

## Determinants of neonatal mortality in a tunisian population

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### R É S U M É

**Prérequis:** En Tunisie, la mortalité périnatale constitue un problème de santé publique. Elle est estimée à 28 ‰ dont 15 ‰ de mortinatalité et 15 ‰ de mortalité néonatale précoce. La moitié des décès des enfants de moins de cinq ans est d'origine périnatale et la mortalité néonatale représente les deux tiers de la mortalité infantile. En Tunisie, les données publiées sur la mortalité néonatale et ses causes sont rares.

**Objectif:** Evaluer l'incidence de la mortalité néonatale sur une durée de deux ans, préciser ses principaux facteurs de risque et ses causes.

**Méthodes:** Cohorte prospective colligeant toutes les naissances vivantes enregistrées entre Janvier 2007 et Décembre 2008 à l'hôpital Charles Nicolle de Tunis. Tous les décès néonataux survenant avant ou après sortie de l'hôpital ou des nouveau-nés transférés dans d'autres hôpitaux puis décédés, ont été inclus. Les naissances vivantes issues d'une interruption médicale de grossesse ont été éliminées. Les causes des décès ont été codées selon la classification internationale des maladies dans sa dixième édition (CIM10).

**Résultats :** 88 décès néonataux ont été enregistrés sur 7285 naissances vivantes (NV) soit un taux de mortalité néonatale de 12‰ NV dont 88.7% de mortalité néonatale précoce (10.8‰). Les facteurs de risque directs de la mortalité néonatale étaient la prématurité (ORa=6.03- IC95%:[2-18.13] p=0.001), la détresse respiratoire néonatale (ORa=16.12 - IC95% :[5.67-45.78] p<10-3), l'asphyxie périnatale (ORa=11.49- IC95% :[3.68-35.92] p<10-3), l'infection nosocomiale ORa=8.71- IC95% : [1.77-42.70] p=0.008, et le retard de croissance intra-utérin ORa=7.11- IC95% :[2.23-22.69] p=0.001. 80.6 % des causes initiales et 88.6 % des causes immédiates des décès étaient regroupées dans le chapitre affections dont l'origine se situait dans la période périnatale.

Les troubles hypertensifs maternels et l'immaturité extrême secondaire à la prématurité spontanée étaient responsables respectivement de 13.6 % et 10.2% des causes initiales des décès néonataux.

**Conclusion:** la mortalité néonatale demeure élevée, dominée par les affections dont l'origine se situe dans la période périnatale. Le caractère multifactoriel de la mortalité néonatale implique une stratégie d'intervention multidisciplinaire, engageant la prévention pré et périnatale.

### M O T S - C L É S

mortalité néonatale, nouveau-né, prématurité, CIM-10.

### S U M M A R Y

**Background:** In Tunisia, perinatal mortality remains a public health problem, currently estimated at 28 ‰, including 15 ‰ of still birth rate and 10 to 15 ‰ of early neonatal mortality rate. The recent investigations show that about half of the deaths at less than five years old are of perinatal origin and that neonatal mortality represents two thirds of infant mortality. Published data regarding neonatal mortality and the causes of death are sparse.

**The aim:** to evaluate the neonatal mortality rate over a 2 year period in our population study and to present data collected prospectively on the risk factors and the causes of all neonatal deaths.

**Methods:** a prospective cohort compiling all live births reported between January 2007 and December 2008 at Charles Nicolle hospital (Tunis-Tunisia). All the neonatal deaths that occurred before or after discharge or transferred to other hospitals and subsequently died are included. Births from termination of pregnancy were excluded from all the analyses. Causes of deaths were assigned according the International Classification of Diseases, Tenth Revision (ICD10).

**Results:** 88 neonatal deaths were recorded over 7285 live births (LB) that is a NMR of 12‰ LB. Early neonatal death occurred in 79 cases (88.7%), that is an ENMR of 10.8‰ LB.

Risk factors directly related to neonatal mortality were prematurity (aOR=6.03- 95%CI: [2-18.13] p=0.001), neonatal respiratory distress (aOR=16.12 - 95%CI: [5.67-45.78] p<10-3), perinatal asphyxia (aOR=11.49- 95%CI: [3.68-35.92] p<10-3), nosocomial infection aOR=8.71- 95%CI: [1.77-42.70] p=0.008, and small for gestational age aOR=7.11- 95%CI: [2.23-22.69] p=0.001. 80.6 % of underlying causes and 88.6 % of immediate causes of death are gathered in the chapter "Certain conditions originating in the perinatal period". Maternal hypertensive disorders and extreme immaturity due to spontaneous prematurity were respectively responsible for 13.6 % and 10.2% of underlying causes of neonatal death.

