In-hospital mortality of very preterm infants in a Tunisian neonatal intensive care unit: Prevalence and risk factors

Mortalité intra-hospitalière des grands prématurés dans un centre de soins intensifs néonatals Tunisien : prévalence et facteurs de risque

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RÉSUMÉ

Introduction : La prématurité représente un problème majeur de santé publique et elle est associée à une lourde mortalité et morbidité. En Tunisie, peu d'études se sont intéressées à ce domaine.

Objectif : Etudier la prévalence et les facteurs de risque de la mortalité intra-hospitalière des grands prématurés.

Méthodes : Nous avons mené une étude rétrospective monocentrique. Nous avons inclus toutes les naissances vivantes d'âge gestationnel inférieur à 32 SA 6 j, admises au service de réanimation néonatale de l'hôpital Charles Nicolle de Tunis, durant une période de deux ans (2011-2012). Nous avons exclus les anomalies congénitales majeures. Pour déterminer les facteurs de risque de mortalité intra-hospitalière nous avons créé et comparé deux groupes : groupe des « survivants » jusqu'à la sortie de l'hôpital et groupe « Décès » avant la sortie. Une analyse par régression logistique multi variée a été utilisée pour étudier l'association entre les facteurs de risque et la mortalité intra-hospitalière. P est considéré significatif si < 0.05.

Résultats: Durant la période d'étude, 7606 naissances vivantes ont été enregistrées, parmi eux 113 étaient des grands prématurés. Il s'agissait de très grands prématurés dans 13% des cas. Le sex-ratio était de 0.8. Le poids de naissance moyen à l'admission était 1338±349g et l'âge gestationnel moyen était 30 SA±1,7. La durée moyenne d'hospitalisation était de 26 jours ±17 jours avec un poids moyen à la sortie de 1942±249g. Une maladie des membranes hyalines a été diagnostiquée chez 42% des cas, une anémie néonatale précoce dans 64% des cas, une hémorragie intra-ventriculaire dans 15% des cas, une infection liée aux soins dans 37,6% des cas. Un décès intra-hospitalier a été noté dans 32 % des cas. Les facteurs de risque de la mortalité intra-hospitalière étaient : la maladie des membranes hyalines, le très très faible poids de naissance (<1000g), la très grande prématurité et les troubles hémodynamiques.

Conclusion : La grande prématurité compte 1,4% des naissances vivantes. Le taux de mortalité intra-hospitalière des grands prématurés est trop élevé et associé principalement à la maladie des membranes hyalines. Une amélioration de la prévention et de la prise en charge de la grande prématurité est indispensable.

Mots-clés

Prématurité, Unité de soins intensifs néonatals, morbidité, mortalité.

SUMMARY

Background: Prematurity is a major public health problem and it's associated with a high mortality and morbidity. In Tunisia, few investigations studied this area.

Aim: To determine the rate and the risk factors of in-hospital mortality of very preterm infants.

Methods: We conducted a retrospective monocentric study. We included all premature Infants born at less than 326 weeks of gestation (< 33 Weeks) without major congenital anomalies admitted from January 2011 to December 2012 in the neonatal intensive care unit (NICU) of Charles Nicolle Hospital (Tunis-Tunisia). To determine in-hospital mortality related risk factors, we created and compared two groups: group of "Survivors" until discharge from our hospital and group of "Dead" before discharge. Multivariable logistic regression models were used to assess the association between risk factors and in-hospital mortality. P-value < 0.05 was considered statistically significant.

Results: During the study period, 7606 livebirths (LB) were recorded; among them 113 were very premature infants. The prevalence of high prematurity was 1,4 % LB. Very premature infants were divided in 24 extremely preterm infant (13%) and 89 moderately preterm infants (87%). Mean weight at admission was 1338g (±349g) and the mean gestational age was 30 weeks (±1,7). The mean hospital stay was 26 days (±17days) with an average weight at discharge of 1942g (±249). Neonatal morbidity was mainly caused by respiratory distress (42%), early neonatal anemia (64%), intraventricular hemorrhagea (15%), associated-care health infection (37,6%). In hospital mortality rate was 32 %. Mortality risk factors identified through multivariate analysis were: extreme premature infant (p<0,05), extremely low birth weight (p<0,01) and circulatory disorders (p<0,05).

