# **Original Research Article**

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# Syndrome of inappropriate antidiuretic hormone secretion in neonates with birth asphyxia at tertiary care centre

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#### **ABSTRACT**

Background: Syndrome of inappropriate antidiuretic hormone is an important metabolic complication of perinatal asphyxia. This study aims to study the occurrence of syndrome of inappropriate antidiuretic hormone in different grades of perinatal asphyxia and to find out the correlation of syndrome of inappropriate antidiuretic hormone to gestational age and birth weight in birth asphyxiated babies.

Methods: It was a hospital-based cohort study. 50 neonates with different grades of asphyxia were enrolled in the study and 50 controls were taken. Syndrome of inappropriate antidiuretic hormone was diagnosed based on calculated plasma osmolality, serum and urine sodium, urine specific gravity and analyzed with different grades of birth asphyxia and birthweight and gestation age.

Results: The occurrence of SIADH in birth asphyxiated babies was 26% and none of the babies in control group developed SIADH. The occurrence was more in the severely asphyxiated babies (53.8%), followed by moderate (30.8%) and then mildly asphyxiated babies (15.4%). Hyponatremia was seen in 26% of birth asphyxiated babies and can be used as a marker of SIADH. In relation to gestation age and birth weight there was no statistically significant correlation between SIADH and different grades of asphyxia. Mortality was high among the neonates who developed

Conclusions: The occurrence of SIADH was 26% in asphyxiated neonates and high in severe asphyxia and gestation age and birth weight beard no significant co relation.

Keywords: Birth asphyxia, Birth weight, Gestation age, Hyponatremia, Neonates, SIADH (Syndrome of Inappropriate Antidiuretic Hormone)

#### INTRODUCTION

Perinatal asphyxia is one of the most common primary cause of mortality (28.8%) and morbidity among neonates in India and is the commonest cause of still births (45.1%).1 Incidence of perinatal asphyxia in India is about 6 in 1000 live birth. An APGAR score of less than 7 at one minute and at 5 minutes respectively is seen in 8.4% and 2.45%.<sup>2</sup> Asphyxia results in hypoxemia, hypercapnia, mixed respiratory and metabolic acidosis and various metabolic complications-one of the metabolic complications is Syndrome of inappropriate ADH secretion leading to water overload.3 ADH secretion occurs in the first 3 days after an asphyxia Insult. This syndrome has been manifested by hyponatremia and corresponding hypo-osmolality, inappropriately elevated urine osmolality, and continued renal excretion of sodium in the absence of dehydration and in the presence of elevated levels of ADH. Seizures and a bulging anterior fontanelle are the prominent clinical signs, apparently related to the water intoxication.<sup>4</sup> The diagnosis of syndrome of inappropriate antidiuretic hormone presumes no volume related stimulus to anti diuretic hormone release such as reduced cardiac output or abnormal renal or thyroid function.<sup>5</sup> Immediate aggressive treatment of these abnormalities could modify the entire outcome of the babies.<sup>6</sup> Insufficient data regarding syndrome of inappropriate antidiuretic hormone in neonates making it difficult to optimize fluid and electrolyte support and precise guidelines for fluid and electrolyte therapy in these neonates. Keeping this in mind and working under such circumstances this study is designated to evaluate the occurrence of syndrome of inappropriate antidiuretic hormone in different grades of perinatal asphyxia and its correlation to gestation and birth weight.

#### **METHODS**

It's a cohort study conducted between November 2015 and May 2017 at neonatal intensive care unit of Vani Vilas and Bowring and lady Curzon hospital attached to BMCRI. 100 newborn babies of which 50 are of different grades of asphyxia were the cases and 50 term and preterm newborns were taken as control.

#### Inclusion criteria

Newborn babies with APGAR score less than 7 at 1 minute were taken as study group and Newborn babies with APGAR score more than or equal to 7 at 1 minute-Babies from postnatal wards, babies admitted for preterm care were taken as control group.

#### Exclusion criteria

Babies with Mother having history of febrile illness 2 weeks prior to delivery, Babies with congenital malformation, Respiratory distress syndrome, Septicemia, meningitis, Acute renal failure, Intracranial hemorrhage.

After obtaining written informed consent from the parents of eligible babies about the study, cases were taken as babies with APGAR score <7 at 1 minute of birth and divided into 3 groups based on the modified sarnat h and sarnat m staging/ levene scoring system of hie for preterm neonates at birth as mild, moderate and severe birth asphyxia. Of 63 babies of birth asphyxia enrolled in the study, 13 were excluded as 2 babies had congenital malformation, 7 babies had sepsis, 2 babies had RDS and 2 babies died within 2 days of birth as shown in Figure 1. Clinical and laboratory parameters were analyzed.

