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Research Article

# COMMUNITY BASED STUDY USING VERBAL AUTOPSY TO ASCERTAIN CAUSES OF DEATH IN A RURAL COMMUNITY OF EASTERN INDIA EXPOSED TO ARSENIC IN GROUND WATER

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**A B S T R A C T**

Chronic arsenic exposure is a major public health threat, especially so in Indo-Bangladesh delta along lower Gangetic plains. A study was conceptualized to understand the causes of death in a rural population of West Bengal, exposed to high arsenic level in ground water. A cohort of 8206 persons was revisited after a decade. Information was obtained for 1044 persons, expired since last visit. Verbal autopsy method was adopted to ascertain cause of death. Arsenic exposure history was also obtained. Diseases of nervous system (27.3%), respiratory system (21.6%) and cancer (11.6%) were three leading causes, accounting for more than half of all deaths. Majority of deaths occurred at home (79%). No significant gender difference was observed in survival pattern. Though deaths were more among those exposed higher arsenic level, but the difference was not statistically significant. Substantial proportion of deaths from stroke and cancer calls for immediate attention towards mitigation measures. Differences were noted for causes leading to death in the arsenic exposed community compared to other areas.



## INTRODUCTION

Arsenicosis occurs in humans as a consequence of chronic exposure to metalloid arsenic. It results in anatomical and physiological dysfunction, with a potential to affect almost all organ system. Though the typical manifestation of arsenicosis involves skin, disease pathology is associated with myriad ailments like, respiratory diseases, hematological problems, renal disorders, neurological problems, obstetrical complications, ischemic heart disease, non-cirrhotic portal hypertension, diabetes mellitus and also cancers of various organs. (Sengupta *et al*, 2008; WHO factsheet; Guha mazumdar *et al*, 2008; Guha Mazumder *et al* 2010; NRC,1999). Hence it won't be erroneous to surmise that chronic arsenic exposure can influence the mortality and morbidity profile of a community exposed to this environmental threat. Local evidence also indicates a significantly higher level of chronic lung disease and peripheral neuropathy among the exposed group out of the 10469 persons examined in the district of Nadia, West Bengal earlier in 2010(Guha Mazumder *et al*, 2010)

Primary source of arsenic is groundwater, which enters our system through drinking water or otherwise.

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It is estimated that at least 140 million people in 50 countries are exposed to drinking water containing arsenic at levels above the WHO guideline value of 10 µg/L(WHO fact sheet). Being an environmental carcinogen, presence of inorganic arsenic (WHO factsheet) is a constant threat for humans and animals living in those geographical terrains. Though no continent is spared, it is more commonly seen in Indian subcontinent, mainly in the lower Ganga-Brahmaputra delta region of Indo-Bangladesh plains and in China (Ghosh P *et al* 2008, Das NK *et al* 2008, Huang *et al*, 2015).

Medical disciplines have always been inquisitive to find morbidities and environmental factors which are acting as key drivers to shape the mortality profile in a specific community. This knowledge would help in reducing preventable deaths as far as possible. But, it is not always feasible to ascertain the exact cause of death in every individual. In areas where majority of deaths are occurring at home or outside hospital it is more difficult to confirm the disease pathology leading to death in absence of reliable clinical records. Often researchers and scientists rely on information available from the relatives or accompanying persons about the events leading to death of the deceased person. This is a common practice and is used routinely for maternal death surveillance (MDSR surveillance guideline, GoI) or infant death review (Child death review

guideline, GoI) or AEFI death investigation (AEFI surveillance guideline, GoI).

