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A point of care test for interleukin-6 in amniotic fluid in preterm prelabor rupture of membranes: a step toward the early treatment of acute intra-amniotic inflammation/infection

Piya Chaemsaithong, MD[1,2], **Roberto Romero, MD, D.Med.Sci.**[1,3,4], **Steven J. Korzeniewski, PhD**[1,2,4], **Alicia Martinez-Varea, MD**[1,2], **Zhong Dong, PhD**[1,2], **Bo Hyun Yoon, MD, PhD**[1,5], **Sonia S. Hassan, MD**[1,2], **Tinnakorn Chaiworapongsa, MD**[1,2], and **Lami Yeo, MD**[1,2]

[1]Perinatology Research Branch, Program for Perinatal Research and Obstetrics, Division of Intramural Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH, Bethesda, MD and Detroit, MI

[2]Department of Obstetrics and Gynecology, Wayne State University, Detroit, Michigan, USA

[3]Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI

[4]Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, MI

[5]Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Korea

Abstract

Objective—Preterm prelabor rupture of membranes (preterm PROM) accounts for 30–40% of spontaneous preterm deliveries and thus is a major contributor to perinatal morbidity and mortality. An amniotic fluid (AF) interleukin-6 (IL-6) concentration is a key cytokine for the identification of intra-amniotic inflammation, patients at risk of impending preterm delivery, and adverse pregnancy complications. The conventional method to determine IL-6 concentrations in AF is an enzyme-linked immunosorbent assay (ELISA). However, this technique is not available in clinical settings, and the results may take several days. A lateral flow-based immunoassay, or point of care (POC) test, has been developed to address this issue. The objective of this study was to compare the performance of AF IL-6 determined by the POC test to that determined by ELISA for the identification of intra-amniotic inflammation in patients with preterm PROM.

Materials and Methods—This retrospective cohort study includes 56 women with singleton pregnancies who presented with preterm PROM. Amniocentesis was performed at the time of diagnosis, and AF was analyzed using cultivation techniques for aerobic and anaerobic bacteria as well as genital mycoplasmas. AF Gram stain and AF white blood cell counts were determined. AF IL-6 concentrations were measured using both lateral flow-based immunoassay and ELISA. The primary outcome was intra-amniotic inflammation defined as AF ELISA IL-6 ≥ 2,600 pg/ml. A previously determined cut-off of 745 pg/ml was used to define a positive POC test.

Address correspondence to: Roberto Romero, MD, D. Med. Sci., Perinatology Research Branch, NICHD, NIH, DHHS, Wayne State University/Hutzel Women's Hospital, 3990 John R, Box 4, Detroit, MI 48201, USA, Telephone: (313) 993-2700, Fax: (313) 993-2694, prbchiefstaff@med.wayne.edu.

Conflict of Interest: The authors declare no conflicts of interest.

Results—1) The POC test for AF IL-6 concentrations had 97% sensitivity and 96% specificity for the identification of intra-amniotic inflammation, as defined using ELISA among patients with preterm PROM; and 2) the diagnostic performance of the POC test for IL-6 was strongly correlated to that of an ELISA test for the identification of intra-amniotic inflammation and was equivalent for the identification of acute inflammatory placental lesions and microbial invasion of the amniotic cavity (MIAC).

Conclusion—A point of care AF IL-6 test can identify intra-amniotic inflammation in patients with preterm PROM. Results can be available within 20 minutes – this makes it possible to implement interventions designed to treat intra-amniotic inflammation and improve pregnancy outcomes.

Keywords

acute chorioamnionitis; acute funisitis; amniocentesis; biomarkers; ELISA; microbial invasion of the amniotic cavity (MIAC); preterm labor; rapid interleukin-6

Introduction

Prelabor rupture of membranes (PROM) is a common complication of pregnancy [1–6], occurring in 10% of term patients [7–10]. Preterm PROM accounts for 30–40% of spontaneous preterm deliveries [11] and is a major cause of perinatal morbidity and mortality [3,12–19].

