Hypoglycaemia and hypocalcaemia as determinants of admission birth weight criteria for term stable low risk macrosomic neonates

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Abstract

Background: Large for gestational age (LGA) accounts for about 6.3% of admissions in kenyatta national hospital, newborn unit. As a policy all IGA's, defined by birth weight of 4000g and above are admitted for 24hours to monitor blood glucose levels. The rational for this policy is questionable and contributes to unnecessary burden on resources needed for new born care.

Objective: To study birth weight related incidence of hypoglycemia and hypocalcaemia in stable low risk lgas in knh and use it to establish a new admission weight based criteria.

Patients and methods: prospective cohort study done in new born-unit, post natal and labour wards of knh. Term lga neonates (birth weight = 4000g) were recruited as subjects and controlled against term appropriate weight (aga) neonates.

Results: the incidence of hypoglycemia and hypocalcaemia in lgas was 21% and 9% respectively. Hypoglycemia was rarely encountered after 12 hours of life in lgas. Hypoglycemia and hypocalcaemia showed a direct upward relationship with weight beyond 4250g. No significant difference in incidence of hypoglycemia and hypocalcaemia between controls and 4000-4249g category to justify their routine admission to newborn unit.

Conclusion: the study identified 4275g as new admission birth weight criteria for stable term low risk IGA's admission.

Keywords: Macrosomia, Hypoglycemia, Hypocalcaemia, birth weight.

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Background

Macrosomia, an indication for admission into the neonatal unit of Kenyatta National Hospital (KNH) accounts for about 6.3% of admissions per year Most of LGA's admitted are however discharged following an uneventful in- patient stay. Other complications of LGA'S are rare, making hypoglycemia as the main indication for admission. The LGA admission rate had shown an upward trend from 1.8% in 1992 to 6.3% in 2000.(1) Current weight based policy of admission not only contribute to the admission of neonates who are not deserving but also exposed them to nosocomial infections and is a financial burden to the institution and parents.

A large for gestational age neonate is defined as neonate whose birth weight has exceeded the expected for the gestation of pregnancy represented as birth weight above 90th percentile of Lubchenco growth curve. At term birth weight cut -off of 4kg is diagnostic of macrosomia(2). The incidence worldwide is estimated at 10%. Improved medical care and reduced socio-environmental factors which affect birth weight negatively, have resulted in increasing birth weight trends.

Maternal diabetes is the classical condition associated with fetal macrosomia, however minor derangements of glucose metabolism without gestational diabetes is a documented risk factor.(3,4) Maternal obesity is associated with 4-12 fold increased likelihood of fetal macrosomia (5,6), as well as excess weight gain in a non obese pregnancy (>13.3 kg)(7). Interestingly, in one study pre-eclampsia and gestational hypertension which had previously been associated with small for gestational age deliveries (SGA) was associated with fetal macrosomia(8). Birth weight has also been shown to be a factor of parity, with average birth weight with successive pregnancy increasing by 80-120g up to the 5th pregnancy (9). Male neonates have an average larger birth weight of about 150g compared to females.(10,11) The proportion of males amongst LGA neonates is about 60-65 % compared to females.

Genetic and congenital disorders associated with high birth weights include; Beckwith-Wiedmann

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Syndrome, Carpenter's Syndrome, Weaver's Syndrome, Soto's Syndrome, Nevo Syndrome, Ruvalcaba-Myhre Syndrome and Fragile X Syndrome [12]. Socio-economic factors and fetal microenvironment also impact on birth weight. Smoking, [13] hard drugs, some therapeutic agents can also lower birth weight while improved socio-economic status is thought to increase birth weight. Maternal nutritional status also influences birth weight. Mothers of low birth weight neonates have been shown by Jansen et al, to have reduced weight for height, triceps skin fold thickness and mid-upper arm circumference, all of which are markers of maternal malnutrition. The same study also showed the importance of maternal weight gain in pregnancy as a determinant of birth weight. Mothers with low weight gain tallying with borderline malnutrition however delivered appropriate weight neonates, thus suggesting that fetal growth may be safeguarded at the expense of maternal reserves at that degree of malnutrition[14]. Other contributory factors include: maternal birth weight and stature,[15] immunological disorders like rhesus isoimmunization, advanced maternal age and idiopathic polyhydramnios. [16]

Geographical variations in mean birth weight have been demonstrated by Meredith's review, the smallest neonate groups with mean birth weight of 2400g are from Torricelli Mountains of New Guinea and the largest in Anguila and Nevis in the Caribbean (3880g). [17]

