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FREQUENCY OF HYPOCALCAEMIA AMONG FULL TERM NEONATES WITH SEVERE BIRTH ASPHYXIA

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ABSTRACT

Although neonates with severe birth asphyxia are known to be at increased risk of early onset hypocalcaemia, the magnitude of problem is not well documented. The objective of this study was to determine the prevalence of neonatal hypocalcaemia among full term infants with severe birth asphyxia in tertiary care hospital. In this cross sectional study, conducted at Nishtar Hospital and medical university, Multan city, Pakistan. The total Serum Ca concentration of 137 full term infants with 1 min APGAR score of less than 3 or equal to 3, were measured using the O-cresulphthalein Complexon Method. All the study neonates (SEVERE BIRTH ASPHYXIA) were examined and their clinical findings were documented and clinical history taken from their mothers. Overall prevalence of early onset neonatal hypocalcaemia (Total S.Ca <8 mg/dL) among asphyxiated neonates was 21.1% Total S.Ca level of asphyxiated neonates of diabetic mothers was significantly low 21(77.7%) and no of asphyxiated neonates of vit-D deficient mothers having hypocalcaemia was also significant 42(30.7%) and most of the mothers of asphyxiated neonates were belonged to poor socioeconomic status even not having proper balanced diet.

KEYWORDS: birth asphyxia, hypocalcaemia, O-cresulphthalein Complexon.

INTRODUCTION

"An abnormally low serum calcium in neonatal life that is observed clinically and on biochemical tests is called neonatal hypocalcaemia".[1]

Neonatal hypocalcaemia is observed with relative frequency and exact incidence or prevalence cannot be evaluated because of Multi-factorial diagnosis. But its occurrence varies by gestational age of neonates and perinatal diseases i.e 50% of low-birth-weight neonates have Hypocalcaemia and nearly all very-low-birth-weight neonates have hypocalcaemia. 25-50% of IDM and neonates of pre-ecclamptic mothers have hypocalcaemia in first 24-48 hours.

Most popular contributory factors for early neonatal hypocalcaemia include Preterm babies, Perinatal asphyxia, infant of Diabetic mother, Intra uterine growth restriction; Small for gestational age is the independent risk factor for ENH,[2] while late neonatal hypocalcaemia may be the result of exogenous Phosphate load (Cow milk, high phosphate containing formula milk) ,maternal Hyperparathyroidism, Hypomagnesaemia, maternal Vit-D deficiency, congenital hypo parathyroid disease of newborns (Digeorge Syndrome).

Most common cause of neonatal hypocalcaemia is Birth Asphyxia/Perinatal Asphyxia which is defined as the condition resulting from deprivation of Oxygen to new born infant that lasts long enough during the birth process to cause physical harm, usually to the brain.

Major contributory factor in early neonatal period is transient deficiency of parathyroid hormone which results in Vit-D deficiency and ultimately hypocalcaemia occurs.[3] Early onset hypocalcaemia is usually asymptomatic and diagnosed on routine screening as compared to late onset hypocalcaemia. Slowly developing hypocalcaemia is usually asymptomatic but there is no therapeutic cut off to be symptomatic. Neonatal hypocalcaemia may present with hypotonia, tachycardia, tachypnea, apnea or wheezing (Broncho-spasm), poor feeding, vomiting (pylorospasm), seizures, jitteriness or tetany.[4]

Diagnosis of neonatal hypocalcaemia is based on total or ionized calcium levels (Total Ca<8mg/dl in term and Ca<7mg/dl in preterm babies. While ionized calcium <4.8mg/dl in term and <4mg/dl in preterm babies.[5] However, Neonatal Hypocalcaemia should be investigated thoroughly to rule out the maternal or neonatal problems. This includes total & ionized S-

Calcium, PTH, levels of Vit-D metabolites (1-OH and 1,25-Di-OH cholecalciferol) S-Mg levels, S-Electrolytes, S-Glucose, S-phosphorus, S-Mg levels, ECG (QT interval>0.4 sec due to prolonged systole).