**Conclusion:** Neonatal mortality remains high, dominated by the conditions originating in the perinatal period. The multitude of the risk factors implies the need for a multidisciplinary strategy of intervention, engaging the pre and perinatal prevention.

### K E Y - W O R D S

neonatal mortality, newborn, premature birth, ICD-10.

Neonatal mortality (NM) remains a major public health problem in developing countries. A two-third reduction of mortality in children less than five years old by 2015 is one of the United Nations millennium development goals [1]. Despite a decline in mortality in children in this age group, in the last few decades, neonatal mortality numbers have not changed substantially [1]. The recent investigations show that about half of the deaths at less than five years old are of perinatal origin and that NM represents two thirds of infant mortality [2, 3].

In Tunisia, in spite of the progress made over the last decades, perinatal mortality (PNM) remains a public health concern given its rather high frequency, currently estimated at 28 ‰, including 15 ‰ of still birth rate and 10 to 15 ‰ of early neonatal mortality rate (NMR). Published data regarding NM and the causes of death are sparse.

The aim of this report is to evaluate the NMR over a 2-year period in our population study and to present data collected prospectively on the risk factors and the causes of all neonatal deaths, according the international classification of diseases (ICD10) [4].

## SUBJECTS AND METHODS

We followed a prospective cohort compiling all live births reported between January 2007 and December 2008 at Charles Nicolle hospital (Tunis-Tunisia).

All the neonatal deaths that occurred in our neonatal unit (level two) before or after discharge or transferred to other hospitals and subsequently died are included.

Systematic phone calls with the parents are carried out, at one week and one month of life, to make sure of the state of their child during the neonatal period, after hospital discharge.

Births from termination of pregnancy were excluded from all the analyses.

Early Neonatal Mortality Rate (ENMR) is defined as death during the first completed six days of life per 1000 live birth (LB). Late Neonatal Mortality Rate (LNMR) is defined as death between 7 and 27 days per 1000 LB.

All deaths are discussed by three consultants in the unit. The consultants assigned causes of deaths, according the International Classification of Diseases, Tenth Revision (ICD10).

The underlying cause of death "Ia" (or primary cause of death) is the disease or injury that initiated the train of morbid events leading directly to death.

The immediate cause of death "Ib" is the disease, injury, or complication that directly precedes death, which is the ultimate consequence of the underlying cause of death.

The underlying cause of death and the immediate cause of death are linked in a cause-and-effect relationship when read from bottom to top.

The contributive causes of death "II" are other significant conditions contributing to the death, but not related to the disease or condition causing it.

A multivariate analysis in logistic regression was used to

identify the risk factors directly related to neonatal death. The logistic regression was used to calculate for each factor directly related to the event, an adjusted Odds ratio.

## RESULTS

Over the 2 year period, there were 88 neonatal deaths over 7 285 live births (LB) that is a NMR of 12‰ LB. Early neonatal death occurred in 79 cases (88.7%), that is an ENMR of 10.8‰ LB (79/7285). 42/88 (47.7%) deaths occurred in the first 24 hours of life. Late neonatal death occurred in 9 cases (10.2%), that is a LNMR of 1.23 ‰ LB (9/7285).

Of the 88 neonatal deaths, there were 57 (64.7%) males and 31 (35.3%) females with a male/female ratio of 1.83.

Neonatal outcome could not be specified in 1 059 cases (14.5%). The new-borns whose neonatal outcome after discharge could not be specified, had significantly less gravidic maternal morbidity (18.6% versus 25.1%  $p<10^{-3}$ ) and less neonatal morbidity (18.1% versus 22.4%  $p=0.002$ ) than the remainder of the new-borns having survived the neonatal period.

Crude odds ratios and adjusted odds ratios after multivariate analysis in logistic regression for risk factors of neonatal mortality are shown in tables 1 and 2.

**Table 1:** Odds ratios for risk factors of neonatal mortality

<b>History of still birth</b>	3.52	[1.59-7.75]	0.001
<b>Multiple pregnancy</b>	3.47	[1.82-6.62]	$<10^{-3}$
<b>Small for gestational age</b>	6.40	[4.06-10.09]	$<10^{-3}$
<b>Maternal hypertensive disorders</b>	3.30	[2.04-5.32]	$<10^{-3}$
<b>Gestational diabetes</b>	2.58	[1.52-4.36]	$<10^{-3}$
<b>Early neonatal infection</b>	10.27	[3.93-26.79]	$<10^{-3}$
<b>Nosocomial infection</b>	53.09	[27.90-101.01]	$<10^{-3}$
<b>Neonatal respiratory distress</b>	88.15	[53.33-145.70]	$<10^{-3}$
<b>Prematurity</b>	23.56	[15.05-36.87]	$<10^{-3}$
<b>Spontaneous prematurity</b>	22.05	[13.41-36.28]	$<10^{-3}$
<b>Perinatal asphyxia</b>	66.75	[40.81-109.20]	$<10^{-3}$

