

## Trimester Pregnancy Loss and Congenital Fetal Defects at the Douala General Hospital, Cameroon: A Case Study

This article was published in the following Scient Open Access Journal:

Women's Health & Gynecology

Received August 09, 2016; Accepted September 30, 2016; Published October 07, 2016

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### Abstract

**Background:** An estimated 276,000 babies die every year worldwide within 4 weeks of birth from congenital anomalies. The situation in Cameroon may be different but certainly misleading because of underreporting of malformations.

**Case:** DY, a 33-year-old G7P3043, was admitted to our Department because of multiple congenital birth defects. Diagnosis was based on clinical diagnosis of restricted growth and ultrasonography at 23 weeks gestation. Labour was induced with vaginal misoprostol that led to the delivery of a fetus weighing 390g. The patient was discharged two days later and counseled on contraception.

**Conclusion:** Congenital malformations are common in Cameroon. Establishment of comprehensive databases would be helpful for surveillance of new exposures, and for prevention, management, and health care planning.

**Keywords:** Congenital malformations, Fetal defects, Ultrasonography, Misoprostol, Termination, Pregnancy, Second trimester

### Introduction

An estimated 276,000 babies die every year worldwide within 4 weeks of birth from congenital anomalies [1]. The most common congenital disorders are heart defects, neural tube defects and Down syndrome. Hemoglobinopathies (including thalassemia and sickle-cell disease) and glucose-6-phosphate dehydrogenase deficiency account for 6% of all congenital disorders [2].

Worldwide surveys have shown that birth prevalence of congenital anomalies varies greatly from country to country. It is reported at about 3% in the United States, [3] 2.5% in India [4] and 2 to 3% in the United Kingdom [5]. The congenital malformation incidence in a Turkish survey was 3.65 percent [6] but prevalence in a Turkish province also reported 2.9/1000 births [7].

The prevalence of congenital birth defects is as low as 1.07% in Japan [8]. In Western Australia, birth defects occurred in 4.5% to 5.7% of live births from 2005 to 2008 [9]. These variations of prevalence may be explained by social, racial, ecological, and economic influences [5].

Among the investigating tools for diagnosis of congenital abnormalities, ultrasound has become invaluable for detection of fetal abnormalities in the antenatal period. However, it has previously been reported that fetal structural abnormalities affecting the fetal skull, brain, abdominal wall, limbs, stomach and bladder can be detected at 11-14 weeks scan in only 22.3 % of the cases. A second trimester anomaly scan is therefore suggested in a routine antenatal care to increase the prenatal detection of the fetal defect [10].

The prevalence of congenital malformations in most countries in sub-Saharan Africa is difficult to assess because of underreporting [11,12].

In a study at the University of Nigeria Teaching Hospital (UNTH), out of 617 newborns, 17 had congenital abnormalities, giving a prevalence of 2.8% [13]. In Cameroon, the reported prevalence of neural tube defects in Yaounde was 1.99/1000 births [14,15] and the prevalence of congenital birth defects at the Douala General

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Hospital was 1.64% [16]. We give a report of a case with multiple congenital malformations diagnosed by ultrasound and insist on the importance of second trimester ultrasound scanning in low-income countries.

## Case Report

DY, a 33-year-old G7P3043, blood group O Rhesus positive, is married and is an accountant by profession. Her LMP was 04/12/2015 and EDD 11/09/2016. She was admitted at our Department for therapeutic abortion because of malformations diagnosed by ultrasound scanning. She has a history of 3 consecutive spontaneous abortions at 20, 16 and 17 weeks' gestation at the 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> pregnancies. The following tests were done after these abortions: anticardiolipin antibodies, lupus anticoagulant antibodies, antinuclear antibodies, listeria serology and the indirect Coomb's test. Test results were all normal. Genetic studies were also done and no abnormalities were found. She delivered her 6<sup>th</sup> and 7<sup>th</sup> pregnancies at 38 and 39 weeks' gestation after benefiting from a cervical cerclage. She is asthmatic and regularly uses beta-mimetics (Salbutamol) to control her crisis. There is no family history of diabetes mellitus, hypertension, sickle cell anemia, preterm deliveries or spontaneous abortions; and no family history of sudden unexplained fetal death, birth defects or abnormalities. She has completed her rubella vaccine and tetanus toxoid. Her husband is a 37-year-old banker who provides for her emotionally and socially, and this pregnancy was planned.

She also reported flu-like symptoms before she realized that she was pregnant, for which she took some traditional medicines recommended by her mother that remedied the condition.

