

Research Article

Causes of death through verbal autopsy: findings from a sub-study of single dose oral cholera vaccination in urban Dhaka, Bangladesh

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Background

Verbal autopsy can play a key crucial to identify significant causes of death in a developing country like Bangladesh where post-death pathological or forensic examination is not common. Single-dose Cholera Vaccination in Bangladesh (SCVB) was an individually randomized, placebo-controlled, double-blind study where verbal autopsy had been conducted for the participants who died within three months of receiving study agents This study aim was to determine the major causes of death through a verbal autopsy in a defined urban population.

Methods

The trial was conducted in urban slums of Dhaka among persons aged one year and older. A census was carried out bi-annually in the study area (Mirpur) including collecting death information from every household. Screening data on death was matched with the vaccination database to confirm whether the participants received the investigational products (IP) or not. The trained physician conducted a verbal autopsy usually within 7 days of notification.

Results

The screening period for verbal autopsy was from May 22 to July 18, 2014. Among 250 detected deaths, 99 received study agents (50 vaccines and 49 placebos). The Verbal autopsy could not be completed for 10 deaths due to the unavailability of a next of kin respondent. Of the total of 240 verbal autopsies performed, 217 were in adults aged 18 years and above, 6 in 5-17 years of age, and rest were ≤ 5 years. The Most common causes of death were non-communicable diseases. 163 deaths occurred at home, 59 in a hospital and others died in different places. No significant difference in cause of death among vaccine and placebo group was found from this analysis.

Conclusions

Verbal autopsies usefully identified probable causes of death in participants in an oral cholera vaccine trial. The findings highlight that in this urban slum, noncommunicable diseases account for most of deaths.

Mortality is an important health indicator and crucial for setting priorities for health interventions. Globally 56 million people die each year from different causes including non-communicable diseases (73.4%), communicable diseases, maternal, neonatal and nutritional causes (18.6%) or

injuries (4.4%).¹ Nevertheless, in low- and lower-middle-income countries imperfect unfailing information is available on mortality rates and causes of death due to much y unregistered death. Precise information on overall and cause-specific mortality is vital to prioritize health systems

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activities and appropriately and efficiently invest the limited public health and health care resources. Despite this need, confirmed medical information is not available in more than 70% of the global deaths.^{1,2} The standard method for determining the cause of death is certification by an attending physician. This approach may yield skewed results in many low- and middle-income countries, as many deaths do not occur in hospitals especially in rural and suburban areas. Ninety per cent of deaths in rural areas of Bangladesh occur at home and no death certificates are given from which one can derive a cause of death. Even when available and accessible, death certificates may not be fulfilled or trustworthy sources of the cause of death data are collected.^{3,4} This is mainly due to the lack of infrastructure, the high cost of data collection, inadequate access to diagnostic tests and limited post-mortem pathology services. In situations where medical certification of cause of death is lacking, and via interviewing the deceased's caregivers, verbal autopsy (VA) is a frequently used practical method for discovering plausible causes of mortality at the community level.^{5,6} Verbal autopsy (VA) is a methodology that can address this gap to collect information at the community level on factors contributing and to establish the cause(s) of death.

VA methodology was first developed for investigating epidemics. Later on it was used to evaluate outcomes of specific interventions and national mortality surveillance systems, particularly in low-income countries such as Bangladesh.⁷ Several studies have shown that VA provides more valid information on the causes of death determination than routine death certificate data in many developing countries.^{3,7,8} In Bangladesh, an individually randomized, placebo-controlled double-blind single dose oral cholera vaccine (OCV) trial was conducted in 2014 in urban Dhaka to evaluate the effectiveness of single dose of OCV in non-pregnant persons aged one year and older an urban slum.^{9,10} VA was conducted in the study area to identify the number of deaths within about three months after completion of vaccination and the probable causes of death. The 'Verbal Autopsy' aims to identify the number of deaths and the probable causes of death in this time period after receiving the investigational product. We hypothesized that this might account for the possible causes of death in this period after receiving vaccination not associated.

