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Follow-up at two years of age and early predictors of non-compliance in a cohort of very preterm infants

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ABSTRACT

Aim: To examine the rates of follow-up at two years of age and perinatal factors associated with non-compliance in an observational population-based cohort of very preterm children enrolled in a routine follow-up program.
Method: Data review of infants born between 2008 and 2012 in the Observatoire de La Grande Prématurité, Reunion Island cohort. All singletons born alive before 33 weeks of gestational age and resident on the island at two years of age were included. Patients were considered compliant if they were timely evaluated between 20–28 months of age, or non-compliant if they were not evaluated or evaluated after 28 months of age.
Results: Of the 802 survivors (mean gestational age of 30.3 ± 2.0 months, mean birthweight of 1364 ± 396 g), 468 (58.4%) were examined between 20–28 months, 119 (14.8%) after 28 months of age, and 215 (26.8%) were never evaluated, respectively. In multivariate analysis, factors associated with non-compliance were higher parity (>2), past history of preterm delivery, maternal diabetes (preexisting or gestational), appropriate for gestational status, and centre of birth.
Conclusion: Sustainable follow-up of vulnerable neonates remains a challenge in clinical practice. Early predictors of non-compliance can be used to define individualized and local follow-up strategies in these infants at high risk for developmental disabilities.

1. Introduction

Improvement in care of very preterm infants have led to increased survival among those infants, but lifelong consequences remain substantial [1,2]. Preventing adverse neurodevelopmental outcomes in early childhood for those high-risk survivors represents a major challenge, and longitudinal follow-up programs have become routine recommendation and a standard of care [3,4]. Such programs enable a continuation of care and precocious appreciation of developmental issues which may lead to appropriate early interventions, with long-term academic and social benefits [3–5]. However, in published data, the follow-up of preterm infants seems difficult to achieve with attendance rates varying from 50 to 100% at two years of age, raising the importance of early identification of risk factors for non-compliance [1,6–13]. Follow-up studies that provide outcome data for preterm infants are predominantly the result of expensively-funded research efforts, but it is also important to examine the follow-up and outcomes that occur via routine clinical care as there may be potential for bias in observational studies [6]. Indeed, the characteristics of patients lost to follow-up and their influences on the real incidence of disability are still ambiguous, and conclusions from previous European, American or Australian cohort studies may not be extrapolated everywhere [7,9,14–17]. Moreover, for units, existence of local data via audits or benchmarking is useful to improve the quality of care by reorganization.

In France, recent data showed that 2.4% of live births occurred before 33 weeks gestational age (GA), corresponding to nearly 19,000 infants per year [2,18,19]. In the population-based French EPIPAGE 2 cohort study, 83.6% of these infants survived at hospital discharge, of whom

Abbreviations: BW, birth weight; CNIL, Commission Nationale de l'Informatique et des Libertés; GA, gestational age; NFU, neonatal follow-up program; NICU, Neonatal Intensive Care Unit; OGP, Observatoire De La Grande Prématurité De La Réunion; SD, standard deviation; SGA, small for gestational age.

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16% (>2500 infants per year) had at least one severe neonatal morbidity [2]. In La Réunion Island, a French overseas department (850,000 inhabitants and about 14,000 births per year), preterm birth is a significant health issue, with a higher burden than in mainland France [20]. The primary aim of this study was to examine the rates of follow-up at two years of age and maternal, prenatal and early postnatal characteristics associated with non-compliance in the population-based cohort of preterm infants enrolled in the Observatoire de La Grande Prématurité de La Réunion (OGP) between 2008 and 2012. The secondary aim was to estimate the respiratory, psychomotor and neurosensorial development of those high-risk infants at two years of age, which was never determined locally in a population-based setting.

2. Methods

2.1. Study design

Review and analysis of two-year follow-up data of a population based-cohort.

2.2. Population

OGP prospectively collects data in all the preterm infants born before 33 GA in the seven maternity units of the island and admitted alive in the two local tertiary-level Neonatal Intensive Care Units (NICU). Clinical and demographic data in mothers and neonatal characteristics during delivery, tertiary-level NICU interventions and outcomes for hospitalized infants are recorded in this observational French overseas database since 2008. At hospital discharge, the parents or guardians were informed orally and by means of a written notice on the goals and schedules of the follow-up. Briefly, follow-up of survivors was carried out by trained in-house neonatologists at one month, 4, 9, 12, 18, and 24 months of corrected age. Appointments were proposed by NICU administrative agents by phone and/or mail, and patients not showing up were recalled at least twice postally and/or telephonically. Upon discharge, parallel home specific interventions such as physiotherapy or psychomotor therapy, and/or early intervention programs within a non-hospital multidisciplinary specialized unit (Centre d'Action Médico-Sociale Précoce- CAMSP) were initiated for infants with impaired neurologic development. Auditory and visual examinations were controlled by age 6 to 12 months. The costs of follow-up visits and interventions were covered by the French national social insurance, and no specific financial incentives were offered to parents. At the two-year visit, infant outcomes were collected by the follow-up neonatologist, using a standardized form.