Microbial invasion of the amniotic cavity (MIAC) is detected in approximately 30% of patients with preterm PROM using cultivation techniques [20–34], and in 50% when using a combination of cultivation and molecular methods [35,36]. Moreover, the frequency of MIAC increases from 30% at the time of PROM to 75% at the onset of labor [37]. The result of amniotic fluid (AF) culture may take days. In contrast, the assessment of intra-amniotic inflammation could be done rapidly through analysis of AF. Previous studies have shown that the outcomes of patients with preterm PROM and intra-amniotic inflammation without detectable microorganisms (sterile intra-amniotic inflammation) is similar to that of patients with microorganisms in the amniotic cavity detected using cultivation or molecular techniques [35,36,38]. Indeed, patients with sterile intra-amniotic inflammation are at risk for adverse pregnancy outcomes whether they present with preterm labor and intact membranes [39,40] or a short cervix [41]. Thus far, AF interleukin-6 (IL-6) performs best among a wide variety of tests in detecting intra-amniotic infection/inflammation, as well as in the identification of patients at risk of impending preterm delivery and neonatal complications [26,42–49].

The standard method to determine IL-6 is enzyme-linked immunosorbent assay (ELISA). However, the results take time and are often not available in time for clinical decisions. Even though an ELISA can be performed in 8 hours, laboratories often batch specimens, and these assays are run only a few times per week, limiting the availability of results for acute patient management decisions (such as those required in obstetrics). A lateral flow-based immunoassay point of care (POC) test for IL-6 was developed to address this issue. This rapid test has been used to detect sepsis in neonates [50,51] and adults [52], as well as

inflammation of the cerebrospinal fluid [53]. Recently, we reported that the results of such as test correlate strongly with IL-6 determinations assessed by ELISA (Spearman's ρ = 0.92) [54]. Moreover, the diagnostic performance for the identification of intra-amniotic inflammation in patients with preterm labor with intact membranes was comparable to that of AF ELISA IL-6 [55]. Other groups have used a POC test to determine IL-6 concentrations in vaginal fluid to assess the risk of impending preterm delivery, one included asymptomatic patients at risk of preterm delivery [56] and another included patients with preterm PROM [57]. Kacerovsky et al used a POC test to determine IL-6 in AF from patients with preterm PROM to identify MIAC and acute histological chorioamnionitis [58]. The objective of this study was to compare the diagnostic and prognostic performance of an AF IL-6 POC test to IL-6 determined by ELISA in identifying intra-amniotic inflammation in patients with preterm PROM.

Material and Methods

Study population

This retrospective cohort study included women with singleton pregnancies and preterm PROM. Patients were identified by searching the clinical database and Bank of Biological Samples of Wayne State University, the Detroit Medical Center, and the Perinatology Research Branch of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) (Detroit, MI). The inclusion criteria were: 1) singleton gestation; 2) trans-abdominal amniocentesis between 20 and 35 weeks; 3) available AF for the performance of microbiologic studies; and 4) neonatal outcomes were known. Patients were excluded from the study if they had: 1) a chromosomal or structural fetal anomaly; or 2) placenta previa.

Patients with the diagnosis of preterm PROM were counseled by their treating physicians about the potential value of identifying microorganisms in AF. Women who agreed to undergo an amniocentesis were asked to donate additional AF other than that required for clinical studies and allow collection of clinical information for research purposes. Further management of these patients was at the discretion of the attending physician. All patients provided written informed consent and the use of biological specimens and clinical data for research purposes were approved by the Institutional Review Boards of NICHD and Wayne State University.

Biological samples and analysis

AF was transported in a capped sterile syringe to the clinical laboratory where it was cultured for aerobic and anaerobic bacteria, including genital mycoplasmas. AF not required for clinical assessment was centrifuged for 10 min at 4°C shortly after and stored at −70°C until analysis. Evaluation of white blood cell (WBC) count, glucose concentration, and Gram stain of AF were also performed after collection. The presence of intra-amniotic infection/inflammation was assessed by determination of AF IL-6 concentration by ELISA. AF IL-6 concentrations were measured for research purposes only, and the results were not used in patient's management.

