarean section at 16%.[33] Another prospective study, from Pakistan, found high rates of induction of labour (63%) in patients with isolated oligohydramnios compared to 14% in women without oligohydramnios, and caesarean deliveries were required in 42% of cases compared with 18% of controls. Fetal distress was the most frequent indication for caesarean section (63%). The authors however found no significant difference between the groups with regard to perinatal morbidity and mortality.[34]

A prospective study conducted by Mushtaq et al, which compared women with oligohydramnios and controls, found that 45% vs 13% of women respectively had a non-reassuring fetal heart rate, and that caesarean delivery was performed in 64% of cases vs 29% of controls; 52% of caesarean sections in the case group were done for fetal distress, compared with 28% in the control group.[35] The comparative rates of MSAF were 32% and 22% respectively. Comparisons between respective Apgar scores showed no statistical significance (10% vs 8% had Apgar scores <7 at 1 minute, and 2% vs 1% had Apgar scores <7 at 5 minutes). In the study group 8% of the newborns required NICU admission compared with 6% in the

control group, and this was also not statistically significant. There was one stillbirth in the oligohydramnios group (0.7%).[35]

Background of the study

While there is some conflicting evidence on adverse obstetric and perinatal outcomes associated with oligohydramnios in the literature, most studies as discussed above show significant associations with adverse obstetric and perinatal outcomes. To our knowledge, there is no published study on oligohydramnios and its effect on pregnancy outcomes in the South African setting. Therefore, the incidence of the oligohydramnios is unknown in our population and the associated perinatal and obstetric outcomes have not been described.

Aim of the study

The aim of our study was to describe the perinatal and obstetric outcomes in pregnancies diagnosed with oligohydramnios.

Objectives

1. To describe the short-term perinatal outcomes of singleton pregnancies with oligohydramnios.
2. To describe the obstetric outcomes in pregnancies diagnosed with oligohydramnios.
3. To describe the fetal and maternal co-morbidities associated with oligohydramnios

Methodology

Setting

The study was conducted in the Chris Hani Baragwanath Academic Hospital (CHBAH) obstetric unit, which is attached to the Faculty of Health Sciences at the University of the Witwatersrand. The facility is a tertiary hospital and is a major referral centre for hospitals in

Johannesburg and bordering districts and provinces. The hospital conducts over 21 000 deliveries each year. The obstetric unit has a dedicated fetal assessment centre (FAC), which together with the maternity ultrasound unit performs about 25 000 ultrasound examinations each year. Pregnant patients are referred to the hospital for maternal conditions such as cardiac disease, hypertensive disorders, diabetes, auto-immune diseases and other disorders. Fetal indications for referral include IUGR, monochorionic twin pregnancies and structural anomalies detected on screening ultrasound. Initial ultrasound assessment is performed by the registrars and sonographers, and problem cases are then referred to the FAC.

Study Population

The study included women who were diagnosed with oligohydramnios at the FAC.

Study design and sample

This was a prospective longitudinal observational study. The data were collected over a six-month period from November 2018 to May 2019, and the researcher recruited 97 pregnant women.

Recruitment

Patients were prospectively recruited at the FAC when the diagnosis of oligohydramnios was made. The ultrasound scans were performed by the maternal-fetal specialists and sub-speciality registrars in the department. AFI was assessed using the Phelan method and oligohydramnios was defined as an AFI of $<5^{th}$ centile for gestational age on GE Viewpoint Database version 4.00.05. Upon recruitment, patients were consented by the FAC staff and the researcher (Appendix A). Informed consent was obtained to examine the patients' records and the records

of their newborns. A study number was allocated, and a trial sticker was attached onto each patient's folder with her trial number.

All study patients were booked on the GE Viewpoint Database version 4.00.05 and scanned using the GE Voluson P8 ultrasound machine with a wide-band convex transducer (2-5 MHz) (General electric healthcare, Wisconsin, USA). Maternal demographics, past obstetric history, fetal growth findings and Doppler studies were recorded on the database. All patients had printed ultrasound reports from the Viewpoint placed in their folders and one copy was filed for the researcher to collect. Eligible patients were also identified by the sonographers and registrars. These patients were then referred to the FAC for confirmation of the diagnosis and recruitment into the study as described above.

Inclusion criteria:

- Any gestational age at diagnosis
- Any order of parity
- Singleton pregnancy
- AFI $<5^{th}$ centile for gestational age
- Women aged $\geq$18 years
- Oligohydramnios from any cause except membrane rupture

Exclusion criteria:

- Declined to participate in the study

Obstetric and perinatal outcomes recorded:

- Mode of delivery
- Indication for caesarean section
- Number of patients who underwent a medical termination of pregnancy
- Gestational age at delivery
- Maternal co-morbid conditions
- Maternal infections

Short-term perinatal outcomes recorded:

- Prenatal diagnosis of congenital abnormalities (structural or chromosomal)
- Prenatal diagnosis of minor abnormalities (external physical features that did not inhibit major function, e.g. clinodactyly, polydactyly, low-set and rotated ears and ocular hypertelorism)
- Prenatal diagnosis of major abnormalities (malformations causing significant functional and cosmetic impairment or which are life-limiting, e.g. neural tube defects, hypoplastic left heart, ventral wall defect and craniofacial clefts)
- Diagnosis of IUGR (defined antenatally as an estimated fetal weight or abdominal circumference $<3^{rd}$ centile).
- Low birth weight babies (defined as having a birth weight $<10^{th}$ centile for gestational age and/or birth weight of <2.5 kg).
- Presence of MSAF intrapartum, described as thin or thick
- Diagnosis of fetal distress, made by the attending doctor on duty

