A PEARL Study Analysis of National Neonatal, Early Neonatal, Late Neonatal, and Corrected Neonatal Mortality Rates in the State of Qatar during 2011: A Comparison with World Health Statistics 2011 and Qatar's Historic Data over a Period of 36 Years (1975-2011)

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ABSTRACT

Objective: To prospectively ascertain Qatar's national Neonatal Mortality Rate (NMR), Early Neonatal Mortality Rate (ENMR), and Late Neonatal Mortality Rate (LNMR) during 2011, compare it with recent data from high-income countries, and analyze trends in Qatar's NMR's between 1975 and 2011 using historic data. **Study Design:** A National prospective cohort-study. **Materials and Methods:** National data on live births and neonatal mortality was collected from all public and private maternity facilities in Qatar (1st January-December 31st 2011) and compared with historical neonatal mortality data (1975-2010) ascertained from the database of maternity and neonatal units of Women's Hospital and annual reports of Hamad Medical Corporation. For inter country comparison, country data of 2009 was extracted from World Health Statistics 2011 (WHO) and the European Perinatal Health report (2008). **Results:** A total of 20583 live births were recorded during the study period. Qatar's national NMR during 2011 was 4.95, ENMR 2.7, LNMR 2.2, and cNMR 3.33. Between 1975 and 2011, Qatar's population increased by 10-fold, number of deliveries by 7.2 folds while relative risk of NMR decreased by 87% (RR 0.13, 95% CI 0.10-0.18, P<0.001), ENMR by 91% (RR 0.09, 95% CI 0.06-0.12, P<0.001) and LNMR by 58% (RR 0.42, 95% CI 0.23-0.74, P=0.002). The comparable ranges of neonatal mortality rates from selected high-income West European countries are: NMR: 2-5.7, ENMR 1.5-3.8, and LNMR 0.5-1.9. **Conclusions:** The neonatal survival in the State of Qatar has significantly improved between 1975 and 2011. The improvement has been more marked in ENMR than LNMR. Qatar's current neonatal mortality rates are comparable to most high-income West European countries. An in-depth research to assess the correlates and determinants of neonatal mortality in Qatar is indicated.

Key words:
Adjusted neonatal mortality, corrected neonatal mortality, early neonatal mortality, late neonatal mortality, neonatal mortality, Qatar

INTRODUCTION

The global neonatal survival has improved significantly between 1970 and 2010,[1] though the results remain grossly uneven between countries and regions.[2,3] Among the countries which have done extremely well are the 6 Gulf Cooperation Council (GCC) countries in the Middle East; United Arab Emirates (UAE), Qatar, Bahrain, Kuwait, Oman, and Saudi Arabia.[1-3] The State of Qatar is a sovereign country in the Middle East, which is undergoing very rapid development since 1995 due to its exponentially growing Liquid Natural Gas (LNG)-based economy. According to the recently published retrospective analyzes [4-10] and World Health Organization reports,[11] the neonatal, perinatal, and maternal mortality rates in the State of Qatar are comparable to most high-income countries. We conducted the current prospective, well-designed, national, population-based, epidemiologic study to ascertain Qatar's Neonatal Mortality Rate (NMR), Early Neonatal Mortality Rate (ENMR), and Late Neonatal Mortality Rate (LNMR) during 2011, to study the trends during the last 36 years (1975-2011), and

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to compare Qatar's 2011 neonatal mortality rates with the World Health Statistics 2011 (2009 data)[11] and European Perinatal Health Report 2008.[12]

MATERIALS AND METHODS

PEARL study-A national perinatal epidemiologic research project

PEARL Study (Perinatal Neonatal Outcomes Research Study in the Arabian Gulf) is Qatar's prospective National Perinatal Epidemiologic Study funded by QNRF (Qatar National Research Fund-grant # QNRF-NPRP-09-390-3-097). The study is a joint collaborative research project between Hamad Medical Corporation (HMC), Doha, Qatar and the University of Gloucestershire, Gloucester, United Kingdom. The project aims at building a National Neonatal Perinatal Registry for Qatar called Q-Peri-Reg, which will be used to quantify maternal, neonatal and perinatal mortality, morbidities, and their correlates. The current study was conducted during the first year of the project. The PEARL study data collection team is comprised of 13 full time physicians (including 1 research fellow, 2 research associates, and 10 research assistants). The study is approved by the Research Ethics Committee (IRB) of Hamad Medical Corporation (protocol #9211/09), which is responsible for providing ethical approval to all health care research projects in the State of Qatar.

