Original Research Article

Sudden unexpected natural deaths of adults in southeastern Nigeria; a 12 years autopsy review.

A**bstract:**

Background: Sudden unexpected natural death (SUNDs) though a global health problem continues to pose serious challenges in our environment. Evaluation of the causes and risk factors will provide baseline data for planning and implementation of desired urgent interventions.

Objectives: To determine the patterns of adult sudden unexpected natural deaths in southeastern Nigeria.

Methods: This is a twelve years retrospective descriptive review of sudden unexpected natural death cases at the Department of Morbid Anatomy, University of Nigeria Teaching Hospital, Ituku-Ozalla Enugu, Nigeria from the year 2007 to 2018. Data from the case notes and autopsy reports of these cases were collected and analyzed.

Results: One hundred and two (102) SUNDs were identified constituting 13.6% of all autopsies done in our hospital during the twelve years period under review. There were 76 (74.5%) males and 26 (25.5%) females giving a ratio of 2.9: 1, and a mean age of 48.2 years ± 16.0 SD. Cardiovascular disease (26.5%) was the commonest cause of SUNDs followed by respiratory (21.6%), central nervous system (16.7%), gastrointestinal system & liver (12.7%), cancer related (8.8%), renal (7.8%), diabetes complications (3.9%) and miscellaneous (2.0%). The major specific causes were Hypertensive heart disease (16.7%), pneumonia (6.9%), subarachnoid hemorrhage (5.9%), and aspiration pneumonitis (5.9%). Most SUNDs (13.7%) peaked bi-modally in the 36-40yrs and 61-65yrs age groups. Hypertension (25.5%), cancer (8.8%), and nonspecific bacterial infections (8.8%) were the most prevalent risk factors identified.

Conclusion: Cardiovascular, respiratory, and central nervous system disorders are the major group causes of adult SUNDs in southeastern Nigeria with hypertensive heart disease being the predominant specific cause occurring mostly in middle aged married men. Identifying high risk patients of hypertension could allow for timely interventions and prevention of sudden death.

Key-words: Autopsy, Adults, Sudden unexpected natural deaths, Southeastern, Nigeria.

Introduction:

Sudden unexpected natural death (SUND) is a global health problem posing serious challenges in developed countries [1-3] as well as in developing countries [4-5] were it is adjudged to be worse due to the near absence of standard emergency medical services. The incidence of sudden natural death continues to rise in developing countries like ours due to evolving lifestyle and population demographics [6, 7] as well as the ongoing epidemiological transition resulting in high burden of both communicable and noncommunicable diseases [8-10]. Sudden unexpected natural death can be defined as death within 24hours of onset of symptoms in a person not known to be suffering from any dangerous disease, injury or poisoning. It is defined by the World Health Organization as "Death within 24 hours from the onset of symptoms" [11]. However, Forensic Medicine for Lawyers by Mason defines it as "Unexpected death following so rapidly from the onset of symptoms that the cause of death could not be certified with confidence by a medical practitioner familiar with the patient" [12]. Thus giving a more inclusive definition since the specific time frame cannot be ascertained in up to 40% of cases, especially when death occurs during sleep [13]. Hence it refers to those deaths which are not preceded by significant symptoms; excluding deaths from violent or traumatic deaths.

While the availability of detailed research data, adequate intervention programs and technological advances have resulted in declining incidence of sudden death in developed countries, the lack of accurate incidence estimates as well as near absence of emergency medical services continue to fuel

the rise in incidence of sudden death in developing countries like ours making it pertinent for urgent interventions. A previous attempt to report on the patterns of medical mortality from our environment have been based on clinical and ancillary investigations by clinicians without autopsy practice [14]. The nature of sudden death means that an accurate diagnosis is difficult to achieve without an autopsy [15-17], hence a limitation in this previous report [14]. Also because sudden unexpected natural deaths are not legally bound for autopsy in Nigeria unlike deaths caused by accidents, homicides, and suicide which are major indications for medico-legal autopsy [18], many SUND cases are not investigated.

