OBSTETRICS

Reproductive outcomes in subsequent pregnancies after a pregnancy complicated by open maternal-fetal surgery (1996–2007)

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OBJECTIVE: The reproductive and gynecologic outcomes for women after the pregnancy complicated by open maternal-fetal surgery (OMFS) were evaluated.

STUDY DESIGN: The retrospective review identified 93 women with OMFS from a single institution (1996–2007). Consent and questionnaires were sent to women. Institutional review board approval was obtained from the Committee for Protection of Human Subjects.

RESULTS: The total return rate was 57.3%. Total pregnancies reported were 47, with 36 delivering after 20 weeks' gestation. The uterine dehiscence and rupture rates were 14% and 14%, respectively. Fetal anomalies occurred in 4 subsequent pregnancies. Normal conception occurred in 98% of subsequent pregnancies. Gynecologic issues were reported by 8 women, with infertility, abdominal pain, and ovarian and uterine factors.

CONCLUSION: The reproductive outcomes of uterine dehiscence (14%) and rupture (14%) in a subsequent pregnancy continue to be a major counseling issue for OMFS. Fertility and gynecologic factors do not appear to be increased for women undergoing OMFS.

Key words: fetal anomalies, in utero therapy, maternal-fetal surgery, maternal-fetal surgery risk, open maternal-fetal surgery outcomes, uterine dehiscence, uterine rupture

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Open maternal-fetal surgery (OMFS) for fetuses with physiologic life-threatening anomalies (fetal or immediate neonatal onset) or anomalies with significant childhood morbidity but increased risk of mortality is rare and is limited to quaternary multidisciplinary hospital programs with expertise in this experimental fetal therapy field. This is the second report from the Center for Fetal Diagnosis and Treatment at the Children's Hospital of Philadelphia (Philadelphia, PA) detailing the reproductive outcomes for women after the pregnancy complicated by maternal-fetal surgery. The first report summarized the outcomes from 1996–2002.[1]

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The objective of this second article is to continue to follow the reproductive outcomes for this unique group of women to enhance the knowledge, risk assessment, and informed consent process for these families. The continued determination of the fetal benefit risk and the maternal risk benefit is mandatory for appropriate ethical considerations for fetus and mother. This second report uses the same ascertainment tools to allow comparison over the extended period of time from February 1996–March 2007.

Materials and Methods

The study population was obtained from women undergoing OMFS at the Children's Hospital of Philadelphia (CHOP) from Feb. 1, 1996–March 30, 2007. The closing date of March 30, 2007, was chosen to allow adequate time for the most recent OMFS mothers' population to have additional reproductive outcomes. ex utero intrapartum treatment (EXIT) surgical delivery is not part of this cohort.

Review of the database identified 118 women and their fetuses who had had OMFS. In this present cohort, women and their fetuses who had undergone OMFS as part of the randomized National Institute of Child Health and Human Development (NICHD) Management of Myelomeningocele Study (MOMS) were excluded from this analysis, because their subsequent pregnancy outcomes are part of the MOMS protocol.

Therefore, review of the database identified 93 women and their fetuses who had had OMFS at CHOP within the identified time period. The indications for the 93 OMFSs included the original pre-MOMS 57 nonlethal (elective) myelomeningocele malformations (MMCs) and the congenital anomalies with lethal potential (high risk for severe pulmonary hypoplasia or cardiac-related hydrops) requiring emergency OMFS, including congenital diaphragmatic hernia surgery (CDH) (11 left sided, 1 right sided), cystic adenomatoid malformation of the lung (CCAM) (7 left sided, 7 right sided), extralobar bronchopulmo-

TABLE 1
The number of pregnancies following OMFS

Pregnancy	Number
No	20
Yes	27
1	16 (59%)
2	6 (22%)
3	2 (7%)
4	2 (7%)
5	1 (4%)
Total pregnancies	47

OMFS, open maternal-fetal surgery.

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nary sequestration (n = 1), mediastinal teratoma (n = 2), bronchial atresia (n = 1), pulmonary leiomyofibroma (n = 1), and sacrococcygeal teratoma (SCT) (n = 5).

CHOP recommends a repeat cesarean section at 36 weeks with no lung maturity testing in the subsequent pregnancies, which possibly increases the late preterm delivery rate.