PEARL study definitions

PEARL study uses the following WHO definitions,[13] based on ICD-10,[14] to ascertain, analyze, and report its neonatal perinatal data.

Live birth for reporting purposes

The birth of a fetus with a birth weight of ≥500 grams, or, if missing, ≥22 completed weeks of gestation, or if missing, crown heel length ≥25 cm, which after separation from his/her mother, has any signs of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscle, whether or not the umbilical cord has been cut or the placenta is attached.

Live birth for international comparison

The birth of a fetus with a birth weight of ≥1000 grams, or, if missing, ≥28 completed weeks of gestation, or if missing, crown heel length ≥35 cm, which after separation from his/her mother, has any signs of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscle, whether or not the umbilical cord has been cut or the placenta is attached.

Mortality rates

All mortality rates are calculated per 1000 live births.

Neonatal mortality

Death of a live born term baby (37 completed weeks of gestation) during the first 28 days (day 0 to day 27) of life.

Early neonatal mortality

Death of a live born baby during first 7 days of life (day 0 to day 6 of life irrespective of gestation at birth).

Late neonatal mortality

Death of a live born baby between day 7 and day 27 of life. Pearl study uses this criterion only for babies born at term (≥37 completed weeks of gestation). For preterm babies (≤36^{+6} weeks of gestation), PEARL study has developed an intrinsic methodology[15] of adjusting neonatal period for prematurity. The prematurity adjusted neonatal mortality is calculated as follows:

Prematurity adjusted neonatal mortality

For all preterm babies, an extended neonatal period is calculated using Table 1, in order to compensate for their prematurity. For example, a baby born at 24 completed weeks of gestation is born 90 days earlier before he/she would have been term (37 completed weeks of gestation). After becoming term (at 37 weeks), the baby's neonatal period will be counted, like any other term baby i.e., for another 28 days. This will make up a total of 118 days of neonatal period for a baby born at 24 completed weeks of gestation. During this extended neonatal period (118 days), the baby usually stays in neonatal intensive care unit (NICU). In case the baby dies during this period, his/her death is classified as neonatal death. However, some extremely preterm babies stay in NICU longer than their adjusted neonatal period, usually due to complications of prematurity and/or of intensive care procedures. In this case, their death after the adjusted neonatal period is classified as post-neonatal death.

Table 1: PEARL study method of estimation of adjusted neonatal mortality

Gestation (Weeks)	Adjustment for prematurity (days)	+ Term neonatal period (days)	Total neonatal period (days)
24	90	+28	118
25	83	+28	111
26	76	+28	104
27	69	+28	97
28	62	+28	90
29	55	+28	83
30	48	+28	76
31	41	+28	69
32	34	+28	62
33	27	+28	55
34	20	+28	48
35	13	+28	41
36	6	+28	34

During the adjusted neonatal period, the first 7 days after birth will be considered as early neonatal period irrespective of the gestation at birth and the rest of the adjusted neonatal period as late neonatal period. Therefore, for an extremely preterm baby born at 24 weeks of gestation, the total neonatal period will be 118 days with first 7 days (day 0-6) counted as early neonatal period and the remaining 112 days (day 7-118) counted as late neonatal period. Table 1, developed by The PEARL study, has been used in this paper to adjust the neonatal period for preterm babies born at various gestational ages, and to calculate their adjusted neonatal mortality rates for valid comparative analyzes with other studies.

In addition, PEARL study has also developed a methodology,[15] as given below, of calculating corrected neonatal mortality after exclusion of cases with futile outcome.