World Health Organization have come up with standard norms and guidance notes on how to conduct this so-called "verbal autopsy". World Health Organization (Verbal Autopsy standard, WHO) defines it as a method to ascertain cause of death based on an interview with next of kin or other care givers which is applied for deaths without certified medical cause. Gold standard for finding cause of death is autopsy which can find about 10% of the conditions leading to death, missed by clinician during antemortem period (Goldman *et al*, 2018). Autopsies are not a universal practice in any part of the globe; medical certification if available can be considered best possible document eliciting the cause of death in an individual. However, there are discrepancies in causes mentioned in medical certification compared with set standards derived from clinical and laboratory evidence(Prado H *et al*, 2011) or autopsy report( Sehdev AES *et al*, 2001). It appears that precise identification and certification of cause of death is painstaking and no system may possibly be completely devoid of any error. Hence, an effective and practical way can be verbal autopsy, which can act as a satisfactory substitute of medical certification of cause of death, in many countries with suboptimal health manpower. A systematic review reinforced the importance of verbal autopsy in generating critical evidence pool for policy makers and programme managers in different countries;, especially so where many of deaths remain uncertified by medical professionals (Thomas LM *et al*, 2018). Verbal autopsies do not incur exorbitant costs. A study published in 2015 reported cost of this process was INR 757/- for each death investigated during 2004-07 in a rural community of 185629 in India (Joshi R *et al*, 2015). India also has the experience of doing large scale verbal autopsy as reported by million death study reports (CGHR report, GoI). In collaboration with registrar general of India, the project listed probable causes of death amongst 14 million people between 1998 to 2014 using verbal autopsy method (Krishnan A *et al*, 2019). An estimated 20% of all reported deaths or 14% of all deaths are medically certifiedin the country (Krishnan A *et al*, 2019). Office of the Registrar General of India has launched an initiative to bridge the gap. In collaboration initiative with AIIMS New Delhi a project termed Mortality in India was established through Verbal Autopsies (MINErVA). This network has a wide base among reputed government and private medical colleges from different parts of the country to carry out this herculean activity (Krishnan A *et al*, 2019).

The report on Medical certification of cause of death (RGI report, GoI) as compiled by Office of the Registrar General, Govt. of India. is based upon 14,56,023 total medically certified deaths accounting for 21.1 per cent of total registered deaths in respect of 35 States/UTs of India who supplied data for the report. Following are the leading cause-groups of deaths constituting around 86.5 per cent of total medically certified cause of deaths: Diseases of Circulatory System (32.9 per cent), Diseases of Respiratory System (9.4 per cent), Certain Infectious and Parasitic Diseases (9.4 per cent), Certain Conditions Originating in the Perinatal Period 5.9 per cent) , Neoplasm (5.7 per cent)) , Injury, Poisoning and Certain other Consequences of External Causes (4.5 per cent)(RGI report GoI). A special verbal autopsy (VA) study of 48 000 adult deaths in Chennai during 1995–97 was conducted to arrive at the probable underlying cause of death and to measure cause specific mortality rates for Chennai. The VA reduced the proportion of deaths attributed to unspecified medical causes and unknown causes from 37% to 7% in early adult life and middle age (25–69 yrs) and has yielded fewer unspecified causes (only 10%) than the death certificate. The sensitivity of VA to identify cancer was 94% in the age group 25–69(Gajalakshmi V *et al*, 2002).

In neighbouring country a 13-year follow-up study in Matlab (Rahman M *et al*, 2019), Bangladesh showed higher mortality in arsenic exposed young adults due to cancers and due to cerebro-vascular disease, cardio-vascular disease, and respiratory disease. Another study reported from Bangladesh that 198 people died from diseases of circulatory system, accounting for 43% of total mortality in the population of 11,746 men and women exposed to arsenic and followed up for an average of 6.6 years. The study revealed cardiovascular mortality increased substantially beyond As level 12 μg/L(Chen Y *et al*, 2011)

Various studies (Guha Mazumder *et al*, 20110) (Rahman MM *et al*, 2014) have generated substantial evidence of arsenic contamination in the ground water in Nadia, West Bengal. A recent study could establish evidence of bioaccumulation of arsenic in locally produced rice crops in Nadia district (Halder D *et al*, 2013). The dangers of chronic high level arsenic exposure are well known (Sengupta *et al*, 2008; WHO factsheet; Guha mazumdar *et al*, 2008; Guha Mazumder *et al* 2010; NRC, 1999). All the study reports from Nadia point towards a high risk pocket in terms of arsenic exposure; its potential adverse impact on health must already be having its toll on the exposed population, albeit surreptitiously. Another stud (Guha Mazumder *et al*, 2020) reported higher incidence of skin cancer in Nadia among the people exposed to As level >50 μ/L.