A diagnosis of hypocalcaemia is based only on ECG criteria which is likely to yield a high false positive rate. Neonates suspected to have hypocalcaemia by ECG criteria which should have the diagnosis confirmed by measurement of serum calcium.[6]

Early onset hypocalcaemia in neonates who are asymptomatic regress spontaneously by third day of life and requires no treatment until very severe (<6mg/dl or ionized Ca<3mg/dl). Late onset hypocalcaemia should be treated by cause accordingly i.e. Low phosphorus containing formula milk and oral Ca supplementation in phosphorus overload conditions, and Vit-D or its metabolites in Hypo parathyroid disorders. Hypocalcaemic seizures, tetany and apnea should be treated with Ca preparations (10% Ca Gluconate, which provides elemental calcium content of 9mg/dl) at doses of 30-50mg of elemental Ca/Kg/day(in 4-6 divided doses), according to response of the patients. Symptomatic hypocalcaemia should be treated with a continuous infusion for at least 48 hours.[7]

Monitor the Ca-levels in neonates at risk for neonatal hypocalcaemia (preterm babies or VLWB<1500g at 12,24 & 48 hours of life). Neonatal Hypocalcaemia owing to maternal Hypo vitaminosis D should be dealt with concurrent recommendation of Vit-D in pregnancy and for breast feeding mothers and especially the exposure of newborns to sunlight. Breast feeding instead of formula milk to be continued.

Term & preterm infants are at risk of developing metabolic bone diseases during the 1st weeks of life due to deficiency of Ca & P influenced by maternal vit-D deficiency in the long term. Severely vit-D deficient mothers prone their children to the ultimate risk of more acute skeletal disturbances in the infancy; consequences of which include hypocalcaemia leading to tetany, convulsions and occasionally cardiomyopathy or mylofibrosis in the 1st six months of life.[8] One of the most common late complication of hypocalcaemia is Rickets, characterized by loss of bone mass and micro architectural degeneration of bone tissue, which leads to increased bone brittleness and consequent fragility fractures.

No data have been found in our local population about this research topic so the result of international studies cannot be generalized on our local population due to lack of awareness about the proper nutrition of mothers and breast feeding habits, subsequent unsatisfactory supplementation by formula milks and prematurity. So, the purpose of our research is to determine the frequency of hypocalcaemia in neonates in our local population and suggest different risk factors associated with it and to overcome the complications beforehand associated with this prolonged hypocalcaemia in future.

MATERIAL AND METHODS

Study Design
Hospital based cross sectional study.

Setting
This study will be carried out in department of Pediatric Unit of Nishtar Hospital Multan (Pediatric Emergency and both wards).

Duration of Study
Six month after approval of synopsis.

Sample Size[10]
Sample size is calculated by following formula

$$n = \frac{Z^2 Pq}{d^2}$$

where least proportion (hypocalcaemia in term neonates)
p = 22.6
with q = 1-P d = 7 and
Confidence level = 93% where n = 137

Sampling Technique
Non-probability random sampling.

Inclusion Criteria
- Babies age; from birth to 28 days of life in the tertiary health centre.
- Babies within serum calcium level <8mg levels
- Properly signed informed written consent

Exclusion Criteria
- Neonates who are having inborn metabolic errors
- Neonates who are having chromosomal aberrations or congenital heart defects.
- Preterm neonates.

Operational Definition
Total Ca < 8 mg/dl (2mmol/dl) or ionized Ca^+ less than 4.8 mg/dl (1.2mmol /dl) in term neonates is defined as hypocalcaemia[5] .It is classified into early onset (first four days) and late onset hypocalcaemia (five to 28 days)[10]

Severe Birth Asphyxia ⟶ 1-minute Apgar score < or = 3 and / or umbilical Artery pH < 7.10.
Early Onset hypocalcaemia ⟶ Hypocalcaemia during first 4 days of life.
Late onset Hypocalcaemia ⟶ Hypocalcaemia after 4 days of life.
Neonatal period: ⟶ It is defined as first 28 days of life of a new born infant of any gestation.
Full-term baby ⟶ A baby born between 37 and 42 weeks of gestation.
Low birth weight ⟶ A baby born with less than 2500gm weight.
Very Low birth weight ⟶ A baby born with less than 1500gm weight.