Conclusion: Very preterm infant represented 1,4 % of all live births. The mortality rate of very premature infant is still high and mainly associated to neonatal respiratory distress. Improving prevention and neonatal management still very required.

Key-words

Prematurity, neonatal intensive care unit, morbidity, mortality.

INTRODUCTION

Prematurity is a major public health problem. It is the principal cause of death among newborns and the second leading cause of death, after pneumonia, in children under five, especially in developing countries [1]. Despite the improvement in neonatal intensive care over the past decade, prematurity is still responsible of high rate of morbidity and mortality.

There is no published study reporting related morbidity and mortality of preterm infants less than 32^6 weeks of gestation in Tunisian NICUs.

The aim of this study was to determine the rate and the risk factors of in-hospital mortality of preterm infants, born less than 32^6 weeks of gestation (WG) in a Tunisian tertiary intensive care unit.

METHODS

We conducted a retrospective monocentric study in the NICU of Charles Nicolle Hospital of Tunis, a tertiary neonatal care center, over two years period (1st January 2011 to 31 December 2012). We included all preterm infants born between 26 and 32^6 WG. We excluded infants with congenital anomalies and births from termination of pregnancy. This study analyzed retrospectively maternal and infant data collected from the medical record. We recorded maternal variables including sociodemographic characteristics; educational level, age, maternal behaviors (tobacco, parity, comorbidities, drug use during pregnancy, prenatal care visits, antenatal steroids, pregnancy complications and antibiotics); intrapartum variables including chorioamnionitis, premature rupture of membranes, and delivery method; infant characteristics including birth weight, gestational age (obstetric estimate), sex, Apgar scores, in hospital morbidities and outcome. To determine in-hospital mortality related risk factors, we created and compared two groups: group of “survivors” until discharge from our hospital and group of “dead” before discharge. Epi Info 6.04d was used for statistical analysis. Statistical significance was calculated using $\chi 2$. Multivariable logistic regression models were used to assess the association between risk factors and in-hospital mortality. P-value < 0.05 was considered statistically significant.

RESULTS

During the study period, 7606 LB, 332 admissions in NICU and 113 very preterm infants (26-326WG) were recorded. Thus, the incidence of prematurity was 1,4 % of total live births. Very preterm infants accounted for 34 % of all admissions in NICU.

Prematurity was induced in 36 % of all cases. In-hospital mortality rate was 32 %.

Related in-hospital mortality risk factors identified through multivariate analysis were: extremely premature infant (p=0,002), very low birth weight (p=0,024) and circulatory disorders (p=0,003).

General maternal, pregnancy and intrapartum descriptive characteristics are presented in table I. The rate of assisted procreation and multiple births accounted for 12,5% and 22,1 % respectively.

Table 1 : Maternal, pregnancy and intrapartum descriptive characteristics

Maternal:	
Age (year), mean±SD	30 ± 5,4
Comorbidities (%)	11
Parity mean±SD	2 ±1
Pregnancy:	
Regular prenatal visits	92,8
Dysgravida (%)	49,6
Diabetes (%)	22
Hypertension (%)	33,6
Preterm Labor (%)	15,9
Chronic fetal distress (%)	21,2
Antenatal steroids (%)	59,3
Intrapartum:	
Multiple births (%)	22,1
Chorioamnionitis (%)	13,3
PROM (>12h) (%)	23,9
Maternal antibiotics (%)	15,9
Cesarean delivery (%)	63,4

SD: standard deviation, PROM: Prolong rupture of membranes

Main causes of very preterm birth were preterm labor in 64% and gravida hypertension in 20,5%. Antenatal steroids were administered in 59,3% and the cure was complete in 86,5%. The delivery was performed by cesarean section in 63,4%. The principles neonatal characteristics are summarized in table II

In-hospital mortality occurred within seven days in 21,2%. The principle cause of death was health care associated infection (HCAI) in 76 %. Mortality risk factors identified through univariate analysis are presented in Table III. Extremely premature infant, very low birth weight and circulatory disorders were the direct in hospital mortality risk factors.

