



THE AGA KHAN UNIVERSITY

eCommons@AKU

Department of Obstetrics & Gynaecology

Division of Woman and Child Health

October 2013

Validation of Verbal Autopsy Tool for Ascertaining the Causes of Stillbirth

Sidrah Nausheen Aga Khan University

Sajid B. Soofi Aga Khan University

Kamran Sadiq *Aga Khan University*

Atif Habib Aga Khan University

Ali Turab Aga Khan University

See next page for additional authors

Follow this and additional works at: http://ecommons.aku.edu/ pakistan_fhs_mc_women_childhealth_obstet_gynaecol Part of the <u>Maternal and Child Health Commons</u>, and the <u>Obstetrics and Gynecology Commons</u>

Recommended Citation

Nausheen, S., Soofi, S. B., Sadiq, K., Habib, A., Turab, A., Suhag, Z., Bhatti, Z., Ahmed, I., Bhutta, Z. A., Memon, Z., Bahl, R., Khan, M. I., Bhutta, S. (2013). Validation of Verbal Autopsy Tool for Ascertaining the Causes of Stillbirth. *PLOS ONE*, 8(10). **Available at:** http://ecommons.aku.edu/pakistan_fhs_mc_women_childhealth_obstet_gynaecol/45

Authors

Sidrah Nausheen, Sajid B. Soofi, Kamran Sadiq, Atif Habib, Ali Turab, Zamir Suhag, Zaid Bhatti, Imran Ahmed, Zulfiqar A. Bhutta, Zahid Memon, Rajiv Bahl, M. Imran Khan, and Shireen Bhutta

This article is available at eCommons@AKU: http://ecommons.aku.edu/pakistan_fhs_mc_women_childhealth_obstet_gynaecol/ 45

Validation of Verbal Autopsy Tool for Ascertaining the Causes of Stillbirth

Sidrah Nausheen¹, Sajid B. Soofi¹, Kamran Sadiq¹, Atif Habib¹, Ali Turab¹, Zahid Memon², M. Imran Khan⁴, Zamir Suhag¹, Zaid Bhatti¹, Imran Ahmed¹, Rajiv Bahl³, Shireen Bhutta⁵, Zulfiqar A. Bhutta^{1,6,7*}

1 Division of Women & Child Health, Aga Khan University, Karachi, Pakistan, 2 Maternal and Newborn Health Program, Research & Advocacy Fund, Islamabad, Pakistan, 3 Department of Child and Adolescent Health and Development, World Health Organization, Geneva, Switzerland, 4 International Vaccine Institute, Seoul, Korea, 5 Department of Obstetrics & Gynecology, Jinnah Postgraduate Medical Center, Karachi, Pakistan, 6 Centre of Excellence in Women & Child Health, Aga Khan University, Karachi, Pakistan, 7 Center for Global Child Health, Hospital for Sick Children, Toronto, Canada

Abstract

Objective: To assess performance of the WHO revised verbal autopsy tool for ascertaining the causes of still birth in comparison with reference standard cause of death ascertained by standardized clinical and supportive data.

Methods: All stillbirths at a tertiary hospital in Karachi, Pakistan were prospectively recruited into study from August 2006- February 2008. The reference standard cause of death was established by two senior obstetricians within 48 hours using the ICD coding system. Verbal autopsy interviews using modified WHO tool were conducted by trained health workers within 2- 6 weeks of still birth and the cause of death was assigned by second panel of obstetricians. The performance was assessed in terms of sensitivity, specificity and Kappa.

Results: There were 204 still births. Of these, 80.8% of antepartum and 50.5% of intrapartum deaths were correctly diagnosed by verbal autopsy. Sensitivity of verbal autopsy was highest 68.4%, (95%CI: 46-84.6) for congenital malformation followed by obstetric complication 57.6%, (95%CI: 25-84.2). The specificity for all major causes was greater than 90%. The level of agreement was high (kappa=0.72) for anomalies and moderate (k=0.4) for all major causes of still birth, except asphyxia.

Conclusion: Our results suggest that verbal autopsy has reasonable validity in identifying and discriminating between causes of stillbirth in Pakistan. On the basis of these findings, we feel it has a place in resource constrained areas to inform strategic planning and mobilization of resources to attain Millennium Development Goals.

Citation: Nausheen S, Soofi SB, Sadiq K, Habib A, Turab A, et al. (2013) Validation of Verbal Autopsy Tool for Ascertaining the Causes of Stillbirth. PLoS ONE 8(10): e76933. doi:10.1371/journal.pone.0076933

Editor: Waldemar A Carlo, University of Alabama at Birmingham, United States of America

Received May 6, 2013; Accepted September 4, 2013; Published October 9, 2013

Copyright: © 2013 Nausheen et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: This study was funded by World Health Organization, Geneva, and Award Number: C6/181/502. The funding body provided clearance for the project design but apart from field visits to review progress did not influence the field trial or the data analysis procedures. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

* E-mail: zulfiqar.bhutta@aku.edu

Introduction

Every year 3.2 million babies are still born, with no signs of life and about 3.3 million babies die in neonatal period worldwide [1,2] yet stillbirths are given far less attention than it deserves. A bulk of these stillbirths (an estimated 98%) occurs in resource constrained countries of sub Saharan Africa and south Asia resulting mostly from antepartum or intra partum complications [3]. Most of the still births in these areas occur at home and thus remain un-notified and un-registered. The dearth of data thwarts perinatal health planning as it depends upon the availability of accurate data [4]. The need for collecting accurate information about the timing, causes and

the burden of stillbirths and early neonatal deaths is therefore critical for maternal and child health care planning.

