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Original article

Data study on preterm newborns with gestational age of 32 weeks or less in a perinatal hospital in Portugal

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Abstract

Introduction: Despite advances in the knowledge of the circumstances surrounding preterm delivery, in a considerable number of cases there are still some unknown aspects.

Aims: The objective of the current work is to characterize and analyze data relating to familial antecedents and the gestation of preterm newborns with 32 or less weeks of gestational age at birth admitted to the neonatal intensive care unit of a differentiated perinatal hospital in Portugal.

Material and methods: Through the use of a prospective, descriptive and opportunistic questionnaire and by reviewing the mother's and newborn's case notes, data was collected focusing on information relating to the newborn, pregnancy, mother, household and family history, based on a sample of 51 mothers and 65 newborns.

Results: The sample included more than 50% of the preterm newborns born in the period of time studied. The main results showed that 52.9% of the mothers were aged 18-34 years, most of them had a favorable socioeconomic position, and 49% suffered from congenital/chronic disease. About 25.4% of pregnancies were the result of medically assisted reproduction and 25.5% involved invasive prenatal diagnosis. About 60.8% of the women needed hospitalization during pregnancy and the main reason for hospitalization in the delivery room was labor induction (45.1%). With regards to newborns, 2 had congenital malformations, a minority had fetal growth restriction and 3 died.

Conclusions: In this descriptive study we registered the fact that preterm mothers had important pre-existing chronic conditions and many needed hospitalization during pregnancy. The preterm birth was medically induced in about 45% of cases due to maternal/fetal pathology. This data can be the starting point for a case-control study.

Keywords

Newborn, prematurity, neonatal intensive care unit, maternal chronic disease, preterm induced birth.

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Introduction

Preterm birth (PTB) is defined as delivery occurring before 37 weeks (w) of gestation. The determinants of prematurity have been the subject of many studies and from different perspectives. The three major events that determine PTB are: the onset of spontaneous labor (SL) with intact membranes, premature rupture of membranes (PRM) and the medical decision to opt for to labor induction (LI) or cesarean birth due to maternal or fetal factors [1]. The global incidences identified for each of these situations are respectively 45-50%, 30% and 15-20% [2]. There are several situations for which the causality and pathogenesis of PTB are documented, namely the activation of the hypothalamic-pituitary-adrenal axis associated with maternal anxiety/depression or fetal stress, systemic or organ infection, decidual bleeding and pathological uterine distension [3-5]. Although the etiology of PTB is considered multifactorial, it is unclear whether it results from the interaction of several pathways or is the independent effect of a single factor [2]. Despite the great advances in Obstetrics and Neonatology, in a considerable number of cases of prematurity the causes are still unknown.

Prematurity is a complex public health problem since it is the main determinant of neonatal morbidity and mortality, accounting for about 27% of worldwide neonatal deaths each year. The risk of neonatal mortality is higher the lower the gestational age (GA), but this relationship is not linear. The premature neonate will be at greater risk of short-term and long-term morbidity compared with a term neonate [3]. The neonates with GA of less than 32 w and weighing less than 1,500 grams (g) are those at higher risk of death, neurodevelopmental disorders, respiratory problems and gastrointestinal diseases [2-8]. The need for newborns' (NBs) hospitalization in a specialized healthcare unit, such as Neonatal Intensive Care Units (NICUs), and the need for subsequent follow-up due to chronic clinical repercussions from prematurity result not only in more severe physical and psychological consequences but also in significant economic costs.

In Portugal, for every 100 NBs 8 are premature [9]. According to the National Statistical Institute, from 2010 to 2015 the percentage of premature live births increased from 7.7% to 8% [10].

The factors that have been associated with PTB are [11-20]: maternal history of gynecological/obstetric pathology (uterine malformations, uterine leiomyomas or history of cervical insufficiency/surgery), history of previous PTB (22% risk of PTB in the next pregnancy), history of abortion/s in the 2nd trimester, maternal age younger than 18 and older than 40 years, African American ethnicity, family history of PTB, maternal underweight, maternal overweight or obesity, chronic disease (such as autoimmune disease or depression associated with selective serotonin reuptake inhibitors therapy), periodontal disease, lifestyle factors (smoking, alcohol or drug use, maternal malnutrition, domestic violence, motor vehicle crash, low socioeconomic status, anxiety) and low education level. The pregnancy-related causes listed as risk factors are: short interval since last pregnancy (< 6 months between the date of the last delivery and the date of the last menstrual cycle), assisted reproduction technologies, inadequate prenatal care, multiple pregnancies, preeclampsia, early vaginal bleeding in pregnancy, cervical insufficiency, urogenital (including asymptomatic bacteriuria) or systemic infections, maternal diabetes and PRM.

