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EVIDENCE OF GLUCOSE GRADIENT ALONG THE UMBILICAL CORD: IMPLICATIONS FOR PETAL DEVELOPMENT

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ABSTRACT

This study established the relationship between maternal blood glucose and fetal blood glucose levels as determined in cord blood. The study involved 30 Nigerian Women who delivered normally at the Maternity Annex of the University of Calabar Teaching Hospital. Maternal blood samples were taken by venepuncture soon after delivery. Cord blood samples were taken at two locations, 6cm from the placenta and 8cm from the fetus. All blood samples were analysed for glucose soon after collection. The results showed a mean maternal blood glucose of 4.7±0.7 mmol/L. Placental end cord blood glucose was 3.4±0.5 mmol/L while the fetal end cord blood glucose was 2.5±0.6 mmol/L. Placental and fetal end glucose levels were 71±15% and 52±17% respectively, of maternal level. The cord blood glucose values correlated positively with the maternal glucose level, with correlation coefficients (r) of 0.89 for 'placental end' glucose and 0.86 for 'fetal end' glucose. These findings predict that mild maternal hypoglycemia could cause severe hypoglycemia in the fetus with attendant consequences.

KEY WORDS: Glucose, fetus, mother, gradient.

INTRODUCTION

The fetus depends on its mother for the supply of nutrients and oxygen. Nutrients are made available to the fetus from maternal sources through the placenta. The major nutrient transferred from the mother to the fetus is glucose (Worthington et al., 1977). Some amino acids, fructose and triglycerides are also transferred. Essentially the fetus receives high carbohydrate and low fat supply from the mother (Cheek, 1975). Glucose is the major nutrient utilized by the fetus. The fetal uptake of glucose and glycogenic amino acids has been shown to be so rapid that maternal fasting glucose levels usually fall below normal (Young, 1971). The resulting maternal hypoglycemia has been described as "accelerated starvation" by Freinkel (1965). The high fetal demand for glucose may be a crucial developmental requirement for the fetus. Animal and human experiments have suggested that a critical period of brain growth may exist during which deprivation of high energy nutrient even in mild form may produce irreversible impairment of brain development (Wenick, 1969). Earlier studies suggested that fetal blood glucose varied between 70 - 80% of maternal levels and is at equilibrium with maternal glucose (Cornblath and Reisner, 1965; Cornblath and Marsgan, 1961). Factors which affect maternal blood glucose level also cause developmental changes in the fetus. For example, infants of diabetic mothers have long been known to be prone to high mortality and morbidity and to be oversize at birth (Bennewitz, 1826). The high birth weight has been attributed to the large supply of glucose to the fetus leading to excess cytoplasmic growth (Cheek, 1975). It is also suspected that the large numbers of still births in developing countries is related to poor maternal nutrition (Fiander, 1992).

This study was conducted to determine the relationship between maternal blood glucose and the cord blood glucose of full term infants. Cord blood glucose is an index of glucose supply to the fetus. Such data are needed for accurate prediction of the glucose supply to the fetus once maternal levels are known.

SUBJECTS AND METHODS

The study involved 30 pregnant Nigerian women attending the Maternity Annex of the University of Calabar Teaching Hospital. Only pregnant women who were healthy and had no apparent complications were included in the study. All subjects had normal deliveries at full term. On the day of delivery cord blood samples were collected at two locations on the cord (a) 6cm from the placental and (b) 8cm

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from the fetal end. Care was taken to avoid contamination with maternal blood. Maternal blood samples for blood sugar were collected by venopunture soon after delivery. All blood samples were collected into fluoride-oxalate bottles and analysed for glucose within 3 hours. The birth weights of the neonates were also recorded.

GLUCOSE ANALYSIS

This was done according to the glucose oxidase method of Trinder(1968). To 2.9ml of protein precipitant 0.1ml of blood was added mixed and centrifuged. One millilitre of the clear supernatant was add to 3.0ml of colour reagent and the absorbance was read at 515nm after 10min incubation at 37°C. Glucose values were calculated by comparing absorbance of test with those of glucose standards put through the same process.

The protein precipitant consisted of 10g of sodium tingstate, 9.0g of sodium chloride, 10g of disodium hydrogen phosphate dissolved in about 800ml of water. Sufficient 1.0M Hcl (about 25ml) was added to bring the pH to 3.0. 1.0g of phenol was then added and the volume made up to 1L. The colour reagent was prepared by mixing 75ml sodium dehydrogen phosphate (0.33M), 215ml distilled water, 5ml fermicozyme 653AM glucose oxidase (Hughes and Hughes Ltd., Brentfood Essex), 5ml peroxidase RZ 0.6 (Sigma). 300mg sodium azide and 100mg 4-aminophenazone were added to the mixture.