The focus of global attention has long been on the intrapartum and immediate postnatal period [5] with still birth receiving less prominence in global, international health policy. The reported still birth incidence in south Asia is 32/1000 births which is critical [2] and about similar number is unreported, but without knowledge of the underlying causes and without addressing them in health policies Millennium Development Goals (MDGs) is a far cry from reality.

In the absence of a comprehensive registration system, verbal autopsy is the only tool for gathering cause specific mortality data from the community. Verbal autopsy is an indirect method of ascertaining the cause of death from

information about symptoms, signs and circumstances preceding death, obtained from the caretakers of the deceased. Global perinatal and neonatal mortality rates are emerging from Asia [6-8] and Africa yet most of these studies have small sample size, do not use standardized tool and are based in health centers [9]. Therefore there is a need for validation of the verbal autopsy tool so that it can be used in community based studies in other resource constrained settings.

Verbal autopsy has been used extensively over years for ascertaining the cause of child death [10]. Validation studies have shown reasonable sensitivity and specificity of childhood verbal autopsy for major causes of childhood death in comparison with physician's certification of death [11,12] but have shown poor diagnostic accuracy for establishing causes of neonatal death [6]. The childhood verbal autopsy was thus revised by an informal group of WHO in 2002 to include specific modules for still birth and neonatal death [13]. Over last few years this revised VA has been used in studies [6] but its performance has not been systemically assessed.

Our study aimed at validating the performance of a standardized verbal autopsy tool in estimating cause specific mortality for major causes of neonatal death and stillbirths. The objective of this paper is to assess the sensitivity, specificity and level of agreement of revised WHO verbal autopsy in ascertaining the cause specific mortality fractions (CSMF) for major causes of stillbirth in comparison with a reference standard cause of death ascertained by standardized clinical and supportive radiology and laboratory data collected prospectively in the hospitals. Validation for neonatal mortality is discussed in another comparison paper although data was collected contemporaneously.

DESIGN AND METHODOLOGY

Methods

The study was conducted in two major cities of Pakistan, Karachi and Hyderabad with collaboration of WHO in three tertiary care hospitals. The stillbirths (the subjects in this study) were recruited only from OBS/GYN unit of Jinnah Postgraduate Medical Center. Karachi whereas neonatal deaths were recruited from Civil Hospital Hyderabad and National Institute of Child Health, Karachi. Data was prospectively collected from August 2006 to February 2008 over 18 month. All stillbirths admitted in the hospital during the study period to mothers, who resided within 100 kilometers of the hospital, consented to be included in study, and were more than 28 weeks pregnant were included. Additionally, assignment of cause of death within 48 hours of stillbirth was another criterion for inclusion. Total 315 stillbirths were admitted to hospital in study period, 20 of them resided in remote areas and did not met the inclusion criteria whereas 13 refused to participate. Thus 282 cases were recruited form the hospital. Verbal autopsy could not be performed in 83 cases "Figure 1" of which 58 gave wrong address, 8 refused to participate, 12 shifted their home and 5 were not at home. Thus 204 cases including 5 sets of twin babies were included in final analyses. The hospital record information was considered as reference data and verbal autopsy data (verbatim) from community was used as study data.

Ascertaining the Reference Cause of Death- Hospital Records

Details of the events around stillbirths that took place in the hospital were recorded by two trained medical officers (graduates). The medical history, problems in previous pregnancy, antenatal care, complications of pregnancy and labor were recorded on a standardized labor delivery record form. All available laboratories & other investigations were also recorded in this form. Besides that addresses and contact details were also recorded to conduct verbal autopsy. The forms were then checked for completeness and errors by supervisors.

Two gualified (FCPS) expert Obstetricians with more than 10 years of clinical experience reviewed the available information, hospital records (history, lab investigation, death certificate, radiological evidence) for all stillbirths and assigned a reference standard primary cause of stillbirth in the light of International statistical classification of diseases and related health problems, 10th revision (ICD-10) They received extensive training in 3 days workshop before starting the study on methodology and cause assignment. They were kept independent and blinded to each other in determining the cause of death. In order to standardize the assignment of primary cause of death, a standardized instruction manual for guiding physicians in the assignment of cause of death was developed and used across the study sites. The manual provided information on the process of assigning a cause of death, including ascertainment of adequacy of information, case definitions, "Figure 2" list of causes of death, and the hierarchy of causes of death .The hierarchy of cause of death was adapted from Neonatal and Intrauterine Death Classification according to Etiology, NICE [15], "Figure 3". The purpose was to assign a single primary cause of death as deceased may have more than one causes. Events that took place first, are placed higher in the hierarchy than events happening later. For example, if a still born with a lethal congenital anomaly was born premature, the cause of death was recorded as congenital anomaly.