Corrected neonatal mortality

Some live born babies are either very sick or are clinically considered non-viable at birth by the attending physician or may be born with lethal congenital anomalies incompatible with life. These babies may not be resuscitated in labor room or provided intensive care because of futility. These neonatal deaths, which usually occur in labor and delivery suites, may not be reported in unit-based studies (Evans and Levene, 2001).[16] Similarly, legal frameworks, clinical guidelines, and practice of termination of pregnancies vary widely between countries and cultural groups, which affects overall perinatal and neonatal mortality (Papiernik *et al*., 2008).[17] These variations in policy and practice generate variations between populations of very preterm births among countries. The corrected neonatal mortality rate not only removes these variations in policy and practice, it also provides a rational basis for comparing survival data on viable babies when they are provided an equitable modern neonatal intensive care.

Data collection

Data on live births and neonatal mortality was collected using pre-designed, structured questionnaire. The State of Qatar had completely moved from home deliveries to hospital-based deliveries by 1974. Hence, facility-based neonatal perinatal data virtually represents Qatar's national population based data. PEARL study data was collected prospectively by a trained full time research team from all 5 maternity units in Qatar (1 January-31 December 2011), which includes 2 public maternity hospitals (Women Hospital and Al Khor Hospital) and 3 private maternity hospitals (Al Ahli Hospital, Doha clinic, and Al Emadi Hospital). Data was also collected from Hamad General Hospital, which does not have a maternity unit. However, it does have the largest emergency department, general pediatric and pediatric intensive care unit where neonatal deaths can happen.

All babies with a birth weight of ≥500 grams who were born with any signs of life were included in birth and death statistics irrespective of gestational age at birth or futility. One of the twins, born at 26 weeks gestation, had a birth weight of 430 grams due to intrauterine growth restriction. His surviving twin had a birth weight of 650 g. Hence, he was included in the birth and mortality statistics. Another 6 babies, who also died in the NICU, were classified as post-neonatal deaths using the prematurity adjustment criteria given in Table 1. Hence, these 6 NICU deaths were excluded from neonatal mortality statistics.

Data for comparison: Sources

For comparative analysis, Qatar's neonatal mortality data (1975-2010) was ascertained from the annual reports of Neonatal Unit Women's Hospital and annual reports published by the Department of Medical Statistics and Epidemiology at HMC, Qatar.[10] These reports are published on behalf of Qatar's National Health Authority (Department of Health) and are available electronically on www.hmc.org.qa and as hard copy from the department of statistics HMC.[9,10] For inter-country comparative analysis of neonatal mortality, we used 2009 data from World Health Statistics published by WHO in 2011.[11] For comparative analysis of early and late neonatal mortality rates, we used data from European Perinatal Health Report published by Europeristat project in 2008.[12]

Statistical analysis

Data was entered into Epi Data version 3.0 and analyzed using SPSS version 18.0. Chi-square test of significance was used to identify any significant differences between categorical variables, which were computed as frequency and percentages. A two-sided $P<0.05$ was taken as significant. The Relative Risk (RR) of mortality with 95% CI was calculated using 1975 data as reference. Significance of trends in neonatal mortality between 1975 and 2011 was measured by using trend Chi square statistics.

RESULTS

The total live births during the study period were 20583; of these, 87% were delivered in public hospitals and 13% in private hospitals [Figure 1]. All neonatal deaths occurred in tertiary care hospitals (NICU and labor room Women's Hospital and PICU Hamad General Hospital), except one labor room death of an anencephalic baby (gestational age 28 weeks, birth weight 800 g) who died in a secondary care hospital following parent's antenatal decision to not resuscitate him. A total of 102 neonatal deaths were recorded after adjustment for prematurity as per Table 1. During 2011, Qatar's national NMR was 4.95 (*n* 102), ENMR 2.7 (*n* 56), and LNMR 2.2 (*n* 46). A total of 33.3% babies (*n* 34) died due to futility; 2 due to non-immune hydrops

(1 of them also had an underlying cystic adenamatoid malformation), 7 due to extreme clinical immaturity, 11 due to lethal congenital anomalies (e.g., anencephaly, holoprosencephay, complex congenital heart disease), and 14 due to chromosomal and non-chromosomal syndromes. The chromosomal syndromes included Trisomy 13, Trisomy 18, Trisomy 20, and interstitial deletion of chromosome 13. The non-chromosomal syndromes included Potter's syndrome and Meckle Gruber syndrome. Among the 34 futile cases, 25 died after a Do Not Resuscitate (DNR) order (care withheld) after parental consent (14 had antenatal parental counseling and DNR while 11 had post-natal parental counseling and DNR). Twenty-nine futile cases died during the early neonatal period (22 during the first 24 hours) and 5 during the late neonatal period; 18 died in labor room and 16 in NICU. Qatar's cNMR during 2011, after excluding 34 futile cases and based on 68 non-futile cases, was 3.3.

