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| **Supplementary Table 1:** PAS biomarkers candidates in maternal circulation. | | | | | | | |
| Type | Biomarker | Study | Aim | Trimester | Total cases | Trends in PAS | AUC |
| Peptides and proteins | AFP | Dreux et al.[1], 2012; Lyell et al.[2], 2015; Oztas et al.[3], 2016\*; Pekar-Zlotin et al.[4], 2018; Berezowsky et al.[5], 2019 | PAS diagnosis/(hysterectomy or not) | First/second | 621†/736†/316†/76/301 | ↑ | -/-/0.742/-/0.573 |
| PAPP-A | Desai et al.[6], 2014\*; Lyell et al.[2], 2015; Büke et al.[7], 2018; Penzhoyan et al.[8], 2019\* | PAS diagnosis | First/Second | 82/736†/88/87 | ↑ | - |
| β-hCG | Dreux et al.[9], 2012; Desai et al.[6], 2014\*; Büke et al.[7], 2018; Berezowsky et al.[10], 2019, Pekar-Zlotin et al.[11], 2018; | PAS diagnosis | First/Second | 621†/82/88/301†/76 | ↑/↓ | -/-/-/0.662/- |
| H-hCG | Einerson et al.[12], 2019\*; Al-Khan et al.[13], 2020\* | PAS diagnosis | Second/Third | 60/88 | ↓, - | 0.68/- |
| IMA, Thiol | Uyanikoglu et al.[14], 2018\* | PAS subtypes | Third | 78 | ↑, ↓ | - |
| CK, CK-MB | Ersoy et al.[15], 2016\* | PAS diagnosis | Pre-operation | 100 | -, - | -/- |
| Troponin Ⅰ | Ersoy et al.[15], 2016\* | PAS diagnosis | Pre-operation | 100 | ↑ | 0.808 |
| ProBNP | Ersoy et al.[15], 2016\* | PAS diagnosis | Pre-operation | 100 | ↑ | 0.831 |
| IL-8, Decorin | Al-Khan et al.[13], 2020\* | PAS diagnosis | Second/Third | 88 | -, ↑ | - |
| TRAIL-R2 | Oztas et al.[16], 2016\* | PAS diagnosis | Pre-operation | 82 | ↓ | - |
| Vascular endothelial factors | VEGF, PIGF, sFlt-1 | Wehrum et al.[17], 2011\*; Biberoglu et al.[18], 2016; Uyanıkoğlu et al.[19], 2018\*; Schwickert, et al.[20], 2021 | PAS diagnosis/PAS subtypes | Third/ Pre-operation | 90/98/44/99 | ↓, ↓, ↓ | -/-/-/0.729 (0.915‡) |
| VEGFR2, sTie2, PAI-1, ATⅢ | Shainker et al.[21], 2020 | PAS diagnosis | Third | 26 | ↑, ↑, ↓, ↑ | - |
| DNA | cffDNA | Samuel et al.[22], 2013 | PAS diagnosis | Third | 20 | - | - |
| RNA | cffRNA, | El Behery et al.[23], 2010\* | PAS diagnosis/PAS subtypes | Third | 35 | ↑ | - |
| cffRNA  (β-hCG) | Zhou et al.[24], 2014 | PAS diagnosis | Third | 68 | ↑ | - |
| cffRNA (hPL) | Kawashima et al.[25], 2014\*; Li et al.[26], 2019 | PAS diagnosis | Third | 110/68 | ↑ | 0.97/- |
| miRNA (miR‐490-3p, miR-133a-3p) | Yang et al.[27], 2020\* | Operation-related blood volume loss | Pre-operation | 20 | ↑ | - |
| miR-139-3p | Chen et al.[28], 2020 | PAS diagnosis | Third | 186 | ↓ | 0.73 |
| miR-196a-5p | Chen et al.[28], 2020 | PAS diagnosis | Third | 186 | ↓ | 0.74 |
| miR-518a-3p | Chen et al.[28], 2020 | PAS diagnosis | Third | 186 | ↓ | 0.59 |
| miR-671-3p | Chen et al.[28], 2020 | PAS diagnosis | Third | 186 | ↓ | 0.70 (0.91‡) |
| Cells | cTBs | Afshar et al.[29], 2021\* | PAS diagnosis | First/Second/Third | 168 | ↑ | 0.942 (0.976‡) |
| ATⅢ: antithrombinⅢ; AFP: alpha-fetoprotein; β-hCG: beta- human chorionic gonadotropin; BNP: ProBNP: Pro-brain natriuretic peptide; cffDNA: cell-free fetal DNA; cffRNA: cell-free fetal RNA; cTBs: circulating trophoblasts; CK: creatine kinase; CK-MB: creatine kinase-MB; H-hCG: hyperglycosylated human chorionic gonadotropin; HPL: human placental lactogen; IL-8: interleukin-8; IMA: ischemia modified albumin; miRNA: MicroRNA; PAI-1: plasminogen activator inhibitor 1; PAPP-A: pregnancy associated plasma protein A; PAS: placenta accreta spectrum; PIGF: placenta growth factor; sFlt-1: soluble Fms-like tyrosine kinase 1; VEGF: vascular endothelial growth factor; VEGFR2: vascular endothelial growth factor receptor 2; TRAIL-R2: tumor necrosis factor related apoptosis-inducing ligand receptor 2. \*All PAS cases confirmed by the histopathologic confirmation only. †The large cohort was from the prenatal screening program. ‡Single biomarker combined with other index including other biomarkers, clinical risk factors or imaging findings. | | | | | | | |

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