Scientific Research Publishing

Open Journal of Pediatrics, 2023, 13, 50-62
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

Acute Bilirubin Encephalopathy: A Propos of 151 Cases Collected during a Multicentric Study in Senegal

Serigne Tawa Ndiaye[1*], Yaye Joor K. B. Dieng[1], Papa Moctar Faye[1], Mohameth Mbodj[1], Sofietou Dieye[1], Khadim Bop[1], Papa Souley Sow[1], Amadou Sow[2], Ndeye Fatou Sow[1], Ibrahima Diop[1], Aziz Faye[1], Sadio Konate[1], Ibrahima Diagne[3], Mousatapha Ndiaye[4], Ousmane Ndiaye[1]

[1]Centre Hospitalier National D'Enfants Albert Royer, Dakar, Senegal
[2]Centre Hospitalier Municipal Abass Ndao, Dakar, Senegal
[3]Gaston Berger University, Saint Louis, Senegal
[4]Cheikh Anta Diop University, Dakar, Senegal
Email: *mabeyend@gmail.com

How to cite this paper: Ndiaye, S.T., Dieng, Y.J.K.B., Faye, P.M., Mbodj, M., Dieye, S., Bop, K., Sow, P.S., Sow, A., Sow, N.F., Diop, I., Faye, A., Konate, S., Diagne, I., Ndiaye, M. and Ndiaye, O. (2023) Acute Bilirubin Encephalopathy: A Propos of 151 Cases Collected during a Multicentric Study in Senegal. *Open Journal of Pediatrics*, **13**, 50-62.
https://doi.org/10.4236/ojped.2023.131006

Received: March 29, 2022
Accepted: January 7, 2023
Published: January 10, 2023

Abstract

Introduction: Bilirubin encephalopathy is a debilitating complication of severe neonatal unconjugated bilirubin jaundice. The aim of this study was to determine the frequency of occurrence of this complication and to describe the diagnostic and prognostic aspects in Senegal. **Materials and Methods:** This was a multicenter, descriptive and analytical study conducted in 32 neonatal units of various levels, with retrospective (January to December 2020) and prospective (January to August 2021) collection. All neonates hospitalized for acute bilirubin encephalopathy were included. The diagnostic criteria were the presence of jaundice associated with neurological signs (muscle tone disorders, abnormal movements, convulsions, etc.), with no other obvious etiology found. The data were entered and analyzed using SPSS version 23 software. The significance threshold was retained for a p-value < 0.05. **Results:** We registered 151 patients. The mean age was 6 days and the sex ratio was 2.5 (clear male predominance). The majority of newborns were from Dakar (51%). Twenty-two (22%) were premature and 32% had low birth weight. Half of the newborns (50%) came from home and 87% were exclusively breastfed. The average time to consult was 3 days. Neurological signs were dominated by decreased primitive reflexes (74%), abnormal movements (59%) and lethargy (50%). Dehydration (30%) and anemia (26%) were often associated. The mean bilirubin level was 416 umol/l. Neonatal infections (19%) and Rhesus (16.7%) and ABO (8.7) incompatibility were the main causes. One third (33%) of patients had received intensive phototherapy and

only 2% had received exchange blood transfusion. The case fatality was 48.9%. **Conclusion:** Bilirubin encephalopathy remains a major concern in Senegal. It is associated with high mortality and numerous neurological sequelae. Progress in terms of early detection and appropriate management is urgently needed on a national scale.

Keywords

Icterus, Encephalopathy, Phototherapy, Lethality

1. Introduction

Jaundice is a yellow discoloration of the mucous membranes and integuments due to hyperbilirubinemia and is the most common symptom in neonatology [1]. In the newborn, when this jaundice is predominantly unconjugated bilirubin, it exposes the child to a formidable complication responsible for a high mortality rate and disabling neurosensory sequelae: bilirubin encephalopathy. This occurs when unconjugated bilirubin not bound to albumin, which is fat-soluble, crosses the blood-brain barrier and attaches itself to the basal ganglia. The clinical manifestations combine a frank, non-cholestatic cutaneous-mucosal jaundice with non-specific neurological signs (disturbed consciousness, lethargy, inability to suck, abnormal movements, muscle tone disturbance, acute plaintive cry, apnea) [2]. Prevention of this complication is based on early detection and appropriate management of rhesus incompatibility in maternity wards by administering anti-D serum. At birth, the management of jaundice by blue light phototherapy is the main therapeutic intervention, with new intensive phototherapy techniques that have significantly reduced the risk of progression to kernicterus. Exchange blood transfusion remains a current therapeutic intervention in severe forms of free bilirubin jaundice [1].

