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Part 2: What resources for management, for what results?

Perinatal Asphyxia in a Hospital Setting in a Developing Country

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Keywords: Newborn; Perinatal asphyxia; Hypoxic-ischemic encephalopathy; Controlled hypothermia; Magnetic resonance imaging; Neonatal deaths.

Abbreviations: AEEG: Amplified Electroencephalogramm; CHUP-CDG: Centre Hospitalier Universitaire Charles De Gaulle; CPAP: Continuous Positive Airway Pressure; CT: Computed Tomography; EEG: Electroencephalogramm; HIE: Hypoxic-Ischemia Encephalopathy; MRI: Magnetic Resonance Imaging; NU: Neonatal Unit; PNA: Perinatal Asphyxia; US: Ultrasound.

Abstract

Bakground: Perinatal asphyxia is one of the three major causes of neonatal morbidity and mortality, along with prematurity and neonatal sepsis. The study was conducted with the aim to describe the means of diagnosis and treatment, as well as, the outcome of management in a developing country in order to contribute to reduce the neonatal morbidity and mortality associated with this major public health problem.

Methods: A cross-sectional retrospective study was conducted from 1 January 2019 to 31 October 2021 at the neonatology unit of the Centre Hospitalier Universitaire Pédiatrique Charles de Gaulle, Ouagadougou, Burkina Faso (West Africa). All neonates with an Apgar score of less than 7 at the 5th minute of birth were included.

Results: The incidence of perinatal asphyxia was 22.3%. Hypoglycaemia (40.4%), hypocalcemia (14.4%), hypernatremia (10%), hyperkalemia (34.5%), acidosis (25.1%), and renal failure (82%) were reported. Transfontanellar ultrasound revealed hemorrhagic (58%) and anoxic-ischemic (23.9%) lesions. Normal discharges accounted for 69.5% of cases. The case fatality rate was 29.9% and sequelae were observed in 26.7% of cases.

Conclusion: In order to improve the management of perinatal asphyxia and reduce its impact on neonatal mortality in our developing countries, the technical resources of our hospitals should be strengthened.

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Introduction

Perinatal Asphyxia (PNA), also known as neonatal asphyxia occurs due to insufficient blood flow and oxygen to the foetus before, during, or shortly after birth. A thorough investigation is essential to establish a timely diagnosis, to evaluate and take emergency measures, and to establish the short-, medium- and long-term prognosis of PNA. In Burkina Faso, PNA continues to be a major cause of neonatal morbidity and mortality [1-4].

The study was conducted with the aim to examine the para clinical, therapeutic, and outcome aspects of PNA. The information gathered will provide a better understanding of this condition, with a view to improving its management and reducing neonatal morbidity and mortality in Burkina Faso and other countries with limited resources.

Material and methods

The study took place in the Neonatology Unit (NU) of the Centre hospitalier universitaire pédiatrique Charles de Gaulle (CHUP-CDG) in the city of Ouagadougou, the capital of Burkina Faso. This unit, with a capacity of 40 beds, has been operational since 2019. It carries out approximately 530 hospitalizations/year. The staff is made up of five pediatricians, 40 nurses, nursing assistants, and laborers. The equipment includes neonatal resuscitation tables, radiant warmers, incubators, central oxygen supply, ventilation equipment (self-inflating balloons, masks, goggles), conventional and intensive phototherapy devices, monitoring scopes, and electric mucus aspirators. On the other hand, Continuous Positive Airways Pressure (CPAP) devices and respirators for newborns are not available. Medications (caffeine, anticonvulsants, antibiotics, etc.) are made available through a hospital pharmacy which dispenses individually by name. Neither neuroimaging modalities such as Magnetic Resonance Imaging (MRI) nor Electroencephalograms (EEG, aEEG) are available in the hospital. Transfontanellar ultrasound cannot be performed at the patient's bedside. In the treatment, the method of neuroprotection by controlled hypothermia is not practiced. As the CHUP-CDG does not have a maternity ward, the admission of newborns is direct by transfer from the city's maternity wards in most cases.

The variables studied are presented in **Table 1**.

Table 1: Variables studied in perinatal asphyxia, Ouagadougou, Burkina Faso, 2021.

