

# Deaths of children aged under 5 years and related factors in the Islamic Republic of Iran: a population-based case-control study

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وفيات الأطفال الذين تقل أعمارهم عن 5 سنوات والعوامل المتصلة بها في جمهورية إيران الإسلامية: دراسة حالات وشواهد سكانية المرتكز

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الخلاصة: أجريت هذه الدراسة لتحديد العوامل العائلية والاجتماعية والاقتصادية المرتبطة بوفيات الأطفال الذين تقل أعمارهم عن 5 سنوات. فقد أجريت دراسة متداخلة لحالات وشواهد تركز على السجلات بشأن وفيات جميع الأطفال الذين تقل أعمارهم عن 5 سنوات في ولاية كوهجيلويها وبوير أحمد في جمهورية إيران الإسلامية. تم اختيار شاهدين لكل وفاة اختياراً عشوائياً من بين أطفال لهم نفس العمر والجنس ومكان الإقامة (186 حالة و 372 شاهداً). فكان التشوه الخلقى (37.6%) والولادة قبل الوقت المتوقع (29.0%) السببين الأكثر شيوعاً للوفاة بين الأطفال الذين تقل أعمارهم عن 5 سنوات. ولم يرد ذكر أي مرض من الأمراض التي يمكن الوقاية منها باللقاحات كسبب للوفاة. ووجد أن أقوى العوامل المرتبطة بالوفيات هي القرابة بين الأبوين (OR = 3.92; 95%CI = 2.27 - 6.85;  $p < 0.01$ ) بالنسبة للأقارب من الدرجة الأولى مقارنة مع عدم وجود قرابة عائلية؛ والعنف المنزلي ضد الأم أثناء الحمل (OR = 3.13; 95%CI = 1.6 - 6.17;  $p < 0.001$ ). لقد كانت الأسباب الرئيسية لوفاة الأطفال الذين تقل أعمارهم عن 5 سنوات في الولاية التشوه الخلقى والولادة قبل الوقت المتوقع.

ABSTRACT The study was conducted to determine the family, social and economic factors associated with deaths of children aged under 5 years. A registry-based nested case-control study was conducted of the deaths of all children aged under 5 years in Kohgiluyeh and Boyer-Ahmad Province in the Islamic Republic of Iran. For each death, two controls were randomly selected among children of the same age, sex and place of residence (186 cases and 372 controls). Congenital abnormality (37.6%) and preterm birth (29.0%) were the two most frequent causes of death among children aged under 5 years. No vaccine-preventable disease was reported as the cause of death. The strongest associations were found with consanguinity of the parents (OR = 3.92; 95% CI = 2.27-6.85 for being first cousins in comparison with no family relation;  $P < 0.001$ ) and with domestic violence to the mother during pregnancy (OR = 3.13; 95% CI = 1.60-6.17;  $P < 0.01$ ). The main causes of death of children aged under 5 years in the Province were congenital abnormality and prematurity.

## Décès d'enfants de moins de cinq ans et facteurs associés en République islamique d'Iran : étude cas-témoin populationnelle

RÉSUMÉ La présente étude a été menée pour déterminer les facteurs familiaux, sociaux et économiques associés aux décès des enfants de moins de cinq ans. Une étude cas-témoin nichée reposant sur les données de registres a été menée sur les décès de tous les enfants de moins de cinq ans dans la province de Kohgiluyeh et Boyer-Ahmad en République islamique d'Iran. Pour chaque décès, deux témoins étaient sélectionnés de façon aléatoire parmi les enfants du même âge, sexe et lieu de résidence (186 cas et 372 témoins). Les malformations congénitales (37,6 %) et les naissances prématurées (29,0 %) constituaient les deux causes de décès les plus fréquentes parmi les enfants de moins de cinq ans. Aucune maladie à prévention vaccinale n'a été rapportée comme cause de décès. Les associations les plus fortes étaient liées à la consanguinité des parents (OR = 3,92 ; IC à 95 % = 2,27-6,85 pour les cousins de premier degré en comparaison avec les sujets n'ayant aucun lien de parenté ;  $p < 0,001$ ) et à la violence conjugale envers les mères pendant la grossesse (OR = 3,13 ; IC à 95 % = 1,60-6,17 ;  $p < 0,01$ ). Les principales causes de décès des enfants de moins de cinq ans dans la province étaient les malformations congénitales et la prématurité.