Fetal factors are also relevant, especially fetal growth restriction (FGR), fetal malformations and male sex [7]. The occurrence of PTB does not appear to be related to parental factors [21].

In order to minimize the burden of prematurity for NBs, families and society, it is extremely important to know all the data accompanying PTB.

The purpose of this paper is to characterize and analyze data relative to familial antecedents and

the gestation of preterm NBs born at or below 32 w of GA admitted to the NICU of a differentiated perinatal hospital in Portugal.

Material and methods

A prospective and descriptive study was carried out with a convenience sample of mothers of NBs with GA ≤ 32 w, hospitalized in the NICU of a differentiated perinatal hospital in Portugal. A questionnaire survey was developed and administered for this purpose (after signing an informed consent form) during the period from 1 June 2013 to 31 December 2014 to the mothers while still hospitalized in the period following the PTB. In order to complete/confirm the information, the mother's and the NB's case notes were also consulted. The survey included questions related to the mother's history, pregnancy, family history and NB's.

In the social class evaluation, an adaptation of Machado and Costa's classification was used [22].

Statistical analysis was performed using simple and conditional frequencies for qualitative variables and minimum, median, maximum, mean and standard deviation for the metric scale variables. Data analysis was performed using IBM® SPSS® statistical software for data handling, version 22.

The study was approved by the Ethics Committee of the hospital where it was performed and authorized by the hospital's Clinical Director. A signed written consent was obtained from all the mothers surveyed.

Results

We studied the gestations of 51 mothers and their 65 preterm NBs born at ≤ 32 w of gestation (51% of a total of 127 NBs admitted to the NICU in this period). The mean mothers' age was 32.9 and median 34 years. Some other maternal factors are described in **Tab. 1**. We were able to verify that 86.3% of the mothers were Caucasian, 23.5% had a Body Mass Index (BMI) > 25 and 5.9% had a BMI < 18.5 before becoming pregnant. Regarding nationality, 78.4% of the mothers were Portuguese, 7.8% were from other European countries, 11.8% from African countries and 2% from Brazil; 51% of the mothers were in common-law marriages, 39.2% were married and only 9.8% were single. About 45% of mothers had higher education, 25.5% had primary education, 23.5% had secondary education and 5.9% had vocational training.

Table 1. Characterization of maternal age, parity, history of abortions and history of preterm birth (PTB).

	%
Age (years)	
18-34	52.9 (n = 27)
≥ 35	47.1 (n = 24)
Parity	
Primiparous	49 (n = 25)
2	19.6 (n = 10)
3	17.7 (n = 9)
4 or +	13.7 (n = 7)
History of abortions	
1st trimester	29.4 (n = 15)
2nd trimester	5.9 (n = 3)
History of PTB	9.8 (n = 5)

PTB: preterm birth.

Regarding the mothers' employment, it was verified that 37.3% had jobs as senior managers, leaders and specialists in intellectual and scientific professions; 29.4% were students or unemployed; 27.5% were mid-level technicians/professionals; 5.9% worked in jobs requiring little or no education. As to the fathers, 43.1% held higher education professions, 27.5% technical training professions, 23.5% jobs requiring few or no qualifications and 5.9% were unemployed. As for housing conditions, only 1 family was found to have a ratio of persons/room greater than 2. In 86.3% of the cases the families were nuclear, 5.9% were single-parent families, 5.9% extended families and 2% step families. About 80.4% of the families could rely on financial or care support for the NB from family members or friends, if needed. Apparently, most families had a favorable socioeconomic level ascertained by the indicators father's and mother's profession, mother's education, number of people per room and mother's marital status.

Five mothers had a congenital disease (tetralogy of Fallot, truncus arteriosus, aortic bifurcation aneurysm, hereditary otosclerosis and renal agenesia) and 20 had a chronic disease, namely 5 with cardiovascular disease (e.g. arterial hypertension) and 4 with endocrine disease (such as hypothyroidism, Hashimoto's thyroiditis and polycystic ovaries). There were 3 cases of mothers with autoimmune disease (Behçet's disease, ankylosing spondylitis and type-1 diabetes). Six mothers had a history of gynecological conditions or procedures: 4 with benign pathology of the uterine body (such as fibroids or uterine septum), 2 with endometriosis and 1 with a history of conization. In 33.3% of the families, there was at least 1

member, up to the third degree of relationship with the NB, with a history of congenital or chronic disease (excluding maternal diseases and aging/degenerative diseases in adult relatives), making up a total of 19 members. Of these, we highlight 3 cases of chromosomal congenital disease.