Urine was collected (2-3 ml) by using urinary bags or supra pubic aspiration in neonates on day 3 of life. Specific gravity of urine >1.010 (which is >300 mosm) was taken as raised which was measured by strip method. urinary sodium >30 mEq/l was taken as elevated and was measured by Ion selective electrode method. 2 ml of Venous blood sample was taken at the same time of urine collection for serum sodium levels, glucose, blood urea. Serum sodium levels <135 mEq/l is taken as hyponatremia measured by Ion

selective electrode in an electrolyte analyser. Plasma osmolality is calculated by the formula,

#### = 2[Na] + glucose/18 + BUN/2.8

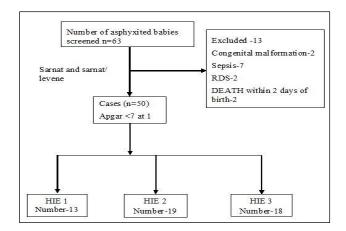


Figure 1: flow chart showing cases included and divided to different grades of asphyxia.

Plasma osmolality of <280 mEq/L is considered low. The diagnosis of syndrome of inappropriate antidiuretic hormone requires demonstration of the following:

- Hyponatremia (<135 mEq/L)
- Low plasma osmolality (<280 mEq/L)
- Elevated urinary sodium concentration >30 mEq/l.
- Urine specific gravity >1.010 (The normal urine osmolality in the newborn is between 75 and 300 mosm which is generally correlated with the specific gravity 1.002 to 1.010).
- Normal renal, adrenal, cardiac, thyroid function.

syndrome of inappropriate antidiuretic hormone (SIADH) is evaluated and compared in different grades of perinatal asphyxia. syndrome of inappropriate antidiuretic hormone (SIADH) is also compared in relation to birth weight and gestational age.

#### Statistical analysis

Data were entered in MS excel and analyzed using SPSS version 23.0. unpaired t-test, Chi square test, Fisher's exact test were employed to test the defined hypothetical parameters. However, the incumbent changes or association of the variables was tested based on the probability value ( $p \le 0.05$ ).

#### **RESULTS**

Of 63 babies of birth asphyxia enrolled in the study, 13 were excluded as 2 babies had congenital malformation, 7 babies had sepsis, 2 babies had RDS and 2 babies died within 2 days of birth. Table 1 compares baseline characters in cases and controls. The mean birth weight and gestational age of babies in study and control group

were comparable. The sex distribution and age at sampling were also comparable.

Table 1: Comparison of baseline characters in cases and controls.

Characters		Cases	Controls
Age (day)		03	03
Sex	Male	24	24
	Female	26	26
Birth Weight (kgs)		2.66±0.599	2.61±0.43
Gestational Age (weeks)		37.4±2.08	37.64±2.06

Among the babies with birth asphyxia, 36% of cases had mild asphyxia, 38% of cases had moderate asphyxia and 26% of cases had severe asphyxia as shown in table 2. Figure 2 shows distribution of cases based on different grades of asphyxia.

Table 2: Perinatal asphyxia staging.

Groups	HIE 1	HIE 2	HIE 3	Nil	Total
Cases	18(36%)	19(38%)	13(26%)	0(0%)	50
Controls	0	0	0	50	50

The mean serum sodium, plasma osmolality, urine sodium, urine specific gravity levels in cases were 129.46±2.90, 276.52±5.96, 33.23±4.58, 1.03±0.005 respectively. It is statistically significant when compared

with controls. Among birth asphyxiated babies, In HIE 1, 2(15.4%) babies had SIADH (syndrome of inappropriate antidiuretic hormone). In HIE 2, 4(30.8%) babies had SIADH and in HIE 3, 7(53.8%) babies had SIADH (syndrome of inappropriate antidiuretic hormone) as shown in table 3. The occurrence of SIADH (syndrome of inappropriate antidiuretic hormone) is more in severely asphyxiated babies. Figure 3 shows SIADH in different grades of asphyxia and it also shows none of the babies in control group had SIADH.

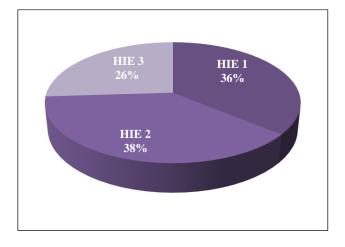


Figure 2: Cases with different grades of asphyxia.

Table 3: SIADH (syndrome of inappropriate antidiuretic hormone) in different grades of asphyxia.

SIADH	HIE 1	HIE 2	HIE3	Total	p value
Absent	16(43.2)	15(40.5%)	6(16.2%)	37	
Present	2(15.4)	4(30.8%)	7(53.8)	13	0.041* < 0.05
Total	18(36%)	19(38.0%)	13(26.0)	50	

<sup>\*</sup>Fisher's exact test

When SIADH was studied in babies with asphyxia in relation to birth weight, as shown in table 4, No asphyxiated babies <1.5 kg had SIADH (syndrome of inappropriate antidiuretic hormone). 4(26.7%) of asphyxiated babies between 1.5 kg and 2.5 kg had SIADH. 9(27.3%) of asphyxiated babies >2.5 kg had SIADH.