If the two Obstetricians failed to agree, the record was reviewed by a third senior obstetrician with clinical experience of 20 years, and the cause on which two of the three agreed was assigned. If all three did not agree on single cause it was labeled as "unclassifiable". We did not have data from autopsy or placental histology.

Assignment of cause of death from Verbal autopsy

The verbal autopsy instrument modified from the WHO/ LSTMH/JHU instrument for the evaluation of stillbirth & neonatal deaths (2000) was used. It was modified slightly to adjust cultural sensitivity and norms and also excluded irrelevant questions according to our study objectives. This questionnaire has different sections for basic information about the deceased neonate and still birth and included both narrative and close ended questions. Instrument was translated into local language Sindhi and back translated in English to

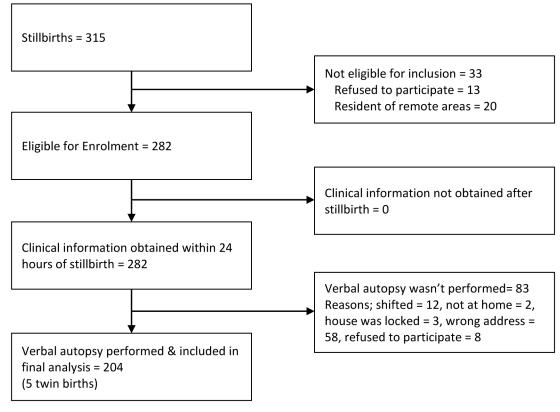


Figure 1: Flow diagram of study

Figure 1. Flow diagram of study.

doi: 10.1371/journal.pone.0076933.g001

ensure content validity. Pretesting of the instrument was also performed to identify the problems that could encounter during instrument administration and drive possible solutions. The verbal autopsy interviews were performed between 2 to 6 weeks after death using the standard questionnaire for stillbirths. A well-trained non-medical female interviewer, with an education level ranging from high school to college graduate conducted the verbal autopsy at home. The mother was the primary respondent; in case of recall bias a female relative present at birth/during illness was asked to assist. However, the health care provider who attended the birth was not interviewed for the verbal autopsy. If the respondent was not available on the first visit, one repeat visit was made to find respondent. Written informed consent in the local language was obtained. During the interview, pictorials of major congenital malformations, low birth weight were shown to aid recall

Assignment of cause of death in the light of given standardized case definition and list of causes of still births "Figure 4" based on those developed by WHO in 2000 [10] was performed by an independent review of the completed verbal autopsy questionnaires by second panel of two expert obstetricians whose experience was similar to the obstetricians working in study hospital. These experts were kept blinded to the clinical information and to the hospital-based, referencecause of death. When there is disagreement between the two, a third obstetrician reviewed the same case and the cause on which two of the three agreed was assigned. If all three did not agree on single cause it was labeled as "unclassifiable". Primary and secondary associated causes of stillbirths were coded; primary cause of death was analyzed.

Training

A six day's training workshop was organized to train the community health workers for verbal autopsy interview and recording of information on the instrument. The training focused on the interviewing techniques, and the concepts used in the instrument. Objectives of the study and underlying meaning of the questions used in questionnaire were elaborated in a class room presentation, small and large group discussions. Audio visual aids were also used as per need. Simulated interview were conducted for practice followed by mock interviews at field site being closely observed by one of the investigators. Feedbacks were given to trainees.

Project medical officers (already working as postgraduate students in same hospital) were trained for three days, in

Figure 2: Case definitions for assigning primary cause of stillbirth

Definitions for Cause of death certification from verbal autopsy stillbirth (adapted from Marsh 2002 & Kalter 1990) (6)

Stillbirths

Fetal deaths before onset of labor: Baby's body macerated, i.e. skin and underlying tissue was pulpy

Intra-partum death: Baby's body not macerated, FHS recorded after onset of labour

Congenital malformations: Include defects incompatible with life e.g. very small head size, mass or defect on the back of the head or spine. Do not diagnose minor congenital malformations as a cause of death e.g. cleft lip, additional digit

Extreme prematurity: Still births when pregnancy was reported to last 7 months or less, pregnancy ended very early or baby was very small at birth

Intra-partum asphyxia: Baby's body not macerated, no major congenital defects and pregnancy lasted 8 or 9 months

Other specific cause: Stillbirth due to any other specific cause, e.g. APH, severe maternal infection

Figure 2. Case definitions for assigning primary cause of stillbirth. doi: 10.1371/journal.pone.0076933.g002

recording information about stillbirth from case files in the hospital on a standardized form.

A 3 days orientation training was arranged for the team of obstetricians to record cause of death in accordance with ICD coding system 10th version and assigning primary single cause as per hierarchy by NICE [15] given in the manual. Both groups received similar training regarding case definitions, list of causes of death and its hierarchy and were explained about utilization of hospital reviews and verbal autopsies in separate groups.

