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Metabolic Emergencies in Newborns in a Subsaharian Neonatology Department: Evaluation of Glucose, Sodium and Potassium Disorders

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Abstract

Introduction: Metabolic neonatal adaptation is a complex phenomenon and metabolic disorders can be frequent in immature newborns or in life-threatening situations. In Low and Middle income countries (LMIC) the difficult access to some diagnostic tests makes the management of the metabolic emergencies challenging. The main objectives of this study were to assess the frequency and circumstances of occurrence and to describe the clinical picture associated with glucose, sodium and potassium disorders in neonates. **Patients and Methods:** Our study was a retrospective and descriptive study conducted in the neonatology unit of National Children Hospital Albert Royer in Dakar (Senegal) from January 1 to December 31, 2014. **Results:** The prevalence of the studied metabolic disorders was 46.7%. The most common metabolic disorder noted was Hyperglycemia followed by Hyponatremia. Thermoregulation disturbances were found particularly in newborns with serum sodium disorders (hyponatremia 33.5% and hypernatremia 59.7%). Neurological signs were noted in case of blood sugar abnormalities (hypoglycemia 26.1% and hyperglycemia 29.8%). Half of the newborns with hyperglycemia (82 cases/50%) had blood sugar levels greater than or equal to 2 g/l. Hypernatremia was severe (Serum sodium> 180 mmol/l) in 12 neonates (16.7%). The main diagnoses retained were sepsis (159 cases/45.4%), prematurity (96 cases/27.4%), intrauterine growth retardation (66 cases/18.9%), malformations (63 cases/18%), perinatal asphyxia (44 cases/12.6%) and malnutrition (36 cases/10.3%). For most metabolic disorders, the correction was late and was done beyond 48 hours. On average, the correction time varied between 3 hours and 6 days. The most frequent complications were cerebral edema (12 cases), brain death (8 cases) and increased intracranial pressure (3 cases). The

most lethal disorders were Hyperkalemia followed by Hyperglycemia. **Conclusion:** Metabolic disorders especially glucose, sodium and potassium disorders are common in newborns. They are medical emergencies that can lead to vital instability and death. Their management is challenging in low-income countries due to the lack of adapted facilities and means to diagnose them. It is therefore important to improve the availability of technical methods and means of biological analysis in hospital laboratories and to monitor closely all newborns for early diagnosis of these disorders.

Keywords

Metabolic Disorders, Newborn, Hypoglycemia, Hyperkalaemia, Hyperglycemia, Hypernatremia

1. Introduction

The neonatal period is a crucial moment during which adaptation mechanisms must swiftly and efficiently occur to allow the newborn, until then completely dependent on its mother, to fully perform its vital functions.

Metabolic neonatal adaptation is a complex phenomenon and metabolic disorders can be frequent in immature newborns or in life-threatening situations. For instance, the prevalence of hypoglycaemia is 1 to 5 cases per 1000 live births, and concerns nearly 30% hospitalized newborns [1] [2]. The prevalence of neonatal hyperglycemia is estimated between 20% and 88% [3] [4]. These metabolic disorders can be life-threatening and require a prompt and adequate management. However, the clinical picture is usually not specific, which makes the availability of biological laboratory tests mandatory, especially in situations of vital distress. In Low and Middle income countries (LMIC) the difficult access to some diagnostic tests makes the management of the metabolic emergencies challenging. The neonatology department of the Albert Royer children's hospital is a major facility in Senegal, a subsaharian country. It regularly welcomes newborns in situations potentially resulting in metabolic disorders such as hypoglycemia, hyperglycemia, hyponatremia, hypernatremia and hyperkalaemia. We led this study, the objectives of which were to assess their frequency and circumstances of occurrence, to describe the clinical symptoms associated with them, to determine their etiologies, to assess their management and to assess their short-term prognosis.

2. Patients and Methods

Our study was conducted in the neonatology unit of National Children Hospital Albert Royer in Dakar (Senegal), a reference unit which offers a capacity of 23 beds.