Between 1975 and 2011, Qatar's population increased by 10-fold and total number of nationwide deliveries by 7.2-folds [Table 2]. During the same period, the relative risk of NMR in Qatar [Figure 2] decreased by 87% (RR 0.13, 95% CI 0.10-0.18, $P<0.001$), ENMR by 91% (RR 0.09, 95% CI 0.06-0.12, $P<0.001$), and LNMR by 58% (RR 0.42, 95% CI 0.23-0.74, $P=0.002$). The trends of improvement in Qatar's NMR, ENMR, LNMR, and PMR are shown in Figure 3. Qatar's 2011 NMR, ENMR, LNMR, and cNMR are comparable to the most recent published rates from many high-income West European counties [Figures 4 and 5].

DISCUSSION

Neonatal mortality, being a component of childhood mortality and hence Millennium Development Goal 4 (MDG 4), has been a focus of all global health improvement strategies and plans of action since 1990. The result is that global neonatal mortality has decreased from an estimated 4 million neonatal deaths per year reported in 2005[18] to an estimated 3.1 million neonatal deaths per year reported in 2008.[1] Unfortunately, this decline in neonatal mortality has been uneven.[1-3] The countries which needed most improvement had the least gain; the main reason being financial, political, administrative, and technical resource restriction.[1-3] Some countries, particularly State of Qatar, Brazil, and Sri Lanka, have done exceptionally well in reducing their neonatal mortality rates.[15]

Qatar is a sovereign state in the Middle East. Geographically, a peninsula spread over 11,437 square km; it is bordered by Saudi Arabia in the South and Persian Gulf on all other sides. Since 2010, Qatar has the highest per capita GDP in the world based on its proven reserves of oil and natural gas.[19] Currently, Qatar is the world's largest Liquefied Natural

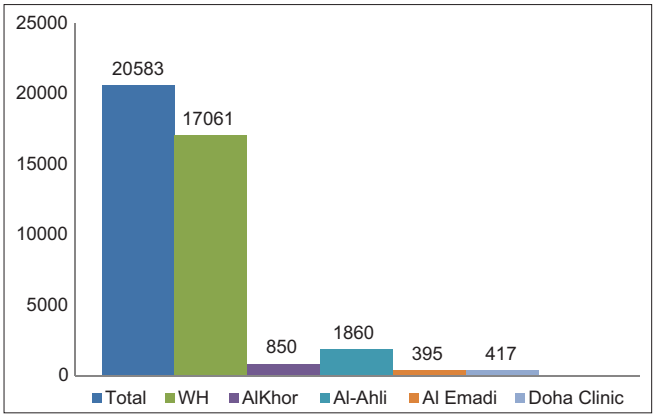

Figure 1: Total facility wise live born babies in Qatar during 2011

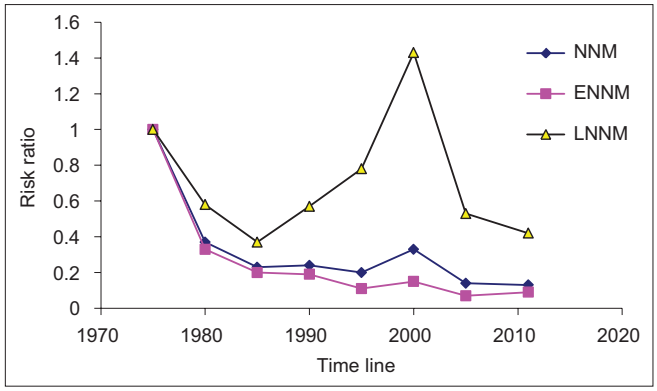

Figure 2: Trends in relative risk of neonatal, early neonatal and late neonatal mortality in Qatar 1975-2011

Table 2: Trends in population, live births, and relative risk of NMR, ENMR, and LNMR in Qatar 1975-2011

