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The evaluation of the predictive value of TNF-alpha concentration in maternal serum in the prediction of neonatal and maternal infection

Ocena wartości predykcyjnej stężenia TNF-alfa w surowicy krwi matki w prognozowaniu wrodzonego zakażenia noworodka oraz zakażenia matki

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Abstract

Introduction: *The consequences of uncomplicated PPROM are serious, and the presence of overt intraamniotic infection (IAI) is associated with a significant increase in both, the maternal and fetal morbidity and mortality rate. TNF-alpha is a cytokine involved in systemic inflammation and plays an important role in modulating the acute phase reaction.*

Aim: *the aim of this study was to evaluate the predictive value of TNF-alpha levels in maternal serum within 6 hours after pprom and in the period of up to 12 hours after delivery, in the prediction of neonatal and maternal infection.*

Material and methods: *The investigation was conducted on a group of 56 women diagnosed with PPROM between 30+0 and 36+6 weeks gestational age. In the period of up to 6hrs from pprom first sample of 10ml of maternal venous blood for laboratory testing was taken and the level of TNF-alpha was measured. A second sample of venous blood was taken within 12hrs from delivery to reassess the TNF-alpha levels. All the participants were divided retrospectively into four groups depending on the occurrence of adverse neonatal and maternal outcome. Measuring the concentration of TNF-alpha in maternal serum was performed using the elisa method (enzyme-linked immunosorbent assay).*

Results: *A statistically significant difference in the second assay (up to 12 hours after delivery) between the patients with and without signs of maternal infection was observed concerning the TNF-alpha serum level. The concentration of this cytokine in maternal serum after delivery was 1.79 and 1.36 pg/ml ($p<0.05$) respectively, whereas within 6 hours from the PPROM in those two groups it was comparable (1.25 vs. 1.37 pg/ml – ns). Analogous observations were made in case of adverse neonatal outcome, where the TNF-alpha serum level within 12 hours after delivery was 1.70 and 1.45 pg/ml ($p<0.05$) and in the period of up to 6 hours from pprom was 1.25 vs. 1.38 pg/ml (ns) respectively.*

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Conclusions:

1. *In our investigation the maternal serum TNF-alpha concentration testing within 6 hours from PPROM between 30+0 and 36+6 weeks of gestation did not allow for the identification of patients who are more likely to develop signs of maternal infection and whose infant was at risk of neonatal infection after delivery.*
2. *In case of pprom between 30+0 and 36+6 weeks of gestation maternal serum TNF-alpha concentration testing in the period of up to 12 hours after delivery may be a useful diagnostic tool for identification of patients with an increased risk of maternal and neonatal infection.*
3. *The lower the gestational age at PPROM and at delivery, the risk of neonatal infection was greater.*

Key words: **preterm premature rupture of membranes** / **tumor necrosis factor-alpha** / / **neonatal infection** / **maternal infection** /

Streszczenie

Wstęp: *Konsekwencje niepowikłanego PPROM są poważne, a dodatkowo obecność jawnej klinicznie IAI związana jest ze znaczącym wzrostem zachorowalności i śmiertelności matki i noworodka. TNF-alfa jest cytokiną biorącą udział w reakcji zapalanej oraz odgrywa istotną rolę w modulacji reakcji ostrej fazy.*

Cel: *Celem pracy była ocena wartości predykcyjnej oznaczenia stężenia TNF-alfa w surowicy krwi matki w czasie 6 godzin od PPROM oraz 12 godzin od porodu w prognozowaniu zakażenia matki i noworodka.*

Materiał i metodyka: *Badanie przeprowadzono w grupie 56 kobiet z PPROM pomiędzy 30+0 a 36+6 tygodniem ciąży. W okresie do 6 godzin od PPROM wykonano podstawowe badania laboratoryjne oraz zmierzono stężenie TNF-alfa w surowicy krwi matki. Ponowne oznaczanie analizowanych parametrów laboratoryjnych oraz stężenia TNF-alfa przeprowadzono w czasie do 12 godzin od porodu. Wszystkie włączone do badania pacjentki podzielono retrospektywnie na cztery grupy, w zależności od wystąpienia niekorzystnego wyniku położniczego matki i noworodka. Pomiar stężenia TNF-alfa w surowicy krwi matki wykonano przy użyciu metody ELISA.*

