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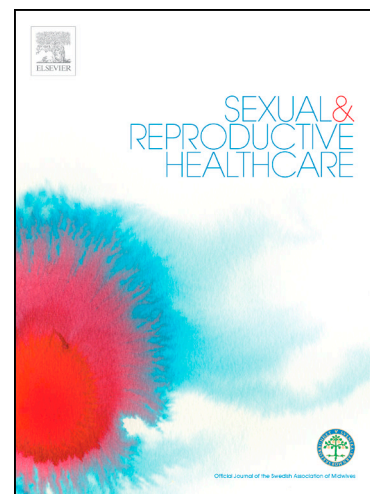
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Cause-specific mortality among women of reproductive age: Results from a population-based study in an Iranian community

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Cause-specific mortality among women of reproductive age: Results from a population-based study in an Iranian community

Introduction

Women in the reproductive age, roughly from 15 to 49 years, comprise a vulnerable group in most low- and middle-income countries as they are confronted with traditional pregnancy-related complications besides the emerging challenges associated with non-communicable diseases (NCDs) and injuries [1]. Due to the vital role played by women in the family and society, unnatural deaths in women of reproductive age could have a major health impact on both the family and community. In addition, all deaths among women of this age group are premature, which occurs before age 70 [2]. Furthermore, there are substantial inequalities in cause-specific mortality in this age group among countries. Consequently, pregnancy-related complications account for the leading cause of death among women of reproductive age in most resource-limited as well as most middle- and high-income countries. The general pattern of adult female's mortality has been associated with a progressive shift towards a larger share of the deaths caused by NCDs and injuries [2].

Population-based data on mortality cause is an integral part of understanding health and tailoring effective public health programs. Globally, few studies have investigated cause-specific mortality in women of reproductive age [1, 3-8]. Investigations conducted in India and Pakistan have shown that the high mortality rates (MRs) in these countries are linked to the pregnancy-related complications. Apart from maternal mortality, neoplasia, infectious diseases such as tuberculosis (TB), hepatitis and diarrhea, as well as cardiovascular diseases and trauma were the main causes of reproductive age deaths [1, 5-8]. However, HIV/TB was the leading causative agent of death among women of reproductive age in South Africa [4].

Despite a national vital registration system in Iran, underestimation of deaths in the country has recently been documented [9]. Therefore, due to the lack of validated population-based death registries in Iran, no detailed estimates are available to indicate cause-specific mortality in women of reproductive age. There are also no research data from population-based studies on female reproductive age mortality in Iran.

Application of the reproductive age mortality survey (RAMOS) method has been suggested as a standard approach to increase the identification of deaths, as compared to

hospital records and official government estimates in resource-limited countries [10]. Moreover, verbal autopsy (VA) has been indicated to be one of the best available techniques for obtaining evidence on the causes of death in resource-limited areas [11]. However, this method has not yet been used to estimate the completeness of the mortality registry in Iran. This paper presents population-based information about the levels and causes of mortality among women of reproductive age in Northwestern Iran, based on the data gathered from the RAMOS. This is a pilot study of a larger survey that examines the true magnitude of maternal mortality and cause-specific mortality using RAMOS and VA methodology in 11 selected provinces in Iran.

Materials and Methods

Population and sampling

RAMOS was carried out in the Northwestern of Iran. The study population comprised of all deaths took place amongst women of the reproductive age (~15-49 years) in West Azerbaijan Province from 1st March 2013 to 31th February 2014. The study area covers a region of 37,059 km² with more than three million populations. The Province is populated mainly by two equal ethnic and religious groups, namely Turks (Shiite Muslims) and Kurds (Sunni Muslims).

Data collection procedure

Our retrospective community-based study included two phases: first, identifying all deaths related to women of reproductive age and second, determining the cause of death. To identify all possible deaths among target age group, we used five different sources of data, including death registration system of the provincial public health network (Ministry of Health records), district organization of civil registration, district legal medicine organization, medical death certificates from private and public hospitals, and local informants who were interviewed during our fieldwork. To perform the first phase of the study, we reviewed the electronic death records from the death registration system of the provincial public health network, which is the most reliable dataset. In this system, mortality data are collected from hospitals, health centers, authorized cemeteries, and other probable sources through a

standard, defined process at provincial health centers [12]. The vast majority of eligible deaths to women of reproductive age (95.5%) were identified using this dataset, i.e. death registration system of the provincial public health network. However, other two sources of data, district organization of civil registration and district legal medicine organization, were investigated separately to verify and complement the data included in the electronic database. Apart from the cases already identified, 23 additional deaths were discovered in the study group, and no new cases of death were identified from medical death certificates or during the fieldwork. These observations indicate that 4.5% of all eligible deaths in the death registration system of the provincial public health network are unaccounted, and the official mortality statistics for women of reproductive age are under-reported. Finally, these records were merged to generate a list of all deaths (510 deaths).

