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Short-Term Outcomes and Complications of Premature Infants with a Birth Weight ≤ 1500g

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Abstract **Original Research Article**

Introduction: Premature infants represent a fragile population due to the immaturity of their vital functions. The prognosis of a premature infant is correlated with the conditions of medical care, both during and after birth, as well as the quality of the environment they are welcomed into. ***Objective***: The aim of our study is to highlight the complications and outcomes of premature infants with a birth weight ≤ 1500g, by identifying the factors of morbidity and mortality, and then comparing our results with other studies. ***Materials and Methods***: This is a retrospective descriptive, epidemiological, clinical, therapeutic, and developmental study conducted over a two-year period, from June 1, 2019, to June 30, 2021, in the neonatology and neonatal resuscitation unit at CHU HASSAN II of Fès. ***Results***: We reported a mortality rate of 54% among the newborns, with the main causes of death being alveolar hemorrhage (43.41%), septic shock (29.45%), and severe respiratory distress (20.93%). The main complications and conditions observed during the hospital stay were: hyaline membrane disease (35.26%), alveolar hemorrhage (26.14%), patent ductus arteriosus (14.93%), hemodynamic instability (56.01%), electrolyte imbalances (44.81%), neonatal jaundice (54.77%), anemia (46.05%), thrombocytopenia (54.77%), apnea of prematurity (51.81%), intraventricular hemorrhage (12.86%), and neonatal infection (85.89%). ***Conclusion***: The results of our study serve as a wake-up call for the necessity of implementing a management and prevention plan to improve the prognosis of premature infants with a birth weight ≤ 1500g.

Keywords: Prematurity – Very Low Birth Weight – Neonatal Morbidity – Neonatal Mortality.

INTRODUCTION

According to the World Health Organization (WHO), prematurity is defined as a birth occurring before 37 completed weeks of gestation, which is before the 25th day since the first day of the last menstrual period, but at least 22 weeks, regardless of the birth weight, but with a minimum of 500g [1]. It is considered a major public health issue. In conjunction with inadequate fetal growth (or intrauterine growth restriction), prematurity is now an indicator of the overall health status of newborns and a key determinant of the child's survival, health, and development [2]. The term "low birth weight" commonly associated with this condition speaks volumes about its prognosis.

Despite the numerous management protocols proposed, the incidence of prematurity has only slightly changed over the past 40 years [3]. Prematurity remains the leading cause of neonatal mortality in both developed and developing countries [3]. The conditions responsible for the deaths of these newborns can also lead to severe lifelong disabilities in those who survive.

The burden of intensive neonatal care due to prematurity significantly impacts healthcare systems. In some Western countries, the prevalence of prematurity ranges from 5% to 9% [4], while in Africa, it exceeds 15% [5]. In Morocco and the Maghreb region, it ranges from 6% to 9%, which is still considered high [6, 7].

It is subdivided into subcategories: low birth weight (birth weight < 2500g), very low birth weight (birth weight < 1500g), and extremely low birth weight (birth weight < 1000g).

Considering the low survival rate of premature infants with very low birth weight and the often irreversible harmful consequences for this neonatal population, it was essential to conduct a review of the

epidemiological, clinical, and developmental profile of these patients.

Thus, the objectives of our study are to determine the hospital frequency of premature newborns in the Neonatology and Neonatal Resuscitation Unit (NNRN) of CHU Hassan II of Fès, to describe the outcomes and short-term complications of premature infants with a birth weight of 1500g or less, as well as the short-term prognosis of this population.

METHOD

The study took place in the Neonatology and Neonatal Intensive Care Unit of the Hassan II University Hospital in Fez, which is a tertiary-level center located on the 3rd floor of the Mother and Child Hospital. The department welcomes newborns referred mainly by the maternity unit of the CHU Hassan II de Fès, provincial hospitals and clinics in the city of Fes and neighboring regions. The department comprises: a day hospital and 2 hospitalization units: a neonatal intensive care unit and a premature babies unit.

241 preterm newborns with a birth weight ≤ 1500 g were selected and included in this cross-sectional, descriptive study, conducted over a two-year period from June 1, 2019 to June 30, 2021.