Wyniki: *W grupie pacjentek z cechami zakażenia, stężenie TNF-alfa w surowicy krwi w okresie do 12 godzin od porodu było statystycznie wyższe w porównaniu do grupy kobiet bez cech zakażenia (1,79 vs. 1,36 pg/ml – p<0,05). W czasie 6 godzin od PPROM stężenie tej cytokiny w surowicy krwi kobiet z obu grup było porównywalne (1,25 vs. 1,37 pg/ml – ns). Podobną zależność stwierdzono w przypadku wrodzonego zakażenia noworodka, gdzie stężenie TNF-alfa po porodzie także było istotnie wyższe w grupie kobiet, u noworodków których stwierdzono cechy zakażenia wrodzonego (1,70 vs. 1,45 pg/ml – p<0,05), a w okresie do 6 godzin od PPROM było na podobnym poziomie wartości (1,25 vs. 1,38 pg/ml – ns).*

Wnioski:

1. *W przeprowadzonym badaniu oznaczenie matczynego, osoczowego stężenia TNF-alfa w okresie do 6 godzin od PPROM pomiędzy 30+0 a 36+6 tygodniem ciąży nie umożliwiło rozpoznanie pacjentek bardziej narażonych na zakażenie oraz tych, których noworodek miał większe ryzyko rozwoju zakażenia wrodzonego po porodzie.*
2. *Oznaczenie stężenia TNF-α w okresie 12 godzin od porodu może być przydatnym narzędziem diagnostycznym w identyfikacji pacjentek o zwiększonym ryzyku wystąpienia zakażenia matki i noworodka.*
3. *Im niższy był wiek ciążowy w chwili PPROM i porodu, tym ryzyko zakażenia noworodka było wyższe.*

Słowa kluczowe: **przedwczesne pęknięcie błon płodowych przed terminem** / **czynnik martwicy nowotworów alfa** / **zakażenie noworodka** / **zakażenie matki** /

Introduction

PROM occurring at a frequency of 8-10% is defined as a rupture of the membranes before the onset of uterine contractions regardless of gestational age [1]. However PPROM defined as pooling the amniotic fluid determined before 37th week of pregnancy affects about 2-3% of all pregnancies and 30-40% of cases of preterm delivery [1]. The etiology of this condition is multifactorial and is not fully understood, but most researchers recognize an infectious agent as key to its development. The presence of microorganisms in the amniotic cavity is determined in nearly half of all pregnant women experiencing premature rupture of membranes, but only some of these women will develop intraamniotic infection [2]. In addition, a little more than 10% of women with the diagnosis of intraamniotic infection based on histological examination present its clinical symptoms [2]. PPROM is also associated with a different latency period from rupture of membranes to delivery and the ongoing subclinical inflammation not always has enough time to develop into an overt intraamniotic infection. The consequences of uncomplicated PPROM are serious, and the presence of overt IAI is associated with a significant increase in both, the maternal and fetal morbidity and mortality rate [1, 3]. Congenital infection of the fetus, which clinically in the newborn may manifest itself as sepsis, bacteremia, congenital pneumonia, otitis media, omphalitis or conjunctivitis is observed in 30-40% of cases of premature rupture of membranes comparing to 10-20% of preterm births uncomplicated by

PPROM, whereas maternal infection is usually determined as an intraamniotic infection or postpartum infection (puerperal fever, endometritis, wound infection after cesarean section or after episiotomy) [1, 4].

As a result of stimulation of the immune system by the presence of fragments of bacteria i.e. lipopolysaccharide (LPS) or their metabolic products, the concentration of TNF-α increases significantly, mainly due to its secretion by the activated macrophages [5-9]. The effect of TNF-α on each organ in many cases corresponds to the function of interleukin-6 (IL-6). Similarly, this cytokine crosses the blood-brain barrier, where it modulates the thermoregulatory center and participates in the fever response of the organism during infection. In addition, through its impact on other centers located in the hypothalamus it stimulates the hypothalamic-pituitary-adrenal axis to increase the production of corticotrophin and suppresses appetite by affecting the center for hunger and satiety [5-10]. It also regulates the immune response of the organism against the presence of pathogens in the tissues of the body by stimulating the acute phase response, resulting among others in the rise of CRP. This cytokine also enhances the passage of cells of the immune system to the area where pathogenic microorganisms are present, mainly due to its chemotactic properties for neutrophils [5-10]. Furthermore, it stimulates phagocytosis by macrophages, the production of IL–1 and PGE2 (prostaglandin–E2) and plays an important role in the pathogenesis of premature uterine contractions and hence premature delivery [1].

