

SUMMARY

Preterm prelabour rupture of membranes (PPROM) represents a serious pregnancy complication associated with approximately 30% of preterm deliveries. PPRM might be complicated by the presence of microorganisms and/or their nucleic acids in amniotic fluid termed microbial invasion of the amniotic cavity (MIAC), and the elevation of various inflammatory mediators in the amniotic fluid referred to as intra-amniotic inflammation (IAI). Based on their presence or absence, four subgroups of PPRM can be defined: i) intra-amniotic infection (presence of both MIAC and IAI), ii) sterile IAI (IAI alone), iii) colonisation of the amniotic cavity (MIAC alone), and iv) absence of both MIAC and IAI.

Although gestational age at delivery is the most important factor affecting the risk of neonatal morbidity and mortality, the presence of MIAC and/or IAI might worsen neonatal outcomes. Therefore, precise assessment of the intra-amniotic environment seems essential for ideal personalised management of PPRM pregnancies.

Modern ultrasound machines allow a very detailed examination of the foetus. The effort to identify surrogate ultrasound markers of MIAC and/or IAI represents a logical research step in this field. One of the most promising results has been found on doppler assessment on blood flow in the foetal splenic vein, a part of the foetal portal system. Therefore, the first specific aim of this study was to evaluate the pulsatile index (PI) of the splenic vein, the main portal stem, the left portal vein, and ductus venosus in the foetuses from PPRM pregnancies with respect to the presence or absence of IAI. The second specific aim of this study was to identify PI's diagnostic indices on the selected parts of the foetal portal system to predict IAI in females with PPRM.

Both specific aims were performed in the same study population, consisting of 81 females with PPRM. The presence of IAI was associated with higher PI in the splenic vein but no differences were observed in the left portal branch, ductus venosus, and portal stem between pregnancies with and without IAI. The PI value of 0.36 on the splenic vein was identified to be optimal to predict IAI in pregnancies complicated by PPRM.

Aside from the ultrasound assessment, the direct evaluation of amniotic fluid is the most precise method to investigate the intra-amniotic environment. Several promising markers of inflammation have been proposed, including a family of granzymes, particularly extracellular granzyme A. Therefore, the third specific aim of this study was to establish an association between concentrations of extracellular granzyme A in amniotic fluid and the presence of MIAC and/or IAI. The fourth specific aim was to determine the diagnostic indices of extracellular granzyme A in amniotic fluid.

The third and fourth specific aims were performed in the same study population, consisting of 166 females with PPRM. The concentration of extracellular granzyme A in amniotic fluid was elevated in the presence of sterile IAI. A concentration of amniotic fluid extracellular granzyme A of 33.4 pg/mL was found to be an optimal cut-off value to predict the presence of sterile IAI in PPRM pregnancies.