SARNAT- STAGING

	Grade 1 Mild	**Grade 2 Moderate**	**Grade 3 Severe**
Alertness	Hyper alert	Lethargy	Coma
Muscle Tone	Normal/increased	Hypotonic	Flaccid
Seizures	None	Frequent	Uncommon
Pupils	Dilated, Reactive	Small, Reactive	Variable, fixed
Respiration	Regular	Periodic	Apnea
Duration	<24 hours	2-14 days	Weeks

APGAR-scoring

Acronym	**Score of 0**	**Score of 1**	**Score of 2**
Appearance (skin color)	Blue/pale	Blue in extremities/ Body Pink	No cyanosis
Pulse	Absent	<100/ minute	>100 /minute
Grimace (reflex irritability)	No response	Grimace /Feeble cry when stimulated	Cry or Pull away when stimulated
Activity	None	Some Flexion	Flexed arms and legs that resists extension
Respiration	Absent	Weak , irregular, gasping	Strong cry

Data Collection Procedure

Patients fulfilling the inclusion criteria from emergency and pediatric department of Nishtar Hospital and University Multan will be included in this study after permission from ethical committee and research department. On inclusion criteria, informed written consent will be taken from each patients attendants ensuring confidentiality and fact that there is no risk involving the patients while taking part in this study. Data will be collected for basic demographics (age and gender), APGAR-scoring, history of Diabetes and anti-epileptic drugs in mothers, nutritional status of mothers and feeding of neonates.

A biochemical test for serum calcium level will be done to confirm the hypocalcaemia in severely asphyxial neonates. Patients admitted with the history of severe birth asphyxia and low APGAR-scoring according to operational definition will be noted on especially designed Performa (annexure-I).

Data Analysis

All data entered using software SPSS version 18. Frequency and percentage will be used for gender, APGAR-scoring, history of Diabetes and use of anti-epileptics in mothers, socioeconomic status, feeding of neonates while Mean and standard deviation for age. Chi-square test will be applied to compare the efficacy between 2 groups. P-value will be considered significant if $P \leq 0.05$. Stratification of age and socioeconomic status will be done to control the effect modifier.

RESULTS

The demographic characteristics of the study sample are shown in tables and figures. In this study, among the total of 137 neonates who constituted the study population,107 (78.1%) neonates with severe birth asphyxia had S.Ca more then 8 mg/dL while 30 (21.1%) neonates had S.Ca less than 8 mg/dL (Hypocalcaemic) . Among total of 137 neontes,96 (70%) were male and 41(30%) were females among these 96 male neonates 18(18.75%) had S.Ca level <8 mg/dL (Hypocalcaemia) and 12 (29.26%) of 41 females had S.Ca level < 8 mg/dL, **as shown in Table No.1.**

Gender * S.Ca Crosstabulation

		S.Ca		
		8 or more	**less than 8**	**Total**
Gender	**Male**	**78**	**18**	**96**
	Female	**29**	**12**	**41**
Total		**107**	**30**	**137**