Ethical consideration

This study was approved by Ethical Review Committee of Aga Khan University and institutional review board (IRB) of WHO. Individual written informed consent was sought from each verbal autopsy respondent before entry into the study. Confidentiality of data was maintained throughout the study and was only accessible to the senior project staff. Participants in the study were allocated unique ID number.

Quality assurance

The quality was ensured by weekly review meetings and supervisory field visits. Random field visits were done by WHO member, the funding body, to ensure adequacy of procedures both in hospital and field. The verbal autopsy interview forms were double checked for completeness by supervisor before data entry. A random 5% of verbal autopsy interviews were also attended by the study supervisor. Compliance checks were done be once daily visit of the supervisor for validity of data. Daily progress report was generated and any problems faced were discussed with supervisor. 2% work of each field interviewer was verified by approaching the respondents directly by Social Scientist and Supervisor. Scheduled and random unscheduled visits for observation of fieldwork procedures and independent blind re-interviews were also conducted.

Data management & Analysis

Data was processed using the Visual FoxPro data management software (Fox Pro v 6.0 Microsoft Corp Seattle WA USA). Data entry was done using a standardized database

Figure 3: Hierarchy for assigning primary cause of stillbirths >28 weeks gestation (Draft, adapted from Winbo 1998)

Hierarchy of the cause of stillbirth (to be assigned in this order if criteria are met)	Fetal deaths before onset of labour (macerated, no FHS before onset of labour)	Intrapartum death (fresh stillbirth, FHS heard after onset of labour)	
1	Congenital anomalies	Congenital anomalies	
2	Extreme prematurity	Extreme prematurity	
3	Other specific cause	Other specific cause	
4	-	Intrapartum asphyxia	

Figure 3. Hierarchy for assigning primary cause of stillbirths >28 weeks gestation (Draft, adapted from Winbo 1998). doi: 10.1371/journal.pone.0076933.g003

structure. The database and range and consistency checks were prepared centrally with inputs from all sites. Range and internal consistency checks were performed regularly. The outcome measures were sensitivity and specificity of the verbal autopsy in ascertaining cause of death and cause specific mortality fractions. Verbal autopsy diagnoses were compared with the reference diagnoses using simple chi sq analyses. Sensitivity $\pm 10\%$ precision and specificity $\pm 5\%$ precision determined compared to the reference standard for all diseases.

The chance corrected level of agreement between reference diagnoses and verbal autopsy was assessed using an interratter agreement Kappa statistics (Cohen, 1960) with 95% confidence interval. Based on criteria originally proposed by Landis and Koch (25) kappa *K* value over 0.75 were taken as excellent agreement ,between 0.4 - 0.75 as moderate agreement , 0.21- 0.4 as fair agreement and below 0.2 as poor agreement.

Results

Data was collected over 18 months from August 2006 to February 2008. Total 315 still births were recruited 13 did not gave consent and 20 resided in remote areas and thus not included in the study. 83 cases were excluded on the basis of shifting, wrong address or the home being locked "Figure 1".

During study time 204 causes of still birth were identified in hospitals settings thus 204 hospital records were received by reviewer 1 and reviewer 2 and in case of discrepancy the assigned expert reviewed the case. Consensus observed between both reviewers for hospital record was 75.5% and 50 cases were discrepant, which were reviewed by expert similarly 60 cases were discrepant in VA forms thus causes of death similar in hospitals record and verbal autopsy was 46.1% [Table 1]. Table 2 shows baseline characteristics. Mean maternal age was 28 years. Most of the mothers were found to be anemic, Hemoglobin- 9.9 gm which depicts nutritional deprivation and poor socioeconomic status of the family. The mean gestational age and birth weight of these still births were 35.7 (±SD) weeks and 2.6 kg (+SD).

Cause specific mortality fractions of the births were compared between hospital records and verbal autopsy [table 3]. Nearly 75% of these still births occurred due to antenatal complications, however intrapartum accidents were observed less frequent. Antepartum hemorrhage was seen in 24% of cases in both verbal autopsy and hospital records. Pregnancy induced hypertension was found in 12% in hospital records and 14% in verbal autopsy. Other leading causes included obstetric complications, congenital malformations and maternal diseases. Unexplained antepartum deaths were only 7.4% in hospital records. Leading cause of still birth in our study is Antepartum hemorrhage (24%) followed by obstetric complications (16.2% for hospital record and 20.6% for verbal autopsy), "Figure 5".

Diagnostic accuracy

Out of 204 still births, 80.8 % of ante partum and 50.5 % of intra partum deaths were correctly diagnosed by VA, however the specificity for ante partum and intra partum death was 50% and 80.8% respectively (table 4). Sensitivity of verbal autopsy is highest 68.4% for diagnosing congenital malformation followed by obstetric complications (57.6%); maternal diseases 57.1% and Antepartum hemorrhage 55.1%.