Clinical Definitions

Gestational age was determined by the last menstrual period and confirmed by ultrasound examination, or by ultrasound examination alone if the sonographic determination of gestational age was not consistent with menstrual dating. Preterm PROM was diagnosed using a sterile speculum examination with documentation of pooling of AF in the vagina in association with a positive nitrazine test and/or positive ferning tests when necessary. Clinical chorioamnionitis was diagnosed when maternal temperature was ≥37.8 °C and two or more of the following criteria were present: uterine tenderness, malodorous vaginal discharge, maternal leukocytosis (>15,000 cells/mm^3), maternal tachycardia (>100 beats/min), or fetal tachycardia (>160 beats/min) [59–61]. The diagnosis of acute histologic chorioamnionitis was made on the basis of the presence of acute inflammatory changes in the examination of the extra-placental chorioamniotic membrane roll and/or chorionic plate of the placenta using criteria previously described [62,63]. Funisitis was diagnosed when neutrophil infiltration was detected in the umbilical vessel walls or Wharton's jelly using criteria previously reported [64,65]. Intra-amniotic inflammation was diagnosed when AF IL-6 determined ELISA concentration was ≥2,600 pg/ml [36,39,46]. MIAC was defined according to the results of AF culture. Intra-amniotic infection was defined as a combination of MIAC with intra-amniotic inflammation.

Analysis of amniotic fluid samples for IL-6 concentrations

AF IL-6 concentrations (pg/ml) were determined both by ELISA and by the lateral flow-based immunoassay POC test. For ELISA, AF IL-6 concentrations were determined by immunoassays obtained from R&D Systems (Minneapolis, MN, USA). The POC determination of AF IL-6 concentrations (pg/ml) was performed using a lateral flow-based immunoassay POC test (Milenia QuickLine® IL-6; Milenia Biotec, Bad Nauheim, Germany). The details and performance of ELISA [46,66–71] and POC immunoassays have been previously described [54]. We used a cut-off value of 745 pg/ml for the AF IL-6 POC test, similar to the cut-off value for intra-amniotic inflammation in preterm labor with intact membranes identified previously [55]. The IL-6 POC test inter- and intra-assay coefficients of variations are 15.5%, and 12.1%, respectively.

Study outcomes

The primary outcome was the presence of intra-amniotic inflammation (defined as an AF IL-6 ELISA concentration of ≥2,600 pg/ml). Secondary outcomes included the presence of a positive AF culture, and the presence of acute inflammatory lesions of the placenta (acute histologic chorioamnionitis and/or acute funisitis). The relationships between acute histologic chorioamnionitis and AF IL-6 concentrations were examined in 26 patients who delivered within 3 days after amniocentesis. This interval was chosen to preserve a meaningful temporal relationship between the results of amniocentesis and placental pathology.

Statistical Analysis

The Kolmogorov-Smirnov test was used to assess normality of arithmetic data distributions. The Kruskal-Wallis and Mann-Whitney U tests were used to make comparisons among and

between groups for arithmetic variables. The Chi-square or Fisher's exact test was used for comparisons of categorical variables, as appropriate. Survival analysis was used to compare the amniocentesis-to-delivery interval between groups. The interval from amniocentesis-to-delivery of women who did not undergo spontaneous labor (delivered for maternal or fetal indications) was treated as a censored observation, with a censoring time equal to the amniocentesis-to-delivery interval. Statistical analysis was performed using SPSS 19 (IBM Corp, Armonk, NY, USA) and SAS 9.4 (Cary, NC, USA). A p value < 0.05 was considered statistically significant.

Results

Characteristics of the study population

Fifty-six women diagnosed with preterm PROM were included in this study. Their clinical characteristics are displayed in Table 1. The median gestational age at amniocentesis was 28.8 [interquartile range (IQR) 25.7–31.5] weeks. The prevalence of MIAC and intra-amniotic inflammation was 25% (14/56) and 60.7% (34/56), respectively. The frequency of preterm delivery at <28 and at <34 weeks of gestation was 33.9% (19/56), and 96.4% (54/56), respectively. The prevalence of acute histological chorioamnionitis and acute funisitis was 57.9% (15/26) and 46.2% (12/26), respectively.

