RESEARCH ARTICLE

DETERMINING THE MAIN CAUSE OF DEATH ASSOCIATED WITH MATERNAL MORTALITY BY FOCUSING THE AUTOPSIES ON CADAVERS

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ABSTRACT

Background: Identifying and controlling medical and social risk factors contributing maternal mortality leads to minimize the rate of mortality particularly in developing nations. The present study aimed to determine risk factors associated with maternal death by focusing the autopsies on cadavers.
Methods: In this retrospective study, the hospital recorded files related to 122 pregnant women aged 15 to 45 years who died because of perinatal death that referred to Legal Medical Center between April 2009 and April 2014 were reviewed. All specimens extracted by autopsy had been sent to pathology and toxicology laboratories for further diagnostic assessments.
Results: Based on determining the cause of death in forensic medicine center or in hospital, the main causes for death because of clinical reasons (n = 115) was eclampsia in 17.2%and 10.4%, DIC in 14.9% and 8.7%, and uterine atony in 12.1% and 7%, respectively. In hospitals, the causes of death remained unclear in 25.9% that the diagnoses were finalized in legal medicine center as eclampsia, amniotic fluid emboli, cardiovascular and valvular disorders and malignancies. In total, 115 pregnant women died because of clinical causes and 7 of non-clinical causes including choking, hanging, drug overdose, poisoning with Co gas, suicide and car accident. Multivariable logistic regression analyses for determining the main determinants of maternal death could show that in both subgroups with in and out of hospital death, lower number of gravity was only predictor for maternal death.
Conclusion: The main causes for maternal death are potentially affected by different geographical, clinical, social, and cultural factors leading introduction of a wide risk variants. As shown in our survey, prim gravity was shown to be the main determinant for maternal death.

INTRODUCTION

About eight hundred women die diurnal from pregnancy-related causes that most of these causes are preventable. Approximately, 99% of these deaths occur in developing countries, especially in areas with lower socioeconomic status including in sub-Saharan Africa followed by South Asia (Conde-Agudelo *et al*., 2005 and Patton *et al*., 2009). In fact, younger age and residency in rural areas have been introduced as the two major factors leading high maternal death in these communities (Say *et al*., 2014). Fortunately, by developing maternal healthcare in recent decade, maternal mortality considerably reduced that from 1990 to 2015, global maternal death dropped by 44% (Say *et al*., 2014). It is now targeted to reduce global maternal mortality to less than 70 per 100.000 births by 2030(4). Along with two main causes for maternal mortality including young age and poor socioeconomic status, pregnancy-related complications have kept their causal roles which are responsible for 75% of deaths (Cousens *et al*., 2009).

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These complications include severe bleeding, maternal infections, preeclampsia, abortion, and HIV infection (Knight *et al*., 2016; Bauserman *et al*., 2015; McCall *et al*., 2016; Nair *et al*., 2009; and Viswanath *et al*., 2015). In this regard, development of maternal safe cares, identifying risk factors for maternal mortality, and employing comprehensive intervention strategies such as risk factors following and monitoring are three vertices of the maternal death prevention triangle. In fact, by identifying and controlling variety of medical and social risk factors contributing maternal mortality, the rate of mortality can be considerably reduced particularly in developing nations. The present study aimed to first describe maternal mortality rates in Iran by autopsy on cadavers and then to determine maternal, pregnancy-related, delivery and postpartum risk factors associated with maternal mortality.

MATERIALS AND METHODS

In this retrospective study, the hospital recorded files related to pregnant women aged 15 to 45 years who died because of perinatal death that referred to Legal Medical Center between April 2009 and April 2014 were reviewed. All cadavers had

been assessed by autopsies of vital organs including uterine, heart, kidneys, brain, and lung to determine the main etiologies of death. The toxicological samples were also extracted from vitreous, gastric contents, visceral organs, bile and urine. All specimens extracted by autopsy were sent to pathology and toxicology laboratories for further diagnostic assessments. All abnormal findings such as bleeding, fractures, or presence of abnormal fluids or change in shape or color of tissues were also recorded. Along with assessment of specimens derived from cadavers, medical history and parameters which might be probable risk factors for maternal death including mother age, gravity and parity, history of hypertension or gestational diabetes, mood of delivery, place of death (in or out of hospital), history of abortion, history of any active infections, or smoking were all collected by reviewing the recorded files. The first study endpoint was to determine the rate of maternal death based on assessment of autopsies and the second was to determine main correlates of maternal death. For statistical analysis, results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Normality of data was analyzed using the Kolmogorov-Smirnoff test. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with expected count of less than 5 were observed. Quantitative variables were also compared with t test or Mann-Whitney U test. For the statistical analysis, the statistical software SPSS version 16.0 for windows (SPSS Inc., Chicago, IL) was used. P values of 0.05 or less were considered statistically significant.