The inclusion criteria were as follows: neonates with a gestational age of less than 37 weeks of amenorrhea and a birth weight of less than or equal to 1500g, whatever the reason for hospitalization. We isolated a total of 241 cases. Excluded were all term and post-term neonates with a birth weight less than or equal to 1500g, premature babies with a birth weight greater than 1500g, as well as those whose gestational age and/or weight were not specified on the record, and incomplete records.

To carry out this work, we collected information in two stages: Firstly, the files were identified by consulting the hospitalization registers for the years 2019, 2020 and 2021. This first step made it possible to extract information on the number, sex, gestational age and reason for hospitalization, as well as some evolutionary data such as death or survival of premature babies. It also enabled us to count all hospitalizations in the department. In a second phase, data from patient records and the computer archive were collected in ascending chronological order from June 2019 to June 2021, using a pre-established data processing form.

Statistical analyses were performed using JAMOVI software for Windows2016 (). Qualitative variables were presented as frequencies and percentages, while quantitative variables were presented as mean standard deviation (SD) or median (interquartile range, IQR).

RESULTS

During the period of our study (from June 1, 2019 to June 30, 2021), the Neonatology and Neonatal Resuscitation Unit at CHU Hassan II of Fez admitted 2736 newborns. Among these, 1127 were hospitalized in the preterm unit, resulting in a hospitalization rate of 41.19%. There were 241 premature infants with a birth weight of 1500g or less, accounting for 21.38% of all premature infants and 8.80% of all hospitalizations in the unit.

Birth asphyxia was assessed using the Apgar score, which was calculated at the 1st and 5th minutes for 202 newborns. The score was <7 at the 1st and 5th minutes in 41.58% and 17.32% of cases, respectively (84 and 35 cases). The mean Apgar score at the 1st minute was 6.28 ± 2.15.

A clinical examination for congenital malformations was performed on 234 newborns (97.09%). The detected malformations were distributed as follows: 3 cases of clubfoot, 2 cases of congenital hip dislocation, 1 case of toe morphological anomalies, 1 case of microcephaly, 1 case of facial dysmorphism, 3 cases of cryptorchidism, and 1 case of polymorphic syndrome.

Regarding the reasons for hospitalization: Respiratory distress (RD) occurred in 78.42% (189) of premature infants, making it the primary reason for hospitalization. This was followed by feeding difficulties. Additionally, 2.07% of all admissions included premature infants who had no underlying pathology and were therefore hospitalized for simple monitoring.

The age at admission ranged from 15 minutes to 13 days of life. The hospitalization rate during the first hour of life was 29.46% (71 cases). The delay in care was primarily attributed to a lack of available spaces in the unit.

In our series, 220 newborns, accounting for 91.28%, experienced respiratory distress (RD) at birth or during hospitalization. The main causes were transient respiratory distress (delayed resorption), hyaline membrane disease (HMD), and alveolar hemorrhage (AH), identified in 45.45%, 38.63%, and 28.63% of cases, respectively. Other causes of respiratory distress included 6 cases of aspiration (2.72%) and 3 cases of spontaneous pneumothorax (1.36%).

Among the 85 newborns with hyaline membrane disease (HMD), 32 had stage I/II HMD, 37 had stage III, and 16 had stage IV. The indication for intratracheal surfactant instillation was made for 69 of these patients. Sixty received a single dose, while 9 received a second dose due to lack of improvement in symptoms.

All newborns in our sample received nasal oxygen therapy or spontaneous ventilation with ambient air during their stay. A total of 128 (53.11%) were intubated due to the worsening of respiratory symptoms.

Hemodynamic instability led to the administration of vasoactive drugs (epinephrine and/or dobutamine) in 135 newborns (56.01%). A systematic echocardiogram was performed on all newborns, revealing patent ductus arteriosus (PDA) in 36 premature infants (14.93%). Among these, 30 newborns (83.33%) received medical treatment. The two medications used were ibuprofen and paracetamol. Twenty-three newborns received ibuprofen alone, 4 received paracetamol alone, and 3 received a combination of both medications. The route of administration was exclusively intravenous.

We recorded 35 cases of hypoglycemia and 18 cases of hyperglycemia, accounting for 14.52% and 7.46%, respectively. Neonatal jaundice occurred in 132 newborns, representing 54.77%. Phototherapy was the first-line symptomatic treatment for all affected patients (132). No cases of kernicterus were reported.

