

Original Research Article**Investigation of an outbreak of acute methanol poisoning in a Southwest state of Nigeria, April 2015****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 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.

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

28 **Keywords:** Disease outbreaks, sudden death, methanol, Nigeria

29

30 1. Introduction

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

45 In response to the outbreak, the SMOH through her Epidemic Management
46 Committee and the WHO established an Incident Management Centre (IMC)
47 modelled after the Emergency Operating Centre (EOC) for the elimination of wild
48 polio virus and control of Ebola virus disease in Nigeria.[9,10] Strategic groups,
49 which included Epidemiology and surveillance, Case management, Infection control

50 and Burial as well as Advocacy and communication subgroups served as the
51 implementation units of the IMC. To verify the diagnosis and identify the risk factors
52 for the outbreak, the Epidemiology and surveillance sub group, made up of
53 representatives from the SMOH, the WHO, the LGA and the Nigeria Field
54 Epidemiology and Laboratory Training Programme (NFELTP) conducted
55 epidemiological and laboratory investigations from the 15-30 April. The report of the
56 investigation is presented in this report.

57 **2. Materials and methods**

58 ***2.1 Outbreak setting:***

59 Nigeria is the most populous country in Africa, with a population of 148 million in
60 2007, and a growth rate of 3.8% per annum. Nigeria has six regional zones with
61 varying ecologies, climates and population characteristics.[11, 12] Ondo State is one
62 of the 36 states in the Federal Republic of Nigeria in the Southwestern geopolitical
63 zone of the country. The State has 18 LGAs with three senatorial districts; Ondo
64 North, Central and South and a 2015 projected total population of about 4,489,756
65 based on the 2006 population census.[12] The current outbreak was restricted to two
66 of the five LGAs in the southern district. The vast majority of the population consists
67 of peasant farmers cultivating food and cash crops at a small-scale level.

68 ***2.2 Field work preparation:***

69 The Epidemiology and surveillance subgroup of the IMC developed an operational
70 case definition based on clinical and epidemiological features common to the
71 cases/deaths found. A data-collection tool was also designed to collect data from
72 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

98 levels and community informants in Irele and the other four neighbouring LGAs
 99 (Odigbo, Ese Odo, Okitipupa and Ilaje) were trained using the operational case
 100 definition to enhance community active case searches for immediate notification of all
 101 cases detected. At community level, heads of household were asked if any member of
 102 the household had reported sudden onset of headache, blurring of vision, loss of sight,
 103 restlessness and coma or death within Irele and other neighbouring LGAs.

104 ***2.4 Descriptive epidemiology:***

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

114 ***2.5 Analytical epidemiology:***

115 To identified potential risk factors, a case-control study design was conducted among
 116 cases that were found alive and stable as well as relatives of fatal cases (data obtained
 117 by proxy). For each case/relative of a dead case who consented to participate, three
 118 control subjects matched on sex and age group were recruited in the neighbourhood;
 119 one to the right, one to the left and one in front on exiting the compound of the case.
 120 Where no eligible control subject was found in the immediate household of the case
 121 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 Absorption 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.

147 **2.7 Public health response:**

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

157 **3. Results**

158 **3.1 Descriptive epidemiology:**

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

162 **Table 1: Sociodemographic characteristics of cases of methanol poisoning, Ondo**
 163 **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	<i>n</i> = 33	
Yes	31	94
No	2	6
Local gin (Ogogoro) consumption 24–48 h before symptom onset	<i>n</i> = 34	
Yes	32	94
No	2	6
Contact with herbicide/pesticide	<i>n</i> = 33	
Yes	1	3

No 32 97

164

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

172 **Table 2: Frequency distribution of symptoms of methanol poisoning, Ondo State,**
 173 **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

174

175

176 **3.2 Analytical epidemiology:**

177 A total of 19 cases (four alive and 15 proxies) and 57 controls responded. All were
 178 males, with 63% of cases and 79% control respondents being < 50 years (p=0.29).
 179 Alcoholic beverage consumption before the onset of symptoms in cases (OR=12.2
 180 95% CI: 2.9–84.5) and most especially consumptions of locally brewed gin (OR=17.2
 181 95% CI: 4.6–84.0) were significantly associated with being a case in the outbreak
 182 (Table 3).

183 **Table 3: Risk factors for methanol poisoning in Ondo State, Nigeria, April 2015**

Potential risk factors	Cases n=19 ()*	Control n=57 ()*	Unadjust ed 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) 24-48hrs before

symptoms onset

Yes	16 (55)	13 (45)	17.2	4.6-84.0 ⁺
No	3 (6)	44 (94)		

184 *Percentages calculated across row totals.

