TESTING THE ACCURACY OF A NEW VERBAL AUTOPSY INSTRUMENT FOR NEONATES

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Abstract
This study was conducted to develop and assess a New VA Instrument for neonates. This retrospective, cohort, randomized study was conducted in Chennai, attracting clinical information from the members of the family which had a neonatal death during the immediate past one year. The Data, collected from the Institute of Child Health and Hospital for children, Chennai. In testing the Accuracy in determing cause of death, the New Instrument validated against Gold standard Hospital Diagnosis and also, in juxtaposition with the WHO VA tool.While WHO VA tool consumes approximately 35 minutes, the new VA tool interview lasts for 15 minutes. It is time-efficient, reliable and accurate.

Cause specific mortality is a vital   indicator for assessing demographic change and for planning public health interventions[1]. Many developing countries and even some developed countries still lack up-to-date data on the causes of death especially neonatal deaths, because of various factors[2].In this scenario, verbal autopsy (VA) proves to be one of the reliable methods to compile the 'community or Population diagnoses' of major causes of diseases[3]. Verbal autopsy is an approach to ascertain probable cause of death by interviewing relatives and caretakers of the deceased[4]. The current study was aimed to develop and assess a new verbal autopsy instrument for Neonates which would be simple, reliable, accurate, time efficient and user friendly.

It was a retrospective cohort randomized study conducted in the Metropolitan City of Chennai and the surrounding field areas. It attracted clinical information from the members of the family, otherwise known as the respondents who had a neonatal deathduring the immediate past one year. The Data was collected from the Institute of Child Health and Hospital for Children, Chennai and then was subjected to the Inclusion - Exclusion Criteria.

The study tool is a newly designed Verbal Autopsy instrument for ascertaining the CoDs of neonates, formatted in a single paper, double-sided layout with eight sections and thirty nine questions. Questionnaire standardized by arranging the questions from easy to difficult ones, and from casual to more probing ones. The new VA tool was added with the starting and ending time of the cardinal symptoms. This can be the deciding factor in determining the starting point of the problem and the main CoD, especially when there are multiple CoDs. Administering WHO VA tool consumes approximately 35 minutes, whereas the new VA tool interview lasts for 15 minutes only.

After getting necessary permissions from appropriate authorities and after training the staff, field study was done. After a positive telephonic confirmation with the family of the deceased, their houses were visited by the social worker. Written consent was obtained from the respondent and then the study was carried out. The interview was conducted after a mourning period of 4 to 6 weeks after death and within 6 months. Based on overall admission, overall deaths and death prevalence during the particular period in the ICH &HC , the calculated sample size was 74. From among the chosen 445 subjects for study, 258 subjects were selected for regular study after applying inclusion- exclusion criteria and after obtaining willingness to participate in the study. Then month-wise classification of subjects and then equi-distribution of each unit into two, randomly allocating one to each tool, were done. The identities of both the social workers and the physicians were blinded for avoiding bias. For the sake of transparency, reliability and objectivity,50% of the 2 categories of equally distributed units were allotted to social worker A and the other 50% to Social Worker B. The entire subject was methodically coded by two independent Physicians. In case of disagreement of coding procedures within the physicians, coding would be arrived at Reconciliation. I fit does not settle at reconciliation, adjudication from a third Physician and Investigator would be sought for finalization of results. Then the CoD was compared separately against the gold standard hospital diagnosis.

Data maintenance: All the forms were checked for the completeness, consistency and errors while filling the forms. Quality checks were also conductedin10%ofquestionnaire by the Investigator independently and compared with social workers for agreement. All the data stored electronically on the researcher's personal laptop, which was password protected, not available for public review or scrutiny. The data will be double checked by the guide and will be used for research purpose only. Relevant data will be exported from MS excel file to SPSS .Statistical Analytical methods like SPSS, Open Epi software were used for data analysis.

The danger of misclassification is an important limitation of verbal autopsy that needs to be addressed. Hospital-based validation studies of verbal autopsy are helpful to understand the patterns of misclassification error in verbalautopsy[5]. Misclassification not only affects estimates of levels of cause-specific mortality fractions but it also affects estimates of: (1) changes in cause-specific mortality fractions over time and (2) differences in cause-specific mortality fractions between two population groups[6]. Maude and Ross have shown that when specificity is less than perfect, the verbal autopsy method underestimates the difference between two cause-specific mortality estimates. Furthermore, this underestimation can be substantial, greatly reducing the power of studies designed to detect differences in cause-specific mortality rates over time or between two populations. The sample sizes required to overcome this problem can be very large[7].

The S.W.O.T Analysis of the Study
There were a number of Strengths, Weaknesses, Opportunities and Threats linked to the study design and analysis. Some of the weaknesses, however, were predicted at the start of the study in which measures were considered while the discussion and conclusion parts were being constructed.

Strengths (internal): Data cleaning and manipulations were done manually (i.e.258 observations were treated individually rather applying common commands). This ensured high data management quality and fewer errors. On the other hand, the good study sample size was (n=129 for each tool) with equal distribution of age-sex groups. Being conducted in such a dynamic setting, this study benefited from the rapid social, political and epidemiological transitions and constant migrations. These factors were well suited to the study interest.

On the analytical level, this research work also considered several analytical measures prior to reaching study conclusion (CSMF, Kappa Statistics/ degree of agreement and Sensitivity and specificity measures) which strengthen the study conclusion.

Weaknesses (internal): Data of some variables contained relatively high number of missing data which might have introduced study bias. For example, the study had to exclude potential variables (e.g. respondent relationship to deceased, which treatment was received first and the SES). These were potential variables which could contribute to the study findings and conclusion. On the other hand, diseases classifications were introduced according to the ICD-10 systematic coding.

