FOETUS AND NEWBORN RESPONSES TO HIGH ALTITUDE, ADAPTATION OR STRUGGLE FOR OXYGEN?

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Reduced oxygen availability at high altitude is associated with reduced intrauterine growth retardation of the foetus and a reduction in birth weight and linear dimensions of the newborn. From a review of published literature on foetus and newborn physiological responses to high altitude, the following remarks can be made.

Growth

The low birth weights of high altitude native populations compared to low altitude populations appear to be mainly secondary to placental hypoxia resulting from maternal hypoxia (Khalid et al., 1997). Placental hypoxia is present despite the relative increase in the placental weight (increased dilatation of the capillaries sinusoids with accompanying thinning of the villous membrane), which is a mechanism which increases the volume and surface of the placenta and improves oxygenation (Monge and León-Velarde, 1991; Burton et al., 1996). But, on the other hand, Frisancho (1970) have hypothesized that the low birth weight observed at high altitude, could be an adaptive response to reduce oxygen requirements rather the consequence of intolerance of intra-uterine hypoxia.

Foetal undernutrition, evaluated by body composition (triceps and subscapular skinfold thickness, and brachial fat cross-sectional), seems not to be responsible for the reduced newborn dimensions observed at high altitude, hypoxia may exert a direct effect on human foetal growth (Balley and Haas, 1986). The foetal growth disruption at high altitude occurs during the last trimester of gestation when fat deposition and limb growth are most notably affected (Haas et al., 1977). In the earlier stages it seems that pre-implantation and early post-implantation stages are at increased risk when compared to sea level (Clegg, 1978).

When human embryos and foetuses were studied histologically in order to analyze the endochondral ossification process at high altitude (3,600 m.) a delay in the appearance of the embryonic stages of chondrogenesis and endochondral ossification was found. However, no changes were found in the development of the appendicular skeleton when compared with the same gestational ages at sea level (Cubillo de Trigo et al., 1987).

Nevertheless, Zamudio et al., 1995a have shown that reduced uterine blood flow and altered pelvic blood flow distribution during pregnancy at high altitude may contribute to the altitude-associated reduction in infant birth weight. Women who presented the latter characteristics may present an incomplete vascular adjustment to pregnancy and may be predisposed to development of preeclampsia or transient hypertension (Zamudio et al., 1995b). High altitude women who developed preeclampsia had less blood volume expansion, particularly during the third trimester, which was also associated with smaller infants (Zamudio et al., 1993).

In fact, Zamudio et al. (1993) have found that in comparison with literature observations, altitude-associated difference in birth weight was smallest in Tibetans, intermediate in South America, and greatest in high altitude populations from North America. However, there is not to date adequate information to determine whether or not the developmental responses of the high altitude native are population-specific, based on a genetic structure different from that of sea level populations.

Lung function
Based in lung volume and compliance studies, Mortola et al. (1990) have pointed out that the respiratory system compliance of high altitude newborns (3,600 m.) is increased at birth, which most likely would be the result of foetal hypoxia. Additionally, newborns maintain their metabolic rate with no major alterations in ventilation, the use of a greater fraction of the inspired O2 at high altitude is probably an indication that functional and structural alterations have been stimulated by foetal hypoxia (Mortola et al., 1992).

Haematology
The notion that the reduced birth weight reported for high altitude infants is induced by intrauterine hypoxia has also been tested by comparing hematological values of high-altitude and low-altitude newborn infants, since the human foetus can respond to intrauterine hypoxia with enhanced erythropoiesis. Haematocrit, hemoglobin concentration, and the proportion of hemoglobin F have been found higher among newborn infants at high altitude, who also display evidence of enhanced erythropoiesis. This fact supports the proposal the high-altitude foetus experiences a greater degree of hypoxia in utero than does the low-altitude foetus (Balley and Haas, 1986). However, some authors have not found differences in haematocrits and PO2 values between neonates studied at high altitude and sea level (Howard et al., 1957; Sobrevilla et al., 1971). Additionally, methaemoglobin concentration measured in the umbilical cord of newborns born at 3,600 m, were more than 4% higher. A decrease in enzymatic reduction systems and an increase in intraerythrocytic oxidant systems are claimed to be the underlying causes of the findings (Ergueta and Clavijo, 1975).

Amniotic fluid
With regards to the amniotic fluid volume, high altitude populations have shown a greater proportion of women with polyhydramnios and a lower proportion with oligohydramnios, indicating and association between high altitude and an increase in amniotic fluid index. The mechanism and clinical significance of this effect are unknown (Yancey and Richards,1994).

Cardiopulmonary adaptation
In Lhasa (3,650 m.; Tibet), Niermeyer et al. (1995) have found, after controlling by gestational age and Apgar score, that Tibetan newborns had higher arterial oxygen saturation at birth and during the first four months of life than Han newborns (newborns with a Chinese origin), which suggest that genetic adaptations may be also involved in the foetus adequate oxygen transport capacity. When foetal electrocardiograms were studied at 4330 m., the cardiac foetal rhythm was found regular and it did not differ from that seen at sea level. However, high altitude

foetuses showed significantly lower cardiac rates between 21 and 24 weeks of gestation (Inga, 1978).
In the newborn, the right ventricular pressure/left ventricular pressure ratio remains in the normal or mildly elevated range from 6 hours to 4 months of age. Despite low O2 saturation in the first week to months after birth at 3,100 m. the newborn rarely show evidence of severe pulmonary hypertension (Niermeyer et al., 1993).

Endocrine Studies
Foetal hypothalamic-pituitary-thyroid function at high altitude has been evaluated mainly in Peruvian populations. Serum concentrations of cortisol and corticosterone were measured in newborns at 4,300 m. and compared with a sea level group (Guerra-Gracía et al., 1977). Normal adrenal function was found in the high altitude newborns. Serum levels of T4, T3, and TSH were measured in cord and maternal blood. Foetal and maternal hormone levels at 3,000 m. were comparable to those of sea level, but maternal and foetal TSH was lower at 3,000 m. than at sea level. There was a progressive and significant decrease of T4, levels with the altitude of residence. High altitude newborns showed a lower TSH pituitary reserve, a lower and delayed rate of secretion of thyroid hormones and a delayed maturation in the peripheral metabolism of iodotyronines (Pretell et al., 1977; Villena, 1987).

Altogether, the work done to evaluate the foetus and newborn physiological responses to high altitude seems to indicate that the foetus must develop several adaptive responses to reduced oxygen availability. Whether these responses represent a benefit or a constraint for the integral development of an infant at high altitude must be elucidated in the near future.

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