ECRONICON OPEN ACCESS

EC MICROBIOLOGY
Review Article

Intraamniotic Infection (Chorioamnionitis): Presentation, Diagnosis, and Management

Fayzah Ahmed Andegani[1]*, Amani Nabil Yamani[2], Shaden Abdulmohsin Almojel[3], Nadia Abdul Hakeem Mulla Yadgar[4], Faez Mohammad Zagzoug[5], Faten Saud Aljehani[6], Doha Jawad Alsafwani[7], Suad Mousa Alsomali[7], Safaa Mahmood Alhasani[8], Mohammed Wadea Alkhonizi[9], Yazed Mohammad Ibrahim Bin Samman[10] and Hind Waleed M Mousa[7]

[1]King Abdulaziz Hospital – Jeddah, Saudi Arabia

[2]Prince Mohammad Bin Abdulaziz Hospital, Madinah, Saudi Arabia

[3]Princess Nourah Bint Abdulrahman University, Riyadh, Saudi Arabia

[4]Saudi German Hospital, Jeddah, Saudi Arabia

[5]King Abdulaziz University, Medical Service Center, Jeddah, Saudi Arabia

[6]October 6 University, Egypt, Saudi Arabia

[7]Medical University of Warsaw, Poland and Saudi Arabia

[8]Batterjee Medical College for Sciences and Technology, Jeddah, Saudi Arabia

[9]Pavol Jozef Šafárik University, Kosice Slovakia, Saudi Arabia

[10]Umm-Alqura University, Makkah, Saudi Arabia

***Corresponding Author:** Fayzah Ahmed Andegani, King Abdulaziz Hospital – Jeddah, Saudi Arabia.

Received: October 24, 2020; **Published:** November 30, 2020

Abstract

Introduction: Clinical intraamniotic infection (IAI) or simply chorioamnionitis is defined as acute inflammation of the membranes and chorion of the placenta. The condition is typically caused by polymicrobial bacterial infection following rupture of membranes. It is the most common cause of peripartum infection.

Aim of Work: In this review, we will discuss the latest available evidence regarding the diagnosis and management of Chorioamnionitis.

Methodology: A thorough systematic search on scientific database including PubMed search engine and Google Scholar search engine regarding all studies discussing chorioamnionitis. Relevant available full articles were reviewed and included.

Conclusion: A presumptive diagnosis of chorioamnionitis can be made in women with fever ≥ 39.0°C or 38.0°C to 38.9°C on two occasions 30 minutes apart, without another clear source plus one or more of increased baseline fetal heart rate > 160 beats/min for ≥ 10 minutes, maternal white cell (WBC) count > 15,000/mm3, and purulent-appearing fluid coming from the cervical os. Management of women with presumptive or confirmed chorioamnionitis involves antibiotics and delivery. Broad spectrum antibiotics should be administered following a diagnosis of chorioamnionitis in favor of both the mother and fetus. The suggested first line include ampicillin (2g intravenously) every six hours plus gentamicin (5mg/kg intravenously) once daily. Delivery should be achieved by prompt induction or augmentation of labor.

Keywords: *Chorioamnionitis; Intraamniotic Infection; IVI; Triple 1*

Introduction

Clinical intraamniotic infection (IAI) or simply chorioamnionitis is defined as acute inflammation of the membranes and chorion of the placenta. The term Histologic chorioamnionitis has been used to describe cases without the typical clinical or microbiological findings associated with acute infection. Chorioamnionitis is an older term that is still widely used. In 2015, a strict diagnostic criteria with new term "triple 1" were introduced to refer to intrauterine infection or inflammation or both [1]. However, this terminology has not been commonly adopted although the criteria are being used [2].

The condition is typically caused by polymicrobial bacterial infection following rupture of membranes. It is the most common cause of peripartum infection. A systematic review estimated that it occurred in 3.9 percent of all women giving birth [3]. However, the reported incidence varies greatly between studies due to several factors including the type of study, prevalence of risk factors, different diagnostic criteria [4]. In addition, the incidence varies between preterm and term pregnancies. Preterm delivery is associated with a higher incidence ranging from 40 to 70 percent mostly due to premature rupture of membranes (PROM) [5].