Paper context

Verbal autopsy (VA) is a methodology that can address this gap to collect information at the community level on factors contributing and to establish cause(s) of death. The results of the study provide a comprehensive picture of broader cause categories of deaths in an urban slum of Dhaka city. The results contribute to the existing knowledge on the cause-specific mortality among the selected population.

METHODS

VERBAL AUTOPSIES

Verbal autopsies were done as a sub-study of Single-Dose Oral Cholera Vaccine in Bangladesh (SCVB) in an urban area of Mirpur, Dhaka, Bangladesh. Total 205,513 participants were randomly administered orally either vaccine or placebo between January 10 and February 4, 2014, with 204,700 (102 552 vaccine participants and 102 148 placebo receivers) included in the per-protocol analysis. Data collectors have visited each house in the intervention areas to collect information on births, deaths, migrations (in/out), missed in previous census, change in marital status, pregnancies and other events twice in a year. Those who have been missed during the data collection period termed as 'not in census' (NIC). The screening for deaths started on May 22, 2014 and routine screening was completed on July 18, 2014. Study staff screened all eligible households. During the screening, the study team identified and notified deaths through household visits. VA was performed at the home of the deceased participant to determine the cause of death after receiving the investigational products (vaccine or placebo). After notification of the deaths, VAs were carried out by a trained study physician with an autopsy questionnaire prepared according to WHO guidelines.⁸ After that, the screening data was matched with the vaccination database to confirm whether the participants received the investigational products or not within three months of intervention. VA was conducted within about 3 months post-investigational product (IP) administration and usually within 7 days after death notification. The physicians conducted VAs during visits to the homes of the deceased with the guidance of field staff to locate the home's location.

Before VA, written informed consent was obtained from a family member of the deceased or relative (adult, > 18 years of age) for an interview about the terminal illness and events of the decedent. In this respect, we tried to select a person who could actually provide correct, reliable, and necessary information about the deceased person. A physician captured the data through an in-depth interview. The questionnaire included socio-demographic data, previously diagnosed medical conditions and a checklist of signs and symptoms that preceded the death. When available, hospital records, laboratory findings and death certificate were documented in the review process. The causes of death (COD) were categorized in different body systems (i.e. diseases of the nervous system, cardiovascular diseases, neoplasm, respiratory diseases, digestive diseases, natural death, diarrhea, diseases of the genitourinary system, endocrine/nutritional, metabolic diseases and others) mentioned in ICD-10. While interview, we characterized people as a natural death, there was no documented likely cause of death or underlined cause.

ANALYSIS

The data were collected through a preset questionnaire. Clinically analysed the causes of Death (COD) considering

most frequent causes of death categorized as diseases of the nervous system, cardiovascular diseases, neoplasm, respiratory diseases, digestive diseases, natural death, diarrhea, diseases of the genitourinary system, endocrine/nutritional, metabolic diseases, and others. Frequency distribution for categorical variables, median with inter-quartile range (IQR) for dimensional variables was inspected for the distribution of study participants' basic demographic characteristics and disease status. The bivariate statistical analyses are presented as frequency with percentage for COD by age, gender, study experiment groups and type of health care consultation by age and gender. Crude odds ratios (OR) were calculated using logistic regression to measure the odds changes for each cause of death by gender and ORs were adjusted by age considered as a confounding factor in the model. All *P* values and 95% confidence limits were two-sided. The analysis was performed using Stata version 13 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP.).