- Apgar scores <7 at 1 and 5 minutes, and diagnosis of birth asphyxia made by paediatricians on clinical examination after delivery (using a combination of Apgar score, cord blood gases and Thompson score)
- Newborn admission to the transitional neonatal care unit immediately after delivery and whether discharged or transferred to the NICU; neonates were followed up for the first 72 hours of life
- Stillbirths and early neonatal deaths. Stillbirths were classified as fresh or macerated, and early neonatal deaths were defined as deaths occurring within the first seven days of life
- Diagnosis of congenital infection made in the neonatal unit

Follow-up and delivery

As per protocol, these patients were reviewed every four weeks to assess fetal growth and Doppler studies by the FAC. AFI and SDP were measured at each visit. Women were delivered at 38-39 weeks' gestation as per CHBAH unit protocol, if there was no earlier indication for expedited delivery. Patients with co-morbid medical problems may have required delivery before term for maternal indications. Induction of labour was planned under continuous fetal monitoring in the labour ward as per unit protocol. Patients who had one or more previous caesarean sections were delivered by repeat operation at 38-39 weeks. Caesarean section was reserved for obstetric indications.

The researcher determined that the study patient was admitted or delivered by:

- Daily searches for study patients in the admission ward, first stage area, labour ward and theatre registers

- Requesting medical staff to inform the researcher when a study patient was admitted or delivered. The patients were identified by the trial stickers on their folders. Staffs were notified about the study at academic meetings and with poster notifications.
- Requesting recruited patients to contact the researcher by text message on admission or after delivery

Data Collection

Each patient's data (FAC reports, and pregnancy, labour, delivery and neonatal details) were entered onto a data collection sheet (Appendix B). No identifying information were entered, and patients were identified by their unique individual study numbers.

Statistics

Descriptive statistical analyses were performed. Categorical variables were summarised using frequencies and percentages, and continuous variables were summarised with means (and standard deviations), and medians (and interquartile ranges), if the data were not normally distributed. For comparison of outcomes, the Chi-squared test was used to compare categorical variables, and the Student's t-test was used to compare normally distributed continuous variables. The statistical analysis was performed using Stata version 15 software (Statacorp, College Station, Texas, USA).

Ethics approval and hospital consent

An application for ethics approval was made to the Human Research Ethics Committee of the University of Witwatersrand and obtained (reference number M180670, Appendix C). An application was made to the CHBAH Chief Executive Officer (Appendix D) and to the departmental heads of Obstetrics and Gynaecology and Paediatrics for permission to conduct the study in their departments.

Funding

All costs incurred were borne by the researcher. Patients were not rewarded for participating in the study.

Intention to disseminate

The research was presented in March 2020 as a poster presentation at the Congress of the South African Society of Obstetricians and Gynaecologists, in the Drakensburg, Kwazulu-Natal, South Africa. The findings were also presented at both the departmental and university academic meetings and there is an intention to publish the study findings.

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Chapter 2. Submissible article

Short term perinatal and obstetric outcomes in singleton pregnancies with oligohydramnios: a prospective study

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Abstract

Background

Oligohydramnios is best defined as an amniotic fluid volume <5th centile expected for a certain gestational age. It is a common complication that affects from 0.8-5.5% of pregnancies and 12% of pregnancies that go beyond 41 weeks.

Objectives

The objectives of this study were to describe the perinatal and obstetric outcomes as well as fetal and maternal co-morbidities in singleton pregnancies diagnosed with oligohydramnios, in a South African setting.

Methods

This was a prospective longitudinal observational study conducted at the Chris Hani Baragwanath Academic Hospital's fetal medicine and obstetric unit. Women were recruited over a period of six months following ultrasound diagnosis of oligohydramnios (amniotic fluid index <5th centile for gestational age). Sixty-one files were retrievable for analysis and descriptive statistical analysis was used.

Results

The caesarean section rate for the study population was 59.0%, with 72.2% of caesarean sections performed for fetal distress. Among the 35 women with co-morbid conditions, 23 (65.7%) had hypertensive disorders of pregnancy. The low birth weight proportion was 62.3% and a majority of the neonates were born at <38 weeks of gestation (54.1%), with 16.3% of the fetuses having intrauterine growth restriction. Overall, 49.1% showed evidence

of fetal distress, 20.4% had low Apgar scores and 8.2% had meconium-stained amniotic fluid. Thirteen live-born neonates (24.1%) required resuscitation and 35.2% were admitted to the neonatal intensive care unit.

Conclusion

Oligohydramnios is associated with a high risk of caesarean section due to fetal distress. There is also an association with maternal hypertensive disorders. Patients with oligohydramnios should be managed with intensive antepartum and intrapartum surveillance to improve the perinatal outcomes.