The OGP database has been notified to the French Data Protection Authority (CNIL: Commission Nationale de l'Informatique et des Libertés) as CNIL n° 1250024.

The OGP participants eligible to follow-up at two years and included in our study were: infants (1) born before 33 weeks GA between January 2008 and December 2012, (2) surviving to discharge, (3) and supposed to be alive and resident on the island at two years of age. Infants (1) who were known to be dead after discharge, (2) who were known to have moved out of the island between discharge and evaluation or (3) for whom follow-up was not offered (refusal of parents or unreachable parents at discharge), were excluded.

2.3. Data collection

Maternal demographic and socio-economic characteristics included age at childbirth, immigrant status, marital status, educational level, employment status, and travel distance from home to consultation centre. Maternal medical factors were self-reported alcohol consumption or smoking habit, obesity (defined as a body mass index ≥30 kg/m^2), diabetes (preexisting or gestational) or hypertensive disorders (pregestational and gestational). Obstetrical data included past obstetrical history.

Neonatal data included gender, GA, birthweight (BW), small for gestational age status (SGA) defined as a BW < 10th centile according to the French AUDIPOG curves [21,22], congenital malformations, multiple birth, bronchopulmonary dysplasia defined as any ventilatory support at 36 weeks' postmenstrual age [23], patent ductus arteriosus treated surgically or using prostaglandin inhibitors, neonatal and nosocomial sepsis, necrotizing enterocolitis, grade III or IV intraventricular hemorrhage based on Papile's classification [24], periventricular leukomalacia, postnatal growth restriction defined as a discharge weight less than the 10th percentile for postmenstrual age according to AUDIPOG curves, discharge destination (home or transfer to a lower-level unit), mode of nutrition, abnormal neurologic examination and perception of social parental environment (favorable, slightly unfavorable, very unfavorable) by the attending neonatologist at discharge. For infants examined at two years of age, neurodevelopmental data concerned motor development (age at independent walking, gross motor examination), sensorineural impairments (visual impairment identified and/or requiring glasses, hearing loss identified and/or requiring aids), language delay, and subjective perception of parental environment were reported by the follow-up neonatologist. Standardized tests were not used. Other medical data included persistent wheezing, hospitalization for respiratory pathologies and number of rehospitalizations after neonatal discharge.

2.4. Outcome measures

The primary outcome measure was timely attendance to the routine follow-up consultation between 20 and 28 months of chronological age. Patients were categorized as compliant if they were timely evaluated between 20–28 months of age (compliant group) or non-compliant if they were not evaluated or evaluated after 28 months of age (non-compliant group). The follow-up rate was defined as the proportion of infants evaluated between 20–28 months of age. The difficulty to achieve attendance (i.e. number of appointments) was not taken in consideration. Patients involved in other study protocols were neither identified nor excluded. Given the possibility of multiple biases induced by follow-up of survivors of multiple gestation, those infants were excluded from analysis, unless there was a unique survivor at discharge [9].

We first compared perinatal factors associated with non-compliance. Secondarily, we compared the clinical outcomes through follow-up between infants who were compliant and those who were evaluated after 28 months of age.

2.5. Statistical analysis

Categorical data were reported as numbers and percentages, continuous data as means with standard deviation (SD) or medians with 25th and 75th percentile. Fisher exact test or the Chi-2 test were used to compare categorical variables; continuous variables were compared with the Mann-Whitney *U* test or Student *t*-test.

Identification of predictive factors for non-compliance at two years of age was conducted using multiple logistic regression models to account for confounding factors: the dependent variable was attendance (yes/no), the independent variables considered in the model were those with a *P*-value <0.20 in the bivariate analysis or variables known to be predictive for attendance in the literature. The Hosmer-Lemeshow test was used to determine the goodness of fit of the logistic regression model.

A *P*-value <0.05 was considered statistically significant. Odds ratios (OR) of risk factors were given with 95% confidence intervals (95% CI). Statistics were performed in Stata 11.2 (StataCorp, Texas, USA).