Aim

The aim of this study was to evaluate the predictive value of TNF-alpha levels in maternal serum within 6 hours after PPROM and in the period of up to 12 hours after delivery, in the prediction of neonatal and maternal infection.

Materials and methods

The investigation was conducted on a group of 56 women diagnosed with PPROM between 30+0 and 36+6 weeks gestational age. From January 2012 to May 2013, all patients in the Division of Perinatology and Women's Diseases, Poznan University of Medical Sciences, Poznan, Poland were involved in the analysis. Before entering the study all patients were informed in detail about the aim of the study and their written consent was obtained. The study was approved by the Bioethical Committee of Poznan University of Medical Sciences (572/12).

All enrolled patients in the analysis were Caucasian and of Polish origin. Their general health condition was satisfactory without any severe comorbidity and without any current infections. In the group of analyzed patients there were 41 primigravidas and 15 multigravidas. The mean age of the patients was 29 years, whereas mean gestational age at PPROM was 34 weeks gestational age. The latency period from PPROM to delivery was 5 days and the mean gestational age at delivery was 35 weeks.

The patients were enrolled in the analysis after fulfilling the following criteria:

- the diagnosis of PPROM between 30+0 and 36+6 weeks of gestation,
- the enrollment in the analysis within 6hrs from PPROM,
- no signs of intraamniotic infection on the basis of clinical examination and laboratory tests: (body temperature ≤ 37,0°C, leukocyte level ≤ 15 G/l, CRP level ≤ 10,00 mg/l, maternal heart rate <100 bpm, fetal heart rate <160 bmp, normal odor of amniotic fluid),
- singleton pregnancy,
- satisfactory general health condition without any severe comorbidity and without any current infections.

In case of the diagnosis of any fetal congenital abnormalities or polyhydramnios, the patient was excluded from the study. The characteristics of participants are shown in Table I.

All the participants were divided retrospectively into four groups depending on the occurrence of adverse neonatal and maternal outcome. Adverse neonatal outcome was understood as a neonatal infection, which was diagnosed when a minimum of one of the following situations was determined: fetal bacteremia, fetal sepsis, congenital pneumonia, congenital otitis media, congenital conjunctivitis or omphalitis. Adverse maternal outcome was understood as a maternal infection, which was diagnosed when one of the following situations was determined: intraamniotic infection, puerperal fever, endometritis, infection of the wound following an episiotomy, wound infection after cesarean section.

During the enrollment in the analysis a gynecological examination was performed using the sterile speculum to confirm the pooling of amniotic fluid from the cervical canal and the culture from the cervical canal was collected. Sample of 10 ml of venous blood for laboratory testing was taken and the level of leukocytes, CRP and TNF-alpha was measured. Thereafter, all the participants who met the inclusion criteria were observed in the perinatology or delivery ward.

After 6hrs of PPROM, each patient received prophylactic antibiotic therapy (Cephalexin or Erythromycin), which was continued until delivery or for a minimum of 7 days. Steroid therapy (Betamethasone) was given up to the 34th week of gestation. Tocolytics (Fenoterolum) were administered only in case of regular contractions. After 12hrs from delivery a second sample of venous blood was taken to reassess the leukocyte, CRP and TNF-alpha levels.

All laboratory tests were performed in The Central Laboratory of Gynaecology and Obstetrics Hospital No. 3 in Poznan. Morphology evaluation was performed using the flow cytometry method and a semiconductor laser. CRP was measured by immunoturbidimetry enhanced with particles (Roche). Measuring the concentration of TNF-alpha was performed using the ELISA method – Human TNF-alpha Immunoassay (R&D Systems Inc.; USA; Catalog No HSTA00D).

For statistical analysis, SigmaStat3.5 was used (Systat Software Inc., USA). Analysis of the distribution of the variables tested was based on the Shapiro-Wilk test. The assessment of the statistical significance of the observed differences is based on the t-test, paired t-test, Mann-Whitney Rank Sum Test and Wilcoxon test sequence pairs. For statistical evaluation of the methods the significance level $p<0.05$ was adopted. To assess the predictive value of the newborn infection and maternal infection, sensitivity, specificity, and the area under the ROC curve (AROC – Area under Receive Operating Characteristic) was calculated (Medical Package v.10.0 Statistica; StatSoft, Inc., Tulsa, OK USA). The individual AUC ranges were assigned to the appropriate classification (0.9-1.0 = very good, 0.8-0.9 = good, 0.7-0.8 = satisfactory, 0.6-0.7 = moderate, 0.5-0.6 = fail).

