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Trends in infant mortality rates in Hungary between 1963 and 2012

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ABSTRACT

Aim: This study investigated annual and seasonal death trends for infants of less than one-year-of-age in Hungary between 1963 and 2012 and analysed commonly accepted risk factors.

Methods: Data on the numbers of live births and infant deaths were obtained from the published nationwide population register. Negative binomial regression was applied to investigate the yearly trends in rates and also the effect of possible risk factors - low birth weight, maternal education and sex - on infant mortality. Cyclic trends were investigated using logistic regression.

Results: Annual infant mortality declined significantly ($p<0.001$) from 42.9 to 4.9 per 1,000 live births per year during the study period and significantly increased ($p<0.001$) in the low birth weight group and lower maternal education groups. A significant ($p<0.001$) cyclic trend in mortality was revealed, with a peak in deaths in late February for all infants and a double peak, in May and November, in the group of cases who died during the early neonatal period.

Conclusion: This Hungarian study suggests that there was a significant seasonal effect on neonatal and infant mortality at the end of winter between 1963 and 2012. We speculate that this may have been related to respiratory infections.

Keywords: Hungary, infant mortality, neonatal mortality, respiratory infections, seasonal variations

Key Notes:

- This study investigated annual and seasonal death trends for infants of less than one-year-of-age in Hungary from 1963-2012.
- Annual infant mortality declined significantly during the study period and significantly increased in the low birth weight and lower maternal education groups.
- A significant cyclic trend in mortality was revealed, with a peak in deaths in late winter for all infants and peaks in May and November for early neonatal infants.

INTRODUCTION

Infant mortality has been investigated in several countries and certain risk factors, including socio-economic, geographic and environmental, have been implicated (1,2). Infant mortality rates have decreased in developed countries in the last two decades (3,4), including Hungary. However, Hungary had the 22nd highest rates of infant mortality out of 24 European countries in the 2010 and 2011 tables produced by the Organization for Economic Co-operation and Development, (4). Nevertheless, in a recent paper, the Hungarian infant mortality rate of 4.6 per 1,000 live births in 2013 was slightly lower than the Central European average of 5.6 per 1,000 live births per year, but was higher than the reported Western European average of 3.2 per 1,000 live births (5). In spite of these annual reported trends in Hungarian infant mortality, rates have not yet been investigated in any detail.

In the present study, changes in infant mortality rates, annual trends and the effect of some possible risk factors related to deaths under the age of one year were investigated during the 50-year interval between 1 January 1963 and 31 December 2012 in Hungary. Furthermore, seasonality analyses, which are analyses of cyclic trends in the infant mortality rates, were also carried out.

METHODS

Study population

Investigation of annual trends and risk factors

Infant death was defined as death after live birth and before the age of one year. Data on the numbers of live births and infant deaths were obtained from the published nationwide population register of the Hungarian Central Statistical Office (6). The 50-year period between 1963 and 2012 was considered in this analysis. Annual birth and infant death data were available, with birth weight, sex, maternal age and maternal education, for both live births and infant death cases throughout the full 50-year period. Complete information was available for birth weight and sex. Maternal age was missing for 261 (0.19%) of the records and maternal education was missing for 344 (0.27%). Maternal age was also categorised using younger or older than 35-years-of-age. Maternal education was categorised as no primary school attended,

primary school attended, vocational or secondary grammar school attended and higher education, which was regarded as the default group in the risk analyses. A birth weight of less than 2,500 g was regarded as a low birth weight.

The data concerning the cause of infant deaths were published annually by the Central Statistical Office. These data were classified according to the ICD10 codes. The main categories were: congenital malformation and certain conditions originating in the perinatal period, infectious and parasitic diseases, diseases of the nervous system and sense organs, diseases of the respiratory system, diseases of the digestive system and other cause of infant death, for example neoplasms, diseases of the circulatory system. The unknown or missing causes of deaths were officially classified into other causes of deaths (6).

Investigation of seasonal trends

The age of the infant death was categorised for neonatal (zero to 27 days) and post-neonatal (28-364 days) mortality according to World Health Organization recommendations. The numbers of infant deaths were available at zero, one to six, seven to 13 and 14-27 days and at one to two, three to five and six to 11 months. Hence, the numbers of death in the early neonatal period (zero to six days) were calculated by adding the numbers of deaths that occurred within 24 hours and during one to six days after birth. Furthermore, the numbers of both monthly live birth and infant deaths, including the date of death, were available. However, monthly data on the cause of infant deaths were not available.

Statistical methods

Because the observed variance was greater than the mean of the death and birth variables, this is known as over-dispersion. Therefore the negative binomial regression method with the Huber–White estimator was applied to investigate the trends across annual rates and investigate the effect of possible risk factors - low birth weight, maternal education and sex – in relation to infant mortality (7). Relative risks (RR) and 95% confidence intervals (95% CIs) were calculated. Trends in the annual number of infant deaths by cause of death were also investigated.