Kappa

Level of agreement between reference cause of death and verbal autopsy was good for congenital malformation [kappa =0.72] and moderate for all major causes of still birth (k > 0.40) [Table 3]. There was lower accuracy and level of agreement for

Figure 4: Definitions used in study conducted to validate the World Health Organization's verbal autopsy tool for stillbirth (10)

Antepartum death: Macerated still born; or a fresh stillborn with evidence of no fetal heart activity before the onset of labour.

Intra-partum death: Fresh still birth with evidence of fetal heart activity or fetal movements after the onset of labour.

Congenital malformations: Only lethal or potentially lethal malformation that markedly increases mortality risk eg anencephaly, large meningomylocele, duodenal atresia, tracheo-oesophageal fistula or major cardiac malformations.

Hyrops fetalis: Characteristic appearance on ultrasonography or on physical examination of the still born baby

Maternal diseases existing before pregnancy:

- Diabetes Mellitus: diagnosed diabetes mellitus prior to pregnancy.
- Chronic Hypertension: Hypertension diagnosed prior to pregnancy or before the 20 weeks of pregnancy.
- Epilepsy: History of having epileptic convulsions or taking anti-epileptic medical treatment during pregnancy.
- Renal Disease: severe renal insufficiency
- Hepatosis: clinical symptoms and elevated liver enzymes.

Pregnancy induced hypertension: blood pressure >140/90 mm Hg and proteinuria on at least two separate occasions , swelling of face and hands, blurring of vision, severe headache.

• Eclampsia : if associated with convulsions or unconsciousness.

Antepartum haemorrhage: vaginal bleeding (sometimes retained in uterus) after 22 weeks gestation.

- Placenta Previa: bleeding not associated with pain, usually with relaxed uterus
- Abruptio placentae: bleeding associated with intermittent or constant abdominal pain, the uterus is usually tense and/or tender

Obstetric complications:

- Malpresentations: All presentations of the fetus other than vertex.
- Cord Prolapse: The umbilical cord lies in the birth canal below the fetal presenting part, or the umbilical cord is visible at the vagina following rupture of membranes.
- Obstructed labour: Fetal distress and third degree moulding, together with arrest of dilatation and descent in the active phase of labour in the presence of adequate uterine contractions.
- Uterine rupture: Intra-abdominal or vaginal bleeding with severe abdominal pain usually associated with a tender abdomen, loss of uterine contour and easily palpable fetal parts.

Figure 4. Definitions used in study conducted to validate the World Health Organization's verbal autopsy tool for stillbirth (10).

doi: 10.1371/journal.pone.0076933.g004

birth asphyxia and hypertension as a cause of still birth, which may be due to difficulties in providing precise description of these causes by the mother.

	Hospital	
	Record	Verbal autopsy
Reviewed cases by both reviewers	204	204
Consensus observed between both reviewers	75.5%	70.6%
Discrepant cases reviewed by third reviewer and finalized	50	60
Causes of stillbirth similar in hospital record and verbal autopsy	46.1%	

Table 2. Baseline characteristics of stillbirths.

Characteristics of mother/stillborn	Stillbirths [N=204]		
Age of the mother (years), mean [SD]	28.6 [5.4]		
Antenatal visits made, n [%]	83 [42.8]		
Hemoglobin of mother (g/dl), mean [SD]	9.0 [2.0]		
Gestation age (weeks), mean [SD]	35.7 [3.3]		
Birth weight (grams), mean [SD]	2658.8 [952.8]		
Lethal Congenital anomaly, n [%]	13 [6.7]		
Multiple births, n [%]	6 [3.1]		
Main respondent [verbal autopsy]	[N=204]		
Age (years), mean [SD]	28.2 [6.1]		
Education (years), mean [SD]	8.0 [2.9]		

doi: 10.1371/journal.pone.0076933.t002

Table 3. Cause specific mortality fraction for stillbirth as per clinical verbal autopsy diagnosis.

	Clinical Diagnosis,	Verbal Autopsy, n	1	
Causes of stillbirth	n (%) [N=204]	(%) [N=204],	KAPP	AP-value
Antepartum	156 (76.5)	150 (73.5)	0.295	<0.001
Intrapartum	48 (23.5)	54 (26.5)		
Congenital	19 (9.3)	16 (7.8)	0.72	<0.001
malformations	19 (9.5)	10 (7.0)	0.72	-0.001
Maternal disease	7 (3.4)	10 (4.9)	0.45	<0.001
Pregnancy Induced	26 (12.7)	30 (14.7)	0.34	<0.001
Hypertension	20 (12.7)	30 (14.7)	0.34	<0.001
Antepartum	49 (24)	49 (24)	0.41	<0.001
haemorrhage	43 (24)	45 (24)		
Obstetric complication	33 (16.2)	42 (20.6)	0.4	<0.001
Asphyxia not explained				
by any maternal	15 (7.4)	12 (5.9)	0.09	0.02
condition				
Others	55 (27)	45 (22.1)	0.31	<0.001

doi: 10.1371/journal.pone.0076933.t003

Discussion

This study is one of the largest validations of verbal autopsy for still birth in the region. We are aware of only two community based studies in resource limited settings, for diagnostic accuracy of verbal autopsy against reference standard cause of still birth; those are from rural Ghana [14] and Chandigarh, India [24]. Two other still birth diagnostic accuracy studies [15,16] are reported but they examined vital registration data and are from developed countries. Currently over 35 Demographic Surveillance Sites (DSS) in 18 countries, the Sample Registration System(SRS) sites in India and Disease Surveillance Points(DSP) system in China regularly use VA on a large scale, primarily to assess the cause of death of a defined population [17,19].