Table I. Characteristics of participants.

	Participants (n=56)
Age (years)	
mean ± SD	29 ± 4.54
median	29
min/max	19/42
Gestational age at the enrollment in the analysis (weeks)	
mean ± SD	34 ± 2
median	35
min/max	30/36
Gestational age at delivery	
mean ± SD	35 ± 2
median	35
min/max	31/38
The latency period from PROM to the delivery	
mean ± SD	5 ± 9
median	2
min/max	1/57
Body temperature at the enrollment in the analysis (°C)	
mean ± SD	36.8 ± 0.2
median	36.8
min/max	36.4/37.0
Leukocyte level at the enrollment in the analysis (G/l)	
mean ± SD	10.71 ± 2.91
median	11.02
min/max	2.0/15.00
CRP level at the enrollment in the analysis (mg/l)	
mean ± SD	5.31 ± 4.8
median	3.52
min/max	0.90/10.00

Results

To the group of patients who delivered a newborn without any signs of neonatal infection 39 women were assigned, whereas 17 women were allocated to the group who delivered a newborn with an adverse neonatal outcome. Out of 56 participants in total, 11 patients had an adverse maternal outcome. The gestational age at PPROM and at delivery was statistically lower in the group of adverse neonatal outcome compared to the group of newborns without any signs of neonatal infection (33 *vs.* 34 and 34 *vs.* 35 gestational weeks respectively). No differences in gestational age at PPROM and at delivery concerning maternal outcome were noticed. In the case of adverse maternal outcome the latency period from PPROM to delivery was significantly longer compared to the group of patients without any signs of maternal infection. The gestational age at the enrollment in the analysis, latency period from PPROM to delivery and the gestational age at delivery depending on the perinatal outcome are shown in table 2. A statistically significant difference in the second assay (up to 12 hours after delivery) between the patients with and without signs of maternal infection was observed concerning the TNF-alpha serum level. The concentration of this cytokine in maternal serum after delivery was 1.36 and 1.79 pg/ml respectively, whereas within 6 hours from the PROM in those two groups was comparable. Analogous observations were made in case of adverse neonatal outcome. The TNF-alpha serum level was 1.45 and 1.70 pg/ml respectively.

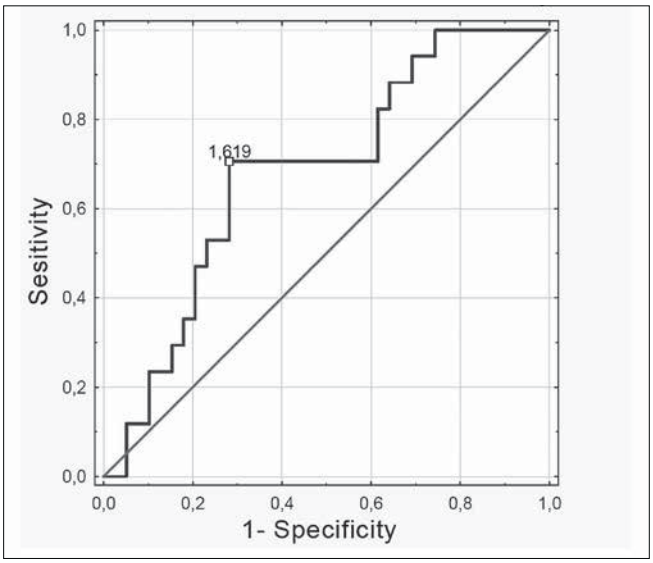

Figure 1. The prediction of the maternal infection based on the maternal serum TNF-alpha concentration in the period of up to 12 hours after delivery.

