

Review Article

Hyaline membrane disease in premature infants: clinical, therapeutic and evolutionary aspects

Abstract

Introduction: Hyaline membrane disease is an anatomoclinical entity related to a quantitative or qualitative insufficiency of pulmonary surfactant.

Patients and methods: This was a retrospective study conducted at the National Reference Center for Neonatology and Nutrition, spread over a period of one and a half years.

Results: Antenatal corticotherapy was given in only 20% of cases.

Pregnancy pathology was divided between preeclampsia, gestational diabetes and gestational hypertension. 66.6% of deliveries were by caesarean section before the onset of labour. Mean gestational age was 33.9 ± 1.5 weeks' amenorrhea, with 10% of patients less than 30 weeks' amenorrhea of gestational age.

Mean weight was 1677 ± 463 g. The very low birth weight population (birth weight < 1500) represented 46.6%. Females predominated, with a sex ratio of 1.12. Tracheal intubation with respiratory assistance was used in 66.6% of cases. 73% of neonates received exogenous surfactant, due to the extent of hypoxemia. Progression was favourable in only 26% of cases.

Conclusion: In Morocco, MMH is a major cause of neonatal morbidity and mortality, requiring rapid diagnosis and early management.

Keywords : Hyaline membrane disease, Antenatal corticotherapy

Introduction:

Respiratory distress is one of the main causes of morbidity and mortality in the neonatal period. It is a symptom common to several pathologies, including hyaline membrane disease (HMD). This pathology is an anatomoclinical entity linked to a quantitative or qualitative insufficiency of pulmonary surfactant.

MMH occurs preferentially in premature infants. Its incidence is inversely proportional to gestational age (GA).

Vital prognosis is closely linked to the degree of prematurity, and death may be inherent to

the severity of HMM, but also to associated complications.

The aim of our study is to evaluate the frequency of hyaline membrane disease (HMD) in relation to other etiologies of neonatal respiratory distress in premature infants, to estimate its incidence and to analyze its various clinical, therapeutic and evolutionary characteristics in relation to data in the international literature.

Patients and methods:

This is a retrospective study carried out at the National Reference Center for Neonatology and Nutrition, CHU Ibn Sina, Rabat, over a period of one and a half years, from January 2020 to May 2021. We developed data sheets on which we recorded the clinical and therapeutic characteristics and the evolution of the disease.

To carry out this retrospective study, we selected from among newborns admitted to the neonatal intensive care unit of the National Reference Centre for Neonatology and Nutrition, a population of children fulfilling the following criteria:

- A gestational age (GA) \leq 37 weeks of amenorrhea, established on calculation of the theoretical duration of gestation from the first day of the last menstrual period and early ultrasound data (before 12 weeks of amenorrhea) whenever this examination has been performed. Clinical evaluation of term according to morphological and neurological criteria was used as a secondary criterion for term assessment;

- The existence of a neonatal respiratory distress syndrome related to hyaline membrane disease, diagnosed in the presence of early respiratory distress with oxygen dependence requiring assisted ventilation, and a radiological appearance combining low pulmonary expansion, diffuse alveolar syndrome with a homogeneous decrease in lung parenchyma transparency and an aeric bronchogram.

We excluded from our study:

- Cases of hyaline membrane disease associated with various pathologies: major

malformations, congenital heart disease and chromosomal aberrations.

- Newborns less than 27 weeks' amenorrhea and/or with a birth weight ≤ 750 grams, for whom a collegial decision to abstain from resuscitation had been made.

Maternal characteristics (medical history, infectious anamnesis, number of gestation and parity), course of pregnancy (follow-up, antenatal corticosteroid therapy, pregnancy pathology), birth circumstances (mode of delivery, acute fetal distress (AFS)), characteristics of the newborn (GA, sex, weight, minor or major malformative pathology) and characteristics of neonatal respiratory distress (clinical and radiological aspects, management and evolution).

Results:

This study involved a total of 60 premature newborns according to the above criteria.

Infectious anamnesis was positive in 30% of cases.

Primiparous in 30% of cases.

Pregnancy was monitored in 56% of cases, and antenatal corticosteroids were given in 20% of cases.

Pregnancy-related pathology was divided between preeclampsia, gestational diabetes and gestational arterial hypertension.

Delivery was by caesarean section in 66.6% of cases, $\frac{3}{4}$ of which were performed outside labour.

Mean duration of labor was 17h.

The average GA in our series was 33.9 ± 1.5 weeks' amenorrhea; in 10% of cases, premature babies were born at less than 30 weeks' amenorrhea.

The mean birth weight in our series was 1677 ± 463 gr. The very low birth weight population (birth weight < 1500) represented 46.6%. Considering all premature babies born during the study period, the incidence of hyaline membrane disease decreased with increasing birth weight.

The proportion of boys was 47% versus 53% for girls, giving a sex ratio of 1.12. 54.6% of newborns had an Apgar score >7 at the first minute, indicating poor adaptation to extrauterine life.

The average response time was five hours. We used tracheal intubation with respiratory assistance in 66.6% of cases.

The average time of assisted ventilation with $FIO_2 \geq 30\%$ was 6 days. 73% of newborns received exogenous surfactant due to the importance of hypoxemia.

The rate of pneumothorax was 3%, especially when the treatment time was long and the diagnosis was late. 6% of the subjects had pulmonary artery hypertension. 5% of the primates developed bronchopulmonary dysplasia.