Opportunities (external): There is wide International attention to the applied health instrument i.e. VA (current proposed call by the WHO) which makes this study in a good place to address the concerns of the CoDs of neonates in the in the developing world. This study would also give the opportunity to evaluate the need for a newly designed VA and what measures could be established to harmonise this method across different regions and settings.

Threats (external): The applied concept of this study was based on the VA in generating the VA tool and compares it to the gold standard (InterVA) to investigate lay-perception on illness in this setting. One future interest could be to validate this study finding in different settings across India

ACCURACY OF THE INSTRUMENT (MAIN STUDY)

Cause of Neonatal deaths as determined through Hospital diagnosis versus New VA tool-Main study

Diagnostic Criteria	ICD code	Hospital Deaths	New tool Deaths	Matched	Unmatched
Sepsis	P369	34	35	32	3
C.Malformations	Q	25	24	22	2
Pneumonia	P239	18	18	16	2
Prematurity	P073	17	17	16	1
Birth Asphyxia	P021-P2	18	18	16	2
Low birth weight	P071	17	17	16	1
Total		129	129	118	11

ICD Code: International Classification of Diseases, Matched: means number of cases correctly diagnosed by New tool, Unmatched: number of cases wrongly diagnosed by New Tool

Validation of New VA tool with Hospital records based on various Diagnostic test measures-Main studies

Diagnostic c Criteria	ICD code	Sensitivity with 95%CI	Specificity with 95%CI	PPV with 95%CI	NPV with 95%CI	DA with 95%CI
Sepsis	P369	94.12 (80.91, 98.37)	96.84 (91.12, 98.93)	91.43 (77.62, 97.04)	97.87 (92.57, 99.41)	96.12 (91.25, 98.33)
C.Malformations	Q	88 (70.04, 95.83)	98.08 (93.26, 99.47)	91.67 (74.15, 97.68)	97.14 (91.93, 99.02)	96.12 (91.25, 98.33)
Pneumonia	P239	88.89 (67.2, 96.9)	98.2 (93.67, 99.5)	88.89 (67.2, 96.9)	98.2 (93.67, 99.5)	96.9 (92.3, 98.79)
Prematurity	P073	94.12 (73.02, 98.95)	99.11 (95.12, 99.84)	94.12 (73.02, 98.95)	99.11 (95.12, 99.84)	98.45 (94.52, 99.57)
Birth Asphyxia	P021-P2	88.89 (67.2, 96.9)	98.2 (93.67, 99.5)	88.89 (67.2, 96.9)	98.2 (93.67, 99.5)	96.9 (92.3, 98.79)
Low birth weigh	P071	94.12 (73.02, 98.95)	99.11 (95.12, 99.84)	94.12 (73.02, 98.95)	99.11 (95.12, 99.84)	98.45 (94.52, 99.57)
Over all		91.47 (85.38, 95.17)		100 (96.85, 100)		91.47 (85.38, 95.17)

ICD Code: Internal Classification of Diseases, CI: Confidence Interval, PPV: Positive Predictive Value, NPV: Negative Predictive Value

Cause of Neonatal deaths as determined through Hospital diagnosis versus WHO VA tool-Main study

Diagnostic Criteria	ICD code	Hospital Deaths	New tool Deaths	Matched	Unmatched
Sepsis	P369	32	33	32	1
C.Malformations	Q	27	26	24	2
Pneumonia	P239	20	20	19	1
Prematurity	P073	20	20	19	1
Birth Asphyxia	P021-P2	15	15	14	1
Low birth weight	P071	15	15	14	1
Total		129	129	122	7

ICD Code: International Classification of Diseases, Matched: means number of cases correctly diagnosed by new tool, Unmatched: number of cases wrongly diagnosed by New Tool.

Validation of WHO VA tool with Hospital records based on various Diagnostic test measures-Main studies

Diagnostic Criteria	ICD code	Sensitivity with 95%CI	Specificity with 95%CI	PPV with 95%CI	NPV with 95%CI	DA with 95%CI
Sepsis	P369	100 (89.28, 100)	98.97 (94.39, 99.82)	96.97 (84.68, 99.46)	100 (96.15, 100)	99.22 (95.74, 99.86)
C.Malformations	Q	88.89 (71.94, 96.15)	98.04 (93.13, 99.46)	92.31 (75.86, 97.86)	97.09 (91.78, 99)	96.12 (91.25, 98.33)
Pneumonia	P239	95 (76.39, 99.11)	99.08 (94.99, 99.84)	95 (76.39, 99.11)	99.08 (94.99, 99.84)	98.45 (94.52, 99.57)
Prematurity	P073	95 (76.39, 99.11)	99.08 (94.99, 99.84)	95 (76.39, 99.11)	99.08 (94.99, 99.84)	98.45 (94.52, 99.57)
Birth Asphyxia	P021-P2	93.33 (70.18, 98.81)	99.12 (95.2, 99.84)	93.33 (70.18, 98.81)	99.12 (95.2, 99.84)	98.45 (94.52, 99.57)
Low birth weigh	P071	93.33 (70.18, 98.81)	99.12 (95.2, 99.84)	93.33 (70.18, 98.81)	99.12 (95.2, 99.84)	98.45 (94.52, 99.57)

ICD Code: Internal Classification of Diseases, CI: Confidence Interval, PPV: Positive Predictive Value, NPV: Negative Predictive Value.

Comparative Characteristics of New VA Instrument and WHO VA Instrument

Characteristics	New VA Instrument	WHO VA Instrument
Number of Sections	8	10
Number of Questions	39	145
Number of Pages	2	9
Typical Interview Duration	15	36
Overall Sensitivity	91.47	94.57
Overall Specificity	100	100
Overall Diagnostic Accuracy	91.47	94.57

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