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Investigation of an Outbreak of Acute Methanol Poisoning in a Southwest State of Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Authors DA, AAF, OEF, PM and RMV did the study design and wrote the protocol. Authors AAF, EI, EA, Adefisoye Adewole, OF, MO, KO and Akinyode Akinfemi did the statistical analysis and literature searches while analyses of study was done by author AAF. All authors read and approved the final manuscript.

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ABSTRACT

Aims: An outbreak of sudden deaths with clinical features suggestive of acute methanol poisoning was reported. An epidemiological investigation was conducted to verify the diagnosis and identify risk factors.
Methodology: A joint team of officials of the Ondo State Ministry of Health, the World Health Organization, and the Nigerian Field Epidemiology and Laboratory Training Programme residents investigated the outbreak which was limited to two Local Government Areas of Ondo State, in Southwest Nigeria. An incident management coordination approach, modelled after the emergency operation centre for the elimination of polio virus and ebola virus disease in Nigeria was used. Field

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survey involving active case searches of health facilities, households and neighbourhoods using an operational case definition was carried out. Blood and urine specimen, including remnant of home-made alcoholic beverages were collected for analysis of viral antigens, heavy metals and methanol. A case-control study was also carried to identify potential risk factors.

Results: A total of 37 cases were found with 27 deaths inclusive (case fatality rate; 73%), most (76%) of whom were in the age group ≤ 49 years. The odd of being a case was 17 fold higher among those who consumed a locally brewed gin. Laboratory reports from samples from remnants of gin consumed as well as human samples; urine and blood, were consistent with acute methanol poisoning.

Conclusion: There is a need for enforcement of regulatory measures to address the consumption of illicitly produced alcoholic beverages to forestall future outbreaks.

Keywords: Disease outbreaks; sudden death; methanol; Nigeria.

1. INTRODUCTION

On 14 April 2015, the disease surveillance and notification officer of the Irele local government area (LGA) of Ondo State was notified of a cluster of sudden deaths involving five persons at Irele and Ayadi communities in the LGA. The State Ministry of Health (SMOH) and the World Health Organization (WHO) State office were notified immediately. Following this, an investigating team from the State was at the communities on the 15 April and confirmed a total of 12 deaths and two cases with histories of sudden onset of headache, blurring of vision, loss of sight, restlessness, seizure and deaths, features suggestive of acute methanol poisoning [1-8]. However, the traditional institutions and the community members strongly believed that the ailments and deaths were the wrath of a local deity, on those who stole or conspire in the stealing of ancient artefacts at the shrine of the god. Whereas, many on social and traditional news media platforms, have attributed the deaths to a strange illness or Ebola virus disease outbreak, which was rampaging the west African countries of Liberia, Guinea and Sierra Leone at the same period [9,10].

In response to the outbreak, the SMOH through her Epidemic Management Committee and the WHO established an Incident Management Centre (IMC) modelled after the Emmergency Operating Centre (EOC) for the elimination of wild polio virus and control of Ebola virus disease in Nigeria [9,10]. Strategic groups, which included Epidemiology and surveillance, Case management, Infection control and Burial as well as Advocacy and communication subgroups served as the implementation units of the IMC. To verify the diagnosis and identify the risk factors for the outbreak, the Epidemiology and surveillance sub group, made up of representatives from the SMOH, the WHO, the LGA and the Nigeria Field Epidemiology and Laboratory Training Programme (NFELTP) conducted epidemiological and laboratory investigations from the 15-30 April. The report of the investigation is presented in this report.

2. MATERIALS AND METHODS

2.1 Outbreak Setting

Nigeria is the most populous country in Africa, with a population of 148 million in 2007, and a growth rate of 3.8% per annum. Nigeria has six regional zones with varying ecologies, climates and population characteristics [11,12]. Ondo State is one of the 36 states in the Federal Republic of Nigeria in the Southwestern geopolitical zone of the country. The State has 18 LGAs with three senatorial districts; Ondo North, Central and South and a 2015 projected total population of about 4,489,756 based on the 2006 population census [12]. The current outbreak was restricted to two of the five LGAs in the southern district. The vast majority of the population consists of peasant farmers cultivating food and cash crops at a small-scale level.