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## Introduction

Childhood mortality has a profound effect on the life expectancy of a community and is considered an important index of a country's health and socio-economic status (1–3). A primary health care network has been established in the Islamic Republic of Iran over the past three decades to deliver effective health services to the most vulnerable segments of the population, such as mothers and children. Improvements in access to primary health care have resulted in dramatic reductions in maternal and early childhood morbidity and mortality, which are considered the key achievements of the national health care system (4,5). The rate of death of children aged under 5 years (per 1000 live births) was reduced from 287.9 in 1967 to 16.8 in 2013 (6). Safe water, vaccination, safe delivery and other basic health and public services have not only reduced overall mortality rates but have also shifted the causes of morbidity and mortality from infectious to non-infectious diseases.

Thus, the common causes of death among children in the Islamic Republic of Iran have become prematurity, low birth weight and congenital birth defects (4). Many factors contribute to childhood mortality, including the environment, health and social and family factors (1,7,8). The patterns of factors that contribute to the leading causes of death in children must be known to enable targeted planning of programmes for further reductions. We conducted a case–control study, with comprehensive, population-level information collected as part of “family health care file” registrations, complemented by a questionnaire survey. The aim of the study was to determine the causes of death of children aged under 5 years and associated factors in Kohgiluyeh and Boyer-Ahmad Province in southern Islamic Republic of Iran during 1 year.

## Methods

### Setting

Kohgiluyeh and Boyerahmad Province in the southwest of the country has an area of 16 249 km<sup>2</sup> and a population of 635 000 (Fig. 1). The Province has 1.12% live births, but represents 3.35% of all deaths of children aged under 5 years in the country (9). Iranian national health legislation requires that all pregnant mothers and children be registered in the national health services network in order to receive basic health care, including vaccination, monitoring of growth and development and nutritional supplements, from birth to 7 years of age. The demographic, social and health information for the families are recorded in a “family health care file”.

### Selection of deaths

We selected all deaths of children aged under 5 years in the Province that occurred during an Iranian calendar year equivalent to 20 March 2011 to 19 March 2012. All deaths had been registered in their corresponding health centre, and information on each child had been included in the family health care file prior to their death. The Iranian Ministry of Health and Medical Education requires that a specific procedure be followed for the deaths of all children reported by public health experts or general practitioners, starting with completion of a children's death investigation form. The form is sent to a death investigation expert committee consisting of a paediatrician, an obstetrician and an epidemiologist, which confirms the probable cause of death.

### Selection of controls

Control children were selected from a list of all children who were under 5 years of age, alive on 19 March 2012 and registered in the national health services network. In view of the link to the provision of health care services, the coverage of the register is considered to be virtually complete (10). Two control



Figure 1. Kohgiluyeh and Boyer-Ahmad Province (highlighted)

children were randomly selected for each death by frequency matching on age (month), sex and urban or rural residence. Of the 372 mothers who were invited to participate, only four refused (1%). Replacements were selected for the four refusals by the same criteria as above. We could not use a higher ratio of controls to cases because of the small number of eligible controls in this relatively small population.

### Sampling and power

During the study period, 186 children aged under 5 years died; all were included in the study. To ensure that there were no unreported deaths of children aged under 5 years, we checked all deaths registered at local birth and death offices. An a posteriori power analysis suggested adequate (at least 80%) statistical power for detecting relevant associations at the 5% level. For example, the analyses had 90% power to detect a difference as small as 5% in the place of birth between the two groups.

