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Original Article

Epidemiological Aspects of Neonatal Mortality Due To Intrauterine Infection in Kazakhstan

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Abstract

Background: In this study, we examined the epidemiological aspects of neonatal mortality due to intrauterine infections with regard to regional characteristics.

Methods: Consolidated report of the Ministry of Health and Social Development of the Republic of Kazakhstan on children deceased during their first 28 days of life due to intrauterine infections (P23 – congenital pneumonia, P35-39 – infectious diseases specific to the perinatal period) in the country and its regions for 2010 - 2014 was used in this investigation. Descriptive and analytical methods of medical statistics and epidemiology were used as the main method of this 5-year (2010-2014) retrospective study.

Results: Overall, 3,298 neonatal deaths from intrauterine infections were recorded in Kazakhstan during the period of 2010-2014, 1,925 of which were early and 1,373 were late neonatal deaths. The average annual rate of neonatal mortality rate from intrauterine infection in the country amounted to 1.73±0.23‰ (95% CI=1.27-2.19‰), whereas trends during the study period decreased (T=−15.3%). Regional characteristics of neonatal mortality were established. Different levels for cartograms of neonatal mortality from intrauterine infections were defined: low (up to 1.28‰), average (from 1.28‰ to 2.12‰) and high (by 2.12‰ and above). Neonatal mortality in the early and late periods was also analyzed.

Conclusion: This is the first epidemiological study of neonatal mortality from intrauterine infection, which contains a detailed space-time evaluation. The results of this investigation can be used to improve the state program to combat infant mortality.

Keywords: Neonatal mortality, Intrauterine infections, Trends, Cartograms, Kazakhstan

Introduction

Infant mortality rate is one of the demographic factors that most clearly reflect the level of state development and its economic and social changes. It also represents the level of development of the healthcare system and affects the government's expenses (1, 2).

Infectious diseases are the leading cause of high morbidity and mortality among young children and adolescents. It was found that one third of child deaths in the world occur in newborns, and the major cause of them is infection (3). Worldwide, the main direct causes of newborn deaths are premature labor (28%), severe infections (26%), asphyxia (23%), and neonatal tetanus (7%) (4).

In all regions of the world, there is a decrease in neonatal mortality, and the progress has been slow in regions with high rates of neonatal mortality. Furthermore, global health programs should pay more attention to neonatal mortality for the more effective implementation of the Millennium Development Goals 4 (to reduce child mortality by two thirds) (5, 6).

In this paper, we present the epidemiological aspects of death from intrauterine infections in Kazakhstan.

Materials and Methods

Consolidated report of the Ministry of Health and Social Development of the Republic of Kazakhstan on children deceased during their first 28 days of life due to intrauterine infections (P23 – congenital pneumonia, P35-39 – infectious diseases specific to the perinatal period) in the country and its regions for 2010-2014 was used in this study, where the number of deceased was calculated by place of death. Additionally, data reported by the Statistics Committee of the Ministry of National Economy of the Republic of Kazakhstan on the number of live births for 2010-2014, was used for further analysis (7). Descriptive and analytical methods of medical statistics and epidemiology were used as the main method of this 5-year (2010-2014) retrospective study. Justification of the basic formulas presented in this article is omitted as all the calculations are described in detail in the guidelines and statistics textbooks (8-10). However, a few of them are represented below.

Early neonatal mortality (ENM) was calculated as follows:

$$\text{ENM} = \frac{\text{number of infant deaths under age of 7 days [0–168 hrs]}}{\text{number of live births}} \times 1\,000$$

Late neonatal mortality (LNM) was calculated as follows:

$$\text{LNM} = \frac{\text{number of infant deaths on 2–4th week of life [168 hrs–27 days 23 hrs 59 min]}}{\text{number of live births}} \times 1000$$

Neonatal mortality (NM) was calculated as follows:

$$\text{NM} = \frac{\text{number of infant deaths under age of 28 days [27 days 23 hrs 59 min]}}{\text{number of live births}} \times 1\,000$$

Trends of mortality rates are determined by the ordinary least squares method:

$$y = a + bx$$

where y – aligned value; x – conditional series of numbers, symmetrically located with regard to zero; a – conditional average; b – alignment coefficient.

Geometric mean, equal to the n-th root of the product of annual rates, is used to calculate the average annual growth rates and/or increase of dynamic series:

$$T_{\text{пр}} = \sqrt[n]{T_1 \times T_2 \times T_3 \times \ldots T_n}$$

where T is the annual rate of growth and/or increase of dynamic series and n is the number of rates.