The realization of multifactorial etiology, regional differences, secular changes and observed upward trend led to the development of regional time-specific gestational age-weight growth curves like Colorado, Illinois and Portland. When Colorado standard developed in 1963 was compared to the Illinois standard developed 20 years later, Colorado 10th and 90th percentiles corresponded to 3rd and 80th Illinois standard respectively. The same study showed 9.8% of appropriate weight term neonates diagnosed as macrosomics by Colorado[18] Using similar justification birth weight criteria for term stable LGA admission has been revised to 4100g [19] 4250g [18] and 4500g [20] in some centers. This study aims to determine birth weight related incidence of hypoglycemia and hypocalcaemia in stable low risk LGAs and use it to determine a new weight based admission criteria.

Patients and methods

A prospective cohort study was done in the Newborn unit, labour and postnatal wards of KNH. All admitted term LGA's whose parents consented, were consecutively recruited and matched to controls according to mode of delivery up to the desired sample size and excluded if: referral, diabetic mother, on dextrose infusion or septic, asphyxiated or with congenital anomalies. Sample size was calculated using the formula: m' =sq{c (a/2)*sqrt [(r+1)*pq] -c (1-b)*sqrt[r*p 1q1 + p2q2]}/ (r*sq[p2-p1]). Confidence interval = 95%, Power =80 %.Incidence of hypoglycemia in term AGA =2.7 %.Incidence of hypoglycemia in macrosomic = 27 %.Unexposed to exposed Ratio = 1:1. Incidence rates based on Singhal PK et al study [21] Birth weight was taken using a standard neonatal weight scale.

A total of 160 subjects were stratified into groups of

Table 1: socio-demographic description of interviewees

	Sub category	LGA %(n=100)	AGA % (n =40)
Age	11-20 yrs	15 (15%)	9 (22.5%)
	21-30 yrs	63 (63%)	23 (57.5%)
	31-40 yrs	22 (22%)	8 (20%)
Educational level	Primary	7 (7%)	7 (17.5%)
	Secondary	73 (73%)	23 (57.5%)
	Tertiary	20 (20%)	10 (25%)
Parity	>3	92 (92%)	34 (85%)
	<3	8 (8%)	6 (15%)

40 neonates in weight categories based on ZY 20 baby scale.4000-4249, 4250-4500, 4500 and above. 40 stable neonates weight 2500-3999kg were recruited as controls. A questionnaire was administered to the mothers to obtain socio-demographic, obstetric and medical data. Baseline random capillary blood glucose, using precision glucometer, was done from a heel, finger or earlobe prick before the first feed and between the 2 and 3 hours of life. Thereafter 4-hourly blood glucose levels were done. Three milliliters of venous blood was drawn aseptically to determine serum calcium level corrected to albumin using cresolphthalein-complexone method (CPC) at the 20th hour of life. Albumin correction was done by adding 0.8mg/dl (0.02mmol/l) of calcium to every 1g of albumin below 3.5g/dl. Neonates were followed up for only 24 hours to determine whether they suffered hypoglycemia or hypocalcaemia.

Hypoglycemia was treated using 10% dextrose solution at 5ml/kg bolus and a maintenance drip of 10% dextrose. Hypocalcaemia was not treated because the laboratory method for its assessment was long and there was delay in getting the results. Data was analyzed using SPSS 11.5 program. Statistical significance was set at $p<0.05$ with 95% confidence interval. Significant risk ratio was defined as relative risk >1, with lower bound confidence interval equal to or >1 or with both lower and upper confidence interval bounds below 1. Receiver operator characteristic curve was used to determine admission cut off birth weight. The following definitions were used.

1. LGA: Term neonate with birth weight of 4000g and above
2. Control: Stable term neonate with birth weight 2500-3999g.
3. Hypoglycaemia: Random capillary blood glucose less than 2.0mmol/l (35mg/dl) in the first 3 hours of life or less than 2.2mmol/l (40mg/dl) in the next 21 hours of life.
4. Hypocalcaemia: Serum calcium concentration less than 8mg/dl or 2mmol/l in the first day of life.

Results

The study was conducted for one year period. A total of 140 neonates were recruited, 40 neonates in categories 2500-3999g, 4000-4249g and 4250-4499g each and 20 neonates in category =4500g. The weight range in the study was2500g to 6100g, with a median of 4125g. There were 83 (59.3%) males and 57 (40.7%) females. The rest of socio-demographic description is shown in table 1.