The verbal autopsy tool in our study has shown a specificity of 80.8% and a sensitivity of 80% for ante partum death. The specificity of most of the causes of death in our study being more than 90% is consistent with literature, which reports diagnostic accuracy of verbal autopsy to be acceptable at the individual level if the sensitivity and specificity are at least 90%. At the population level, the Verbal autopsy is deemed to have reasonable diagnostic accuracy if sensitivity is at least 50%, specificity at least 90% and CSMF is within 20% of the true value [23].

High sensitivity and specificity for congenital malformation 98.4%, in our study is consistent with results from Chandigarh [24]. However, it is contrary to what is reported earlier from rural Ghana [14]. One explanation could be the extensive training which was given to CHWs for digging out diagnoses and inclusion of supportive radiologic and laboratory data in assigning the cause of death .Secondly the verbal autopsy interviews within 6 weeks and preferably by mother has further reduced the chances of error.

Another, strength of our study is the minimization of unexplained deaths by using standard case definitions for assigning cause of death, extensive training of staff, doctors and reviewing by 2^{nd} and 3rd reviewer. Similar results are shown by Aggarwal [24] from Chandigarh. However previous studies from Ghana [14,15] reported 58-60% of unexplained ante partum deaths.

Cause specific mortality fractions found in the study are useful for strategic planning in both maternal and neonatal health care programs. High antepartum still birth rate (75%) than intrapartum (25%) is consistent with world literature which states about 2.2 million of stillbirths occur during last trimester but before the onset of labor [20], and also by Aggarwal [24]. Cause mortality fractions for stillbirth vary considerably in literature. We report leading cause of stillbirth as antepartum hemorrhage whereas multicenter study in low resource countries by Engmann C, et al [25] reported maternal and neonatal infections to be the major cause. Over two-thirds of the stillbirths are attributable to causes, for which preventive and therapeutic interventions are available, namely pregnancyinduced hypertension, antepartum hemorrhage, underlying maternal illness and obstetric complications. Interventions like better obstetric care, more rapid response to intrapartum complications, reducing delays at home and transportation should be integrated into antenatal and childbirth care. Secondly, the diagnostic accuracy of verbal autopsy suggests that the distribution of causes of death as determined by verbal autopsy can be confidently used to plan public health interventions.

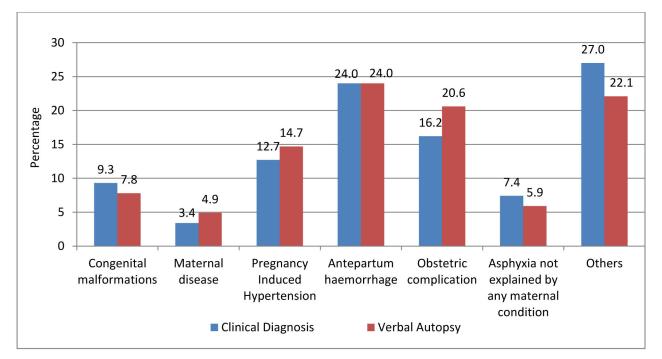


Figure 5: Cause specific mortality fraction for stillbirth as per clinical and verbal autopsy diagnosis

Figure 5. Cause specific mortality fraction for stillbirth as per clinical and verbal autopsy diagnosis. doi: 10.1371/journal.pone.0076933.g005

Reported literature on verbal autopsy vary markedly over the globe in terms of case definition, cause of death, classification system and reviewing verbal autopsy for assigning cause of death and this diversity makes it difficult to compare data [22]. In this regards WHO and its collaborators developed this modified verbal autopsy tool for neonatal death as well as stillbirths to identify the underlying causes of neonatal deaths and still birth, which has recently been used by Aggarwal [24]. We found it very effective, easy to use as the case definitions are simple to understand and applicable. It is for this reason, that the number of unexplained still births has been markedly reduced in our study.

There are limitations in this study. The reference cases were facility-based series in urban setting and may not be the representative of community as risks, exposure, interventions differ markedly .Therefore we report 16% of cases with obstetric complication whereas published studies from low income developing countries reports obstetric complication as leading cause of still birth[21] although the CSMFs were similar to community studies in West Africa[14] and other Global studies [2] .We used obstetricians reviews for assigning the cause of death which is the most commonly used method for assigning cause of death from verbal autopsy although the results vary considerably [7]. A disadvantage of this method is the lack of objectivity and inter-observer variability which we have addressed in our study by providing standard objective

Table 4. Sensitivity and Specificity of verbal autopsy against clinical diagnosis (hospital record).