95% confidence interval was calculated according to the following formula:

$$95\%\ \text{CI} = M \pm 1{,}96 \times m$$

The cartogram compiling method used in this investigation was proposed by Igissinov in 1974 [11]. It is based on the derivation of a standard deviation *(σ)* from an average of *(x)*. The scale levels were calculated as follows: *σ* was taken as an interval, the maximum and minimum levels of disease were defined by the following formula: $x \pm 1.5\sigma$, with the minimum level of $x-1.5\sigma$ and a maximum equal to $x+1.5\sigma$. Afterwards, the scale levels of the cartogram were determined: i) $(x-1.5\sigma)+\sigma$; 2) $(x-1.5\sigma)+2\sigma$; 3) $(x-1.5\sigma)+3\sigma$, etc.; categorization of the indexes was derived from the $x \pm 0.5\sigma$ formula, corresponding to the average level ($x-0.5\sigma$ and $x+0.5\ \sigma$); the values distant from the average incidence by *σ*, show lower $((x-0.5\sigma)-\sigma)$ and higher $((x-0.5\sigma)+\sigma)$ values.

The materials were viewed and processed on computer (using software package Microsoft Office: Excel, Word, Access; BIOSTAT, EpiInfo 7).

Results

Overall, 3,298 neonatal deaths from intrauterine infections were recorded in Kazakhstan during the period of 2010-2014, 1,925 of which were early and 1,373 were late neonatal deaths. Distribution by regions of the country is presented in Table 1.

The average annual intrauterine infection neonatal mortality rate in the country amounted to 1.73±0.23 per 1,000 of live births (95% CI=1.27-2.19‰). Over time, neonatal mortality rate decreased from 2.20‰ (2010) to 1.10‰ in 2014 (Fig. 1). After alignment of this indicator, the downward trend (T=−15.3%) was also set.

Table 1: Distribution of neonatal death from nosocomial infection in regions of Kazakhstan in 2010-2014

Region/city	Neonatal mortality, Number (%)		
	Overall	Early	Late
North Kazakhstan region	39 (1.2)	21 (1.1)	18 (1.3)
West Kazakhstan region	73 (2.2)	52 (2.7)	21 (1.5)
Pavlodar region	76 (2.3)	32 (1.7)	44 (3.2)
Astana city	97 (2.9)	69 (3.6)	28 (2.0)
Atyrau region	117 (3.5)	66 (3.4)	51 (3.7)
Aktobe region	122 (3.7)	68 (3.5)	54 (3.9)
National organizations	148 (4.5)	61 (3.2)	87 (6.3)
Kostanay region	154 (4.7)	62 (3.2)	92 (6.7)
Mangistau region	158 (4.8)	92 (4.8)	66 (4.8)
Akmola region	161 (4.9)	128 (6.6)	33 (2.4)
Karagandy region	181 (5.5)	130 (6.8)	51 (3.7)
Kyzylorda region	182 (5.5)	121 (6.3)	61 (4.4)
Zhambyl region	207 (6.3)	121 (6.3)	86 (6.3)
East Kazakhstan	223 (6.8)	147 (7.6)	76 (5.5)
Almaty region	244 (7.4)	171 (8.9)	73 (5.3)
South Kazakhstan	322 (9.8)	148 (7.7)	174 (12.7)
Almaty city	794 (24.1)	436 (22.6)	358 (26.1)
Republic of Kazakhstan	3,298 (100.0)	1,925 (100.0)	1,373 (100.0)

A high proportion of neonatal deaths occur in Almaty (24.1%).

