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ABSTRACT:

Pre-eclampsia is known to be associated with various placental morphologic changes as well as fetal growth restriction. Growth restricted neonates are at increased risk of hypoglycaemia in the first three days of life. The aim of the study was to examine the relationship between occurrence of neonatal hypoglycaemia and the relative placental weight in mothers with pre-eclampsia.

The blood glucose concentrations of 69 neonates born to mothers with pre-eclampsia were determined three times daily during the first three days of life. The birthweight of each of the neonates as well as the corresponding weight of the placenta were determined and recorded. The relative placental weight was calculated using the formula: Weight of placenta x 100/Birthweight of the infant. Overall prevalence of neonatal hypoglycaemia was 47.8%. Of the 69 neonates, severe neonatal hypoglycaemia (blood glucose < 1.6 mmol/L) was prevalent in 10 (14.5%) and 15(21.7%) had blood glucose level between 1.6 and 2.5 mmol/L.

The relative placental weight did not differ with the severity of maternal pre-eclampsia. No statistically significant correlation was obtained between the relative placental weight and neonatal hypoglycaemia.

Key Words: Hypoglycaemia, neonates, placental weight, pre-eclampsia;
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INTRODUCTION:

Neonatal hypoglycaemia (blood glucose concentration below 2.6mmol/L) is one of the common clinical care problems encountered in some neonatal units [1]. The frequency is influenced by the cut-off point used for blood glucose concentration [1, 2]. In a study in Nepal, when the cut-off point for blood concentration was below 2.6mmol/L the incidence was 41.0%; the incidence dropped when a cut-off point below 2.0mmol/L was applied [2].

Pre-eclampsia is an established pregnancy-associated clinical condition that leads to fetal growth restriction [3-5]. It has been suggested that fetal growth restriction in pre-eclampsia might depend on abnormal placental development [3, 6]. For instance, shallow trophoblastic invasion of decidual arteries can precipitate pre-eclampsia with the attendant reduction in placental perfusion and insufficient transport of nutrients to the developing fetus which in turn leads to fetal growth restriction [4, 7-9]. Vascular spasm in the placental bed is believed to cause placental infarction, resulting in deterioration in the metabolism between the mother and her fetus with fetal growth restriction as a consequence [8, 10].

Some investigators have reported occurrence of placental growth retardation in pre-eclampsia [11, 12]. Some of the principal pathological changes of the placenta in pre-eclampsia include decidual arteriopathy, infarcts, abruptio placentae and Tenney-Parker changes [11, 13]. All these pathological features are not always present [13]. Khong et al [14] in their study of 39 patients with pre-eclampsia reported that the placental lesions were unrelated to maternal parity, degree of proteinuria, severity and duration of hypertension, or its therapy. Considering the various placental morphologic changes in pre-eclampsia and the resultant fetal growth restriction, it may be surmised that the relative placental weight could predict the likelihood of neonatal hypoglycaemia among infants born to mothers with pre-eclampsia.

The present study, therefore, sought to examine the relationship between occurrence of neonatal hypoglycaemia and relative placental weight in maternal pre-eclampsia.

PATIENTS AND METHODS:

All neonates delivered at St Philomena Catholic Hospital (SPCH), Benin City between January and December 2010 to Nigerian women with pre-eclampsia were recruited into the study. Ethical clearance and permission for the study were approved by the hospital authority. The mothers were given a detailed verbal

explanation of the study and their permission sought before enrolment.

The criteria for diagnosis of pre-eclampsia and enrolment of the mother-infant pair into the study were:

An increase in either systolic or diastolic blood pressure greater than 30 mmHg or 15 mmHg respectively above the booking blood pressure (BP) plus proteinuria (using albustix) of one plus (1+) and above in the absence of urinary tract infection (UTI).

An intrapartum BP = 140/90 mmHg obtained on at least two occasions not less than 6 hours apart during delivery plus presence of proteinuria as indicated above.

A single reading of 110 mmHg diastolic BP or more with proteinuria as indicated above was accepted as pre-eclampsia.

The Korotkoff sound phase 5 (disappearance phase) which is more reproducible, correlated better with intra-arterial measurements of diastolic BP and is more closely related to outcome was used [10].

Nigerian women who did not smoke or drink alcohol and had not been diagnosed with diabetes mellitus or sickle cell anaemia and were not on medication, such as propanolol or drugs such as narcotics were recruited into the study.

Gestational diabetes mellitus was excluded by routine determination of blood glucose concentration in all pregnant women attending antenatal care clinic in our hospital.

Pregnant women with random or fasting blood glucose concentrations below 8.0mmol/L or 6.0mmol/L respectively, were deemed to be free from gestational diabetes mellitus [15].