### Data collection

Data were collected in 2012 and analysed in 2013. Most information was obtained from the family health care file, including the mother's education and occupation, age at marriage and pregnancy and history of miscarriages and previous pregnancies. Information on the mother's weight gain and regular

smoking was recorded at each visit to a health centre for routine pregnancy care (on average, 13 visits per pregnancy). The birth characteristics included gestational age (number of weeks from the date of the last normal period) and birth weight. All participants also participated in a structured interview at which information was obtained on social, economic and family factors including consanguinity of the parents, family size, place of residence at birth, mother's education, mother's smoking status, mother's job and satisfaction with the family income and domestic and sexual violence during the pregnancy. All interviews were conducted in a friendly, quiet, private environment by trained female interviewers with a university degree in midwifery or public health. The questionnaire was tested in a pilot study with 53 mothers in Kohgiluyeh and Boyer-Ahmad Province who had children aged under 5 years. As questions about family income were considered to be sensitive and the answers thus potentially unreliable, an indirect question was used, the mothers being asked to report their satisfaction with the family income on a scale of 1–5 (very dissatisfied to very satisfied) (11,12). Violence against mothers was recorded by asking the mothers to report any physical or sexual abuse they had experienced during the pregnancy, after a brief explanation and assurance of confidentiality. The pilot study indicated that the reliability or internal

consistency of the questionnaire was good (Cronbach's alpha = 0.7).

The study protocol was approved by the Yasuj University of Medical Sciences ethical committee, and all mothers agreed to participate after reading and signing an informed consent form before the interview; verbal consent was obtained from mothers who were illiterate.

### Statistical methods

Associations between continuous and categorical variables with deaths of children aged under 5 years were tested by Student's t and chi-squared tests, respectively. Multivariate logistic regression was used to analyse the association of each variable with deaths of children aged under 5 years after control for other variables. The final model was built in a backwards selection strategy. Data were analysed with the R statistical package (version 3.0.1).

## Results

In total, 186 deaths of children aged under 5 years occurred during the study period. For each case, two children of the same sex and age were randomly selected from eligible children with the same place of residence (372 controls in total).

Congenital abnormality (37.6%) and preterm birth (29.0%) were the most prevalent causes of death (Table

1). None of the deaths was due to a vaccine-preventable disease, and other infectious diseases, including diarrhoea and pneumonia, were responsible for only 12.9% of all deaths.

The health, family and social characteristics of the cases and controls are presented in Tables 2 and 3. The cases weighed less than controls at birth (2.42 kg vs 3.16 kg,  $P < 0.001$ ) and were born earlier (35.05 vs 38.48 weeks,  $P < 0.001$ ) than the controls. The mothers of the case children were more likely than those of control children to be multiparous (15.6% vs 0.8%,  $P < 0.001$ ) and to have had at least one previous miscarriage (17.7% vs 10.2%,  $P = 0.015$ ). Moreover, the mothers of the case children gained less weight during their pregnancy (8.37 kg vs 9.96 kg,  $P < 0.001$ ) and were more likely to have experienced domestic violence than controls (18.8% vs 6.5%, respectively,  $P < 0.001$ ). They had attended fewer visits for maternal care (average, 7.06 vs 8.49 visits,  $P < 0.001$ ). The mothers of the case children were also less satisfied with their family income (55.4% case mothers and 75.9% controls were very satisfied or satisfied,  $P < 0.001$ ). In addition, more common between the parents was commoner among the cases than controls: being first cousins was 20.4% more likely among the parents of the case children than the controls ( $P < 0.001$ ). No significant associations were found between the death of a child aged under 5 years and birth order, birth

Table 1. Causes of death of children aged under 5 years by age group

Cause of death	Age group			All
	< 1 month	1–12 months	1–5 years	
Prematurity	54 (50.9%)	0	0	54 (29.0%)
Congenital abnormality*	31 (29.2%)	24 (63.2%)	14 (34.1%)	70 (37.6%)
Respiratory illness	10 (9.4%)	4 (10.5%)	1 (2.4%)	15 (8.1%)
Diarrhoea	2 (1.9%)	4 (10.5%)	3 (7.3%)	9 (4.8%)
Domestic or traffic accident	1 (0.9%)	4 (10.5%)	13 (31.7%)	18 (9.7%)
Other	8 (7.5%)	2 (5.3%)	10 (24.4%)	20 (10.8%)
Total	106	38	41	186