Year	Population*	Total live births	NM	NMR	RR (95% CI) *P* value	ENM	ENMR	RR (95% CI) *P* value	LNM	LNMR	RR (95% CI) *P* value
1975	171,000	2853	104	36.45	Reference	89	31.2	Reference	15	5.25	Reference
1980	229,000	6609	88	13.32	0.37 (0.28-0.48)<0.001	68	10.29	0.33 (0.24-0.45)<0.001	20	3.03	0.58 (0.30-1.12)=0.100
1985	320,000	9767	81	8.29	0.23 (0.17-0.30)<0.001	62	6.35	0.20 (0.15-0.28)<0.001	19	1.95	0.37 (0.19-0.73)=0.002
1990	439,000	10759	96	8.92	0.24 (0.19-0.32)<0.001	64	5.95	0.19 (0.14-0.26)<0.001	32	2.97	0.57 (0.31-1.04)=0.064
1995	642,000	9995	74	7.40	0.20 (0.15-0.27)<0.001	33	3.30	0.11 (0.07-0.16)<0.001	41	4.10	0.78 (0.43-1.41)=0.408
2000	744,000	11074	134	12.10	0.33 (0.26-0.43)<0.001	51	4.6	0.15 (0.10-0.21)<0.001	83	7.5	1.43 (0.82-2.47)=0.202
2005	863,000	13242	67	5.06	0.14 (0.10-0.19)<0.001	30	2.26	0.07 (0.05-0.11)<0.001	37	2.8	0.53 (0.29-0.97)=0.035
2011	1,707,756	20583	102	4.9	0.13 (0.10-0.18)<0.001	56	2.7	0.09 (0.06-0.12)<0.001	46	2.2	0.42 (0.23-0.74)=0.002

*Population reference bureau. (2010). World population data sheet 2010. (www.prb.org); NMR - Neonatal mortality rate; ENMR - Early neonatal mortality rate; LNMR - Late neonatal mortality rate

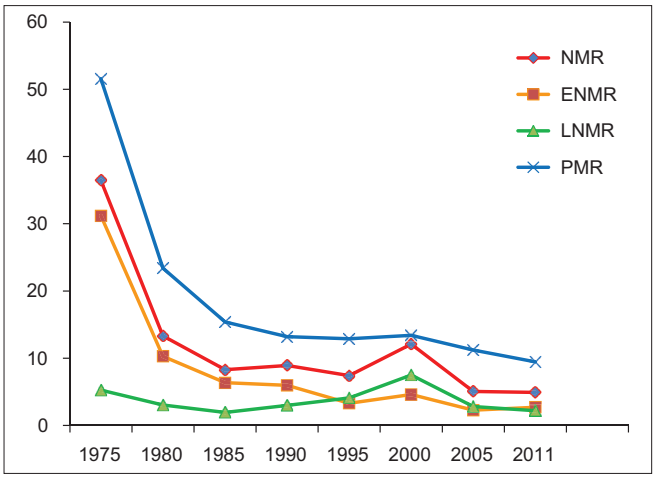

Figure 3: Trends in Qatar's NMR, ENMR LNMR, and PMR over a period of 36 years (1975-2011)

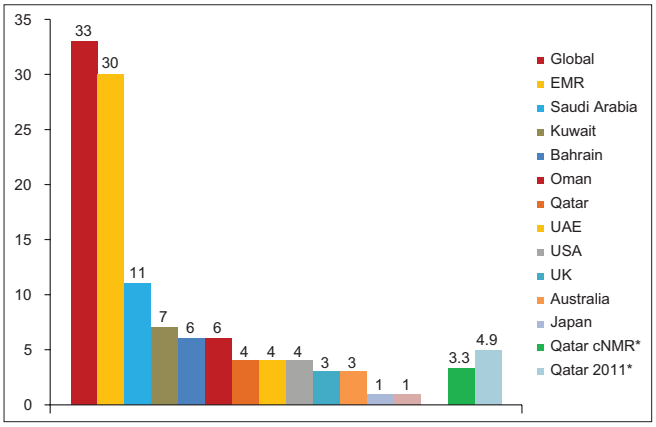

Figure 4: Comparative analysis of Qatar's neonatal and corrected neonatal mortality rates during 2011 with global, Eastern Mediterranean Region (EMR), GCC countries, and some developed world countries (Source: World Health Statistics 2011)