Risk factors directly related to neonatal mortality were prematurity (a OR=6.03- 95%CI: [2-18.13]  $p=0.001$ ), neonatal respiratory distress (aOR=16.12 - 95%CI: [5.67-45.78]  $p<10^{-3}$ ), perinatal asphyxia (aOR=11.49- 95%CI: [3.68-35.92]  $p<10^{-3}$ ), nosocomial infection aOR=8.71- 95%CI: [1.77-42.70]  $p=0.008$ , and small for gestational age aOR=7.11- 95%CI: [2.23-22.69]  $p=0.001$ .

We studied the relationship between adequacy of prenatal care

**Table 2:** Odds ratios for risk factors directly related to neonatal mortality

Risk factor	Crude odds ratio (cOR)	95% confidence intervals	Adjusted odds ratio (aOR)	95% confidence intervals	p
Spontaneous	22.05	[13.41-36.28]	6.03	[2-18.13]	0.001
<b>Prematurity</b>					
Neonatal respiratory distress	88.15	[53.33-145.70]	16.12	[5.67-45.78]	<10 <sup>-3</sup>
<b>Nosocomial infection</b>	53.09	[27.90-101.01]	8.71	[1.77-42.70]	0.008
<b>Perinatal asphyxia</b>	66.75	[40.81-109.20]	11.49	[3.68-35.92]	<10 <sup>-3</sup>
<b>Small for gestational age</b>	6.40	[4.06-10.09]	7.11	[2.23-22.69]	0.001

and neonatal mortality based on the national schedule of prenatal visits. We did not find a statistically significant difference: 57 neonatal deaths over 3 951 LB (1.4 %) with adequate prenatal visits versus 24 over 1 717 L B (1.4%) with inadequate prenatal visits (NS).

45 cases of neonatal death over 3 930 LB(1.1%) were recorded when at least three antenatal ultrasounds (11-12 WG, 22-24WG, 32-33WG) were performed versus 41 deaths over 1 685 (2.4%) with inadequate antenatal ultrasound timing, OR=2.12 CI95%= [1.38-3.25] p<10-3.

The causes of death during the neonatal period, according to the ICD10, are shown in tables 2, 3 and 4.

80.6 % of underlying causes “Ia” and 88.6 % of immediate causes of death “Ib” are gathered in the chapter “Certain conditions originating in the perinatal period”. Table 2

Maternal hypertensive disorders were responsible for 13.6 % of

**Table 3:** Classification of neonatal deaths according the International Classification of Diseases (ICD 10)

CHAPTER	ICD 10	XVI	XVII	IV	unspecified
CODE		P00-P96	Q00-Q99	E00-E90	
		Certain conditions originating in the perinatal period		Congenital malformations and deformations	Endocrine, nutritional and metabolic diseases
<b>Initial causes (Ia)</b>	Number	71	9	2	6
	%	80.6	10.2	2.2	6.8
<b>Immediate causes (Ib)</b>	Number	78	3	1	6
	%	88.6	3.4	1.1	6.8
<b>Contributive causes : II</b>	Number	46	2	0	40
	%	52.2	2.2	0	45.4

**Table 4:** Primary causes Ia- Certain conditions originating in the perinatal period

CAUSES	ICD-10	Number	%
<b>Fetus and newborn affected by maternal factors and by complications of pregnancy, labour and delivery.</b>	P00-P04	32	36.3
Fetus and newborn affected by maternal hypertensive disorders	P00.0	12	13.6
placenta praevia	P02.0	2	2.2
placental transfusion syndromes	P02.3	2	2.2
<b>Disorders related to length of gestation and fetal growth.</b>	P05-P08	21	23.8
Light for gestational age	P05.0	2	2.2
Extreme immaturity	P07.2	9	10.2
Other preterm infants	P07.3	7	8
<b>Respiratory and cardiovascular disorders specific to the perinatal period</b>	P20-P29	12	13.6
Severe birth asphyxia	P21.0	4	4.5
Mild and moderate birth asphyxia	P21.1	3	3.4
Other respiratory distress of newborn	P22.8	4	4.5
<b>Infections specific to the perinatal period</b>	P35-P39	3	3.4
Sepsis of newborn due to streptococcus, group B	P36.0	2	2.2