It welcomes newborns and infants under the age of two months with an average of nearly 800 newborns per year, all "out born".

The biological tests necessary for their care are carried out in the Hospital's

biological analysis laboratory. In case of emergency, the capillary blood sugar and serum electrolytes such as sodium and potassium are available.

This was a retrospective and descriptive study conducted over a period of one year, from January 1 to December 31, 2014.

We included in the study all preterm and full-term newborns hospitalized with at least one of the following disorders:

- Hypoglycemia: capillary blood sugar < 0.5 g/l;
- Hyperglycemia: capillary blood sugar ≥ 1.25 g/l;
- Hyponatremia: Serum sodium level < 135 mmol/l;
- Hypernatremia: Serum sodium level > 145 mmo/l;
- Hypokalaemia: Serum potassium level < 3.5 mmol/l;
- Hyperkalaemia: Serum potassium level > 5.5 mmo/l.

The files of all hospitalized neonates were consulted. When at least one of the metabolic disorders studied was noted, the data were collected on a form established for this purpose. For each file with metabolic disorders, the parameters collected were the socio-demographic data and the clinical presentations. Regarding the metabolic disorders, we collected the age of the patients at their onset, the number of episodes, the minimum and maximum level of glucose, sodium and potassium. We also collected data about the treatment they received and the evolution.

The collected data were first coded and then entered, using the EPI DATA software. They were analyzed using SPSS 2 software. Given the specific objectives of the study, both univariate and bivariate analyses were performed. The univariate analysis consisted of determining the dispersion and central tendency characteristics of each variable studied. For associations between categorical variables, the Chi-square test was used. When the conditions of applicability of the latter were not met, a Fischer test was used.

3. Results

3.1. Epidemiological Aspects

Seven hundreds and forty nine newborns were admitted to the hospital. Among them, 350 had presented at least one episode of metabolic disorder, which represented a prevalence of 46.7%.

The most common metabolic disorder noted was Hyperglycemia (164 cases/21.8%) followed by Hyponatremia (151 cases/20.1%). Hypoglycemia occurred earlier than other disorders (mean age 6.37 days) while Hyperkalaemia was the latest disorder to occur (mean age 11.31 days). The frequency of the metabolic disorders studied and the age of onset are summarized in Table 1. The sex ratio was 1.38. Ninety six patients (12.8%) were born premature. Table 2 displays the distribution of the metabolic disorders according to the gestational age.

3.2. Clinical and Biological Aspects

The main clinical signs observed are summarized in Table 3. Thermoregulation

Table 1. Frequency of metabolic disorders and Age (in days) of their onset.

Metabolic disorder	Frequency	Mean age ± SD
Hypoglycemia	84 (11.2%)	6.37 ± 7.83
Hyperglycemia	164 (21.8%)	7.69 ± 8.83
Hyponatremia	151 (20.1%)	9.82 ± 9.95
Hypernatremia	72 (9.6%)	10.96 ± 7.53
Hypokalaemia	14 (1.8%)	9.87 ± 9.12
Hyperkalaemia	64 (8.5%)	11.31 ± 8.20

SD: Standard deviation of the mean.

Table 2. Distribution of the metabolic disorders according to the gestational age.

Metabolic disorder	N	Preterm	Full term
Hypoglycemia	84	39 (46.4%)	45 (53.6%)
Hyperglycemia	164	63 (38.4%)	101 (61.6%)
Hyponatremia	151	42 (27.8%)	109 (72.2%)
Hypernatremia	72	12 (16.7%)	60 (83.3%)
Hypokalaemia	14	5 (37.5%)	9 (64.3%)
Hyperkalaemia	64	10 (15.6%)	54 (84.4%)

Table 3. Distribution of clinical signs according to metabolic disorders.