We considered anemia to be a hemoglobin level below 13 g/dl. 111 cases of neonatal anemia were recorded (46.05%). The average hemoglobin level was 10.04 ± 2.21 g/dl, with extremes ranging from 3.2 to 12.9g/dl. We considered thrombocytopenia to be a platelet count below 150,000 elements/mm³. 132 newborns (54.77%) developed thrombocytopenia during their hospitalization. The average platelet count was 69,590 ± 59,601 elements/mm³, with extremes ranging from 3,000 to 136,000elements/mm³. 75 newborns (30.70%) received transfusions with labile blood products (LBPs). The most commonly used LBP was red blood cell concentrate (RBC), administered to 68 patients, followed by fresh frozen plasma (FFP), administered to 35 patients, and platelet concentrate (PC), administered to 26.

The sucking reflex was present in 32 (13.27%) premature infants, weak in 167 (69.29%), and absent in 42 (17.42%). At birth, primitive reflexes were present in 121 (50.20%) newborns, weak in 96 (39.83%), and absent in 15 (6.22%). At least one apnea episode occurred in 51.86% (125) of the newborns. The pharmacological treatment used was caffeine. 117 newborns received loading and maintenance doses, while 8 did not receive them due to a lack of medication in the department. Intraventricular hemorrhages were the main detected lesions, found in 31 newborns (12.86%).

The diagnosis of neonatal infection (NI) was made in 207 newborns (85.89%). The analysis of various clinical, biological, and microbiological data allowed us to define three classes of NI:The infection was classified as confirmed in 35 newborns (16.90%) based on positive bacteriological findings, as probable in 36 newborns (17.39%) based on suggestive clinical context and/or biological abnormalities with negative bacteriological results, and as possible (or unlikely) in 136 newborns (65.70%) based on a suggestive clinical context and/or biological abnormalities without bacteriological evidence. A bacteriological examination was performed in 71 newborns, and the result came back positive with germ isolation in 35 newborns. The most frequently identified pathogen was *Klebsiella pneumoniae* (71.42%).

We regrettably reported the death of 129 premature infants, representing a hospital mortality rate of 54%. Alveolar hemorrhage was the leading cause of neonatal mortality (43.41%), followed by septic shock (29.45%) and severe respiratory distress (20.93%).

In our study, we were able to identify several causes and factors contributing to the occurrence of preterm births, many of which were intertwined. Maternal infection was found to be the most frequent cause, present in 30.30% of cases. This was followed by multiple pregnancy, responsible for 14.11% of preterm births, and the combination of maternal infection with multiple pregnancy, identified in 10.79% of cases. Preeclampsia, a common pregnancy complication, was observed in 22.40% of patients. However, in 15.36% of cases, prematurity remained unexplained, highlighting the complexity and multifactorial nature of this phenomenon.

DISCUSSION

Adaptation to Extra-Uterine Life

The Swedish study by S. Cnattingius *et al*., [8], based on a large national cohort of preterm infants born between 1992 and 2016, showed that low Apgar scores at 5 minutes and 10 minutes were associated with higher relative risks of neonatal mortality ($p<0.05$). Similarly, a retrospective study by Bernard Barzilay *et al*., [9], conducted at Shamir Medical Center in Tel Aviv, involving very low birth weight preterm infants born between 1997 and 2013, demonstrated the same finding. The results revealed that the Apgar score was inversely associated with an increased risk of death in preterm newborns. Our study further supports the validity of the Apgar score in assessing mortality risk among very low birth weight preterm newborns. The analysis showed that an Apgar score below 7 at 5 minutes of life (indicating poor adaptation to extra-uterine life) was statistically correlated with neonatal mortality risk ($p = 0.028$).

Respiratory Disorders

Neonatal respiratory distress is defined as any breathing difficulty encountered before the age of 28 days, linked to disturbances in gas exchange leading to cerebral anoxia. It is an emergency where clinical examination, etiological investigation, and symptomatic treatment must be conducted simultaneously to avoid death or severe sequelae caused by hypoxemia [10]. In our series, the incidence rate of neonatal respiratory

distress (NRDS) (across all pathologies) was 91.28%. Its occurrence was statistically associated with the risk of neonatal mortality (P=0.001).

