

CAUSES, MANAGEMENT AND OUTCOMES OF POLYHYDRAMNIOS AT A LEVEL 2 HOSPITAL IN CAPETOWN



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Table of Contents

Title Page	1
Declaration	2
Plagiarism Declaration	3
Acknowledgement	4
Table of Contents	5
Abstract	6
Chapter 1 Introduction	9
1.1 Background	
1.2 Causes	
1.3 Management	
1.4 Outcomes	
1.5 Rationale	
1.6 Specific Aims and Objectives	
Chapter 2	13
2.1 Study Design	
2.2 Study Subjects	
2.3 Sampling Technique	
2.4 Measures	
2.5 Data Management Plan	
2.5.1 Data Collection	
2.5.2 Data Entry, Storage, Confidentiality	

2.6 Statistical Consideration

2.6.1 Sample Size

2.6.2 Statistical Analysis

2.7 Ethical Consideration

2.8 Conflict of Interest

2.9 Data Dissemination

Chapter 3: Results 16

3.1 Causes

3.2 Management Protocols

3.3 Outcomes

Chapter 4: Discussion 23

4.1 Causes

4.2 Management

4.3 Outcomes

Chapter 5: Conclusion 27

Chapter 6: References 28

Chapter 7: Attachments 31

7.1 Data collection sheet

7.2 Sample size calculation formula

Abstract

Introduction:

Polyhydramnios is defined as excessive accumulation of amniotic fluid and has an estimated incidence of 0.2% – 3.9%. It is associated with both maternal and fetal adverse outcomes. Mild polyhydramnios is often idiopathic and pregnancy outcomes in this group are usually no worse than in the general population of pregnant women. In contrast, conditions such as congenital anomalies, chromosomal abnormalities, or diabetes mellitus are often found in patients with moderate and severe polyhydramnios. Neonatal and maternal adverse outcomes, can be up to five times higher in this subgroup.

Methodology:

We conducted a retrospective cohort study at a Level 2 hospital in Cape Town. Folders of women diagnosed with polyhydramnios on ultrasound examination were reviewed. We recorded demographic data as well as information on underlying causes, management and outcomes. We summarised continuous variables using the mean (standard deviation) and categorical variables using count (percentage). We tested the association between categorical variables using the chi-square test. Statistical significance was set at $p < 0.05$.

Results:

A total of 136 patients with polyhydramnios (80 mild and 56 moderate + severe) were included from January 1, 2018 to December 31, 2020. Cases of idiopathic polyhydramnios accounted for 81.7% of the mild and 77.2% of the moderate + severe polyhydramnios group. Composite maternal and fetal adverse outcome occurred in 19/136 (14.0 %) polyhydramnios cases. Preterm labour occurrence was significantly higher in the moderate + severe polyhydramnios group (9/56; 16 %) compared to the mild polyhydramnios group (3/80; 3.8%, $p = 0.01$). There was a statistically significant difference in the occurrence of the composite adverse outcome in the moderate + severe group compared to the mild group [13/56(23.2 %) vs 6/80 (7.5 %) $p = 0.001$]. Elective delivery at 38 – 40 weeks for polyhydramnios was associated with an increased risk of composite perinatal adverse outcome (7.6% vs 3.4%) compared to those that awaited spontaneous

labour or were delivered for other obstetric reasons. The difference was however not statistically significant ($p = 0.14$).

Conclusions:

Most cases of polyhydramnios are idiopathic, regardless of category. Adverse outcomes are, however, significantly lower in the mild group compared to the moderate + severe group. The rate of adverse outcome in the mild group is comparable to the background risk in the general population. Elective admission and delivery of patients for polyhydramnios between 38–40 weeks may be associated with adverse outcome compared to awaiting spontaneous labour or delivery indicated for other obstetric reasons.

1. Introduction

1.1 Background

Polyhydramnios is defined as excessive accumulation of amniotic fluid and has an estimated incidence of 0.2% – 3.9% (Hamza et al., 2013). It is associated with both maternal and fetal adverse outcomes. The frequency of its detection depends on the proportions of low-risk to high-risk patients seen and how frequently ultrasonography is used in pregnancy (Dashe et al., 2002).