185 ⁺Statistically significant (p<0.05)

186

187 **3.3 Laboratory:**

188 The blood and urine samples sent for PCR tests were negative for all viral antigens.

189 Normal levels of Pb, Cu and Cd were also found in the specimens. Methanol was

190 detected in the urine at a level of 0.018 g/l. The levels of methanol in the three blood

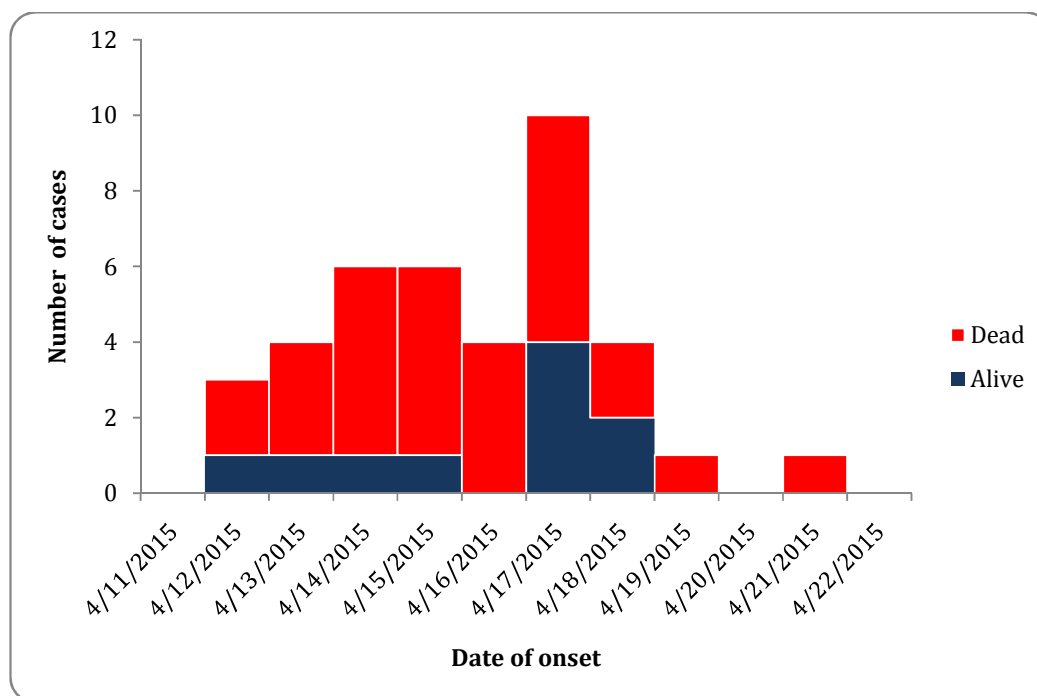
191 samples were 0.28, 0.21 and 0.05 g/l. The methanol levels in the three drinks were

192 125, 9.6 and 65 g/l. In addition, five of the 15 drink samples sent to NAFDAC had a

193 high concentration of methanol ranging from 4.5 to 16.9%.

194 3.4 Public health response impact:

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



198
199 **Figure 1. Epidemic curve of methanol poisoning outbreak in Ondo State, Nigeria**
200 **April, 2015**

201 4. Discussion

202 In this outbreak, we verified the diagnosis based on the highly suggestive clinical,
203 epidemiological and laboratory findings. Although many of the patients reported late
204 to the health facilities or died before notification, the reported symptoms of blurring
205 of vision, loss of sight, respiratory distress, and headache were common among cases
206 and were consistent with previous methanol poisoning outbreaks.[1-8] A similar
207 situation was reported in Kenya, where > 60 people were killed, and many more were
208 blinded or ill after drinking homemade alcohol laced with methanol to make it

209 stronger.[1] This report informed the direction of our thought early in the
210 investigation, even when local perception was different and media reports were
211 carrying news about a strange disease or Ebola virus disease outbreak in the affected
212 communities.

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

228 The case fatality rate reported in our investigation was higher compared to
229 previous outbreaks.[1-8] Paasma *et al.*[5] reported a 44% case fatality rate in an
230 outbreak of methanol poisoning in Estonia in 2001; Zakharov *et al.*[8] reported a case
231 fatality rate of 34% in a similar outbreak in the Czech Republic in 2012; Taleb and
232 Bahelab,[7] reported a case fatality rate of 9% in a large methanol poisoning outbreak
233 in Libya in 2013 and Abdolkarim,[6] reported a case fatality rate of 15% in an

234 outbreak of methanol poisoning involving 20 persons in Iran in 2013. The high case
235 fatality rate in our series could be attributed to the wrong community perception of
236 the cause of death, leading to lateness in seeking orthodox medical help. However, the
237 high case fatality found was consistent with a typical outbreak of methanol poisoning
238 as methanol poisoning is an acute medical emergency, which if not recognized in time
239 and treated on a sound pharmacological and toxicological basis, can lead to
240 considerable morbidity as well as mortality.[3]

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

252 Furthermore, the epidemic curve in this investigation suggests a common
253 source pattern of epidemic, which is consistent with our finding that majority of the
254 cases consumed a locally brewed gin popularly called “ogogoro”. The fact that no
255 health worker or family contacts were affected supported the non-contagious nature of
256 the disease. The outbreak was limited to the contiguous LGAs of Irele and Odigbo in
257 the southern senatorial district of the State. Timely investigation and institution of
258 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 48hours 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.

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