Epidemiologically, the frequency of this neonatal complication has decreased significantly in developed countries in recent decades, thanks to advances in early detection and management, although a small upward trend has been noted recently [3] [4] [5] [6].

In contrast to our low-income countries, global estimates show that the prevalence of acute bilirubin encephalopathy is much higher, as in sub-Saharan Africa (SSA) with higher morbidity and mortality [7] [8] [9]. This much higher incidence can be explained by several factors: poor prevention in maternity wards (anti-D serum), lack of effective strategies for early detection, low awareness of jaundice risks among health care providers and communities, insufficient availability of phototherapy devices in neonatal units and maternity wards...

In Senegal, Faye reported 30 cases at the Centre Hospitalier National d'Enfants Albert Royer, corresponding to 1.14% of hospitalizations in neonatology [10]. However, in recent years, we have observed a resurgence of cases in neonatal units. This is why we undertook to carry out this study, the general objective of

which was to determine the frequency of occurrence of this complication and to describe the diagnostic and prognostic aspects in Senegal.

2. Methodology

This was a multicentric study opened to all facilities with a neonatology unit at the national level. The cases were collected in 32 neonatal units of various levels, spread over the 14 regions of Senegal (Table 1). This was a retrospective (January to December 2002) and prospective (January to August 2021), descriptive and analytical, cross-sectional data collection. All newborns hospitalised for acute bilirubin encephalopathy were included in this study. The diagnostic criteria were the presence of jaundice associated with neurological signs (tonus disorders, abnormal movements, convulsions), with no other obvious etiology found (meningitis, asphyxia, inborn errors of metabolism, etc.). Newborns whose records were incomplete were not included. A data collection form was drawn up for this purpose. It was shared with all neonatal units. The parameters studied were: epidemiological data, maternal data, perinatal data, clinical data, biological data, therapeutic data and evolutionary data (see data collection form in the annex). The data were entered and analyzed using SPSS version 23 software. The significance threshold was retained for a p-value < 0.05 (Chi-square test).

3. Results

Epidemiologically: we collected 151 newborns, of which 14 records were not usable. In the end, the analysis concerned 137 patients. The average age at admission was 6 days (1 and 15 days). The majority of newborns (78%) were admitted during the first week of life. There was a male predominance (sex ratio 2.5). The majority of newborns came from the Dakar region (51%).

Regarding maternal data and background: the average age of the mothers was 26 years (13 years and 44 years) and the majority of the mothers were pauciparous (42%).

A family history of neonatal jaundice was found in 59% of newborns.

Regarding perinatal data: seventy-nine patients (57.6%) had a vaginal delivery, 22% were born prematurely and 32% had a low birth weight.

Regarding diagnostic aspects: half of the newborns were from home (50%), 87% were exclusively breastfed and the mean age of the patients at the time of admission was 6 days. Forty patients (33%) had early onset jaundice (Figure 1). The mean time to consultation was 3 days (1 and 12 days). Neurological signs were dominated by: decreased primitive reflexes (74%), abnormal movements (59%) and high-pitched cry (50%) (Table 2). Dehydration (30%) and anaemia (26%) were the most frequent associated signs.

Biologically, the mean bilirubin level was 416 umol/l and the majority (64%) had a bilirubin level above 350 umol/l (Figure 2). The Coombs test was performed in only 8% of the patients and the IAT in 4%. G6PD activity testing was not performed in any of our patients.

The etiology was found in only 72 cases (52%). Neonatal infections (19%) and rhesus (16.7%) and ABO (8.7%) incompatibilities were the main causes found (Table 3).

Table 1. Characteristics of the different structures.