The incidence of hypoglycemia was 12.5% in controls. At 4000-4249g the incidence of hypoglycemia increased in tandem with weight from 7.5% to 50% in weight-category >4500g. The cumulative risk of hypoglycemia in the term LGA neonates was 21% compared to 12.5% in control. The incidence of hypoglycemia in LGAs was highest in the 1st 12 hours of life, 19%). This contributed to 90.5% of the cumulative incidence at the end of the first 24 hours of life. Beyond 12 hours of life, the incidence was 2 %. (p=0.006)

Table 2: factors associated with hypoglycaemia

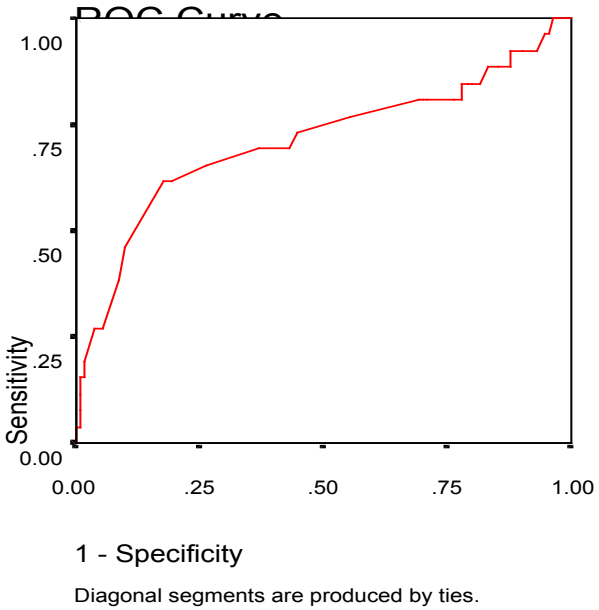
Factor	Hypoglycaemia yes	Hypoglycaemia No	Relative risk 95% ci	P-value
LGA	21	79	1.68 (0.68, 4.15)	0.24
AGA	5	35		
Weight category				
4000-4249g	3	37	0.6 (0.08, 3.19)	0.71*
2500-3999g	5	35		
4250-4499g	8	32	1.6 (0.57, 4.47)	0.36
2500-3999g	5	35		
4500g +	10	10	4 (1.58, 10.14)	0.002
2500-3999g	5	35		

Hypoglycemia occurred more in LGA, s than AGAs, with the relative risk progressively increasing with birth weight. A similar trend was observed on determinant risks of hypocalcaemia.

Table 3: factors associated with hypocalcaemia

Factor	Hypocalcaemia	Hypocalcaemia No	Relative risk 95% ci	P-value
LGA	9	91		
AGA	2	38	1.8 (0.36, 18.6)	0.73
Weight category				
4000-4249g	0	40		
2500-3999g	2	38	0 (0, 5.3)	0.49
4250-4499g	3	37		
2500-3999g	2	38	1.5(0.17,19.33)	1
4500g +	6	14		
2500-3999g	2	38	6 (1.22, 88.03)	0.01

Figure 1: receiver operator characteristic curve for hypoglycaemia versus birth weight



An ideal admission cut off is one with highest possible sensitivity and specificity. Using ROC curve an ideal admission birth weight for LGAs based on hypoglycemia is 4275g. This has sensitivity of 65.4% and specificity of 73.7%. When hypocalcaemia is used as a determinant of admission birth weight for LGA's a cut off weight of 4325g is identified. This has sensitivity 72.7% and specificity of 78.3%.

Discussion

This was a hospital based prospective cohort study designed to establish the incidence of hypoglycemia and hypocalcaemia in stable term LGAs controlled with stable term AGA neonates during the first 24 hours of life. Selection of the control group in the study was made on the basis of birth weight while considering the inclusion/exclusion criteria. This did not strictly adhere to the definition of appropriate for gestational age as estimated gestational age by Dubowitz was not matched to birth weight. The study did not achieve the desirable sample size in neonates above 4500g. This could partly be explained by the fact that most neonates above that weight were of diabetic mothers or had other risk factors that made them to be excluded.