RESULTS

In total, 122 cadavers were assessed. Assessing the trend of the change in maternal death (Figure 1) from 2009 to 2014 showed the highest and the lowest mortality rates in 2010 and 2009 respectively.
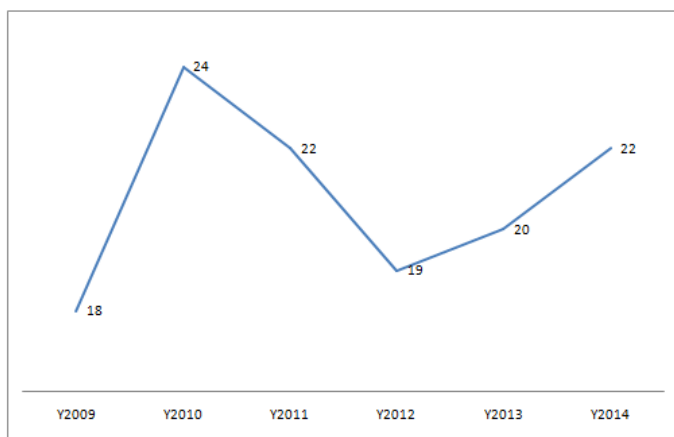

Figure 1. Trend of the change in maternal death according to the year of report

The mean age of patients was 30.6 ± 6.1 years ranged 15 to 45 years with an average gestational age of 31.0 ± 9.3 weeks ranged 5 to 41 weeks. Overall, 18% of deaths occurred beforedelivery and 7.5% on first 24 hour and 74.5% between second days to Forty-second day. Table 1 indicates The main causes of maternal death based on hospital-based and legal medicine-based diagnoses, the main causes for death because of clinical reasons (n = 115) was eclampsia in 17.2%

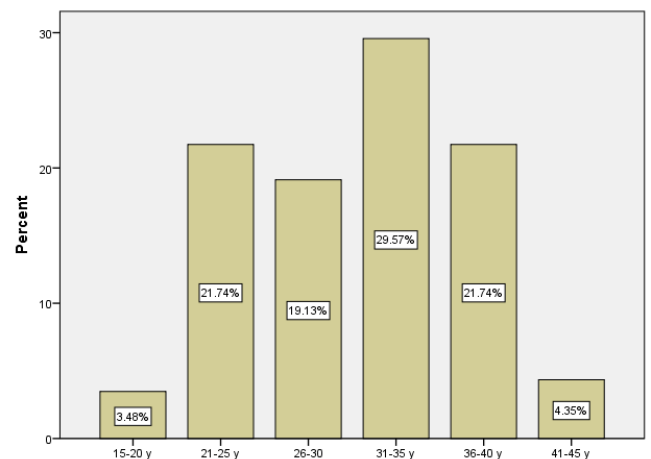and10.4%, DIC in 14.9% and 8.7%, and uterine atony in 12.1% and 7%, respectively.

Figure 2. Age distribution in maternal death

Table 1. The main causes of maternal death based on hospital-based and legal medicine-based diagnoses

In hospitals, the causes of death remained unclear in 25.9% that the diagnoses were finalized in legal medicine center as eclampsia, amniotic fluid emboli, cardiovascular and valvular disordersand malignancies. It was shown an agreement between the diagnoses based on hospital and legal medicine assessments (Kappa value of 0.67). The highest death occurred in age range of 31 to 35 years (29.5%) followed by in the age range of 36 to 40 years (21.7%) and 21 to 25 years (21.7%) (Figure 2). Most of the patients were prim gravid (42.6%). Regarding mood of delivery, cesarean section was recorded in 65.4% and vaginal delivery in 35.6%. Of 115 deaths assessed, 81.7% occurred in first trimester, 9.6% in second trimester, and 8.7% in third trimester. History of smoking and opium use was recorded in 10.4% and 2.6%, respectively. Also, 30.4% had history of abortion. History of multiple pregnancies was also found in 2.6% as twin and triple pregnancies in 0.9% and 1.7%, respectively. Gestational diabetes was revealed in 15.7% with the average blood glucose of 173.5 ± 47.5mg/dl. Pregnancy-related hypertension was also reported in 27.0%. In total, the main cause of maternal death was shown to be ectopic pregnancy in first trimester (33.3%), ectopic pregnancy in second trimester (30.0%), and eclampsia in third trimester (12.8%) (Table 2). In this regard, the highest mortality rate was recorded in ninth month followed by in eighth month of pregnancy with the rates of 63.5% and 12.2% respectively. In total in different years, the most frequent cause of maternal death was Eclampsia and DIC and Uterine bleeding (Table 3).

