Abstract

Background: Preeclampsia (PE) is associated with maternal morbidity and mortality globally, but especially in Bolivia where rates are third highest worldwide. The exact pathophysiology of PE is still unknown, but previous studies have shown insulin signaling pathway dysfunction and hypoxia as plausible mechanisms in PE development. This study aimed to examine protein expression of the insulin signaling pathway and correlate the proteins with hypoxia in PE placentas compared to normotensive controls at high-altitude to discover more about the PE pathogenesis. **Methods:** Patients were recruited from the Hospital Materno-Infantil in La Paz, Bolivia (3,600-4,100m). Maternal blood samples were taken to measure erythropoietin receptor (EpoR) as a marker of hypoxia. Umbilical venous and arterial blood was sampled along with placental biopsies. Western capillary electrophoresis was used to measure protein expression of IRS1, pIRS1, IRS2, AKT, pAKT, and pGSK3B. **Results:** 65 maternal-infant pairs with 29 PE cases and 36 controls were recruited for this study. Compared to controls, PE placentas were found to have greater pAKT, greater pIRS1, and lower pGSK3B expression levels. There was also a trend seen in PE placentas having greater IRS2 expression levels, although not statistically significant. There was no significant difference in IRS1 or AKT protein expression between PE cases versus normotensive controls. There was a negative correlation between IRS1, pIRS1, IRS2 with EpoR. There was a positive correlation seen between pGSK3B with EpoR. There was no correlation between Akt and EpoR. **Conclusion:** PE placentas showed dysfunction in the insulin signaling cascade concerning for insulin resistance. Hypoxia was determined to be a significant factor in this insulin signaling pathway, suggesting that hypoxia can interfere with normal functioning of this cascade. This study demonstrated how insulin signaling disruption and hypoxia can play a role in the pathophysiology of PE at high altitude.