Table 2 describes clinical characteristics among the 14 patients diagnosed with MIAC, including AF IL-6 concentrations determined by both the POC and ELISA assays, and the presence or absence of acute inflammatory lesions of the placenta. The most frequent organism identified in AF was *Ureaplasma urealyticum*, occurring in 50% (7/14). Twenty-one percent (3/14) had a polymicrobial infection.

Amniotic fluid interleukin-6 point of care in the identification of intra-amniotic inflammation

Table 3 describes the diagnostic performance of the POC AF IL-6 test for the identification of intra-amniotic inflammation (AF IL-6 ELISA ≥2,600 pg/ml). It also shows that the POC and ELISA tests were equivalent in identifying patients with MIAC, as well as those with acute inflammatory lesions of the placenta, since sensitivity and specificity differed by <5% and 95% confidence intervals for each estimate overlapped.

A single patient whose AF IL-6 ELISA concentration (2,402 pg/ml) approached (but did not reach) the threshold for being considered as intra-amniotic inflammation (AF IL-6 ELISA ≥ 2,600 pg/ml) had a positive POC IL-6 test, constituting a false-positive test result. The amniocentesis-to-delivery interval was 68 days, and the patient delivered spontaneously at 36.3 weeks of gestation without MIAC or acute placental inflammatory lesions of placenta. The POC test also failed to identify one case of intra-amniotic inflammation (i.e., a false negative). This patient was induced due to preterm PROM and delivered at 32 weeks of gestation, but did not have MIAC or acute inflammatory lesions of placenta. Hence, it is difficult to determine whether this patient had a false-positive ELISA IL-6 test result.

Pregnancy outcomes of patients with positive POC AF IL-6

AF glucose was significantly lower but AF WBC count was significantly higher in patients with positive POC tests than in those with negative results (p=0.01 for both) (Table 4). The frequency of MIAC was not different among these groups (p=0.34). Patients with a positive POC test had a significantly lower gestational age at amniocentesis, gestational age at delivery, and neonatal birthweight than those with negative POC tests (p=0.005, 0.008, and 0.03, respectively) (Table 4). The frequency of delivery at less than 28 weeks of gestation and acute histological chorioamnionitis tended to be higher in patients with positive POC tests than in those who had negative tests (p=0.06 for both).

Discussion

Principal findings of the study

1) A positive POC test for AF concentrations of IL-6 in women with preterm PROM had 97% sensitivity and 96% specificity for the identification of intra-amniotic inflammation as defined by ELISA; and 2) results of the POC test were equivalent to those determined by ELISA in identifying patients with MIAC as well as those with acute inflammatory lesions of the placenta. These findings suggest that a POC test for AF concentrations of IL-6 can be used in place of ELISA for the identification of intra-amniotic inflammation in women with preterm PROM.

AF IL-6 determined by a point of care test in preterm PROM

It is well-established that intra-amniotic infection or intra-amniotic inflammation is associated with adverse pregnancy and neonatal outcomes [40,41,46,72,73], and that patients with intra-amniotic inflammation without detectable microorganisms have a similar outcome to those with intra-amniotic inflammation associated with the presence of microorganisms [38,39,41,46,72–74]. Therefore, a key issue in determining outcome is the presence or absence of inflammation.

Acute histologic chorioamnionitis (a maternal host response) [62,63,75] and funisitis (a fetal host response) [64,76] are associated with adverse pregnancy outcomes. [16,68,75–108]. The AF concentration of IL-6 correlates better with the presence and magnitude of acute histologic inflammatory lesions of the placenta than the presence or absence of microorganisms in the amniotic cavity [35,36,38,68,70,72]. This is not surprising, because IL-6 is an inflammatory mediator. Microorganisms detected in the amniotic cavity may vary in virulence, capacity to elicit an inflammatory response, and sometimes, a positive culture may be the result of contamination instead of true infection [109–113].