Polyhydramnios can be classified into mild (25–29.9 cm), moderate (30–34.9 cm) and severe (>35 cm) groups based on the amniotic fluid index (Alexander et al., 1982). Amniotic fluid index (AFI) is a common way of quantifying amniotic fluid at ultrasonography. It is calculated by obtaining the sum of vertical dimensions of amniotic fluid from four cord-free and limb-free quadrants of the uterus. Amniotic fluid volume varies with gestational age, peaking at an AFI of 18 around 30–32 weeks' gestation (Magann et al., 2000). The volume of amniotic fluid at any stage of gestation depends on the balance between its production from fetal urine, lung and oral secretions and its uptake through fetal swallowing and intermembranous absorption (Brace, 1997). A fetus close to term will produce between 500 and 1200 mL urine and swallow between 210 and 760 mL amniotic fluid per day. Increased production and/ or reduced reabsorption can result in polyhydramnios (Magann et al., 2000).

1.2 Causes of Polyhydramnios

Approximately 50%-60% of cases of polyhydramnios are unexplained and referred to as idiopathic (Smith et al., 1992; Karkhanis & Patni, 2014). An underlying cause is found in only 17% of cases in mild polyhydramnios, compared to 91% in moderate to severe polyhydramnios (Many et al., 1995; Hamza et al., 2013). The commonly listed causes of polyhydramnios include fetal malformations, maternal diabetes mellitus, multiple pregnancies, fetal anaemia, fetal neuromuscular conditions and viral and bacterial infections (Hamza et al., 2013). Fetal abnormalities such as oesophageal atresia, duodenal atresia and some

neuromuscular conditions which impair the swallowing reflex are associated with polyhydramnios (Karkhanis & Patni, 2014). Viral infections usually cause polyhydramnios through increased cardiac output associated with fetal anaemia and resultant increased urinary production (Fayyaz & Rafi, 2012). Approximately 18.8% of pregnant women with diabetes mellitus have polyhydramnios. The mechanism is believed to be increased fetal urine production secondary to hyperglycaemia (Alfadhli et al., 2015). Other rare causes of polyhydramnios, such as placental tumours, have also been documented in the literature (Abdalla et al., 2014).

Laboratory investigations used to identify the aetiology include HbA1c and oral glucose tolerance test to exclude diabetes mellitus, screening for maternal toxoplasmosis, cytomegalovirus, and parvovirus, screening for atypical antibodies and the Betke-Kleihauer test to check for feto-maternal haemorrhage (Karkhanis & Patni, 2014). Furthermore, a detailed fetal ultrasound scan should be performed to check for structural abnormalities and, when doubt exists for conditions such as tracheo-oesophageal fistulas, a magnetic resonance imaging (MRI) scan may be helpful (Alexander et al., 1982). Middle cerebral artery dopplers may also be performed when fetal anaemia is suspected. Chromosomal abnormalities are known to be present in 10% of fetuses with sonographic anomalies and polyhydramnios, but in only 1% when ultrasound is considered normal (Karkhanis & Patni, 2014). In cases where fetal malformation or soft markers are present, fetal karyotyping may be advised to detect chromosomal abnormalities (Karkhanis & Patni, 2014).

1.3 Complications of Polyhydramnios

Maternal dyspnoea, preterm labour, premature rupture of membranes, abnormal fetal presentation, placental abruption, postpartum haemorrhage and umbilical cord prolapse have been described as possible obstetric complications due to overdistention of the uterus (Smith et al., 1992; Many et al., 1995; Dorleijn et al., 2009). A cluster-randomised trial of ultrasound-diagnosed polyhydramnios within five low and low-middle income countries in Africa and Asia showed significantly higher rates of obstructed labour (7% vs 4%) and fetal malposition (4% vs 2%), while the incidence of preterm birth was not different among pregnancies complicated by polyhydramnios and those not (11% vs 13%) (Bauserman et al., 2019). A study by Many et al. (1995) on the association between preterm labour

and polyhydramnios suggested that the underlying cause of polyhydramnios, rather than the relative excess of amniotic fluid, appeared to determine the occurrence of preterm labour. Polyhydramnios has also been shown to be associated with higher birth weights, higher rates of caesarean sections for fetal indications, low neonatal 5-minute APGAR scores, higher rates of admission to neonatal intensive care units (NICU) and increased perinatal mortality (Lallar et al., 2015).