To identify the cause of death, we investigated all cases by performing household visits and completing a standard VA questionnaire with relatives of the deceased women and/or health care providers [13]. The structured questionnaire contained detailed data regarding personal information, socio-economic background, place of death, treatment received for illness before death, and the symptoms of the decease. These interviews were complemented by medical certification and autopsy reports. As a routine in 18 districts and 28 hospitals in West Azerbaijan Province, pathologists perform post-mortem examinations. In deaths occurring outside hospitals, post-mortem examination is carried out by physicians in a legal medicine organization to establish the cause of death before permission for interment is given. These proceedings could prevent the probable alterations in the VAs 'accuracy of information'. For instance, suicide of a family member may bring a sense of guilt and shame on families and make them change their response to the questions, which can be prevented by using medical certification and autopsy report.

Quality control measures included checking for completeness of questionnaires, double completing VA questionnaire (if needed), and missing data. Supervisors of the research at the district and provincial levels monitored and controlled the data according to the plan. One obstetrician, one clinical epidemiologist, and one maternal and child health physician reviewed each of the VAs and medical records to establish the most probable cause of death where medical certification is unavailable or unreliable. Agreement of two reviewers was sufficient to make the classification. Discordant results were renegotiated to obtain agreement. International Classification of Diseases, tenth version (ICD-10) definitions was used [14]. Fieldwork was conducted between August 1, 2014 and January 30, 2015, for the VAs, and from February to March 2015 for the review of the records. A written informed

consent was obtained from each respondent before interview. The confidentiality of data was guaranteed to the respondents. Permission to carry out the study and ethical clearance were obtained from the ethical committee of the Urmia University of Medical Sciences, Urmia, Iran.

Evaluation of the data

Data from Iranian National Population and Housing Censuses conducted in 2011 were the source of the number and characteristics of general population [15]. Total reproductive age female populations for 2011 were collected directly from national censuses. To estimate the population size for year 2013, mean population growth rates was used. Cross-tabulation of categorical variables and vital status were performed using Chi-square tests of significant differences within the variable groups and a woman's vital status.

Crude MRs were used as the ranking criterion because the population denominator of each rate is constant across all cause-of-death categories. Crude MRs were typically expressed per 100,000 populations and were often rounded to two decimal places. Data were analyzed using Statistical Package for the Social Sciences (SPSS), version 18 (SPSS, Inc., Chicago, IL, USA).

Results

A total of 901,161 women of reproductive age were identified as living in West Azerbaijan, Iran, between March 2013 and February 2014. Among them, 510 (0.06%) died, and VA interviews were successfully conducted for all of the cases. The main source of information for the VA of five cases was the local healthcare provider; three families refused to be interviewed and two families could not be found at home after two visits.

Approximately one in ten deaths occurred between the ages of 15 and 19 years, and most deaths happened in women aged 45-49 years (25.9%; Table 1). Although most of the populations were alive in the urban area (64%), deaths in the rural area significantly outnumbered those in the urban setting (50.6%; $P < 0.001$). The marital status of the 510 deceased women revealed that 135 (26.5%) were unmarried, 329 (64.5%) married, and 46 (9%) divorced or widowed. While most of the women were illiterate or had completed utmost nine years in school, 22.9% of those who died had accomplished more than nine years of

education. There were significant differences between dead and alive women when last seen across the categories of ethnic (religious) status ($P < 0.001$; Table 1).

Death in 58% of cases was occurred naturally due to a disease being the cause of death, i.e. disease-related mortality. Death distribution by characteristics of target group showed that non-natural deaths were significantly associated with age, education, and ethnic relations and were more prevalent among educated women and Sunni Muslims (Table 2). The top two unnatural causes of death were suicide in 92 victims, followed by accident in 83 victims. Death distribution by age demonstrated that about half of the suicide cases (48.9%) were among reproductive age group women in the third decade of life. In contrast, natural deaths increased expectedly with age among women of reproductive age (Table 3).