Metabolic disorders	N	Dehydration	Undernutrition	Seizures	Respiratory Distress	Cardiac Arrest-Shock
Hypoglycemia	84	31 (36.9%)	13 (15.4%)	18 (21.4%)	40 (47.6%)	19 (22.6)
Hyperglycemia	164	60 (36.5%)	18 (10.9%)	39 (23.7%)	105 (64%)	53 (32%)
Hyponatremia	151	41 (27.1%)	14 (9.2%)	36 (23.8%)	82 (54.3%)	23 (15.2%)
Hypernatremia	72	43 (59.7%)	22 (30.5%)	21 (29.1%)	19 (26.3%)	18 (25%)
Hypokalaemia	14	7 (50%)	2 (14.2%)	5 (35.7%)	8 (57.1%)	2 (14.2%)
Hyperkalaemia	64	29 (45.3%)	14 (21.8%)	25 (39%)	32 (50%)	28 (43.7%)

disturbances were found particularly in newborns with serum sodium (hyponatremia 33.5% and hypernatremia 59.7%) and blood glucose disorders (Hypoglycemia: 30.9%/Hyperglycemia: 39.6%). Neurological signs were noted in case of blood sugar abnormalities (Hypoglycemia:26.1%/Hyperglycemia:29.8%) and hyperkalaemia (31.2%). The patients presented an average of 1.71 ± 1.5 episodes of hypoglycaemia with a maximum of 9 episodes.

Half of the newborns with hyperglycemia (82 cases/50%) had blood sugar levels greater than or equal to 2 g/l.

Eleven newborns (7.3%) had severe hyponatremia ≤ 120 mmol/l.

Hypernatremia was severe (Serum sodium > 180 mmol/l) in 12 neonates (16.7%).

There was only one case of major hypokalaemia at 1.90 mmo/l and 10 cases (15.6%) of severe hyperkalaemia. The different blood test values are summarized in Table 4.

The main diagnoses retained were neonatal Sepsis (159 cases/45.4%), Prematurity (96 cases/27.4%), Intrauterine Growth Retardation (66 cases/18.9%), Malformations (63 cases/18%), Perinatal Asphyxia (44 cases/12.6%) and Malnutrition (36 cases/10.3%). Sepsis was the most common diagnosis in patients with hyperkalemia (42 cases/65.62%) followed by hypernatremia (47 cases/65.27%), hyperglycemia (81 cases/49.39%) and hypoglycemia (39 cases/46.42%).

3.3. Therapeutic Aspects

The correction period of metabolic disorders could not be collected in all newborns. When it could be noted, for most metabolic disorders, the correction was late and was done beyond 48 hours. On average, the correction period varied between 3 hours and 6 days. Table 5 displays distribution of patients according to the period of correction of the metabolic disorders. The intravenous glucose correction intakes were on average 8.3 ± 5.6 g/kg/day in case of hypoglycaemia and 8.1 ± 4.2 g/kg/day in case of hyperglycaemia. To correct hyponatremia, newborns received an average of 7.08 ± 4.1 mEq/kg/day of sodium and 4.1 ± 3.4 mEq/kg/day to correct hypernatremia.

Potassium intakes were 3.5 ± 0.8 mEq/kg/day in case of hypokalaemia and

Table 4. Distribution of metabolic disorders according to blood levels of glucose, sodium and potassium.

Metabolic disorders	Unit	Mean level ± SD	Minimum level	Maximum Level
Hypoglycemia	g/l	0.2898 ± 0.14	0.02	0.49
Hyperglycemia	g/l	2.4 ± 1.1	1.45	6
Hyponatremia	mmol/l	128 ± 5.3	108	134
Hypernatremia	mmol/l	163 ± 14.5	146	199
Hypokalaemia	mmol/l	2.6 ± 0.32	1.9	3.4
Hyperkalaemia	mmol/l	6.74 ± 1.5	5.6	15

Table 5. Distribution of patients according to the time of correction of the metabolic disorders.