1.4 Interventions

One study showed that up to one-third of cases of polyhydramnios, especially mild ones, resolved spontaneously without any treatment (Moise, 1991). Treatment is usually recommended only for maternal discomfort and dyspnoea (Rode et al., 2007; Hamza et al., 2013). Amniodrainage and pharmacological techniques can be used to reduce the amniotic fluid volume and prevent complications (Cabrol et al., 1987). There are no randomised controlled studies to show the optimum amount of amniotic fluid to be drained, or whether tocolysis or prophylactic antibiotics should be used. There is general agreement that the procedure should be stopped when ultrasound examination shows an AFI between 15 and 20 cm. Amniodrainage is complicated in 1%-3% of cases by preterm labour, placental abruption, and premature rupture of membranes, chorioamnionitis or hyponatremia (Cabrol et al., 1987)). An optimum environment is needed to be able to respond timeously to these complications. Indomethacin, a prostaglandin synthetase inhibitor, has also been used to successfully reduce amniotic fluid volume (Cabrol et al., 1987). However, complications of indomethacin such as early closure of the fetal ductus arteriosus and episodes of fetal intracranial bleeding have been reported. If indomethacin is used, weekly AFI checks and fetal echocardiography are recommended to check for oligohydramnios and closure of the ductus arteriosus, respectively. Sulindac, another non-steroidal anti-inflammatory drug, has been shown to have a better side effect profile than indomethacin (Jayagopal et al., 2007). There are no randomised controlled studies comparing expectant management versus intervention in the prevention of complications of polyhydramnios. However, intervention is usually reserved for severe maternal discomfort. In addition, routine cervical length measurement has not been shown to improve outcome. (Hershkovitz et al., 2006).

Some obstetricians routinely admit patients with polyhydramnios for observation and some will electively induce labour before 40 weeks' gestation (Backley et al.,

2019). They argue that, if labour and rupture of membranes occur in areas where prompt actions can be taken to avoid any potential complications, maternal and fetal adverse outcomes may be better.

However, no studies have shown any benefits to these practices when there is no obstetric indication (Karkhanis & Patni, 2014).

1.5 Rationale for the Study

Based on the above-mentioned complications associated with polyhydramnios and the possibility that these may vary across the different severity categories, management protocols need to be implemented accordingly. Currently, different clinicians employ different management strategies and the evidence is unclear as to optimal management strategies, including the use of cervical length surveillance to predict preterm labour, investigations such as TORCH (Toxoplasmosis, rubella, cytomegalovirus and herpes infections) screen and oral glucose tolerance tests, amnioreductive therapy, and elective admission and induction of labour between 38 and 40 weeks to avoid the risk of abruptio placentae and cord prolapse. We intend to use information from our study to inform cost-effective and evidence-based ways of investigating and managing patients with polyhydramnios.

1.6 Specific Objectives

- To assess maternal and perinatal outcomes in patients with polyhydramnios.
- To compare perinatal outcomes between mild versus moderate and severe polyhydramnios
- To compare causes of polyhydramnios between different severity groups of polyhydramnios
- To compare perinatal outcome measures for patients admitted in the ward and those undergoing induction of labour at 40 weeks or earlier versus those who had spontaneous labour. These comparisons will be made within and across severity groups.
- To compare perinatal outcome measures between different management protocols.

2. Research Design and Methods

2.1 Study Design

We conducted a retrospective cohort study comparing causes, management and outcomes in women with mild polyhydramnios vs moderate + severe polyhydramnios diagnosed on ultrasound scan by any of the sonographers at Mowbray Maternity Hospital (MMH) from January 1, 2018 to December 31, 2020. Cases were found in the ultrasound scan register.

2.2 Study Subjects

All women with polyhydramnios diagnosed on ultrasound between January 1, 2018 and December 31, 2020 were sampled until the required sample size was reached.

Inclusion Criteria

- AFI > 25 on ultrasound diagnosed after 24 weeks' gestation
- Followed up and delivered at MMH or referred for delivery at Groote Schuur tertiary hospital (GSH)
- Ultrasound reports available

Exclusion criteria

- Missing folders
- Did not deliver at MMH or GSH
- Missing ultrasound reports

2.3 Sampling Technique

A total of 201 ultrasound reports with AFI >25 were identified between January 1, 2018 and December 31, 2020. Of these, 63 were moderate + severe and the rest were mild. All the moderate and severe cases with available folders (56) were

included. After applying the inclusion and exclusion criteria, 80 of the 138 mild cases were included. A total of 136 patient folders were analysed.

2.4 Measures

Data were recorded on demographics, risk factors for polyhydramnios, different management strategies, and adverse maternal and fetal outcomes. Composite adverse outcome was defined as occurrence of any adverse outcome whether maternal or fetal. All the measured data can be found in the data collection sheet attached in the annexure.