STATISTICAL ANALYSIS

The significance of any differences between the maternal blood glucose and cord blood at any of the two sites of the cord or between blood glucose of the two cord samples were assessed by the Student's 't' test. Correlation plots of maternal glucose against cord blood glucose at each of the two points of sample collection were made and the respective correlation coefficients were calculated. Correlation between fetal birthweight and cord blood glucose were also determined.

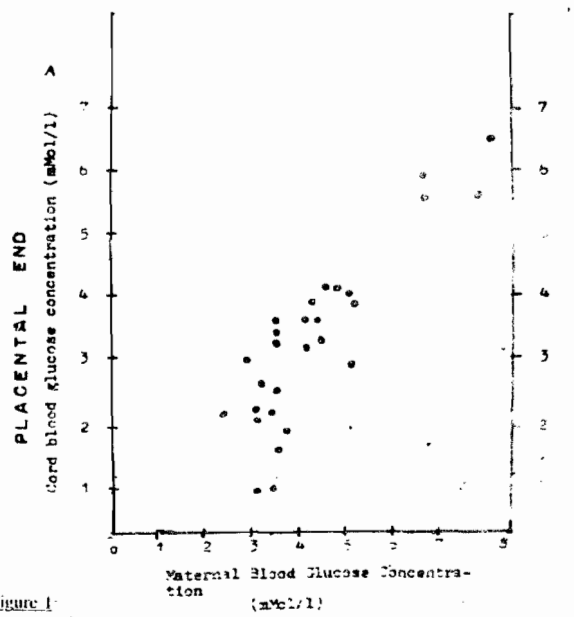

Figure 1: Correlation plot between placental end cord blood glucose and maternal blood glucose r = 0.89, n = 30, p<0.005

RESULTS

The cord and maternal blood glucose levels obtained are shown in table 1. The mean maternal blood glucose level was significantly higher ($p<0.001$) than cord blood glucose at any of the two sites of sample collection. Blood collected from the placental end of the cord had significantly higher glucose concentration ($p<0.001$) than blood collected from the fetal end (table 1). Both the placental and fetal end cord blood glucose levels

Glucose Gradient along unbilical cord.

Table 1: Maternal and Cord blood glucose levels

Parameter	Maternal	CORD Blood		P Values
		Placental end	Fetal end	
Blood glucose mm0l/L	4.7±0.7	3.4±05	2.5±0.6	1. Maternal vs Placental end $p<0.001$ 2. Maternal vs Fetal and $p<0.001$ 3. Placental end vs Fetal end $p<0.001$
n	30	30	30	
Mean Birth wt. of neonate (kg)	3.13±0.48			

Mean ± SD

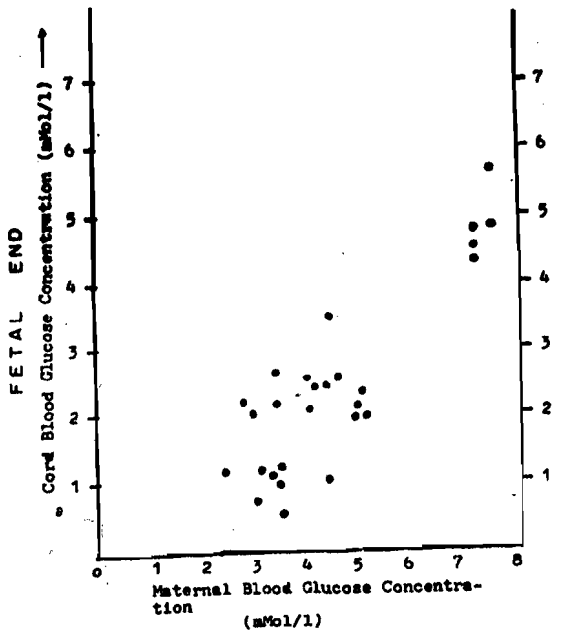

Figure 2:
Correlation plot between fetal end cord blood glucose and maternal blood glucose

r = 0.86, n = 30, p<0.005

correlated with maternal blood glucose positively and significantly ($p<0.005$) with correlation coefficients of 0.89 and 0.86 respectively (figures 1 and 2). Fetal birth weight also correlated positively and significantly ($p<0.05$) with cord blood glucose from both the placental end ($r = 0.68$) and fetal end ($r = 0.64$).

DISCUSSION

The fetus is totally dependent for its nutrition on maternal supply of nutrients. Different nutrients appear to be transferred through the placenta at different rates and by different mechanisms, so that maternal and fetal concentrations of some important nutrients differ substantially. For instance free amino acid concentration in fetal plasma is known to be higher than maternal plasma levels, yet transfer from, the mother to the fetus continues against the concentration gradient (Hill and Young, 1971). Glucose is rapidly transferred through the placenta to the fetus. The transfer is so rapid that maternal hypoglycemia may occur (Freinkel, 1965).