Data on the month of the death were aggregated over the study period. Cyclic trends in these monthly data were investigated using the Walter-Elwood method (8) and the logistic regression method using both sine and cosine functions (9). This statistical test was used to retain the information on the connection of time periods by describing the seasonal pattern as one sine and one cosine function. These functions can be incorporated in a regression model that allows the investigation of single or double peaks of seasonality. Monthly cyclic trends (seasonality) were investigated in babies who died in the early neonatal period of zero to six days, by looking at babies who died within 24 hours after birth and babies who died during the first week after birth.

P-values of less than 0.05 were considered to be statistically significant. The Type I error was reduced using Bonferroni corrections. P-values were multiplied by the total number of significance tests. All analyses were performed using STATA Software version 9.0 (Stata Corp LP, College Station, Texas, USA)

RESULTS

During the 50-year interval, there were 6,336,976 live births (3,247,936 boys and 3,089,040 girls) and 136,537 infant deaths (77,751 boys and 58,786 girls) in Hungary. There were 47,055 (34.5%) within the first 24 hours of delivery, 87,757 (64.3%) during the early neonatal period and 17,134 (12.5%) during the late neonatal period. Thus 104,891 (76%) of the infant deaths occurred during the first 28 days after birth. The number of normal and low birth weight infant deaths were 43,578 (32%) and 92,959 (68%), respectively.

The annual infant mortality rate declined by 88.6% from the maximum of 42.9 per 1,000 births in 1963 to the minimum of 4.9 per 1,000 births in 2012 (Figure 1). There was a significant RR trend per annum of 0.954 (95% CI 0.953–0.955; $p < 0.001$). A similar decreasing trend was detected for the annual rate of early neonatal deaths with an annual RR of 0.944 (95% CI 0.941–0.948; $p < 0.001$).

A significantly increased risk of infant mortality was found in boys, with an RR of 1.23 (95% CI 1.19–1.28, $p < 0.001$), than girls. A significantly increased risk of infant

death with an RR of 1.73 (95% CI: 1.64 , 1.83; $p<0.001$) was found in mothers over the age of 35 compared to mothers under this age.

The proportion of mothers in the no primary school completed group decreased from 32.3% to 7.2% during the 50-year period. However, the proportion of mothers in the only primary school completed group decreased by only 24% from 56.8% to 32.8% in the last 20 years of the study. The 10-year interval aggregated numbers of infant deaths in the different maternal education groups are summarised in Table 1. The proportion of infant deaths was 5.7% in the group of mothers with longer education. In contrast, the overall proportion of mothers in the only primary school and no school groups were 52.2% and 20.6%, respectively. Thus, the risk of an infant's death was higher in mothers with lower levels of education than those with higher levels of education (RR=1.31, 95% CI 1.30-1.32, $P<0.001$). For those whose mothers only completed secondary grammar or vocational school the RR was 1.28 (95% CI 1.25–1.31). For those whose mothers only completed primary school the RR was 1.72 (95% CI 1.67–1.75). For those whose mothers did not complete primary school the RR was 2.23 (95% CI 2.17–2.29). However, the highest risk of infant mortality with an RR of 20.2 (95% CI 19.9–20.4 $p<0.001$) was observed in the low birth weight group compared with the normal birth weight group. Nevertheless, similar significantly declining ($p<0.001$) annual trends in infant mortality rates by sex, birth weight, maternal education and maternal were found in all subgroups as well as overall.

Table 2 shows numbers of infant deaths together with the cause of death. Similarly, the trends were significantly ($p<0.001$) decreased in annual infant mortality during the study period in the all cause of death categories as well as in all infant mortality during the study period (Table 2).

The monthly cyclic trends of mortality were investigated among all infants and, separately, in the groups of cases who died during the early neonatal period, within 24 hours after birth and during the first week after birth. The monthly numbers of babies who died within 24 hours of birth, infant deaths and early neonatal deaths used in the seasonal analyses are given in Table 3. A significant cyclic trend in all infant mortality was revealed by the logistic regression model, with a peak of deaths

during late February ($p < 0.001$). Similarly, a significant cyclic trend was found with a peak of deaths during March both in the group of cases who died within 24 hours after birth ($p < 0.001$) and in the group of cases who died during the early neonatal period ($p < 0.001$), respectively. In a sensitivity analysis, the Walter–Elwood method was applied to investigate the cyclic trends and this provided similar peaks to the logistic regression method. The peaks were in February for all infant deaths ($p < 0.001$) and in March in both the group of cases who died within 24 hours after birth ($p < 0.001$) and in the group of cases who died during the early neonatal period ($p < 0.001$). Seasonality models with double peaks were also investigated using the logistic regression method. In double peak models neither the sine nor cosine variables were significant for all infants. However a significant ($p = 0.045$) double peak in May and November was detected in the group of cases who died during the early neonatal period. The cyclic trends are depicted in Figure 2.