RESULTS

Between January and August 2014, 250 death cases were identified during the VA surveys. Relatives of the deceased for 10 cases could not be reached as they had migrated out of the study area (Figure 1). Half (49%) of the deaths were observed in 60 years of age or above, 26% in 45-59 years of age, and only 10% death in less than 18-year-old. The overall median (IQR) age at death was 59 (43-71) years and 139 (58%) deaths were men. Most of the deaths occurred at home (68%) followed by those at hospital (24.6%). 13.8% of the deceased were unmarried and 67.5% lived with a married partner. The highest proportion of deaths was observed among people who have no formal education whereas only 2% had eleven and more years of the school experience. 30% of the deceased suffered from high blood pressure, 21% from heart disease and 23% from diabetes. In addition, 21% and 16% had a history of stroke and different types of cancer history respectively. Sixty five percent of the deaths occurred in the dry season (March – June), 28% in the wet season (July – October) and the rest of the deaths occurred in other seasons. The most frequent causes of death were related to nervous system diseases (20%) followed by cardiovascular diseases (17%), cancer (15%), respiratory illness (14%), natural death (7%), digestive diseases (5%), diarrhea (2%), genitourinary system diseases (3%), and endocrine, nutritional, metabolic diseases (3%) and other causes (13%) (Table 1). Majority of the CODs are detected as non-communicable diseases. The other causes include road traffic accidents, burn, electrocution, drownings, suicide, heat stroke and heights falling.

We observed a significant (*P* -value=0.003) relationship between causes of death and deceased age. Of all causes of death, respiratory illness (22%) was a major contributor among children and adolescents followed by diarrhea, cancer, diseases of nervous and cardiovascular system (9% of deaths each). Among adults the major causes of death were nervous system diseases (22%), cardiovascular diseases (18%), cancer (16%), respiratory illness (13%), natural

death (8%), genitourinary system diseases (4%), endocrine, nutritional & metabolic diseases (4%), and diarrhea (0.9%). Percent of causes of death among male and female were statistically significant (*P* -value=0.023); among the deceased men, cardiovascular diseases (23%) and nervous system diseases (22%) were predominant causes of death followed by respiratory illness (15%) and cancer (14%). Among the deceased women, deaths were mainly due to diseases of the nervous system (19%) followed by cancer (16%) and natural death (14%). Of 240 deceased, 47 deaths were in the vaccine group and 48 in the placebo group for any cause of death. We did not find any significant variation of causes of death among vaccine and placebo group (*P* -value=0.098): Nervous system diseases (17% vs 23%), cardiovascular diseases (19% vs 8%), cancer (19% vs 12%), respiratory illness (17% vs 6%), aging (6% vs 2%), genitourinary system diseases (2% vs 8%), endocrine, nutritional and metabolic diseases (6% vs 4%) and others (67% vs 33%). Digestive diseases as a COD represented 8% among the placebo group only. The data from the SCVB study revealed that the proportion of deaths that were vaccinees (49%) and placebo recipients (51%) groups were similar (Table 2).

Seventy-four percent of the deceased had made a visit to a healthcare provider during a terminal illness, them, 39% relied on traditional medication provided by the untrained provider (e.g., drug-seller, village practitioner, spiritual/religious healers, etc.), 35% sought care from the doctor/hospital, and 26% of them did not seek any medical care at all. Consultation from a medical doctor/hospital was higher among adults than elderly (45% for 18-44-year old, 44% for 45-59-year old and 29% for ≥60-year old) who were comparatively more dependent on conventional medicines (41%). However, <5-year-old deceased children were also more likely to have been treated with traditional medication (41%). Thirty-nine percent of men sought care from doctors/hospitals, and 41% of women were more likely to seek care from traditional medication (Table 3).

A comparative analysis of causes of death was performed between male and female deceased people. Crude and adjusted (with age in years) models suggest that most male death causes did not differ from those among women except for cardiovascular diseases. The odds of having cardiovascular as COD among men were three times likely (OR=2.9; 95%CI: 1.3, 6.5) than women. In addition, odds of ageing as COD among men are 86% less likely (OR=0.14; 95% CI: 0.04, 0.49) than women (Table 4).