Introduction

Oligohydramnios is an amniotic fluid volume (AFV) <5th centile for a certain gestational age.[1] Phelan et al described it as an AFI (amniotic fluid index) <5 cm using the four-quadrant measurement of the AFV,[2] whereas Chamberlain et al described it as the single deepest vertical pocket <2 cm using the single deepest pocket (SDP) method.[3] Shank et al showed that using an AFI <5th centile for gestational age to describe oligohydramnios was a better predictor of fetuses at risk for adverse outcomes than an AFI definition of <5 cm described by Phelan et al.[1]

Oligohydramnios occurs in 0.8-5.5% of pregnancies. It is most frequent in the third trimester and complicates up to 12% of pregnancies that go beyond 41 weeks of gestation.[4,5] There are two peaks in the incidence, from 13-21 weeks and from 34-42 weeks.[5] The most common cause of oligohydramnios is rupture of membranes before the onset of labour, which complicates approximately 8% of pregnancies. Other causes include congenital fetal abnormalities, uteroplacental insufficiency with intrauterine growth restriction (IUGR), poor maternal hydration, postdates pregnancy, medication like nonsteroidal anti-inflammatory drugs and angiotensin converting inhibitors, and maternal conditions such as hypertensive disorders and diabetes mellitus.[6,7]

Congenital fetal abnormalities generally cause severe oligohydramnios, either from absence of functional renal tissue, which prevents the formation of urine, or obstructive uropathy, which prevents entry of urine into the amniotic sac. Fetal urinary system malformations include bilateral renal agenesis, ureteral atresia, posterior urethral valves, bilateral ureterojunction obstruction, bilateral multicystic dysplastic kidneys, and infantile polycystic kidney disease.[7-10] Fetal complications of oligohydramnios include cord compression leading to fetal hypoxia,

musculoskeletal abnormalities like facial distortion and clubfoot, pulmonary hypoplasia, IUGR, and amnion nodosum, which is the presence of nodules on the surface of the amnion.[11]

Oligohydramnios has been associated with adverse obstetric and perinatal outcomes, including induction of labour, caesarean section for fetal distress, instrumental delivery, medical termination of pregnancy (MTOP), IUGR, low Apgar scores, meconium-stained amniotic fluid (MSAF), stillbirths, and admission to neonatal intensive care unit (NICU).[12,13] Clinical management depends on the gestational age at which the diagnosis is made. A planned birth in a tertiary hospital obstetric unit is recommended.[14]

There is consensus in the literature that oligohydramnios is associated with a risk of adverse perinatal and obstetric outcomes. Given the absence of data on outcomes of oligohydramnios in South Africa, the aim of this study was to describe the obstetric and perinatal outcomes in pregnancies diagnosed with oligohydramnios in a South African setting.

Methods

The study was conducted in the obstetric unit of Chris Hani Baragwanath Academic Hospital (CHBAH), which is attached to the Faculty of Health Sciences at the University of the Witwatersrand. The facility is a tertiary hospital, which is a major referral centre for hospitals in the Johannesburg area and adjacent districts and provinces. CHBAH conducts over 21 000 deliveries per year. The obstetric unit has a dedicated fetal assessment centre (FAC). The centre and the maternity ultrasound unit perform about 25 000 ultrasound examinations per annum. Patients are referred for maternal conditions such as cardiac disease, hypertensive disorders, diabetes and autoimmune disorders, as well as for fetal conditions like IUGR, monochorionic twin pregnancies and structural abnormalities detected on ultrasound. At referral, ultrasound

screening is initially performed by maternity ultrasound unit sonographers or obstetric registrars, who then refer the patients to the FAC.

Permission to conduct the study was obtained from the Human Research Ethics Committee of the University of Witwatersrand (reference number M180670), and from the CHBAH Chief Executive Officer.

A prospective longitudinal observational study was undertaken from November 2018 to May 2020. The inclusion criteria were singleton pregnancy, AFI <5th centile for gestational age, and maternal age >18 years. Women with co-morbid conditions and pregnancies with suspected or confirmed congenital abnormalities were included. Women with clinically confirmed premature rupture of membranes and those who declined to participate were excluded. Women were recruited at any gestational age from the second trimester. Ninety-seven pregnant women were recruited into the study. Oligohydramnios was defined as an AFI <5th centile for the gestational age as per CHBAH protocol.

All study patients were booked on the GE Viewpoint Database version 4.00.05 and scanned using a Voluson P8 ultrasound machine with a wide-band convex transducer (2-5 MHz) (General electric healthcare, Wisconsin, USA). Maternal demographic information, past obstetric history, fetal growth, and Doppler studies were recorded on the database. All women meeting the inclusion criteria were recruited into the study by the staff of the FAC. Informed consent was obtained to analyze the records of both study participants and their newborns. A study number was allocated, and a trial sticker was attached to the patient's folder with her trial number.

As per hospital protocol, the participating patients were reviewed every four weeks by the FAC to assess fetal growth and to perform Doppler studies. A fetal medicine viewpoint report was issued at each visit to the patient, and one copy was filed for the researcher. Patients were delivered at 38-39 weeks' gestation as per hospital protocol if there was no maternal or fetal indication for expedited delivery before term. Patients who had one or more previous caesarean sections were delivered by caesarean section at 38-39 weeks.

The following information was captured on data sheets: maternal demographic information, gestational age at delivery, mode of delivery, co-morbidities and infections, birth weight, congenital anomalies and neonatal outcomes. Congenital abnormalities were defined as either structural and confirmed, or suspected chromosomal abnormalities. A minor abnormality was defined as an external physical feature that which did not inhibit major body function, and a major abnormality was defined as a life-limiting malformation, or one causing significant functional or cosmetic impairment.

IUGR was determined antenatally as an estimated fetal weight or abdominal circumference $<3^{rd}$ centile as per hospital protocol. Low birth weight babies were defined as those with a birth weight <2.5 kg. MSAF, if present, was recorded as thin or thick. The diagnosis of fetal distress was made by the attending obstetric doctor on duty at the time of the event. Apgar scores were recorded at 1, 5 and 10 minutes, as was stillbirth. Neonatal outcome was recorded as admission to the transitional neonatal unit or to the NICU, as well as early neonatal death. All newborns were followed up for the first 72 hours after birth.