2.5 Data Management Plan

2.5.1 Data Collection

Cases of polyhydramnios were identified from the ultrasound department register and the patient folders were retrieved. Data on causes, investigations, management and outcomes in the mothers and neonates were extracted from the patient files. Data were captured onto a data collection sheet (see attached below).

2.5.2 Data Entering, Storage and Confidentiality

Captured data were entered on an excel spread sheet. Electronic data was backed up daily, weekly, and monthly. All data were kept anonymised. Only hospital numbers appeared on data capture sheets and these were kept in lockable cabinets.

2.6 Statistical Considerations

2.6.1 Sample Size

Previous studies have estimated adverse perinatal outcomes to be between 7% and 44% depending on the degree of the polyhydramnios (Barkin et al., 1987; Krispin et al., 2020; Khan & Donnelly, 2017; Taskin et al., 2013). Based on these estimations we calculated sample sizes of 72 per group (total 144) to achieve an 80% power to detect a difference of 18% of the composite outcome between the mild and moderate + severe groups, assuming an event rate of 10% (average of 7%

and 13%) in the mild group and 28% (average of 23% and 33%) in the moderate + severe group at an alpha level of 0.05. These computations were done based on the chi-square test of the null hypothesis that there was no difference between the moderate + severe and mild groups. We analysed 136 medical records (56 moderate + severe and 80 mild polyhydramnios cases). Statistical analysis was done using STATA 15.

2.6.2 Statistical Analysis

We summarized continuous variables using the mean (standard deviation) and categorical variables using count (percent). We report the proportion (percentage) with the composite outcome with the corresponding 95% confidence intervals. We tested the association between categorical variables using the chi-square test. Statistical significance was set at $p < 0.05$.

2.7 Ethical Considerations

Approval for the study was granted by the University of Cape Town's Human Research Ethics Committee, approval number (HREC REF 213/2021). Permission to collect data was obtained from the relevant authorities at Mowbray Maternity Hospital. Since the study is a retrospective folder review, the requirement for individual patient consent was waived.

2.8 Conflict of Interest

No conflict of interest declared.

2.9 Data Dissemination and Future Considerations

The dissemination of data will be by publishing our study in a peer-reviewed journal, use of conferences, workshops and seminars.

3. Results

We included 136 patients in the study. Demographic data are shown in Table 1.

Table 1: Demographic Data of the Cohort (n =136)

	Mild polyhydramnios	Moderate + severe polyhydramnios
Age (mean)	29 (17-44)	30 (18-42)
Parity (median)	2 (0-6)	2 (0-8)
HIV positive n (%)	16 (20)	14 (25)
Atypical Ab* n (%)	4 (5)	0 (0/56)
The AFI category n (%)	80 (59)	56 (41)
Median AFI	26.2 (25 - 29)	32 (30 – 46)
Median gestational age at diagnosis in weeks n (range)	33 (26 – 41)	34 (24 -40)

*Atypical Ab – Atypical antibodies

3.1 Causes

3.1.1 Diabetes Mellitus (Pre-existing or GDM)

Incidence of diabetes mellitus was similar in the 2 groups. Of the 80 cases with mild polyhydramnios, 13 (16.3%) had either pre-existing or gestational DM, while 9 of the 56 (16.1%) participants with severe polyhydramnios had either pre-existing or gestational DM.

3.1.2 Fetal Anomalies

Significantly more patients with moderate and severe polyhydramnios 6/47 (12.8%) had fetal anomalies compared to those with mild polyhydramnios, 2/70 (2.9%) p = 0.02. Nineteen patients did not have a fetal anomaly scan.

Table 2: Fetal Congenital Abnormalities (n =8)

Fetal Anomaly	Gestational Age at Diagnosis	Polyhydramnios Group
6 fingers bilaterally	28 weeks	Mild
Dilated renal pelvis bilaterally	33 weeks	Mild
Dilated renal pelvis bilaterally	32 weeks	Moderate
Talipes	36 weeks	Moderate
Short long bones	29 weeks	Moderate
Atrioventricular septal defects, micrognathia, hypotelorism	38 weeks	Severe
Hydropic baby	28 weeks	Severe
Micrognathia, rocker bottom feet	27 weeks	Severe

3.1.3 Karyotyping

No patients had fetal karyotyping performed. Most of the anomalies detected were on scans done after 24 weeks' gestation and the window for termination of pregnancy was past. In addition some of the detected anomalies did not have a high association with chromosomal abnormalities.