Table 2: General characteristics of neonates.

Sex ratio (M/F)	0,83
Gestationnal age (WG) mean±SD	30 ±1,78 (26-32^{6})
Gestationnal age <28^{6} WG (%)	13
Birth weight (g) mean±SD	1338± 349 (660-2200)
<1000g (%)	14,2
IUGR (%)	35,4
Apgar at 5 mn<7 (%)	9,7
Intubation (%)	15
RDS (%)	39,8
Apnea (%)	45,1
Invasive mechanical ventilation (%)	66,6
Bronchopulmonary dysplasia (%)	3,5
Health care–associated infection (%)	37,6
Early neonatal anemia (%)	64
Intraventricular hemorrhagea (%)	15
Circulatory disorders (%)	54,9
Length of hospitalization (day) mean±SD	26,8±17,4
Term at discharge (WG) ±SD	35±1,2
Weight at discharge (g) mean±SD	1940±249

IUGR: intrauterine growth restriction, SD: standard deviation

Table 3: Related in-hospital mortality risk factors

	Dead	Survivors	p	OR IC$_{95\%}$
Dysgravida (%)	66.7	42.1	0.015	2.7 [1.2-6.3]
Acute fetal distress (%)	41.7	22.4	0.045	2.47 [1.05-5.8]
Apgar score <7 at 5n	22,2%	4,1%	<0,001	6.7 [1.6-27.3]
VLBW	33.3	5,3	<0,001	9 [2.6-30.5]
RDS	57.6	34.2	0.023	2.6 [1.1-6]
Invasive mechanical ventilation	87.9	44.7	<0,001	8.9 [2.8-27.9]
HCAI	59.4	31.6	0.007	3.16 [1.3-7.4]
Circulatory disorders	90.9	42	<0,001	13.7 [3.8-49]
Early anemia	81,3	55.9	0.01	3.4 [1.2-9.3]

RDS: respiratory distress syndrome, VLBW: very low birth weight, HCAI: Health care-associated infection

DISCUSSION

In our study, very preterm infants accounted for 1,4% of LB and 34 % of all admissions in NICU. The same rates was reported in others studies [2,3]. The rate of in-hospital mortality was high (32%). However, it was significant compared to the survival data of very preterm infants in resource-limited countries [4]. In our study, the principle cause of death was HCAI in 76 %.

The main risk factors of mortality were the very low birth weight (< 1000 g), the extreme prematurity (<29 WG), and circulatory disorders (p<0,05). The same results were reported in others studies [5].

This study has limitations, it was retrospective, monocentric, and as in most studies focusing on the special populations of very preterm or very low birth weight infants (about 1-1.5% of total births), sample size may be not large enough to detect the risk factors associated to neonatal outcomes.

In our study, the delivery was performed cesarean section in 63,4%. The same rate of cesarean delivery was reported in European studies [6]. There are no recommendations to prefer cesarean delivery in case of very preterm delivery [7].

The rate of respiratory distress syndrome (RDS) was significant, 42,2% of our study population. In EPIPAGE study, the incidence of RDS was inversely proportional to gestational age especially in absence of antenatal steroids injections, 43,8 percent at 30 WG to 23,9% at 32 WG [8,9]. Indeed, the rate of antenatal steroids prescription was insufficient (59,3% of all cases). In EPIPAGE study, antenatal steroids were administered in 84 % of very preterm infants [10]. American studies recommended an aim of 80 % of antenatal steroids cover of very preterm infants born before 34 WG [11,12]. Invasive mechanical ventilation was needed in 66,6 % of all cases. The rate of BPD was 3,5 % of all cases. This rate was under-estimated by the high rate of in-hospital mortality of extremely premature infants. EPIPAGE study reported a rate of 5,7% of BPD in very preterm infant (<32^{6}WG) [13].