Regions	Names Structures	Types Structure	Capacity in neonatology	Number of convention cameras	Number of cameras. intensive
Dakar	CHAN	EPS 3	25	4	0
	HALD	EPS 3	30	3	0
	HDJ	EPS 3	20	4	0
	GASPARD	CS	9	1	0
	CHNEAR	EPS 3	39	8	7
	IHS	EPS 1	19	0	0
	HOGIP	EPS 3	12	2	0
	PIKINE	EPS 3	26	5	0
	PMS	CS	8	2	0
	HPD	EPS 3	25	1	1
	CHRB	EPS 1	10	3	0
Diourbel	CHRDHL	EPS 2	16	1	0
	FAWZENI	EPS 3	30	1	0
	NDAMATOU	EPS 1	14	0	1
Fatick	CHF	EPS 2	8	1	0
Kafrine	CHRKA	EPS 2	6	1	0
Kaolack	CHRK	EPS 2	12	2	0
Kedougou	CSK	CS	8	2	0
Kolda	CHRKO	EPS 2	8	2	0
Louga	CHRASML	EPS 2	13	1	0
matam	CHRM	EPS 2	8	1	0
	CHR	EPS 2	13	2	0
Saint Louis	CHRRT	EPS 2	6	0	0
	CHRSL	EPS 3	17	2	0
Sedhiou	CHRS	EPS 1	8	1	0
Tamba	CHRT	EPS 2	10	3	2
Thies	MBOUR	EPS 1	6	1	2
	CHREAST	CS	18	2	0
	TIAVAOUNE	EPS 1	9	3	0
Ziguinchor	HPZIG HRZIG	EPS 2 EPS 2	15 16	2 3	1 1

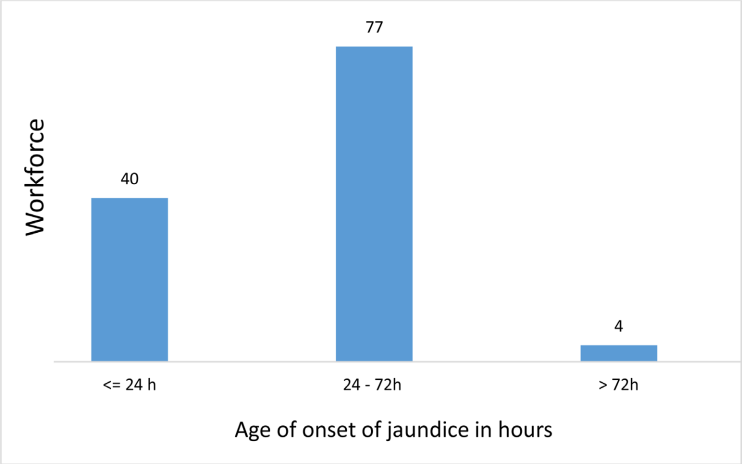

Figure 1. Repair of patients by age of onset of jaundice.

Table 2. Distribution of cases by neurological signs.

Neurological signs	Workforce	Percentage %
Decreased archaic reflexes	102	74
Abnormal movements	81	59
High-pitched scream	68	50
Lethargy	68	50
Head rejection	58	42
Hypertonia in opistotonos	45	33
Consciousness disorders	37	27
Seizures	35	26
Breathing pause	30	22
Upward gaze paralysis	22	16