At term, the overall incidence of intrauterine infection is estimated to be 1 - 4 percent [4]. However, this increases to 7 percent with the presence of PROM, 40 percent with PROM for more than 24 hours, and 20 percent of women who have more than eight digital vaginal examinations [6].

Chorioamnionitis is associated with potentially serious maternal, fetal, and neonatal adverse effects. In this review, we will discuss the latest available evidence regarding the diagnosis and management of Chorioamnionitis.

Methodology

We conducted a thorough systematic search on scientific database including PubMed search engine and Google Scholar search engine for all studies discussing chorioamnionitis. All relevant available full articles were reviewed and included. The terms used in the search were: Chorioamnionitis, intraamniotic infection, IVI, triple 1, assessment, risk factors, and management.

Pathogens and pathogenesis

Chorioamnionitis is typically polymicrobial disease caused usually by vaginal or enteric flora. About two-thirds of women with Chorioamnionitis have at least two isolates per specimen of amniotic fluid. Transplacental transmission of infection to maternal circulation, on the other hand, are more likely to be nonpolymicrobial.

Genital mycoplasmas (As *Ureaplasma* and *Mycoplasma* species) are the most common isolates and may be detected in the absence of other organisms.[7] Some experts, however, believe that this is due to contamination or colonization from the lower genital tract rather than a true infection because these organisms are highly prevalent (more than two-third) in the lower genital tract. However, repeated data support pathogenicity of these organisms [7]. Other incriminated pathogens include anaerobes (As *Gardnerella vaginalis, Bacteroides* spp), enteric gram-negative bacilli, and group B *Streptococcus*. Anaerobes are encountered more frequently in preterm chorioamnionitis than in full term women [8].

Migration of lower genital tract flora through the cervical canal is the most common route of infection. Hematogenous route from bacteremia is uncommon and when it occurs, however, the pathogen infects the intervillous space or results from amniotic cavity contamination due to invasive procedure. Another speculated pathway of Infection is from the peritoneum via the fallopian tubes, but this likely rare [9]. Bacterial infection activates the maternal and fetal inflammatory response systems and generally leads to labor and/or rupture of membranes.

Risk factors and clinical presentation

The most important risk factors for chorioamnionitis are prolonged labor and higher duration of ruptured membranes. Other factors that may be associated with IVI include multiple digital vaginal examinations, cervical insufficiency, meconium-stained amniotic fluid, presence of genital tract organisms (from sexually transmitted infections, group B *Streptococcus*, or bacterial vaginosis), and positive history of previous chorioamnionitis [10]. Association between infections rate and number of digital examinations could be explained by prolonged labor rather than due to the number of digital examinations as an independent risk factor [11].

Chorioamnionitis often occurs in women with premature rupture of membranes (PROM) but can also occur with intact membranes. The clinical findings are usually nonspecific. Fever presents in all women, however, about 70 - 90 of these women have leukocytosis. Tachycardia appears in 50 - 80 percent of women (HR > 100/min); fatal tachycardia (HR > 160/min) is slightly less prevalent. One fourth at maximum show uterine tenderness. Bacteremia is most common when chorioamnionitis is associated with group B *Streptococcus* or *Escherichia coli* infection with 18 and 15 percent of cases respectively. As most cases of chorioamnionitis are due vaginal or enteric flora, however, bacteremia is seen in 5 - 10 percent of women with IVI.

It is essential to bear in mind that chorioamnionitis could be subclinical, which by definition does not present with the above clinical findings. Subclinical infection may manifest as preterm labor with intact membranes or as preterm premature rupture of membranes.

Pregnant with chorioamnionitis may present (or undergo) in complications. The infection is associated with an increased risk of labor abnormalities, which increase the risk for cesarean delivery, uterine atony, postpartum bleeding, and need for blood transfusion [12]. The severity of dysfunction labor is affected by the type of bacteria. Women with persistent high-virulence in the amniotic fluid have more labor abnormalities than women with low-virulence organisms [13]. The exact pathophysiologic mechanisms for labor dysfunction in not fully understood and many factor may have a role. The association between chorioamnionitis and both labor abnormalities and postpartum bleeding suggests dysfunctional myometrial contractility caused by inflammation [12].