2.2 Field Work Preparation

The Epidemiology and surveillance subgroup of the IMC developed an operational case definition based on clinical and epidemiological features common to the cases/deaths found. A data-collection tool was also designed to collect data from relation/household members of cases retrospectively and prospectively to identify risk factors associated with the ailment. The data obtained from cases/deaths on the Integrated Disease Surveillance and Response (IDSR) line list used for initial notifications were scanty as almost all the cases were seen dead and the community members were not volunteering to

provide information because of their strong perception that the ailment was as a result of the wrath of the traditional god on persons who either connived or were directly involved in the stealing of the idols at the shrine. The draft of the data tool designed was peer-reviewed, finalized and adopted after sharing with the WHO zonal and the country offices. Surveillance officers from the SMOH and partner agencies were dispatched to the community to commence data collection and active case searches for reported and unreported cases/deaths. This was after they were trained on the use of an excel based data collection platform, where the data-collection tool was uploaded.

2.3 Case Identification

A field survey was conducted with the informed consent and approval of relevant state and public health authorities. It involved active case searches of households and neighbourhoods where cases had been reported, as well as of all health facilities in the LGAs of Irele and Odigbo and neighbouring LGAs to identify additional cases using the operational case definition. Information, Education and Communication materials, including radio and television jingle on case identification, and reporting were also made available to the general public. For case identification, a case was defined as any person who had or died suddenly from complaints of any or combination of the following symptoms: headache, blurring of vision, loss of sight, restlessness, seizure, coma or any related symptoms within Irele and other neighbouring local government areas from four weeks before the primary case on the 11 April 2015. Moreover, disease surveillance focal persons at the health facility levels and community informants in Irele and the other four neighbouring LGAs (Odigbo, Ese Odo, Okitipupa and Ilaje) were trained using the operational case definition to enhance community active case searches for immediate notification of all cases detected. At community level, heads of household were asked if any member of the household had reported sudden onset of headache, blurring of vision, loss of sight, restlessness and coma or death within Irele and other neighbouring LGAs.

2.4 Descriptive Epidemiology

All identified cases were line-listed with an excel based electronic line-list template automatically generated from the data-collection tool. The line-list included data on the LGA, the location of the settlement, the age and sex of the cases, occupation, ingestion of locally brewed alcohol, as well as the date of onset of illness and clinical features. Other data included whether or not a specimen had been taken (a “yes” or “no” response) and the status of the case, i.e. alive or dead. The data were exported from the computer database and analysed using SPSS® software version 16.0. Descriptive epidemiological analyses were generated showing the distribution of cases by person, place and time.

2.5 Analytical Epidemiology

To identified potential risk factors, a case-control study design was conducted among cases that were found alive and stable as well as relatives of fatal cases (data obtained by proxy). For each case/relative of a dead case who consented to participate, three control subjects matched on sex and age group were recruited in the neighbourhood; one to the right, one to the left and one in front on exiting the compound of the case. Where no eligible control subject was found in the immediate household of the case in all directions, the next household was visited until one is found. An adapted, standardized, closed-ended questionnaire was used to collect data on the demographic and potential exposure variables. A participant anonymity was carefully protected. Data were entered using SPSS and comparisons made between the cases and controls demographic and exposure variables. The demographic variables were compared using Chi-square test or Fishers’ exact test as appropriate. The strength of association of risk factors was estimated by the odds’ ratios and their confidence intervals.

2.6 Laboratory Investigation

Blood and urine specimens were collected from the two cases alive at the onset of investigation to rule out infective causes. These specimens were sent to the National Reference Laboratory for Viral Haemorrhagic Fever and the WHO-AFRO Reference Laboratory for Ebola Virus at the College of Medicine/Lagos University Teaching Hospital. Polymerase Chain Reaction (PCR) tests for Ebola, Lassa, Enterovirus, Dengue, Yellow fever, Chikungunya and Rift valley fevers were conducted on the blood and urine specimens. As evidence mounts on the possibility of acute poisoning, urine and blood specimens as well as remnants of locally brewed gin were collected for toxicology analysis at the University College Hospital (UCH), Ibadan and

Nigeria National Agency for Food and Drug Administration and Control (NAFDAC) laboratories. At the UCH, about 7ml of blood (4ml heparinised and 3ml EDTA) and 40ml of urine from 3 cases were received. These were in addition to samples of three alcoholic beverages obtained from the cases. Samples were analysed for lead (Pb), Zinc (Zn), Copper (Cu) and Cadmium (Cd) by Atomic Absoption Spectrophotometry (AAS) and methanol levels using Gas Chromatography (GC) techniques. Fifteen samples of locally brewed alcoholic beverages from drinking joints reported by cases where consumption had taken place in the last 24 to 48 hours before symptoms or deaths as well as remnants from cases were sent to the NAFDAC laboratory.