All data collected was entered on a study data sheet. Descriptive statistical analyses were performed. Categorical variables were summarised using frequencies and percentages, and

continuous variables were summarised with means (and standard deviations), and medians (and interquartile ranges), if the data were not normally distributed. To assess and rule out if there was any association between maternal comorbidities and fetal outcomes, we used Chi-squared tests. The Chi-squared tests were used to establish if there were significant differences between the observed and expected frequencies for fetal distress and Apgar scores among women with and without co-morbidities at 5% level of significance. All statistical analysis were performed using Stata version 15 software (Statacorp, College Station, Texas, USA).

Results

Ninety-seven pregnant women with oligohydramnios were recruited for the study after meeting the inclusion criteria. Only 61 maternal records were retrievable for analysis at the end of the study. The remainder was lost to follow-up as records could not be found at the hospital records department. It is unclear if these patients were delivered at our facility or at other facilities. The Johannesburg metro region is an area with a significant number of migrants and our facility serves most of these patients. It is our suspicion that most patients tend to return to their area of origin closer to term in order to give birth where they have better family support and care. The other plausible explanation could be the large number of patients our facility serves together with the inadequacies of staff that could have led to poor record keeping, and therefore records not being found.

The mean age of the participants was 29.8 years, with 9 (14.8%) being >35 years old and 52 (85.2%) aged 18-34 years. There were 40 multigravidas (65.6%) and 21 primigravidas (34.4%). Twenty-three neonates delivered at ≥38 weeks' gestation, of which 22 (95.7%) had a birth weight ≥2.5 kg. Thirty-three neonates delivered at <38 weeks' gestation and 1 neonate (3.0%) had a birth weight ≥2.5 kg. Overall, 38 (62.3%) of the neonates were born with a birth

weight <2.5 kg. Twenty-one were of very low birth weight (<1.5 kg), of which 12 were of extremely low birth weight (<1 kg). Tables 2.1 and 2.2 summarise the obstetric and perinatal outcomes.

Table 2.1. Obstetric outcomes (n=61)

Variable	**n (%)**
Intrauterine growth restriction:	
Present	10 (16.3%)
No intrauterine growth restriction	51 (83.7%)
Gestational age at delivery:	
<38 weeks	33 (54.1%)
≥38 weeks	28 (45.9%)
Fetal distress (n=55):	
Present	27 (49.1%)
No fetal distress	28 (50.9%)
Meconium-stained amniotic fluid:	
Present	5 (8.2%)
No meconium staining	56 (91.8%)
Mode of delivery:	
Caesarean section	36 (59%)
Normal vaginal	25 (41%)

Table 2.2 Perinatal outcomes (n=61)

Variable	**n (%)**
Live birth, Apgar score at 5 minutes (n=54)	
<7	11 (20.4%)
≥7	43 (79.6%)
Stillbirth (n=7):	
Fresh stillbirth	2 (28.6%)
Macerated stillbirth	5 (71.4%)
Birth weight:	
<2.5 kg	38 (62.3%)
≥2.5 kg	23 (37.7%)
Major congenital abnormalities:	
Present	5 (8.2%)
No congenital abnormalities	56 (91.8%)
Neonatal resuscitation (n=54):	
Yes	13 (24.1%)
No	41 (75.9%)
Neonatal intensive care unit admission (n=54):	
Yes	19 (35.2%)
No	35 (64.8%)

There were 54 live births (88.5%) and 7 stillbirths (11.5%), with all stillbirths born at <38 weeks' gestation with a birth weight <2.5 kg. There were two fresh stillbirths due to severe preeclampsia complicated by abruptio placentae, and five macerated stillbirths, all associated with severe preeclampsia. Five mothers (8.2%) had MTOPs, of which four were done for early-onset severe preeclampsia, and one was done for a lethal congenital abnormality affecting the cardiac, renal and skeletal systems.

Among the five fetuses with congenital abnormalities, four had severe malformations relating to the urinary system. Two of these had renal agenesis with associated cardiomegaly, pericardial effusion and pulmonary hypoplasia (one with additional pelvic and lower limb deformities). The third fetus had posterior urethral valves with bilateral hydronephrosis, and the fourth had sirenomelia and bilateral multicystic dysplastic kidneys. There was also one infant who had known gastroschisis and developed evidence of fetal distress before onset of labour, requiring caesarean section. This neonate was admitted to the NICU and was scheduled for surgical repair.

Among the neonates showing evidence of fetal distress (n=27), 19 (70.4%) were born with a birth weight <2.5 kg. Thirteen (24.1%) of 54 live-born infants required resuscitation after birth, and 19 (35.2%) were admitted to the NICU. The main reasons for admission were very low birth weight as well as respiratory distress syndrome. One infant required intubation and ventilation. Among neonates with birth weights <2.5 kg (n=38), 10 (26.3%) had IUGR and 5 (13.2%) had major congenital abnormalities as described above. Eight of the cases with IUGR (80%) were associated with hypertensive disorders. Among births by caesarean section (n=36), fetal distress was a reason for a majority of the operations (n=26; 72.2%) (Table 2.3). There were five early neonatal deaths (a rate of 8.9%). Four of these deaths were due to lethal congenital anomalies, and one occurred in an extremely premature infant that weighed less than 1 kg.