**Table 5:** Immediate causes Ib: Certain conditions originating in the perinatal period

CAUSES	CIM10	Number	%
<b>Respiratory and cardiovascular disorders specific to the perinatal period</b>	P20-P29	48	54.5
Severe birth asphyxia	P21.0	14	16
Respiratory distress syndrome of newborn	P22.0	8	9
Other respiratory distress of newborn.	P22.8	6	6.8
Respiratory distress of newborn, unspecified	P22.9	12	13.6
Pneumothorax originating in the perinatal period	P25.1	2	2.2
Neonatal cardiac failure	P29.0	1	1.1
<b>Infections specific to the perinatal period.</b>	P35-P39	20	22.7
Other bacterial sepsis of newborn	P36.8	13	14.7
Bacterial sepsis of newborn, unspecified	P36.9	6	6.8
<b>Haemorrhagic and haematological disorders of fetus and newborn</b>	P50-P61	3	3.4
Unspecified intraventricular (nontraumatic) haemorrhage of fetus and newborn	P52.3	1	1.1
Congenital anemia from fetal blood loss	P61.3	1	1.1
<b>Other disorders originating in the perinatal period</b>	P90-P96	6	6.8

underlying causes of neonatal death. Table 3

Extreme immaturity due to spontaneous prematurity was responsible for 10.2% of underlying causes of death. Table 3 Severe birth asphyxia, respiratory distress syndrome and infections specific to the perinatal period were responsible respectively for 16 %, 9% and 22.7 % of immediate causes of death. Table 3

Deaths due to congenital malformations accounted for 10.2% of primary causes of deaths.

## DISCUSSION

In Tunisia, NMR dropped considerably over the last 30 years; from 46.6 ‰ in 1972 to 14.5‰ in 2002. The substantial decline in both early and late neonatal mortality during the 1980s is largely due to the socio-economic and cultural development and various measures taken in order to reduce infant mortality such as the national plans of perinatality, anti-diarrheal fight and vaccination. Published data regarding NMR are sparse and represent hospital rates. Our prospectively collected data, covering all the neonatal period, offered to us a more accurate assessment of the rate. The missing data concerned new-borns with lesser perinatal risks and thus does not seem to affect the results.

However, our population does not represent a good cross section of the Tunisian population. Our NMR of 12.2 ‰ LB do reflect the national NMR.

38% of the deaths of children of less than five years happen in the first month of life, mainly in the first week, and even in the first 24 hours of life [5,6]. Our analysis confirmed the well-known vulnerability of the first week of life, particularly the first 24 hours, found on a worldwide scale by WHO [5, 6].

The high ENMR underlines the importance to identify and prevent the risk factors and the underlying causes of ENM to reduce neonatal and infant mortality.

Nearly two thirds of the neonatal deaths are due to affections of perinatal origin [5]. In our population, fetus and newborn affected by maternal factors and by complications of pregnancy, labour and delivery represented on the whole 36.3% of underlying causes of neonatal death. Our analysis indicates that hypertensive disorders, spontaneous preterm delivery and perinatal asphyxia were the main primary obstetric events that led to newborn deaths.

13.6 ‰ of underlying causes of neonatal death were due to maternal hypertensive disorders. This could be due, in part, to induced prematurity and thus of its complications particularly the respiratory distress syndrome, responsible for 9% of immediate causes of death.

The impact of prenatal care on perinatal outcomes is largely established, primarily in terms of perinatal mortality and birth asphyxia. A lack of prenatal care has been shown to negatively impact pregnancy outcomes and is associated with increased rates of perinatal death [7,8,9]. In our series, we did not find an impact of the adequacy of prenatal care, in terms of timing of antenatal visits and ultrasounds on neonatal mortality. But the quality of prenatal care, more difficult to appreciate, plays a central role in the prevention of spontaneous prematurity, maternal hypertensive disorders and their complications [8,9,1].

Our study emphasize the urgent need to develop and evaluate strategies for the identification and management of complications of pregnancy, labour and delivery, especially spontaneous prematurity, maternal hypertensive disorders and birth asphyxia.

The development of neonatal intensive care units with qualified personnel would contribute to reducing neonatal morbidity and mortality especially in premature newborn.

Improvements in the quality of information systems, with a more rigorous approach in the classification of causes of death are necessary to have complete data, accessible and reliable in order to facilitate the realization of national investigations.

Achievement of millennium development goal for child survival depends on improved quality of clinical care for mothers, emergency obstetric care and emergency neonatal care. Our ultimate objective is to reduce neonatal mortality from 15.5 ‰ to 8 ‰ between the year 2000 and 2015.

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