\*Age at death was missing for one case

Table 2. Birth characteristics of cases and controls

	Cases No. (%)	Controls No. (%)	P
<b>Sex</b>			
Male	101 (54.3%)	202 (54.3%)	1.00
Female	75 (45.7%)	170 (45.7%)	
<b>Birth order</b>			
	Mean=2.28, SD=1.54	Mean=2.31, SD=1.40	
1	83 (44.6%)	136 (36.6%)	0.09
2-3	66 (35.5%)	167 (44.9%)	
4-7	37 (19.9%)	69 (18.5%)	
<b>Birth weight (kg)</b>			
	Mean=2.422, SD=0.940	Mean=3.164, SD=0.538	
< 2	59 (31.7%)	7 (1.9%)	< 0.001
2-2.5	16 (8.6%)	15 (4.0%)	
2.5-3.5	75 (40.3%)	236 (63.4%)	
3.5-4.9	21 (11.3%)	114 (30.6%)	
<b>Gestational age (weeks)</b>			
	Mean=35.05, SD=4.88	Mean=38.48, SD=1.98	
< 37	82 (44.1%)	23 (6.2%)	< 0.001
37-42	101 (54.3%)	343 (92.2%)	
> 42	3 (1.6%)	6 (1.6%)	
<b>Multiple birth</b>			
No	157 (84.4%)	369 (99.2%)	< 0.001
Yes	29 (15.6%)	3 (0.8%)	

interval, family size (4.8 for cases vs 4.5 for controls,  $P > 0.05$ ) or mother's education, job or smoking status ( $P > 0.05$ ).

After full adjustment for other variables, the odds for death of children aged under 5 years were increased by low birth weight, consanguinity of parents, history of abortion or domestic violence, smaller family size and residence in rural areas ( $P < 0.05$  for all comparisons, Table 4). Maternal weight gain and the number of prenatal visits were not associated with deaths of children aged under 5 years, after adjustment. Consanguinity of the parents (OR = 3.92, 95% CI = 2.27–6.85, for children of first-cousin marriages compared with no family relation,  $P < 0.001$ ) gave the highest odds ratios. The other factor strongly associated with deaths of children aged under 5 years was domestic violence against the mother (OR = 3.1, 95% CI = 1.60–6.17,  $P < 0.001$ ). When the analyses were restricted to cases who survived at least 12 months ( $n = 131$ ) and their controls, we found a strong protective effect of breastfeeding

for at least 6 months (OR = 0.12, 95% CI = 0.06–0.24,  $P < 0.001$ ).

## Discussion

In the Islamic Republic of Iran, as in many other developing countries, a significant reduction in common infectious diseases has made non-infectious disease more common causes of death among children aged under 5 years of age (13). We found that only 12.9% of the registered deaths of children aged under 5 years in Kohgiluyeh and Boyer-Ahmad Province were due to infectious causes, and, importantly, none of the deaths was due to vaccine-preventable diseases. This national achievement is considered to be (at least partly) the consequence of notable improvements in access to basic health and public services (including mother and child health care, vaccination, safe drinking-water and education) and a significant improvement in public welfare during the past three decades (5).

Our study suggests that the distribution of causes of childhood mortality in our country differs from global patterns, including in particular higher rates of congenital abnormalities and preterm births (7, 13). The frequency of congenital abnormalities appears to be even higher in the Province (37%) than in the country as a whole (17%) (14).

Our results show that consanguinity of parents is strongly associated with the death of children aged under 5 years, even after adjustment for various other factors. The association was revealed by examining children's death investigation forms, which are available even for rural areas (15). Parental consanguinity is alarmingly common in the Province: 21% of the parents of cases and 41% of those of controls were first cousins and 52% and 72% were other relatives, respectively. Although we found no official report on national or regional rates of consanguinity, it may explain, at least in part, the high rate of congenital abnormalities in the Province (16,17). We