2.7 Public Health Response

Public enlightenment on the avoidance of home-made alcohol using mass media; radio and television, was instituted within 72 hours of the investigation. In addition, information, education and communication (IEC) materials on case reporting as well as on avoidance of the alcohol beverages were developed and distributed. Apart from daily press briefing by the officials of the SMOH, meetings were also held with the representatives of sellers of the home-made alcohol beverages to halt the sale of their products. Case treatment centers were established at the two communities where cases were stabilised using adapted treatment protocol [2-8], before referrals or discharges were made as required.

3. RESULTS

3.1 Descriptive Epidemiology

A total of 37 cases, including 27 fatalities in Irele and Odigbo LGAs, which produced a case fatality rate of 73%, was found. Most of the cases/deaths were male (97%, *n* = 36) and occurred in Irele LGA (89%, *n* = 33) as shown in Table 1.

Table 1. Sociodemographic characteristics of cases of methanol poisoning, Ondo State, Nigeria, April 2015

Variables	Frequency	%
Age group (yr)		
<30	6	16
30-39	14	38
40-49	8	22
50-59	6	16
>60	3	8
Mean (SD) age:	40.4 (12.5)	
Sex distribution		
Male	36	97
Female	1	3
Occupation		
Farmers	16	43
Artisans	5	14
Okada riders	5	14
Others	11	30
Location (LGA)		
Irele	33	89
Odigbo	4	11
Alcohol consumption 24–48 h before symptom onset	*n* = 33	
Yes	31	94
No	2	6
Local gin (Ogogoro) consumption 24–48 h before symptom onset	*n* = 34	
Yes	32	94
No	2	6
Contact with herbicide/pesticide	*n* = 33	
Yes	1	3
No	32	97

Also, about half of the cases were farmers (43%, *n* = 16). The age distribution showed that 76% of the cases were aged ≤ 49 years (*n* = 28). Furthermore, 32 (94%) of the 34 cases with data collected on history of consumption of locally brewed gin, reported ingestion 24–48 hours prior to the symptom onset, while only one (3%) of the 33 with information collected on history of use of herbicide/pesticide reported its use. Loss of sight (78%, *n* = 29) and blurring of vision (76%, *n* = 28) were the most reported symptoms, while seizure was the least (5%, *n* = 2), (Table 2).

Table 2. Frequency distribution of symptoms of methanol poisoning, Ondo State, Nigeria, April 2015

Symptoms	Frequency	Percent (%)
Loss of sight (Blindness)	29	78
Blurring of vision	28	76
Headache	17	46
Respiratory distress	13	35
Unconsciousness	7	19
Vomiting	6	16
Fever	6	16
Seizures	2	5

3.2 Analytical Epidemiology

A total of 19 cases (four alive and 15 proxies) and 57 controls responded. All were males, with 63% of cases and 79% control respondents being < 50 years (p=0.29). Alcoholic beverage consumption before the onset of symptoms in cases (OR=12.2 95% CI: 2.9–84.5) and most especially consumptions of locally brewed gin (OR=17.2 95% CI: 4.6–84.0) were significantly associated with being a case in the outbreak (Table 3).

3.3 Laboratory

The blood and urine samples sent for PCR tests were negative for all viral antigens. Normal levels of Pb, Cu and Cd were also found in the specimens. Methanol was detected in the urine at a level of 0.018 g/l. The levels of methanol in the three blood samples were 0.28, 0.21 and 0.05 g/l. The methanol levels in the three drinks were 125, 9.6 and 65 g/l. In addition, five of the 15 drink samples sent to NAFDAC had a high concentration of methanol ranging from 4.5 to 16.9%.

3.4 Public Health Response Impact

The peak of incident cases was reached on the 17 April, a case decline was observed on the 18 and by 22 of April, no new cases were found (Fig. 1). A total of 10 cases were successfully managed at the treatment centres out of which 5 were referred.