The all-cause crude MR for women of reproductive age was 56.59 per 100,000 women (95% CI: 56.49-56.69), varying from 20.65 per 100,000 women (95% CI: 20.57-20.73) for external causes of morbidity and mortality to 0.89 per 100,000 women (95% CI: 0.87-0.91) for endocrine, nutritional, and metabolic diseases (Table 4). Suicide-related death were the most common causes of death with a MR of 10.21 per 100,000 women of reproductive age (95% CI: 10.15-10.27), which includes virtually 18% of all deaths occurring among the women of reproductive age (Table 5).

The preponderant method of suicide was by self-inflicted burns at 45.6% (42 cases), followed by hanging (28.3%), and drug intoxication (22.8%). These three methods comprised about 97% of the total suicidal deaths in this study. The less common methods of suicide were jumping from a height and gunshot wound. Meanwhile, 83 women died of accidents with a MR of 9.21 per 100,000 women of reproductive age (95% CI: 9.15-9.27). Besides death from suicides and accidents, reproductive age women experienced significant excess mortality from various cancer types. Deaths due to cancers of the breast (MR=4.22 per 100,000 women, 95% CI: 4.18-4.26) and digestive organs (MR=4.11 per 100,000 women, 95% CI: 4.07-4.15) accounted for most of the cancer-related mortality. Women who died in pregnancy contributed 3.33% of all deaths in women of reproductive age with a MR of 1.89 per 1,000 women (95% CI: 1.86-1.92).

Discussion

Death among women of reproductive age has indicated negative health outcomes on family and community. Without data on the dimensions and causes of death in this age group, it is impossible to establish strong programs for addressing this issue.

This study represents the first attempt at evaluating all causes and cause-specific mortality in women of reproductive age in Iran. Since five different sources of data were used to identify all possible deaths among target age group, the data provides a fair idea of existing situation in this region. Further, the age and etiology distribution of death differ among different populations under study. The main factors associated with all-cause mortality were woman's age, area of residence, education, and ethnic status. Our findings indicated that the women living in rural areas, Kurd women, and those uneducated are at the higher risk of dying during reproductive age in Northwestern Iran. This picture may not be surprising since significant development inequalities in socioeconomic status, ethnic diversity, the low level of human development index (HDI) (0.66), and low Gini coefficient, an indicator used for measuring inequality in income or wealth, (0.38) have been documented in this province [16, 17]. A study from Iran has revealed an association between declining maternal mortality and increasing HDI, which is a combination of life expectancy, level of education, and income within the study area [17].

In the current large population-based study, we showed that MR among the target group was 56.6 per 100,000 women in the province having more than three million populations over the periods 2013-2014. Our calculations of the all-cause crude MR for women of reproductive age are similar to the same age groups of women in USA in 2012 (MR=66.6 per 100,000) [16] and in Sweden in 1988-2008 (MR=68.1 per 100,000) [3], but lower than those women in South Africa in 2000-2009 (MR=14.6 deaths per 1,000) [4] and in Karachi, Pakistan, in 1989 (MR=151 per 100,000) [5].

Cause-of-death ranking is a useful tool for clarifying the relative burden of cause-specific mortality. Further, our analysis indicated that the leading causes of unnatural deaths in descending order of frequency were suicide, accidents, medical negligence, homicide, and legal execution. Suicide was particularly the most common manner of unnatural death in the study group (MR=10.21 per 100,000 women, 95% CI: 10.15-10.27), and it accounted for about one sixth of total deaths (17%) in this population. According to the World Health Organization (WHO) report, approximately 804,000 people globally died as a result of suicide in 2012, with an annual rate of 8.0 per 100,000 females worldwide[18]. In line with our findings, a previous injury-specific study has also reported the public health burden of suicide among reproductive age female population in Iran. They found that women of the target group are more likely to be involved in violence and injuries related to suicide [19]. This observation can be attributed to gender inequality, which has been shown to be growing in some areas in low- and middle-income countries [6, 20, 21]. Moreover, some studies have

indicated increasing trend of suicide in the women of reproductive age in high-income countries [22]. These findings signal the need for more efforts to improve the overall health of women in this region through understanding and addressing the suicidal behavior and safety education to prevent suicide-related mortality among women of reproductive age. This practice should be supported by creation of a national strategy for suicide prevention to effectively reduce the high percentage of this behavior among Iranian women. We recommend the employment of United Nations guidelines in the development of a national strategy with emphasis on inter-sectoral collaboration, multidisciplinary approaches, and continued evaluation and review [23].