It was found that 18 mothers had a history of at least 1 abortion in the first or second trimester (3 had 2 abortions and 4 more than 3 abortions). In 8 mothers the cause was unknown, in 5 it was due to extra-uterine/anembryonic pregnancy, 1 due to placental pathology, 1 due to uterine malformation, 1 due to fetal malformation and 2 due to voluntary termination of pregnancy. In the characterization of abortions, it was decided to exclude cases of feticide from the gestation under study. Regarding the time elapsed since the gestation in question and the last gestation, in 5.9% of the mothers this period was less than 6 months, in 3.9% the period was between 6 and 11 months and in 7.8% from 12 to 17 months. Only 2 puerperal women reported that their mother had a history of PTB and 5 had a history of at least 1 previous PTB.

As for the variables directly related to the 51 pregnancies studied, 31.4% were twin pregnancies. Of these, labor occurred in 25% between 25 w and 27 w + 6 days (d) of gestation and 75% between 28 w and 32 w + 6 d. The mean GA was 29.5 w and the median was 30 w. Out of the total pregnancies, 25.4% were the result of medically assisted reproduction (**Tab. 2**).

Regarding maternal habits, 21.6% of the women smoked during their pregnancies and 15.7% were passive smokers. Only 1 puerperal woman consumed illicit drugs during pregnancy, more specifically cannabinoids. No puerperal women mentioned consuming alcohol after learning they were pregnant. Concerning anxiety, 7.8% of pregnant women had to take oral therapy for this disorder.

Only 21.6% of the mothers reported having made physical efforts such as household chores, babysitting or sports during pregnancy. Only 1 woman (2%) reported a fall from the standing position, which did not affect the date of delivery.

Tab. 3 shows the main complications of these pregnancies as well as the need for invasive prenatal diagnosis. In 2 cases of twin pregnancies there was alteration in the fetal karyotype and in 2 pregnancies feticide was performed on the affected fetus. In 1 case, fetal-fetal anastomoses were ablated in the context of feto-fetal transfusion syndrome. In the total of 12 pregnancies diagnosed with FGR, 4 were diagnosed in twin pregnancies (this diagnosis occurred only in 1 fetus).

About 60.8% of the pregnant women were hospitalized at least once in an obstetrics unit, with later discharge or transfer to the delivery room.

As to the clinical reason that led to the hospitalization in the delivery room of the pregnant woman, 45.1% of cases were due to medical decision to induce labor or perform cesarean delivery due to maternal or fetal factors (LI), 39.2% due to the onset of SL and 15.7% due to PRM (**Tab. 4**).

Table 2. Characterization of the type of pregnancy and medically assisted reproduction.

	%
Type of pregnancy	
Singleton	68.6 (n = 35)
Multiple	31.4 (n = 16)
Medically assisted reproduction	
ICSI	13.7 (n = 7)
IVF	3.9 (n = 2)
Ovulation induction	3.9 (n = 2)
IUI	3.9 (n = 2)

ICSI: intracytoplasmic sperm injection; IUI: intrauterine insemination; IVF: *in vitro* fertilization.

Table 3. Characterization of the factors related to clinical intercurrences during pregnancy.

	%
Hypertensive disorders during pregnancy	
Preeclampsia	11.8 (n = 6)
HELLP syndrome	3.9 (n = 2)
Gestational hypertension	5.9 (n = 3)
Maternal diabetes	9.8 (n = 5)
Invasive prenatal diagnosis	
Amniocentesis	21.5 (n = 11)
CVS	2.0 (n = 1)
Cordocentesis	2.0 (n = 1)
Cervical incompetence	25.5 (n = 13)
Placental disorders	
Previa	7.8 (n = 4)
Abruption	5.9 (n = 3)
FGR	23.5 (n = 12)
Infections	
UTI	15.7 (n = 8)
Vaginosis	7.8 (n = 4)
Chorioamnionitis	5.9 (n = 3)
Respiratory/gastrointestinal	7.9 (n = 4)

HELLP: "Hemolytic anemia, Elevated Liver enzymes, Low Platelet count"; CVS: Chorionic villus sampling; FGR: fetal growth restriction; UTI: urinary tract infection.

Table 4. Characterization of the reason for hospitalization in the delivery room, according to gestational age.

		GA		Total
		25 w to 27 w + 6 d	28 w to 32 w + 6 d	
SL	%	38.5 (n = 5)	39.5 (n = 15)	39.2 (n = 20)
PRM	%	30.8 (n = 4)	10.5 (n = 4)	15.7 (n = 8)
LI	%	30.8 (n = 4)	50 (n = 19)	45.1 (n = 23)

GA: gestational age; SL: spontaneous labor; PRM: premature rupture of membranes; LI: labor induction.