In previous studies, our group reported that AF IL-6 concentrations measured using a POC test were strongly correlated with those determined by conventional ELISA [54]. Moreover, the diagnostic performance of the POC AF IL-6 test was comparable to that of IL-6 determined by ELISA (sensitivity and specificity >90%) and impending spontaneous preterm delivery in patients with preterm labor with intact membranes [55].

In this study, we demonstrated that the AF IL-6 POC test is sensitive and specific for the identification of intra-amniotic inflammation in patients with preterm PROM. Only one patient (2.9%, 1/36) had a false-negative AF POC IL-6 determination (IL-6 POC < 745 pg/ml but had ELISA IL-6 ≥ 2,600 pg/ml). Moreover, the AF IL-6 concentrations determined by the POC test had equivalent diagnostic performance to that measured by ELISA for the identification MIAC and placental lesions consistent with acute inflammation.

Other point of care tests in preterm PROM

It was previously reported that a rapid metalloproteinase-8 test has clinical value in the determination of intra-amniotic inflammation in patients with preterm PROM [114]. This test has a sensitivity of 90% and a specificity of 92% in the identification of intra-amniotic infection/inflammation and was an independent predictor of interval to delivery and significant neonatal morbidity [114]. We report herein that an AF IL-6 POC test can be used as an alternative to assess the likelihood of intra-amniotic inflammation in patients with preterm PROM. Both tests have optimal properties of a POC test, namely: 1) sensitive and specific for the determination of intra-amniotic inflammation; 2) simple to perform; 3) inexpensive to set up; 4) operator independent; 5) rapid in obtaining the result (within 20 minutes); and 6) low maintenance (for the kit).

Strengths and limitations

The strengths of this study include: 1) the POC test was not used to inform treatment; 2) we included a homogenous group of patients with preterm PROM rather than additionally including patients with preterm labor with intact membrane who have a lower prevalence of intra-amniotic infection/inflammation; and 3) AF IL-6 concentrations were determined using both a POC test and ELISA. However, the study had a small sample size and, since we used cultivation to identify microorganisms in the amniotic cavity, non-culturable bacteria may not have been detected.

Conclusion

Amniotic fluid IL-6 concentrations determined using a POC test can identify intra-amniotic inflammation in patients with preterm PROM with strong diagnostic performance. Further studies are warranted to determine whether treatment with antibiotics and/or anti-inflammatory agents informed by the POC test might improve pregnancy outcomes in this setting.

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Table 1

Clinical characteristics of the study population

Characteristics	Preterm prelabor rupture of membrane (n=56)
Maternal age (years)	26.5 (21.7–31.5)
Nulliparity	33.9% (19/56)
Prior preterm delivery	17.9% (10/56)
Gestational age at amniocentesis (weeks)	28.8 (25.7–31.5)
Amniotic fluid glucose (mg/dl)	17 (10–27)
Amniotic fluid white blood cell (cell/m^3)	20 (1–145.5)
Microbial invasion of the amniotic cavity (%)	25% (14/56)
Intra-amniotic inflammation (ELISA IL-6 ≥ 2,600 pg/ml) (%)	60.7% (34/56)
Gestational age at delivery (weeks)	30.8 (27.1–32.9)
Interval from amniocentesis to delivery (days)	3 (1–12.75)
Delivery at < 28 weeks of gestation (%)	33.9% (19/56)
Delivery at < 34 weeks of gestation (%)	96.4% (54/56)
Acute histological chorioamnionitis (%) *	57.9% (15/26)
Acute funisitis (%) *	46.2% (12/26)
Acute inflammatory lesions of placenta (%) *	57.9% (15/26)

Data presented as median (interquartile range) or % (n)

* Included only patients who had interval from amniocentesis to delivery ≤ 3 days.

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Table 2

Clinical characteristics, amniotic fluid inflammatory response, and acute inflammatory placental lesions in patients with microbial invasion of the amniotic cavity using cultivation techniques.