Variables studied	
Investigations	• Biology: blood glucose, ionogram, hemogram • Imaging: Transfontanellar US, brain Computed Tomography (CT) scan
Therapeutics	• Resuscitation, drugs, fluids, electrolytes
Outcomes	• Within 24 hours, in the first week • Length of hospital stay • Exit mode • Sequelae

Results

Of the 1,599 newborns hospitalized in the NU during the period, 331 cases of PNA were found, representing an overall hospital frequency of 20.7%.

Biological tests

The results of biological tests such as blood glucose, blood ionogram, and creatinine levels are shown in **Table 2.**

The results of the hemogram are shown in **Table 3.**

Table 2: Distribution of asphyxiated newborns according to biological test results, Ouagadougou, Burkina Faso (n = 331).

Biological test and result	Number of cases	%
Blood glucose (mmol/L)		
Mean ± SD [minimum, maximum]	4.31 ± 4.71 [0.1, 30]	
Hypoglycemia (<2.5)	116	40.4
Hyperglycemia (>4.5)	94	32.8
Normal (2.5-4.5)	77	26.8
Serum calcium (mmol/L)		
Mean ± SD [minimum, maximum]	2.31 ± 0.57 [0.2, 8.4]	
Normal (2-3)	233	80.1
Hypocalcemia (<2)	42	14.4
Hypercalcemia (>3)	16	5.5
Natremia (mmol/L)		
Mean ± SD [minimum, maximum]	137.42 ± 5.77 [116, 157]	
Normal (130-145)	228	81.8
Hypernatremia (>145)	28	10.0
Hyponatremia (<130)	23	8.2
Kalemia (mmol/L)		
Mean ± SD [minimum, maximum]	5.38 ± 1.67 [3, 20]	
Normal (3.5-5.5)	169	61.5
Hyperkalemia (>5.5)	95	34.5
Hypokalemia (<3.5)	11	4.0
Serum Bicarbonate (mmol/L)		
Mean ± SD [minimum, maximum]	17.33 ± 5.73 [1, 38]	
Normal (14-28)	187	71.1
<14 (acidosis)	66	25.1
>28 (alkalosis)	10	3.8
Serum creatinine (µmol/L)		
Mean ± SD [minimum, maximum]	85.5 ± 4.55 [14, 380]	
Renal failure (>90)	246	82.0
Normal (20-90)	54	18.0

Table 3: Blood count in asphyxiated newborns, Ouagadougou, Burkina Faso 2021 (n = 331).

Blood count	Number of cases	%
Leukocytes (x10 /mm^3)		
Mean±SD [minimum, maximum]	15.8±7.4 [1.8, 49.1]	
Normal (10-30)	238	75,5
Leucopenia (<10)	66	21,0
Hyperleukocytosis (>30)	11	3,5
Haemoglobin level (g/dL)		
Mean±SD [minimum, maximum]	15.2±2.4 [3.2, 20]].	
Normal (14-20)	228	72,4
Anaemia (<14)	87	27,6
Platelets (x10 /m^3)		
Mean±SD [minimum, maximum]	208.8±84.7 [8, 486]	
Normal (150-400)	245	77,8
Thrombocytopenia (<150)	61	19,4
Thrombocytosis (>400)	9	2,8

Medical imaging examinations

Table 4 shows the results of the imaging tests (Transfontanellar US, brain CT) carried out on newborns.

Treatment.

Table 5 shows the treatment given to asphyxiated neonates such as resuscitation, drugs, fluids, and electrolytes.

Table 4: Distribution of asphyxiated newborns according to medical imaging results, Ouagadougou, 2021, Burkina Faso.

Test and result	Number of cases	%*
Transfontanellar US (n = 176)		
Haemorrhage (subependymal, ventricular)	102	58,0
Anoxic-ischaemic lesions	42	23,9
Normal	33	18,7
Brain CT (n = 5)		
Cortical atrophy	3	60,0
Leukoencephalomalacia	3	60,0
Cerebral oedema	1	20,0

*The percentage may exceed 100% because a newborn could have several lesions at the same time.

Table 5: Distribution of asphyxiated newborns according to treatment, Ouagadougou, 2021, Burkina Faso (n = 331).