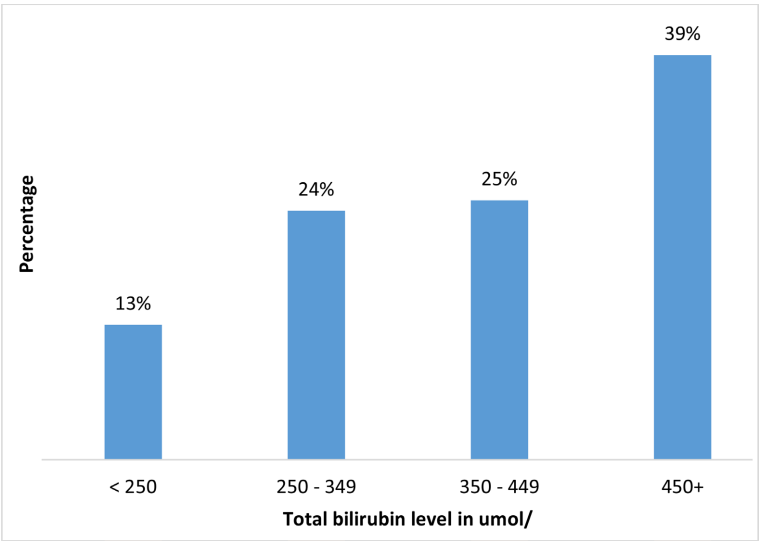

Figure 2. Distribution of cases by total bilirubin level.

Table 3. Distribution of cases according to the cause found.

Cause retained	Workforce	Percentage %
Infection	26	19
Rh alloimmunization	23	16.7
ABO alloimmunization	12	8.7
Prematurity	10	7.2
Alloimmunization subgroup	1	0.7
Cause not found	65	47
Total	137	100

Table 4. Correlation between deaths and signs.

		Deaths		p-value
		No	Yes	
Term of pregnancy	Premature	14 (47%)	16 (53%)	p = 0.029
	Term	49 (51%)	47 (42%)	
Hypertonia in opistotonos	Yes	23 (40%)	35 (60%)	p = 0.050
	No	36 (62%)	22 (38%)	
Breathing pauses	Yes	9 (30%)	21 (70%)	p = 0.037
	No	49 (59%)	34 (41%)	
Maximum bilirubin level in umol/L	<250	6 (46%)	7 (54%)	p = 0.559
	250 - 349	17 (71%)	7 (29%)	
	450+	22 (57%)	17 (43%)	

Therapeutic and evolutionary aspects: 45 patients (33%) had received intensive phototherapy, and only 2% had received exchange blood transfusion. Fourteen neonates (10%) did not receive phototherapy because it was unavailable. The case fatality rate was 48.9%. Deaths were significantly correlated with prematurity (p = 0.029). The occurrence of opistotonic hypertonia (p = 0.050) and respiratory pauses (p = 0.037) were significantly found to be poor prognostic signs (Table 4).

4. Discussion

We recorded 151 cases of acute bilirubin encephalopathy. In comparison, the reported prevalence in Western countries are much lower [11] [12] [13]. From 2011 to 2012, the National Reference Centre for Perinatal Haemobiology had identified only 5 cases of kernicterus in Ile de France [12]. In the United States From 1992 to 2004 over 13 years, a Pilot Registry of nuclear jaundice was set up and recorded 125 cases of nuclear jaundice [3]. In Canada, from 1999 to 2000, Suad F. recorded 12 cases of kernicterus [14]. However, global estimates show that the prevalence of acute bilirubin encephalopathy is much higher in

low-income countries, particularly in Sub-Saharan Africa (SSA), with a higher morbidity and mortality rate [7] [15]. In Nigeria, one study found a 15.3% incidence of bilirubin encephalopathy in 159 newborns treated for hyperbilirubinemia [9]. This high incidence of kernicterus in our study may have several explanations: poor prevention of rhesus alloimmunisation in maternity wards, lack of effective strategies for early detection of kernicterus in maternity wards, coupled with a policy of early discharge of newborns from maternity wards, poor awareness of the risks of kernicterus among health care providers, insufficient availability of phototherapy devices in neonatal units and maternity wards (**Table 1**).

There was a male predominance (sex ratio of 2.5). This result is in line with that of several authors [14] [16] [17]. There may be a genetic factor explaining this tendency to male predominance [18].

The majority (70%) of cases were full term newborns and 22% of cases were preterm newborns. But this reflects the fact that detection was not systematically performed in preterm infants. Preterm and low birth weight newborns have an increased risk of developing bilirubin encephalopathy compared to normal birth weight newborns. Indeed, hyperbilirubinemia is more frequent and its evolution more prolonged in the premature newborn compared to the full-term newborn, due to the immaturity of the purification systems, in particular at the hepatic level, and its toxicity for the central nervous system is more marked because the blood-brain barrier is itself more permeable due to the immaturity of the cell junctions. Cases of kernicterus have been reported for low bilirubin levels in premature newborns [19] [20].