Neonatal respiratory distress (NRDS), whether of medical or surgical origin, is primarily summarized by three conditions: hyaline membrane disease (HMD), caused by pulmonary surfactant deficiency; delayed absorption of alveolar fluid, which causes moderate respiratory distress generally with a favorable outcome; and pulmonary infection, presenting as an infectious alveolitis mimicking HMD [11]. In our study, the main causes of NRDS were transient respiratory distress (delayed fluid absorption), hyaline membrane disease (HMD), and alveolar hemorrhage (AH), identified in 45.45%, 38.63%, and 28.63% of cases, respectively. NRDS was more severe in cases of lower gestational age. This finding is also reported by Amri F in their study [7]. It also occurred in cases of absence of antenatal corticosteroid therapy and vaginal birth. The use of antenatal corticosteroid therapy helped prevent the occurrence of HMD, confirming the data in the literature [12].

Apnea of prematurity also presents a concerning problem due to its frequency and the potential consequences. Apneas are defined as respiratory pauses, sometimes prolonged (>20 seconds), accompanied by bradycardia (less than 100 beats per minute) and/or desaturation with cyanosis [11-13]. Apneas can be essential due to the immaturity of respiratory control centers or can indicate an underlying pathology (anemia, gastroesophageal reflux, neurological disorders, infection…) [11]. Generally, they only appear after a few hours or days of life and are consistently observed in infants born before 28 weeks of gestation. In our population, at least one episode of apnea occurred in 51.86% (125) of newborns.

Neonatal Infection

Neonatal infections can either cause or complicate prematurity and remain a major cause of morbidity and mortality today. The susceptibility of preterm infants to neonatal infections is multifactorial but largely relies on the immaturity of their various immune systems. This immaturity can be a handicap during the hospital stay, a period in which the premature newborn is prepared for discharge to home. During this time, preterm infants are exposed to infections they share with other patients. These infections are much more frequent in preterm infants than in full-term newborns, likely reflecting their immune immaturity, which is more profound the greater the prematurity [11].

In our series, the incidence of neonatal infections (NI) was 85.89%. This rate is almost identical to the one reported by Barkat A. *et al*., which was 84.1%. The diagnosis of NI was made based on a combination of anamnesis, clinical, and biological evidence. Infection was classified as confirmed in 16.90% of newborns with a positive bacteriological result. Infection was considered probable in 17.39% of newborns based on suggestive clinical context and/or biological abnormalities with negative bacteriological results. Infection was classified as possible (or unlikely) in 65.70% of cases, based on a suggestive clinical context and/or biological abnormalities without bacteriological proof. Statistical analysis demonstrated that neonatal infection is significantly associated with neonatal mortality ($p<0.001$).

Neurological Complications

The incidence of intraventricular hemorrhage (IVH) in preterm infants varies widely in the literature depending on the nature of the studied population (Table 1), ranging from 20.9% according to Marba *et al*., [14], to 64.4% according to Sajadian N. *et al*., [15]. In our population, IVH occurred in 31 newborns, resulting in an incidence rate of 12.86%. This rate is significantly lower than those reported in the literature. The risk of developing IVH was inversely proportional to gestational age (GA) and birth weight (BW) ($p < 0.01$ for each).

Table 1: Incidence of Intraventricular Hemorrhage (IVH) in the Literature

Author	Population Characteristics	Incidence (%)
Sajadian N. *et al*., (15)	< 37 weeks GA and < 1500g	64.4
Lee *et al*., (16)	< 34 weeks GA	27.8
Adegoke *et al*., (17)	< 1500g	24.1
Marba *et al*., (14)	< 1500g	20.9
Our series	< 37 weeks GA and < 1500g	12.86

There is no specific treatment for intraventricular hemorrhage (IVH). Management consists of addressing the factors that promote IVH and providing symptomatic treatment for the consequences of significant IVH (hypotension, anemia, acidosis, shock, treatment of seizures). After birth, it is essential to avoid any sudden changes in temperature and blood volume [18]. Prenatal pharmacological prevention through antenatal maternal corticosteroid therapy significantly reduces the incidence of IVH of all grades. The protective mechanisms of corticosteroids appear to be related to improved respiratory function, stabilization of blood pressure, and a maturational effect on the germinal zone.

