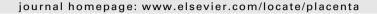
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# Histologic Chorioamnionitis is More Common after Spontaneous Labor than after Induced Labor at Term

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#### ABSTRACT

Objective: Inflammation of the chorioamniotic membranes (histologic chorioamnionitis) is a risk factor for adverse neonatal outcome. Labor has many common features with inflammatory processes; therefore, an important question is whether the frequency of histologic chorioamnionitis in spontaneous labor at term is higher than that of women in labor after induction. This study was conducted to address this question.

Study design: The frequency of histologic chorioamnionitis was compared between patients who delivered after the spontaneous onset of labor versus those who delivered after induction of labor at term in singleton gestations ( $\geq$ 37 weeks). Patients in whom uterotonic agents were used during the latent phase of labor were excluded.

Results: (1) The overall frequency of histologic chorioamnionitis was 20.2% (107/531); (2) histologic chorioamnionitis was significantly more frequent in women who delivered after the spontaneous onset of labor than in those who underwent induction of labor (24.3% [81/333] versus 13.1% [26/198], p < 0.005). This difference remained significant after adjusting for parity, gestational age at delivery, total duration of labor, the interval from rupture of membranes to delivery and the mode of delivery. Conclusion: Histologic chorioamnionitis is more common in women who delivered after the spontaneous onset of labor than in those who underwent induction of labor at term.

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#### 1. Introduction

Histologic chorioamnionitis is frequently diagnosed in placentas delivered at term and in preterm gestations, and is a risk factor for the occurrence of infection-related and non-infection-related perinatal and maternal morbidity and mortality [1–6]. Recent studies indicate that histologic chorioamnionitis is significantly more common in patients with spontaneous preterm birth than in those with indicated preterm birth (60% versus 9%) [7]. However, there is a paucity of information about the risk of histologic chorioamnionitis according to the type of labor (i.e., spontaneous onset versus induction of labor) in term gestations. This study was performed to examine this question.

#### 2. Materials and methods

#### 2.1. Study design

Histologic examination of the placenta was performed in patients who delivered live term singleton neonates (gestational age from 37+0weeks to 42+0weeks) after labor between October 2004 and October 2005 at the Seoul National University Hospital. Patients were divided into 2 groups according to the onset of labor before delivery, regardless of the mode of delivery: group 1 included women who delivered after the spontaneous onset of labor (n = 333), and group 2 included women who delivered after the induction of labor (n = 198). Cesarean delivery was performed for obstetrical indications during labor. Group 2 consisted of patients whose labor was induced using oxytocin and/or prostaglandin E1 (misoprostol, Pfizer Pharmaceuticals Korea, Seoul, Korea) or prostaglandin E2 (dinoprostone pessary, Bukwang Pharmaceutical, Seoul, Korea). Patients in whom uterotonic agents (oxytocin or prostaglandin) were used during the latent phase of labor (cervical dilatation less than 4 cm) after the spontaneous onset of labor were excluded from the analysis because these cases represent neither group 1 (spontaneous onset of labor) nor group 2 (induced labor) and could possibly confound the results. Patients in whom oxytocin was used in the active phase of labor (cervical dilatation more than 4 cm) after spontaneous onset of labor were included in group 1.

Partograms are routinely used in our unit to plot changes in cervical dilatation and fetal descent. Given the difficulties in determining when labor begins, we chose

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to calculate the duration of labor from the onset of the active phase of labor, which was defined as 4 cm of dilatation. The duration of the active phase of labor, as well as the second stage, was assessed using the partograms. The Institutional Review Board of the Seoul National University approved the collection and use of the information for research purposes. The Seoul National University has a Federal Wide assurance negotiated with the Office for Human Research Protection of the Department of Health and Human Services of the United States.

#### 2.2. Histologic chorioamnionitis

Placentas were subjected to histopathologic evaluation. Histologic chorioamnionitis was defined as the presence of acute inflammatory changes on examination of a membrane roll and chorionic plate of the placenta; funisitis was diagnosed in the presence of neutrophil infiltration into the umbilical vessel walls or Wharton's jelly, according to criteria previously described in detail [8]. Briefly, the inflammation of amnion and chorio-decidua was defined as the presence of at least one focus of more than 5 neutrophils and considered as severe inflammation if there is diffuse neutrophil infiltration. The inflammation of the chorionic plate was defined as the presence of at least one focus of 10 or more neutrophil foci or diffuse inflammation in the subchorionic fibrin, and considered as severe inflammation if there was diffuse and dense infiltration of neutrophils into the connective tissue of the chorionic plate, or placental vasculitis. Funisitis was defined as neutrophil infiltration confined to umbilical vessel walls and considered as severe funisitis if there was extensive neutrophil infiltration into Wharton's jelly.

#### 2.3. Statistical analysis

Proportions were compared with the use of Chi-square test or Fisher's exact test as appropriate. Continuous variables were compared with the use of Student t-tests. Logistic regression analysis was performed to evaluate the contributing factors to the occurrence of histologic chorioamnionitis. p < 0.05 was considered significant.

#### 3. Results

#### 3.1. Study population

A total of 738 patients delivered live newborns at term during the study period. One hundred and sixty nine neonates were delivered before the onset of labor by cesarean delivery and 38 patients in whom the uterotonics were used during the latent phase of labor were excluded. Histologic examination of placenta was not available in 2 patients, of whom one patient delivered by cesarean section before the onset of labor and the other patient delivered with uterotonics used during the latent phase of labor. A total of 531 patients met the inclusion criteria.