Chorioamnionitis may lead to localized postpartum infection. Women undergo cesarean delivery, which is common, are at increased risk for wound infection, septic pelvic thrombophlebitis, pelvic abscess, and endomyometritis [14]. Sepsis may occur as a result of chorioamnionitis. In one large population based study in the United States, 18 percent of maternal sepsis were associated with chorioamnionitis [15]. Another study showed that 1.4 percent of women with established chorioamnionitis developed sepsis due to lack of identification upon initial presentation [16]. Hence, the risk of life-threatening sequelae is low with prompt adequate management with broad spectrum antibiotics. Obtaining a lactate level can be helpful since an elevated level can be a sign of sepsis and is associated with an adverse maternal outcome. Serum lactate level correlates with the severity of sepsis and should be used to follow the therapeutic response.

Diagnostic evaluation

In most case scenario, a presumptive diagnosis of chorioamnionitis is adequate for initiating maternal therapy. However, when the diagnosis is uncertain because of absence of typical clinical findings as maternal fever or overlap with other source of infection, evaluation of amniotic fluid can confirm or exclude the diagnosis. Amniotic fluid culture remains the "gold standard" and the most precise test for the diagnosis, but is constrained by the fact that conclusive results may take days to obtain, which is too long to be practically useful. Results can be obtained more feasibly from many other tests including white blood cell (WBC) concentration, gram stain, glucose concentration, and leukocyte esterase level. Unfortunately, the majority of these tests have relatively low predictive value for a positive amniotic fluid culture and even lower ability to predict neonatal sepsis [17].

WBC concentration can be calculated using a coulter counter (abnormal result > 30 cells/mm^3). Sensitivity and specificity were 64 and 95 percent respectively in one study of 120 patients with preterm labor and intact membranes [18]. Gram stain usually performed on an unspun specimen of amniotic fluid as centrifuging does not significantly improve the sensitivity of the test. The sample should be

examined under 20 to 30 high-power fields should be examined. As the amniotic fluid is sterile in uncomplicated pregnancies with intact membranes, the presence of any bacteria and leukocytes (at least six leukocytes per high-power field) is suspicious for chorioamnionitis [19]. In one meta-analysis based on two studies with a total of 288 women with preterm labor and intact membranes, Positive gram stain had sensitivity and specificity of 65 and 99 percent respectively [20]. Glucose concentration could be assessed by an autoanalyzer tests (abnormal result < 15 mg/dL). The sensitivity of glucose ≤ 14 was 85 percent while the sensitivity and specificity was 87 percent as shown in individual patient - level meta-analysis [20]. The combination of positive Gram stain of glucose level and gram stain did not in significant increase in both sensitivity and specificity. Finally, Leukocyte esterase activity can be tested by a urine dipstick reagent with sensitivity ranging from 85 to 91 percent and specificity from 95 to 100 percent [21,22]. In patients with preterm labor, the combined result of all previous 4 tests has sensitivity of 90 percent and specificity of 80 percent for predicting positive results of amniotic fluid culture. However, since the prevalence of chorioamnionitis is relatively low, this combination of tests has a high false-positive rate (about 67 percent); thus, the decision should be made with extreme caution particularly when the intervention involves delivery of an immature fetus. Accordingly, amniocentesis is not advised to exclude subclinical chorioamnionitis before attempts to prolong pregnancy in patients with preterm labor or cervical insufficiency.

Complete blood count (CBC) is essential. Blood culture in patient with chorioamnionitis is not routinely used. Physician should order a blood culture when sepsis occurs or is being suspected. C-reactive protein (CRP) in maternal serum has no role in the diagnostic evaluation. It is concluded in one meta-analyses that elevated maternal CRP level did not appear to be useful for early diagnosis or predicting neonatal sepsis but was moderately predictive of histologic chorioamnionitis [23]. Available studies demonstrated a very heterogeneous wide range for sensitivity and specificity of CRP. Diagnostic tests for other infections, such as urinalysis and urine culture, are obtained if the diagnosis of chorioamnionitis versus another cause of fever and leukocytosis is uncertain.