For this pregnancy, she started antenatal care visits at 12 weeks' gestation and underwent the following investigations: HIV, HBsAg, VDRL, TPHA, Toxoplasma and Rubella serology, all negative. She was positive for *Mycoplasma hominis* after a vaginal swab and was treated with doxycycline. Thick and thin films for malaria and urine culture were negative. An ultrasound scan done at 9 weeks' gestation (patient requested) prior to her first ANC visit at our hospital confirmed a singleton intrauterine pregnancy evolving normally. She received iron and folic supplements from 12 weeks' gestation when she started her 1<sup>st</sup> ANC visits and her 1<sup>st</sup> dose of sulphadoxine-pyrimethamine combination at 14 weeks' gestation for malaria prevention.

Patient was reviewed at 19 weeks' gestation; fundal height (FH) was 16 cm and fetal heart rate and movements were regular. She was seen again on 16/05/2016 at 23 weeks 2 days gestation. At this visit, there was discordance between the FH and gestational age (GA). The FH remained at 16 cm as the previous visit but the fetal heart rate and movement were normal. An ultrasound scan was requested that revealed: protrusion of intestinal loops through the anterior abdominal wall just below the umbilicus suggestive of omphalocele, asymmetric intracranial and absent cerebral folds with a unilateral fluid-containing cavity suggestive of a ventricle. There were craniofacial abnormalities with absent eye-balls (Figures 1 and 2). Patient was counseled for medically induced (therapeutic) abortion and a signed informed consent obtained from her to carry out the procedure.

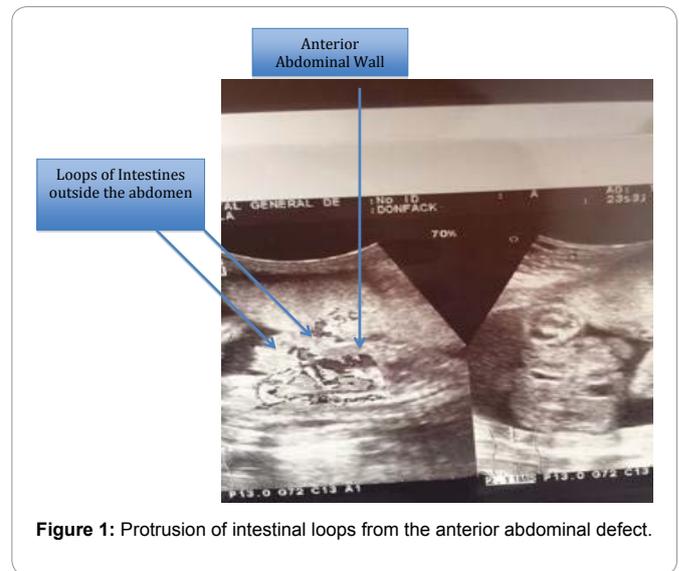


Figure 1: Protrusion of intestinal loops from the anterior abdominal defect.

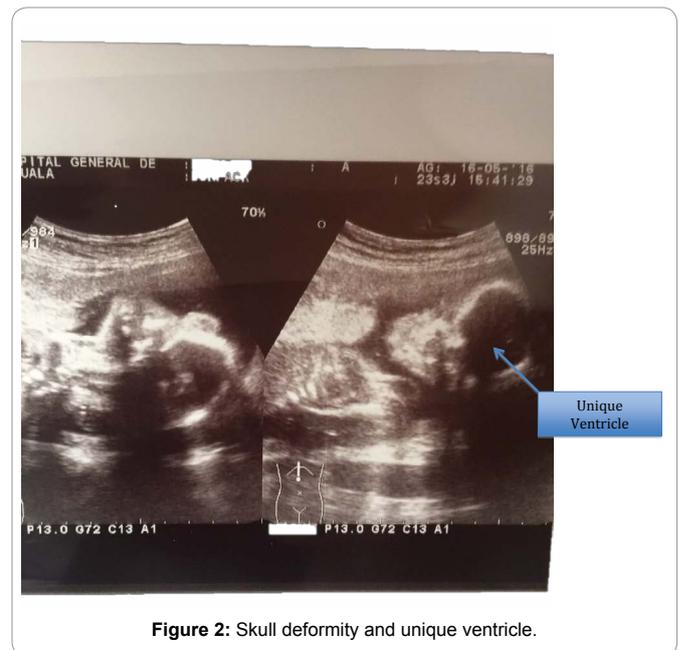


Figure 2: Skull deformity and unique ventricle.

Her review of system was unremarkable and her physical examination showed a woman with class 1 obesity BMI=33 kg/m<sup>2</sup>. She was not pale, and was anicteric, with no abnormal physical findings.