3.1.4 Toxoplasmosis, Rubella, Cytomegalovirus and Herpes (TORCH) Screen

Of the 136 patients, only 2 had TORCH screens done and both of them were negative.

In the mild polyhydramnios group a cause associated with the polyhydramnios was found in 15/80 (18.8%), while in the moderate + severe group, a cause was found in 13 of the 56(22.8%).

3.2 Management Protocols

Table 3: Management Protocol Comparisons between the 2 Groups (n = 136)

	Mild Polyhydramnios	Mod – severe polyhydramnios	p-value
Follow up scans	54/80 (67%)	25/56 (45%)	0.08
Poly improved	18/54 (33.3%)	9/25 (36%)	0.13
Admitted to ward for observation from 36 weeks	8/80 (10%)	13/56 (23%)	0.04
Delivered between 38 and 40weeks	33/80 (41%)	33/56 (58%)	0.04
Amniodrainage	0/80	0/56	-
Indomethacin	0/80	0/56	-
Sulindac	0/80	0/56	-
*OGTT	69/80 (86%)	49/56 (86%)	-

*OGTT – oral glucose tolerance test

3.2.1 Cervical Length Measurement

Cervical length measurement has been described as a means of identifying patients at risk for preterm labour. In our study, most cases were diagnosed after 34 weeks' gestation when this was no longer relevant. Of those diagnosed before 34 weeks' gestation, only 2 had cervical length measured and these were normal.

3.2.2 Follow up Scan

Of the 79 patients that had follow-up scans, 18 of 54 (33.3%) of mild polyhydramnios improved while 9 of 25 (36%) of moderate + severe improved

with no statistical difference between the 2 groups. The remainder did not have follow up scans because of their late diagnosis.

3.2.3 Admission to the Ward

Eight of the 80 (10%) mild polyhydramnios cases were admitted to the ward from 36 weeks gestation for observation awaiting delivery at 38 weeks, while 14 of 56 (24.6%) moderate + severe were admitted awaiting delivery to prevent rupture of membranes at home.

3.2.4 Elective Delivery between 38 – 40 weeks

Sixty-three of the 136 polyhydramnios cases underwent induction of labour between 38 and 40 weeks so as to avoid spontaneous labour at home with the possibility of cord prolapse. Those who did not undergo elective induction of labour due to polyhydramnios included 12 patients who delivered before 38 weeks' gestation due to preterm labour or preterm pre-labour rupture of membranes (PPROM) and 60 patients who awaited spontaneous labour or were delivered for other obstetric indications between 38 and 40 weeks.

3.3 Outcomes

Table 4: Outcomes Compared Between Mild and Moderate + Severe Groups of Polyhydramnios (n = 136)

	Mild Polyhydramnios n (%)	Mod –Severe Polyhydramnios n (%)	p-value
Preterm Labour	3/80 (3.8%)	9/56 (16.1%)	0.01
Cord Prolapse	1/80 (1.25%)	0/56	0.40
PPROM	1/79 (1.25%)	6/56 (10.7%)	0.01
Abruptio Placentae	0/80	0/56	
Shoulder Dystocia	1/80 (1.25%)	2/56 (3.57%)	0.36
5 min Apgar <7	2/80 (2.5%)	3/56 (5.36%)	0.42
Admission to NICU	2/80 (2.5%)	8/56 (14.3%)	0.01
Need for Assisted Ventilation	2/80 (2.5%)	7/56 (12.5%)	0.02
HIE	0/80	2/56 (3.57%)	0.17
Birth Trauma	1/80 (1.25%)	0/56	1.00
Composite Adverse Outcome	6/80 (7.5%)	13/56 (23.2%)	0.01

3.3.1 Preterm Labour and PPROM

A total of 12/136 (8.8%) patients had preterm labour (See table 4). Preterm labour occurred in 9/56 (16%) of patients in the moderate + severe group polyhydramnios group and 3/80 (3.8%) in the mild polyhydramnios group (p = 0.01).

PPROM occurred in 6/56 (10.7%) of the moderate + severe polyhydramnios group and 1/79 (1.25%) of the mild polyhydramnios group ($p = 0.01$). There were thus statistically significant differences in the two groups for both preterm labour and PPRM.

3.3.2 Placental Abruption, Cord Prolapse and Postpartum Haemorrhage

There were no cases of placental abruption. There was one case of cord prolapse which occurred in a patient from the mild polyhydramnios group. There were 3 cases of shoulder dystocia, 1 from the mild and 2 from the moderate + severe polyhydramnios groups, respectively. There were 2 cases of postpartum haemorrhage, 1 from each group, and both cases were unrelated to uterine atony.

