

**Evaluation of Maternal Risk Factors and Delivery and Neonatal Outcomes of Premature Rupture of Membrane: A systematic review study**

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## **Running title:** Evaluation of Maternal Risk Factors

### **Abstract**

**Context:** Premature rupture of membrane is an important complication during pregnancy and is responsible for one third of preterm labors, which is associated with the neonatal and delivery outcomes.

**Objective:** The present study aimed to investigate the risk factors of premature rupture of membrane and its delivery and neonatal implications.

**Data Sources:** For this study, the articles on the databases including PubMed, Cochrane Library, ISI and Google Scholar up to 2017 were searched. The keywords used were premature rupture of membrane, neonatal, risk factors, maternal and delivery.

**Study Selection:** The inclusion criteria were: articles on the relationship between maternal risk factors and premature rupture of membrane(PROM); neonatal outcomes of PROM; the delivery outcomes of PROM; the study of mothers and infants; English and Persian language articles; and sufficient information on the state of the PROM. The articles investigating amniotomy or that only their abstract were available were excluded from the study.

**Data Extraction:** The data extracted from the above mentioned databases were illustrated with the following titles in the Excel software: authors' names and surnames, year; type of study; place of study; case group; control group; maternal risk factors; delivery outcomes, and neonatal outcomes of PROM, and the results of the study.

**Results:** Out of 90 articles, 15 articles were finalized including 1 prospective study, 5 cross-sectional papers, 6 retrospective articles and 3 historical cohort studies. Maternal risk factors included: age, parity, education, occupation, diabetes, blood pressure, cervical length along with abortion history, history of infection, upper urinary tract infection, sexual transmitted disease. Moreover, delivery complications were: cesarean section, oligohydramnios, chorioamnionitis, placental abruption. Neonatal complications included: prematurity, respiratory distress syndrome, asphyxia, infection, meningitis, sepsis, pneumonia, perinatal mortality, patent arterial duct, necrotizing enterocolitis, IVH, pulmonary hypoplasia, hyperbilirubinemia, and antibiotic intake.

**Conclusion:** Based on the results of this study, the most important risk factors for PROM, were diabetes and maternal hypertension which were associated with neonatal and maternal complications. The most important maternal and neonatal complication is infection.

**Keywords:** Premature rupture of membrane, risk factors, neonatal, maternal, Complication

## 1. Context

A premature rupture of membrane (PROM) means a rupture of membrane before the onset of labor pain in pregnancies less than 37 weeks (1). PROM occurs in 3 to 8% of pregnancies and causes one third of premature labors (2). In the case of a rupture in membrane, if the risk of an increased infection prevails over the risk of prematurity, it is recommended that delivery be performed (1). A prolonged premature rupture of membrane means the premature rupture of membrane for more than 18 hours, which is associated with an increased risk of neonatal infections of up to about 10-fold (3). The prevalence of PROM is different in several countries and populations, and many factors affect its occurrence. Therefore, its etiology is complex and multifactorial. Two-thirds of PROM cases occur spontaneously or for unknown reasons (4). However, other cases are due to structural defects in the membrane due to deficiency of collagen content in the membrane, protrusion of the membrane due to Isthmus-cervical incompetence, and activation of catabolic enzymes like collagenase, the fetal membranes weakens due to enzymatic degeneration in inflammatory or infectious processes and mechanical stresses (1, 5, 6), and secretion of proteolytic enzymes from cervicovaginal flora or infectious amniotic fluids (7). One of the main causes of the occurrence of PROM is infection (often bacterial infection) that stimulates the release of pro-inflammatory cytokines from decidua and amniotic membranes. Therefore, many bioactive materials, such as prostaglandins and metallo- proteases, are released. So, prostaglandins stimulate uterine contractions, and metalloproteases cause cervical ripening and ultimately cause the rupture of membrane (8).