Table 2.3. Indications for caesarean sections (n=36)

Indication	**n (%)**
Fetal distress	20 (55.6%)
Repeat caesarean section	4 (11.1%)
Severe pre-eclampsia	3 (8.3%)
Severe pre-eclampsia and fetal distress	3 (8.3%)
Repeat caesarean section and fetal distress	3 (8.3%)
Failed induction of labour	2 (5.7%)
Placenta praevia	1 (2.8%)

Thirty-five women (57.3%) had associated co-morbidities, with the majority (n=23; 65.7%) having hypertensive disorders of pregnancy (Table 2.4). The other women with co-morbid conditions included three with cardiac disease. One had a replaced pulmonary valve with moderate regurgitation and significant stenosis. The second woman had severe mitral regurgitation, and the third had rheumatic heart disease with mild mitral regurgitation. Other women with medical co-morbidities included one with hyperthyroidism, hypertension and mitral regurgitation associated with mitral valve prolapse. Another had chronic hypertension with cardiomyopathy and congestive cardiac failure that was treated successfully, but who then developed superimposed severe pre-eclampsia. Among the two women with renal disease, one had chronic renal failure and hypertension and the other developed acute kidney injury as a result of severe acute pneumonia. Three women were diabetic. All women with co-morbidities,

except one with chronic hypertension, delivered neonates with birth weights ≥2.5 kg, and their fetuses had normal doppler studies with the only concerning finding being oligohydramnios.

Table 2.4. Maternal co-morbidities (n=35)

Medical condition	
Hypertensive disorders	23 (65.7%)
Diabetes	3 (8.6%)
Respiratory disorders	3 (8.6%)
Cardiac disorders	3 (8.6%)
Systemic infections	1 (2.9%)
Central nervous system disorders	1 (2.9%
Hyperthyroidism and cardiac disease	1 (2.9%)

Inferential analyses were conducted to assess if there was an association between maternal co-morbidities and perinatal outcomes. However, this showed no statistically significant association at a 5% level of significance (Table 2.5 and Table 2.6). Out of the 61 women a total of 55 and 54 women had data on fetal distress and newborn Apgar scores. For these women, chi-squared test showed no statistical difference in the occurrence of fetal distress (X^2= 0.4462 P-value = 0.504) and low Apgar scores (X^2= 0.2264 P-value = 0.634) at 1 degree of freedom and 5% level of significance. Based on these findings the null hypotheses were not rejected

and were considered true, that is, there is no significant association between having maternal co-morbidities and these fetal outcomes.

Table 2.5. Relationship between maternal co-morbidities and Fetal distress (n=55)

	Fetal Distress		
Co-morbidity	No	Yes	Total
No	12 (46.15%)	14 (53.85%)	26
Yes	16 (55.17%)	13 (44.83%)	29
Total	28 (49.09%)	27 (49.09%)	55

Chi-squared test statistic (X^2) = 0.4462 P-value = 0.504

Table 2.6. Relationship between maternal co-morbidities and Low Apgar scores (n=54)

	Low Apgar scores		
Co-morbidity	No	Yes	Total
No	20 (76.92%)	6 (23.08%)	26
Yes	23 (82.14 %)	5 (17.86 %)	28
Total	43 (79.63%)	11 (20.37%)	54

Chi-squared test statistic (X^2) = 0.2264 P-value = 0.634

Discussion

Oligohydramnios is defined as an AFI <5th centile for gestational age and is a common complication of pregnancy.[1] Oligohydramnios occurs in 0.8-5.5% of pregnancies and is associated with both adverse obstetric and perinatal outcomes.[4,5]

The mean maternal age of the women in this study 29.8 years, and this was consistent with the studies conducted by Mushtaq et al,[15] and Neveiro-Fuentes, et al.[16] However, 85.2% of the study participants were aged 18-34 years, which may explain the mean maternal age. In addition, the study excluded women <18 years of age, and few women fall pregnant beyond the age of 35 years in the local population (CHBAH annual maternity statistics, 2018/19). The incidence of oligohydramnios was higher in multigravid women (65.6%) compared with primigravid women (34.4%). There are inconsistent findings in the literature that suggest a relationship between maternal parity and oligohydramnios, with a higher prevalence noted in multigravid women.[17-20]

Thirty-six women (41%) delivered by caesarean section. This was a relatively high caesarean section rate. The most common indication was fetal distress, often in association with pre-eclampsia and previous caesarean section. This finding is consistent with other studies, which also show an association between oligohydramnios and an increased caesarean section delivery rate.[21,22] Oligohydramnios may lead to umbilical cord compression, MSAF, poor tolerance of labour, fetal acidosis and low Apgar scores. At CHBAH, fetal scalp blood sampling and internal pressure transducers are not used for intrapartum monitoring. The diagnosis of fetal distress was made purely on cardiotocograph tracings by the doctors on call, who use the NICE (United Kingdom National Institute for Health and Care Excellence) guidelines as per hospital protocol.[14] The high rate of fetal distress may be explained by the use of continuous fetal

monitoring that allowed for early detection of pathological traces and a lower threshold for delivery by caesarean section.

MSAF was found in 8.2% of the women in the study. No neonates developed meconium aspiration syndrome. While this finding was unremarkable with no control group, other studies have shown an increased detection of MSAF among women with oligohydramnios. Fetal intrapartum passage of meconium is due to vagal stimulation from umbilical cord compression, leading to hypoxic stress resulting in an increase in peristalsis and relaxation of the anal sphincter. In addition to oligohydramnios, other factors that have been shown to cause MSAF include placental insufficiency, maternal hypertensive disorders, intrauterine infections, fetal acidosis, and maternal substance abuse like tobacco and cocaine. The finding of intrapartum MSAF is an indication for intensive fetal heart rate monitoring. It is therefore recommended that women with oligohydramnios be referred for delivery to a hospital with capabilities for electronic intrapartum fetal monitoring, as well as caesarean section facilities, and NICU support. This is also important in counselling before induction of labour in women with oligohydramnios.