The study was approved by the Committee for Protection of Human Subjects at CHOP, institutional review board #2007-6-5394. The women were sent via postal mail the same questionnaire that was used and published in the first study and a letter describing the purpose of the study (asking them to participate in this retrospective study evaluating postoperative problems, fertility, psychologic concerns, and subsequent obstetric outcomes), as well as 2 copies of the consent form and a stamped return envelope.

For the 93 patients who were sent the study material, there were a total of 47 responders (50.5%), with 11 return-to-sender returns, 53 second-reminder mailings, and 24 e-mail reminders. Telephone contact was not a part of the institutional review board approval. Written consent from the maternal patient and a completed questionnaire regarding the reproductive history after the index OMFS case were required for data inclusion. Exclusion criteria for the subsequent reproductive outcomes were no consent given or no response by the maternal patient.

Information from the questionnaires was put into a standard Microsoft Excel database (Microsoft Corp, Redmond, WA). The questionnaire used for this and the previous study were not validated. Valid statistical comparisons between the OMFS and standard obstetric populations are not possible because of the treatment and selection biases within the OMFS population, but less validated comparisons can be considered.

The interpregnancy interval for adverse and normal outcomes, as well as gestational age at fetal surgery for adverse and normal outcomes, was analyzed as normally distributed continuous variables with a 2-sided Student *t* test. The indication for the fetal surgery (elective vs emergent) and its effects on subsequent adverse or normal outcomes were analyzed by χ^2 for categorical variables. A *P* value of less than .05 was considered significant for each analysis.

RESULTS

Forty-seven of 82 (sent and received as indicated by 11 packages that were unopened and marked return to sender) questionnaires were completed and returned with consent to participate (57.3%). Thirty-three patients completed both the 2004 and 2008 questionnaire, with 12 women having additional pregnancy(ies) (36.4%) in both time periods, 11 patients (33.3%) had further pregnancies in only the 2004–2008 period , and 10 (30.3%) did not have any pregnancies after the maternal-fetal surgery.

For the group that responded to both study periods, there were a total of 21 pregnancies in the 2004 report, with an additional 22 pregnancies in the 2008 report. Reasons for decreased questionnaire returns would include length of follow-up in 1996–2008 and change of residence, and the most recently treated MOMS patients were excluded.

The primary indication for OMFS in the study was 32 MMCs (68%), 9 CCAMs (19%), 4 CDH surgeries (8%), 1 SCT (2%), and 1 mediastinal teratoma (2%). Table 1 reports the number of women reporting a pregnancy and the number of pregnancies for each woman following the OMFS pregnancy. The total number of 47 pregnancies had the gestational age at delivery reported as less than 20 weeks of 11 (23%), 1 at 20–23 ± 6 weeks (2%), 1 at 24–27 ± 6 weeks (2%), 15 at 28–36 ± 6 weeks (32%), and 19 at greater than 37 weeks (40%).

Table 2 summarizes the subsequent pregnancy outcomes following the OMFS pregnancy. The obstetric risks in the subsequent pregnancy continue to be the major prenatal counseling issue for women, with the present incidence of uterine dehiscence and rupture of 14% and 14%, respectively, with no fetal/neonatal or maternal deaths. Only 1 cesarean hysterectomy was reported in this cohort in a pregnancy with a preterm labor at 28 weeks and placenta accreta.

This follow-up cohort is too small to be able to predict placental implantation problems in a subsequent pregnancy, but an increased risk is probable with 2 hysterotomy scars (fundal for OMFS, anterior low transverse for delivery) being present at the subsequent pregnancy.

Table 3 summarizes the fetal outcome in subsequent pregnancies following the OMFS pregnancy. Subsequent pregnancy fetal outcomes did not show any increase in congenital anomalies above the natural development background. The method of conception following the OMFS pregnancy was most commonly normal conception (n = 46) but with assisted reproduction required for 1 pregnancy.

Table 4 reviews the gynecologic outcomes following the OMFS and the subsequent pregnancies (a woman's gynecologic issue is reported only once in this table). The gynecologic conditions reported by this cohort did not appear to indicate any increased risk for infertility, abdominal adhesions beyond the recognized surgical incidence for multiple surgeries, or ovarian or uterine pathology. A small number of maternal comments indicated problems with unexplainable chronic abdominal pain and difficult menstruation.

Statistical comparisons did not identify any significant associations within