The diagnosis of chorioamnionitis is usually based on clinical findings alone. Maternal fever is the key criterion without another identifiable source, which is a manifestation of systemic inflammation; other criteria are insensitive. National Institute of Child Health and Human Development Workshop expert panel suggests diagnostic criteria in 2015 which was endorsed by the American College of Obstetricians and Gynecologists (ACOG) [24]. A presumptive diagnosis of chorioamnionitis can be made in pregnant with fever ≥ 39.0°C or 38.0°C to 38.9°C on two occasions 30 minutes apart, without another clear source plus one or more of the following: Baseline fetal heart rate > 160 beats/min for ≥ 10 minutes, excluding accelerations, decelerations, and periods of marked variability; Maternal white cell (WBC) count > 15,000/mm^3 in the absence of corticosteroids; Purulent-appearing fluid coming from the cervical os visualized by speculum examination. Patients with isolated fever ≥ 39.0°C (102.2°F) should be managed as having suspected chorioamnionitis, as they are at high risk of an adverse clinical infectious outcome [25]. These criteria omitted the importance of maternal tachycardia (heart rate > 100 beats per minute) and fundal tenderness for clinical diagnosis. The presence of risk factors strengthen the presumptive diagnosis of chorioamnionitis.

A confirmed diagnosis of IAI can be made in women with all previous finding plus one or more of objective laboratory findings that include positive Gram stain of amniotic fluid, low glucose level in amniotic fluid, positive amniotic fluid culture, high WBC count in amniotic fluid in the absence of a bloody tap, or histopathologic evidence of infection or inflammation or both in the placenta, fetal membranes, or the umbilical cord vessels.

In women with preterm labor and intact membranes, elevated levels of interlukin-6 (IL-6) in cervicovaginal fluid tend to be predictive of microbial amniotic cavity invasion [26]. Infection, preterm birth, and chronic fetal inflammatory syndrome are associated with elevated cytokine levels in amniotic fluid and fetal blood [17].

Increased IL-6 in the setting of chorioamnionitis may carry more significance as prognostic factor for adverse outcomes than a positive culture of amniotic fluids alone. Regardless of microbial culture results, composite perinatal morbidity and mortality rates were lower in pregnancies with IL-6 levels < 2.6 ng/mL compared with pregnancies with IL-6 levels > 11.3 ng/mL.

At present, the technological complexity of the assays, the absence of laboratory specifications, and minimal data on test features restrict this testing to research purposes in many countries including the United State. In some countries, however, a rapid test has become available and provides results within 20 minutes [27]. Preliminary evaluations indicate that the sensitivity and specificity of the test for intraamniotic inflammation in preterm pregnancies with ruptured or intact membrane are as high as 93 to 97 and 91 to 96 percent respectively [28].

Management

Management of women with presumptive or confirmed chorioamnionitis involves antibiotics and delivery. Bactericidal concentrations in the fetus and amniotic fluid is achieved within 30 to 60 minutes after initiation, but chorioamnionitis can only be cured by delivery of the infected products of conception. The lack of efficacy of antibiotics alone could be explained by biofilms formed by bacteria, which are resistant to antibiotic treatment [29].

Initially, broad spectrum antibiotics should be administered following a diagnosis of chorioamnionitis in favor of both the mother and fetus. Prompt initiation of antimicrobial therapy may reduce the frequency and severity of neonatal infection [30]. The chosen antibiotic should be parenteral broad spectrum that coverage for common pathogens. The suggested first line include ampicillin (2g intravenously) every six hours plus gentamicin (5 mg/kg intravenously) once daily. A single daily dose of gentamicin is equally or even more effective, convenient, and adequate fetal serum level than thrice-daily (standard) dosing and safe when used intrapartum or postpartum [31]. Pregnant with renal insufficiency should receive adjusted dose of gentamicin; serum levels and creatinine clearance should be monitored to guide dosing in these patients.