Hematopeietic Disorders

The causes of anemia in preterm newborns are numerous, including early clamping of the umbilical

cord, hemorrhagic delivery, impaired erythropoiesis, increased physiological hemolysis, multiple blood draws, iron deficiency, and more [11]. These causes can manifest in the first days of life as well as during the first weeks. In our study, anemia was present in 46.5% of cases. Hemostasis disorders, on the other hand, are primarily due to vascular fragility and decreased coagulation factors, characteristics that are particularly pronounced in preterm infants [11].

Metabolic Disorders

In preterm infants, neonatal jaundice is more frequent, earlier, prolonged, and more intense than in full-term newborns due to the immaturity of bilirubin metabolism [11]. Additionally, preterm infants exhibit relative hypoalbuminemia, as the developing body prioritizes the production of structural proteins over transport proteins [19]. In our study, the incidence rate of neonatal jaundice (across all etiologies) was 54.77%.

Mortality

Prematurity remains the leading cause of neonatal mortality worldwide, particularly in developing countries. The figures vary from one study to another, which can be attributed to differences in methods for calculating mortality: some authors base their statistics on the overall rate of preterm births, while others consider only live births. Additionally, the size of the studied populations and age groups differ across studies. In developed countries, the survival rate of preterm infants has significantly increased, thanks to optimized maternal-fetal care. Since the mid-1990s, data concerning the mortality of preterm infants born after 32 weeks of amenorrhea (WA) has not been reported in these countries, which now focus on the outcomes of very preterm infants.

In the series by Gupta *et al*., [20], the mortality rate for preterm infants with gestational age (GA) less than 37 weeks and birth weight (BW) less than 1500 g was 21.33%. In comparison, in the series by Tsou *et al*., [21], the mortality rate for preterm infants with GA between 27 and 36 weeks and BW less than 1500 g was 12.5%.

Table 2: Mortality Rates in the Literature

Author	Population Characteristics	Mortality Rate (%)
Gupta *et al*., (20)	< 37 weeks GA and < 1500g	21.33
Tsou *et al*., (21)	26-36 weeks GA and < 1500g	12.5
Iriondo *et al*., (22)	< 1500g	13.47
AlQurashi *et al*., (23)	23-33 weeks GA and < 1500g	18.8
Fernández *et al*., (24)	24-32 weeks GA and < 1500g	26
Our series	< 1500g	54

The two main factors associated with neonatal mortality in the above series were gestational age and birth weight.

CONCLUSION

Our study highlights valuable data that will contribute to advancing scientific knowledge about the risk factors influencing morbidity and neonatal mortality among very low birth weight preterm infants in our context.

Our results show that the incidence of prematurity remains high, despite significant progress made in obstetrics and neonatology. Very low birth weight preterm infants exhibit increased morbidity and mortality, with rates rising as gestational age and birth weight decrease. Early diagnosis and appropriate management of these conditions are essential to prevent negative effects on the newborn, which can range from minor damage to severe complications that may compromise vital prognosis.

The main complications observed were hyaline membrane disease (HMD), patent ductus arteriosus (PDA), nosocomial neonatal infections (NNIs), hematological disorders, and intraventricular hemorrhages (IVHs). Rapid identification of these conditions is crucial for remediation. Among the major causes of neonatal death, we identified alveolar hemorrhage and neonatal sepsis, for which specific, tailored, and immediate therapeutic measures must be implemented to prevent often fatal outcomes.

To improve the prognosis for preterm infants and strengthen preventive actions, we emphasize the importance of:

- Early identification of pregnant women at risk of preterm birth to offer preventive treatment outside of emergency situations.
- Coordination and collaboration among professionals in perinatal networks (obstetricians, neonatologists, midwives, etc.).
- Enhancing the skills of healthcare personnel to improve the quality of prenatal consultations.
- Active involvement of pregnant women in monitoring their pregnancy.
- Adequate equipping of neonatal services according to needs.

This integrated approach would enable better prevention and management of prematurity, aiming to reduce neonatal morbidity and mortality in our context.

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