Table 1 compares the clinical characteristics of mothers and neonates. Patients who delivered after the spontaneous onset of labor had a significantly lower mean gestational age at delivery, a shorter time interval between rupture of membranes and delivery and lower rate of nulliparity than those who delivered after induction of labor (p < 0.05). However, there were no significant differences in the mean duration of labor and birth weight between the two groups of patients (p > 0.05, Table 1). Cesarean delivery was significantly more frequent in group 2 (p < 0.05). The frequency of maternal fever on the day of delivery was higher in group 2 than in group 1 although the difference was not statistically significant (p = 0.06).

The indications for induction of labor were: (1) post-term pregnancy (n = 57); (2) premature rupture of membranes (n = 42); (3) maternal medical diseases (n = 37); (4) fetal indications (n = 19) including fetal growth restriction, non-reassuring fetal status or fetal anomalies; (5) oligohydramnios (n = 17); and (6) others (n = 26).

#### 3.2. Frequency and distribution of histologic chorioamnionitis

The overall frequency of histologic chorioamnionitis was 20.2% (107/531, Table 2). Histologic chorioamnionitis was more common

**Table 1**Clinical characteristics of the mothers and neonates according to whether labor began spontaneously.

	Group 1 (Spontaneous labor, $n = 333$ )	Group 2 (Induced labor, $n = 198$ )	p value
Clinical characteristics			
Maternal age (yr)	$30.9\pm3.5$	$31.5\pm3.4$	NS
Gestational age at delivery (wk)	$39.7 \pm 1.0$	$40.0\pm1.2$	< 0.05
Nulliparity	183/333 (55.0%)	133/198 (67.2%)	<0.05 <sup>c</sup>
Labor duration (min)	$260.0 \pm 193.1$	$243.4 \pm 176.7$	NS
ROM duration (min)	$243.3 \pm 414.5$	$518.6 \pm 749.9$	< 0.001
Cesarean delivery	27/333 (8.1%)	33/198 (16.7%)	<0.05 <sup>c</sup>
Maternal fever <sup>a</sup>	50/329 (15.2%)	43/198 (21.7%)	0.06 <sup>c</sup>
Neonatal characteristics	3		
Birth weight (gm)	$3240.8 \pm 411.1$	$3298.7 \pm 475.6$	NS
SGA	28/333 (8.4%)	23/198 (11.6%)	NS <sup>c</sup>
AS1 < 4	1/333 (0.3%)	5/198 (2.5%)	$< 0.05^{d}$
AS5 < 7	1/333 (0.3%)	5/198 (2.5%)	< 0.05 <sup>d</sup>
Cord pH	$7.285 \pm 0.058$	$7.262 \pm 0.069$	< 0.001
Meconium staining	73/333 (21.9%)	38/198 (19.2%)	NSc
Admission to NICU (adjusted <sup>b</sup> )	2/333 (0.6%)	2/198 (1.0%)	NS <sup>d</sup>

Values are given as mean  $\pm$  SD.

ROM: rupture of membranes, SGA: small for gestational age, AS1: 1 min Apgar score, AS5: 5 min Apgar score, NICU: neonatal intensive care unit, NS: not significant.

- <sup>a</sup> Highest body temperature of more than 38.0 °C on the day of delivery.
- <sup>b</sup> NICU admission due to major anomalies were excluded.
- <sup>c</sup> Chi-square test.
- d Fisher's exact test.

in women who delivered after the spontaneous onset of labor (group 1) than in those delivered after the induction of labor (group 2) (24.3% versus 13.1%, p < 0.005).

The chorio-decidual interface was the most frequent site of inflammation, and the differences were significant between groups

**Table 2**Frequency, site and severity of histologic chorioamnionitis and funisitis in each group.

	Group 1 (Spontaneous labor, $n = 333$ )	Group 2 (Induced labor, $n = 198$ )	p value
Histologic chorioamnionitis	81/333 (24.3%)	26/198 (13.1%)	<0.005
Site of inflammation			
Amnion	17/333 (5.1%)	4/198 (2.0%)	NS <sup>a</sup>
Mild	10/333 (3.0%)	3/198 (1.5%)	
Severe	7/333 (2.1%)	1/198 (0.5%)	
Chorio-decidua	81/333 (24.3%)	26/198 (13.1%)	$< 0.005^{b}$
Mild	59/333 (17.7%)	21/198 (10.6%)	
Severe	22/333 (6.6%)	5/198 (2.5%)	
Chorionic plate	11/333 (3.3%)	4/198 (2.0%)	NS <sup>a</sup>
Mild	6/333 (1.8%)	1/198 (0.5%)	
Severe	5/333 (1.5%)	3/198 (1.5%)	
Funisitis	22/333 (6.6%)	12/198 (6.1%)	NS <sup>b</sup>
Mild	12/333 (3.6%)	7/198 (3.5%)	
Severe	10/333 (3.0%)	5/198 (2.5%)	

NS: not significant.

The inflammation of amnion and chorio-decidua was defined as the presence of at least one focus of more than 5 neutrophils and considered as severe inflammation if there is diffuse neutrophil infiltration. The inflammation of the chorionic plate was defined as the presence of at least one focus of 10 or more neutrophil foci or diffuse inflammation in the subchorionic fibrin, and considered as severe inflammation if there was diffuse and dense infiltration of neutrophils into the connective tissue of the chorionic plate, or placental vasculitis. Funisitis was defined as neutrophil infiltration confined to umbilical vessel walls and considered as severe funisitis if there was extensive neutrophil infiltration into Wharton's jelly. Mild inflammation was defined when the inflammation did not meet the criteria of severe inflammation.

- <sup>a</sup> Fisher's exact test.
- <sup>b</sup> Chi-square test.

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