Thirty-five women (57.4%) had associated co-morbidities. Hypertensive disorders of pregnancy were the commonest co-morbidities in the participants. This is similar to a study conducted by Madhavi et al,[23] who found the incidence of hypertensive disorders among women with oligohydramnios to be 52%. This finding was not unexpected as maternal hypertensive disorders are associated with placental insufficiency, which may cause fetal growth restriction and chronic fetal hypoxia resulting in oligohydramnios. According to standard protocols, women with hypertensive disorders of pregnancy undergo intensive ultrasound surveillance because of the risk of fetal growth restriction, thus increasing the

detection rate of oligohydramnios. In this study, related to severity of maternal hypertensive disease, four mothers had MTOPs done in the second trimester and early third trimester. Among the non-hypertensive women with co-morbid conditions, fetal and neonatal complications, other than the observed oligohydramnios, were infrequent.

The rate of preterm delivery (<37 completed weeks' gestation) in this study was 54.1%. This was mainly attributable to severe hypertensive disorders requiring expedited delivery, often related to the presence of non-reassuring fetal heart rate patterns, abnormal Doppler studies (absent or reversed umbilical artery end-diastolic flow or abnormal middle cerebral artery flow indicating redistribution), and/or severe maternal conditions like imminent eclampsia, liver dysfunction, renal dysfunction and HELLP syndrome (haemolysis, elevated liver enzymes, low platelets). Hypertensive disorders can result in complications such as maternal stroke, eclampsia, HELLP syndrome, abruptio placentae, IUGR and fetal distress. The International Society for the Study of Hypertension in Pregnancy recommends that women with preeclampsia who exhibit severe features, i.e. organ dysfunction including signs of adverse fetal affectation, be delivered promptly to prevent adverse outcomes.[24] The majority of women with co-morbidities (65.7%) in the study had hypertensive disorders, this may have prompted delivery before term based on both maternal health status and fetal condition. Nevertheless, oligohydramnios on its own can lead to non-reassuring fetal heart rate patterns requiring expedited preterm delivery.[13,25,26]

The stillbirth rate was high (11.5%), with most stillbirths occurring in association with severe hypertensive disorders. Fetal death often occurred during the MTOP. Sharma et al associated fetal deaths in their study with early onset of oligohydramnios.[27] Generally, the earlier the onset of oligohydramnios, whatever the cause, the worse the prognosis. Fetal congenital

abnormalities, while not frequent in this study (n=5), involved mostly the urinary system with resulting anuria. This finding was not surprising.

This study found that 16% of the fetuses had IUGR, comparable to findings by Chudal et al,[28] who reported IUGR in 13% of their fetuses. Hypertensive disorders were present in most cases of IUGR in this study. Severe hypertensive disorders affect the development and function of the placenta. This increases the risk of IUGR secondary to placental insufficiency.[29] The fetus adapts to resultant hypoxia by shunting blood flow to essential organs and decreasing blood flow to the kidneys, leading to reduced urine output and oligohydramnios.

Twenty percent of live-born babies in this study had Apgar scores <7 at 5 minutes. This relatively high proportion is comparable to other studies of oligohydramnios.[30,31] The low Apgar scores may be explained by an increased risk of fetal distress as a majority of the neonates who had low Apgar scores had fetal distress. The fact that 24% of neonates required resuscitation after birth highlights the importance of trained doctors being present at delivery of women with oligohydramnios, also with facilities able to provide intubation and ventilation if needed. Thirty-one percent of neonates in the study required admission to the NICU and this finding is similar to those of other studies.[32] As expected, the main reasons for the admissions were low birth weight and prematurity-related problems. The five early neonatal deaths, related to lethal congenital anomalies and extremely low birth weight (<1 kg), were not preventable. Oligohydramnios has been shown to be associated with low birth weight,[33] particularly in patients with associated medical conditions as demonstrated in a systematic review conducted by Rabie et al.[13] In this study, 62% of neonates born were born with a birth weight <2.5 kg, with a large proportion weighing <1 kg at birth.

Several studies have reported maternal comorbidities as markers of poor fetal outcomes.[34,35] This study found no association between maternal comorbidities and fetal distress as well as low Apgar scores. A possible explanation for these results may be the small sample size that was used. Further studies with larger sample sizes, is therefore recommended to validate the findings of our study and to ensure that such relationships are explained in such settings.

Limitations

A limitation of this study is that patients were often delivered at other institutions and therefore lost to follow up. Some maternal and neonatal records were incomplete, making it difficult to include these patients in the study. The other major limitation was the large proportion of files of affected pregnancies that were not retrievable for analysis from the hospital records department.

Conclusion

Oligohydramnios is a common finding in pregnancy, most frequently due to rupture of membranes. Oligohydramnios is also associated with maternal hypertensive disorders of pregnancy as well as fetal congenital anomalies and IUGR. There is also an increased risk of adverse obstetric and perinatal outcomes, commonly the risk for caesarean delivery due to fetal distress. This study had almost 30% of the participants lost to follow up, but it demonstrated some of the maternal and fetal risks associated with oligohydramnios, including hypertensive disorders, high caesarean section rate, MSAF, fetal abnormalities, low Apgar scores, preterm births with very low birth weight, and admission to NICU, as have been shown in studies from other countries.

