especially gestational hypertension and preeclampsia.

These findings support the ‘immunologic theory,’ suggesting that immunologic intolerance between mother and fetus may play an important role in the pathogenesis of preeclampsia.

Obstetric providers should be aware of the increased risk associated with pregnancies achieved via donor oocytes and follow these high-risk pregnancies with closer surveillance.

Bedside assessment of amniotic fluid interleukin-6 in preterm prelabor rupture of membranes

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OBJECTIVE: The objective of the study was to determine the diagnostic indices and predictive values by bedside assessment of amniotic fluid interleukin-6 (IL-6) concentration in the identification of microbial invasion of the amniotic cavity (MIAC) and/or histological chorioamnionitis (HCA) in patients with preterm prelabor rupture of membranes.

STUDY DESIGN: One hundred twenty-four women with singleton pregnancies were included in this study. The amniotic fluid was sampled by transabdominal amniocentesis at the time of admission. IL-6 concentrations were assessed with an immunoassay.

RESULTS: The presence of MIAC, HCA, or the coexistence of both was associated with higher amniotic fluid concentrations of IL-6 in both a crude and adjusted analysis. The amniotic fluid concentration of IL-6 of 1000 pg/mL was determined to be the best cutoff value for the prediction of MIAC (sensitivity of 50%, specificity of 95%, positive predictive value of 82%, negative predictive value of 81%, and likelihood ratio of 8.4) or both MIAC and HCA (sensitivity of 60%, specificity of 94%, positive predictive value of 75%, negative predictive value of 88%, and likelihood ratio of 9.4).

CONCLUSION: The bedside assessment of amniotic fluid IL-6 seems to be an easy, rapid, and inexpensive method for the prediction of MIAC or both MIAC and HCA in pregnancies complicated by preterm prelabor rupture of membranes.


BACKGROUND AND OBJECTIVE

Preterm prelabor rupture of membranes (PPROM) is often complicated by microbial invasion of the amniotic cavity (MIAC), intraamniotic infection or inflammation, and histological chorioamnionitis (HCA). Traditional markers from the maternal blood (C-reactive protein, white blood cell count) and amniotic fluid (white blood cell count, glucose, Gram stain) are still used to detect MIAC and HCA. The evaluation of amniotic fluid interleukin (IL)-6 appears to be superior to that of amniotic fluid white blood cell count, amniotic fluid glucose, or Gram stain for this purpose.

The primary aim of this study was to determine the diagnostic indices and predictive values by bedside assessment of amniotic fluid IL-6 concentration in the identification of MIAC and/or histological chorioamnionitis in patients with PPROM.

MATERIALS AND METHODS

From January 2012 through July 2013, a prospective cohort study was conducted on pregnant women at 24+0 or 36+6 weeks of gestational age who were admitted to the Department of Obstetrics and Gynecology, University Hospital Hradec Králové, Czech Republic. Pregnant women 18 years old or older with singleton pregnancies complicated by PPROM were invited to participate.

Ultrasound-guided transabdominal amniocentesis was performed upon admission but before the administration of antibiotics, corticosteroids, or tocolytics. Noncentrifuged amniotic fluid

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(100 μL) was used for the bedside assessment of IL-6 concentration (Milenia QuickLine IL-6; Biotec GmbH, Giessen, Germany).

**RESULTS**

We recruited 124 women with PPROM at gestational age 24±0 to 36±6 weeks. The overall rate of MIAC was 31% (38 of 124). HCA was found in 71% of women (89 of 124). Funisitis was identified in 43% (53 of 124). The presence of both MIAC and HCA was observed in 24% of women (30 of 124).

Amniotic fluid IL-6 concentration was greater in women with than without MIAC both upon crude analysis (median, 1024 pg/mL; range, 50–10000, vs median, 214 pg/mL; range, 50–6072, respectively; P = .0003) and in an analysis adjusted for gestational age and parity (P < .0001). A cutoff value of 1000 pg/mL was found to be optimal for the prediction of MIAC, with a sensitivity 50%, specificity 95%, positive predictive value (PPV) 82%, negative predictive value (NPV) 81%, area under the receiver-operating characteristic curve (AUC) 70%, and likelihood ratio 8.4.

The presence of HCA was associated with higher amniotic fluid IL-6 concentrations than the absence of HCA upon crude analysis (median, 358 pg/mL; range, 50–10,000, vs median, 144 pg/mL; range, 50–1516, respectively; P = .0002). A cutoff value of 327 pg/mL was identified as optimal for the prediction of HCA with a sensitivity 53%, specificity 83%, PPV 89%, NPV 41%, AUC 71%, and likelihood ratio 3.1.

Women with both MIAC and HCA had higher amniotic fluid IL-6 concentrations than the others (Figure). A cutoff value of 1000 pg/mL was found to be optimal for the prediction of the presence of both MIAC and HCA, with a sensitivity 60%, specificity 94%, PPV 75%, NPV 88%, AUC 78%, and likelihood ratio 9.4.

When women were divided into 4 subgroups based on the presence or absence of MIAC and/or HCA, we observed differences in the amniotic fluid IL-6 concentrations (P < .0001). Women with both MIAC and HCA had the highest median concentration of IL-6 among the subgroups.

**COMMENT**

Amniotic fluid IL-6 concentrations have been traditionally evaluated by enzyme-linked immunosorbent assay or Luminex (Luminex Corporation, Austin, TX), neither of which can provide results quickly; therefore, neither is useful for clinical decision making. In this study, IL-6 was assessed at the bedside in a procedure requiring only 100 μL of amniotic fluid that could provide results within 20 minutes. Our
Bedside results confirmed that amniotic fluid IL-6 concentrations were elevated when MIAC, HCA, or both were present. Moreover, bedside amniotic IL-6 concentrations were shown to be useful for the prompt prediction of MIAC either alone or with HCA with good specificity in the clinical setting.

Besides having a bedside test available, clinicians need a clear cutoff value to interpret its results. From a practical point of view, the cutoff value must be easy to remember. We believe a cutoff value of 1000 pg/mL of amniotic fluid IL-6 works well.

PPROM pregnancies complicated by both MIAC and HCA seem to comprise the worst-case scenario subgroup of PPROM because of their highest intraamniotic and fetal inflammatory response. In this study, the highest intraamniotic inflammatory response, as determined by amniotic fluid IL-6, peaked when both MIAC and HCA were present. This subgroup of women had higher amniotic fluid concentrations of IL-6 than the 3 other subgroups (MIAC alone, HCA alone, and neither). Moreover, no differences in IL-6 concentrations among these 3 subgroups were found.

In conclusion, the bedside assessment of amniotic fluid IL-6 seems to be a simple, rapid, inexpensive method for the prediction of MIAC or both MIAC and HCA in pregnancies complicated by PPROM.

**CLINICAL IMPLICATIONS**

- Bedside assessment of noncentrifuged amniotic fluid interleukin-6 immediately after the sampling procedure in the labor and delivery department seems to be an easy, rapid, inexpensive method for the prediction of microbial invasion of the amniotic cavity or both microbial invasion of the amniotic cavity and histological chorioamnionitis in pregnancies complicated by premature preterm rupture of the membranes.

- The results of this study confirm earlier findings regarding the association between intrauterine infection and chorioamnionitis and interleukin-6 levels in biobanked amniotic fluids.