3.3.3 Neonatal Outcomes

APGAR scores < 7 were not statistically different between the 2 groups with 2/80 (1.25%) of the mild polyhydramnios group having the outcome compared to 3/56 (3.56%) of the moderate + severe polyhydramnios group ($p = 0.42$).

A total of ten babies were admitted to NICU. Of these 2/80 (2.5 %) were from the mild and 8/56 (14.3%) from the moderate + severe group. The difference between the 2 groups was statistically significant ($p = 0.01$).

Significantly more babies born to mothers with moderate + severe polyhydramnios required assisted ventilation compared to those born to mothers with mild polyhydramnios. Nine babies required assisted ventilation (2/80 (2.5 %) from the mild and 7/56 (12.5 %) from the moderate + severe group ($p = 0.02$).

Only 2 babies had signs of hypoxic ischaemic encephalopathy (HIE) and both were from the moderate + severe group.

3.3.4 Composite Outcomes

The adverse composite outcome occurred in 19/136 (14.0%) of cases. A statistically significant difference was found in the occurrence of the composite

outcome in the moderate + severe group compared to the mild group [13/56(23.2%) vs. 6/80 (7.5%); $p = 0.001$].

More women delivered between 38 – 40 weeks for polyhydramnios had the composite adverse outcome, with 5/66 (7.6%) compared to 2/58 (3.4%) of those that awaited spontaneous labour of delivery for other indications. The difference was not statistically significant, $p = 0.14$. Our study did also not have enough power to detect a difference if there was any.

4. Discussion

A total of 136 women with polyhydramnios were included in the study. Of these 80 had mild polyhydramnios and 56 had moderate + severe polyhydramnios.

Polyhydramnios was classified as idiopathic in 15/80 (18.8%) in the mild polyhydramnios group, compared to 13/56 (22.8%) of the moderate + severe group.

Prevalence of gestational or pre-existing gestational diabetes was similar in both groups (16.3% and 16.1% in the mild and moderate + severe groups, respectively). There were significantly more congenital anomalies in babies of mothers with moderate + severe polyhydramnios than in those with mild polyhydramnios (12.8% vs 2.9%).

There was a significantly greater association between preterm labour and moderate + severe polyhydramnios than with mild polyhydramnios (16.1% vs 3.8%). NICU admissions and ‘need for assisted ventilation’, were both significantly more associated with moderate + severe polyhydramnios than with mild polyhydramnios.

There was a greater association between elective delivery for polyhydramnios at 38 – 40 weeks and adverse perinatal outcome than with either awaiting spontaneous labour, or delivery indicated by other obstetric reasons. For those delivered at 38 – 40 weeks, 5/66 (7.6%) had the composite adverse outcome as compared to 2/58 (3.4%) of those that awaited spontaneous labour. The difference was, however, not statistically significant, and our study was not powered enough to detect this difference.

4.1 Causes

Hamza et al. (2013) reported the finding of underlying disease in only 17% of cases with mild polyhydramnios, compared to 91% with moderate to severe polyhydramnios. Our findings for the mild polyhydramnios group were comparable with this; however, in the moderate + severe group, a cause was found in only 22.8% of cases; significantly lower than the 91% reported in Hamza's study. This may be related to the fact that the study was conducted at a secondary level hospital. Cases with concerns of either maternal discomfort or congenital anomalies would have been referred directly to the tertiary centre. Reports from other studies may be from tertiary centres, resulting in the higher prevalence of associated causes (Hamza et al., 2013; Taskin et al., 2013; Kyriacou et al., 2021; Hara et al., 2006). None of our patients had karyotyping. Of the 8 patients referred to the tertiary centre by us for either anomalies or severe maternal discomfort, all were > 30 weeks' gestation; 2 declined amniocentesis and the rest had anomalies that were not severe enough to offer karyotyping and termination of pregnancy after 24 weeks' gestation.

Maternal diabetes, either pre-existing or GDM, was the most commonly found cause in both the mild and moderate + severe polyhydramnios groups (15.9% and 15.8%, respectively). This is comparable to results from most published studies. Hamza et al. (2013) quoted an incidence of 5 – 26% while Moore (2017) quoted 8.5%.