Pregnancies with oligohydramnios should therefore undergo detailed maternal and fetal evaluation, and ideally be managed at a centre capable of offering regular fetal ultrasound surveillance. Continuous fetal monitoring is advised during labour due to the high risk of fetal distress, with facilities for emergency caesarean section. There should also be the capability to offer advanced neonatal resuscitation and intensive care.

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Appendix A: Data Sheet

DATA SHEET

Study number: Enrolment Date:

Booking date: Booking GA: Rh: RVD: Hb:

Age: Parity: Gravidity:

GA at Enrolment: EFW: AFI: SDP:

Number of follow up visits:

Measurement	28 weeks	32 weeks	36 weeks	38 weeks	>38 weeks
AFI					
SDP					

Date of Delivery:

Obstetric Outcomes

Mode of Delivery: GA at Delivery:

IOL: Yes/NO CS: Yes/No

Delivery by CS

Indication:

Fetal distress: CAT 1: CAT 2: CAT 3:

MSAF: Thin: Thick:

Grade1: Grade2: Grade3:

Other delivery

comment……

……

……

……

Perinatal outcomes

Live Birth: Yes/No

Stillbirth: Yes/No

APGARS: 1min: 5min:

Birth weight: Length: HC:

Baby Resuscitated: Yes/No if yes.

Comment……

……

……

NICU admission: Yes/No if yes

Comment……

……

…….

Chromosomal / Congenital abnormalities: Yes/No if yes

Comment……

……

……

Other

comment……

……

……

Appendix B*:* Information sheet.

Good day, my name is Dr Ally Morudu. I am a doctor training to be a specialist in obstetrics and gynaecology here at Chris Hani Baragwanath Hospital. I am conducting research in order to obtain a master's degree (MMed). My research will look at short term perinatal and obstetric outcomes of term, singleton pregnancies with oligohydramnios.

The findings will help understand current knowledge regarding perinatal and obstetric outcomes and what we can do to improve-protocols

I invite you to partake in my research. All that is required is for you to participate in our monthly follow up protocol were you will be examined and ultrasonography performed on you and at the end of your pregnancy information will be collected from your file for analysis. I assure you that your personal information will be kept highly confidential. Only your study number will appear on the forms, which will be kept by me and my supervisor. Your file number will not appear on my research. The data sheet will not contain any identifiable information and will be destroyed once data analysed.

You will not receive any remuneration or reward for partaking in the study. You may change your mind at any point even if you have signed. Your treatment and care shall not be jeopardized in any way if you decide not to participate in the study. Ethics approval has been obtained from the University of Witwatersrand and the Human Research Ethics Committee.

You may contact me at any time concerning my research. My cell number is 0718204785.

Human Research Ethics Committee contact details:

Prof P Cleaton Jones, Tel 011 717 2301, email: peter.cleaton-jones1@wits.ac.za

Ms Z Ndlovu/ Mr Rhulani Mkansi/ Mr Lebo Moeng at the Administrative Officers Tel: 011 717 2700/ 2656/ 1234 /1252 email: zanele.ndlovu@wits.ac.za; Rhulani.mkansi@wits.ac.za; and Lebo.moeng@wits.ac.za

Appendix C: Consent Form

Informed consent sheet.

If you are willing to partake in my study, please kindly sign that you have understood all that has been explained to you.

Thank you for your participation.

Participant……

Witness……

Researcher……

Date……

Appendix D: Hospital Chief Executive Officer approval

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 5th June 2018

TITLE OF PROJECT:

Short term perinatal and obstetrics outcomes in Singleton pregnancies with Oligohydramnios: A Prospective Study

UNIVERSITY: Witwatersrand

Principal Investigator: Dr L A Morudu

Department: Obstetrics & Gynaecology

Supervisor : Dr J Jeebodh

Permission Head Department (where research conducted): Yes

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Academic Hospital. The CEO / management of Chris Hani Baragwanath Academic Hospital is accordingly informed and the study is subject to:-

- Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.
- The Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- The MAC will be informed of any serious adverse events as soon as they occur
- Permission is granted for the duration of the Ethics Committee Approval.

.....
Recommended
(On behalf of the MAC)
Date: 5/6/2018

.....
Approved/Not Approved
Hospital Management
Date: 06/06/18

Appendix E: HOD approval

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

PERMISSION TO CONDUCT RESEARCH AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PRINCIPAL RESEACHER:

FULL NAME: LEFIHLILE ALLY MORUDU

DESIGNATION: MEDICAL REGISTRAR (O&G)

CONTACT NUMBER: 0718204785

EMAIL: allymorudu@gmail.com

NAME OF SUPERVISOR: DR. J. JEEBODH

TITLE OF RESEARC: SHORT TERM PERINATAL AND OBSTETRIC OUTCOMES ITY SINGLETON PREGNANCIES WITH OLIGOHYDRAMNIOS

STUDY SITE/S: CHRIS HANI BARAGWANATH HOSPITAL

BRIEF OUTLINE OF METHODOLOGY
This is a prospective observational study where patients will be recruited, consented & enrolled on diagnosis of Oligohydramnios, then followed up until delivery where certain variables will be measured.

PROTOCOL: ATTACHED

DATA SHEET: ATTACHED.