The cumulative incidence of hypoglycemia in LGAs was 21%. Previous investigations have reported incidence in LGAs of 4-27 % [21, 22] which is within our findings. In those studies no weight stratification was done and LGAs were wholesomely grouped in one category. Weight related incidence of hypoglycemia showed a direct upward relationship as weight increases. In the 4000-4249g category the incidence was 7.5%, 20% in 4250-4499g and 50% in the rare>4500g. In the control group the incidence was 12.5% comparable to findings of other studies. [22-24] Comparison made between the cumulative risk of hypoglycemia in controls and 4000-4249g category was not statistically significant. This implies that there is no justification in treating these groups differently. Between 4250-4499g the incidence of hypoglycemia almost tripled that of the preceding group. The sharp increase in the incidence suggests a possible transient abnormality in glucose metabolism predisposing the neonates to hypoglycemia that is beyond control by feeding alone. Neonates in weight category above 4500g had three-fold risk of hypoglycemia compared to the control. The highest incidence of hypoglycemia (50%) in weight category above 4500g could be a true hypoglycemia risk.

In LGAs, 90.5% of recorded hypoglycemia occurred in the first 12th hours while the rest in subsequent hours of life. The finding could be partly explained by the feeding practice in our ward, where the calculated feeds are introduced slowly and gradually increased to maximum feeds over sometime. Despite the inability of this study to correlate the time maximum feeds were attained versus hypoglycemia, by 12th hour of life hypoglycemia was rarely encountered. This finding concurs with others where hypoglycemia was rarely encountered after 12hours of life. [11] It might be reasonable to stop random blood sugar screening at 12th hour of life especially where resources are scarce. Blood sugar followed a predictable pattern, with postnatal dip followed by stabilization at levels between 2.8-5.2mmol/l. [25] Postnatal dip in this study is prolonged up to 4-12 hours of life and can be attributed to delayed or inadequate feeding.

Hypocalcaemia was documented in 7.9% of the study population. The majority of hypocalcaemia was in the macrosomic neonates with cumulative incidence of 9%. This was almost twice compared to the normal weight neonates and concurs with another previous study. [26] The pathophysiology of this hypocalcaemia is still postulative. As weight increased above 4250g, hypocalcaemia was found to be increasing progressively with the highest frequency in weight >4500g (30%). Apparently in the category 4000-4249g no single case of hypocalcaemia was noted while in appropriate term neonates the incidence was 5%. The reason why hypocalcaemia was not encountered in the 4000-4249g group is not known. Possible erroneous inclusion of controls with undiagnosed birth asphyxia, due to poor APGAR scoring or poor documentation of delivery notes could possibly explain the higher occurrence of hypocalcaemia in that group. When comparison was made in the different LGA subcategories with control, only neonates in weight category >4500g had significant risk for hypocalcaemia. The numbers involved in risk calculations were small and might have affected the power of the study. Probably a larger study is suggested to address hypocalcaemia in LGA's.

In an attempt to identify a new admission weight criteria, various cut off weights; 4000g, 4250g and 4500g were compared with pooled neonates below the cut off weight. With the current admission cut off weight employed in new born unit, KNH, (= 4000g) there was no significant risk of either hypoglycemia or hypocalcaemia in neonates compared to control. This finding might be due to the low cumulative incidence of both hypoglycemia and hypocalcaemia in category 4000-4249g. Above 4250g a tendency of increasing risk of hypocalcaemia and hypoglycemia is noted. When the admission weight cut off is 4250g, there is an obvious significant risk of hypoglycemia and hypocalcaemia. Neonates with birth weight > 4250g had 3 times risk of hypoglycaemia and 6 times risk of hypocalcaemia than those between 2500-4249g. When admission cut off is 4500g the relative risk increased up to 3.75 and 7.2 for hypoglycaemia and hypocalcaemia respectively.

An admission weight cut off of 4250g is the most

appropriate as it marks a point where significant risk of hypoglycaemia and hypocalcaemia occurred. Using different methodologies other studies have adjusted LGA cut off admission weight to 4100g, [19] 4250g [18] and 4500g.[20] Change of admission weight criteria for stable term low risk LGA neonates in KNH, from 4000g to 4250g would lead to reduction in numbers of LGA admission by about 40%.Overall this translates to a reduction from 6.3% to 3.78% of the total admissions per year. This will have an impact of reducing pressure on hospital resources and improvement in doctor/nurse-patient ratio hence improvement in the quality of care offered. To the parents it will relieve off financial burden especially now when both the mother and neonate are charged a daily bed fee. This recommendation can also be applied in similar settings within Africa.

Conclusion

The incidence of hypoglycaemia was directly related to and progressively increased with birth
weight. The risk of hypoglycaemia was highest in the first 12 hours of life. Neonates with birth weight 4000-4250g did not suffer significant hypoglycaemia or hypocalcaemia to justify their routine admission to NBU. The study recommends admission weight criteria for stable low risk term LGA neonates be revised from 4000g to 4275g.

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Contribution of Authors:

We declare that this work was done by the author(s) named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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