4.2 Management

Only 2 patients had TORCH screens and both were negative. In our unit this is reserved for patients with either a prior history of symptoms suggestive of viral infection or where ultrasound features of fetal infection were found. Fayyazi & Rafi (2012) suggested that TORCH screen may not be beneficial in patients with isolated polyhydramnios. In their study, all 66 patients with isolated polyhydramnios tested negative for TORCH infections. Hamza et al. (2013) also suggested this test be reserved for patients with ultrasound features suggestive of intrauterine infection.

In our study, only 2 patients had cervical length measured as a method of predicting preterm labour. These patients had presented with threatened preterm labour and cervical length was performed in order to decide whether tocolysis and antenatal corticosteroids should be administered. An observational study by

Hershkovitz et al. (2006) showed that women with polyhydramnios had a gradual shortening of cervical length with advancing gestational age. However, this finding was not related to the severity of polyhydramnios. Two separate meta-analyses, (Hamza et al., 2013; Karkhanis & Patni, 2014) recommended cervical length surveillance and administration of antenatal corticosteroids in those with progressive shortening of the cervix due to the risk of preterm labour. We did not have enough measurements to recommend or discourage this practice.

Odibo et al. (2016), Tashfeen et al. (2013) and Taskin et al. (2013) reported that significantly more cases of mild polyhydramnios showed resolution on follow-up scans compared to those with moderate and severe polyhydramnios. Our study showed no difference in resolution rates, with 18 of 54 (33.3%) cases of mild and 9 of 25 (36%) of moderate + severe polyhydramnios improving ($p = 0.395$). There was no difference in the occurrence of the composite adverse outcomes in patients admitted to the ward from approximately 36 weeks' gestation to await delivery at 38 weeks' gestation: 1/21 (4.8%) compared to those that were managed as outpatients awaiting spontaneous labour or delivery at 38 weeks' gestation: 6/103 (5.8%) $p = 0.31$. This may be because, although there may be a theoretical benefit to inpatient management, adverse perinatal outcomes were related to unnecessary interventions in admitted patients. Our study was however not sufficiently powered to detect any such difference. We did not find any studies comparing inpatient versus outpatient management in patients with polyhydramnios.

There was a greater association between elective delivery for polyhydramnios at 38 – 40 weeks and composite adverse perinatal outcome than with either awaiting spontaneous labour, or delivery indicated by other obstetric reasons (7.6% vs 3.4%). The difference was not statistically significant ($p = 0.14$). This may be because inductions of labour have their own associated complications that may impact perinatal outcomes (Hamza et al., 2013). We could not find any studies comparing induced delivery between 38 – 40 weeks' gestation solely for polyhydramnios and awaiting spontaneous labour or inductions for other obstetric indications. Most international guidelines, however, do not support induced delivery for polyhydramnios without other obstetric indications.

In our study, no patient received amnioreductive therapies (pharmacotherapy or amniocentesis). Many studies have shown that NSAIDs (indomethacin and Sulindac) alone or with amniodrainage are effective in reducing amniotic fluid levels to normal (Cabrol, 1987; Moise, 1991; Rode, 2007; Jayagopal, 2007). NSAIDs can cause oligohydramnios and early closure of the fetal ductus

arteriosus; hence, weekly AFI is necessary to identify these complications early (Hamza et al., 2013). However, these forms of management remain controversial.

4.3 Outcomes

The composite adverse maternal and fetal outcome occurred in 18/139 (12.9%) of all cases. Other published studies have shown even higher rates of adverse perinatal outcomes, with a retrospective observational study in India by Lallar et al. (2015), showing up to 51% maternal adverse outcome in patients with idiopathic polyhydramnios. Another retrospective observational study by Omar (2005) also showed an increase in composite adverse outcome in patients with idiopathic polyhydramnios. This was confirmed in 2 separate meta-analyses by Hamza et al. (2013) and Karkhanis & Patni (2014).

The composite adverse maternal and fetal outcome was significantly higher in the moderate + severe group compared to the mild group, 13/56 (23.2 %) vs. 6/80 (7.5%) $p = 0.001$. A study in Mali by Andamel et al. (2020) estimated the adverse maternal and fetal composite outcome to be around 7.1%. This is comparable to the adverse composite outcome (7.5%) in our mild polyhydramnios group. This supports our hypothesis that adverse outcomes are significantly more common in moderate and severe polyhydramnios, while these outcomes are not any higher in the mild group compared to the general population. We did not find any study comparing the composite adverse outcome between mild and moderate + severe polyhydramnios.