The risk factors for PROM including: maternal risk factors including the history of PROM in previous pregnancies (the risk of recurrence of 16-32% in comparison with the risk of 4% in non-complicated term pregnancies), vaginal bleeding before delivery, long-term use of steroids, vascular collagen disorders such as Ehlers Danlos syndrome, systemic lupus erythematosus), abdominal trauma, preterm labor history, cigarette smoking, drug abuse, anemia, low BMI (under 19.8 kg / m<sup>2</sup>), food deficiencies including ascorbic acid and copper, low socioeconomic status (9), history of hypertension, abortion , cesarean section (10),smoking, black race/ethnicity, access to hospital care services, marital status, parity, history of preterm labor, exposure to diethylstilbestrol in the uterus, pregnancy complications such as gestational diabetes or overt diabetes, maternal weight gain, diagnostic procedures such as cerclage and amniocentesis (6),mother age less than 20 and over 35 years, blood group, Gravidity, Pelvic stenosis, maternal fatigue during work (11), lack of treatment

during pregnancy, sexually transmitted infections (12), history of cervical surgery, genital infections (chorioamnionitis or mycoplasma or chlamydia accumulation), maternal diseases (pulmonary, hypertension, and diabetes) (13).

Uterine- placental risk factors including uterine abnormalities (such as uterine septum), placental abruption (may cause 10 to 15% of premature rupture of the membrane), cervical failure, previous cervical conization, cervical shortening in the second trimester (below 2.5 cm), excessive dilation of the uterus (polyhydramnios, multiple pregnancy), chorioamnionitis, vaginal examinations (with non-sterile speculum or vaginal ultrasonography), cervical cerclage and abnormal vaginal discharge (9, 10). Neonatal risk factors include multiple pregnancies (premature rupture of the membranes complicated 7-10% of twin pregnancies) (9), inappropriate position of the fetus (11), high birth weight (12).

The premature rupture of the membrane presents 2 to 20% of delivery complication and is associated with 18 to 20% of perinatal deaths (1). PPRM is associated with many neonatal complications including respiratory distress syndrome, neonatal sepsis, and fetal death. The most common maternal complication of PPRM is infection. Chorioamnionitis occurs in 13-60% of pregnant women and postpartum infection or endometritis in 2 to 13% of women (6). Maternal complications of PROM include severe bacterial infection (0.8%) that can lead to maternal death (0.14%), increased cesarean sections, placental abruption (9-12%), disseminated intravascular coagulation, sepsis, endometritis (2 to 13%), Asherman syndrome, menstruation delay (14- 16), cervical incompetence, labor disorder, postpartum hemorrhage (17). Fetus complications include perinatal infection, cord compression due to oligohydramnios (15), hyaline membrane disease, intraventricular hemorrhage, sepsis, umbilical cord prolapse, fetal distress and increased fetal death. Prolong rupture of the membrane is associated with an increased risk of infection and chorioamnionitis, which increases the incidence of cesarean section (17).

Since the cause of the PROM is unclear, there is no effective way to prevent it. On the other hand, considering the importance of PROM for the delivery, maternal and neonatal outcomes, the early identification of risk factors for PROM and their control can reduce the occurrence of maternal and neonatal outcomes of PROM and promote the health of mothers and neonates.

**2. Objective:** The present study systematically reviews the risk factors and outcomes of premature rupture of the membrane.

### **3. Data Sources**

**Evaluation of the Maternal risk factors and maternal and neonatal outcomes of the premature rupture of membrane:** After a preliminary review of the articles, a list of risk factors and the outcomes of the premature rupture of the membrane were provided for systematic review, and articles that only examined maternal risk factors for the premature rupture of membrane, as well as maternal and neonatal outcomes were studied. In this regard, articles containing maternal risk factors, delivery outcomes, neonatal outcomes, or a combination of them were included.

**Search strategy:** The PubMed, EMBASE, and Google Scholar databases were used to conduct systematic reviews and to find studies including maternal risk factors, delivery outcomes, and neonatal outcomes of PROM. To search the articles, the keywords "PROM", "Risk Factors" and "Outcome" were used. There were 90 studies had the inclusion criteria that were collected using the EndNote software in a separate library file. Of these, 40 duplicate articles were eliminated. The articles were evaluated in terms of title and abstract and 30 articles were eliminated at this stage. Of the remaining 20 papers, 5 papers were omitted due to incomplete data, the absence of full text, the uncertainty of the type of study, and the target group. Finally, 15 articles related to the research topic were studied.