Cause of still birth	Sensitivity		Specificity	
	n/N	% [95% CI]	n/N	% [95% CI]
Antepartum	126/156	80.8 [73.9,86.1]	24/48	50.0 [36.4,63.6]
Intrapartum	24/48	50.0 [36.4,63.6]	126/156	80.8 [73.9,86.1]
Congenital malformations	13/19	68.4 [46.0, 84.6]	182/185	98.4 [95.3, 99.4]
Maternal disease	4/7	57.1 [25.0, 84.2]	191/197	97.0 [93.5, 98.6]
Pregnancy Induced Hypertension	12/26	46.2 [28.7, 64.5]	160/178	89.9 [84.6, 93.5]
Antepartum haemorrhage	27/49	55.1 [41.3, 68.1]	133/155	85.8 [79.4, 90.4]
Obstetric complication	19/33	57.6 [40.8, 72.7]	148/171	86.5 [80.6, 90.8]
Asphyxia not explained				
by any maternal condition	2/15	13.3 [3.7, 37.8]	179/189	94.7 [90.5, 97.1]
Others	24/55	43.6[31.4,56.7]	128/149	85.9[79.4,90.6]

doi: 10.1371/journal.pone.0076933.t004

case definitions and hierarchy of causes of death to the physicians reviewing verbal autopsy interviews. Further, the method is labor intensive and is difficult to use in routine monitoring of causes of death, such as from Sample Registration Surveys in India and China [18,19]. An interesting alternative is the use of pre-decided computer algorithms. However, In spite of all limitations Quigley MA et al [23], strongly recommended physician reviews as it provided more accurate results in his study than application of computerized algorithms [23]. Obstetrician reviews in our study also limits its generalizability to other low-resource settings where obstetricians are unavailable and many births occur at home or other community settings. However, Engmaan C, et al [25] has recently used verbal autopsy interviews in non-hospital community based still births and early neonatal deaths in four low resource countries including Pakistan where cause assignment of death was done by two local physicians with reasonable sensitivity.

Ascertainment of cause of still birth by two expert obstetricians, who worked independent and blind to each other and involvement of third obstetricians, in cases of discrepancy has decreased the bias as well as chances of error but this is an expensive approach and would be difficult to apply in community due to wide spread shortage of physicians in many low income countries. Verbal autopsy reviews by nonphysicians after adequate training is therefore considered by many authors. However Engmann C, et al [26] reported an agreement of only 50% between physicians and nonphysicians panels on ascertainment of cause of perinatal death. Thus further research is required before non-physicians are asked to determine perinatal cause of death in low income settings.

Conclusion

Our results suggest verbal autopsy tool as having reasonable validity in determining and discriminating between causes of stillbirth, thus can be used to estimate CSMFs of stillbirth at community level. However, as these validation results are hospital based care must be taken while interpreting

References

- Oestergaard MZ, Inoue M, Yoshida S, Mahananni WR, Fiona M et al. (2011) Neonatal Mortality levels for 193 countries in 2009 with trends since 1990: A Systemic Analysis of Progress, Projections, Priorities. PLOS Med 8(8) : e1001080.
- Stanton C, Lawn JE, Rahman H, Wieczynska K (2006) Still birth rates delivering estimates in 190 countries. Lancet 367: 1487-1494. doi: 10.1016/S0140-6736(06)68586-3. PubMed: 16679161.
- Lawn JE, Shibuya K, Stein C (2005) No cry at birth. Global estimates of intra partum still birth and intra partum related neonatal deaths. Bull WHO 83: 4009-4417.
- The Lancet (2005) Editorial Stumbling around in the dark. Lancet 365 (1983).
- Lawn JE, Cousens S, Zupan J (2005) 4 million neonatal deaths: When? Where? Why? Lancet 365: 891-900. doi:10.1016/ S0140-6736(05)71048-5. PubMed: 15752534.
- Marsh DR, Sadruddin S, Fikree FF, Krishnan C (2003) Validation of verbal autopsy to determine the cause of 137 neonatal deaths in Karachi Pakistan. Pediatr Perinatal Epidemiol 17: 132-142. doi: 10.1046/j.1365-3016.2003.00475.x.
- Free man JV; Christian P, Khatry SK, Adhikari RK, LeClerq SC et al. (2005) Evaluation of neonatal verbal autopsy using physician review verses algorithm based cause of death assignment in rural Nepal Pediatrics & Perinatal epidemiology 19: 323-331.
- Baqui AH, Darmstadt GL, Williams EK, Kumar V, Tu Kiran et al. (2006) Rates, timing and causes of neonatal death in rural India. Implications

data of still births that occur at home. Assignment of cause of death by obstetricians is an expensive and labour intensive method and can be replaced by general physician or nonphysician in low income settings after further research .The introduction of uniform and reliable method to drive causes of death and standardization of the VA questionnaire and field operating procedures are important steps towards further improvement of the VA process. High antepartum deaths mostly due to antepartum hemorrhage and hypertension warrants public health interventions and allocation of appropriate resources to women in the immediate antenatal period to achieve Millennium Development Goals.