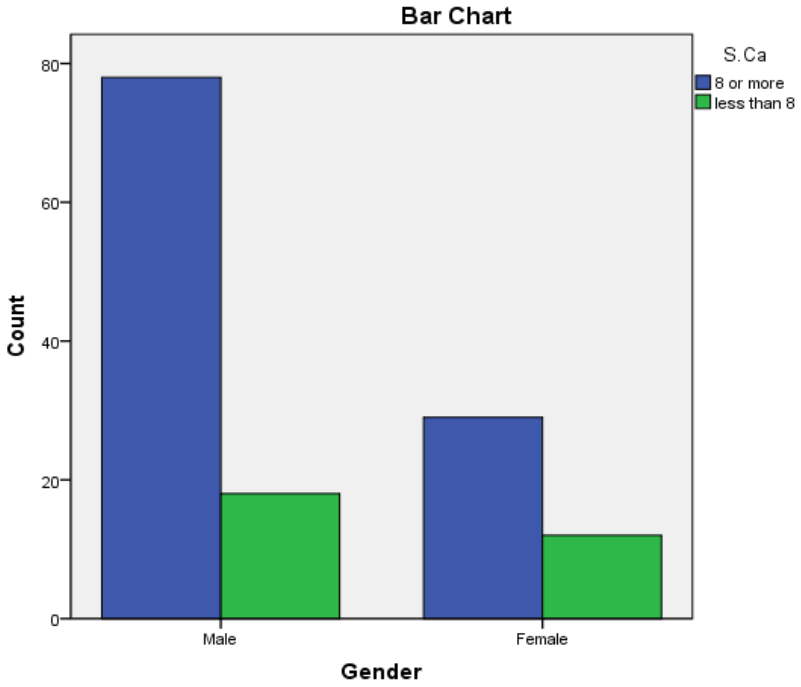

Figure No. 1: Showing the comparison btw gender and S.Ca among the Severely Birth Asphyxic neonates.

History of fits in neonates of SEVERE BIRTH ASPHYXIA were present in 48(35%); with significant P=0.000 and fits were absent in remaining 89(65%) neonates, **as shown in Table No.2.**

History.Fits * S.Ca Crosstabulation

		S.Ca		Total
		8 or more	less than 8	
History.Fits	Yes	24	24	48
	No	83	6	89
Total		107	30	137

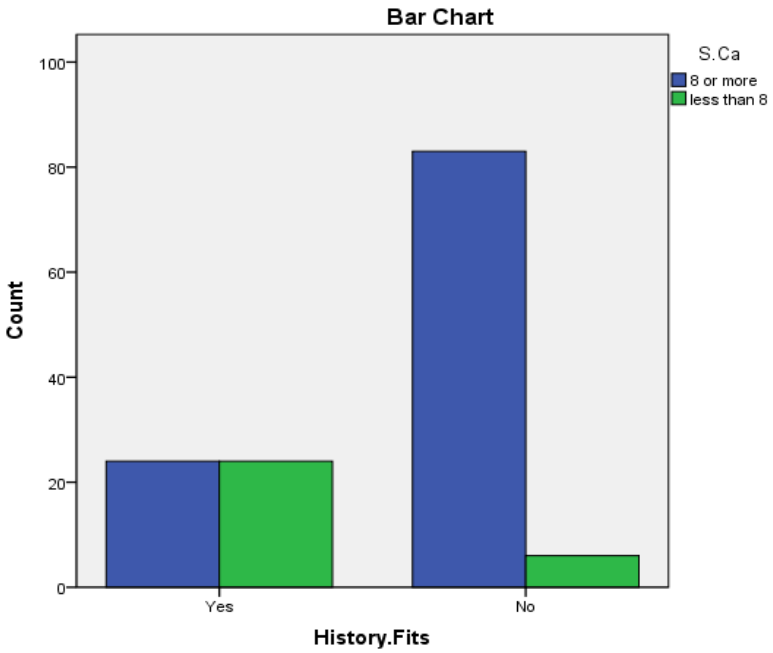

Figure No. 2: Showing comparison btw the fits and S.Ca among the Severely Birth Asphyxic neonates.