In total, 7 pregnant women died because of nonclinical causes including choking, hanging, drug overdose, poisoning with Co gas, suicide and car accident. The mean age of women in this subgroup was 26.3 ± 2.5 years ranged 24 to 30 years. None of the patients had history of hypertension, diabetes, multiple pregnancies or abortion. Only one of them was smoker. The mean gestational age was 22.6 ± 10.5 weeks ranged 5 to 28 weeks. The mean gestational age was significantly longer in those who died out of hospital (32.6 ± 7.9 weeks versus 23.3 ± 12.3 weeks, p < 0.001). Also, the mean number of gravity was higher in former group (3.3 versus 1.5, p = 0.03).

Table 1. The main causes of maternal death based on hospital-based and legal medicine-based diagnoses

	In hospital diagnosis	In forensic medicine diagnosis
Eclampsia	12 (10.4%)	15 (17.2%)
DIC	10 (8.7%)	13 (14.9 %)
Uterine atony	8 (7%)	11 (12.1%)
Decolman	6 (5.2%)	6 (6.5%)
ICH	6 (5.2%)	8 (8.6%)
Pulmonary emboli	7 (6.3%)	5(5.5%)
Sepsis	4(3,5%)	5(5.5%)
Malignancy	3(2,6%)	3(3.2%)
peritonitis	3(2,6%)	3(3.2%)
TTP	3(2,6%)	------------------------
Cardiac disease	5 (4.5%)	9 (9.9%)
Hellepsyndrom	2(1.7%)	------------------------
Massive uterine bleeding	5 (4.3%)	10 (11%)
pereclampsia	2(1.7%)	4(4.6 %)
Sepstic abortion	3(2,6%)	3(3.2%)
ARDS	2(1.7%)	2(2.2%)
Amniotic fluid emboli	---------------------	5(5.5%)
Ectopic pregnancy	1(.9%)	3(3.2%)
Multi organ failer	1(.9%)	4(4.6 %)
Placenta accrete	1(.9%)	------------------------
pneumonia	1(.9%)	1 (1.1%)
Uterine rupture	1(.9%)	3(3.2%)
Preforation	-----------------------	2(2.2%)

Table 2. Common Cause for pregnancy death

Pregnancy Trimester	Patients number	Death Cause
Third	94	Eclampsia=12.8%
Second	11	Ectopic pregnancy=30%
First	10	Ectopic pregnancy=33.3
Total	115	

Table 3. The main causes of maternal death based on the year of report

Year	Common causes of death		
2009	Uterine/vaginal bleeding	Placental abruption	Eclampsia
2010	DIC	Uterine/vaginal bleeding	Eclampsia
2011	Emboli	Uterine/vaginal bleeding	Eclampsia
2012	DIC	Uterine/vaginal bleeding	Sepsis
2013	Placental abruption	Uterine/vaginal bleeding	Eclampsia
2014	Eclampsia	Uterine/vaginal bleeding	Heart disease

Table 4. The main causes of maternal death adjusting for baseline variables

Factor	B	S.E.	P-value	OR	95.0% CI for OR	
					Lower	Upper
Trimester	1.503	1.411	0.287	4.497	0.283	71.431
Gravida	-0.828	0.403	0.04	0.437	0.199	0.962
Gestational age	0.081	0.207	0.696	1.084	0.723	1.627
MAH	-1.126	1.036	0.277	0.324	0.043	2.469
Constant	1.357	1.184	0.252	3.886		

Those women died out of hospital was significantly younger that other ones (29.4 ± 8.1 years versus 31.0 ± 5.8 years, p = 0.02). There was no difference between the patients died in and out of hospital in hypertension (25.5% versus 28.5%, p = 0.20) and gestational diabetes (15.7% versus 0.0%, p = 0.070), however history of smoking was higher in those who died in hospital (9.6% versus 0.9%, p 0.05). Multivariable logistic regression analyses for determining the main determinants of maternal death (Tables 4) could show that in both subgroups with in and out of hospital death, lower number of gravity was only predictor for maternal death (OR = 0.437, P = 0.040).