Another key finding of the present study is the method of suicide among the reproductive age group women. We found that self-inflicted burn (45.6%) was the major method of suicide among women of reproductive age. Attempted suicide by burning (self-immolation) is distinctly different from the self-mutilation by burning, and the resulting burn size is much larger and fatal than that incurred as a result of self-mutilation [24]. Suicidal intent by burning is relatively less frequent in North America and Europe than in the Middle East, Africa, and South Asia, where its prevalence is as high as 11% [25, 26]. Notably, India has the highest number of self-immolation cases in the world, and the majority of victims in this country are young women [25]. Although little research has focused on self-immolation in the reproductive age group, some limited studies have found it as a major public health problem for young women [19, 27, 28]. However, our research showed that women of reproductive age are more likely to be involved in self-mutilation related to suicide. Results presented here confirm the findings of earlier studies [29, 30] in this setting, where self-mutilation is particularly common among the young women whose living situations are characterized by dysfunction family, poverty, and illiteracy. Sensitizing health policy-makers, increasing community awareness, setting up public health programs supporting women, identifying at-risk individuals, teaching stressor-coping strategies, proliferating suicide prevention campaigns, and spreading sensitization messages in the media are some of the recommended strategies for self-immolation and suicide prevention [25].

The causes of natural death were commonly observed in 58% of deaths, mostly due to neoplasms (31%) and circulatory system diseases (9.8%). The leading cause of neoplasm-related deaths in this region was malignant neoplasms of breast [7.4% of all deaths, MR of 4.22 per 100,000 women of reproductive age (95% CI: 4.18-4.26)]. From an epidemiological point of view, there is no certain evidence to explain this phenomenon because the strongest risk factor for breast cancer, as a western lifestyle-related cancer, is age, and it is expected a

woman's risk of the disease increases as she gets older. Moreover, there is no data in the literature regarding the prognostic effect of age at diagnosis of breast cancer in different parts of Iran; young and relatively old women have a similar risk of dying from breast cancer [31]. Globally, age-standardized death rate for all ages was 7.4 (6.4-8.1 per 100,000), and for women in the Middle East, breast cancer was the major factor for premature death in all countries in 2013 [2]. Results presented here confirm the findings of an earlier study in this setting [32] where MR from breast cancer among women of all ages had an increasing trend and reached to 4.92 per 100,000 in 2010. The results of that study and ours indicate the high mortality of breast cancer among younger women (women of reproductive age) in Iran. To reduce burden of breast cancer, preventive and screening programs, especially for young women, are highly recommended.

Deaths related to pregnancy, childbirth, and the puerperium (maternal mortality) account for only 3.33% of all deaths occurring among reproductive age women in our study setting. Although for three decades, a continuing focus for women's health in low- and middle-income countries has been on reductions in maternal mortality, attention to non-maternal causes of death for women of reproductive age such as suicide, accidents, and neoplasms is highly needed.

In summary, we received mortality information using RAMOS methodology coupled with VA data, which allowed us to estimate overall and cause-specific mortality among reproductive age females resident in West Azerbaijan Province, Iran. Despite the attention given and efforts being made to prevent mortality related to pregnancy, childbirth, and the puerperium in Iran, we showed that maternal mortality is responsible for a small fraction of all deaths occurring among target population of women. Attention to other causes of death and health issues for women of reproductive age such as suicide, accidents, and breast cancer is obviously required. Alongside with the existing national maternal mortality surveillance system, the Ministry of Health and Medical Education of Iran should scale up the current efforts to reverse the public health burden of other prevalent causes of death such as suicide, accidents, and breast cancer among women of reproductive age.

Our study has at least two strengths. First, the same as any other population-based study, we were able to study nearly all deaths of the three million populations of women of reproductive age due to multiple data sources. Second, to the best knowledge of the authors, this is the first time in the literature that information about the levels and causes of reproductive age female mortality using data gathered from the RAMOS is reporting in Iran.