The mean age at admission was 6 days of life. This mean age is generally reported as [3] [9]. Jaundice was early in onset in 40% of the newborns and half of the newborns (50%) had come from home. This is generally reported in the literature [3] [14] [17]. This can be explained by a lack of screening and follow-up of neonatal jaundice in neonatology units for multiple reasons: home births, short length of stay in maternity wards, delay between discharge from maternity wards and the first post-natal consultation which often exceeds the first week of life, delay in identification of jaundice in black skin by parents, socio-cultural beliefs, non-availability of neonatology units in some areas. Thus, in our series, the average delay of consultation was 3 days. This figure is comparable to that found by most authors [16] [19].

Neurological signs were dominated by: decreased archaic reflexes (74%), abnormal movements (59%), high-pitched cry (50%). The same signs were described by Faye P. M. in different proportions [10].

The mean bilirubin level was 416 umol/l. Several authors have looked at the indirect bilirubin concentration at which treatment should be initiated [20]-[25]. However, there is not necessarily a correlation between bilirubin levels and the occurrence of kernicterus, especially in preterm infants.

We found only 52% of the causes. These etiologies were dominated by neonatal infections (19%) followed by fetomaternal incompatibilities in the rhesus system (16.7%) and ABO system (8.7%). These same causes were reported by

Faye P.M. in different proportions: neonatal infections 33.3%, ABO incompatibilities 33.3% rhesus 20%. [10]. Similar proportions have been reported by several authors in Africa [7] [16] [19]. Haemolysis is the main cause of severe jaundice, whether it is linked to fetomaternal incompatibility or maternal-fetal infection or to a corpuscular anomaly [6] [26] [27]. G6PD deficiency is described as a frequent cause of severe jaundice in developed countries and in the Maghreb [3] [5] [14] [28]. In our patients, few investigations were performed in this sense but there would certainly be cases of G6PD deficiency among the 65 newborns (48%) whose etiologies were not explored. This is certainly due to the insufficient means of investigation in our hospitals, but also to the low socio-economic level.

Concerning the therapeutic and evolutionary aspects: only 33% of patients had benefited from intensive phototherapy against 58% under conventional phototherapy and only 2% from exchange transfusion. In the FAYE study, exchange transfusion was performed in 7 newborns (23.3%) [10]. The low use of intensive phototherapy in our study can be explained by the unavailability of phototherapy equipment in some neonatal units, especially in the periphery, as indicated in **Table 1**. Exchange transfusion is an intervention that requires a certain technicality, training, blood and pharmaceutical products, and consumables, which are often not available in some centers.

The case fatality rate was 48.9%. This figure is comparable to the 44.8% found by Merine S. [29] and 36.5% by Ogunlesi [30]. In contrast, Diala found 22% deaths in his study [9]. Deaths were significantly correlated with prematurity ($p = 0.029$).

Preterm newborns are considered to be at increased risk of kernicterus compared to term newborns [31] [32]. Ogunlesi previously reported prematurity, low birth weight and severe anaemia as important risk factors for mortality in patients with bilirubin encephalopathy [29]. This high mortality could be explained by the precariousness of the clinical condition of the premature baby and above all by the lack of equipment necessary for their overall management.

Our study has certain limitations. Our study was hospital-based, which did not allow us to deduce a general prevalence of this complication in Senegal. Nevertheless, we consider that this incidence of cases is excessive in view of the seriousness of kernicterus, if we consider that there is probably an underestimation, as many cases go unnoticed, especially when the newborn is preterm. As a retrospective study, we have not been able to assess the long-term evolution of bilirubin encephalopathy

5. Conclusion

Bilirubin encephalopathy remains a major public health concern, due to the high mortality and numerous neurological sequelae. Infections and fetomaternal incompatibility are the most frequent causes in our context. Progress in terms of early detection and adapted management must be obtained urgently on a na-

tional scale.