Table 3. Risk factors for methanol poisoning in Ondo State, Nigeria, April 2015

Potential risk factors	Cases n=19 ( )*	Control n=57 ( )*	Unadjusted odd ratio	95% CI
Marital status				
Currently married	17 (29)	42 (71)	3.0	0.7-21.2
Single/separated	2 (12)	15 (88)		
Educational status				
Low	12 (34)	23 (66)	2.5	0.9-7.7
High	7 (17)	34 (83)		
Alcohol consumption 24-48 hrs before the onset of symptoms				
Yes	17 (43)	23 (58)	**12.2**	**2.9-84.5** +
No	2 (6)	34 (94)		
Recent travel history				
Yes	2 (10.5)	8 (14.0)	0.7	0.1-3.5
No	17 (26)	49 (74)		
Occupation (Farming)				
Farming	10 (32)	21 (68)	1.9	0.7-5.6
Others	9 (20)	36 (80)		
Consumption of local gin (Ogogoro) 24-48 hrs before symptoms onset				
Yes	16 (55)	13 (45)	**17.2**	**4.6-84.0** +
No	3 (6)	44 (94)		

**Percentages calculated across row totals.*
+Statistically significant (p<0.05)

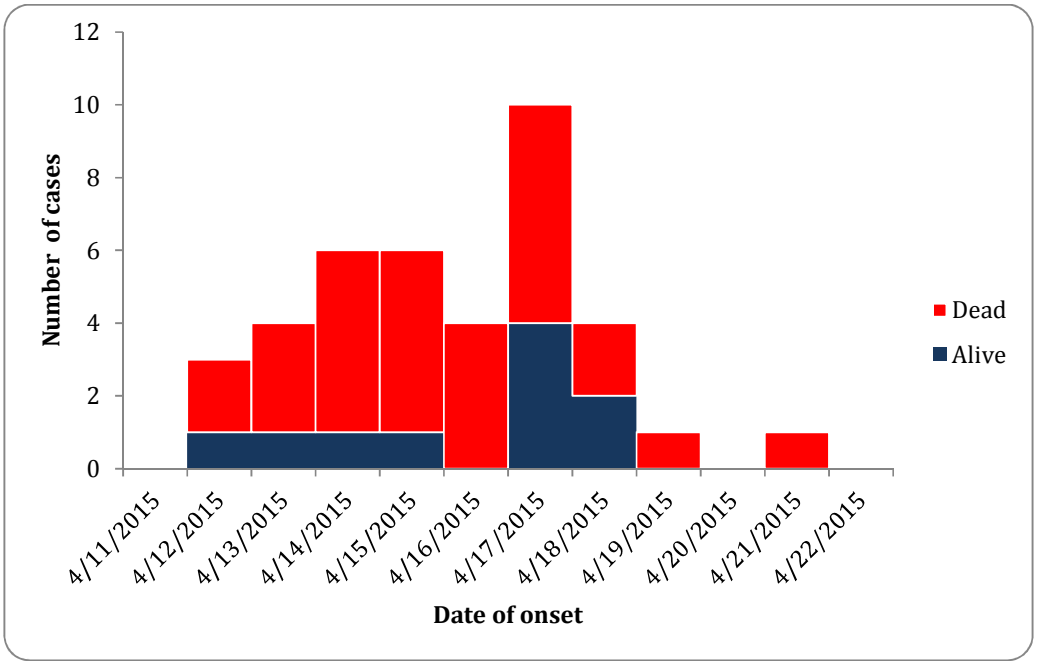

Fig. 1. Epidemic curve of methanol poisoning outbreak in Ondo State, Nigeria April, 2015

4. DISCUSSION

In this outbreak, we verified the diagnosis based on the highly suggestive clinical, epidemiological and laboratory findings. Although many of the patients reported late to the health facilities or died before notification, the reported symptoms of blurring of vision, loss of sight, respiratory distress, and headache were common among cases and were consistent with previous methanol poisoning outbreaks [1-8]. A similar situation was reported in Kenya, where > 60 people were killed, and many more were blinded or ill after drinking homemade alcohol laced with methanol to make it stronger [1]. This report informed the direction of our thought early in the investigation, even when local perception was different and media reports were carrying news about a strange disease or Ebola virus disease outbreak in the affected communities.

The levels of methanol detected in the blood and urine of the victims tested supported methanol toxicity. In many of the previous methanol outbreaks, diagnosis was not verified by methanol determination. However, unlike the outbreak reported in Estonia [5], in which all patients had detectable serum methanol levels, we were only able to determine these in three patients. Four main reasons may have been responsible. First, victims did not report to the health facilities and the few that did, reported late. Second, the laboratory capabilities of the facilities and experiences of attending clinicians for methanol determination were limited. Third, the perception of the community of the cause of illness and a general negative attitude towards autopsy did not allow the team to perform an autopsy, despite having a clinical pathologist among the investigating team. Lastly, toxicological analysis of samples took a long time due to lack of preparedness of the laboratories to handle specimens in an outbreak setting and inadequate infrastructure, such as erratic electricity supply for processing specimens. This may have led to the reduced levels of methanol detected in samples over the period of storage.