The present study has a few limitations: our study was limited to its external validity. Although our data covers strongly the whole target population of the province, the external validity of these findings may not be accurate. Further, the study setting includes only 1.4% of the country population, and the ethnic (religious) characteristics of the province is unique in the country; therefore, it seems that our results cannot be generalized to the overall country. On the other hand, the present type of data collection method may have trivialized deaths because of incomplete recording of deaths and the low quality of data generated, as well as due to under-registration of deaths. We tried to decrease underestimation using five datasets, but our study is not an exception and death cases presented here should be interpreted as minimum cases due to inevitable underestimation. To ensure complete death case ascertainment, active data sharing is needed among public health network, organization of civil registration, and legal medicine organization.

Conclusions

Unexpectedly, pregnancy-related mortality accounts for only about 3% of all deaths occurring among reproductive age women in Iran. Meanwhile, death related to suicide was the most common cause of mortality among this age group of women. Therefore, attention to health issues and other causes of death, such as suicide and malignancies, for women of reproductive age is definitely required. Undoubtedly, there is a need for further research on policies that provide preventive services for the women of reproductive age.

Conflict of interest

The authors have no financial and non-financial conflicts of interest to be declared.

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Table 1

Socio-demographic characteristics of women of reproductive age in West Azerbaijan, Iran (2013-2014)

Variable	Women alive n (%)	Women dead n (%)	P value
Overall (n=901161)	900651 (99.94)	510 (0.06)	
Age in years			<0.001
15-19	146978 (16.3)	53 (10.4)	
20-24	172371 (19.1)	68 (13.3)	
25-29	160260 (17.8)	68 (13.3)	
30-34	137040 (15.2)	60 (11.8)	
35-39	105828 (11.7)	64 (12.5)	
40-44	98643 (11.0)	65 (12.8)	
45-49	80041 (8.9)	132 (25.9)	
Area of residence			<0.001
Urban	576441 (64.0)	252 (49.4)	
Rural	324210 (36.0)	258 (50.6)	
Marriage			<0.001
No	250602 (27.8)	135 (26.5)	
Yes (living with husband)	612219 (68.0)	329 (64.5)	
Yes (Divorced or dead husband)	37830 (4.2)	46 (9.0)	
Employment			0.065
Practitioner	67608 (7.5)	53 (10.4)	
Unemployed or student	833043 (92.5)	457 (89.6)	
Highest level of education			<0.001
More than nine years	423440 (47.0)	117 (22.9)	
Equal or less than nine years	299618 (33.3)	202 (39.6)	
No school	177593 (19.7)	191 (37.5)	
Ethnic (religious) group			<0.001
Azeri (Shiites Muslims)	686433 (76.2)	252 (49.4)	
Kurd (Sunni Muslims)	205211 (22.8)	254 (49.8)	
Others	9007 (1.0)	4 (0.8)	

Table 2

Manner of death distribution by characteristics of reproductive age women in West Azerbaijan, Iran (2013-2014)

Characteristic	Natural Death (n=296)		Non-Natural Death (n=214)		P value
	n	%	n	%	
Age in years					
15-19	23	7.8	30	14.0	0.00
20-29	54	18.2	82	38.3	
30-39	78	26.4	46	21.5	
40-49	141	47.6	56	26.2	
Area of residence					
Urban	156	52.7	96	44.9	0.88
Rural	140	47.3	118	55.1	
Marriage					
No	89	30.1	46	21.5	0.49
Yes (living with husband)	178	60.1	151	70.6	
Yes (Divorced or dead husband)	29	9.8	17	7.9	
Employment					
Practitioner	34	11.5	19	8.9	0.38
Unemployed or student	262	88.5	195	91.1	
Highest level of education					
More than nine years	71	24.1	46	22.2	0.00
Equal or less than nine years	97	33.0	96	46.4	
No school	126	42.9	65	31.4	
Ethnic (religious) group					
Azeri (Shiites Muslims)	158	53.4	94	43.9	0.04
Kurd (Sunni Muslims)	136	45.9	118	55.1	
Others	2	0.7	2	0.9	

Table 3

Manner of death distribution by age range of reproductive age women in West Azerbaijan, Iran (2013-2014)