Conflicts of Interest

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

References

[1] Cortey, A., Renesme, L., Raignoux, J., Bedu, A., Casper, C., Tourneux, P., *et al.* (2017) Management of Jaundice in the Newborn ⩾ 35 GW: From Screening to Follow-Up after Discharge. Guidelines for Clinical Practice. *Archives de Pédiatrie*, **24**, 192-203. https://doi.org/10.1016/j.arcped.2016.11.011

[2] Maisels, M.J. (2009) Neonatal Hyperbilirubinemia and Kernicterus—Not Gone but Sometimes Forgotten. *Early Human Development*, **85**, 727-732. https://doi.org/10.1016/j.earlhumdev.2009.09.003

[3] Johnson, L., Bhutani, V.K., Karp, K., Sivieri, E.M. and Shapiro, S.M. (2009) Clinical Report from the Pilot USA Kernicterus Registry (1992 to 2004). *Journal of Perinatology*, **29**, S25-S45. https://doi.org/10.1038/jp.2008.211

[4] Manning, D., Todd, P., Maxwell, M. and Platt, M.J. (2007) Prospective Surveillance Study of Severe Hyperbilirubinaemia in the Newborn in the UK and Ireland. *Archives of Disease in Childhood-Fetal and Neonatal Edition*, **92**, F342-F346. https://doi.org/10.1136/adc.2006.105361

[5] Sgro, M., Campbell, D. and Shah, V. (2006) Incidence and Causes of Severe Neonatal Hyperbilirubinemia in Canada. *CMAJ Canadian Medical Association Journal*, **175**, 587-590. https://doi.org/10.1503/cmaj.060328

[6] Cortey, A. (2012) Jaundice in Newborns: The Return of Kernicterus. *Arch Pediatrics*, **19**, 897-899. https://doi.org/10.1016/j.arcped.2012.06.018

[7] Onalo, R. (2013) Neonatal Hypothermia in Sub-Saharan Africa: A Review. *Nigerian Journal of Clinical Practice*, **16**, 129-138. https://doi.org/10.4103/1119-3077.110120

[8] Olusanya, B.O., Ezeaka, C.V., Ajayi-Obe, E.K., Mukhtar-Yola, M. and Ofovwe, G.E. (2012) Paediatricians' Perspectives on Global Health Priorities for Newborn Care in a Developing Country: A National Survey from Nigeria. *BMC International Health and Human Rights*, **12**, Article No. 9. https://doi.org/10.1186/1472-698X-12-9

[9] Diala, U.M., Wennberg, R.P., Abdulkadir, I., Farouk, Z.L., Zabetta, C.D.C., Omoyibo, E., *et al.* (2018) Patterns of Acute Bilirubin Encephalopathy in Nigeria: A Multicenter Pre-Intervention Study. *Journal of Perinatology*, **38**, 873-880. https://doi.org/10.1038/s41372-018-0094-y

[10] Faye, P.M., Dieng, Y.J., Deme, I., Cissé, D.F., Kane, M., Cissé, D.F., *et al.* (2020) Neonatal Bilirubin Encephalopathy: Study of 30 Cases at Albert Royer National Children Hospital of Dakar. *Open Journal of Pediatrics*, **10**, 116-124. https://doi.org/10.4236/ojped.2020.101010

[11] Alkén, J., Håkansson, S., Ekéus, C., Gustafson, P. and Norman, M. (2019) Rates of Extreme Neonatal Hyperbilirubinemia and Kernicterus in Children and Adherence to National Guidelines for Screening, Diagnosis, and Treatment in Sweden. *JAMA Network Open*, **2**, e190858. https://doi.org/10.1001/jamanetworkopen.2019.0858

[12] Johnson, L. and Bhutani, V.K. (2011) The Clinical Syndrome of Bilirubin-Induced Neurologic Dysfunction. *Seminars in Perinatology*, **35**, 101-113. https://doi.org/10.1053/j.semperi.2011.02.003

[13] Ebbesen, F., Andersson, C., *et al.* (2005) Extreme Hyperbilirubinaemia in Term and Near-Term Infants in Denmark. *Acta Paediatrica*, **94**, 59-64.