Treatment	Number of cases	%
Resuscitation		
Oxygen	168	50,8
Nasopharyngeal obstruction	112	33,8
Warming	107	32,3
Mask ventilation	18	5,4
External cardiac massage	5	1,5
Drugs		
Antibiotic (cefotaxime, gentamicin)	324	97,9
Phenobarbital	133	40,2
Diazepam	79	23,9
Paracetamol	33	10,0
Adrenalin	7	2,1
Fluids		
Glucose 10%	330	99,7
Bicarbonate 14‰	13	3,9
Ringer lactate	10	3,0
Isotonic saline	2	0,6
Electrolytes		
Calcium gluconate	325	98,2
Sodium chloride	105	31,7
Potassium chloride	104	31,4

Outcomes

Within the first 24 hours, hypotonia was observed in 75.8% of cases, hypertonia in 4.2%, convulsions in 28.4%, coma in 18.4%, and respiratory distress in 8.8%. At one week of age, convulsions persisted in 8.8% of cases. The average length of hospitalization was 9.88 days ± 8.93 [1, 73].

In 69.5% of cases, the newborns were discharged normally. There were 99 deaths, giving a case fatality rate of 29.9%. The specific mortality rate was 6.2% (99/1,599). During the study period, a total of 355 deaths due to PNA were recorded, giving a proportional mortality rate of 27.9% (99/355). Of the 232 newborns discharged alive, 62 (26.7%) had various sequelae which include convulsions (51.6%), hypotonia (45.2%), and sensory problems such as blindness and deafness (3.2%).

Discussion

In the present study, hypoglycaemia was common in asphyxiated neonates (40.4% of cases). Similarly, a case-control study conducted by Bahatkar *et al.* [5] shows significant hypoglycaemia in asphyxiated newborns as compared with non-asphyxiated newborns. According to some authors, hypoglycaemia is an important risk factor for perinatal brain damage and adverse outcomes, particularly in newborns requiring resuscitation following Hypoxic-Ischemic Encephalopathy (HIE). In the event of stress, preterm newborns are more exposed to hypoglycaemia than those born at term [6]. In contrast to hypoglycaemia, hyperglycemia was also observed in almost a third of cases of asphyxia, but we believe that this is probably iatrogenic hyperglycemia. Indeed, in our context, it is not uncommon for blood samples to be taken after the start of the infusion of glucose serum in the referring health center or in the emergency room of our NU. Systematic measurement of blood sugar in all newborns on admission, particularly those suffering from asphyxia, would make it possible to detect hypoglycaemia and take urgent corrective measures to avoid the development of brain lesions that could damage the newborn.

The electrolyte abnormalities observed in this study (hyper or hyponatremia, hyper or hypokalemia, hyper or hypocalcemia, acidosis or alkalosis) were probably related to the pathophysiology of PNA itself. Several studies [5,7,8] conducted among normal-weight term newborns report that hyponatremia, hypocalcemia, and hyperkalemia correlate with the degree of asphyxia and Apgar scores in asphyxiated newborns. Hence, regular monitoring of the blood ionogram in asphyxiated newborns is utmost crucial to detect and correct metabolic disturbances.

The majority (82%) of asphyxiated newborns in this study had acute renal failure. This frequency is higher than that reported by other authors in asphyxiated term newborns [9] (44.6%). PNA can damage the kidneys of the newborn due to decreased blood flow to the kidneys during the period of asphyxia leading to a reduction in glomerular filtration rate and an accumulation of metabolic waste products in the blood, ultimately resulting in renal failure. Most visceral damage recovers in the event of survival; only severe kidney damage can sometimes leave sequelae [10]. It is therefore important to monitor renal function carefully in newborns who have suffered PNA and to treat any renal failure urgently to avoid complications.

Overall, the hemogram was little disturbed in this study. The inflammatory response to hypoxia-ischemia or possible maternal-fetal infection may result in hyperleukocytosis or leukopenia. Anemia was observed in 27.6% of cases and is multi factorial in origin.