Delivery should be achieved by prompt induction or augmentation of labor. Cesarean delivery reserved for standard obstetric indications. Once antimicrobial therapy is initiated, there is no evidence that the duration of labor correlates with adverse neonatal outcome; [6] therefore, shortening labor does not justify cesarean delivery. In addition, as mentioned earlier, cesarean delivery in the presence of chorioamnionitis carries increased risk of wound infection, endomyometritis, and venous thrombosis [32]. If cesarean delivery is decided, women with chorioamnionitis should receive additional anaerobic coverage to the intrapartum antibiotic regimen because anaerobes play a major role in complications associated with post-cesarean endometritis. The addition of anaerobic coverage has reduced failure rates of post-cesarean endometritis. The recommended choice is either metronidazole 500 mg orally or intravenously or clindamycin 90 0 mg intravenously every eight hours. It is worth mentioning that a single dose of 500 mg azithromycin intravenously may be added as it is part of his routine antibiotic prophylaxis for cesarean delivery [33].

There is no concrete data regarding postpartum continuity of antimicrobial therapy. Some experts choose to administer additional dose of antibiotic after both vaginal delivery and cesarean section. These approaches are based on evidence from a few small randomized trials and observational studies in pre-delivery women treated for chorioamnionitis that compared the outcomes of women treated with no or one postpartum antibiotic dose with those treated with multiple postpartum antibiotic doses [30]. The use of multiple doses of antibiotics in these trials was not associated with a substantial reduction in treatment failure (usually characterized as persistent fever) compared with less intensive treatment. Some authors continue to administer antibiotics after delivery to all patients for at least 24 hours until they are afebrile and asymptomatic. Given the limited number of participants and postpartum febrile events in the available studies and the discrepancies between studies on patient characteristics and treatment regimens, this is a rational alternative strategy. It is suggested by one retrospective study that women underwent cesarean section are most likely to benefit from this approach since they had a higher prevalence of persistent fever after delivery [34]. ACOG committee opinion on chorioamnionitis states that additional antibiotic doses are not required after vaginal delivery and at least one additional dose is indicated after cesarean delivery [24]. There is no evidence that oral antibiotics are beneficial after discontinuation of parenteral therapy.

Sufficient evidence regarding the best management of chorioamnionitis in patient allergic to penicillin is lacking. Some experts improvise with substituting vancomycin for ampicillin. Gentamicin once daily plus intravenous clindamycin every 8 hours is an acceptable alternative, unless GBS coverage is indicated. In these cases, clindamycin should only be used if clindamycin-inducible resistance testing is negative.

Regarding fetal monitoring, continuous electronic fetal monitoring is to detect development of fetal compromise due to chorioamnionitis. Fetal infection is not associated with a specific pattern of periodic fetal heart rate changes, except mild baseline tachycardia in some cases. While there is no evidence suggesting that use of a scalp electrode increases the risk of neonatal sepsis in the setting of chorioamnionitis, it is prudent to use only when an external device does not provide adequate information.

Acetaminophen is typically administered to reduce fever. The combination of maternal fever and fetal acidosis increase the risk of neonatal encephalopathy by 12.5 percent. One study has suggested that each one of these factors may be considered as an independent risk factor for encephalopathy with odd ratio 8.1 and 11.5 for maternal fever and neonatal acidosis respectively [35]. Hence, this supports the use of antipyretics in women with chorioamnionitis. Additionally, Reduction of fever with antipyretics may also reduce fetal tachycardia, thereby avoiding the tendency to perform a cesarean delivery because of an abnormal fetal heart rate pattern.

Conclusion

The most important risk factors for chorioamnionitis are prolonged labor and higher duration of ruptured membranes. However, it can also occur with intact membranes. The infection is associated with an increased risk of labor abnormalities, which increase the risk for cesarean delivery, uterine atony, postpartum bleeding, and need for blood transfusion.