The causes that led to the medical decision to LI in the 23 cases identified, include, in descending order of frequency, FGR (6 cases), preeclampsia (4 cases), placental abruption (3 cases), placenta previa, fetal isoimmunization, chorioamniotitis, HELLP syndrome (2 cases for each entity), feto-fetal transfusion syndrome and exacerbation of maternal disease (1 case each).

Out of the 65 NBs, 55.4% were females. Eighteen were extreme preterm NBs (< 28 w – 27.7%), while the majority of NBs (72.3%) were born between 28 w and 32 w + 6 d. As to preterm NBs born between 25 w and 27 w + 6 d, their mean weight was 872 ± 0.16 g, median 854 g, with approximately equivalent frequencies of extremely low weight, very low weight and low weight NBs. In the group with GA between 28 w and 32 w + 6 d, the mean weight was 1,480 ± 0.31 g, median 1,425 g, with a prevalence of low birth weight of 48.9% and extremely low birth weight of 4.3%.

When assessing the weight percentiles adjusted for GA, 15 NBs were in percentiles between 3 and 10, 36 in percentiles between 10 and 50 and 14 in percentiles of 50 or higher.

Three cases with Apgar score below 7 at 5 minutes were identified in the gestational period between 25 w and 27 w + 6 d and 1 case in the gestational period between 28 w and 32 w + 6 d.

Two neonates with GA between 28 w and 32 w + 6 d were born with congenital anomalies: 1 with Morgagni hernia and another with unilateral renal agenesis.

There were 3 cases of neonatal mortality: 1 with GA of 26 w due to acute abdomen with hemoperitoneum secondary to gastric perforation; 1 with GA of 25 w + 6 d due to hyaline membrane disease and 1 with a GA of 28 due to intra-parenchymal and sub-capsular hepatic hematoma.

Discussion and conclusions

It is important to know all data concerning PTB in one's regional population. With the evolution of technology, the survival of moderate and extreme preterm NBs is increasing, albeit with possible morbidity, and the focus should be placed on the implementation of multiple medical and socioeconomic strategies to prevent PTB and improve early access to differentiated care.

With this study we verified that most of the mothers were aged 18-34 years, had a favorable socioeconomic status, a history of at least 1 hospitalization during the current pregnancy and LI due to maternal, fetal or both factors as the precipitant of premature birth. We found no differences in the number of previous gestations (primiparous/multiparous). The high number of mothers with congenital/chronic disease (49%) and the high percentage of women who were overweight before pregnancy (23.5%) are also noteworthy. Of course, a case-control study would have made some of this data more relevant, but that was not the purpose of this project. As for some documented PTB risk factors (such as infection, history of PTB, time since last gestation and chronic autoimmune disease), they were not prevalent in our sample, but they should be taken into account as they may be determinants of preterm delivery, and again a control group would be necessary to draw some conclusions.

In our sample, 25.4% of the pregnancies were the result of medically assisted reproduction (61.5% of these cases resulted in twin pregnancy). Although lately a clear decrease in trigeminal pregnancies has been noticed (which strongly influenced premature delivery), prematurity due to twinning is still strongly associated with these techniques [12] and it would again be important to have a control group to validate the results. Likewise, in 25.5% of pregnancies it was necessary, for several reasons, to perform an invasive prenatal diagnosis which corresponds to a higher frequency than the general population [23].

Regarding the factors related to NBs, unlike most report in the literature, our sample did not show a predominance of the male gender. It included a small number of cases with diagnosed congenital malformations and only a minority

presented a diagnosis of FGR during gestation. It should also be noted that, in most cases of extreme prematurity, survival was possible. However, despite the success in survival at discharge from the NICU, it would be desirable to investigate the occurrence and severity of sequelae in the short, medium and long term in order to provide timely therapeutic interventions.

In the evaluation of the results obtained, we consider that the main limitations should be taken into account, in particular the fact that a full-term neonatal control group was not included and that a convenience type of sample was used (although it included the majority of NBs hospitalized in the study period). Also, from the methodological point of view, the possibility of an information bias (despite the systematic confirmation of the information provided by the puerperal women through the clinical files) should be considered.

This article constitutes a comprehensive descriptive work regarding the study of data of families and mothers of preterm babies born at a GA of 32 w or less. A more preventive approach regarding modifiable factors such as smoking, medically assisted reproduction, pre-gestational BMI and time since the last pregnancy can be recommended in our population. The present work could be a starting point for a larger and multicenter case-control study for the evaluation of risk factors for PTB.

Declaration of interest

The Authors declare that there is no conflict of interest. Funding: none.

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