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CIRCULATING BIO-MARKERS AS A NON-INVASIVE DIAGNOSTIC TEST TO PREDICT LOSS OF PREGNANCY

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The hypothesis of induction of intolerance suggests the role of unique dendritic cell (DC) subsets, NK cells and its ability to prime type 1 regulatory T (Treg) cells in recurrent pregnancy loss (RPL). Thus, we attempted to find if the indices of peripheral Treg/DCs/NK cells and their Th1/2/17 responses can be developed as biomarkers to predict pregnancy loss. Antenatal women with history of RPL (6-20 weeks of singleton pregnancy; n=25), with threatened abortions (TA; 6-20 weeks; n=25), with normal (control) singleton pregnancy (6-12 weeks; n=50), median age of 26±4 yrs were enrolled. Cases with history of chronic diseases/ known anatomical anomalies of womb/genetic or infectious etiology of previous miscarriage were excluded. PBMCs were used to identify dendritic cells as monocytoid and plasmacytoid, co-stimulatory (CD83) and PDL (CD274). Treg cells were also investigated (FACS ARIA III). Cytokines (IL-2/4/6/10/17A, TNF, IFN) were measured using BD™ CBA Human Cytokine Kit. Student t-test/chi-square/Pearson correlation was used to analyse the results and statistically significant if the P value was <0.05. The incidence of pDCs decreases significantly in RPL (1.9±0.56) compared to TA (1.8±0.55; <0.001) and controls (3.09±0.6; <0.001). Treg cells were found to be significantly lowered in RPL patients, 2.02±0.25 (<0.001) and 2.57±1.05% in TA cases, as compared with 3.04±0.69% in normal controls. Expression of activated T-cell was not significantly observed between RPL and control. NK cells were elevated in RPL (7.77±0.74) and TA (4.13±0.58) compared to controls (3.08±0.57). Levels of IL-2, INF , TNFα were found to be higher (<0.001) in TA and RPL cases compared to controls. Th1/Th2 ratio decreases significantly in RPL as compared to normal (<0.001). IL-17A was significantly elevated in RPL (5-fold; 13.2±1.03 ph/ml) and TA (2-fold; 6.9±2.7 pg/ml) as compared to control (2.9±0.6 pg/ml; <0.001), revealing a close association of these conditions with the increased production of Th17 cells. ROC showed IL-2 and IL-17A to be able to distinguish between RPL and TA significantly from control with AUC ranging from 85-98%.

Conclusion & Significance: Significant decreased expression of pDC and Tregs, increase in NK cells and IL-17, exhibit impaired immune regulatory mechanisms in pregnancy which may lead to pregnancy loss. IL17A showed to be one of the most sensitive and accurate marker predicting pregnancy losses. Thus, we propose that analysis of these circulating immune cells in peripheral blood and associated cytokine markers could be used as non-invasive diagnostic test for preganancy loss and miscarriage risk assessment. In future, this test may provide a scientific evidence for improved treatment modalities and immature DCs could be used as an alternative therapy in RPL/TA cases

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