No.	Organisms	GA at delivery (weeks)	ELISA IL-6 (pg/ml)	Point of care IL-6 (pg/ml)	AF WBC (cell/mm^3)	AF glucose (mg/dl)	Acute histological chorioamnionitis	Acute funisitis
1.	*Haemophilus influenza beta lactamase*	32^{+1}	1765.62	428	0	15	Acute chorioamnionitis	Umbilical arteritis
2.	*Ureaplasma urealyticum*	29^{+4}	963.7	262	20	32	No	No
3.	*Ureaplasma urealyticum*	31^{+4}	2169.02	537	0	35	No	No
4.	*Ureaplasma urealyticum, Mycoplasma hominis, Streptococcus viridian*	25^{+6}	949.97	350	4773	1	Necrotizing chorioamnionitis	Umbilical arteritis
5.	*Bacteroides ureolyticus,* Gram-negative bacilli	29^{+5}	5416.71	2054	10	27	Acute chorioamnionitis	Umbilical arteritis
6.	*Streptococcus pneumoniae*	22^{+6}	120 378.2	4245	723	10	Acute chorioamnionitis	Umbilical phlebitis/chorionic vasculitis
7.	*Streptococcus mitis*	22^{+2}	167 371.76	5310	144	1	Acute subchorionitis	Umbilical arteritis
8.	*Streptococcus species*	24^{+2}	157 500.9	8432	760	10	Acute chorioamnionitis	No
9.	*Bacteroides ureolyticus*	20^{+1}	326 190.4	3305	19	N/A	Acute chorioamnionitis	Umbilical phlebitis/chorionic vasculitis
10.	*Ureaplasma urealyticum*	27^{+1}	9910.19	3488	20	22	Acute chorioamnionitis	Umbilical arteritis
11.	*Ureaplasma urealyticum*	30^{+4}	27 213.11	3570	1080	10	Acute chorioamnionitis	Umbilical arteritis
12.	*Ureaplasma urealyticum*	31^{+1}	7413.27	1108	26	19	No	No
13.	*Streptococcus group B, Prevotella species*	30^{+1}	39 379.07	3403	28	15	Necrotizing chorioamnionitis	Umbilical arteritis
14.	*Ureaplasma urealyticum*	27^{+4}	284 940	4748	660	19	Subchorionic microabscesses	Umbilical arteritis

N/A: not available; WBC: white blood cell count; AF: amniotic fluid.

Acute subchorionitis/chorionitis = acute histologic chorioamnionitis stage 1;

Acute chorioamnionitis = acute histologic chorioamnionitis stage 2;

Necrotizing chorioamnionitis and subacute chorioamnionitis = acute histologic chorioamnionitis stage 3;

Subchorionic microabscessess = severe acute histologic chorioamnionitis;

Umbilical phlebitis/chorionic vasculitis = acute funisitis stage 1;

Umbilical arteritis = acute funisitis stage 2;

Necrotizing funisitis = acute funisitis stage 3.

Table 3

Diagnostic performance of point of care AF IL-6 concentrations and ELISA AF IL-6 for identification of intra-amniotic inflammation, intra-amniotic infection, and placental lesions consistent with acute inflammation