DISCUSSION

Among different factors increasing the risk for maternal mortality, uterine bleeding, eclampsia, and infections have the most important places, however different geographical patterns of these factors have been identified. In the present study, although various factors were more associated with maternal death, but only prim parity was determinant for maternal mortality. In other word, multiparity could reduce the risk for maternal death more two times compared to primipar individuals. Different direct and indirect maternal factors have been identified that are associated with increased risk for maternal death such as postpartum hemorrhage; anemia, malaria, and heart disease; infection; unsafe abortion; eclampsia; obstructed labor, ectopic pregnancy, embolism, and anesthesia complications (Nour *et al.*, 2008). More importantly, most of these factors are preventable by both curative and interventional approaches. For instance, efforts to address or treat postpartum hemorrhage and infection at health-care facilities made by providing appropriate drugs and

antibiotics, manual removal of the placenta, blood transfusion, and if needed, hysterectomy can result in significantly reducing the risk for maternal death (Nour *et al*., 2008). However, because of the different risky nature of death-related risk factors in different geographical characteristics, identifying the prominent risk factors in every region especially in developing African and Asian countries is important. Even, low social or cultural factors have been also revealed as the main risk factor. In a study by Yego *et al* in Kenya in 2014 (Yego *et al*., 2014). the most important factor associated with maternal mortality included having no education relative to secondary education followed by history of underlying medical conditions, doctor attendance at birth, having no antenatal visits, and being admitted with eclampsia. In another similar study in Senegal in 1997 (Garenne *et al*., 1997). The leading causes of death were puerperal sepsis and other infections, hemorrhage, eclampsia, ruptured uter, and anemia, but along with clinical causes, the role of some factors associated with health system failures such as medical equipment failure, late referral, lack of antenatal visit, and lack of available personnel at time of admissionhave been also identified as the determinant. In a great survey among Indian population in 2014 (Montgomery *et al*., 2014), both clinical causes (in more than 80% of pregnant women) and social reasons (social poorer states) were shown to be correlates for maternal death. In another study on Ethiopian population in 2015 (Godefay *et al*., 2015), it was indicated that women who were not members of the voluntary Women's Development Army, women whose husbands or partners had below-median scores for involvement during pregnancy, women with a pre-existing history of other illness, and those who had never used contraceptives, and also those women with previous pregnancy complications were at risk for maternal death. Ndour *et al* (2013), also showed in a study on Malian population in 2013 that patients with uterine rupture, hemorrhage or prolonged/obstructed labor, and those who have an emergency ante-partum cesarean delivery have an increased risk of in-hospital mortality, especially if they are referred from another health facility.

Reviewing the literature on reported risk factors for maternal death in Iran led to a variety of factors affecting maternal death. In a study at center region of Iran in 2016 (Karimi-Zarchi, 2016), bleeding was the most common cause of maternal mortality (30%), and it was associated directly with maternal mortality. Furthermore 20% of the mothers died due to heart disease and cardiac complications, which were associated indirectly with maternal mortality.In another survey in Isfahan in 2015 (Beigi *et al*., 2015), it was shown that lack of knowledge and skills in the medical team, unfamiliarity with their duties, lack of health care-based on protocols, lack of follow-up after discharge and inadequate supervision of inspectors on academic qualified doctors, and lack of referral the mothers' to the health care center were the main determinants for death. In another Iranian survey in 2014 (Farrokh-Eslamlou *et al*., 2014), the most common causes of maternal deaths were obstetric hemorrhage in 36.6% of cases and hypertensive disorders of pregnancy in 25.7%.In a study by Poorolajal *et al* in the west of Iran in 2014, (Poorolajal *et al*., 2014). The main risk factors were advanced ages, underweight status, overweight or obese condition, multi-gravidity, and preterm labor. In our study, although the prevalence of some factors was significantly different between survived and non-survived mothers, but adjusting baseline

characteristics introduced only primiigravidity as the main risk factor for maternal death that seems to be an indirect cause for death because of its-related comorbidities. In total, the causes for maternal death can be divided into two direct and indirect cases. The main direct causes of maternal deaths which account for up to 80% of cases including obstetric hemorrhage, puerperal sepsis, pregnancy-induced hypertension (including eclampsia), obstructed labor and ruptured uterus, and complications of unsafe abortion. Besides, indirect causes account for 20 to 25 percent of maternal deaths and are attributable to illnesses aggravated by pregnancy including anemia, HIV/AIDS, systemic disorders, and ectopic pregnancies. As shown by our study, even some non-clinical causes may be also risky such as physical violence and accidents that should be also taken into consideration. In final, it should be pointed that a wide range of social, nutritional, and clinical factors can affect maternal health status emphasizing attention to manage preventable factors to minimize maternal death.

Conclusion

The main causes for maternal death are potentially affected by different geographical, clinical, social, and cultural factors leading introduction of a wide risk variants. As shown in our survey, prim gravity was shown to be the main determinant for maternal death.

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