Labour was induced with 400 µg misoprostol tablets inserted vaginally every 6 hours that led to the delivery of a female fetus that weighed 390 g, 17 hours later.

On examination of the fetus, the umbilical cord was wrapped round the left leg, with two turns nuchal cord (Figure 3). There was gastroschisis with protrusion of the intestines through the anterior abdominal wall defect lateral and to the left of the umbilicus (Figure 3). Both eyes and nose were absent and there was a tubular projection from the forehead (Figure 3). There was also polydactyly (six fingers on each hand and six toes on each

foot) and deformation of the bones of the lower limbs (Figures 4 and 5).

Patient did not permit autopsy or samples to be collected for genetic studies. She was counseled on contraception and discharged from hospital two days later.

## Discussion

Birth defects are defined as a series of structural, functional and metabolic disorders. According to the literatures, they are a major source of infant and child morbidity and mortality and single or multiple defects can occur in one or several organs of the children [1].

The causes of congenital abnormalities are often multifactorial, but sometimes no apparent causes are identified [1].

### Use of medications in early pregnancy

Our patient had some flu-like symptoms before she discovered she was pregnant and was treated by unknown herbal (traditional) substance. More than 50% of pregnant women take prescription or nonprescription (over-the-counter) drugs or use social drugs (such as tobacco and alcohol) or illicit drugs at



Figure 3: Exteriorization of intestinal loops from the abdominal defect, cord wrapped round the left leg and tubular protrusion on the forehead and absent nose.



Figure 4: Polydactyly.



Figure 5: Polydactyly and deformation of the bones of the lower limbs.

some time during pregnancy. On the whole, use of drugs during pregnancy is increasing [17]. In general, drugs should not be used during pregnancy unless absolutely necessary because they can harm the fetus. About 2 to 3% of all birth defects result from drugs taken to treat a disorder or symptom [17].

Before taking any drug (including over-the-counter drugs) or dietary supplement (including medicinal herbs), a pregnant woman should consult her health care provider who may recommend certain vitamins and minerals.

Drugs taken in pregnancy reach the fetus primarily by crossing the placenta, the same route taken by oxygen and nutrients needed for fetal growth and development. Such drugs can affect the fetus in several ways. They can:

- Act directly on the fetus, causing damage, abnormal development (leading to birth defects), or death.
- Alter the function of the placenta, usually by causing blood vessels to narrow (constrict) and thus reducing the supply of oxygen and nutrients to the fetus from the mother. Sometimes the result is a baby that is underweight and underdeveloped.
- Cause the muscles of the uterus to contract forcefully, indirectly injuring the fetus by reducing its blood supply or triggering preterm labor and delivery.

Affect the fetus indirectly. For example, drugs that lower the mother's blood pressure may reduce blood flow to the placenta and thus reduce the supply of oxygen and nutrients to the fetus. The timeframe when medications could have a teratogenic effect on the fetus is the first 20 days after fertilization [6,18,19] and the 3<sup>rd</sup> to 8<sup>th</sup> week of pregnancy during organogenesis [18,19].

### Risk factors of congenital malformations

This patient had a history of three consecutive abortions at 20, 16 and 17 weeks' gestation at the 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> pregnancies. Causes like thrombophilia that are associated with first and second trimester pregnancy wastage were not assessed on this patient [20,21]. In another study, 155 couples with two or more consecutive pregnancy losses disclosed uterine morphologic abnormalities in 27%, chromosomal abnormalities in 21

individuals (7.7%, or 15.4% of the couples), and at least one abnormal diagnostic test suggestive of a cause for recurrent pregnancy loss in 106 (68%). A positive test for antinuclear antibody was found in 7.5% of the women, whereas the expected rate in a population of this age is less than 2%. Cervical cultures for *Ureaplasma urealyticum* (T-strain mycoplasma) were positive in 48% of the women and 28% of these women had a genetic or uterine abnormality to explain their pregnancy losses. Thyroid function profiles and cervical cultures for *Mycoplasma hominis* provided no significant information in the evaluation in these couples. With the exception of women with a positive antinuclear antibody, the overall prognosis for later pregnancies was quite good whether the diagnostic evaluation of the couple was normal (77% subsequent live births) or abnormal (71% subsequent live births). The significance of the positive antinuclear antibody in these women is unclear, but further studies and long-term evaluation are necessary to determine the relationship between recurrent pregnancy losses and later development of collagen-vascular diseases [22].