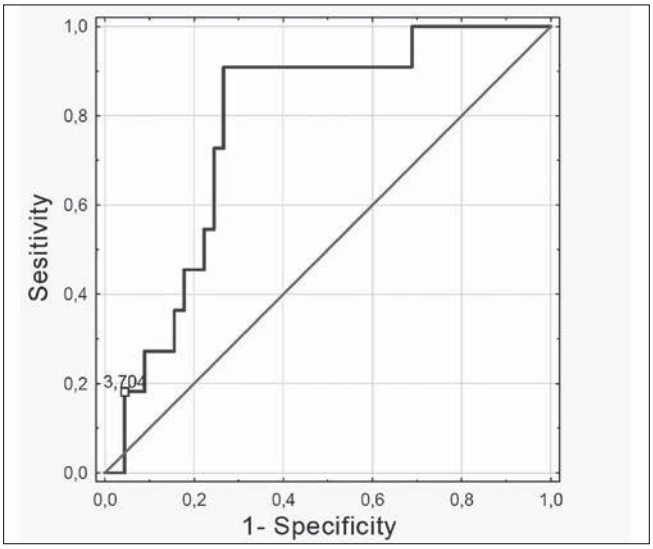

Figure 2. The prediction of the maternal infection based on the maternal serum TNF-alpha concentration in the period of up to 12 hours after delivery.

There were no statistically significant differences between groups with and without signs of infection in antenatal maternal serum concentration of leukocytes and CRP – concerning neonatal and maternal adverse outcome. After delivery, the concentration of both the CRP and leukocytes increased, however significant differences between groups (with and without signs of infection) only in the case of postpartum CRP were observed. Maternal serum concentration of leukocyte, CRP and TNF-alpha depending on the perinatal outcome are shown in table 3, whereas the maternal serum TNF-alpha concentration levels depending on the collection time of the sample are shown in table IV.

Based on the results of maternal serum TNF-alpha concentration in the period of up to 6 hours from PROM and within 12 hours after delivery we analyzed the predictive value of these tests in the anticipation of neonatal and maternal infection.

Table II. The gestational age at the enrollment in the analysis, latency period from PPROM to delivery and the gestational age at delivery depending on the perinatal outcome.

	No signs of neonatal infection (39 newborns)	Adverse neonatal outcome (17 newborns)	P	No signs of maternal infection (45 patients)	Adverse maternal outcome (11 patients)	P
Gestational age at the enrollment in the analysis (weeks) mean ± SD median min/max	 34 ± 1.6 34 30/36	 33 ± 2.1 33 30/36	**p<0.05** Mann-Whitney Rank Sum Test	 34.4 ± 1.8 35 30/36	 33 ± 2.5 34 30/36	ns Mann-Whitney Rank Sum Test
The latency period from PPROM to delivery (days) mean ± SD median min/max	 6 ± 9.9 2 1/57	 5 ± 5.7 2 1/20	ns Mann-Whitney Rank Sum Test	 4 ± 4.8 2 1/21	 12 ± 16.2 4 1/57	**p<0.001** Mann-Whitney Rank Sum Test
Gestational age at delivery (weeks) mean ± SD median min/max	 35 ± 1.5 35 31/38	 34 ± 2.0 34 31/36	**p<0.05** Mann-Whitney Rank Sum Test	 34.7 ± 1.7 35 30/38	 33.9 ± 2.0 35 31/36	ns Mann-Whitney Rank Sum Test

Table III. Maternal serum leukocyte, CRP and TNF-alpha concentration depending on the perinatal outcome.