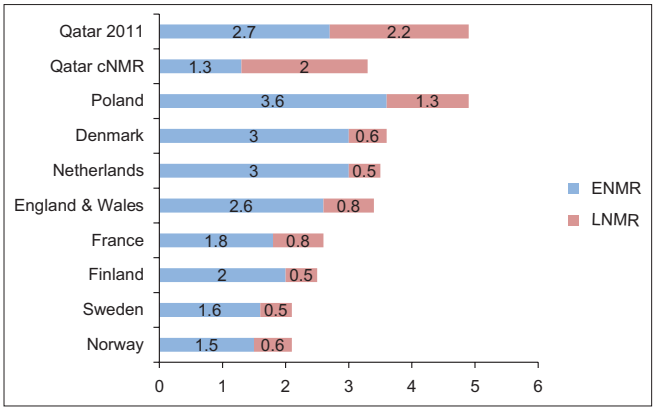

Figure 5: Comparative analysis of Qatar's early and late neonatal mortality rates with some of the European countries (Source: Europeristat Report 2008)

Gas (LNG) producer.[19] Qatar's economic boom, which started in mid-1990's, has resulted in exponential increase in its population [Table 2] due to economic migration.[20] Qatar's current population (1.7 million) is comprised of 20% native Qataris and 80% expatriates (Arab nations 20%; India 20%, Nepal 13%, Pakistan 7%, Sri Lanka 5%, Philippines 10%, and other countries 5%).[9,19] The life in Qatar is changing rapidly due to heavy investment in infrastructure and systems development. United Nations has classified Qatar as one of 42 countries possessing a very high human development index. Qatar had been allocating 15% of its national budget for health care till 2010.[10] The health care budget was increased to 27% of national budget in 2011. In addition, Qatar is investing a lot of funds in health-related research, which is a part of its strategic goal to develop a knowledge-based society.[21] Though Qatar's population increased 10-fold between 1975 and 2011, the major increase happened between 2005 and 2011 when the population doubled from 0.86 million to 1.7 million due to massive economic migration [Table 2]. There was a corresponding 7.2-fold increase in the number of live births. However, during the same period, NMR decreased 7.4-fold and RR of NMR 87% ($P<0.01$). The improvement in NMR, ENMR, and LNMR was part of an overall improvement in reproductive health [Figure 3], which included a similar and simultaneous decline in maternal mortality, still birth rate, and perinatal mortality rates (PMR).[10] During 2011, Qatar's perinatal mortality rate was 9.55/1000; stillbirth rate 6.85/1000 and maternal mortality rate 9.85/100,000 (the country had only two maternal deaths during the whole year). Qatar's maternal mortality rate had been zero for several years during mid 1990s and then from 1999 to 2002.[10] It is plausible that Qatar's heavy health care investments, combined with reduction in poverty and high levels of female literacy, could have contributed to Qatar's significantly improved neonatal, perinatal, and maternal survival rates.[6-10]

There is a wide variation in the reporting of births and neonatal deaths among institutions, countries, and regions due to variations in the limits of viability, definitions of live birth, and neonatal period.[17,22,23] Hence, comparative analysis of reported neonatal mortality rates between the countries becomes a challenge for the perinatal epidemiologist. WHO has published guidelines for standardization of births and deaths[13,14] which, unfortunately, lack universal compliance. Increasing survival of extremely preterm babies with resultant prolonged stay in NICU results in many very late deaths, which will technically be classified as "post-neonatal infant deaths" and not "neonatal deaths." Unfortunately, there is no standardized universal method of adjusting neonatal mortality for prematurity though most of previous works have used 36 weeks post-menstrual age as cut-off. According to the ICD-10, preterm period ends at 36^{+6} weeks of gestation. However, ICD-10 does not provide any guideline on how to adjust neonatal period for a preterm baby. Hence, to fill this gap in knowledge, PEARL study has

developed its own intrinsic method of calculating neonatal mortality rate adjusted for prematurity [Table 1] without changing the basic definitions of neonatal mortality given in ICD-10. Since all deaths in NICU may not qualify as neonatal deaths while many neonatal deaths occur outside NICU; unit-based neonatal mortality estimates are not representative of population-based neonatal mortality rates. Qatar has a unique obstetric set up in which >99.5% deliveries in the state are conducted in maternity hospitals, and 100% of births (live and stillborn) have a reliable birth weight available. Hence, the use of WHO criteria and ICD-10 definitions of neonatal mortality were possible at a national level in PEARL study; the estimates essentially represent a population-based study. Based on these criteria, Qatar's prematurity adjusted national NMR during 2011 (4.95/1000) is comparable with the NMR of most high-income countries published in the World Health Statistics 2011, though the estimated NMR of other countries published in this report may not necessarily have followed the same reporting criteria as ours.