### **4. Study Selection**

**Inclusion criteria:** Articles were selected based on the following criteria:

1) The population of study were neonates or mothers; 2) Premature rupture of the membrane is confirmed; 3) Maternal risk factors of premature rupture of the Membrane were evaluated; 4) Neonatal outcomes of the premature rupture of the membrane were evaluated; 5) Articles are in English and Persian language; and 6) There is sufficient information about the condition of the premature rupture of the membrane.

**Exclusion criteria:** The following articles were excluded from the study to provide relevant articles.

1) Articles reviewing amniotomy; 2) Articles examining factors other than maternal risk factors; 3) Articles not addressing the neonatal outcomes; and 4) Articles only available for their abstract.

## 5. Data Extraction

**Data extraction and evaluation of the quality of the articles:** Articles with full text from the above mentioned databases were downloaded. The data extracted from them were illustrated with the following titles in the Excel software: authors' names and surnames, year; type of study; place of study; case group; control group; maternal risk factors; delivery outcomes, and neonatal outcomes of PROM, and the results of the study.

Of the 100 papers found, 15 papers with a sample size of 3225 neonates were finally examined. The articles were from 1997 to 2017. 4 articles (26.66%) reviewed the maternal risk factors and 1 (6.67%) article reviewed the delivery outcomes, 1 article (67.6%) examined neonatal complications and 9 articles (60%) dealt with the combination of these factors.

## 6. Results

**6.1. The prevalence of studies on the risk factors and outcomes of PROM:** A review of related studies conducted between 1997 and 2017 showed that most studies examined the combination of risk factors, maternal and delivery outcomes of PROM. Also, 4 studies examined maternal risk factors, 1 study studied delivery outcomes and 1 study investigated neonatal outcomes of PROM.

**6.2. Controversies among the Studies:** The studies on the risk factors and neonatal and delivery outcomes of PROM were different in terms of inclusion criteria, population, case group definition, research methodology, sample size, and location. There were 1 prospective study, 5 cross-sectional studies, 6 retrospective articles, and 3 historical cohort studies (Table 1).

**6.3. Global distribution of the studies on the risk factors and delivery and neonatal outcomes of PROM:** from these reviewed articles 4 (26.66%) are done in Iran, and then in the United States (2 studies, 13.33% %), India (2 studies, 13.33%), Oman (1 study, 6.66%), Indonesia (1 study, 6.66%), Ireland (1 study, 6.66%), the Netherlands (1 Study (6.66%), Canada (1 study, 6.66%), Brazil (1 study, 6.66%) and Nigeria (1 study, 6.66%).

**6.4. Maternal risk factors for PROM (4 articles):** In a case-control study, Saremi et al. (2012) investigated maternal risk factors including vaginal culture, abortion history, cervical length on 121 subjects as control (without the rupture of membrane) and 121 subjects as a group. The results of the study showed that there was no significant relationship between the number of pregnancies, cerclage and vaginal culture with premature rupture of the membrane (18).

In a study of the historical cohort of Al Riyami et al. (2013), 44 women with preterm premature rupture of the membrane were surveyed for risk factors associated with multiple maternal complications as well as adverse outcomes in Omani women. The results of the study showed that the most important risk factor was the history of infection in 24 of the research subjects. Also, there was no significant relationship between gestational age, parity, maternal age, maternal BMI and cesarean section. Infection had a significant role both as a risk factor and in the occurrence of a PROM, which was present in 27% of the research subjects. In a final conclusion, the researchers stated that the co-infection was high in patients with a very early premature rupture of the membrane (6).

In a case-control study, in order to evaluate the risk factors for risk of premature rupture of the membrane, Maryuni et al. (2017) compared 114 mothers with premature rupture of the membrane (case group) with 228 mothers without premature rupture of the membrane (control group). According to multivariate analysis, education was the most important risk factor for PROM (19).

In a case-control study, Doody et al. (1997) examined the risk factors of PROM in people with a history of PROM. Therefore, 208 women were enrolled as case group (women with history of sequential PROM) and 848 women as control group (women with a single PROM history). PPROM recurrence was associated with parity 2 or more (4.3 times). The highest incidence of recurrence of PROM (PROM term or PPROM) was associated with a non-white race (1.9 times) and parity 2 or more (2 times) (20).

Mishra et al. (2017) studied the risk factors of PROM in India. In this study, 120 patients with PROM were studied. The cause of most PROM cases was unclear and was associated with the history of PROM. Most cases of PROM occurred in housewives aged 20 to 30 years old (21).