DISCUSSION

The study results provide a comprehensive picture of broader cause categories of deaths in an urban slum of Dhaka city. The results contribute to the existing knowledge on cause-specific mortality among the selected population. Infectious diseases are the primary cause of death among the pediatric population while non-communicable diseases and co-morbidities are the most common cause among adults. Diseases of the nervous system (20%) are the predominant cause among all deaths followed by cardiovascular diseases (17%), cancer (15%), and respiratory ill-

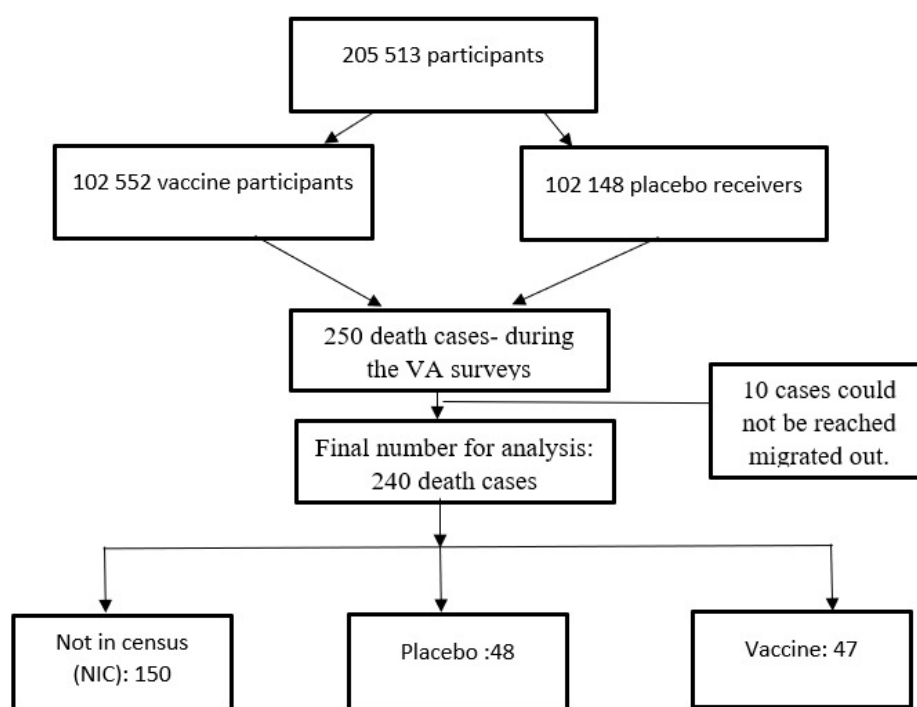


Figure 1. Total number of verbal autopsy person of single dose oral cholera vaccination in urban Dhaka

ness (14%). NCDs are currently the leading cause of death in low- and middle-income nations.^{11–13} Heart disease, diabetes mellitus, malignancy, and chronic respiratory disorders are the most common NCDs in Bangladesh.¹⁴ The total death rate was higher among men than among women.

The study's major was that trained physicians were involved in conducting the VA and they have used a structured questionnaire to obtain all the required information from the deceased household. Once notified of a death, the physician immediately visited the household and interviewed the immediate next of kin, preferably the main caregiver reducing recall biases. Each one was verified against study ID numbers to minimize selection errors. Our study had several limitations. First, the supporting documents were not sufficient to reach the definite cause of death. Secondly, we conducted a population-based instead of hospital-based survey and could not undertake a validation study for verbal autopsy survey, to obtain a 'gold standard' and estimates of sensitivity and specificity for VA in our setting. In spite of these limitations, our findings provide some vital information on the major causes of deaths and trends in an urban area of Bangladesh. Our findings corroborate those from a report on mortality profile Bangladesh, 2011. Deaths due to non-communicable diseases are on the rise and on the other hand communicable diseases are declining.¹⁵ Similar findings were observed from other studies conducted in Bangladesh and India.^{3,4} In case of children <5 years the leading cause of death was respiratory illness which is consistent with a previous study.¹⁶ In spite of differences in causes of death by gender, the results are also consistent with other studies that show higher death rates among men than women, irrespective of cause.³ Similarly, consultation with health care providers was higher for men than for women.⁴ As expected, this study did not find any

statistically significant association of CODs among the vaccine and placebo groups. This study has a reflection of a true image of COD in defined urban areas of Bangladesh. . In limitation, this was a nested study within a bigger one, and the efficacy comparison was not performed since the design was not ideal.