A presumptive diagnosis of chorioamnionitis can be made in pregnant with fever ≥ 39.0°C or 38.0°C to 38.9°C on two occasions 30 minutes apart, without another clear source plus one or more of the following: Baseline fetal heart rate > 160 beats/min for ≥ 10 minutes, excluding accelerations, decelerations, and periods of marked variability; Maternal white cell (WBC) count > 15,000/mm^3 in the absence of corticosteroids; Purulent-appearing fluid coming from the cervical os visualized by speculum examination. A confirmed diagnosis of IAI can be made in women with all previous finding plus one or more of objective laboratory findings.

Management of women with presumptive or confirmed chorioamnionitis involves antibiotics and delivery. Broad spectrum antibiotics should be administered following a diagnosis of chorioamnionitis in favor of both the mother and fetus. The suggested first line include ampicillin (2g intravenously) every six hours plus gentamicin (5 mg/kg intravenously) once daily. Delivery should be achieved by prompt induction or augmentation of labor.

Bibliography

1. Higgins RD., *et al.* "Evaluation and Management of Women and Newborns With a Maternal Diagnosis of Chorioamnionitis: Summary of a Workshop". *Obstetrics and Gynecology* 127 (2016): 426.

2. Barth WH Jr. "Lost in Translation: The Changing Language of Our Specialty". *Obstetrics and Gynecology* 127 (2016): 423.

3. Woodd SL., *et al.* "Incidence of maternal peripartum infection: A systematic review and meta-analysis". *PLOS Medicine* 16 (2019): e1002984.

4. Newton ER. "Chorioamnionitis and intraamniotic infection". *Clinical Obstetrics and Gynecology* 36 (1993): 795.

5. Yoon BH., *et al.* "Clinical significance of intra-amniotic inflammation in patients with preterm labor and intact membranes". *American Journal of Obstetrics and Gynecology* 185 (2001): 1130.

6. Rouse DJ., *et al.* "The Maternal-Fetal Medicine Units cesarean registry: chorioamnionitis at term and its duration-relationship to outcomes". *American Journal of Obstetrics and Gynecology* 191 (2004): 211.

7. Waites KB., *et al.* "Mycoplasmas and ureaplasmas as neonatal pathogens". *Clinical Microbiology Reviews* 18 (2005): 757.

8. Sperling RS., *et al.* "Intraamniotic infection in low-birth-weight infants". *The Journal of Infectious Diseases* 157 (1988): 113.

9. Park CW., *et al.* "The involvement of human amnion in histologic chorioamnionitis is an indicator that a fetal and an intra-amniotic inflammatory response is more likely and severe: clinical implications". *Placenta* 30 (2009): 56.

10. Seaward PG., *et al.* "International Multicentre Term Prelabor Rupture of Membranes Study: evaluation of predictors of clinical chorioamnionitis and postpartum fever in patients with prelabor rupture of membranes at term". *American Journal of Obstetrics and Gynecology* 177.5 (1997): 1024-1029.

11. Cahill AG., *et al.* "Number of cervical examinations and risk of intrapartum maternal fever". *Obstetrics and Gynecology* 119 (2012): 1096.

12. Satin AJ., *et al.* "Chorioamnionitis: a harbinger of dystocia". *Obstetrics and Gynecology* 79 (1992): 913.

13. Gibbs RS., *et al.* "Quantitative bacteriology of amniotic fluid from women with clinical intraamniotic infection at term". *The Journal of Infectious Diseases* 145 (1982): 1.

14. Hauth JC., *et al.* "Term maternal and neonatal complications of acute chorioamnionitis". *Obstetrics and Gynecology* 66 (1985): 59.

15. Al-Ostad G., *et al.* "Incidence and risk factors of sepsis mortality in labor, delivery and after birth: population-based study in the USA". *Journal of Obstetrics and Gynaecology Research* 41 (2015): 1201.

16. Edwards SE., *et al.* "Modified obstetric early warning scoring systems (MOEWS): validating the diagnostic performance for severe sepsis in women with chorioamnionitis". *Journal of Obstetrics and Gynaecology Research* 212 (2015): 536.e1.