**6.5. Articles on the delivery outcomes of PROM (1 article):** Okeke et al. (2014) conducted a retrospective study of the prevalence and management of PPRM outcomes in Nigeria. This study was conducted on 119 women treated with PROM. The prevalence of PPRM was 3.3% and perinatal death was 7%. Maternal morbidity was about 20% (2).

**6.6. Articles on neonatal outcomes of PROM (1 article):** Silveria et al. (2014) conducted a retrospective descriptive study in Brazil for 166 neonates of mothers with PROM for neonatal outcomes. The results of the study showed a significant relationship between prematurity and long intervals from rupture of the membranes to labor. It was found that gestational age had a fundamental importance for clinical management and predictive evaluation of perinatal outcomes, since the major health problem is associated with PROM is prematurity (22).

**6.7. on the combination of risk factors, maternal and neonatal outcomes of PROM (9 articles):** In the study carried out by Boskabadi et al. (2016), the frequency of maternal risk factors for prolonged rupture of membrane was investigated. A total of 309 neonates were examined for prolonged rupture of membrane (more than 18 hours before labor). Maternal risk factors included diabetes (12.7%), hypertension (9.5%), smoking (8.9%), and history of premature rupture of membrane (8.9%), urinary tract infection (7.2%), Thyroid disorders (5%), history of preterm delivery (4.4%), and cerclage (3.8%) (23). Neonatal problems in this study included jaundice, infections, RDS and asphyxiation, respectively. The common infectious diseases of the neonates with PROM included clinical infection, sepsis, and meningitis, respectively (23).

Sanginabadi et al. (2014), in a cohort study, examined the maternal and neonatal complications of premature rupture of membrane. The research subjects consisted of 50 cases in the control group (hospital care) and 39 case groups (home care). The researchers concluded in a general conclusion that it was not routine to monitor mothers at home, and it would be better if the patient was admitted to the hospital and the doctor decided for each patient individually and on the basis of her conditions (24).

Boskabadi et al. (2011), in a cross-sectional study, examined the outcomes of infants born to mothers with prolonged rupture of membrane (more than 18 hours). Maternal risk factors, antibiotic use and their effects on neonatal outcomes were evaluated. In this study, newborns were divided into three groups: 1) symptomatic neonates within 8 hours after birth; 2) mothers with chorioamnionitis; and 3) asymptomatic neonates. 150 neonates were enrolled in the study. Twelve infants (7.7%) were infected (meningitis, sepsis, pneumonia), and 101

infants (67%) were immature, and 88 (58.6%) had mothers with history of antibiotic use. The most common outcome of PROM was prematurity and related side effects, but infection was the most important corrective complication. Although antibiotic therapy in women with a history of PROM has improved the neonatal outcomes by reducing neonate sepsis and respiratory distress syndrome, but the incidence of meningitis and pneumonia increased (25).

Linehan et al. (2016) developed a descriptive retrospective cohort study of women who had been diagnosed with PROM in the second trimester of pregnancy (14 weeks to 23 weeks and 6 days). The purpose of this study was to investigate the risks to the mother and the fetus. Out of 44667 deliveries, 42 cases were selected during the five-year study. The prevalence of PPRM in the second trimester of pregnancy was 1 in 1000 pregnancies (26).

Yang et al. (2004) retrospectively reviewed the maternal and fetal outcomes of 73 single-pregnancies with PROM (16 to 26 weeks). The prevalence of sepsis was 42.1%, stillbirth was 30.1% and neonatal death was 17.8%, pulmonary hypoplasia was 15.7%, and IVH grade 3 or 4 was 7.9% (27).

Van der Heyden, in a 2013 retrospective cohort study in the Netherland, reviewed pregnancy outcomes and prenatal risk factors of PPRM in 305 pregnant women between weeks 13 and 27. The researchers concluded that perinatal mortality in PPRM in less than 27 weeks occurs in half of the cases. And among the babies that remained alive, there were serious complications in about 40% of cases. Prenatal parameters (low gestational age at PPRM, short interval between PPRM and delivery time, positive vaginal culture, and non-use of antibiotics at admission) could help predict perinatal mortality (28).