Acknowledgements

The authors would like to acknowledge the exceptional support provided by Dr Razia Korejo and her colleagues (Jinnah Postgraduate Medical Center, Pakistan) as verbal autopsy experts to ascertain the causes of stillbirth. We would like to appreciate all the staff of the study for their hard work and support and notably, the excellent support provided by Mr Asghar Ali, (manager grants), Dr Farrukh Raza, Women & Child Health Division, the Aga Khan University, Pakistan. We are also thankful to Dr Nick Brown (Salisbury District Hospital Salisbury, UK) for reviewing and giving feedback on the manuscript.

Author Contributions

Conceived and designed the experiments: ZAB SBS RB. Performed the experiments: ZS KS SBS SN SB. Analyzed the data: ZB IA MIK. Contributed reagents/materials/analysis tools: MIK ZB. Wrote the manuscript: SN SBS. Manuscript review: AH AT ZM Maintaining quality assurance at all stages of the study: RB.

for neonatal health Program. Bull WHO 84: 706-713. PubMed: 17128340.

- Rudan I, Lawn JE, Cousens S, Rowe AK, Boschi-Pinto C et al. (2005) Gaps in policy, relevant information on burden of diseases in children, a systematic review. Lancet 365: 2031-2040. doi:10.1016/ S0140-6736(05)66697-4. PubMed: 15950717.
- Anker M, Black RE, Coldham C, Kaltes HD, Quigley MA et al. (1999) A standard verbal autopsy method for investigating causes of death in infants and children. WHO/CDS/CSR/ISR/99.4. Geneva: WHO. pp. 1-78.
- Quigley MA, Armstrong Schellenberg JR, Snow RW (1996) Algorithms for verbal autopsies: a validation study in Kenyan children. Bull WHO 74: 147-154. PubMed: 8706229.
- Snow RW, Armstrong JRM, Forster D (1992) Childhood deaths in Africa, uses and limitations of verbal autopsy. Lancet 340: 351-355. doi: 10.1016/0140-6736(92)91414-4. PubMed: 1353814.
- WHOstandard Neonatal Verbal autopsy questionnaire, (2003) Revised version. Who/JHU/SNL. Geneva: WHO.
- Edmond K, Quigley M, Charles Z, Samuel D et al. (2008) Diagnostic accuracy of verbal autopsy in ascertaining the causes of stillbirths and neonatal deaths in rural Ghana. Pediatr Perinatal Epidemiol 22: 417-429. doi:10.1111/j.1365-3016.2008.00962.x.
- Winbo IG, Serenius FH, Dahlquist GG, Källén BA (1998) NICE, a new cause of death classification for still births and neonatal deaths. Neonatal and intrauterine death classification according to etiology. Int J Epidemiol 27: 499-504. doi:10.1093/ije/27.3.499. PubMed: 9698143.

- Winbo IGB, Serenius FH, Dahlquist GG, Källen BA (1997) A computer based method for cause of death classification in stillbirth and neonatal death. Int J Epidemiol 26: 1298-1306. doi:10.1093/ije/26.6.1298. PubMed: 9447410.
- INDEPTH Network (2005) An International Network of field sites with continuous Demographic Evaluation of Populations and their Health in developing countries. INDEPTH Network.
- Prospective study of one million deaths in India. Rationale, design and validation results. PLOS Med 3(2): e18. doi:10.1371/journal.pmed. 0030018. PubMed: 16354108 Toronto
- Yang G, Hu J, Rao KQ, Ma J, Rao C et al. (2005) Mortality Registration and surveillance in China; History, current situation and challenges. Popul Health Metrics 3: 3. doi:10.1186/1478-7954-3-3.
- Lawn Joy E, Yawar Yaqoob M, Rachel A, Haris ZA, Bhutta (2009) 3.2 million Stillbirths epidemiology and overview of evidence review. BMC 9(supp 1): 9. doi:10.1186/1471-2210-9-S1-P9.
- Who CWG (2005) The world health report 2005. Making every mother and child county. Geneva: WHO.

- 22. World Health Organization (2005) WHO technical consultation on verbal autopsy tools. Geneva: WHO.
- Quigley MA, Chandramohan D, Rodrigues LC (1999) Diagnostic accuracy of physician reviews, expert algorithm and data derived algorithms in adult verbal autopsies. Int J Epidemiol 28: 1081-1087. doi: 10.1093/ije/28.6.1081. PubMed: 10661651.
- Arun K, Aggarwal I, Vanita J, Rajesh K (2011) Validity of verbal autopsy for ascertaining the causes of still birth. Bull World Health Organ Geneva 89(1): 31-40. doi:10.2471/BLT.10.076828.
- Engmann Č, Garces A, Jehan I, Ditekemena J, Phiri M et al. (2012) Causes of community stillbirths and early neonatal deaths in lowincome countries using verbal autopsy: an International, Multicenter Study. J Perinatol 32(8): 585-592. doi:10.1038/jp.2011.154. PubMed: 22076413.
- Engmann C, Ditekemena J, Jehan I, Garces A, Phiri M et al. (2011) Classifying perinatal mortality using verbal autopsy: is there a role for nonphysicians? Popul Health Metrics 9: 42. doi: 10.1186/1478-7954-9-42.