INTRAUTERINE INFECTIONS DURING PREGNANCY

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Annotation: Preterm birth accounts for nearly one million deaths among children under five years of age, and although its etiopathogenesis is not fully elucidated, ascending intrauterine infection and fetal inflammatory response seem to be the main triggers. The intense inflammatory responsemediated by IL-1b, TNF-a, PAF, IFN-c and IL-6, PGE_2 and MMP-1 and MMP-9 causes fetal mem- brane damage and rupture, increased uterine contractions and biochemical and structural changes in the cervix. Furthermore, preterm neonates have deficient innate and adaptive immune responses characterized by reduced levels of IgG, opsonization and phagocytosis, as well as increased activation of Th1 cells in relation to Th2 cells. Therefore, this triad is favors the occurrence of neonatal complications, such as respiratory distress syndrome, necrotizing entero- colitis, retinopathy of prematurity and bronchopulmonary dysplasia.

Keywords: Prematurity; ascending intrauterine infection; inflammation; inflammatoryresponse; immune system

INTRODUCTION

Preterm birth (PTB) is considered a major public health problem. The WHO [1] estimates that approximately
15 million newborn infants (NB) are born preterm, accounting for 11.1% and that prematurity-relatedcomplications accounted for nearly one million deathsamong children under five years in 2013. In European and Latin American countries, it is estimated that PTB will reach 5% and 8.4%, respectively, whereas inAfrican countries, it may reach 18% [2].
PTB has been defined as delivery before 37 com- pleted weeks of gestation; and it can be classified as extremely preterm (<28 weeks),
very preterm (28 to <32 weeks) and moderate to late preterm (32 to <37 weeks) based on the gestational age (GA).
This syndrome can be divided into two subtypes: *(a) spon-taneous PTB*: spontaneous onset of labor or labor induction after premature rupture of membranes (PPROM); and *(b) provider-initiated preterm birth*: induction of labor or elective cesarean section before37 weeks of complete gestation due to maternal or fetal indications or for non-medical reasons [3].

RESULTS AND DISCUSSION

Even though its etiopathogenesis remains unknown, several factors have been suggested to trigger PTB. African descent, multiple pregnancies, premature pla- cental abruption, uterine rupture, fetal distress, intrau- terine growth restriction, cervical insufficiency, smoking, preeclampsia and diabetes mellitus and obe- sity [3] are a few examples.
However, ascending intrauterine infection is themain mechanism associated with PTB, since it triggers PPROM and chorioamnionitis. In PPROM, the inflamma-tory response favors membrane damage, thus causing the loss of amniotic fluid before 37 weeks of preg- nancy and affecting 24% of PTB. In chorioamnionitis, the inflammatory response may affect the umbilical cord and the chorionic villi blood vessels, causing funi-sitis and chorionic vasculitis [4].

Different types of infections are associated with pre- maturity and other neonatal complications. Among them, it is important to highlight bacterial vaginosis (BV), trichomoniasis, gonorrhea and periodontal infec- tion [5,6].

Repercussions of PTB include respiratory and circu- latory instability, innate changes in fetal development and significant metabolic disorders that affect nearly 60% of newborns; mechanical ventilation needs to beused in more than 80% of the cases, and it is possibleto correlate the higher incidence of respiratory distress syndrome, perinatal anoxia and sepsis with the classifi- cation of PTB and with the Apgar score in the fifth minute of life [7].

Intrauterine infection and fetal inflammatory responseare the main triggers of PTB. Although contamination can occur in different ways, for instance bloodborne infection and during amniocentesis, colonization of the lower genital tract with pathogenic organisms affect a large percentage of preterm pregnancies withPPROM [8] and chorioamnionitis [9]. Ascending infec- tions triggered by *Mycoplasma sp, Ureaplasma sp, Mobiluncus sp, Bacteroides sp, group B Streptococcus sp, Escherichia coli, Enterococcus faecalis, Candida albicans, Klebsiella pneumoniae* and *Gardnerella vaginalis* [9] area few examples.

Bacterial vaginosis (BV) is triggered by the prolifera- tion of anaerobic microorganisms (*Gardnerella vagina- lis, Bacteroides spp, Mobiluncus spp and Mycoplasma hominis*), imparing *Lactobacillus* species. It is character-ized by vaginal pH ranging from 3.8 to 4.2, the pres- ence of discharge, amine odor and clue cells in Pap smear. This entity, diagnosed in approximately 42% of pregnancies, increases up to four times the risk of spontaneous PTB and PPROM [5,10]. A multicenterprospective case-cohort analysis of vaginal smears before 16th week of gestation and between 20–24th weeks, identified and quantified eight BV-associated bacteria and showed a higher risk for PTB in women with high levels of *BV-associated bacteria 1, Leptotrichia/Sneathia* species and *Megasphaera phylo- type 1* [5]. Although the mechanism of injury is poorly elucidated, the etiological agents of BV seem toreach the uterine cavity before or at the beginning of gestation [10].

CONCLUSION

Ascending intrauterine infection has proved to be a major trigger of PTB, since the intense inflammatory response promotes fetal membrane damage and rup- ture. Furthermore, deficient innate immune response is observed, with impaired opsonization and phagocytosis of pathogens, recruitment of inflammatory cells, antigen presentation and activation of the adaptive immune response, as well as a higher susceptibility to several neonatal complications following preterm birth.

Therefore, research aimed at identifying PTB bio-markers for the early diagnosis of this entity is of para-mount importance.

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