Although not very specific and operator-dependent, Transfontanella US remains the first-line examination for exploring the brain in cases of PNA in our context. In this study, this test showed 58% of hemorrhage lesions, which is significantly higher than the 2.4% reported by Ouédraogo [11], a decade ago in the

same hospital. This difference can no doubt be explained by the large proportion (16%) of premature newborns in this study. Indeed, sub ependymal hemorrhages (stages 1, 2 and 3) and peri ventricular leukomalacia lesions would be the prerogative of asphyxiated premature newborns [12]. What's more, Transfontanellar US has now been performed free of charge since 2016, whereas, ten years ago it was paid by parents, which limited its use. Ischemic and infarct lesions, on the other hand, are more frequent in asphyxiated term newborns [12]. They were noted in 23.9% of patients in this study, a higher frequency than that reported by Ouédraogo [11] (3.5%). Here too, the fact that the examination is free of charge has helped to improve diagnosis. Equipping the NU with a mobile ultrasound scanner should be done to easily perform Transfontanella US at the patient's bedside and better monitoring.

In this study, brain CT was utilized to detect the lesions of leuko and encephalomalacia, cerebral edema, and cortical atrophy [12]. Magnetic Resonance Imaging (MRI), which is the gold standard for investigation in PNA, is not available in our hospital. MRI is a useful tool to identify brain lesions in HIE and establish the prognosis.

In this study, the treatments used for PNA, which consisted of infusion of fluids and electrolytes, in particular calcium gluconate, oxygen, and anticonvulsants, were the same as elsewhere [13], except that we did not have CPAP. aminophylline, which is used by other authors [13,14], is not administered under our conditions, according to the PNA management protocol. We only know that the treatment of PNA is essentially symptomatic. As the benefits of controlled hypothermia no longer need to be demonstrated [15], access to this therapy would be an asset for us in the treatment of PNA to improve newborn survival in our context. Strengthening the neonatal resuscitation skills of the birth room staff is essential in the PNA management chain. During the first 24 hours, seizures were noted in 28.4% of asphyxiated newborns which is lower than the rate of 31.9% reported by Coulibaly *et al.* [16]. However, the frequency of seizures in this study is higher than that reported by other authors in South Africa [17] (19.3%). Seizures are less frequent in Sarnat stage 3 because of the deep lesions in the brain that prevent the propagation of electrical discharges [18]. After a week in the hospital, seizures subsided but persisted in 8.8% of asphyxiated newborns. These cases of convulsive malaise are probably linked to the moderate to severe stages of HIE. In our context of countries with limited resources, we do not have EEG or aEEG to monitor these seizures, the importance of which is undoubtedly underestimated.

The hospital stay of 9.9 days observed in this study is similar to that reported in Africa [19] but shorter than a France study [20] (13.5 days). Under our conditions, newborns are discharged as soon as the clinical course is deemed favorable, whereas in Europe, they stay for a longer period in order to perform extensive investigations and better monitoring [20].

The case-fatality rate of 29.9% observed in this study is higher than the rates reported in Africa (10.4% to 26.5%) [16,19,21,22] and Europe (21%) [20]. The CHUP-CDG NU is a reference center for the city of Ouagadougou and the country. It is, therefore, a place where all serious cases flock, which explains the relatively high mortality observed in this study. With a proportional mortality rate of 27.9%, PNA is a major contributor to neonatal deaths, confirming the results reported by other authors [1,2].

After discharge from the hospital, 26.7% of asphyxiated newborns had neurological and sensory sequelae. Unfortunately, the data regarding the post-hospitalization outcome of these newborns was not available. However, the monitoring of surviving neonates who have experienced HIE is very important and must not be neglected as the consequences of HIE can have a significant impact on the long-term health and well-being of these children [17,20].

Limitations and constraints of the study

In the context of a developing country, laboratory (cord p^H, lactacidemia), Medical Imaging (MRI), and therapeutic (controlled hypothermia) shortcomings may give rise to certain biases that limit the scope of this study. In addition, the retrospective nature of the hospital study can indeed introduce a lack of precision in the information collected.

Conclusion

This study has shown that PNA is a major problem in the neonatal unit of a hospital, particularly in a developing country. The successful resolution of this tragedy in our neonatal units requires consistent diagnostic and therapeutic resources for optimal management.

Conflicts of interest

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

Authors' contributions

KN designed the study, analyzed the data, and drafted the manuscript.

BK participated in designing the study and writing the manuscript.

SP participated in data collection, data entry, data analysis, and drafting of manuscript.

LT, SD, AB, MS, CK contributed to the drafting of the manuscript.

DY critiqued and revised the manuscript.

All the authors read and approved the final version of the manuscript.

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