Metabolic Disorders	Within 24 hours	24 - 48 hours	Beyond 48 hours
Hypoglycemia	16 (100%)		
Hyperglycemia	52 (54.7%)	33 (34.7%)	10 (10.5%)
Hyponatremia	4 (9.1%)	14 (31.8%)	26 (59.1%)
Hypernatremia	4 (9.5)	21 (50)	17 (40.5%)
Hypokalaemia	2 (18.2)	4 (36.4)	5 (45.5%)
Hyperkalaemia	0 (0.0%)	21 (65.6%)	11 (34.4%)

0.05 ± 0.2 mEq/kg/day in case of hyperkalaemia

In 56 neonates with a metabolic disorder, we used mechanical ventilation. The other treatments were treatments of the etiology (antibiotics for infections, surgical cures for malformations) but above all symptomatic treatments summarized in Table 6.

3.4. Evolution

The most frequent complications were cerebral edema (12 cases), brain death (8 cases) and increased intracranial pressure (3 cases).

Cerebral edema mainly complicated sodium disorders, Hyperglycemia and Hyperkalemia, while cases of brain death were observed with glucose and sodium disorders. The most lethal disorders were Hyperkalemia (mortality rate: 54.7%) followed by Hyperglycemia (mortality rate: 49.4%) and the least lethal one was Hypernatremia (Table 7).

4. Discussion

The incidence of metabolic disorders in newborns was high in our series (46.72%),

Table 6. Other treatments used.

Treatments	Frequency
Mechanical ventilation	56
Volume expansion	47
Fluid restriction	15
Sodium Bicarbonate	3
Kayexalate	4
Hydrocortisone	27
Salbutamol	12
Calcium gluconate	18
Diuretics	33
Insulin	16
Anticonvulsants	62

Table 7. Mortality rate of the metabolic disorders.

Metabolic disorders	Frequency	Deaths frequency	Deaths percentage
Hypoglycemia	84	29	34.5%
Hyperglycemia	164	81	49.4%
Hyponatremia	151	52	34.4%
Hypernatremia	72	19	26.4%
Hypokalaemia	14	4	28.6%
Hyperkalaemia	64	35	54.7%

but remains lower than that noted in Bamako in 2002 (85.14%).

This Malian study, however, only concerned newborns between 0 and 7 days of life [5]. The Malian series also found a male predominance with a sex ratio of 1.52, close to our results (1.38) [5]. In a study conducted in Japan in 2001, hypocalcemia was more frequent in male newborns [6]. This suggests that boys are at greater risk of developing metabolic abnormalities in the neonatal period.

The prevalence of hypoglycemia found in our study (11.2%) was comparable to the one found in Nepal (11% in term newborns) but lower than the prevalence reported in the Malian study (15%) [5] [7]. In most cases, these frequent episodes of hypoglycemia result from the poor conditions of care in the delivery room and the poor conditions of transfer of the newborns. In our study, we found 39 cases of prematurity (46.4%). The association between prematurity and hypoglycemia has been explained by the low hepatic glycogen reserves in preterm newborns [1]. The studies of Najati and Nong found results akin to ours with a frequency of prematurity of 59.6% and 23.3% respectively [5] [8]. Hypoglycemia was diagnosed on average at 6 days of life, which was higher than the data found by Koivisto, who found a mean age at diagnosis varying between 9 and 39 hours depending on the clinical picture [9]. The high mean age at diagnosis in our series could be explained by the large size of our sample, composed of newborns received at all ages, in particular beyond the 48th hour of life, and for whom the diagnosis was only made on their arrival at our facility. A particular situation that we have observed is the occurrence of hypoglycemia secondary to the lack of food intake associated with dehydration and undernutrition. For all these neonates at high risk of hypoglycemia, preventive strategies should be adopted, including early and fractionated feeding, sometimes continuous enteral feeding, and the use of adequate parenteral nutrition or medication if necessary.

Hyperglycemia was found in 21.8% of cases in our study. It is reported with very variable frequencies: 2.9% in India, between 11 and 13% in Mali [5] [10]. The prevalence increases to 54% in Low Birth Weight (LBW) [10]. In LBW, these hyperglycemia episodes are associated with a risk of undernutrition but above all with a risk of cerebral complications such as haemorrhage [11]. Eighty one cases of hyperglycemia were found to have neonatal sepsis which is an etiology classically found in many studies [12]. Hyperglycemia was found to be a associated with a high mortality rate in our setting. This was also confirmed by other studies [13] [14]. For this reason, the occurrence of hyperglycemia episodes during the monitoring of newborns should be considered as a warning sign to encourage intensified and optimized management.