Table 4: SIADH in relation to birthweight.

Birthweight (kg)	SIADH absent	SIADH present	Total	p value
<1.5	2(100%)	0(0%)	2	1 000%
1.5-2.5	11(73.3%)	4(26.7%)	15	1.000*
>2.5	24(72.7%)	9(27.3%)	33	p>0.05

<sup>\*</sup>Fisher's exact test

The correlation in incidence of SIADH in different birthweight groups was not statistically significant. 4(26.7%) of asphyxiated babies between 1.5 kg and 2.5 kg had SIADH. 9(27.3%) of asphyxiated babies >2.5 kg had SIADH. The co relation in incidence of SIADH in different birthweight groups was not statistically significant.

Table 5: SIADH in relation to gestational age.

Gestational age (WKS)	SIADH absent	SIADH present	Total	p value
32-33	3(100%)	0(0%)	3	0.741*
34-36	7(70%)	3(30%)	10	p>0.05
37-42	27(73.0%)	10(27%)	37	NS

<sup>\*</sup>Fisher's exact test

The correlation in incidence of SIADH in different birthweight groups was not statistically significant. Table 5 shows the relation of SIADH with respect to gestational age. No asphyxiated babies between 32-33 weeks had SIADH. 3(30%) asphyxiated babies between 34 and 36 weeks had SIADH. 10(27%) asphyxiated babies between 37 and 42 weeks had SIADH.

The co-relation in incidence of SIADH in different gestational age groups was not statistically significant.

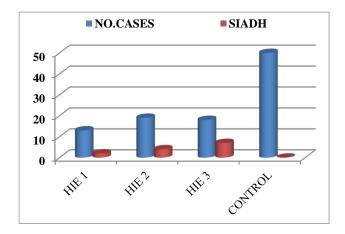


Figure 3: SIADH in different grades of asphyxia in cases and controls.

#### **DISCUSSION**

Perinatal asphyxia is one of the most common cause of mortality and morbidity among neonates. There are previous studies where only hyponatremia is studied and corelated to SIADH, so the true incidence of SIADH is not clearly known. Identification of cases with SIADH to restrict fluids at the earliest to  $2/3^{\rm rd}$  of maintenance fluids till serum sodium value returns to normal is recommended. Incidence of SIADH in HIE stage 1, 2, 3 was 7.4%, 44.4% and 35.7% respectively in a study by Harsh et al5 and the incidence of SIADH was 34% as per study by Phelen et al, whereas it was 15.4%. 30.8% and 53.8% in HIE 1, 2, 3 respectively in the present study.<sup>7</sup>

Incidence of SIADH was maximum in moderately asphyxiated babies as per study by Harsh et al, but in this study, the incidence was maximum in severely asphyxiated babies.<sup>5</sup> Author studied the incidence of SIADH in asphyxia in relation to birth weight. Low birth weight babies had SIADH 26.7% and normal weight babies 27.3% had SIADH. None of the very low birth weight babies had SIADH. There was no significant co relation between SIADH and birth weight. In our study, in preterm babies SIADH was 33.3%, 16.6% and 25% in HIE 1, 2, 3 respectively and in term it was 6.6%, 23.07%, 66.6% in mild, moderate and severe asphyxia respectively. In a study by Harsh et al, in preterm SIADH was 25%, 33.5%, 25% in mild, moderate and severe birth asphyxia respectively and in term it was 50% and 40% in moderate and severe birth asphyxia babies.<sup>5</sup> SIADH was

seen in 14 out of 14 preterm babies in different illness in 1<sup>st</sup> week of life forming an incidence of 100% as studied by Rees et al.<sup>8</sup> In a study by Speer et al, SIADH was seen in 13 out of 13 term babies making incidence of 100%.<sup>9</sup> The difference in incidence of SIADH between ours and other authors may be related to their small sample size and different yardsticks of assessing SIADH. Among the 13 SIADH cases, 7 cases died and 2 other cases which died didn't have SIADH. In a study by Mohammad et al, mortality was significantly high among the neonates who developed SIADH.<sup>10</sup>

#### **CONCLUSION**

The present study showed that SIADH occurs in asphyxiated babies and none of the babies in control group developed SIADH. The occurrence is more in the severely asphyxiated babies, followed by moderate and then mildly asphyxiated babies. In relation to birth weight and gestation age, there was no statistically significant correlation between the incidence of SIADH in different grades of asphyxia and low birth weight and normal weight babies.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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