Discussion

Strengths and weaknesses of the study

Our population data were obtained from published tables. However a long study period of 50 years was used in the analyses, which allowed us to investigate trends in infant mortality rates. Furthermore, our data were obtained from civil registers, which could have been influenced by a certain simplification of categorisation. Additionally, minor changes occurred in the structure of the reported data during the 50-year interval of the study. Over-dispersion did not influence our results as the negative binomial regression method was applied in both risk estimation and the investigation of annual mortality trend.

In the seasonality, monthly cyclic trend analyses we used the Walter-Elwood method, which confirmed the findings of the logistic regression model since both gave similar results. Moreover, the longest study period was used in the seasonality analyses. The main shortcoming of this study is that we did not have information about the cause of infant death using the monthly frequencies to confirm the speculation of the infectious aetiology, although, a significant seasonal peak in February was found and the vast proportion (75%) of deaths occurred in the neonatal period. The month of infant deaths were based on date at death. Therefore in the seasonal analyses the months of births and months of death are only the same in the group of babies who died within 24 hours after birth. There was a small shift

between the months of births and months of death in the group of the early neonatal deaths. However, this shift was undetectable in the group of all infant deaths. Therefore, the double peaks analyses revealed no significant seasonality in the group of all infant deaths. Thus, the effect of infections around birth was described by double peaks models. Moreover, the application of Bonferroni correction reduced the probability of chance findings in our analyses.

Main findings

The annual infant mortality rate declined 10-fold from its maximum value in 1963 to the minimum value in 2012. Nevertheless, a significantly increased risk of infant mortality was observed in the low birth weight group compared with the normal birth weight group and lower maternal education also increased the risk of infant mortality.

A seasonal peak rate was found in February in the analyses that investigated the monthly cyclic trend of infant deaths and a peak mortality rate was revealed in March in the early neonatal mortality. Although, we did not have data on the age or birth weight of infant related to the monthly numbers of death, we might speculate that the significant peak of neonatal and infant mortality could be related to respiratory infections at the end of winter (9).

Comparison with other studies

Similar to other studies in Europe (3,11-14), the rates of both neonatal and infant death significantly decreased in Hungary during the 50-year study period. However, these other studies investigated shorter periods than our study. Nevertheless, the Hungarian infant mortality rate of 4.9 per 1,000 live births in 2011, was higher than the reported Western European infant mortality rate, which was 3.2 per 1,000 live births in 2011 (4,5).

Lin et al (15) investigated sex-specific risks and causes of mortality among low birth weight infants under one-year-of-age and found an RR of 8.99 in boys and an RR of 8.29 in girls. However, in our study a much higher RR of 20.2 for infant mortality was observed in the low birth weight group. Furthermore, a significantly increased RR of 1.23 for infant mortality was found in boys compared with girls.

Some studies described differences in infant mortality among geographic areas within a country (3,16) and Corchia and Orzalesi (16) reported a lower socio-sanitary level in the South compared to the North of Italy. We did not have data on socio-demographic characteristics, but we have found a strong negative correlation between the real income per person of the overall population and the rate of stillbirth in a previous study (17). However, we investigated the relationship between maternal education and infant mortality and found that the lower education of mothers also increased the risk of infant deaths compared to the higher educated groups. This is the same as the study by Ko et al (18), who reported that maternal education levels were also inversely related to infant mortality. Arntzen et al (19) also reported a persistent inverse association between maternal educational level and neonatal death in a population-based study in the Nordic countries, but the published RRs were slightly lower than those were found in the present study. Similarly, Devlieger et al (20) found that increased infant mortality was associated with low levels of maternal education.

Finally, a peak in mortality rates was found in February in an analysis that investigated the monthly cyclic trend of infant deaths using both logistic regression and the Walter-Elwood methods. The later method was also applied in a study of analysis of seasonal variation of birth defects in Atlanta (21). Seasonality of infant deaths was analysed by Hare et al (22) in relation to temperature changes. They reported that seasonal variations in the neonatal death rate were closely related to winter temperatures during the period 1921-1960. Similarly, our findings suggest that the significant peak of neonatal and infant mortality could have been related to respiratory infections at the end of winter. However, further cohort studies should be carried out to investigate this hypothesis, using detailed individual data including age at death, month of death, sex and birth weight.

Conclusions

In this study a number of risk factors and trends were investigated in relation to infant mortality using well established statistical methods. We found seasonal effects related to infant and early neonatal mortality, with peaks in February and March, when the number of diseases from respiratory infections is highest in Hungary.