In this backdrop, a study was conceptualised with the following objectives:

- To ascertain cause of death in rural areas of arsenic affected blocks of Nadia district of West Bengal using verbal autopsy method.
- To find out association if any with arsenic exposure and causes of death in the study population

## METHODOLOGY

The study was conducted in the arsenic affected rural blocks of district of Nadia. Earlier about a decade back, a cross sectional survey was carried out amongst 10469 people to understand the clinical consequences of chronic arsenic exposure[4]. The same households were revisited afterwards. During follow up, it was learnt that 2263 persons have moved else-where and they could not be contacted. The current report is based on data generated for of the remaining 8206 persons. Data on arsenic level of water available from earlier survey were linked with mortality data. The current study was conducted between 2017-2019 for a period of 3 years and earlier phase was between 2006-2007. Households of 8206 persons, enlisted during the earlier survey were visited by the research team. The family member and respondents were explained the purpose of the visit. A written informed consent was obtained prior to interview. Fortunately, no family member refused interview. Sometimes the interviewer needed to reschedule the visit as per mutual convenience. In every family, event of any

death amongst those earlier enlisted was recorded. In case any family member who was not included in the previous list, died during the review period, that information was excluded from this analysis. Cause of death was ascertained by verbal autopsy method. The format was adapted from VA-formats used by RGI (CGHR, GoI). Once the format was finalized after pre-testing, the enumerators were oriented; and experts were also sensitized on the format and also how the information collected was to be interpreted. The semi-structured format used by the enumerator included a description of events preceding the event of death. List of cardinal symptoms like cancer, hypertension, diabetes, tuberculosis etc. were used for probing. Both narrative and close-ended questions were used to assign the underlying cause of death. Initial contact with household was done to obtain consent to participate in the study and was followed by interview to access medical records if the death had occurred in a hospital; this was followed by interview for Verbal Autopsy. Interview of next of kin, relatives, or those acquainted and associated with the deceased was done to extract relevant information preceding death. Information on sequence of events, circumstances leading to death, signs & symptoms of any illness etc. were collected. Specific subset of questions was kept for maternal deaths. Two independent experts (clinicians) reviewed all the information, positive & negative symptoms and opined about the probable cause of death based on available information. Following review of completed questionnaires assignment of ICD codes listed as causes of death was done. In case of any discrepancy third expert was consulted. About 10% of cases were re-evaluated by a separate team for quality check and till date performance of teams were found to be satisfactory. The format captured information on demographic profile of the family and respondents, history and clinical records of ailments of the deceased person, socio-demographic features of the person concerned and a narrative on events leading to death.

***Correlation of arsenic exposure through water in arsenicosis cases during past study***

Data on arsenic level in the water was available for 8173 persons of the initial cohort, of whom 1042 were deceased and 7131 were alive during this survey.

## RESULTS

Out of the listed 8206 persons studied earlier, 1044 persons have died during the interval from last study. Information was obtained from daughter/son in majority of cases (41%) or from spouse (14%). For the rest, information was collected from other relatives like siblings, cousin brother or sister, grandchildren, parents, uncle, aunts etc. or close neighbours who could describe the health conditions and recount the events leading to death of the person. Majority of these deaths occurred at home (79%). Among males it was 77% while for females it was 81%. The difference was not statistically significant (p=0.17). Other than home, majority of death occurred in secondary or tertiary care hospitals and not in primary care settings.

Age of those alive was recorded between 12-106 years, while those deceased ranged from 14 to 109 years. Figure-1 shows the age distribution of the two groups. Median age of surviving cohort was 45 years while those who died it was 70 years.

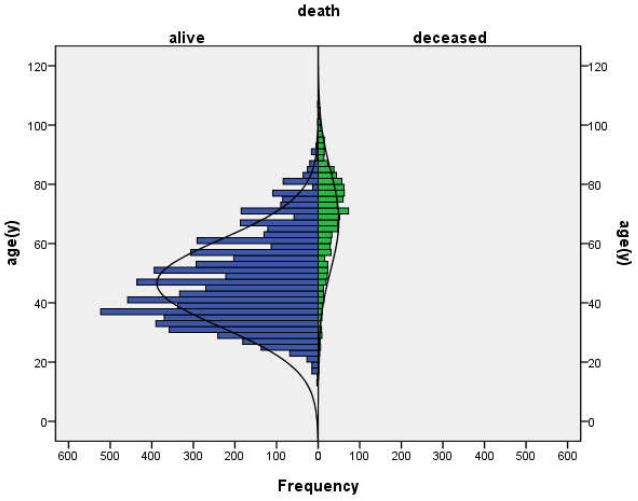


**Fig 1** Age distribution of deceased persons and those alive

Analysis was done in different age groups to understand the potential effect of arsenic exposure on mortality. Table-1 indicates that in all the age categories (below 30 years, 30-60 years and >60 years) mean or median peak arsenic exposure was comparable for deceased and surviving cohorts. The differences in mean or median values was not statistically significant.