The incidence of hyponatremia was 20.1% of hospitalized neonates and was the second most frequent metabolic disorder. In the literature, it is reported in variable frequencies: 9% in Mali, 24% in France, 33% in Nigeria [5] [15] [16].

The clinical picture was essentially neurological and respiratory signs with, in particular, convulsions and respiratory distress. The series by Day in Canada and Tarnow-Mordi in England found the same clinical signs [17] [18]. More than

half of the cases of Hyponatremia presented with respiratory distress. The occurrence of the Syndrome of Inappropriate Anti-diuretic Hormone Secretion (SIADH), common in case of respiratory distress, has been incriminated [19].

Hypernatremia affected nearly 10% of hospitalized newborns, a prevalence higher than that found in many studies: 5.4% in Mali, 3% in Italy and 5.6% in Turkey [5] [20] [21]. Overall, in breastfed newborns, the incidence has been estimated at 1.8% [22].

Dehydration and undernutrition were the main associated pictures. The lack of intake, often related to difficult breastfeeding or a neonatal pathology associated with a refusal to feed, explains this association [23] [24]. For formula-fed neonates, the use of overly concentrated bottles may promote the occurrence of hypernatremia [25]. Supporting mothers during breastfeeding could therefore be an important element in the prevention of hypernatremia. When it occurs, hypernatremia must be corrected progressively over 48 hours. In our series, as in that of Bolat, correction was obtained in less than 48 hours for more than half of the neonates [22]. This exposes to a risk of cerebral oedema which we observed in our study.

The hospital prevalence of hypokalemia was relatively low (1.8%). This was also the case in Mali (2.15%) [5]. In the Nong study, prematurity and LBW increased the risk of hypokalemia. The incidence was 58% in the Boubred study, and 37% with Takanashi [26] [27]. In several studies, hypokalemia was essentially associated with digestive manifestations such as occlusions, which was either a cause or a consequence. Kontogomau in Burkina Faso found 10% hypokalemia cases in neonatal occlusions [28].

In our study, hyperkalaemia represented a hospital prevalence of 8.5%. A similar incidence was found in Bamako in the study by Nong, who found 18 cases of hyperkalaemia (9%), with a greater frequency in low birth weight [5]. The frequency of hyperkalaemia can be very high in very premature babies: it's the so called non-oliguric hyperkalaemia, of which we noted 18 cases out of 64 (28.1%) [29]. A strong correlation has been found between hypotension and hyperkalaemia in premature babies [30]. We also found this notion in our study, with a high frequency of shock in newborns presenting episodes of Hyperkalaemia. Subsequently, Hyperkalaemia was associated with the highest death rate in our study. This high mortality is classic [31] [32]. It is explained by the difficulties of biological or electrical monitoring and by the association of hyperkalaemia with situations of severe distress situations such as sepsis, respiratiory distress or renal failure.

Nevertheless, our study presented some limitations such as the inability to use some medical records that were incomplete. During certain periods of the study, some biological analyses were not available. That might have underestimated the prevalence of the metabolic disorders. It was also difficult to repeat the biological analysis, making it difficult to monitor the metabolic disorders we noted.

5. Conclusion

Metabolic disorders especially glucose, sodium and potassium disorders are com-

mon in newborns. They are medical emergencies that can lead to vital instability and death. Their management is challenging in low-income countries due to the lack of adapted facilities and means to diagnose them. It is therefore important to train medical and paramedical staff in the recognition of metabolic emergencies, but also to improve the availability of technical methods and means of biological analysis in hospital laboratories. This allows for better detection and monitoring of metabolic disorders. It is of utmost importance to promote the availability of capillary micro-methods of biological tests at the newborn's bed, allowing for instantaneous basic tests, generally including serum electrolytes level with arterial blood gases and lactates.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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