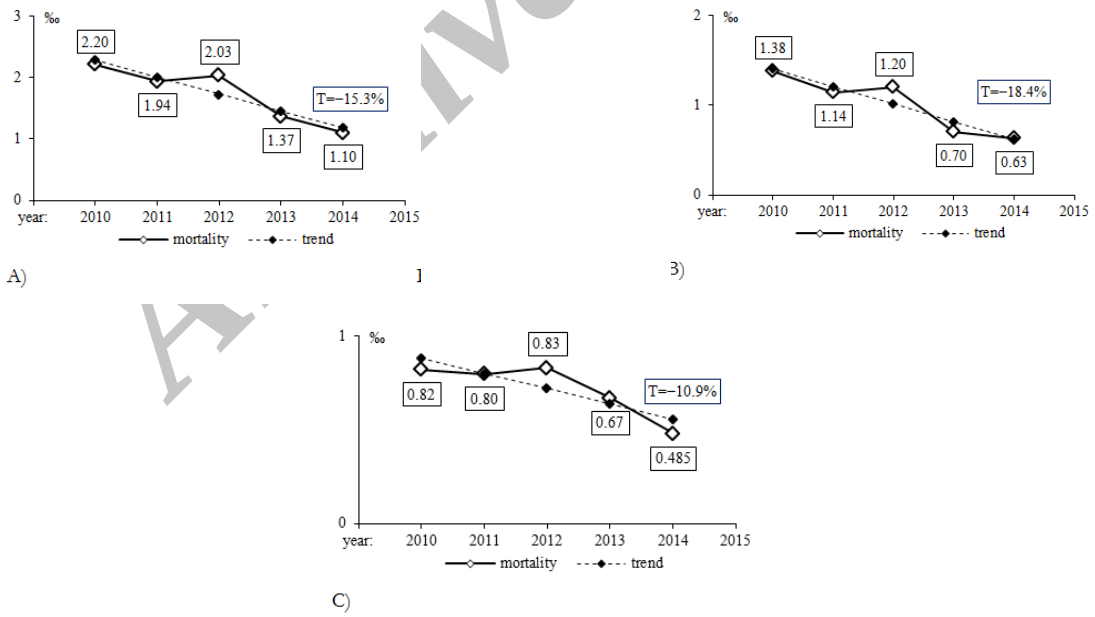

Fig. 1: Dynamics of neonatal mortality (A – overall, B – early, C – late) in the Republic of Kazakhstan in 2010-2014

The average annual early neonatal mortality rate was 1.01±0.16‰ (95% CI=0.69-1.33‰) and late neonatal mortality rate was 0.72±0.07‰ (95% CI=0.57-0.87‰). The differences were not statistically significant (P>0.05) as both mortality rates are affected by the same causal factors. In the dy-

namics, trends tended to decrease, while the rates for late neonatal mortality (T=−10.9%) were less pronounced compared to the early (T=−18.4%).
Neonatal mortality due to intrauterine infection had regional characteristics. For instance, the lowest overall annual average neonatal mortality was established in South Kazakhstan (0.83±0.10‰), North Kazakhstan (0.97±0.25 ‰) and in Astana city (0.93±0.10‰). High average annual mortality rates were attributed to the Akmola region (2.66±0.63‰), Almaty (4.18±0.54‰) and national organizations (Table 2).

Table 2: Average annual indices of neonatal mortality from nosocomial infection by regions in the Republic of Kazakhstan in 1999-2010

	Neonatal mortality								
	Overall			Early			Late		
	P±m, ‰	95% CI, ‰	T, %	P±m, ‰	95% CI, ‰	T, %	P±m, ‰	95% CI, ‰	T, %
South Kazakhstan region	0.83±0.10	0.63-1.03	−10.8	0.38±0.07	0.24-0.53	−15.0	0.45±0.05	0.36-0.54	−7.3
Astana city	0.93±0.10	0.73-1.13	*+0.9*	0.66±0.13	0.39-0.92	*+3.7*	0.27±0.03	0.21-0.34	−5.5
North Kazakhstan region	0.97±0.25	0.48-1.45	*+24.5*	0.52±0.12	0.28-0.76	*+24.4*	0.45±0.14	0.17-0.72	*+24.6*
West Kazakhstan region	1.20±0.24	0.72-1.68	−22.7	0.85±0.22	0.42-1.29	−17.4	0.34±0.18	0.00-0.69	−38.6
Pavlodar region	1.21±0.57	0.08-2.33	−86.0	0.51±0.26	0.01-1.01	−69.3	0.70±0.32	0.06-1.33	−71.2
Almaty region	1.28±0.11	1.05-1.50	−1.2	0.90±0.12	0.66-1.14	−10.5	0.38±0.07	0.24-0.51	*+26.9*
Aktobe region	1.33±0.53	0.29-2.37	−32.7	0.74±0.28	0.19-1.30	−32.3	0.59±0.25	0.09-1.09	−33.2
Karagandy region	1.48±0.18	1.14-1.83	−7.2	1.07±0.14	0.80-1.33	−10.6	0.42±0.06	0.30-0.54	*+2.1*
Atyrau region	1.50±0.60	0.33-2.67	−18.9	0.85±0.32	0.22-1.48	−22.6	0.65±0.31	0.05-1.25	−14.2
Zhambyl region	1.53±0.53	0.49-2.57	−39.3	0.90±0.39	0.13-1.66	−57.3	0.64±0.15	0.35-0.93	−24.8
Republic of Kazakhstan	1.73±0.23	1.27-2.19	−15.3	1.01±0.16	0.69-1.33	−18.4	0.72±0.07	0.57-0.87	−10.9
Kyzylorda region	1.89±0.44	1.02-2.76	−14.5	1.26±0.33	0.60-1.91	−23.5	0.64±0.16	0.33-0.94	*+3.4*
Mangistau region	1.91±0.47	1.00-2.82	−28.3	1.11±0.32	0.49-1.73	−27.7	0.80±0.19	0.42-1.18	−29.2
East Kazakhstan region	1.96±0.38	1.22-2.71	*+2.3*	1.29±0.26	0.78-1.80	*+9.8*	0.67±0.15	0.37-0.97	−10.7
Kostanay region	2.39±0.31	1.78-3.00	−9.5	0.96±0.19	0.60-1.33	−13.7	1.43±0.17	1.08-1.77	−6.7
Akmola region	2.66±0.63	1.43-3.88	−25.6	2.11±0.63	0.88-3.33	−34.6	0.55±0.07	0.41-0.69	*+4.1*
Almaty city	4.18±0.54	3.12-5.24	−15.1	2.30±0.42	1.49-3.12	−19.7	1.88±0.17	1.54-2.22	−9.7
National organizations	5.44±1.13	3.22-7.66	−19.2	2.24±0.53	1.21-3.28	−22.0	3.19±1.04	1.16-5.23	−17.2

