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Preterm uterine contractions ultimately delivered at term: safe but not out of danger

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ABSTRACT

Objectives: Patients with pregnancies complicated with premature uterine contractions (PMC), but delivered at term are considered as false preterm labor (PTL), and represent a common obstetric complication. We aimed to assess obstetric and neonatal outcomes of pregnancies complicated with PMC, but delivered at term, as compared to term normal pregnancies.

Study design: Obstetric, maternal and neonatal outcomes of singleton pregnancies complicated with PMC between 24–33$^{6}/_{7}$ weeks (PMC group), necessitating hospitalization and treatment with tocolytics and/or steroids, during 2009–2014, were reviewed. The study group included only cases who eventually delivered ≥37 weeks, which were compared to a control group of subsequent term singleton deliveries who had not experienced PMC during pregnancy. Neonatal adverse composite outcome included: phototherapy, RDS, sepsis, blood transfusion, cerebral injury, NICU admission.

Results: The PMC group ($n = 497$) was characterized by higher rates of nulliparity ($p = 0.002$), infertility treatments ($p = 0.02$), and polyhydramnios ($p < 0.001$), as compared to controls ($n = 497$). Labor was characterized by higher rates of instrumental deliveries ($p = 0.03$), non-reassuring fetal heart rate tracings ($p < 0.001$) prolonged third stage of labor ($p = 0.04$), and increased rate of post-partum maternal anemia (Hb < 8 g/dL) $p = 0.004$, in the PMC group as compared to controls. Neonates in the PMC groups had lower birth weights compared to controls, 3149 g ± 429 vs. 3318 g ± 1.1, $p < 0.001$, respectively. By logistic regression analysis, PMC during pregnancy was independently associated with neonatal birth-weight <3rd percentile (adjusted OR 4.6, 95% CI 1.5–13.7).

Conclusions: Pregnancies complicated with PMC, even-though delivered at term, entail adverse obstetric and neonatal outcomes, and may warrant continued high risk follow up.

Introduction

Preterm labor (PTL), defined as birth <37 weeks of gestation is a syndrome considered as one of the main causes of perinatal morbidity and mortality. It is identified with different etiological mechanisms, including inflammation, infection, vascular disease, placental dysfunction and uterine over-distension [1]. Several maternal risk factors are associated with PTL, among which are pervious PTL, young maternal age, nulliparity, and grand multiparity, low socioeconomic status, low pre-pregnancy body mass index (BMI) and obesity as well [2–4]. Diagnosis of PTL is challenging, resulting in over diagnosis, thus the majority of women presenting with signs of PTL will eventually deliver at term [5–7].

It is unclear whether the same mechanisms that lead to PTL are also responsible for premature contractions (PMC) and signs of PTL episodes, even-though eventually delivered at term [3]. It could be speculated that signs of PTL may be a marker of an underlying in-utero pathology which may influence the developing fetus. Only few studies focused on the association between pregnancies complicated with PMC and PTL signs, but delivered at term, and neonatal outcome, and demonstrated a higher rate of small for gestational age (SGA) neonates among women with PMC who progressed to deliver at term, as compared to those who delivered prematurely [8,9].

We hypothesized that pregnancies associated with significant PMC might be complicated with in-utero insults, through different

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mechanisms, which would have an impact on the fetus as well as on labor characteristics. Thus our objective was to explore obstetrics and neonatal outcomes of singleton term deliveries of women with PMC necessitating hospitalization and medical treatment, to term deliveries with no such history.

Materials and methods

Patients

The computerized files of all pregnancies complicated by PMC, between 22–$33^{6}/_{7}$ gestational weeks, who were hospitalized at the Edith Wolfson Medical Center, Holon, during 2009–2014, were reviewed. The study group (PMC group) included patients who were hospitalized, according to the attending physician's decision, and who received medical treatment that included tocolytic treatment and/or steroids for neonatal lung maturation, but eventually delivered at term (>37 + 0 weeks). Tocolytic treatment included calcium channel blockers or indomethacin, or intravenous oxytocin antagonist. The control group included the subsequent term singleton deliveries, according to the delivery registry, who had not experienced PMC during pregnancy. Excluded from the study were: multiple pregnancies, women with no prenatal care, preterm premature ruptured membranes, known fetal malformations/genetic abnormalities and cases with uterine malformations. Gestational age was defined according to last menstrual period and/or based on first trimester ultrasound examinations.

The following data were collected from the patients' medical files: demographics, gravity, parity, pregnancy follow-up and co-morbidities as pre-gestational diabetes mellitus (DM), gestational DM (GDM), hypertension, preeclampsia, thrombophilia. History of infertility treatment was considered as any pregnancy achieved by in vitro fertilization (IVF) or ovulation induction. Amniotic fluid index (AFI) was measured and recorded in the standard four-quadrant assessment technique. Oligohydramnios was defined as AFI $\leq$ 5 cm and polyhydramnios as AFI $\geq$ 24 cm [10].