Those excluded from the study were mothers with eclampsia; Infants with rhesus isoimmunisation, polycythaemia and major congenital abnormalities; Infants of diabetic mothers and twins.

Pre-eclampsia was categorized into mild, moderate and severe according to the criteria suggested by Redman with some modifications [16]. In this Classification System, mild pre-eclampsia was defined as a diastolic BP increase of at least 30mmHg and proteinuria of 1+ (using albustix); moderate pre-eclampsia as an increase in diastolic BP of at least 30mmHg and proteinuria of 2+; and severe pre-eclampsia as a diastolic BP increase of at least 30mmHg or a single diastolic BP equal or greater than 110mmHg and proteinuria of 3+. In our hospital, the approved routine treatment of pre-eclampsia consisted of bed rest, anti-hypertensive drugs (Hydralazine, Methyl dopa) and sedatives (Diazepam) as determined by the patient's clinical condition.

Following delivery of the neonate, the umbilical cord was clamped and this was followed by

delivery of the placenta at the appropriate time. The placenta with all its membranes was weighed and recorded.

The corresponding birthweight of each baby was measured to the nearest 50g using a Waymaster Weighing Scale and the value obtained was recorded. From the weights obtained, the relative placental weight was calculated using the formula:

$$\frac{\text{Placental weight} \times 100}{\text{Birthweight of baby}}$$

The relative placental weight was categorized into two groups; those equal or less than 15% and those greater than 15%.

Blood glucose measurement was performed for each neonate three times daily for the first three days of life, using a Glucometer (Acutrend meter product 128485 with glucose test strips) which display results in mmol/L. Neonates whose blood glucose concentration was less than 3.0mmol/L had their blood glucose concentration confirmed in the central laboratory of the hospital, using the standard glucose-oxidase-perioxidase method [17]. If there was a single blood glucose concentration with value less than 2.0mmol/L, the tests were continued for at least one day after the blood glucose concentration has returned to normal or after the therapy had been discontinued. At the time of this study, breast feeding in the neonatal unit/newborn nursery of the hospital was routinely started about 1-2 hours after birth. Some of the babies were given pre-lacteal 5% glucose orally. When the blood glucose concentration of a neonate was less than 1.6mmol/L or a neonate was symptomatic (irrespective of blood glucose concentration), intravenous administration of 10% dextrose in water was started immediately. To ensure reliability of the results, discoloured strips were not used and care was taken to avoid contamination with alcohol skin-cleansers. It was also ensured that the drop of blood covered the whole surface of the test-pad. The packed cell volume of each of the study neonates was also determined.

The Chi-square test and Z-score test were used in ascertaining the significance of differences in proportions with the p-value set at <0.05.

RESULTS:

Seventy one (5.2%) of the 1,360 pregnancies delivered in the hospital during the one-year

study period were complicated by pre-eclampsia. Clinical data of the mothers with pre-eclampsia are shown in Table 1. The distribution of cases into subgroups of mild, moderate and severe did not differ in relation to maternal parity. Two (2.8%) of the 71 neonates delivered by pre-eclamptic mothers were stillborn, leaving 69 live-born babies whose data were further analysed.

The frequency of delivery of neonates with birthweight less than the 10th percentile increased with the severity of maternal pre-eclampsia (Table 2); X^2 =5.26 p>0.05. As shown in Table 3, the relative placental weight was greater than 15% in majority of cases. The severity of maternal pre-eclampsia did not influence the relative placental weight (Table 3).

Table 1: Clinical data of mothers according to severity of pre-eclampsia

Severity of pre-eclampsia	Percent (n)	Mean age in Years	Maternal Parity in percent (n)		
			Para zero	Para 1 – 4	Para ≥5
Mild	42.3 (30)	24.7	44.7 (17)	48.1 (13)	0
Moderate	23.9 (17)	26.3	23.7 (9)	22.2 (6)	33.3 (2)
Severe	33.8 (24)	26.8	31.6 (12)	29.7 (8)	66.7 (4)
Total	100 (71)	25.4	100 (38)	100 (27)	100 (6)

Table 2: Distribution of birthweight percentile of neonates according to severity of maternal pre-eclampsia.

Severity of Pre-eclampsia	Number of neonates	Birthweight of infants by percentile {% (n) of neonates}			Total
		<10th	10 – 90th	>90th	
Mild	29	13.8 (4)	75.9 (22)	10.3 (3)	100 (29)
Moderate	17	17.6 (3)	82.4 (14)	0	100 (17)
Severe	23	39.1 (9)	60.9 (14)	0	100 (23)
Total	69	23.2 (16)	72.5 (50)	4.3 (3)	100 (69)

Table 3: Distribution of relative placental weight according to severity of maternal pre-eclampsia.