Figure-2 shows the survival characteristics of male and female subjects under study. Since the first phase of data collection, on an average about 12 ½ years have elapsed., One in every ten (9.7%) females and one in every six (17.1%) males recruited in first phase, expired during this interval..

**Table 1** Comparison of peak arsenic value amongst deceased and alive persons of different age group (N=8173)

| Age group | Status | Subjects | Std. Deviation | Median | Minimum | Maximum |
|---|---|---|---|---|---|---|
| | Alive | 688 | 0.0847±0.127992 | .04100 | BDL | .899 |
| <30 Y | Deceased | 31 | 0.0967± 0.140263 | .04000 | BDL | .580 |
| | Total | 719 | 0.0852±0.128463 | .04100 | BDL | .899 |
| | Alive | 4987 | 0.0738±0.116283 | .03500 | BDL | 1.362 |
| 30-60Y | Deceased | 246 | 0.875±0.139202 | .04000 | BDL | .890 |
| | Total | 5233 | 0.0744±0.117481 | .03500 | BDL | 1.362 |
| | Alive | 1456 | 0.0769±0.123709 | .03700 | BDL | 1.362 |
| >60Y | Deceased | 765 | 0.0799±0.121675 | .03300 | BDL | .804 |
| | Total | 2221 | 0.0780±0.122993 | .03500 | BDL | 1.362 |
| | Alive | 7131 | 0.0755±0.119029 | .03600 | BDL | 1.362 |
| Total | Deceased | 1042 | 0.0822±0.126528 | .03500 | BDL | .890 |
| | Total | 8173 | 0.0764±0.120024 | .03600 | BDL | 1.362 |

Difference not statistically significant based on one-way ANOVA (p-value=0.064)
Arsenic exposure data was not available for 33 subjects.

**Table 2** Distribution of deceased population according to cause of death and peak arsenic exposure in the past (n=1044)

| Cause of death System Specific | As level<0.01mg/L | As level ≥0.01mg/L | NA | Grand Total |
|---|---|---|---|---|
| Gynecological | | 1(100%) | | 1(0.1%) |
| Maternal death | 1(100%) | | | 1(0.1%) |
| PUO | | 12(100%) | | 12(1.1%) |
| GI system | 8(33.3%) | 16(66.7%) | | 24(2.3%) |
| Septicemia | 5(20.8%) | 19(79.2%) | | 24(2.3%) |
| Liver problems | 9(31%) | 20(69%) | | 29(2.8%) |
| Kidney problems | 9(27.3%) | 24(72.7%) | | 33(3.2%) |
| Unnatural cause | 7(17.9%) | 32(81.1%) | | 39(3.7%) |
| Accidents | 18(33.3%) | 36(66.7%) | | 54(5.2%) |
| Unknown | 24(29.3%) | 56(68.3%) | 2(2.4%) | 82(7.9%) |
| Heart disease | 33(29.2%) | 79(69.9%) | 1(0.9%) | 113(10.8%) |
| Cancer | 25(20.7%) | 96(79.3%) | | 121(11.6%) |
| Respiratory problems | 61(27%) | 165(73%) | | 226(21.6%) |
| Nervous system | 91(31.9%) | 191(67%) | 3(1.1%) | 285(27.3%) |
| Grand Total | 291(27.9%) | 747(71.6%) | 6(0.6%) | 1044 |