17. Gomez R., *et al.* "Premature labor and intra-amniotic infection. Clinical aspects and role of the cytokines in diagnosis and pathophysiology". *Clinics in Perinatology* 22 (1995): 281.

18. Romero R., *et al.* "The diagnostic and prognostic value of amniotic fluid white blood cell count, glucose, interleukin-6, and gram stain in patients with preterm labor and intact membranes". *American Journal of Obstetrics and Gynecology* 169 (1993): 805.

19. Rehbinder EM., *et al.* "Is amniotic fluid of women with uncomplicated term pregnancies free of bacteria?" *American Journal of Obstetrics and Gynecology* 219 (2018): 289.e1.

20. Lisonkova S., *et al.* "Diagnosis of subclinical amniotic fluid infection prior to rescue cerclage using gram stain and glucose tests: an individual patient meta-analysis". *Journal of Obstetrics and Gynaecology Canada* 36 (2014): 116.

21. Riggs JW and Blanco JD. "Pathophysiology, diagnosis, and management of intraamniotic infection". *Seminars in Perinatology* 22 (1998): 251.

22. Hoskins IA., *et al.* "Leukocyte esterase activity in amniotic fluid: normal values during pregnancy". *The American Journal of Perinatology* 7 (1990): 130.

23. Van de Laar R., *et al.* "Accuracy of C-reactive protein determination in predicting chorioamnionitis and neonatal infection in pregnant women with premature rupture of membranes: a systematic review". *European Journal of Obstetrics and Gynecology and Reproductive Biology* 147.2 (2009): 124-129.

24. Committee on Obstetric Practice. Committee Opinion No. 712: Intrapartum Management of Intraamniotic Infection". *Obstetrics and Gynecology* 130 (2017): e95.

25. Ona S., *et al.* "Diagnostic Validity of the Proposed Eunice Kennedy Shriver National Institute of Child Health and Human Development Criteria for Intrauterine Inflammation or Infection". *Obstetrics and Gynecology* 133 (2019): 33.

26. Combs CA., *et al.* "Detection of microbial invasion of the amniotic cavity by analysis of cervicovaginal proteins in women with preterm labor and intact membranes". *American Journal of Obstetrics and Gynecology* 212 (2015): 482.e1.

27. Kacerovsky M., *et al.* "Bedside assessment of amniotic fluid interleukin-6 in preterm prelabor rupture of membranes". *American Journal of Obstetrics and Gynecology* 211 (2014): 385.e1.

28. Chaemsaithong P., *et al.* "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". *Journal of Maternal-Fetal and Neonatal Medicine* 29.3 (2016): 360-367.

29. Kim CJ., *et al.* "Acute chorioamnionitis and funisitis: definition, pathologic features, and clinical significance". *American Journal of Obstetrics and Gynecology* 213 (2015): S29.

30. Chapman E., *et al.* "Antibiotic regimens for management of intra-amniotic infection". *Cochrane Database of Systematic Reviews* (2014): CD010976.

31. Lyell DJ., *et al.* "Daily compared with 8-hour gentamicin for the treatment of intrapartum chorioamnionitis: a randomized controlled trial". *Obstetrics and Gynecology* 115 (2010): 344.

32. Venkatesh KK., *et al.* "Association of chorioamnionitis and its duration with adverse maternal outcomes by mode of delivery: a cohort study". *International Journal of Obstetrics and Gynaecology* 126 (2019): 719.

33. Tita AT., *et al.* "Adjunctive Azithromycin Prophylaxis for Cesarean Delivery". *The New England Journal of Medicine* 375 (2016): 1231.

34. Black LP., *et al.* "Limited course of antibiotic treatment for chorioamnionitis". *Obstetrics and Gynecology* 119 (2012): 1102.

35. Impey LW., *et al.* "The relationship between intrapartum maternal fever and neonatal acidosis as risk factors for neonatal encephalopathy". *American Journal of Obstetrics and Gynecology* 198 (2008): 49.e1.

Volume 16 Issue 12 December 2020