The other common comorbidities were early anemia in 64 %, circulatory disorders in 57% and Associated care health infection (ACHI) in 37,6% of all cases. Anemia is known to be early or late in premature infants, it is favored by the absence of systematic use of human recombinant erythropoietin, but especially by the absence of micromethods for blood samples [14]. The rate of HCAI was high (37,6 %).

The mean hospital stay was 26,8±17,4 days. Indeed, we allowed hospital discharge at 34 WG of postmenstrual age and a birth weight greater than 1600 g.

CONCLUSION

Very preterm births represented 1.3% of total Live births but they were responsible for the large share of related prematurity morbidities. The in-hospital mortality rate was high. The main risk factors of mortality were the very low birth weight, the extreme prematurity and circulatory disorders. Improving prevention and management of neonatal respiratory distress is still highly required.

REFERENCES

1. Liu L, Johnson HL, Cousens S, Perin J, Scott S, Lawn JE, et al.Global. Regional and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. Lancet 2012;379:2151—61.
2. Vendittelli F, Riviere O, Crenn-Hebert C, et al. Réseau sentinelle Audipog 2004–2005. Partie 1 : résultats des principaux indicateurs périnatals. Gynecol Obstet Fertil 2008;36:1091–100.
3. Gouyon-Cornet B, Bréat G et al. Évaluation nationale des besoins en lits de réanimation et soins intensifs néonataks B, Arch Pediatr. 2003 ; 10 :969-78.
4. DE Ballot, Chirwa TF, Cooper PA. Determinants of survival invery low birth weight neonates in a public sector hospital inJohannesburg. BMC Pediatr 2010; 10 (1): 30.
5. Martines J, Paul VK, Bhutta ZA, Koblinsky M, Sukat A, Wal-ker N, et al. Neonatal survival: a call for action. Lancet2005; 365 (9465): 1189-1197.
6. Zeitlin, Lallo DD et al. Variability in caesarean section rates for very preterm births at 28-31 weeks of gestation in 10 European regions: Results of the MOSAIC project. Eur J Obstet Gynecol Reprod Biol. 2010; 149(2):147-52.
7. Boulot P. Mode d'accouchement des enfants de poids inférieur à 2500 g. En cours de travail, quelle voie d'accouchement faut-il choissir? J Gynecol Obstet Biol Reprod. 1998;27 Suppl 2:S295-S301.
8. Truffert P, Maillard F, Burguet A, pour le groupe EPIPAGE. Morbidité pulmonaire du grand premature: incidence et prise en charge, cohorte EPIPAGE 1997. In: Collet M, Treisser A. 31ème Journées de medicine périnatale; Paris: Arnette; 2001.p.175-82.
9. Paumier A, Gras C, Branger B et al. Rupture prématurés des membranes avant 32 semaines d'aménorrhées: facteurs pronostiques prénatals. Gynecol Obstet Fertil. 2008; 36: 748-56
10. Ancel PY, Martin-Marchand L, et le groupe EPIPAGE 2. Prématurité: survie, morbidité et évolution entre 1997 et 2011. 43èmes journées nationales de la société française de medicine périnatale;13-15 novembre 2013; Monaco.Paris:Springer Paris;2013.p3-11.
11. Bonanno O, Wapner RJ. Antenatal corticosteroid treatment: what's happened since Drs Liggins and Howie ? Am J Obstet Gynecol. 2009;200(4):448-57.
12. Wallawe EM, Chapaman J, Stenson B, Wright S. Antenatal corticosteroid prescribing: setting standards of care. Br J Obstet Gyneacol. 1997;104(11):1262-6.
13. Galene Gromez S. Mortalité et morbidité des prématurés nés entre 30 et 34 semaines d'aménorhhée : résultats de l'enquête EPIPAGE (thèse). Médecine : Rouen ; 2005.
14. Shannon KM, Mentzer WC, Abels RI, Wertz M, Thayer- Moriyama J, Li WY, et al. Enhancement of erythopoiesis by recombinant human erythropoietin in low birth weight infants: a pilot study. J Pediatr 1992;120:586–92.