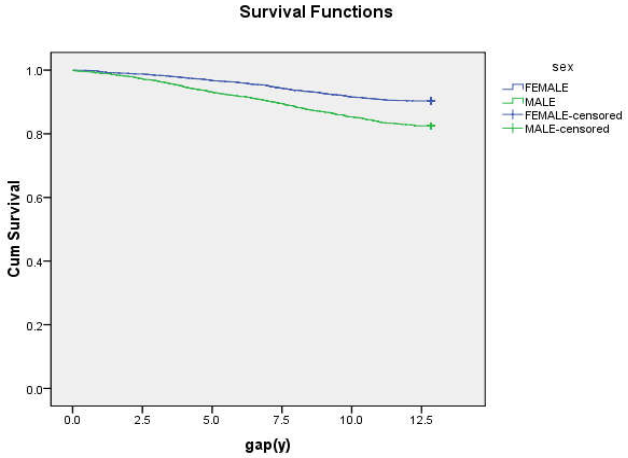


**Fig 2** age wise survival curves since last phase of survey

Survival curve is steeper for males than females, even when adjusted for age. Mean peak arsenic exposure was 0.0755 mg/L among those alive and 0.0822 mg/L among those who died but this difference was not statistically significant (p=0.09). Among the population studied 72% were exposed to peak As level >0.01mg/L. Amongst those exposed to ≥ 0.01 mg/L, 12.8% of the cohort expired and among those exposed to <0.01 mg/L peak arsenic in water, 12.6% persons of the cohort died.

The difference in mortality proportion was not statistically significant (p=0.88). Data on arsenic exposure were not available for 33 subjects.

The major disease groups associated with mortality is listed in table-2.Majority of causes of death occurred due to diseases of Nervous System 285 (27.3%), Diseases of lung 226 (21.6%), diseases of Cardiovascular system 113 (10.8%) and cancer 121(11.2%).No cause could be ascertained in 7.9% of subjects. Further subgroup distribution is enlisted in table-3 Largest number of deaths occurred due to CVA, 271 (95%), Respiratory Failure 75 (33.2%), Heart Failure, 59 (52%) and Myocardial Infarction, 40(35.4%) among the different organ system disease affected respectively. Study of death due to non-communicable diseases (HTN &DM) showed that 42% of deceased subjects had HTN, 24% had DM and 18.5% had both HTN &DM. (Not shown in Table-3). Maximum number (59%) of all causes of unnatural death occurred due to suicide. Death due to cancer occurred in121 (11.6%) subjects out of total death of 1044 subjects. It was observed that 96 (79.3%) out of 121 subjects who died due to cancer had peak arsenic exposure was ≥0.01mg/L. However the difference in number of people who died due cancer with peak arsenic exposure of <0.01mg/L and ≥0.01mg/L was not statistically significant. (p-value: 0.054)

## DISCUSSION

Results of the study were compared with relevant accessible information from various sources. Similar to other reports, in this study also majority of the deaths were not medically certified.

The report on Medical certification on Cause of Death,(Office of Registrar General, Govt of India 2012 )MCCD-2012, is based upon total medically certified deaths (20.0% of total registered deaths) supplied by 31 States/UTs of India(RGI, GoI). Owing to different levels of efficiency of medical certification across the States/UTs, the number of deaths reported therein may lack the representative character in the strict sense. On the other hand, VA reduced the proportion of deaths attributed to unspecified medical causes and unknown causes from 37% to 7% in early adult life and middle age and has yielded fewer unspecified causes (only 10%) than the death certificate (Gajalakshmi V *et al*, 2002)

**Table 3** is to be incorporated. It was there in the original manuscript mailed. In the result section it is also mentioned.

| Major System involvement | Frequency | within group % | Overall % | Organs affected with malignancy | Frequency | within group % | Overall % |
|---|---|---|---|---|---|---|---|
| | Diagnosis | | | Esophagus | 1 | 0.83% | |
| CVA | 271 | 95.10% | | GB | 1 | 0.83% | |
| Paraplegia | 8 | 2.80% | | Pancreas | 1 | 0.83% | |
| Epilepsy | 3 | 1.10% | | Rectum | 1 | 0.83% | |
| Spino-cerebellar ataxia | 1 | 0.40% | | Rib with brain metastasis | 1 | 0.83% | |
| Spinal Tuberculosis | 1 | 0.40% | | Stomach | 1 | 0.83% | |
| Rabies | 1 | 0.40% | | Urethra | 1 | 0.83% | |
| Nervous system problems | 285 | | 27.30% | Colon | 2 | 1.65% | |
| Acute Respiratory Failure | 75 | 33.20% | | Peritoneum | 4 | 3.31% | |
| Respiratory Tract Infection/Pneumonia | 54 | 23.90% | | Bladder | 4 | 3.31% | |
| COPD | 37 | 16.40% | | Kidney | 4 | 3.31% | |
| Asthma | 33 | 14.60% | | Brain | 5 | 4.13% | |
| Pulmonary Tuberculosis/Pl Eff | 27 | 11.90% | | Breast | 5 | 4.13% | |
| Respiratory disease | 226 | | 21.60% | Skin | 6 | 4.96% | |
| Heart failure | 59 | 52.20% | | Blood | 7 | 5.79% | |
| AMI | 40 | 35.40% | | Oral | 8 | 6.61% | |
| Hypertensive heart disease | 6 | 5.30% | | Throat | 9 | 7.44% | |
| Ischemic heart disease | 5 | 4.40% | | Uterus | 11 | 9.09% | |
| Cardiac arrest | 2 | 1.80% | | Lung | 24 | 19.83% | |
| Heart block | 1 | 0.90% | | Liver | 25 | 20.66% | |
| Heart Diseases | 113 | | 10.80% | Cancer | 121 | | 11.59% |