EXPECTED START DATE: 01/08/2018 EXPECTED DURATION: 31/01/2019

ETHICS CLEARANCE? Y / N / (PENDING)

CONFLICT OF INTEREST? Y / (N) DETAILS

COST TO HOSPITAL AND OR PATIENTS? Y / (N)

SOURCE OF FUNDING: N/A.

APPROVAL OF HOD (Y/N)

SIGNATURE | NAME IN PRINT+ DESIGNATION: Yadlam | OFFICAL STAMP+ DATE: CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL MASOKA MOSTI 05 JUN 2018

Appendix F: Human research ethics committee approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Dr LA Morudu
School of Clinical Medicine
Department of Obstetrics and Gynaecology
Chris Hani Baragwanath Academic Hospital

E-mail: allymorudu@gmail.com

CC: Supervisor: Dr J Jeebodh and Dr N Frank <jjeebodh@gmail.com>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 07/11/2018

REF: *R14/49*

PROTOCOL NO: **M180670** *(This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)*

PROJECT TITLE: *Short term perinatal and obstetric outcomes in singleton pregnancies with oligohydramnios*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr LA Morudu

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M180670

NAME: (Principal Investigator)	Dr LA Morudu
DEPARTMENT:	School of Clinical Medicine Department of Obstetrics and Gynaecology Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Short term perinatal and obstetric outcomes in singleton pregnancies with oligohydramnios
DATE CONSIDERED:	29/06/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr J Jeebodh and Dr N Frank
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	07/11/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

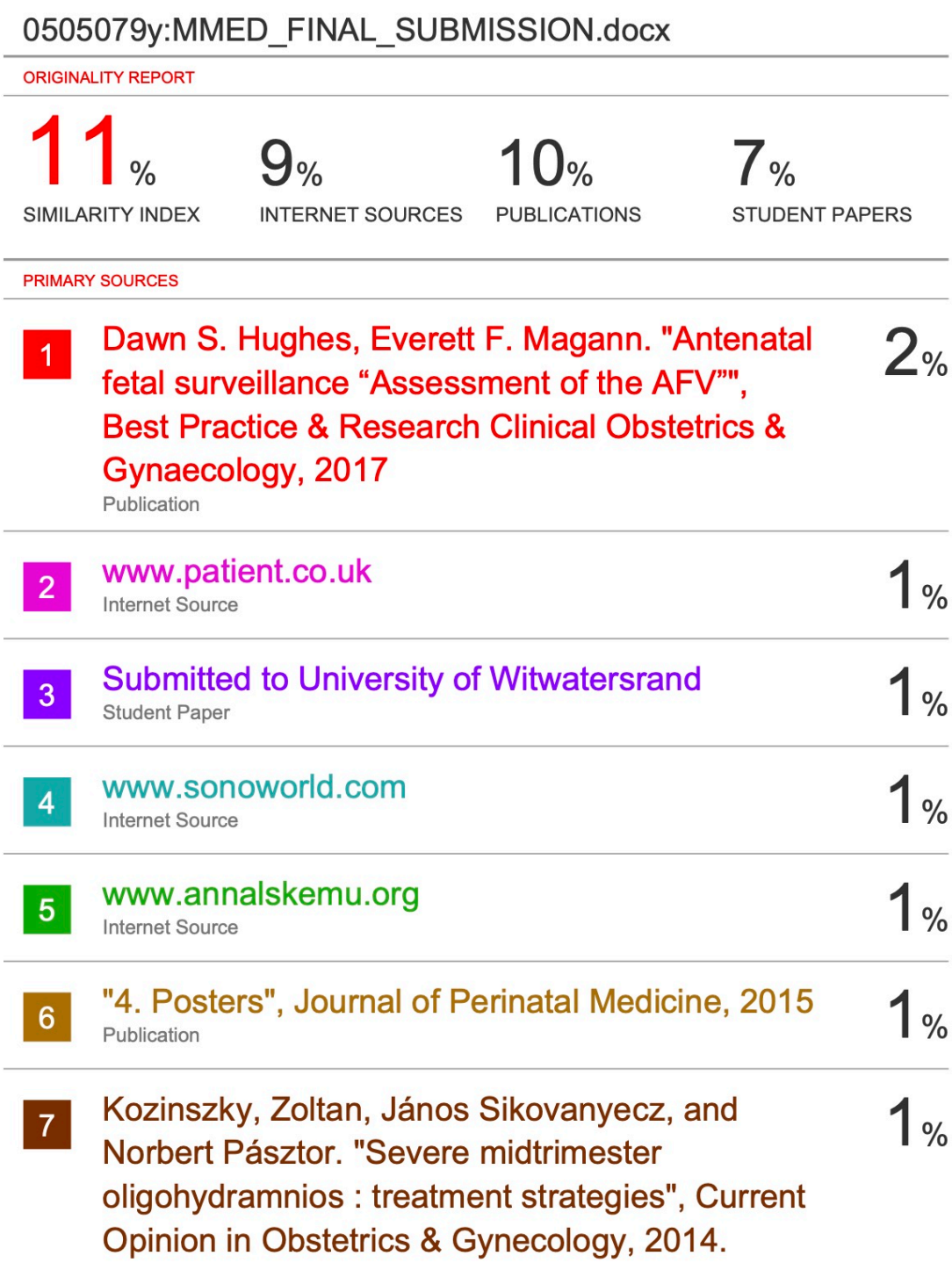
DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on 3rd floor, Phillip V Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date of the meeting when the study was initially reviewed. In this case, the study was initially reviewed in **June** and will therefore reports and re-certification will be due early in the month of **June** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix G: Turnitin Report



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ORIGINALITY REPORT

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