Severity of pre-eclampsia	Number (n) of mothers	Percent (n) of Relative placental weight	
		≤15%	>15%
Mild	30	13.3 (4)	86.7 (26)
Moderate	17	23.5 (4)	76.5 (13)
Severe	24	20.8 (5)	79.2 (19)
Total	71	18.3 (13)	81.7 (58)

Table 4: Frequency of neonatal hypoglycaemia according to relative placental weight.

Relative placental weight	Blood glucose concentration (mmol/L)		
	<1.6	1.6 – 2.5	>2.5
	% (n) of neonates		
≤15% (n = 13)	30.8 (4)[a]	38.4 (5)[c]	30.8 (4)
>15% (n = 56)	10.7 (6)[b]	32.1 (18)[d]	57.2 (32)
Total (n = 69)	14.5 (10)	33.3 (23)	52.2 (36)
p-values:	a vs b >0.05	c vs d >0.05	

Table 5: Distribution of relative placental weigh among normoglycaemic and hypoglycaemic neonates of mothers with pre-eclampsia.

Relative placental weight	Category of neonates		
	Normoglycemic	Hypoglycaemic	
	% (n) of neonates		P-value
≤15% (n = 13)	30.8 (4)	69.2 (9)	
>15% (n = 56)	57.1 (32)	42.9 (24)	>0.05
Total (n = 69)	52.2 (36)	47.8 (33)	

The mean age of the neonates at the time of determination of the first blood glucose concentration was 2.3±0.6 hours (95% Confidence Interval, CI = 2.1-2.5). A total of 33 (47.8%) neonates born to mothers with pre-eclampsia had at least one blood glucose concentration less than 2.6mmol/L (neonatal hypoglycaemia). Of the 69 neonates, 10 (14.5%) had at least one blood glucose concentration less than 1.6 mmol/L (severe neonatal hypoglycaemia). In addition, 8 (11.6%) neonates had 2 or more blood glucose concentration between 1.6 and 2.5 mmol/L and 15 (21.7%) had only one blood glucose concentration between 1.6 and 2.5 mmol/L. Of the 33 hypoglycaemic neonates, 18(54.5%) were diagnosed in the first 12 hours of life and 25 (75.8%) were diagnosed during the first 24 hours of life. Although the prevalence of neonatal hypoglycaemia was higher among infants associated with relative placental weight equal or less than 15%, the difference was not statistically significant Z-statistic=1.83 $p>0.05$(Table 5). Similarly, the severity of hypoglycaemia did not correlate with relative placental weight Z-statistic: a versus b=1.49 $p>0.05$, c versus d= 0.22 $p>0.05$ (Table 4). The glucose values obtained using the Acutrend glucometer correlated well with values obtained from the central laboratory. Only 5(15.2%) of neonates with hypoglycaemia were symptomatic. The symptoms observed were poor feeding (3 cases), lethargy (3 cases), jitteriness (2 cases) and circumoral pallor (1 case).

DISCUSSION:

The overall prevalence (47.8%) of neonatal hypoglycaemia found in this study was lower than the 64.9% reported from Oulu, Finland [18], but higher than 38.0% reported from Nepal [2]. Although the same methodology and definition were used in the present study and in the Nepalese study, the study population in the later was not at risk of hypoglycaemia which may explain the lower prevalence reported in that study [2]. With regard to the higher prevalence rate reported in the Finnish study compared to the present study, one possible explanation might be the differences in feeding practices in the immediate postnatal period. Breast feeding of the newborn infant routinely commenced within 1 to 2 hours after birth in our hospital compared to 24 hours after birth in the Finnish hospital [18]. The pattern of breast-feeding practice has been variously shown to influence the prevalence of neonatal hypoglycaemia, (19, 20] a finding attributed to the ketogenesis-promoting property of breast milk [21]. In addition, skin-to-skin contact with the mother during breast feeding facilitates stable temperature and blood glucose for the neonate [22, 23].

Data from the present study showed that majority of mothers with pre-eclampsia, had relative placental weight greater than 15%, suggesting minimal placental growth retardation. The relative placental weight did not differ with the severity of the maternal pre-eclampsia. Similar finding was reported in the Finnish study [18].

In the present study, although the prevalence of neonatal hypoglycaemia was higher among neonates associated with relative placental weight equal or less than 15%, it was not statistically significant. Similar finding has been reported from Oulu, Finland [18]. Among the hypoglycaemic neonates born to mothers with pre-eclampsia, the severity of the hypoglycaemia did not differ with the relative placental weight. This may be explained, as documented by Benirchke et al [13] that the placental pathological features are not all invariably present. Although the number of neonates with symptomatic hypoglycaemia was small, the two leading symptoms of were poor feeding and lethargy. A study from India has reported a similar finding [24].