In our study, 8.6% of the polyhydramnios patients had preterm labour, but a subgroup analysis showed that 30% of patients with severe polyhydramnios had preterm labour. Our sample size was however not sufficient to comment on this. These values are significantly lower than those reported by Many et al. (1995), which showed an incidence of preterm labour of 18.5% in the mild group compared to 21.8% in the moderate group. We could not find any plausible explanation for this except that these patients were from different patient populations where other factors may influence preterm labour rates.

There was one case of cord prolapse and no cases of placental abruption in our study. Most clinicians who admit patients to await delivery at 38 weeks do this to pre-empt these complications. Our results suggest that this might not be justifiable, considering the economic and social costs associated with hospital admission. We

did not find any comparative studies quoting the incidence of cord prolapse in polyhydramnios.

We did not have any perinatal deaths; however, 6.1% of the neonates had adverse outcomes. Higher rates of perinatal adverse outcomes have been reported in other studies. A study by Avitan, Hutcheon & Mayer (2016) showed adverse perinatal outcomes in up to 30% of patients with pregnancies complicated by polyhydramnios. This could be due to differences in the health systems and resource distribution.

5. Conclusion

Although maternal and fetal adverse outcomes are significantly higher in pregnancies complicated by polyhydramnios, the risks of those outcomes do not seem to be significantly higher than the background risk in the mild polyhydramnios subgroup. Our study findings do not support inpatient management and induction of labour between 38 and 40 weeks for polyhydramnios alone without any other obstetric indications. We do, however, recommend further studies with bigger sample sizes.

Our study findings also suggest that the biggest complication of polyhydramnios is preterm labour, mostly before 34 weeks' gestation. It may be prudent to perform routine cervical length measurement to predict preterm labour and administer corticosteroids in the severe polyhydramnios group where the preterm labour rate was up to 30%.

Up to 50% of pregnancies complicated by severe polyhydramnios had associated congenital anomalies. These could benefit from being referred to tertiary centres for assessed by fetal medicine specialists.

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7. Attachments

7.1 Data Collection Sheet

7.1.1 Demographics

Measure	Result
Age	
Parity	
HIV status	
Atypical antibody status	
Syphilis serology	
AFI	
Gestational age at first detection of polyhydramnios	

7.1.2 Causes

Cause	Yes	No	Not done
Gestational/overt diabetes mellitus			
Fetal congenital anomalies			
Fetal chromosomal abnormalities			
Toxoplasmosis			
Parvovirus			
Rubella			
Cytomegalovirus			
Other causes			

7.1.3 Management

Management	Yes	No
Cervical length surveillance		
Follow-up scan		
Did polyhydramnios improve		
Did polyhydramnios worsen		
Admitted to ward		
IOL between 38 and 40weeks		
Amniodrainage		
Indomethacin		
Sulindac		
Was OGTT or random blood sugar done		

Cervical length measurement	Lengths and gestation measurements were made.	Number of times cervical length measured	Interval between cervical length measurement
Yes/No			

7.1.4 Maternal Outcomes

Outcome	yes	No
Preterm labour/GA at occurrence		
PPROM/PROM/ GA at occurrence		
Malpresentation		
Abruptio placenta/GA at occurrence		
Post-partum haemorrhage		
Shoulder Dystocia		
Composite outcome		
Cord prolapse		

7.1.5 Fetal Outcomes

Outcome	Yes	No
5 minute APGAR < 7		
Admission to NICU		
Need for Assisted ventilation		
Any Sign of Hypoxic Ischaemic Encephalopathy		
Birth Trauma		
Birth Weight		
Composite Outcome		

7.2 Formula for Calculating Sample Size

$$n = (Z_{\alpha/2} + Z_{\beta})^2 \times [p_1(1-p_1) + p_2(1-p_2)] / (p_1 - p_2)^2$$

where $Z_{\alpha/2}$ is the critical value of the normal distribution at $\alpha/2$ (e.g. for a confidence level of 95%, α is 0.05 and the critical value is 1.96), Z_{β} is the critical value of the normal distribution at β (e.g. for a power of 80%, β is 0.2 and the critical value is 0.84) and p_1 and p_2 are the expected sample proportions of the two groups.

$$N = (1.96 + 0.84)^2 \times [0.28(1 - 0.28) + 0.10(1 - 0.10)] / (0.28 - 0.10)^2$$

$$N = 7.84 \times (0.206 + 0.09) / 0.0324$$

$$N = 7.84 \times 0.296 / 0.0324$$

$$N = 71.6$$

$$N = 72 \text{ for each group}$$

The total sample size = 144 participants