Outcomes	Diagnostic performance	Point of care IL-6 test (cut-off 745 pg/ml)		ELISA IL-6 (cut-off 2600 pg/ml)	
		% (n)	95% CI	% (n)	95% CI
Intra-amniotic inflammation [60.7% (34/56)]	Sensitivity	97.1 (33/34)	(84.6–99.5)	100% diagnostic performance. ELISA IL-6 is a gold standard test for the identification of intra-amniotic inflammation.	
	Specificity	95.5 (21/22)	(77.1–99.2)		
	Positive predictive value	97.1 (33/34)	(86.6–99.5)		
	Negative predictive value	95.5 (21/22)	(77.1–99.2)		
	Positive likelihood ratio	21.4 (97.1/4.5)	(3.14–145.0)		
	Negative likelihood ratio	0.03 (2.9/95.5)	(0–0.2)		
Microbial invasion of the amniotic cavity (MIAC) identified by culture [25% (14/56)]	Sensitivity	71.4 (10/14)	(41.9–91.4)	71.4 (10/14)	(41.9–91.4)
	Specificity	42.9 (18/42)	(27.7–59.04)	42.9 (18/42)	(27.7–59.04)
	Positive predictive value	29.4 (10/34)	(15.12–47.5)	29.4 (10/34)	(15.12–47.5)
	Negative predictive value	81.8 (18/22)	(59.7–94.7)	81.8 (18/22)	(59.7–94.7)
	Positive likelihood ratio	1.3 (71.4/57.1)	(0.8–1.9)	1.3 (71.4/57.1)	(0.8–1.9)
	Negative likelihood ratio	0.67 (28.6/42.9)	(0.27–1.64)	0.67 (28.6/42.9)	(0.27–1.64)
Acute inflammatory lesions of placenta (acute chorioamnionitis or acute funisitis) [only patients who delivered within 3 days after amniocentesis were included [57.69% (15/26)]]	Sensitivity	73.3 (11/15)	(44.9–92.1)	73.3 (11/15)	(44.9–92.1)
	Specificity	63.6 (7/11)	(30.9–88.9)	54.6 (6/11)	(23.5–83.1)
	Positive predictive value	73.3 (11/15)	(44.9–92.1)	68.8 (11/16)	(41.4–88.9)
	Negative predictive value	63.6 (7/11)	(30.9–88.9)	60.0 (6/11)	(26.4–87.6)
	Positive likelihood ratio	2.0 (73.3/36.4)	(0.9–4.7)	1.6 (73.3/45.4)	(0.8–3.3)
	Negative likelihood ratio	0.4 (26.7/63.6)	(0.2–1.1)	0.5 (26.7/54.6)	(0.2–1.3)
Acute funisitis [only patients who delivered within 3 days after amniocentesis were included [46.2% (12/26)]]	Sensitivity	75 (9/12)	(42.8–94.2)	75.0 (9/12)	(42.8–94.2)
	Specificity	57.1 (8/14)	(28.9–82.2)	50.0 (7/14)	(23.1–76.9)
	Positive predictive value	60 (9/15)	(32.3–83.6)	56.3 (9/16)	(29.9–80.2)
	Negative predictive value	72.7 (8/11)	(39.1–93.7)	70.0 (7/10)	(34.8–93.0)
	Positive likelihood ratio	1.8 (75.0/42.9)	(0.9–3.5)	1.5 (75/50)	(0.8–2.8)
	Negative likelihood ratio	0.4 (25.0/57.1)	(0.2–1.3)	0.5 (25/50)	(0.2–1.5)

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MIAC: microbial invasion of the amniotic cavity; CI: confidence interval.

Table 4

Pregnancy outcomes according to the results of point of care IL-6 (using cut-off: 745 pg/ml)

	Negative point of care IL-6 (Group 1) (n=22)	Positive point of care IL-6 (Group 2) (n=34)	P value
Amniotic fluid glucose (mg/dl)	25.5 (11.5–32.75)	14 (10–22)	0.01
Amniotic fluid WBC (cell/m^3)	4.5 (0–38)	27 (6.8–262.5)	0.01
Gestational age at amniocentesis (weeks)	30.65 (28–31.78)	27 (22.7–30.48)	0.005
Microbial invasion of the amniotic cavity (MIAC)	18.2% (4/14)	29.4% (10/34)	0.34
Gestational age at delivery (weeks)	31.8 (30.6–33.18)	28.9 (23.48–32.78)	0.008
Delivery < 28 week (n=19)	50% (2/4)	89.5% (17/19)	0.06
Delivery < 34 week (n=54)	95.5% (21/22)	97.1% (33/34)	0.75
Birthweight (grams)	1752.5 (1398.8–2108.8)	1220 (524–1777.5)	0.03
ELISA amniotic fluid IL-6 (pg/ml)	1091.7 (701.1–1965.6)	12 328.1 (6138.7–132 198.2)	<0.001
Acute histologic chorioamnionitis (n=15)	36.4% (4/11)	73.3% (11/15)	0.06
Acute funisitis (n=12)	27.3% (3/11)	60% (9/15)	0.098

AF: amniotic fluid; GA: gestational age; WBC: white blood cell; ELISA: enzyme linked immunosorbent assay; IL: interleukin.

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