Table 3. Maternal and demographic characteristics of cases and controls

	Cases No. (%)	Controls No. (%)	P
<b>Birth interval (years)</b>	Mean=2.28, SD=1.54	Mean=2.31, SD=1.40	
≤ 1	15 (8.1%)	18 (4.9%)	0.18
1-2	20 (10.8%)	40 (10.8%)	
2-3	16 (8.6%)	51 (13.7%)	
> 3	135 (72.6%)	262 (70.6%)	
<b>Family size</b>	Mean= 4.8, SD=1.87	Mean=4.53, SD=1.63	
3	56 (30.1%)	123 (33.1%)	0.52
4-6	16 (54.3%)	51 (54.6%)	
7-13	135 (15.6%)	262 (12.4%)	
<b>Age of mother at pregnancy (years)</b>	Mean= 27.10, SD=6.02	Mean=27.90, SD=5.52	
15-17	13 (7.0%)	10 (2.7%)	0.12
18-34	156 (83.9%)	324 (87.1%)	
35-43	17 (9.1%)	38 (10.2%)	
<b>Age of mother at marriage (years)</b>	Mean= 20.09, SD=3.94	Mean=20.81, SD=4.06	
12-16	33 (17.7%)	48 (12.9%)	0.24
17-25	135 (72.6%)	278 (74.7%)	
26-36	18 (9.7%)	46 (12.4%)	
<b>Previous miscarriage</b>			
Yes	33 (17.7%)	38 (10.2%)	0.02
No	153 (82.3%)	334 (89.8%)	
<b>Weight gained during pregnancy (kg)</b>	Mean= 8.37, SD=3.68	Mean=9.96, SD=3.35	
1-5	47 (25.3%)	36 (9.7%)	< 0.001
6-10	98 (52.7%)	193 (51.9%)	
11-15	32 (17.2%)	121 (32.5%)	
16-19	9 (4.8%)	22 (5.9%)	
<b>Number of prenatal care visits</b>	Mean= 7.06, SD=3.47	Mean=8.49, SD=2.97	
0-4	39 (21.0%)	31 (8.3%)	< 0.001
5-10	118 (63.4%)	267 (73.0%)	
11-18	29 (15.6%)	73 (19.6%)	
<b>Parents' consanguinity</b>			
First cousin	77 (41.4%)	78 (21.0%)	< 0.001
Second cousin and further	57 (30.6%)	119 (32.0%)	
No family relation	52 (28.0%)	175 (47.0%)	
<b>Place of birth</b>			
Urban	44 (23.7%)	115 (30.9%)	0.075
Rural	142 (76.3%)	257 (69.1%)	
<b>Place of death and interview</b>			
Urban	85 (45.7%)	172 (46.2%)	0.93
Rural	(101 (54.3%))	200 (53.8%)	
<b>Mother's education</b>			
Illiterate	32 (17.2%)	55 (14.8%)	0.22
Primary school	54 (29.0%)	108 (29.0%)	
Middle school	38 (20.4%)	62 (16.7%)	
High school	36 (19.4%)	104 (28.0%)	
Higher	26 (14.0%)	43 (11.6%)	
<b>Smoked during pregnancy</b>			
Yes	5 (2.7%)	10 (2.7%)	1.00
No	181 (97.3%)	362 (97.3%)	

Table 3. Maternal and demographic characteristics of cases and controls (concluded)

	Cases No. (%)	Controls No. (%)	P
<b>Mother's occupation</b>			
Housewife	168 (90.3%)	334 (89.8%)	0.43
Teacher	6 (3.2%)	19 (5.1%)	
Employee	8 (4.3%)	16 (4.3%)	
Self-employed	4 (2.2%)	3 (0.8%)	
<b>Income satisfaction</b>			
Very satisfied	19 (10.2%)	57 (15.3%)	0.003
Satisfied	84 (45.2%)	200 (53.8%)	
Neither satisfied nor dissatisfied	52 (28.0%)	83 (22.3%)	
Dissatisfied	16 (8.6%)	23 (6.2%)	
Very dissatisfied	15 (8.1%)	9 (2.4%)	
<b>Domestic violence during pregnancy</b>			
Yes	35 (18.8%)	24 (6.5%)	< 0.001
No	151 (81.2%)	348 (93.5%)	
<b>Sexual abuse during pregnancy</b>			
Yes	18 (9.7)	9 (2.4%)	< 0.001
No	168 (90.3%)	363 (97.6%)	

also observed an association between domestic violence against the mother during pregnancy and an increased risk that her child would die before the age

of 5 years (18). This association is not unexpected, but it calls for action to both prevent domestic violence and to intervene when it is observed.

