Iranian J Publ Health, Vol. 38, No.1, 2009, pp. 48-52

Original Article

Neonatal Mortality Risk Factors in a Rural Part of Iran: A Nested Case-Control Study

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(Received 4 Aug 2008; accepted 18 Feb 2009)

Abstract

Background: Due to complex causal framework of neonatal mortality, improvement of this health indicator is quite gradual and it's decreasing trend is not as great as other health indicators such as infant and under 5 mortality rates.This study was conducted to evaluate neonatal mortality risk factors based on nested case-control design.

Methods: The study population was 6900 neonates who were born in rural areas of Kohgiluyeh and Boyerahmad province (South of Iran). They were under follow up till the end of neonatal period and the outcome of interest was neonatal death. By using risk set sampling method, 97 cases and 97 controls were selected in study cohort.

Results: Prematurity (OR= 5.57), LBW (OR= 7.68), C-section (OR= 7.27), birth rank more than 3 (OR=6.95) and birth spacing less than 24 months (OR=4.65) showed significant statistical association ($P< 0.05$) with neonatal mortality. The Population Attributable Fraction (PAF) was 0.45 for LBW, 0.40 for prematurity, 0.28 for C-section, 0.30 for birth rank more than 3, and 0.16 for birth spacing less than 24 months.

Conclusion: Prematurity, low birth weight, C-section, birth spacing less than 24 months and birth rank more than 3 are important risk factors for neonatal mortality.

Keywords: *Neonatal mortality, Nested case-control study,Risk factors, Iran*

Introduction

Neonatal mortality (death from the birth till 28th day of life) is one of the most important determinants of children health status. Neonatal death has a complex causal framework and improvement of this health indicator is quite gradual. In rural area of Iran, the decreasing trend of neonatal mortality rate was not as great as other health indicators such as infant and under 5 mortality rates. Based on reports of Iran Health Ministry, from 1994 to 2004 in rural areas, the infant mortality rate decreased from 36.3 to 23.7 per 1000 live births and under 5 yr children mortality rate decreased from 45.3 to 29 per 1000 live births whereas neonatal mortality rate had little improvement and decreased from 19 to 16.6 per 1000 live births (1). According to the results of the studies in different regions of Iran, following the implementation of health system network and development of primary health care, infant and under 5 yr mortality rates had substantial decrease but there was not such progress in neonatal mortality rate (2).

The similar trend has been reported in rural areas of Kohgiluyeh and Boyerahmad: Infant mortality rate in this provience decreased from 35 in 1995 to 24 per 1000 live births in 2005, during the same perid under 5 yr mortality rate decreased from 48 to 29 per 1000 live births while neonatal mortality decreased from 21 to 17.5 per 1000 live births (3). The Kohgiluyeh and Boyerahmad Province located in south east of Iran, is one the less developed regions and it's population is estimated at 634299, from which about 52% are living in rural area. Primary Health Care (PHC) is provided by Behvars (especially

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trained health care providers for rural areas) in 370 health houses. The PHC coverage is 97% in this province (3).

A population based case-control study on still birth, neonatal mortality and their determinants in Kurdistan Province (West of Iran) showed that high risk pregnancy and mother illiteracy were among significant determinants. Estimated Odds Ratio (OR) for high risk pregnancy was 2.3(95% Confidence Interval (CI): 1.4-4.7) and OR of illiteracy was 3.1(95% CI: 1.4-6.5). The results did not show significant effect of birth place, sex of neonate and delivery route on neonatal mortality (4).

Most of studies in Iran and also in other countries showed that prematurity (less than 37 weeks of gestational age), congenital anomaly, male sex, delivery interval less than 1 yr and Low Birth Weight (LBW- less than 2500 gram of birth weight) are main risk factors for neonatal deaths, hence there is some variation between different studies done in different locations so it is crucial to examine the main risk factors in each specific location (5-8).

The aim of present study was evaluation of neonatal death risk factors in a substantial sample of Iranian neonates in a part of rural areas by using a relatively new design and modern analytic technique.