With time, the overall neonatal mortality rate in almost all regions of the country tended to decrease. However, in Astana city (T=+0.9%), East Kazakhstan (T=+2.3%) and North Kazakhstan (T=+24.5%) the trends with aligned indices tended to increase (Table 2).
The average annual downward trend of aligned indices of neonatal mortality rate ranged from T=−1.2 (Almaty region) to T=−86.0% (Pavlodar region) (Table 2).
Early neonatal mortality rate due to intrauterine infection was lowest in South Kazakhstan (0.38±0.07‰), Pavlodar (0.51±0.26‰) and North Kazakhstan (0.52±0,12‰) areas. The regions with the highest rates of early neonatal mortality were Akmola region (2.11±0.63‰) and Almaty city (2.30±0.42‰). Additionally, high values were determined in national organizations (2.24±0.53‰).
Early neonatal mortality trends grew only in Astana city (T=+3.7%), East Kazakhstan (T=+9.8%) and North Kazakhstan (T=+24.4%).
The average annual rates of late neonatal mortality were lowest in North Kazakhstan (0.27±0.03‰), West Kazakhstan (0.34±0.18‰) and Almaty region (0.38±0.07‰). High values of late neonatal mortality were established in Kostanai region

(1.43±0.17‰), Almaty City (1.88±0.17‰) and national organizations (3.19±1.04‰). Trends of late neonatal mortality from intrauterine infection grew in Karaganda (T=+2.1%), Kyzylorda (T=+3.4%), Akmola (T=+4.1%), North Kazakhstan (T=+24.6%) and Almaty (T=+26.9%) regions (Table 2).

Cartograms of neonatal mortality

Mapping is one of the leading methods of scientific analysis of epidemiological situation in a country (11-16) that allows further analysis of spatial distribution of the frequency of neonatal mortality. Mapping was carried out based on neonatal mortality rates (overall, early and late). Upon preliminary identification of annual averages in individual health and geographic regions, arithmetic mean (M) ratios and standard deviation (õ) were calculated. Ultimately, the cartograms' scale of stages with grouped mortality rates was determined. It should be noted that the data on national organizations was omitted in this calculation.

Overall, the following groups of areas were defined on the cartogram of neonatal mortality (Fig. 2A):

1. Regions with low rates (up to 1.28‰) – South Kazakhstan (0.83‰), North Kazakhstan (0.93‰), West Kazakhstan (1.20‰) and Pavlodar (1.21‰) region, as well as Astana city (0.93‰);

2. Regions with the average rates (from 1.28‰ to 2.12‰) – Almaty (1.28‰), Aktobe (1.33‰), Karagandy (1.48‰), Atyrau (1.50‰), Zhambyl (1.53‰), Kyzylorda (1.89‰) Mangistau (1.96‰) and East Kazakhstan (1.96‰) regions;