In our study, most of the neonates were of less than 7 days of age 110 (80.3%) while more than 7 days neonates were only 27 (19.7%). Out of 110(80.3%) neonates, 22 (20%) were hypocalcemic, as and 112 (81.75%) of 137 neonates had APGAR score less than 3 or equal to 3 (SEVERE BIRTH ASPHYXIA). Among these 112 neonates 24(21.42%) were hypocalcemic, **as shown in Table No. 3.**

APGAR Score * S.Ca Crosstabulation

		S.Ca		Total
		8 or more	less than 8	
APGAR.Scor	Less than 3 or equl to 3	88	24	112
	less than 6 or equl to 6	19	6	25
Total		107	30	137

H/O Diabetes mellitus in mothers of SEVERE BIRTH ASPHYXIAL neonates were present only 27 (19.72%) but out of these 27,21 (77.7%) neonates were having hypocalcemic, **as shown in Table No.4**; which was very significant (P =0.000). It showed strong relationship of diabetes in mothers to hypocalcaemia in their neonate.

History of Diabetes Mil in Mothers * S.Ca Crosstabulation

		S.Ca		Total
		8 or more	less than 8	
History of Diabetes Mil in Mothers	Yes	6	21	27
	No	101	9	110
Total		107	30	137

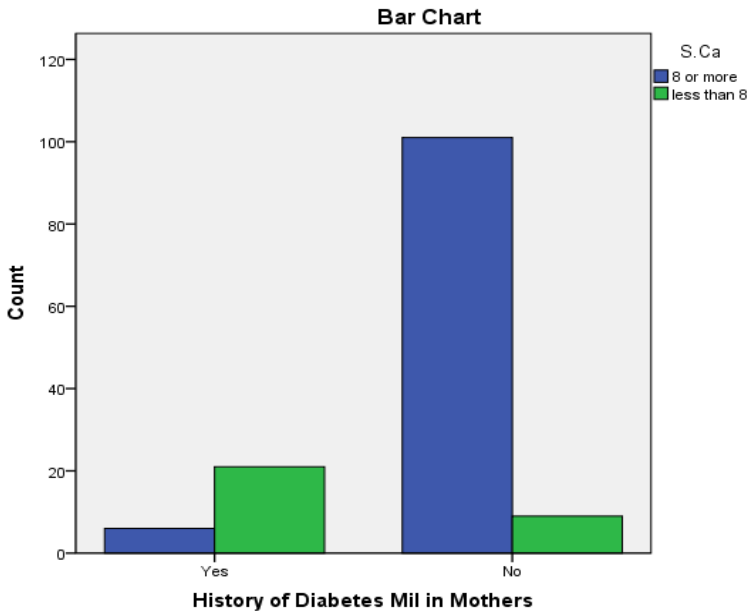

Figure No. 3: Showing the comparison btw History of Diabetes Mil in mothers with S.Ca among the Severely Birth Asphyxic term neonates.

H/O joint pains and vit-D deficiency in mothers of SEVERE BIRTH ASPHYXIAL neonates was present in 42 (30.7%) during their pregnancy while 95(69.3%) mothers had no any H/O joint pains or vit-D deficiency during their pregnancy and out of these 42(30.7%) mothers,8(19%) were having hypocalcaemia,**as shown in Table No.5.**

J.Pain & VitDDef * S.Ca Crosstabulation

		S.Ca		Total
		8 or more	less than 8	
JP.VitDDef	Yes	34	8	42
	No	73	22	95
Total		107	30	137

Antiepileptic drugs-intake during pregnancy was prevalent in only 13(9.5%) and absent in 124 (90.5%) but among these 13(9.5 %) mothers, 4(30.76%) were having neonates of S.Ca less than 8 mg/dL which was quite significant, **as shown in Table No.6.**

Anti.Epileptic * S.Ca Crosstabulation

		S.Ca		Total
		8 or more	less than 8	
Anti.Epileptic	Yes	9	4	13
	No	98	26	124
Total		107	30	137

Most of the neonates belonged to poor socioeconomic backgrounds 89(65%) and remaining 47(34.3%) were from middle socioeconomic backgrounds.

DISCUSSION

In this study, the overall prevalence of early onset neonatal hypocalcaemia among neonates with severe birth asphyxia was 21.1% which was lower than reported by Pacific Journal of Medical Science among their asphyxiated neonates.[11] Their higher prevalence may be accounted by the retrospective nature of their study and the fact that S.Ca was not measured in all their study population.