Material and Methods

This study was conducted as a nested case-control study, that is an efficient modality of case control study with growing use in the health related literature (9- 12) and the study cohort was all the neonates who were born in rural area of Kohgiluyeh and Boyrahmad Province (South of Iran) during a calendar year (from March 2006 till March 2007). All of the cohort members (6900 subjects) were followed by the health house staff, during neonatal period and relevant data were recorded in health file for each neonate. The outcome of interest was the neonatal death during the first 28 d of life and at the time of each case's occurrence the control was selected randomly from among all neonates with same birth date. Thus the sampling method was the risk set sampling with one control for each case and due to occurrence of 97 cases of neonatal death in the studied cohort (6900 newborn), 97 controls were selected, resulting in a total sample size of 194.

For all the cohort members the baseline data were appropriately collected from birth date to the end of neonatal period. The outcome or dependent variable was neonatal mortality set as a dichotomous variable of any death from birth till the end of 28^{th} day of life. The independent variables were sex (male vs. female), gestational age (<37weeks vs. ≥37 weeks), birth weight (<2500gr vs. ≥2500gr), maternal age (<18 or >35 vs. 18 - 35), birth rank (>3 vs. ≤3), delivery route (C-section vs. normal vaginal delivery (NVD)) and birth spacing (<24 months vs. ≥24 months).

The data were analyzed using univariate and multivariate conditional logistic regression models, reporting crude and adjusted matched OR in each analysis. Finally the Population Attributable fraction was computed for the variables remained in the model (13-14).

Results

We identified 97 cases and 97 controls in this well defined cohort of 6900 neonates, based on risk set sampling method. So we can expect NMR of about 14.1 (95% CI: 11.3 to 16.9) per 1000). Descriptive results revealed great discrepancies in frequencies of LBW, prematurity, delivery type (C-section) and birth rank more than 3 in the two groups (Table 1). Next a univariate conditional logistic regression for each variable was performed separately (Table 2) and any risk factors that showed marked association ($P< 0.2$) were selected for the next step analysis. The result of this stage led to exclusion of neonatal sex and maternal age. The conditional logistic regression model included the birth weight less than 2500 gr (OR=9.8, 95% CI=3.90-24.60), gestational age less than 37 weeks (OR=8.8, 95%CI=3.50-22.20), birth spacing (with previous birth) less than 24 months (OR=1.79, 95%CI=.78-4.08), C-section (OR=2.8, 95%CI=

1.36-5.76) and birth rank more than three (OR= 1.8, 95%CI=.96-3.38).

In the final model prematurity (Adjusted Odds Ratio (AOR)= 5.57), LBW (AOR= 7.68), C-section (AOR= 7.27), birth rank more than 3 (AOR= 6.95) and birth spacing less than 24 months (AOR= 4.65) showed significant statistical association ($P< 0.05$) with neonatal mortality (Table 2). As is seen in the table, age of the mother was not related to the outcome both in the univariate and multivariate models, birth rank (not significant in the univariate) becomes significant and birth spacing (significant in the univariate model) loses its significance in the final model.

There is some augmentation/attenuation of the Odds Ratios in the final model too. The OR for gestational age and birth weight attenuates and for the birth rank and delivery route augments in the final model.

The Population Attributable Fraction (PAF) was computed for the variables remained in the final model. Given the assumption that the observed relationships be causal, the PAF was as: 0.45 for LBW, 0.40 for prematurity, 0.28 for C-section, 0.30 for birth rank more than 3, and 0.16 for birth spacing less than 24 months.

Table 1: Descriptive frequencies of risk factors of neonatal mortality in a rural part of Iran-2006

Variables		Cases (%)	Controls (%)
Sex of neonate	female	43 (44.3)	52 (53.6)
	Male	54 (55.7)	45 (46.4)
Birth weight	≥2500gr	47 (48.5)	91 (91.8)
	<2500gr	52 (51.5)	6 (8.2)
Gestational age	≥37 weeks	50 (51.5)	89 (91.8)
	<37 weeks	47 (48.5)	8 (8.2)
Delivery type			
	NVD	66 (68.0)	84 (86.6)
	C-section	31 (32.0)	13 (13.4)
Birth rank	< 3	63 (64.9)	75 (77.3)
	≥ 3	34 (35.1)	22 (22.7)
Birth spacing	≥24 months	46 (47.4)	56 (57.7)
	<24 months	19 (19.6)	13 (13.4)
	First gestation	32 (33)	28 (28.9)
Maternal age (yr)	18-35	84 (86.6)	88 (90.7)
	< 18 or > 35	13 (13.4)	9 (9.3)