Data were also reviewed for labor course, labor complications and mode of delivery. Diagnosis of non-reassuring fetal heart rate (NRFHR) during labor was based on physician documentation, in labor charts, associated with the need for intrauterine resuscitation that included: maternal oxygen, amnioinfusion, cessation of oxytocin infusion, or the need for prompt delivery, as instrumental delivery or cesarean delivery (CD). Prolonged 3rd stage was defined as an interval of 30 min or more between the delivery of the newborn and the completed delivery of the placenta.

Neonatal outcome parameters included: Apgar scores, cord pH, days of hospitalization and the rate of neonatal intensive care unit (NICU) admission. Neonatal birth weight percentile in each case was assigned using the updated Israeli growth charts [11] and small for gestational age (SGA) was defined as less than 3rd percentile. Neonatal adverse composite index was defined as one or more of the following: phototherapy, need for respiratory support, sepsis, blood transfusion, cerebral injury, necrotizing enterocolitis (NEC) or death.

The study was approved by the local Ethics Committee.

Statistics

Continuous variables were calculated as mean ± standard deviation (SD) or median and range as appropriate, and compared with the use of Student *t*-tests. Categorical variables were calculated as rate (%) and compared using the Chi-square test or Fisher's exact test as appropriate. A linear regression module was composed in which birth weight served as the dependent variable and PMC and gestational age served as independent variables. A *p*-value of <0.05 was considered statistically significant.

Results

During the study period 497 patients were hospitalized with suspected preterm labor (PMC group) but eventually delivered at term. The PMC study group characteristics are detailed in Table 1. Mean gestational age (GA) at first hospitalization was 30.2 ± 2.8 weeks. Tocolytic treatment was administered to 414 (83%) patients and steroids to 400 (80.4%). Among non-primiparous patients, 33% of patients had a history of PTL or PMC in previous pregnancy.

Demographics and clinical characteristics of the PMC group as compared to the control group ($n = 497$), are detailed in Table 2. There were no between group differences regarding maternal age or the rate of pregnancy complications, including diabetes mellitus, hypertensive disorders and thrombophilia. The PMC group was notable for higher rates of nulliparity (43% vs. 33%, $p = 0.002$), infertility treatments (7.4% vs. 4%, $p = 0.02$) and polyhydramnios (3.8% vs. 0.6%, $p < 0.001$) as compared to controls.

Labor and obstetrics outcomes among the two study groups are presented in Table 3. As compared to controls, patients in the PMC group delivered earlier – 39.0 ± 1.1 vs. 39.4 ± 1.1 weeks, $p < 0.001$. Though both groups had similar rate of CD, the PMC group exhibited more often NRFHR tracings during labor as compared to controls, 33.1% vs. 23.1%, $p < 0.001$. In addition, a higher rate of instrumental delivery was observed in the PMC group, 9% vs. 5.4%, $p = 0.03$. Third stage of labor was longer among the PMC group ($p = 0.04$), with a higher rate of prolonged 3rd stage ($p = 0.04$) as compared to controls. In addition, PMC patients were more likely to have a hemoglobin of 8 g/dL or less after delivery – 10% vs. 5.2%, $p = 0.004$.

Table 1
PMC group characteristics.

PMC group $n = 497$	
Maternal age (years)	28.4 ± 5.2
Gestational age at first hospitalization[a] (weeks, range)	30.2 ± 2.8 (23–34)
Numerous hospitalizations for PMC (%)	154 (30.9)
Numerous ER referrals for PMC (%)	221 (44.4)
Tocolytic treatment (%)	414 (83.3)
Steroids (%)	400 (80.4)
Previous pregnancy with PMC/PTL (%)[b]	94/282 (33.3)

PMC – premature uterine contractions; ER – emergency room.
[a] Data presented as mean ± standard deviation.
[b] Validated history for PMC/spontaneous PTL, among non-primiparous patients.

Table 2
Demographic characteristics, obstetric history and pregnancy complications of patients with PMC during pregnancy and controls.

	PMC $n = 497$	Control $n = 497$	*p* value
Age[a] (years)	28.4 ± 5.2	29.3 ± 5.0	0.32
Nulliparous (%)	215 (43.2%)	167 (33.6%)	0.002
Previous cesarean section (%)	44 (8.8%)	58 (11.6%)	0.17
Infertility treatments (%)	37 (7.4%)	20 (4%)	0.02
DM[b] (%)	28 (5.6%)	30 (6%)	0.89
Chronic/gestational HTN[c] (%)	5 (1%)	8 (1.6%)	0.57
Thrombophilia (%)	12 (2.4%)	6 (1.2%)	0.23
Preeclampsia (%)	10 (2%)	11 (2.2%)	1.0
Polyhydramnios (%)	19 (3.8%)	3 (0.6%)	<0.001
Oligohydramnios (%)	15(3%)	28 (5.6%)	0.06

[a] Data presented as mean ± standard deviation.
[b] DM – diabetes mellitus, including: GDM and Pre DM.
[c] HTN – hypertension.