The average duration of hospitalization was eighteen days.

Respiratory distress was severe in 45% of cases (Silverman score greater than 3/10).

The majority of patients had stage I HMM (40%)

The majority of patients had hypoxia with or without acidosis associated with pulmonary shunt intra. We noted hypercapnia in 30% of cases (severe forms and/or as part of hypoventilation).

Discussion:

Hyaline membrane disease was first described by Avery in 1959 and has been defined as a quantitative and qualitative deficit of the surfactant [1]. Since then, studies have been conducted to identify the epidemiological, clinical, evolutionary and therapeutic aspects of this disease.

The main risk factors for MMH identified in our study were preeclampsia, pre-birth caesarean, absence of prenatal corticosteroid therapy, gestational age, female sex and very low birth weight.

Caesarean birth was in 66.6% of which 3/4 were performed outside labor. The rate of induced

prematurity for our population was 60%.

Indeed, Herbst and Kallen [2] find that the risk of HMM increases significantly after a Caesarean section, while Malhotra et al. [3] and Wolf and al. [4] find no significant reports. A more recent 6-year (2007-2012) retrospective study attempting to assess the impact of elective cesarean in late premature babies (34 WA-37WA) concluded that these newborns are at a higher risk of developing MMH after elective caesarean. This risk is influenced by each additional week in utero [5].

The use of prenatal corticosteroids is one of the major advances in obstetrics in recent years and allows the prevention of some complications of premature childbirth. It is one of the only prenatal therapies, if not the only one, that has radically improved the neonatal status of premature babies. Its emergence was essentially revealed by Crowley's meta-analysis in 1995 [6] and confirmed in the latest review of the Cochrane collaboration [7].

Our population has been special because of the great prematurity. The average gestational age in our series was 33.9 ± 1.5 WA; in 10% of cases, they were premature babies of less than 30 WA. Similarly, we noted that the incidence of MMH was inversely proportional to gestational age with a highly statistically significant difference.

These data are consistent with those found in the literature [8, 9]. It should be noted that a significant number of newborns develop an HMM or secondary surfactant destruction syndrome. [8]

The average birth weight in our series was 1677 ± 463 gr. The population with very low birth weight (birth weight < 1,500) was 46.6 per cent.

These results are consistent with those in international literature [10, 11].

Conclusion:

The epidemiological data in our study highlight the high levels of HMM in premature babies. The improvement in this figure involves the introduction of a prevention policy involving

various measures, some of which are very simple: monitoring of pregnancy; equipping of laboratory facilities; prompt transfer, in a medicated transport; and strict hygiene measures in neonatology. Other measures must address the various risk factors. Thus, it is essential to initiate prenatal corticosteroid therapy in a timely manner and to reconsider, on a case-by-case basis, the indications of caesarean before labor and especially in situations of intrauterine growth delay by making a proper risk assessment in relation to the benefit of induced prematurity.

References

- 1- Avery ME, Mead J. Surface properties in relation to atelectasis and hyaline membrane disease. *AM J Dis Child.* 1959;97:517-523.
- 2- Herbst A, Kallen K. Influence of mode of delivery on neonatal mortality in the second twin, at and before term. *BJOG.* 2008;115(12):1512-7
- 3- Malhotra D, Gopalan S, Narang A. Preterm breech delivery in a developing country. *Int J Gynecol Obstet.* 1994;45(1):27-34.
- 4- Wolf H, Schaap AH, Bruinse HW, Smolders-de Haas H, Van Ertbruggen I, Treffers PE. Vaginal delivery compared with cesarean section in early preterm breech delivery: a comparison of a long-term outcome. *Br J Obstet Gynecol.* 1999;106(5):486-91.
- 5- Rinaldi M, Maffei G, Cella A, Guglielmi M, Popolo P, Matteo M et al. Respiratory distress syndrome after caesarean section in late preterm infants: a 6-year cohort study. In: *Early Human Development, dir. 5th International Conference on Clinical Neonatology; September 11-13, 2014; Torino, Italy. Ireland: Elsevier Ireland Ltd; 2014. p. 61-79.*
- 6- Crowley PA. Antenatal corticosteroid therapy: a meta-analysis of the randomized trials, 1972 to 1994. *Am J Obstet Gynecol.* 1995;173:322-35.
- 7- Roberts D, Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev.* 2017-mar21;3:CD004454.
- 8- Grisar-Granovsky S, Reichman B, Lerner-Geva L, Boyko V, Hammerman C, Samueloff A et al. Mortality and morbidity in preterm small-for-gestational-age infants: a population-based study. *Am J Obstet Gynecol.*

2012;206(2):150.e1-7. 33.

9-Lorotte-Namouni S, Clamadiou C, Jarreau PH. Détreffes respiratoires du nouveau-né (en dehors des malformations et des maladies génétiques ou constitutionnelles). EMC Pédiatrie. 2004 ;152-170.

10- Al Hazzani F, Al Alaiyan S, Hassanein J, Khadawardi E. Short term outcome of very low birth weight in a tertiary care hospital in Saudi Arabia. Ann Saudi Med. 2011;31:581– 5. 34.

11- Horbar JD, Soll RF, Edwards WH. The Vermont Oxford Network: a community of practice. Clin Perinatol. 2010;37(1):29-47

UNDER PEER REVIEW