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Perinatal mortality or severe neonatal encephalopathy among normally formed singleton pregnancies according to obstetric risk status:" is low risk the new high risk?" A population-based cohort study

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ABSTRACT

Objective: To evaluate the capacity of the current system of obstetric risk stratification at the outset of pregnancy to predict severe adverse perinatal outcome.
Study Design: This retrospective cohort study of singleton pregnancies over a five year period (2009–2013) was performed at the Rotunda Hospital, Dublin, Ireland. High-risk or low-risk status was assigned retrospectively to a large consecutive cohort of women with a normally-formed singleton pregnancy on the basis of factors analyzed at the first prenatal hospital visit. The incidence of severe perinatal morbidity and mortality were compared between high- and low-risk groups to determine the predictive utility of risk stratification at the outset of pregnancy for severe perinatal morbidity.
Results: During the study period, 41,044 patients registered for prenatal care. 25,702;(63%) were deemed low-risk and 15,342;(37%) high-risk. Low-risk women were statistically more likely to be nulliparous ($p < 0.0001$) and to have a spontaneous or operative vaginal delivery ($p < 0.0001$). High-risk women were more likely to be multiparous and to undergo Caesarean delivery ($p < 0.0001$). The perinatal mortality rate was 3.8 per-1000 in low-risk pregnancies and 6.1 per-1000 in the a priori high-risk group ($p = 0.012$). The incidence of severe neonatal encephalopathy (NNE) was 1.8 and 0.65 per-1000 in the low and high-risk groups respectively ($p = 0.0025$).
Conclusion: Where low-risk status is assigned at registration, neonatal encephalopathy is more prevalent. This data is relevant for the design of prenatal care models and demonstrates that assignment of low obstetric risk on the basis of maternal or pre-pregnancy factors alone may erroneously be interpreted as conferring low-risk status to the fetus.

Introduction

A myriad of well described risk factors increase the prospect of poor obstetric outcome. Several studies have identified antepartum and intrapartum events that may adversely affect the developing fetus however many of these factors evolve during pregnancy and are often not present or not apparent when a woman presents for antenatal care at the initial registration visit [1,2]. Furthermore, because low-risk women may be channelled out of medicalised care once risk status is determined, the primary risk assignment may be the only opportunity for medical input into prenatal care.

Obstetric risk stratification purports to streamline perinatal care, such that a community based model can be adopted for women at low obstetric risk, with reservation of more intensive resources for women at higher risk. The Eighth Report of the Confidential Enquiry into Maternal Deaths in the United Kingdom maintains that a risk assessment at the initial antenatal visit is essential in order to enable the stratification of care [3]. Based on risk assignment that is conducted at the outset of pregnancy, low risk women are eligible to seek midwifery led care combined with GP care in the community throughout their pregnancy. Subsequent serial refinement of risk at each visit aims to identify risk factors that arise during the antenatal period. As the pregnancy

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progresses, maternal disease or fetal complications may develop and women who no longer fit the low-risk criteria are appropriately transferred to an obstetric led care model that is better designed to prevent or treat conditions that lead to adverse obstetric outcome. However, while risk stratification at the initial antenatal visit may reduce maternal morbidity, we questioned whether preliminary risk stratification similarly impacts severe perinatal morbidity.

This study examines the capacity of the current system of obstetric risk stratification at the outset of pregnancy to predict severe adverse perinatal outcome in the form of perinatal mortality (PNM) or neonatal encephalopathy (NNE).

Materials and methods

A retrospective review of all women who registered for prenatal care at a single tertiary referral perinatology centre over a five year period (2009–2013) was conducted. Women were stratified according to history-defined medical and obstetric risk. Risk assignment was based on a set of pre-specified criteria obtained at the initial prenatal registration visit. The maternal demographic, medical and obstetric history criteria that reflect whether a patient is deemed suitable for community based care were used to assign risk status as 'high' or 'low'. Women who met any of the criteria that would result in exclusion from the community based model of prenatal care were deemed 'high-risk' for the purpose of this study. The remaining population was classified as low-risk. Hospital databases (Patient Administration System (PAS) and the Hospital In-patient Enquiry (HIPE)) were examined for the risk factors outlined in Table 1, and confirmed with High-Risk Clinic registries and the laboratory database.

Perinatal mortality was defined as stillbirth or death within the first 7 days of life of a baby weighing at least 500 g [4]. Severe neonatal encephalopathy was defined as HIE grade 2 or 3 in a term newborn infant demonstrating: metabolic acidosis with a cord pH of <7 or a base deficit of ≥12 mmol/L; early onset of encephalopathy; multi-system organ dysfunction; and exclusion of other etiology such as trauma, coagulation disorders, metabolic disorders, and genetic causes [5]. Cases of perinatal mortality or of neonatal encephalopathy among normally-formed infants were ascertained from a prospectively-recorded and published hospital register [4]. Cases of PNM and of NNE were thus cross-checked across database sources for maternal risk-status as determined by registration criteria. Individual case records were collected for all such cases of mortality or encephalopathy.