The case fatality rate reported in our investigation was higher compared to previous outbreaks [1-8]. Paasma et al. [5] reported a 44% case fatality rate in an outbreak of methanol poisoning in Estonia in 2001; Zakharov et al. [8] reported a case fatality rate of 34% in a similar outbreak in the Czech Republic in 2012; Taleb and Bahelab [7], reported a case fatality rate of 9% in a large methanol poisoning outbreak in Libya in 2013 and Abdolkarim [6], reported a case fatality rate of 15% in an outbreak of methanol poisoning involving 20 persons in Iran in 2013. The high case fatality rate in our series could be attributed to the wrong community

perception of the cause of death, leading to lateness in seeking orthodox medical help. However, the high case fatality found was consistent with a typical outbreak of methanol poisoning as methanol poisoning is an acute medical emergency, which if not recognized in time and treated on a sound pharmacological and toxicological basis, can lead to considerable morbidity as well as mortality [3].

This epidemiological investigation showed that the outbreak affected mainly men, except one woman. This finding is consistent with previous outbreaks of methanol poisoning associated with illegally produced alcoholic beverages reported globally [1-8]. Ravichandran et al. [2] reported that most of the cases (98%) recorded during an outbreak of methanol poisoning in India in 1984 were male. Likewise, Kute et al. [4] in a similar outbreak in 2009, involving 91 patients, reported that all cases were male. This finding was expected as a result of the strong societal and religious norms that discourage women from drinking alcoholic beverages. The finding that the age group ≤ 49 years was mostly affected was comparable to the study of Ravichandran *et al*. [2], who reported that most cases recorded during the outbreak in Chembur and Ghatkopar were aged 30–40 years.

Furthermore, the epidemic curve in this investigation suggests a common source pattern of epidemic, which is consistent with our finding that majority of the cases consumed a locally brewed gin popularly called “ogogoro”. The fact that no health worker or family contacts were affected supported the non-contagious nature of the disease. The outbreak was limited to the contiguous LGAs of Irele and Odigbo in the southern senatorial district of the State. Timely investigation and institution of control measures could have been responsible for the limited spread. The control measures included an aggressive community sensitization on circulation of methanol poisoned local gin and the need to stop further ingestion meanwhile. This was done through; the distribution of information, education and communication materials, radio and television jingle, engagement of the officials of the associations of manufacturers as well as marketers of the locally brewed gin and a broadcast by the executive governor of the State. The disease surveillance and notification officers at the LGAs were trained in addition, to enhance surveillance activities during the outbreak. Consumption of local gin contaminated with methanol 24 to 48 hours before the onset of illness was identified as the major risk factor for the outbreak based on the findings from the case-control study with neighbourhood controls. All the cases and proxies were male with majority being farmers. Consumption of locally brewed gin 24 to 48hours before the onset of illness of the case increased significantly the odds of having the disease similar to findings from other studies [1-8].

5. CONCLUSION

Finally, despite the timely investigation and control of the current outbreaks, we recognised the limitations our methods may have imposed on our findings. Firstly, we did not determine the methanol levels in all individuals; however, the consistency of symptoms in all cases reported and the fact that other causes of metabolic acidosis such as diabetes ketoacidosis, could not have occurred coincidentally as we have in this outbreak lend credence to methanol poisoning. Secondly, exposure information was obtained by proxy in a majority of cases, making misclassification error possible. In the same vein, recall bias may also have occurred from the data collected retrospectively from cases or the relatives of deceased cases. Stratified analysis to determine if effect modification is present in the magnitude of effects for cases that were interviewed directly and those by proxy lacked precision due to small sample size. In addition, social desirability bias is suspected as community perception about the cause of the outbreak might have stigmatized respondents. However, probing questions were asked to ensure correct responses where possible. The precision of the case-control method was improved by selecting three controls for every case. The investigation confirms previous reports that methanol poisoning, especially from the consumption of illicit alcoholic beverages could result in high morbidity and mortality. There is a need for enforcement of regulatory measures to address the consumption of illicitly produced alcoholic beverages to forestall future outbreaks.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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