Diraviyam et al. (2017) examined the maternal and perinatal effects of PROM in a descriptive study of 141 pre-natal patients between weeks 28 and 36 and 6 days with PROM in India. The most common cause of perinatal mortality in PPRM was prematurity and complications. In late PPRM, the perinatal outcomes were desirable (17).

Smith et al. (2005) studied cross-sectional study of the prevalence, management, and outcomes of PROM in Canadian women. In nine academic centers studied in two weeks, 27 women with PPRM were enrolled. 1168 births occurred at the same time as the prevalence of PPRM was 2.3% (29). The summary of the articles is presented in Table 1.

Table 1. Summary of the studies on maternal risk factors, delivery and neonatal outcomes of PROM							
Authors/year	Method	Place	Case group	Control group	Maternal risk factors	delivery outcomes	Neonatal outcomes
Boskabadi et al. (2016) (23)	Cross-sectional	Iran	309 neonates		Diabetes and hypertension are the most common risk factors for the prolonged rupture of membrane	Caesarean section, oligohydramnios, chorioamnionitis, placental abruption, fetal distress, fever during labor and placenta previa were complications during labor.	Prematurity, respiratory problems, asphyxiation and infection are among the most serious problems.
Saremi et al. (2012)	Case-control	Iran	121 mothers	121 mothers	The length of the cervix, along with the history of abortion, was one of the important and serious factors for the premature rupture of the membrane.		
Al Riyami et al. (2013) (6)	Historical cohort	Oman	44 women with rupture of membrane		The most important maternal risk factor was the history of infection.	PROM causes infections (45%), pre-natal bleeding (25%), and cesarean section (27%).	
Sanginabadi et al. (2014) (24)	Cohort	Iran	39 mothers	50 mothers		The mean age of mothers, the number of pregnancies, the frequency of neonatal death and chorioamnionitis were significantly higher in the case group than in the control group.	Mean weight, Apgar score in first and fifth minutes, gestational week at delivery, mean time between PROM and delivery in case group was significantly lower than control group.
Boskabadi et al. (2011) (25)	Cross-sectional	Iran	150 neonate born to mothers with prolonged rupture of the membrane (more than 18 hours).		The history of PROM (10%), addiction (8%), upper urinary tract infection (5.3%), diabetes mellitus (4.7%), placental		Prematurity (67.3%), respiratory distress syndrome (22.6%), asphyxia (8.6%), meningitis (5.2%), sepsis (4%), pneumonia (1.3%),

					abruption, (4.7%), preeclampsia (3.3%), and cerclage (2%)		and death 4.6%).
Maryouni et al. (2017) (19)	Case-control	Indonesia	114 mothers with premature rupture of membrane	228 mothers without premature rupture of membrane	Age, parity and education are risk factors for PROM		
Doody et al. (1997) (20)	Case-control	USA	208 women with sequential PROM	848 women with one PROM in the previous deliveries	In women with one PROM in the previous deliveries, increased risk of recurrence of PROM was associated with fetal death below 20 weeks of gestation with parity of 2 or more. No factor increased the risk of recurrence of PROM in women with PPRM history.		
Lineban et al. (2016) (26)	Cohort descriptive retrospective	Ireland	42 cases that had prolonged PROM in the second trimester of pregnancy (14 weeks to 23 weeks and 6 days).			Maternal morbidity was sepsis (2.4%), need for antibiotic therapy (38%), placental retention (21%), and postpartum hemorrhage (12%).	Clinical chorioamnionitis was a low prevalence (14%). Neonatal death (77%), RDS (70%), sepsis (30%), necrotizing enterocolitis (20%) and IVH (30%), coagulase-negative staphylococci (20%), patent artery ducts (40%).
Yang et al. (2004) (27)	Retrospective	USA	73 singleton pregnancies with PROM (16 to 26 weeks)			Maternal morbidity was low and includes puerperal endometritis (6.8%), which caused one person to suffer from septicemia, which did not leave a long-time complication.	The prevalence of sepsis was 42.1%, stillbirth rate was 30.1% and neonatal death was 17.8%, pulmonary hypoplasia was 15.7%, and IVH grade 3 or 4 was 7.9%. The risk of neonatal pulmonary hypoplasia is greater than the gestational age at the time of delivery