Unlike the amino acids, fetal blood glucose has been shown in previous studies to be only about 80% of maternal blood glucose (Cornblath and Reisner, 1965; Cornblath and Carsgan, 1961).

In this study, cord blood glucose which is an index of glucose supply to the fetus, has been shown to vary according to the location on the cord from which blood sample is collected. Blood taken 6cm from the placental end of the cord had higher glucose concentration than samples taken 8cm from the fetal end (table 1). Values of glucose at both locations were lower than mean maternal blood glucose levels, and represented 71±15% and 52±17% respectively of mean maternal blood glucose. There appears to be a glucose gradient descending from maternal sources to the fetus. The reason for this gradient is not yet well understood. Rapid utilization of glucose by the fetus (Freinkel, 1965) is a possible contributing factor. In addition it is known that the umbelical cord uses a large amount of energy to maintain its viability and functions, and most of this energy is derived from glucose (Worthington et al., 1977).

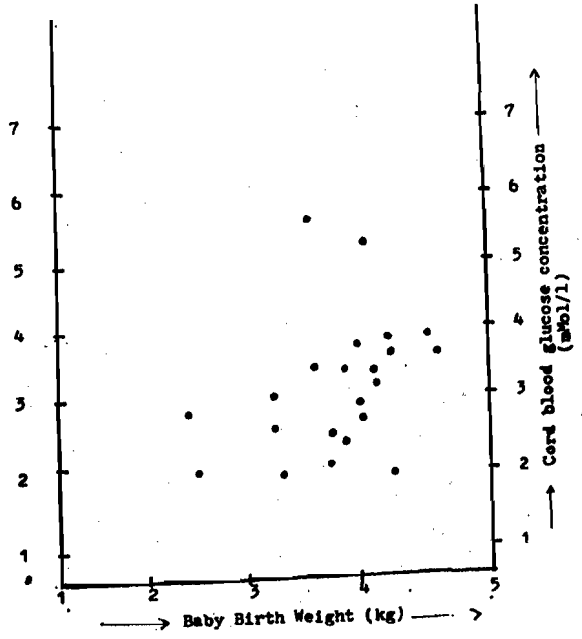

Figure 3:
Correlation plot between placental end cord blood glucose and fetal birth weight.

r = 0.68, n = 30, p<0.05.

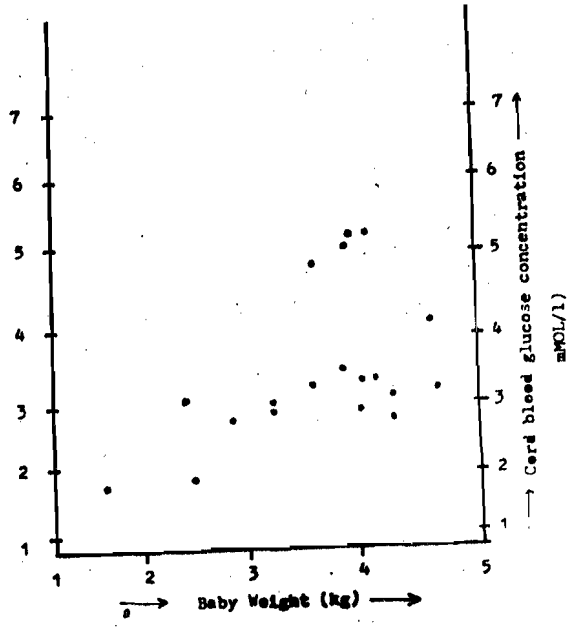

Figure 4:
Correlation plot between fetal end cord blood glucose and fetal birth weight.

r = 0.64, n = 30, p<0.05.

Such glucose utilization by the cord, combined with a high rate of fetal consumption can surely create a glucose gradient between the mother and the fetus. The strong positive correlation between maternal blood glucose and cord blood glucose (fig. 1 and 2) indicates a proportional relationship between cord and maternal blood glucose. It is also worthy of note that cord blood glucose correlates positively and significantly ($p < 0.05$) with fetal birth weight. This suggests the involvement of glucose in fetal development. The observed glucose gradient implies that even mild maternal hypoglycemia may result in profound hypoglycemia in the fetus. This phenomenon may be responsible for low birth weights and the large number of still births and other perinatal deaths in our region (Fiander, 1992; Oyo-Ita et al., 1998).

We recommend that regular blood glucose monitoring should form an important aspect of maternal care during pregnancy, and that fasting by pregnant women for religious or other reasons should be avoided.

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