3. Regions with high rates (from 2.12‰ and above) – Kostanay (2.39‰), Akmola (2.66‰) and Almaty region (4.18‰).

Spatial assessment of early neonatal mortality established the following regions (Fig. 2B):

1. With low levels (up to 0.76‰) - South Kazakhstan (0.38‰), Pavlodar (0.51‰), North Kazakhstan (0.52‰) and Aktobe (0.74‰) region, as well as Astana city (0.66‰);

2. With average levels (from 0.76‰ to 1.29‰) - Atyrau (0.85‰), West Kazakhstan (0.85‰), Zhambyl (0.90‰), Almaty (0.90‰), Kostanay (0.96‰), Karagandy (1.07‰), Mangistau (1.11‰) and Kyzylorda (1.26‰) region;

3. With high levels (from 1.29‰ and higher) - Eastern Kazakhstan (1.29‰), Akmola (2.11‰) and Almaty region (2.30‰).

The cartogram of late neonatal deaths represents the following regions (Fig. 2C):

1. Regions with low rates (up to 0.47‰) – Astana city (0.27‰), West Kazakhstan (0.34‰), Almaty (0.38‰), Karaganda (0.42‰), North Kazakhstan (0.45‰) and South Kazakhstan (0.45‰) regions;

2. Regions with average rates (from 0.47‰ to 0.89‰) – Akmola (0.55‰), Aktobe (0.59‰), Kyzylorda (0.64‰), Zhambyl (0.64‰), Atyrau (0.65‰), East Kazakhstan (0.67‰), Pavlodar (0.70‰) and Mangistau (0.80‰) regions;

3. Regions with high rates (from 0.89‰ and above) – Kostanay region (1.43‰) and Almaty city (1.88‰).

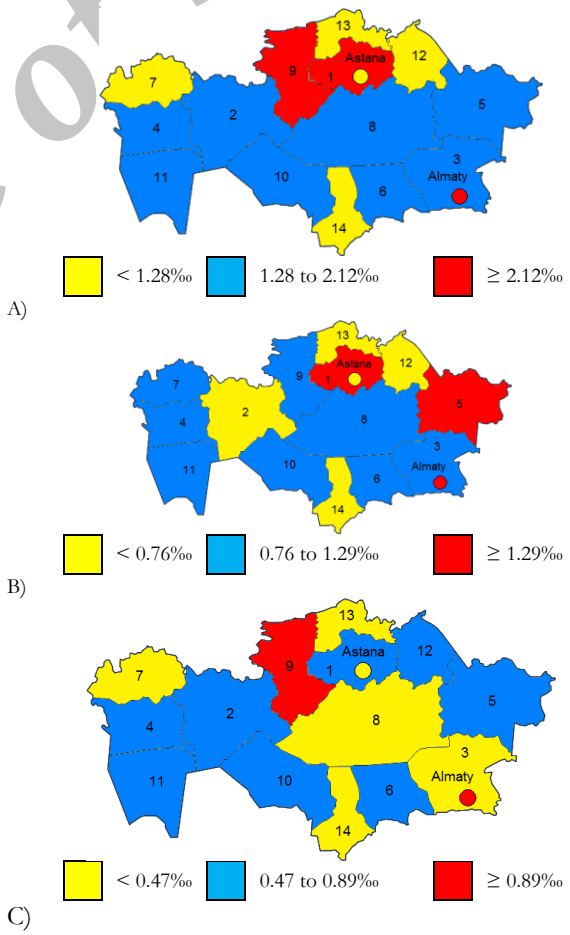

Fig. 2: Cartogram of neonatal mortality from intrauterine infections in Kazakhstan in 2010-2014

Regions: 1. Akmola region 2. Aktobe region 3. Almaty region 4 Atyrau region 5. East Kazakhstan region 6. Zhambyl region 7. West Kazakhstan region 8. Karaganda region 9. Kostanay region 10. Kyzylorda region 11. Mangistau region 12. Pavlodar region 13. North Kazakhstan region 14. South Kazakhstan region