Fetal aneuploidy was the most important cause of pregnancy loss before 10 weeks. At least 50-60% of all miscarriages are associated with cytogenetic abnormalities, the most frequent being trisomy, followed by polyploidy and monosomy X. Most human aneuploidies arise from errors in the first meiotic division of the oocyte, which is initiated prenatally and is not complete until ovulation. An increased rate of sperm chromosome abnormalities has also been reported in couples with recurrent miscarriage, but only 7% of fetal trisomies have been shown to arise from paternal meiotic errors [23]. In this patient, no genetic studies were done.

It has been reported previously that administration of folic acid six months before envisaging a pregnancy and during the first trimester of pregnancy is associated with the prevention of neural tube defects [24]. This patient did not receive folic acid supplementation prior to pregnancy or during the first trimester. Other risk factors associated with congenital fetal malformations like diabetes mellitus, history of sudden fetal death, low socio-economic status, tobacco, use of hard drugs [25] and advanced paternal age [26,27] were not found on this patient. She was an accountant and her husband a banker aged 37.

### Diagnosis of congenital malformations

Several modalities have been recommended for the diagnosis of fetal defects, mainly ultrasonography, CT-scan and magnetic resonance imaging. The most cost-effective modality is ultrasonography at the 20-24 weeks' gestation [28,29]. This is true in low-income countries like Cameroon. With ultrasonography, we are able to study the internal anatomy of the heart, brain, bone, kidneys, etc. [28].

### Treatment of congenital birth defects

#### Surgical management

The treatment will depend on whether there are isolated or multiple anomalies. Cases with omphalocele alone will benefit from surgical repair of the anterior abdominal wall. "Giant" omphalocele implies an abdominal wall defect that is 5 cm or more in diameter with the liver in a central position. Giant omphalocele is often associated with other significant

anomalies. Technically, it is often difficult to close the abdominal wall defect and a staged repair utilizing prosthetic materials may be necessary. The morbidity and mortality associated with this entity remain significant despite advances in management techniques. Hospitalization is often prolonged and costly. For the best outcome in managing patients with giant omphalocele, early attention to hypothermia and other metabolic requirements and long-term attention to nutritional needs are important. Techniques of closing the omphalocele should be adapted to the individual characteristics of the defect, but mobilization and stretching of the abdominal muscles should begin at birth. The term hepatomphalocele, implying "liver-containing omphalocele", is suggested to refer to this particular entity [30-32]. Surgical repair of these malformations is sometimes difficult in low-income countries like Cameroon because of elevated cost of the procedure, difficult post-operative care, and sometimes lack of trained personnel to carry out the procedure.

#### Therapeutic abortion

We decided for a therapeutic abortion on this patient because the fetus had omphalocele, gastroschisis and other associated malformations, especially of the brain. We did not do an autopsy on the fetus to look for cardiac or other internal organ malformations because the patient did not consent to the procedure. This condition is sometimes associated with the VATER/VACTERL association of malformations (Vertebral defects(V), Anal Atresia(A), Cardiac anomalies(C), Tracheo-Esophageal fistula(TE), Renal and Radial anomalies(R), Limbs anomalies(L)) [33,34], gastroschisis, and omphalocele [35].

We used misoprostol to terminate the pregnancy because of the unfavourable bishop score, but also because this was the method of choice at this gestational age. Studies have shown that in second-trimester pregnancy termination, a vaginal misoprostol regimen of 400 µg every 6 hours was 1.9 times more likely to result in delivery within 24 hours from commencement than an oral regimen of 400 µg every 3 hours [36,37]. Our patient delivered the fetus 17 hours after the start of induction.

### Conclusion

Congenital anomalies are common in Cameroon. Establishment of comprehensive databases would be helpful for surveillance of new exposures, and for prevention, management, and health care planning.

### Consent

Written informed consent was obtained from the patients for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal."

### Abbreviations

- LMP: Last Menstrual Period
- FH: Fundal Height
- GA: Gestational Age
- HIV: Human immunodeficiency virus
- VDRL: Venereal Disease Research Laboratory

TPHA: Treponema Pallidum Hemagglutination Assay

BMI: Body Mass Index

## Competing Interests

The authors declare that they have no competing interests

## Author's Contribution

TOE contributed in the management of the patient and in the writing of the manuscript. He is the corresponding author. WT and ENE did the literature search and proofread the manuscript. REM supervised and proofread the manuscript. All authors proofread and agreed on the final version of the manuscript.

## Acknowledgements

We thank the staff of the Department of Obstetrics and Gynecology of the Douala General Hospital for the assistance they gave us in the management of this patient. We also thank the patient for consenting in the publication of the images.

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