Age range (years)	Manner of death					Total (n=510)	
	Suicide (n=92)	Accident (n=83)	Medical negligence (n=28)	Homicide/ Legal execution (n=11)	Natural death (n=296)		
15-19	n	19	10	1	0	23	53
	%	20.7	12.0	3.6	0.0	7.8	10.4
20-29	n	45	23	8	6	54	136
	%	48.9	27.7	28.6	54.5	18.2	26.7
30-39	n	13	18	13	2	78	124
	%						

	%	14.1	21.7	46.4	18.2	26.4	24.3
40-49	n	15	32	6	3	141	197
	%	16.3	38.6	21.4	27.3	47.6	38.6
Total	n	92	83	28	11	296	510
	%	100.0	100.0	100.0	100.0	100.0	100.0

Table 4

Cause of death coded by the ICD-10 chapter deaths to women of reproductive age in West Azerbaijan, Iran (2013-2014) (n=510)

ICD-10 chapter	Cause-specific mortality fraction		Mortality rate/ 100,000 women	95% confidence intervals	
	n	%		Lower	Upper
XX External causes of morbidity and mortality	186	36.47	20.65	20.57	20.73
II Neoplasm	158	30.99	17.53	17.45	17.61
IX Diseases of the circulatory system	50	9.80	5.55	5.50	5.60
XVII Congenital malformations, deformations and chromosomal abnormalities	32	6.27	3.55	3.51	3.59
XV Pregnancy, childbirth and the puerperium	17	3.33	1.89	1.86	1.92
VI Diseases of the nervous system	16	3.14	1.78	1.75	1.81
I Certain infectious and parasitic diseases	15	2.94	1.66	1.63	1.69
IV Endocrine, nutritional and metabolic diseases	8	1.57	0.89	0.87	0.91
All other classified	28	5.49	3.12	3.08	3.16
Total	510	100	56.59	56.49	56.69

Table 5

Cause of death by the ICD–10 codes to women of reproductive age in West Azerbaijan, Iran (2013-2014) (n=510)

Cause of death	ICD-10	Death		Mortality rate/100,000 women	95% confidence intervals	
		n	%		Lower	Upper
All causes	A00-Y89	510	100.0	56.59	56.49	56.69
External causes of morbidity and mortality	V01-Y98	186	36.47	20.65	20.57	20.73
Intentional self-harm (Suicide)	X60-X84	92	18.0	10.21	10.15	10.27
Accidents	V01-X59	83	16.3	9.21	9.15	9.27
Others	X85-Y09, Y35-Y36, Y40-Y84	11	2.2	1.22	1.20	1.24
Malignant Neoplasms	C00-D48	158	31.0	17.53	17.45	17.61
Breast	C50	38	7.4	4.22	4.18	4.26
Digestive organs	C15-C26	37	7.2	4.11	4.07	4.15
Lymphoid, hematopoietic, and related tissue	C81-C96	25	4.9	2.78	2.75	2.81
Eye, brain, and other parts of central nervous system	C69-C72	17	3.3	1.89	1.86	1.92
Respiratory and intrathoracic organs	C30-C39	15	2.9	1.66	1.63	1.69
Female genital organs	C51-C58	14	2.7	1.55	1.52	1.58
Other neoplasms	C43-C44, C73-C80	12	2.3	1.33	1.31	1.35
Diseases of the circulatory system	I00-I99	50	9.8	5.55	5.50	5.60
Cerebrovascular diseases	I60-I69	21	4.1	2.33	2.30	2.36
Other forms of heart diseases	I05-I09, I30-I52	21	4.1	2.33	2.30	2.36
Ischemic heart diseases	I20-I25	8	1.6	0.89	0.87	0.91
Congenital malformations, deformations and chromosomal abnormalities	Q00-Q99	32	6.3	3.55	3.51	3.59
Pregnancy, childbirth and the puerperium	O00-O99, X60-X84	17	3.3	1.88	1.85	1.91
Diseases of the nervous system	G00-G99	16	3.1	1.78	1.75	1.81
Certain infectious and parasitic diseases	A00-B99	15	2.9	1.66	1.63	1.69
Endocrine, nutritional and metabolic diseases	E00-E99	8	1.6	0.89	0.87	0.91
All other classified	-	28	5.5	3.12	3.08	3.16

Highlights

- Suicide was the most common cause of death among young women in northwestern Iran.
- The leading method of suicide was self-immolation for about half of the cases.
- Suicide and breast cancer are major public health problems for young women in Iran.