Discussion

A decrease in neonatal mortality rate due to intrauterine infection was observed in the Republic of Kazakhstan for the period of 2010 – 2014 mainly due to reduction of both early and late neonatal mortality rates, diminishing from 2.20 ‰ in 2010 to 1.10 ‰ in 2014. This indisputably positive fact was noted in many parts of the world (12). Access to health facilities under the State program "100 schools, 100 hospitals" for diagnosis and treatment of women and children, improvement of financial and technological state of hospitals and clinics in accordance with the requirements of modern medicine, development of highly specialized medical assistance as well as the integration and systematic structure of national healthcare system facilitated this progress. Moreover, WHO approved strategies, such as "Safe pregnancy and childbirth", "Breastfeeding promotion and effective perinatal assistance program", "WHO program on breastfeeding and nutrition of young children", "Integrated Management of Childhood Illnesses" were also implemented. Modern perinatal technologies and approaches, also approved by WHO, were introduced into clinical practice in obstetrics and obstetric facilities, such as birth partnership, heat chain, joint stay of mother and child, early discharge from the hospital. Therefore, implementation of these innovations into practical health care helped reduce the number of infant deaths, including neonatal mortality.

Analysis of the causes of death of newborns in the early neonatal period revealed that the infant mortality is preventable under such controlled conditions like birth trauma and birth asphyxia and depends on the tactics of the delivery and the timely and appropriate, non-aggressive intensive care. However, the incidence of pneumonia and fetal intrauterine infection is directly dependent on the presence of chronic viral infections and inflammatory processes in genitals of a mother (13-15). The health status of a newborn is determined by the mother's health and reflects the well-being of prenatal development and birth process. The major source of intrauterine infections is a sick mother that infects the fetus in utero or a newborn, during childbirth, when the child is passing through the birth canal (16-19).

Comparative analysis revealed the prevalence of early neonatal mortality (1.01±0.16‰) over late neonatal mortality (0.72±0.07‰) in neonatal mortality (1.73‰±0.23‰). Comparative analysis of the causes of neonatal mortality showed the difference between early neonatal mortality and late neonatal mortality. Respiratory distress syndrome and birth trauma are the leading causes in early neonatal mortality, whereas mortality birth trauma and intrauterine infection are the most frequently diagnosed causes of death in late neonatal mortality. Intrauterine infections as the cause of death occur 3 times more often than in case of late neonatal mortality compared to the early.

Even though a clear pattern cannot be distinguished between the investigated regions, high average mortality rates, established in the Akmola region, Almaty city and national organizations, can be explained by the fact that hospitalized women were patients with obstetrical history, concomitant extragenital pathologies of cardiovascular, respiratory, renal, endocrine and other systems.

Trends of aligned indices that had a tendency to grow in Astana city, East Kazakhstan and North Kazakhstan regions can be justified by climatic features, leading to frequent acute respiratory viral infections. These regions are characterized by extreme continental climate with sharp seasonal temperature differences, long frosty winters with blizzards, snowstorms and hot dry summers with stronger winds.

Therefore, all these changes take us back to the question of development of medicine, quality of medical services, level of implementation of state programs and quality of registration and report in these regions. Additionally, it is crucial to focus on the following practices and guidelines:

1. In order to improve obstetric services in the

country it is necessary to improve the system of accounting and registration, particularly quality of registration and control of deceased children.
2. To improve the early diagnosis of pathologies of pregnant women and fetuses and to ensure safe delivery, informational and educational activities among the population of the country should take place. Development and organization of effective forms of counseling and preventive work in the organizations of primary health care in family planning are also very important.
3. Public awareness of the need to monitor their health, of the availability of medical care and the existing programs aimed at reducing mortality, for example solidary liability for their own health, should be raised.
4. Operational daily monitoring in all regions needs to be improved. After timely analysis of the updates pregnant women at risk should be transferred to a higher level of specialized care.
5. Training and certification of primary care physicians and specialists of perinatal services in the regions of regions with high rates of neonatal mortality should be organized with accordance to international approaches in providing antenatal services based on the principles of safe motherhood.
6. Results of neonatal mortality from intrauterine infections can be used as a priority in research projects for development of national and regional preventive programs.
7. The results of the spatial assessment (cartograms) of neonatal mortality from intrauterine infection are recommended for targeted research in regions. These investigations should be aimed at improvement of programs to combat diseases and to development of unified state control programs to reduce infant mortality.
8. Improvement of the methodology of epidemiological studies by strengthening the role of integration of epidemiology of infant mortality with science and technology and other areas to develop preventive measures, by identifying population groups with high and low mortality.

Conclusion

This epidemiological study provides recent (2010-2014) detailed information, including spatial and temporal characteristics of neonatal mortality in Kazakhstan. Findings of this investigation can be used for further development of neonatal services with particular focus on social and economic development, geographical location, demographic situation, and health and infrastructure in each region.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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The authors(s) declare that they have no competing interests.

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