CONCLUSIONS

Verbal autopsy allows higher resolution understanding of major health problems and differences in mortality ratios and trends over time. The value of VA depends on quality and standardization. With this method we obtained mortality information which allows us to visualize the pattern of COD by age and sex in an urban slum area where non-communicable diseases are now predominant, although communicable disease are still prevalent. Good cause of death data is essential for developing and accessing public health policies.¹⁷ These findings may be helpful for health managers and policy makers of Bangladesh to set priorities of diseases for interventions as well as future research.

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Table 1. Background characteristics of deceased of a verbal autopsy survey

Socio-demographic characteristics	n (%)
Age (years)	
<5y	17 (7.1)
5y-<18y	6 (2.5)
18y-<45y	38 (15.8)
45y-<60y	62 (25.8)
≥60y	117 (48.8)
Median Age (Interquartile range)	59 (43-71)
Gender	
Male	139 (57.9)
Female	101 (42.1)
Site of death	
Hospital	59 (24.6)
Home	163 (67.9)
Other	16 (6.7)
Don't know	2 (0.8)
Marital Status	
Unmarried	33 (13.8)
Married living with a partner	162 (67.5)
Widowed	39 (16.3)
Divorced	4 (1.7)
Separated	2 (0.8)
Highest level of schooling	
No formal education (0 years schooling)	129 (53.8)
Primary (5 years schooling)	69 (28.8)
Secondary (10 years schooling)	20 (8.3)
Higher (11+ years schooling)	5 (2.1)
Children (<5 years)	17 (7.1)
Occupation	
Employed	71 (29.6)
Unemployed	16 (6.7)
Home-maker	45 (18.8)
Student	6 (2.5)
Pension	2 (0.8)
Other (dependent, beggar, hawker, labor)	83 (34.6)
Children (<5 years)	17 (7.1)
Previously diagnosis diseases of deceased	
High blood pressure	73 (30.4)
Heart disease	51 (21.3)
Diabetes	54 (22.5)
Asthma	39 (16.3)
Cancer	39 (16.3)
Chronic Obstructive Pulmonary Disease (COPD)	12 (5.0)
Stroke	50 (20.8)
Kidney disease	37 (15.4)
Liver disease	31 (12.9)
Season of death	
Wet season (July to October)	66 (27.5)

Socio-demographic characteristics	n (%)
Dry season (March to June)	157 (65.4)
Cause of death (COD)	
<i>Nervous system diseases</i>	49 (20.4)
<i>Cardiovascular diseases</i>	40 (16.7)
<i>Cancer</i>	36 (15.0)
<i>Respiratory illness</i>	33 (13.8)
<i>Digestive diseases</i>	13 (5.4)
<i>Aging</i>	17 (7.1)
<i>Diarrhea</i>	4 (1.7)
<i>Genitourinary system diseases</i>	8 (3.3)
<i>Endocrine, nutritional and metabolic diseases</i>	8 (3.3)
<i>Others</i>	32 (13.3)

Table 2. Distribution of COD (Cause of Death) by age and gender stratification

Causes of Death	Age (years)		Gender		Vaccine Group*	
	<18y	≥18y	Male	Female	Vaccine	Placebo
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
<i>Nervous system diseases</i>	2 (8.70)	47 (21.66)	30 (21.6)	19 (18.8)	8 (17.02)	11 (22.92)
<i>Cardiovascular diseases</i>	2 (8.70)	38 (17.51)	31 (22.3)	9 (8.9)	9 (19.15)	4 (8.33)
<i>Cancer</i>	2 (8.70)	34 (15.67)	20 (14.4)	16 (15.8)	9 (19.15)	6 (12.50)
<i>Respiratory illness</i>	5 (21.74)	28 (12.90)	21 (15.1)	12 (11.9)	8 (17.02)	3 (6.25)
<i>Digestive diseases</i>	1 (4.35)	12 (5.53)	6 (4.3)	7 (6.9)	0 (0.00)	4 (8.33)
<i>Aging</i>	0 (0.0)	17 (7.83)	3 (2.2)	14 (13.9)	3 (6.38)	1 (2.08)
<i>Diarrhea</i>	2 (8.70)	2 (0.92)	1 (0.7)	3 (3.0)	1 (2.13)	0 (0.00)
<i>Genitourinary system diseases</i>	0 (0.00)	8 (3.69)	5 (3.6)	3 (3.0)	1 (2.13)	4 (8.33)
<i>Endocrine, nutritional and metabolic diseases</i>	0 (0.00)	8 (3.69)	6 (4.3)	2 (2.0)	3 (6.38)	2 (4.18)
<i>Others</i>	9 (39.13)	23 (10.60)	16 (11.5)	16 (15.8)	5 (10.64)	13 (27.08)
Total	23 (100)	217 (100)	139 (100)	101 (100)	47 (100)	48 (100)
Fisher Exact test[†]	p-value=0.003		p-value=0.023		p-value=0.098	