[14] AlOtaibi, S.F., Blaser, S. and MacGregor, D.L. (2005) Neurological Complications of Kernicterus. *Canadian Journal of Neurological Sciences*, **32**, 311-315. https://doi.org/10.1017/S0317167100004182

[15] Bhutani, V.K., Zipursky, A., Blencowe, H., Khanna, R., Sgro, M., Ebbesen, F., *et al.* (2013) Neonatal Hyperbilirubinemia and Rhesus Disease of the Newborn: Incidence and Impairment Estimates for 2010 at Regional and Global Levels. *Pediatric Research*, **74**, 86-100. https://doi.org/10.1038/pr.2013.208

[16] Many, M.R., Mashako, Y.K. and Bitwe, R.M. (2018) Clinical Profile and Determinants for Nuclear Jaundice in Newborns at North-Kivu Provincial Hospital in Democratic Republic of Congo. *Annals of African Medicine*, **11**, e2918.

[17] Bhutani, V.K., Johnson, L.H., Maisels, M.J., Newman, T.B., Phibbs, C., Stark, A.R., *et al.* (2004) Kernicterus: Epidemiological Strategies for Its Prevention through Systems-Based Approaches. *Journal of Perinatology*, **24**, 650-662. https://doi.org/10.1038/sj.jp.7211152

[18] Watchko, J.F. and Lin, Z. (2010) Exploring the Genetic Architecture of Neonatal Hyperbilirubinemia. *Seminars in Fetal and Neonatal Medicine*, **15**, 169-175. https://doi.org/10.1016/j.siny.2009.11.003

[19] Baumann, R.J. (2001) Neurology of the Newborn. 4th Edition, WB Saunders Company, Philadelphia, 258-259. https://doi.org/10.1016/S0887-8994(01)00302-2

[20] Watchko, J.F. and Oski, F.A. (1992) Kernicterus in Preterm Newborns: Past, Present, and Future. *Pediatrics*, **90**, 707-715. https://doi.org/10.1542/peds.90.5.707

[21] Mutombo, A.K., Mukuku, O., Kabulo, B.K., Mutombo, A.M., Ngeleka, A.M., Mutombo, J.D., *et al.* (014) Pathological Jaundice in Neonates at Bonzola Hospital, Mbuji-Mayi, Democratic Republic of Congo. *The Pan African Medical Journal*, **19**, 302.

[22] Johnson, L. (1992) Yet Another Expert Opinion on Bilirubin Toxicity. *Pediatrics*, **89**, 829-831. https://doi.org/10.1542/peds.89.5.829

[23] Valaes, T. (1992) Bilirubin Toxicity: The Problem Was Solved a Generation Ago. *Pediatrics*, **89**, 819-821. https://doi.org/10.1542/peds.89.5.819

[24] Hansen, T.W.R. (2011) Prevention of Neurodevelopmental Sequelae of Jaundice in the Newborn. *Developmental Medicine & Child Neurology*, **53**, 24-28. https://doi.org/10.1111/j.1469-8749.2011.04059.x

[25] Ruud Hansen, T.W. (2010) Phototherapy for Neonatal Jaundice-Therapeutic Effects on More Than One Level? *Seminars in Perinatology*, **34**, 231-234. https://doi.org/10.1053/j.semperi.2010.02.008

[26] Ding, Y., Wang, S., Guo, R., Zhang, A. and Zhu, Y. (2021) High Levels of Unbound Bilirubin Are Associated with Acute Bilirubin Encephalopathy in Post-Exchange Transfusion Neonates. *Italian Journal of Pediatrics*, **47**, Article No. 187. https://doi.org/10.1186/s13052-021-01143-z

[27] Veenstra, C., Petersen, W., Vellekoop, I.M., Steenbergen, W. and Bosschaart, N. (2018) Spatially Confined Quantification of Bilirubin Concentrations by Spectroscopic Visible-Light Optical Coherence Tomography. *Biomedical Optics Express*, **9**, 3581-3589. https://doi.org/10.1364/BOE.9.003581

[28] Alkhotani, A., Eldin, E.E.M.N., Zaghloul, A. and Mujahid, S. (2014) Evaluation of Neonatal Jaundice in the Makkah Region. *Scientific Reports*, **4**, Article No. 4802. https://doi.org/10.1038/srep04802

