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MiR-150 enhances immune tolerance by targeting ARRB-2/PDE4 to down-regulate inflammatory cytokines

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MiR-150, a major modulator negatively regulating the development and differentiation of various immune cells is widely involved in orchestrating inflammation. In transplantation immunity, miR-150 can effectively induce immune tolerance, although the underlying mechanisms have not been fully elucidated. In the current study, we found that miR-150 is elevated after blocking CD28/B7 co-stimulatory signaling pathway and impaired IL-2 production by targeting ARRB2. Further investigation suggested that miR-150 not only repressed the level of ARRB2/PDE4 directly but also prevented AKT/ARRB2/PDE4 trimer recruitment into the lipid raft by inhibiting the activities of PI3K and AKT through the cAMP-PKA-Csk signaling pathway. This leads to the interruption of cAMP degradation and subsequently results in inhibition of the NF-kB pathway and reduced production of both IL-2 and TNF. In conclusion, our study demonstrated that miR-150 can effectively prevent CD28/B7 co-stimulatory signaling transduction, decrease production of inflammatory cytokines such as IL-2 and TNF and elicit the induction of immune tolerance. Therefore, miR-150 could become a novel potential therapeutic target in transplantation immunology.

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Anemia and its prevalent factors in gestation with skin problems

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Background: Anemia affects more than 2.5 billion population globally, accounting for more than 35% of the global population. It is a major public health concern in gestation specifically in developing countries like Pakistan. Anemia is considered severe when hemoglobin concentration is <7.0 g/dL, moderate 7.0-9.9 g/dL and mild 10.0-11 g/dL. Anemia is a major cause of morbidity and mortality in gestation and has maternal and fetal consequences.

Objective: To determine the prevalence of anemia, its risk factors and outcomes in gestation.

Methods: A cross sectional study was conducted and a sample of 100 patients was selected. Anemic and non-anemic patients were matched on the grounds of age, parity and child birth data. Sample size was estimated by using the World Health Organization (WHO) software where α=5%, 1-β=90, P1=0.05, P2=0.10, n (sample size)=100. Outcome variable was prevalence of iron deficiency anemia defined as <11 g/dL, plasma ferritin <12 mcg/l or zinc protoporphyrin >35 mcg/dl. Clinical variables with p <0.05 were considered statistically significant and adjusted odds ratio with 95% CI was calculated and were entered in multivariate logistic regression model to determine association. Prevalence of anemia, no education, absence of iron supplementation in gestation and skin problems (pruritis, angular cheilitis, pale skin) were defined in reduced and full models of ANOVA in regression analysis. (Reduced model $Y=\beta0+\beta1X1+\varepsilon$ and the full model $Y=\beta0+\beta1X1+\beta2X2+\beta3X3+\varepsilon$).

Results: Iron deficiency anemia was high 47% if Hb <10.5 g/dl and was statistically significant high 60% in infants of anemic mothers. Educational status [odds ratio (OR) 1.17; 95% (CI): 1.07-1.20], iron supplementation during gestation [(OR) 1.64; 95% (CI): 1.45-1.82], skin problems (pale skin, angular cheilitis, tongue swollen smooth with burning sensation) [odds ratio (OR) 2.78; 95% (CI): 2.17-3.20]. (Reduced model $Y=\beta0+\beta1$ Iron deficiency anemia$+\varepsilon$ and the full model $Y=\beta0+\beta1$ Iron deficiency anemia$+\beta2$ Educational status$+\beta3$ Skin problems (pale skin, angular cheilitis, tongue swollen smooth with burning sensation$+\varepsilon$). Maternal Hb and serum ferritin showed a highly significant positive correlation (r=0.81; p<0.001) mentioning that iron deficiency anemia was the most significant factor for anemia in gestation. Maternal Hb also showed a significant correlation with placental weight (r=0.64; p<0.001), birth weight (r=0.73; p<0.001) and APGAR score (r=0.78; p<0.001). Maternal serum ferritin also positively correlated with cord ferritin (r=0.85; p<0.001).

Conclusion: Iron deficiency anemia and its risk factors have a statistically significant adverse effect on gestation and fetal outcome.

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