	No signs of neonatal infection (39 newborns)	Adverse neonatal outcome (17 newborns)	P	No signs of maternal infection (45 patients)	Adverse maternal outcome (11 patients)	P
Leukocyte level age at the enrollment in the analysis (G/l) mean ± SD median min/max	 11.19 ± 2.85 12.00 6.00/15.00	 9.55 ± 2.92 10.00 4.00/10.00	 ns t-Test	 10.99 ± 2.18 11.00 6.00/15.00	 9.48 ± 3.27 10.00 2.00/14.00	ns Mann-Whitney Rank Sum Test
Leukocyte level age after delivery (G/l) mean ± SD median min/max	 16.56 ± 5.57 15.31 6.60/28.87	 17.92 ± 7.25 15.93 9.20/34.76	 ns t-Test	 17.12 ± 6.32 15.62 6.60/34.76	 16.56 ± 5.26 15.40 9.20/24.45	ns Mann-Whitney Rank Sum Test
CRP level at the enrollment in the analysis (mg/l) mean ± SD median min/max	 5.66 ± 5.66 4.01 0.87/10.00	 5.25 ± 5.33 3.39 1.43/10.00	ns Mann-Whitney Rank Sum Test	 4.71 ± 4.4 3.21 0.91/10.00	 8.92 ± 8.2 4.22 1.4/10.00	ns Mann-Whitney Rank Sum Test
CRP level after delivery (mg/l) mean ± SD median min/max	 29.41 ± 26.0 23.81 1.6/118.1	 83.52 ± 72.3 68.92 12.5/223.4	**p<0.05** Mann-Whitney Rank Sum Test	 25.13 ± 17.6 23.83 1.6/62.4	 130.41 ± 56.9 112.61 68.9/223.4	**p<0.001** Mann-Whitney Rank Sum Test
TNF-alpha level at the enrollment in the analysis (pg/ml) mean ± SD median min/max	 1.51 ± 0.63 1.38 0.83/4.49	 1.43 ± 0.49 1.25 0.79/2.46	ns Mann-Whitney Rank Sum Test	 1.50 ± 0.61 1.37 0.83/4.49	 1.45 ± 0.49 1.25 0.79/2.46	ns Mann-Whitney Rank Sum Test
TNF-alpha after delivery (pg/ml) mean ± SD median min/max	 1.60 ± 0.89 1.45 0.65/5.55	 2.03 ± 0.98 1.70 1.11/4.83	**p<0.05** Mann-Whitney Rank Sum Test	 1.59 ± 0.85 1.36 0.65/5.55	 2.28 ± 1.08 1.79 1.19/4.83	**p<0.01** Mann-Whitney Rank Sum Test

Table IV. The maternal serum TNF-alpha concentration depending on the collection time of the sample.

	TNF-alpha level at the enrollment in the analysis (pg/ml) mean ± SD median min/max	**TNF-alpha after delivery (pg/ml)** mean ± SD median min/max	**p**
No signs of maternal infection (45 patients)	1.50 ± 0.61 1.37 0.83/4.49	1.59 ± 0.85 1.36 0.65/5.55	ns Wilcoxon Signed Rank Test
Adverse maternal outcome (11 patients)	1.45 ± 0.49 1.25 0.79/2.46	2.28 ± 1.08 1.79 1.19/4.83	**p<0.05** Wilcoxon Signed Rank Test
No signs of neonatal infection (39 newborns)	1.51 ± 0.63 1.38 0.83/4.49	1.60 ± 0.89 1.45 0.65/5.55	ns paired t-Test
Adverse neonatal outcome (17 newborns)	1.43 ± 0.49 1.25 0.79/2.46	2.03 ± 0.98 1.70 1.11/4.83	**<0.001** paired t-Test

Table V. ROC curve analysis of the predictive value for adverse neonatal and maternal outcome based on the maternal serum TNF –alpha concentration test.

NEONATAL INFECTION	**AUC**	**SE**	**CI 95%**	**Cutoff point**	**Sensitivity (%)**	**Specificity (%)**
Maternal serum TNF-alpha concentration within 6 hours from PPROM (pg/ml)	0.461	0.088	0.288-0.633	2.461	5.9	97.4
Maternal serum TNF-alpha concentration within 12 hours after delivery (pg/ml)	**0.680**	**0.075**	**0.533-0.827**	**1.619**	**70.6**	**71.8**
MATERNAL INFECTION	**AUC**	**SE**	**CI 95%**	**Cutoff point**	**Sensitivity (%)**	**Specificity (%)**
Maternal serum TNF-alpha concentration within 6 hours from PPROM (pg/ml)	0.484	0.099	0.289-0.679	2.461	9.1	98.7
Maternal serum TNF-alpha concentration within 12 hours after delivery (pg/ml)	**0.778**	**0.069**	**0.643-0.912**	**3.704**	**18.2**	**95.6**

The area under the ROC curve did not exceed the value of 0.8 for tests assessing the possibility of the adverse neonatal and maternal outcome. However, the predictive value of the maternal serum TNF-alpha concentration test within 12 hours after delivery was in the range of the average results (AUC – 0.680) for the possibility of neonatal infection. The proposed cutoff point was 1.619 pg/ml, whereas the sensitivity and specificity was 70.6 and of 71.6 % respectively. Graphical representation of this analysis is provided in Figure 1. Similarly, the predictive value of the maternal serum TNF-alpha concentration test in the period of up to 12 hours after delivery was in the range of satisfactory results (AUC – 0.778) for the possibility of maternal infection. The proposed cutoff point for that test was 3.704 pg/ml, whereas the sensitivity and specificity was 18.2 and 95.6% respectively. Graphical representation of this analysis is provided in Figure 2. Detailed results of the ROC curve analysis of the predictive value for adverse neonatal and maternal outcome based on the maternal serum TNF-alpha concentration are shown in Table V.