[29] Smaili, L., El Alaoui, K., Guerblmous, F., Oulmaati, A., Atmani, S., Bouharrou, A., *et al.* (2010) P085-Maternal-Fetal Incompatibility in the Rhesus System. *Arch Pediatrics*, **17**, 71-72. https://doi.org/10.1016/S0929-693X(10)70486-3

[30] Merine, S.G., Benabdallah, A.C., Benyatou, C. and Benhamla, K. (2014) SFN P-14-L'encéphalopathie hyperbilirubinémique du nouveau-né. *Archives de Pédiatrie*, **21**, 627. https://doi.org/10.1016/S0929-693X(14)71887-1

[31] Ogunlesi, T.A., Dedeke, I.O.F., Adekanmbi, A.F., Fetuga, M.B. and Ogunfowora, O.B. (2007) The Incidence and Outcome of Bilirubin Encephalopathy in Nigeria: A Bi-Centre Study. *Nigerian Journal of Medicine*, **16**, 354-359. https://doi.org/10.4314/njm.v16i4.37337

[32] Gartner, L.M., Snyder, R.N., Chabon, R.S. and Bernstein, J. (1970) Kernicterus: High Incidence in Premature Infants with Low Serum Bilirubin Concentrations. *Pediatrics*, **45**, 906-917. https://doi.org/10.1542/peds.45.6.906

ANNEX

FILE NUMBER **DATE...../...../.....**

Survey Sheet

Characteristics of the Structure

- Name: .....
- Type: .....
- Number of births per year: .....
- Neonatology capacity: .....
- Phototherapy device:
  - Conventional:
    Number: .....
    Functional number: .....
  - Intensive equipment (Tunnel, Reflector) Number: .....
    Functional number: .....
- Number of paediatricians: .....
  - Number of nurses: .....

Epidemiological data

- Full name: .....
- Sex: M ☐ F ☐
- Age: .....
- Telephone: .....
- Address: .....

Maternal data

- Mother's age .....;
- Management .....;
- Parity .....;
- History of neonatal jaundice. .....;

Perinatal data

- Exact wording: .....
- Prematurity ☐; Full term ☐; Post term ☐
- Lower abdomen ☐; Caesarean section ☐
- Cry at birth: yes ☐ no ☐
- Birth weight.....gram
- Breastfeeding: Exclusive breastfeeding ☐; Exclusive formula ☐; Mixed ☐

Clinical data

- Mode of admission: Transfer ☐ Home ☐
- Data on jaundice
  - Age of onset.....days
  - Consultation period.....days
- Neurological signs
  - Refusal to suckle ☐
  - High-pitched cry ☐

- Head rejection ☐
- Upward gaze paralysis ☐
- Breathing pauses ☐
- Apnea ☐
- Convulsions ☐
- Lethargy ☐
- Consciousness disorders ☐
- AR drop ☐;
- Abnormal movements: Reptation ☐; Rolling ☐; Pedalling ☐
- Hypertonia in opistotonos ☐;
- Hypotonia ☐;

■ Other associated signs:

- Pallor ☐
- Fever ☐

Paraclinical

- Dehydration
- Undernutrition

■ Maximum bilirubin.....umol/L

■ G6PD assay ☐

■ Coombs test ☐

■ RAI ☐

Probable or proven cause of jaundice Hemolytic causes

■ ABO alloimmunisation ☐

■ Rhesus alloimmunisation ☐

■ Alloimmunisation in subgroups ☐

■ G6PD deficiency ☐

■ Pyruvate kinase ☐

■ Infectious jaundice ☐

Gluco-conjugation defect

■ Mother's milk jaundice ☐

■ Undernutrition ☐

■ Prematurity ☐

■ Crigler and Najjar ☐

Cause not found ☐

Treatment methods

■ Phototherapy

Type of device: Intensive ☐; Conventional ☐

Duration: .....

■ Exchange transfusion ☐

■ Transfusion ☐

Evolution

Length of stay: .....

➢ Deaths ☐

➢ Survival ☐

Transfer ☐