* 145 death cases were not allocated for either vaccine/placebo group

† Too many cell frequencies close to zero, so, digestive disease, aging, diarrhea, genitourinary system disease, Endocrine, nutritional and metabolic diseases were categorized into a same group to get P-values using Fisher exact test.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by the Research Review Committee and the Ethical Review Committee of the icddr, Dhaka, Bangladesh. Informed consent was obtained from the study participants. This trial is registered at [ClinicalTrials.gov](https://clinicaltrials.gov), number NCT02027207.

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AUTHOR'S CONTRIBUTIONS

FQ, JC, AIK, MTI contributed to the study design and implementation. FQ, AIK contributed to the implementation and

supervision of the study. DRK, FA involved in data cleaning and analysis. DRK supervises the data analysis and took responsibility for the accuracy of the data analysis. All others supported the study in the different components. All authors participated in the writing of the manuscript and had full access to the data in the study. All authors saw and approved the final version of the manuscript.

COMPETING INTEREST

The authors completed the Unified Competing Interest form at <http://www.icmje.org/disclosure-of-interest/> (available upon request from the corresponding author), and declare no conflicts of interest.

Table 3. Distribution of type of health care consultation (medical vs traditional) before death by demographic characteristics

Demographic characteristics	Home, n (%)	Doctor / Hospital, n (%)	Traditional Medication, n (%)	Total
Age stratification (years)				
< 5	4 (23.53)	6 (35.29)	7 (41.18)	17 (7.08)
5-17	5 (83.33)	1 (16.67)	0 (0.00)	6 (2.50)
18-44	7 (18.42)	17 (44.74)	14 (36.84)	38 (15.83)
45-59	11 (17.74)	27 (43.55)	24 (38.71)	62 (25.83)
60 & above	35 (29.91)	34 (29.06)	48 (41.03)	117 (48.75)
Gender				
Male	33 (23.74)	54 (38.85)	52 (37.41)	139 (57.92)
Female	29 (28.71)	31 (30.69)	41 (40.59)	101 (42.08)
Total	62 (25.83)	85 (35.42)	93 (38.75)	240 (100.00)

Table 4. Odds of causes of death among male than female deceased

Causes of Death	Crude OR (95% CI)	Adjusted OR* (95% CI)
<i>Nervous system diseases</i>	1.19 (0.63, 2.26)	1.17 (0.61, 2.23)
<i>Cardiovascular diseases</i>	2.93 (1.33, 6.48)	2.93 (1.33, 6.48)
<i>Cancer</i>	0.89 (0.44, 1.82)	0.89 (0.44, 1.82)
<i>Respiratory illness</i>	1.32 (0.62, 2.82)	1.35 (0.63, 2.91)
<i>Digestive diseases</i>	0.61 (0.20, 1.86)	0.62 (0.21, 1.96)
<i>Aging</i>	0.14* (0.04, 0.49)	-
<i>Diarrhea</i>	0.24 (0.02, 2.31)	0.27 (0.03, 2.64)
<i>Genitourinary system diseases</i>	1.22 (0.28, 5.22)	1.25 (0.29, 5.40)
<i>Endocrine, nutritional and metabolic diseases</i>	2.23 (0.44, 11.30)	2.20 (0.44, 11.16)
<i>Others</i>	0.69 (0.33, 1.46)	0.77 (0.36, 1.69)

*Adjusted by age (in years) at death

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