						to the gestational age at the time of the rupture of membrane. Clinical chorioamnionitis was 37% and histological chorioamnionitis was 67.1%.
van der Heyden et al. (2013) (28)	Retrospective cohort	Netherland	305 pregnancies with PPROM below 27 weeks	Low gestational age at PPROM time, short interval between PPROM and delivery time, positive vaginal culture, and no antibiotic use at admission time		Perinatal mortality was 49%, with serious complications of PPROM were in 41% of infants.
Diraviam et al. (2017) (17)	descriptive	India	141 pre-natal patients between weeks 28 to 36 weeks and 6 days with PROM			18% of newborns had chorioamnionitis. 73% of the newborns were hospitalized for complications of pregnancy, such as RDS (54.54%). Perinatal mortality (2.12%) was due to sepsis. 18.5% of newborns had hyperbilirubinemia. RDS occurred in 33% of ruptured membranes that lasted less than 24 hours until delivery, in 18% of ruptured membranes that lasted longer than 24 hours until delivery. The incidence of sepsis in cases of rupture of themembranes, with a time interval of more than 24 hours until delivery, was 36%, and in cases of rupture of the membrane, which had an interval of less than 24 hours until delivery, was 10%.

Smith et al. (2005) (29)	Cross-sectional	Canada	27PPROM زن با			Neonatal complications of PPROM had an inverse relationship with gestational age. A total of 53% of the placenta were under histopathologic examination after PPROM, which had evidence of chorioamnionitis. The increased risk of chorioamnionitis was associated with a long interval from PPROM to delivery. The prevalence of PPROM was 2.3%.
Okeke et al. (2014) (2)	Retrospective	Nigeria	119 women with PROM treated.	The highest rate of PPROM was in the fertility age range of 26 to 30 years, with the lowest rate of PPROM was in the fertility rates of 16 to 20 years and after 41 years of age.	Maternal morbidity was about 20%.	Perinatal death rate was 7%, and the most important complication of PPROM was infection.
Silveria et al. (2014) (22)	Retrospective	Brazil	166 neonates of mothers with PROM	Maternal risk factors were: UTI (31.5%), chorioamnionitis (2.4%) and sexually transmitted infections (0.6%).		Prematurity, help for respiratory support, neonatal infections and antibiotic use.
Mishra et al. (2017) (21)	Cross-sectional	India	120 mothers with PROM	Most cases of PROM occurred in housewives aged 20-30 with a history of PROM.		

## 7. Discussion

Since PROM is one of the main causes of perineal morbidity and mortality (30), this study was conducted to evaluate the risk factors and neonatal and delivery outcomes of PROM. In this regard, 15 articles were obtained from the search of databases. 4 studies had investigated maternal risk factors, 1 study had evaluated delivery outcomes and 1 study had studied neonatal outcomes of PROM. Most studies in this regard were conducted in Iran (4 studies, 26.66%), and then in the United States (2 studies, 13.33%) and India (2 studies, 13.33%).

High admission of neonates following the occurrence of PROM in the hospital indicates the problems of neonates on the first days of life, and it is recommended early and accurate assessment of mothers in order to reduce neonatal complication (25). On the other hand, PROM increases hospital costs and increases maternal and neonatal hospitalization time. As a result of a PROM complicated term delivery, the average cost of a hospital increases by 40%, while hospital costs for birth with PPRM make up 8 times uncomplicated labors (20). The gestational age at birth is the main determinant of neonatal weight, neonatal complication, need for resuscitation and survival rate in neonates (31). Maternal age is one of the most important risk factors for the occurrence of PROM. Age below 20 years old is associated with a lack of uterine development, and therefore the risk of a PROM is increased. (32). In some studies, the age of 30 years old and older is considered to be a risk factor for PROM (6).

Maternal education plays an important role in the development of PROM. Mothers with high education tend to be aware of their health status and their families as much as their nutritional and medical control during pregnancy. Hence, mothers with high education will identify any changes in pregnancy faster (19).

Multiple birth is one of the reasons for PROM. One theory states that the cause of PROM can be excessive uterine stretch, for example in multiple birth, poly hydramnios, and inappropriate presentation of the fetus. With a large stretch in the uterus, the infection can enter the amniotic sacs during biomechanical processes, and rupture of the membranes can easily occur (33). The results of a study showed that more than 53% of mothers with PROM had cervical length shorter than 35 mm. Hence, short cervical lengths were considered as one of the effective factors in the occurrence of PROM (18).