Table 2: The results of univariate and multivariate conditional logistic regression of neonatal mortality risk factors in a rural part of Iran-2006

Variables	Crude OR	95% CI	*P*	Adjusted OR	95% CI	*P*
Sex:						
Female	1	-	-			
male	1.43	0.82-2.50	0.210			
Birth weight:						
≥2500gr	1	-	-	1	-	-
<2500gr	9.80	3.90-24.60	<0.001	7.68	1.49- 39.55	0.015
Gestational age:						
≥37 weeks	1	-	-	1	-	-
<37 weeks	8.80	3.50-22.20	<0.001	5.57	1.12- 27.60	0.035
Birth rank:						
≤3	1	-	-	1	-	-
>3	1.8	0.96-3.38	0.068	6.95	1.90- 25.28	0.003
Birth spacing:						
≥24 months	1	-	-	1	-	-
<24 months	1.79	0.78-4.08	o.167	4.65	1.13-19.13	0.002
Delivery route:						
NVD	1	-	-	1	-	-
C- section	2.8	1.36-5.76	0.005	7.27	2.05- 25.72	0.033
Mother age (yr):						
18-35	1	-	-			
<18 or >35	1.5	0.61-3.67	0.374			

Discussion

We found 97 neonatal deaths in 6900 births registered in the 12 month period in the rural area of Kohgiluyeh and Boyerahmad Province of Iran. This equals to a Neonatal Death Rate of about 14.1 in 1000 live births (95% confidence interval: 14.1-16.9) that is a little smaller that province statistic 17.5 per 1000 live births in 2005. There are several explanations for this discrepancy. Firstly it may be due to the improvement of this index in recent years. There may be some differences in the data collection methods of this study and country report. Finally, this may be due to the better situation of health care delivery in rural parts comparing urban parts. Irrespective of the cause of discrepancy, there seems to be little influence on the results.

This study has identified; prematurity, LBW, C-section, birth spacing less than 24 months and birth rank more than 3 as potential risk factors for neonatal mortality. Our findings did not show significant effect of mother's age and sex of neonate on neonatal death. The results on prematurity and LBW were similar to our previous study (5). In the present study; sex of neonate was not a risk factor, as similar as the study conducted in Kurdistan province, But delivery route (C-section) which the mentioned study study failed to show significant association with neonatal mortality, was a predictor of outcome in our study (4). Our findings were similar to a case-control study which was conducted in Recife city of Brazil (6) indicating prematurity and LBW as neonatal death risk factors. They did not observe significant OR for delivery route but we identified C-section as an important risk factor. Both studies did not show significant association between neonatal death and maternal age. The significant effect of prematurity and LBW on neonatal mortality in this research was similar to the study which was conducted in Yazd City (7) but against to our results regarding the effect of sex, they did report the significant effect of sex. The present study showed that birth spacing less than 24 months was a risk factor, in contrast to the mentioned study that reported birth spacing less than 12 months as a risk factor. Shirvani et al. survey which was performed more than one decade earlier, showed prematurity, LBW, maternal age older than 35 yr and birth rank higher than 5 as neonatal death risk factors (15). Many published studies have evidenced that low birth weight with or without prematurity plays a role in a complex framework of causality involving genetic and environmental factors related to socio-economic and mother health status (16-18). Although the Population Attributable Fraction was computed for the variables remained in the final model, its results must be interpreted with great caution as the type of design does not support the causative relationship. The OR for C-section (vs. Normal Delivery) was increased from 2.80 to the 7.27 by adjusting for the probable confounding variables (Table 2). As C-section may be accompanied with high risk pregnancy, it was supposed that the OR to be diluted by adding any confounder to the model, but this was not the case in our study and we did not find any explanation for this situation.