Discussion

Preterm premature rupture of membranes and preterm labor is associated with neonatal and maternal infection, increased morbidity and with all the consequences of prematurity, which together affect the final perinatal outcome. In addition, the link between preterm labor, preterm premature rupture of the membranes, intraamniotic infection, neonatal and maternal infection and the increase in plasma levels of TNF-alpha, CRP and leukocytes has been widely documented in literature and was also confirmed in this study [11-15]. Availability of markers that can correctly identify patients who are at risk of occurrence of adverse neonatal and maternal outcome would be invaluable in the selection of the most optimal management of PPROM between 30+0 and 36+6 weeks of gestation. These patients, as they are more likely to fail the expectant management could be eligible for induction of labor prior to the development of intraamniotic infection. The most useful markers of adverse neonatal or maternal outcome should also enable differentiation of patients who

are more prone to developing signs of infection at the moment of rupture of the membranes. They should also be obtained in the least invasive way for the patient. Therefore, in the above study we focused mainly on the evaluation of maternal serum TNF- alpha concentration testing in the group of pregnant women without any sings of ongoing infection.

In the above investigation in the maternal serum TNF-alpha levels some regularity was noticed. Patients with signs of maternal infection and/or whose newborn had signs of neonatal infection had a significantly higher TNF-alpha serum concentration (depending on the time of sampling) compared to the other patients. Maternal serum TNF-alpha level in the group of patients without any signs of maternal infection and those with a healthy newborn remained relatively constant. The consequence of these observations was achieving a satisfactory level of AUC for the test evaluating the maternal serum TNF-alpha concentration in the period of up to 12 hours after delivery in the prediction of maternal infection (AUC 0.778, 95% CI 0.643-0.912, sensitivity 18.2%, specificity 95.6%) and the average level of AUC for the test predicting neonatal infection (AUC 0.680, 95% CI 0.533-0.827, sensitivity 70.6%, specificity 71.8%).

Zhang et al. studied the maternal plasma and amniotic fluid concentration of selected cytokines (IL-6, IL-8 and TNF-alpha) in the group of women with PROM. TNF-alpha concentration in maternal serum before delivery was comparable in both groups, which corresponds to the results obtained in the above investigation. Further more, in the case of women diagnosed with chorioamnionitis, the serum TNF-alpha concentration was significantly higher in comparison with non-infected women. Zhang et al. also noticed that the longer the latency period between PROM and delivery, the more increased level of this cytokine was [16].

Interesting results also showed Shobokshi et al. who analyzed the significance of selected cytokines (among others IL-6 and TNF-α) in the pathogenesis of premature rupture of membranes before 37 weeks of gestation. From the 30 participants diagnosed with PPROM amniotic fluid (collected by amniocentesis) and venous blood samples were obtained. The amniotic fluid and the blood serum levels of these cytokines were measured and the amniotic fluid was cultured. The control group consisted of 20 patients who experienced preterm delivery without preterm premature rupture of membranes. Positive amniotic fluid culture results were found in 24 of 30 cases of PPROM. Over 90 % patients with a positive culture of amniotic fluid had significantly elevated levels of cytokines in the amniotic fluid, indicating ongoing intraamniotic infection. However only 52% of these women had also significantly higher concentrations of the analyzed cytokines in blood serum comparing to the control group [17]. The results of this work may correspond with the results obtained in the above study and indirectly explain the higher number of newborns with neonatal infection than women with signs of maternal infection (17 vs. 11).

Conclusion

In our investigation the maternal serum TNF-alpha concentration testing within 6 hours from PPROM between 30^{+0} and 36^{+6} weeks of gestation did not allow the identification of patients who are more likely to develop signs of maternal infection and whose infant was at risk of neonatal infection after delivery.

In the case of PPROM between 30^{+0} and 36^{+6} weeks of gestation maternal serum TNF-alpha concentration testing in the period of up to 12 hours after delivery may be a useful diagnostic tool for identification of patients with an increased risk of maternal and neonatal infection.

The lower the gestational age at PPROM and at delivery, the risk of neonatal infection was greater.

Oświadczenie autorów:

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