PPROM is important in both aspects of prematurity and infections of newborn, and its complications on the fetus and the neonate are more than that on the mother. Outcomes of PPRM depend on the gestational age and the condition of chorioamnionitis (35). Because

most of the neonatal complications of PPRM are due to preterm labor, prolonging the interval between rupture of the membrane and the occurrence of labor by appropriate interventions may reduce prenatal mortality and morbidity (36).

A prolonged rupture of membrane over 18 hours increases the risk of infection ten times in the baby (25). There is a strong association between PROM and inflammation or intrauterine infection. Moreover, genitourinary tract infection plays an important role in the development of PROM, especially in preterm labors (38).

Asphyxia (40%) and RDS (28%) is the most common neonatal. The incidence of neonatal complications increases with the duration of PROM. Neonatal complication of PROM including: infection (pneumonitis, meningitis and sepsis), pulmonary hypoplasia, deformities of the limbs and body, compression of the umbilical cord and placental abruption(39).In Movahedi et al., Sepsis was found in 3% of neonates with PPRM (40).In a study by Boskabadi et al. (2011), PROM risk factors(40% of mothers)included history of previous PROM, addiction and UTI in pregnancy, respectively (25).

The most serious complication of PROM is chorioamnionitis, which is often associated with adverse maternal and neonatal outcomes related to infection (41). Chorioamnionitis was reported in women with PROM in the study by Medina, 13-60% (42) and in the Boskabadi study, 12.7% (25). Chorioamnionitis, by altering the cervix, causes the loss of integrity of the cervical canal or specific organisms in the vagina that may result in excessive growth of undesirable organisms. So, biochemical changes have been made in the fetus membranes and decidua, which ultimately lead to the release of prostaglandin and cytokines and regulate intracellular messaging which in turn causes the cervix to soften and rupture the membrane. Increasing the activity of the uterus is also common in most cases (43).

In one study, the prevalence of sepsis following PROM was reported to be 5.4 to 14% (45). In the study by Medina, sepsis was found in 5.2% of the cases following PROM (42). In the study conducted by Boskabadi, clinical sepsis, definitive infection and sepsis were reported in 22%, 8% and 4% of neonate, respectively (25). The results of a study show that the use of antibiotics in women with PROM reduces the incidence of neonatal sepsis (42). The results of another study comparing the effect of cefotaxime and ampicillin on cases of premature rupture of membrane on infant infections indicated that the risk of infection in infants of mothers with premature rupture of membrane receiving cefotaxime was significantly lower than that of mothers receiving ampicillin (46).



The side effects of the fetus are directly related to the gestational age at the time of the PROM. Preterm PROM increases the premature mortality by 4 times and morbidity infant by 3 times.. (48).In the study by Boskabadi et al. (2011), severe asphyxia, pulmonary hypoplasia, sepsis, CNS hemorrhage and pneumothorax were among the main causes of neonatal death in PROM cases (25).

With the occurrence of PPRM far from the term, there are certain morbidity and mortality risks for mother and neonate, and this bolds the role of physicians in taking care of a pregnant woman and paying attention to all the risk symptoms and making decisions about the timely termination of pregnancy or the continuation of pregnancy (50).

The strengths of the present study are that, as far as researcher searches are concerned, this study was the only study that reviewed the systematic review of risk factors and neonatal and delivery outcomes of PROM. The limitations of this study include the lack of access to all published articles and reports, the lack of accurate and high quality reports, and the applicability of some articles, the lack of clear and identical criteria in studies on PROM as well as the lack of same definition of the case group in studies.

## **8. Conclusions**

Extensive efforts were made to find out the results of studies on risk factors and maternal, delivery and neonatal complications of PROM. The studies found were different in terms of methodology, methods, risk factors, and outcomes of PROM. PROM is a common problem that may occur at the end of pregnancy. Although prematurity is the most common complication of PROM, but other complications such as sepsis, asphyxia, and respiratory distress syndrome may also occur. Timely identification of maternal risk factors and their proper management helps reduce the incidence and severity of PROM complications. So, performing more studies for investigating of correlation between PROM & other neonatal morbidity such as BPD, pulmonary hemorrhage is necessary.

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