In conclusion, newborn infants of mothers with pre-eclampsia were at increased risk of hypoglycaemia, particularly in the first 24 hours of life but the prevalence of hypoglycaemia did not differ significantly with the relative placental weight.

REFERENCES:

1. Fox G, Hoque N, Watts T. Oxford Handbook of Neonatology, Oxford, Oxford University Press, 2010: 354-356.
2. Pal DK, Manandhar DS, Rajbhandari S, Land JM, Patel N, de Castello AM. Neonatal hypoglycaemia in Nepal I: prevalence and risk factors. Arch Dis Child Fetal Neonatal Ed 2000; 82: F46-F51.
3. Ness RB, Roberts JM. Heterogenous causes constituting the single syndrome of pre-eclampsia: A hypothesis and its implications. Am J Obstet Gynecol 1996; 175: 1365-1370.
4. Odegard RA, Vatten LJ, Nilsen ST, Salvensen KA, Austgulen R. Pre-eclampsia and fetal growth. Obstet Gynecol 2000; 96(6): 950-955.
5. Onyiriuka AN, Okolo AA. Perinatal outcome in patients with pre-eclampsia in Benin City, Nigeria. Trop J Obstet Gynaecol 2004; 21(2): 148-152.
6. Ghidini A, Salafia CM, Pezzullo JC. Placental vascular lesions and likelihood of diagnosis of pre-eclampsia. Obstet Gynecol 1997; 90: 542-545.
7. Roberts JM, Redman CW. Pre-eclampsia: more than pregnancy-induced hypertension. Lancet 1993; 341: 1447-1451.
8. Barker PN. Obstetrics by Ten Teachers, 18th edition, London, Hodder Arnold publishers 20006: 156-164.
9. Cunningham FG, Leveno KJ, BloomSL, Hauth JC, Gilstrap LC, Wenstram KD. Williams Obstetrics,

22nd edition, New York, McGraw Hill Medical Publishing Division, 2005: 761-808.

10. Agboola A. The placenta, umbilical cord and membranes. In: Agboola A(ed), Textbook of Obstetrics and Gynaecology for medical Students, 2nd edition, Ibadan, Heinenmann Educational Books(Nigeria) Plc, 20006: 265-273.
11. Soma H, Yoshida K, Mukaida T, Tabuchi Y. Morphologic changes in the hypertensive placenta. Contrib Gynecol Obstet 1982; 9: 58-75.
12. Naeye RL, Friedman EA. Causes of perinatal deaths associated with gestational hypertension and proteinuria. Am J Obstet Gynecol 1979; 133(1): 8-10.
13. Benirschke K, Kaufmann P. Pathology of the Human Placenta, 2nd edition, New York, Springer-Verlag 1990: 499-529.
14. Khong TY, Pearce JM, Robertson WB. Acute atherosis in pre-eclampsia: maternal determinants and fetal outcome in the presence of the lesion. Am J Obstet Gynecol 1987; 157: 360-363.
15. Abudu OO, Afolabi BB. Diabetes mellitus. In: Agboola A (ed). Textbook of Obstetrics and Gynaecology for Medical Students. 2nd edition. Ibadan, Heineman Educational Books (Nigeria) plc, 2006: 365-370.
16. Redman CWE. Hypertension in Pregnancy. New York, Perinatology Press, 1987.
17. Cheesbrough M. District Laboratory Practice in Tropical Countries (Part I), Cambridge, Cambridge University Press, 2006: 340-348.
18. Koivisto M, Jouppila P. Neonatal hypoglycaemia and maternal toxaemia. Acta Paediatr Scand 1974; 63: 743-749.
19. Huffman SL, Zehner ER, Victora C. Can improvements in breast-feeding practices reduce neonatal mortality in developing countries? Midwifery 2001; 17(2): 80-92.
20. Hoseth E, Joergensen A, Moeller M. Blood glucose levels in a population of healthy, breast fed term infants of appropriate size for gestational age. Arch Dis Child Fetal Neonatal Ed 2000; 83: F117-
21. Hawdon JM, Ward Platt MP, Aynsely Green A. Patterns of metabolic adaptation for preterm and term infants in the first neonatal week. Arch Dis Child 1992; 67: 357-365.
22. Fransson AL, Karisson H, Nilsson K. Temperature variation in newborn babies: importance of physical contact with the mother. Arch Dis Child Fetal Neonatal Ed 2005; 90: F500-F504.
23. Chiu SH, Anderson GC, Burkhammer MD. Newborn temperature during skin-to-skin breast feeding in couples having breast feeding difficulties. Birth 2005; 32(2): 115-121.
24. Singhal PK, Singh M, Paul VK, Deorari AK, Ghorpade MG, Malhotra A. Neonatal hypoglycaemia – clinical profile and glucose requirements. Indian Pediatrics 1992; 29: 167-171.