The obstetric practices also vary worldwide with lack of uniformity of approach towards reproductive futility.[22,23] Social, cultural, and religious set-up of individual society influences the parental choice of antenatal terminations and resuscitation at birth. Hence, countries with higher rates of antenatal terminations are likely to have lower neonatal mortality and *vice versa*.[22,23] Therefore, to make a reasonable comparison, the neonatal mortality rates of countries with low antenatal terminations would need correction for futility. The State of Qatar has very low rate of antenatal terminations. In our current study, 34 cases died due to futility. None of the parents agreed with antenatal termination. Only 14 parents (41%) agreed withholding resuscitation at birth. Hence, to remove this skewedness, we corrected Qatar's 2011 NMR for lethal congenital anomalies and futility. Qatar's estimated cNMR of 3.33 is comparable with the NMR of countries with high antenatal terminations of pregnancies.

There is also an increasing postnatal recognition of futility in labor room and NICUs with consequent increasing trend of withdrawal of care or with holding care.[24-26] A recent study from Kansas reported 61.6% NICU deaths due to care withdrawn and another 20.8% deaths due to care withheld.[24] A similar trend has been reported from other NICU's from USA,[25,26] Norway,[27] and Australia.[28] Some babies are notified as very sick and not for resuscitation by the clinician attending the labor and delivery room. This is an accepted way of emergency clinical decision, which usually involves parental counseling. We had 18 neonatal deaths in the labor room and delivery room, which were included in the total mortality. In Qatar, during 2011, care was withheld (DNR-Do Not Resuscitate) in only 73.5% of futile cases (25 out of 34) and 24.5% of total deaths (25 out of 102). Nine futile cases received full cardiopulmonary resuscitation because the parents did not consent to the DNR order. The barriers to post-birth withdrawal/withholding of care in futile cases are similar to antenatal withdrawal/withholding of care and elective medical termination of pregnancy.

During the last 36 years, there was a significant decline in both early and late neonatal mortality rates in Qatar [Table 2]. However, the decline was more significant in early (P<0.001) than in late NMR (P=0.002). The RR of LNMR in Qatar showed a very distinct second peak during early 2000s [Figure 2]. This was the period when formal tertiary care neonatology was being launched in Qatar. Hence, an increasing number of extremely preterm and low birth weight babies were resuscitated and provided intensive care. Parallel and simultaneous to this change, the country had seen an increasing number of preterm births due to booming assisted reproductive technology. The result was an increase in early survival followed by delayed death of babies born at the limits of viability. Similar pattern had happened in high-income countries during late 1980s and early 1990s.

The Europeristat report 2008 and our study share similarity in methodology of using WHO definitions of neonatal mortality. Hence, we used Europeristat report for comparative analysis of Qatar's early and late neonatal mortality rates. Qatar's 2011 ENMR is only 1.2 times higher than LNMR as compared to most high-income West European countries, in which ENMR is 2- to 3-fold higher than LNMR [Figure 5]. The possible reasons of relatively higher LNMR in Qatar are late recognition of futility, delay or decline in parental consent to withdraw or withhold treatment.

Summary

State of Qatar, with its remarkable neonatal survival rates, more than 99.5% institutional deliveries and heavy investment in maternal and child health research, provides an ideal environment for in-depth study of clinical, socio-cultural and economic correlates, and associations of neonatal mortality. The knowledge generated will provide a strong foundation for further research into the genetic and molecular basis of reproductive wastage.

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Ethical approval: PEARL study is approved by the Institutional Research Ethics Committee of Hamad Medical Corporation State of Qatar (protocol #9211/09).

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