One of the limitations of this study was that we focused on neonatal factors of neonatal death and our suggestion is to extension of nested case-control study to all maternal, neonatal and socio-economic risk factors of neonatal mortality. The another limitation points to the data gathering method; the data of this study were extracted from family health profiles which were recorded by health house staff (Behvars), and we recommend to consider other sources of data such as hospitals, health care providing centers, and finally directly from families (parents) if possible.

Acknowledgments

This research was supported by the School of Public Health and Institute for Public Health Research, Tehran University of Medical Sciences, Iran. We would like to thank Dr K Mohammad for his kind help. Also authors wish to thank Yasuj Medical University staff especially Mrs F Sadeghi,

Mr Z Parisay, Mr K Davari and Mr S Rezaei, for their cooperation in data gathering.
The authors declare that they have no conflict of interests.

References

1. Naghavi M, Jafari N, Jamshidbaigi E, Vasegh SH, Azad AM, Akbari ME (2005). *Health transition in rural areas of Iran*. 1st ed. Barge Rezvan, Tehran, Iran, pp.:92-98.
2. Mansoori A (1999). The evaluation of still birth and neonatal death risk factors in East Azarbayjan and Khorasan [MS thesis]. School of public Health, Tehran University of Medical Sciences, Iran.
3. Chaman R (2004). *Health View in Kohgiluyeh and Boyerahmad province*. 1st ed. Yasuj Medical University press, Yasuj, Iran, pp.:16.
4. Esmaeilnasab N, Majdzadeh R, Nadim A (2002). An Epidemiologic study on still birth, neonatal mortality and their determinant factors in Kurdistan province. *Hakim*, 4:272-77.
5. Chaman R (1998). Evaluation of mortality causes and preparation of life table for population of Kohgiluyeh Township [MPH thesis]. School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.
6. Sarinho S, Filho D, Dasiva G, Lima M (2001). Risk factors for neonatal death in Recife: a case-control study. *J Pediat*, 77 (4): 294-8.
7. Falahzadeh H, Mottahareh G, Rezvan A, Zafar Mohtashami A, Hakimi Kh, Ahmadabadi M, et al. (1999). Estimation of neonatal mortality rate and its related risk factors in Yazd city. *J Shahid Sadooghi Medical University*, 8: 374-80.
8. Shi L, Makinko J, Starfield B, Xu J, Regan J, et al. (2004). Primary care, infant mortality and low birth weight in the state of the USA. *J Epidemiol Community Health*, 58:374-80.
9. Rothman KJ, Greenland S (1998) *Modern Epidemiology*. 2nd ed. Lipincott-Raven, Washington, USA, pp.:108-110.
10. Szklo MN, Javier F (2007). *Epidemiology: Beyond the basics*. 2nd ed. Jones and Bartlett, Ontario, Canada, pp.:26-31.
11. Samet JM, Munoz A (1998). Perspective Cohort Studies. *Epidemiol Rev*, 20(1): 135-6.
12. Norman GR, Streiner DL (1993). Biostatistics: *The Bare Essential*. 1st ed. Mosby, Ontario, Canada, pp.:108-116.
13. Coughlin SS, Benichou J, Weed DL (1994). Attributable Risk Estimation in Case-Conrtol Studies. *Epidemiologic Reviews*, 16: 51-62.
14. Jewell NP (2004). *Statistics for Epidemiology*. Chapman & Hall/CRC, Washington, USA, pp.:51-53.
15. Shirvani F, Khosroshahi N (1995). A survey of frequency and causes of prenatal mortality in Tehran. *J Med School*, 1:69-71.
16. Spencer N, Logan S (2002). Social influence on birth weight. *J Epidemiol Community Health*, 56: 326-27.
17. Wilcoxon MA, Smith SJ, Johnson IR, et al. (1995). The effect of social deprivation on birth weight, excluding physiological and pathological effects. *Br J Obstet Gyn*, 102: 918-24.
18. Clausson B, Lichtenstein P, Cnattingius S (2000). Genetic influence on birth weight and gestational length determined by studies in offspring of twins. *Br J Obstet Gyn*, 107: 375-81.