Table 4. Explanatory variables for deaths of children aged under 5 years in the multivariate logistic regression analysis

	No.	OR (95% CI)	P
<b>Preceding birth interval</b>	558	0.95 (0.88–1.03)	0.24
<b>Birth weight</b>	543	0.36 (0.23–0.56)	< 0.001
<b>Gestational age</b>	558	0.85 (0.77–0.94)	0.001
<b>Place of birth</b>			
Urban	159		
Rural	399	1.79 (1.030–3.18)	0.04
<b>Weight gain during pregnancy</b>	558	1.01 (0.94–1.08)	0.89
<b>Number of maternity visits</b>	558	0.95 (0.88–1.018)	0.15
<b>History of abortion</b>			
No	487		
One	48	2.20 (1.035–4.64)	0.04
Two and more	23	1.04 (0.30– 3.21)	0.95
<b>Consanguinity of parents</b>			
No	155		
First cousin	176	3.92 (2.27–6.85)	< 0.001
Second cousin and further	227	1.62 (0.93–2.83)	0.09
<b>Family size</b>	558	1.24 (1.09–1.41)	0.001
<b>Domestic violence</b>			
No	499		
Yes	59	3.13 (1.60–6.17)	< 0.001

Variables in the saturated logistic model: birth interval from previous sibling, birth order, age of mother at pregnancy, age of mother at marriage, single status, prenatal visits, weight gain during pregnancy, birth weight, history of abortion, consanguinity of the parents, family size, place of residency at birth, mother's education, smoking status of the mother, mother's job and family income satisfaction, domestic violence during pregnancy, sexual violence during pregnancy

Earlier reports suggested an association between maternal occupation and education with childhood mortality (8,19). In our analyses, the effects of maternal occupation and education did not persist after other contributing factors were accounted for. Also, in contrast to some earlier studies, we found no association between birth interval and death of children aged under 5 years (19), perhaps because there has been a major, nationwide reduction in fertility rate in the country, with a decrease of 59.5% between the mid-1980s and the mid-1990s (20), which is considered to be due to more family planning, increases in the average birth interval and improvements in social and health services (4). For example, in our study, only 6.1% of the study children had a birth interval from their older siblings shorter than 2 years. This may have attenuated the associations between previously recognized factors (mainly maternal education and birth interval) and deaths of children aged

under 5 years. We found a strong negative association between breastfeeding and the deaths of children aged under 5 years (21). In our context, this may reflect poorer health and feeding ability among the cases rather than a strong protective effect.

One of the strengths of our study is that it included information on socioeconomic, health and family factors that affect the risk for childhood mortality. We consider that the results can be generalized to many (developing) countries in the Region with similar cultural, social and geographical features. A limitation is that, despite efforts to assure the mothers of the privacy and confidentiality of the information they provided, we cannot exclude possible underreporting of sexual or domestic violence. Furthermore, much of the

information was routinely collected data from family health files and death investigation forms. Although health staff try systematically to ensure that the information they collect is valid and reliable, we cannot exclude possible errors in the information from official sources.

Studies based on national or international sources should be conducted to determine the applicability of the results. As the risk factors identified in this study can be modified, population-based interventions are recommended to apply social and health measures to prevent deaths of children aged under 5 years.

In conclusion, the main causes of deaths of children aged under 5 years in this registry-based, nested case-control study in Kohgiluyeh

and Boyer-Ahmad Province in the Islamic Republic of Iran were congenital abnormality and prematurity, while vaccine-preventable causes of death were extremely rare. Consanguinity of parents and domestic violence were important determinants of the deaths of these children, indicating the need for suitable interventions.

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