Data from the present study showed that neonates with 1_min APGAR score less than or equal to 3 had significantly lower mean total S.Ca concentration than their counterparts with 1_min APGAR score 6 or more. Pacific Journal of Medical Science have reported similar findings.[11] This implies that Birth Asphyxia plays a separate role in early neonatal Calcium hemostasis.

Asphyxial Neonates of diabetic mothers have more hypocalcaemia (Calcium less than 8 mg/dL) as compared to Asphyxiated neonates of non-diabetic mothers. Similar findings has been reported by Demarini S.[12] It shows that diabetes in mothers is strongly related to hypocalcaemia in neonates.

In this study, asphyxiated neonates of mothers having vit-D deficiency have significant hypocalcaemia as compared to those asphyxiated neonates whose mothers are not vit-D deficient. Similar findings have been reported by AycaTorel Erger.[13]

Some limitations of present study must be considered. Firstly, the use of APGAR score in defining the birth asphyxia. The APGAR scoring system[14] although very useful in the measurement of birth asphyxia has its shortcomings in that it doesn't fully define birth asphyxia.[15] it is known that factors(maternal diabetes, anti-epileptic medications, vit-D deficiency) other than asphyxia may affect the APGAR-score of an infant. However, in the review by Addy.[16] He noted that APGAR-Score was the basis of many peoples on the outcome of Birth Asphyxia justifying its use in the present study. Secondly, our inability to measure directly ionized S.Ca concentration and blood gases. This was due to lack of facility for their determination in our hospital. Further study will take this into consideration. Despite these limitation, the study gave an insight into the prevalence of the early onset neonatal hypocalcaemia. In conclusion, hypocalcaemia was common among asphyxiated neonates of diabetic and vit-D deficient mothers.

REFERENCES

1. Jain A.Agarwal, R.sankar, M.J, Deorari A.paul, V.K. Hypocalcaemia in Newborn Indian Journal sof Pediatrics, 2010; 77; 1123-1128
2. Marx SJ. Hyperparathyroid and Hypoparathyroid disorders. N Engl J Med., 2000; 343: 1863-75.
3. Loughead JL, Mimouni F, Tsang RC, Serum ionized calcium in normal neonates. Am J Dis Child., 1988; 142: 516-518.
4. Last full review version August by Alan Lantzy, MD.
5. Oden, J. Bourgeois, M, Neonatal endocrinology, Indian Journal of Pediatrics, 2000; 77: 217-213.
6. Salle BL, Delvin EE, Lapillonne A, Bishop NJ, Glorieux FH, perinatal metabolism of Vitamin D. Am J Clin Nutr, 2000; 71(5 suppl): 1317S-24S.
7. Mimouni F, Tsang RC. Neonatal hypocalcaemia; to treat or not to treat? J Am Call Nutr, 1994; 13: 408-15.
8. Pediatric bone 2nd Ed., metabolic bone disease in the neonatal period and its later sequelae, 2012; P655-677.
9. Ogilvy-Stuart A,Midgley P.Prctical neonatal endocrinology.Cambridge: Cambridge University Press, 2006; 133-142.
10. Pacific Journal of Medicl Sciences, April 2011; 8(1).
11. Alphonus N.Onyiriuka. Department of Child Health, University of Benin Teaching Hospital, PMB IIII, BENIN City, Nigeria. Prevalence of Neonatal Hypocalcemia Among Full Term Infants with Severe Birth Asphyxia.
12. DEMARINI S, Mimouni F.Trang RC Khoury J,Hertzbergv.
13. Ayca Tarel Ergur, Merih Berberoglu, and Gonul Ocal.
14. Apgar V.A proposal for a new method of evaluation of the newborn infant Curr Res Anaesth Analgesia, 1953; 32: 260-267.
15. Sykes G, Melloy P, Johnson P. Do Apgar scores indicate Asphyxia? Lancet, 1982; 1: 494-496.
16. Addy DP. Birth Asphyxia. BMJ, 1982; 284: 1288-1289.