These findings could prove useful in preventive strategies, but further cohort studies should be carried out to investigate this hypothesis using detailed individual data.

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Conflict of interest

The authors declare that they have no conflict of interest.

Statistical validity

Richard McNally and TA Nyári are certified biostatisticians and state that the methods used in this paper are valid.

Publication Ethics

The manuscript does not contain clinical studies or individual patient data.

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Figure legend

Figure 1. Infant mortality rate in Hungary between 1963 and 2012

Figure 2. Seasonal variation in month of infant deaths

Table 1. The numbers of infant deaths and maternal education in Hungary between 1963 and 2012. Mortality rates per 1,000 live births are given by time period and level of education.

School attended	Primary school 0–7 grades Age under 14- years-old		Completed primary school 8 grades Age 14-years- old		Completed secondary school or vocational school Age 17-18 years old		Completed third- level school Age over 18-years- old		Total		No information/ Missing data
	No. of deaths	mortality rates	No. of deaths	mortality rates	No. of deaths	mortality rates	No. of deaths	mortality rates	No. of deaths	mortality rates	
period											No. of deaths
1963-1972	17,390	49.99	27,053	36.11	7,893	28.80	1,478	20.73	53,814	37.31	45
1973-1982	6,854	47.80	25,478	28.06	10,247	22.21	2,690	19.15	45,269	27.38	64
1983-1992	2,317	34.49	12,325	19.34	5,243	13.57	1,827	10.86	21,712	17.25	55
1993-2002	1,129	22.77	4,478	12.83	3,607	7.41	861	5.89	10,075	9.77	86
2003-2012	381	13.84	1,739	9.81	2,309	4.88	874	3.29	5,303	5.63	94
1963-2012	28,071	46.11	71,073	26.80	29,299	14.68	7,730	10.10	136,173	21.52	344

Table 2. Annual number of infant deaths by cause of death in Hungary between 1963 and 2012 (N=136,537)

Cause of deaths	Congenital malformation and certain conditions originating in the perinatal period	Infectious and parasitic diseases	Diseases of the nervous system and sense organs	Diseases of the respiratory system	Diseases of the digestive system	Other diseases	Total
ICD10 codes	Q00–Q99; P00–P96	A00–B99	G00–G99	J00–J99	K00–K93		
Trends*	0.956 (0.954-0.958)	0.960 (0.953-0.967)	0.946 (0.942-0.950)	0.918 (0.912-0.925)	0.899 (0.891-0.907)		0.954 (0.953-0.955)
Period							
1963-1972	41,673 (38.1%)	521 (43.0%)	1,986 (41.9%)	5,836 (50.2%)	2,431 (62.3%)	1,367 (24.6%)	53,814 (39.4%)
1973-1982	36,869 (33.7%)	276 (22.8%)	1,563 (33.0%)	3,724 (32.0%)	1,214 (31.1%)	1,628 (29.3%)	45,274 (33.2%)
1983-1992	17,888 (16.3%)	233 (19.2%)	746 (15.7%)	1,466 (12.6%)	164 (4.2%)	1,230 (22.2%)	21,727 (15.9%)
1993-2002	8,431 (7.7%)	139 (11.5%)	299 (6.3%)	486 (4.2%)	64 (1.6%)	830 (15.0%)	10,249 (7.5%)
2003-2012	4,646 (4.2%)	43 (3.5%)	146 (3.1%)	117 (1.0%)	27 (0.7%)	494 (8.9%)	5,473 (4.0%)
1963-2012	109,507 (100%)	1,212 (100%)	4,740 (100%)	11,629 (100%)	3,900 (100%)	5,549 (100%)	136,537 (100%)

*Relative risk(RR) and 95% confidence interval (95% CI)

Table 3. The monthly numbers of babies who died within 24 hours of birth, infant deaths and early neonatal deaths used in seasonal analyses.

Months	Numbers of babies who died within 24 hours of birth†	Numbers of early neonatal deaths†	Numbers of all infant deaths†	Numbers of live births*
January	4,189	7,682	12,300	532,829
February	3,659	6,858	11,010	497,184
March	4,229	7,793	12,279	549,937
April	4,363	8,010	12,236	522,361
May	4,345	8,101	12,325	544,044
June	3,919	7,369	11,242	534,077
July	3,922	7,345	11,123	569,752
August	3,634	7,017	10,763	551,010
September	3,515	6,579	10,146	537,334
October	3,834	6,959	10,821	513,773
November	3,633	6,840	10,699	483,878
December	3,813	7,204	11,593	508,293
Total	47,055	87,757	136,537	6,344,472*

*The monthly numbers of births included stillbirths between 1963-1968 (6).

†The numbers based on date at death

Figure 1. Infant mortality rate in Hungary between 1963 and 2012

Figure 2. Seasonal variation in month of infant deaths