Causes of death were reported (Kalkonde Y *et al*, 2019) from 86 villages from general population in rural region of Gadchiroli district of Maharashtra, India during 2013 using verbal autopsy interview. There were 1599 deaths over 188,308 person years of observation. The five leading causes of death were diseases of the circulatory system (20.8%), stroke being the leading cause (14.3%), infections and parasitic disorders (18.4%), injuries and other external causes of mortality (10%), peri-natal diseases (6.5%) and diseases of the respiratory system (6.4%).Another study was conducted during 2002-2007 in which trained multi-purpose health workers conducted 2294 verbal autopsy interviews in rural adult population of North India and underlying cause of death was coded by physicians (palanivel C *et al*, 2013). The leading causes of death were diseases of the respiratory system (18.7%) and the circulatory system (18.1%). Infectious causes and injuries and other external causes, each accounted for around 15% of total deaths followed by neoplasms (6.8%) and diseases of the digestive system (4%)[29].

In the current study leading causes of death identified by VA in arsenic exposed population were different from those observed from studies in general population in two regions of India. These were diseases of nervous system (27.3%), respiratory system (21.6%), cancers (11.6%) heart diseases (10.8%). and accidents (5.2%).Further, 8.9% deaths were attributed to accidents and unnatural causes. A study from Bangladesh (Rahman M *et al*, 2019) reported higher incidence of deaths due to cardiovascular, respiratory and cancer in young adults exposed to higher arsenic levels.

It was clearly shown that cancer deaths were higher in this study compared to others. Cancer is one of the leading causes of adult deaths worldwide. In India, the International Agency for Research on Cancer estimated indirectly that about 635 000 people died from cancer in 2008, representing about 8% of all estimated global cancer deaths and about 6% of all deaths in India (IARC factsheet); Thus our observation of 11.6% cancer deaths in arsenic exposed population in Nadia, was higher than the report available regarding incidence of cancer death in general population in India. Another study from India (Dikshit R *et al*, 2012), showed that 7137 deaths were attributable to cancer out of 122 429 deaths for both sexes at all ages during the years 2001–03 in general population. This constitutes occurrence of 5829 cancer death per 100,000 all deaths in the general population .Our observation of 121 cancer death out of 1044 of all death or occurrence of 11590 deaths per 100,000 all deaths was much higher than the reported occurrence of cancer deaths in general population in India.

In the current study death due to Stroke was found to occur in 271 (25%) subjects out of 2044 deaths which occurred out of 8206 population studied. Verbal autopsy survey carried out in a rural community in Maharashtra showed that 229 (14.3%) deaths were caused by stroke outof 1599 deaths during the study period. In that study Stroke was the most frequent cause of death (Kalkonde Y *et al*, 2019). The current observed stroke prevalence in arsenic exposed population was found to be much higher than the reported incidence of stroke from rural population of Maharashra, India.

In our study death was more among those exposed to high level of arsenic but statistical significance was not observed between those exposed to high and low level of arsenic. Report from Bangladesh showed increasing incidence of death (Argos M *et al*, 2010) with increase in ground water level of arsenic, but dose response relationship was not clearly established. In a community where majority of deaths are happening at home and mostly not certified by medical professionals, verbal autopsy was an effective method to ascertain cause of death. Entire district of Nadia is exposed to high arsenic level in groundwater and potential health complications should be analysed to design and implement sustainable mitigation and control measures. The study identified the leading disease conditions causing deaths like stroke, respiratory problems, and cancer. It was noted that cancer and stroke burden was more compared to many other studies in general population. Mortality profile with increased share of stroke and cancer, also indicates the potential burden in terms of morbidity, as well as compromised quality of life. Being a systemic problem, arsenicosis is probably playing a critical role in the web of causation of these non-communicable diseases in this locality.

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