Cases were excluded from the analysis in the event of miscarriage, major congenital malformation, neonatal transfer from a regional hospital, multiple gestation or where a woman was not registered for prenatal care. Rates of PNM and NNE were then compared for low-risk and high-risk groups. Chi-square tests, two-sample t-tests and Wilcoxon rank sum tests were used to compare event rates and associated characteristics. The p-value < 0.05 was considered statistically significant. Database construction, screening of criteria and query evaluation was performed using MS Access Version 15.0. Statistical analysis was performed using SAS Version 9.2.

Table 1
High Risk Criteria at Registration.

High Risk Maternal Characteristics	Number of Cases (n = 15,342)	Prevalence (%)
Weight(Kgs) <45 or >90	2489	16.2
Drug Abuse	124	0.8
Alcohol >7	83	0.5
Parity >5	198	1.3
Age at booking <17 or >45	192	1.3
Miscarriage >= 3	1229	8
Previous Caesarean Section	5293	34.5
Non-English speaking	832	5.4
Poor Obstetric History	1198	7.8
Diabetes I/II	151	1
HIV, Hepatitis B, Hepatitis C	396	2.6
Chronic Lung Disease	4	0.03
Cystic Fibrosis	4	0.03
Haemoglobin <10 g/L	478	3.1
Antibodies	142	0.9
Hyperthyroidism	91	0.6
Hypothyroidism	636	4.1
Thrombophilia	45	0.3
Epilepsy	191	1.2
Chronic Kidney Disease	7	0.05
Hypertension	266	1.7
Cardiac	48	0.3

Results

Complete demographic, maternal and obstetric history data were available on 41,044 registered women delivered of a normally formed singleton infant weighing at least 500 g at birth, at a minimum gestational age of 24 weeks during the study period 2009 – 2013 [5]. This cohort represents 97% of the population who met the inclusion criteria for this study. The remaining 3% were excluded from the analysis. Within this cohort,25,702 women (63%) were identified as low-risk pregnancies by criteria

Table 2
Pregnancy Characteristics, Perinatal Mortality and Causes of Mortality in High and Low Risk Pregnancies.

Pregnancy Characteristics			
Characteristics 2009 - 2013	Low risk (N = 25,702)	High Risk (N = 15,342)	p-value
Nulliparity	13,188 (51.3 %)	5399 (35.2 %)	<0.0001
Spontaneous Vaginal Delivery	15,912 (61.9 %)	6278 (40.9 %)	<0.0001
Operative Vaginal Birth	6,141 (23.9 %)	1941(12.7 %)	<0.0001
Caesarean Section	3,649 (14.2 %)	7123 (46.4 %)	<0.0001
Maternal age	29 ± 5 years	31 ± 5 years	NS
Gestational age at delivery	39 ± 2 weeks	38 ± 2 weeks	NS
Birth Weight at Delivery	3.47 ± 5.5 kg	3.43 ± 6.3 kg	NS
*Perinatal Mortality			
PNM 2009 - 2013	Low risk (N = 25,702)	High Risk (N = 15,342)	p-value
PNM Cases	98	93	–
PNM (per thousand)	3.8	6.1	0.012
Parity (Median [IQR])	0 [0 - 1]	1 [0 - 2]	<0.001
Gestational Age (Mean +/- SD)	32.9 ± 6.3	32.4 ± 6.0	NS
Mean Birth Weight (kg)	2.11 ± 1.17	1.96 ± 1.14	NS
Causes of Mortality			
Causes of Mortality 2009 - 2013	Low risk (N = 25,702)	High Risk (N = 15,342)	p-value
Placental	24 (0.09%)	34 (0.22%)	0.07
Cord	28 (0.11%)	11 (0.07%)	0.004
Infection	9 (0.04%)	8 (0.05%)	0.888
Prematurity	15 (0.06%)	14 (0.10%)	0.961
FMH	2 (0.01%)	0	0.166
Hypoxia	2 (0.01%)	2 (0.01%)	0.958
Uterine rupture	0	1 (0.01%)	0.303
Traumatic delivery	1 (<0.01%)	0	0.329
Maternal bleed	0	1 (0.01%)	0.303
Mec. Asp. & RDS	1 (<0.01%)	0	0.329
SID	0	1 (0.01)	0.303
Unexplained	16 (0.06%)	21 (0.14%)	0.274
Total	*98*	*93*	–

Notes: Mean ± SD and Median [inter-quartile range] are presented for continuous and ordinal data, respectively. The chi-squared test was used for categorical data (PNM rate), the two-sample *t*-test for continuous data (weight, GA) and the Wilcoxon rank-sum test was used for ordinal data (parity).

* Perinatal mortality was defined as stillbirth or death within the first 7 days of life of a baby weighing at least 500 g.