It is the purpose of this study therefore to determine the pattern of sudden unexpected deaths in south eastern Nigeria based on accurate determination of causes of death through autopsy practice and also to discuss how these compare with those of other developing and developed countries. This will provide evidence-based insights for improvement of our health policies and health care delivery [19], pertinent in our quest to be better prepared to manage our own share of this global phenomenon.

Methods:

This is a twelve years retrospective study of autopsies done at the Department of Morbid Anatomy, University of Nigeria Teaching Hospital, Ituku-Ozalla Enugu, Nigeria from the year 2007 to 2018. This is the core referral centre, offering autopsy services to all the five states of the south-east region of Nigeria as well as the adjoining states in the north-central and south-south geopolitical regions of Nigeria. The ethical clearance for this study was obtained from the Health Research Ethics Committee of University of Nigeria Teaching Hospital. Relevant clinical data of the deceased patients such as; autopsy number, age, sex and other clinical information were obtained from the duplicate copies of the consent forms and death certificates in the departmental archives as well as from case notes in our hospital medical record archives.

Complete medical autopsies were conducted in all of these cases and relevant tissue sections were processed into tissue blocks using automatic tissue processor (Leica Microsystems - Wetzlar, Germany). These tissue blocks were cut into slide sections and were stained with routine haematoxylin and eosin (H & E) stains. The slides were examined using binocular light microscope (Leica Microsystems - Wetzlar, Germany) and histological diagnoses were made based on morphological grounds. The causes of sudden deaths were classified into; cardiovascular, central nervous, respiratory, gastrointestinal & liver, renal, cancer related, endocrine (diabetic mellitus complications) and miscellaneous.The results obtained were analyzed using Predictive Analytics Software (PASW) Statistics for Windows, Version 18 (Chicago: SPSS Inc.) and tables and figures are used to clearly present findings.

Results:

One hundred and two (102) cases of sudden unexpected natural deaths (SUNDs) were identified in this study constituting 13.6% (102/ 750) of all autopsies done in our hospital's Morbid Anatomy Department during the twelve years period under review. There were 76 (74.5%) males and 26 (25.5%) females giving a ratio of 2.9: 1 [Table 1]. The age range was from 18 years to 80 years, and the mean age was 48.3 years ± 16.0 SD. Seventy-nine (77.5%) of the SUNDs were married while twenty-three (22.5%) were single until their time of death.

Twenty-seven (26.5%) of the SUNDs were from cardiovascular causes while 75 (73.5%) were from non-cardiovascular causes. The commonest cause of SUNDs were from the cardiovascular with 27 (26.5%) cases, followed by; respiratory system 22 (21.6%) and central nervous system (CNS) 17 (16.7%) [Table 2]. These together accounted for more than half (64.8%) of the entire causes of SUNDs. The other causes include; gastrointestinal system & liver 13 (12.7%), cancer related 9 (8.8%), renal 8 (7.8%), diabetes complications 4 (3.9%) and miscellaneous 2 (2.0%) [Table 2].

The commonest specific cause of SUNDs were Hypertensive heart disease 17 (16.7%), followed by pneumonia 7 (6.9%), subarachnoid hemorrhage (5.9%), and aspiration pneumonitis (5.9%). Other important specific causes include; cerebral infarction (3.9%), saddle pulmonary embolism (3.9%), and diabetic ketoacidosis (3.9%) [Table 2].

Within the cardiovascular causes of SUNDs, hypertensive heart disease (63.0%) caused most of the deaths. Other cardiovascular causes were; coronary artery disease (7.4%), dilated cardiomyopathy (7.4%), hypertrophic cardiomyopathy (7.4%), ruptured aortic aneurysm (7.4%), constrictive pericarditis (3.7%), and mitral valve endocarditis (3.7%) [Table 2]. The major causes amongst the respiratory system were pneumonia (31.8%), aspiration pneumonitis (27.3%), and saddle pulmonary embolism (18.2%), while the least were pulmonary tuberculosis (13.6%) and bronchial asthma (9.1%). The central nervous **system** deaths were mainly from subarachnoid hemorrhage (35%) and cerebral infarction (23.5%), followed by intracerebral hemorrhage (17.6%), meningitis (17.6%) and cerebral abscess (5.9%). All the cases of subarachnoid hemorrhage and intracerebral hemorrhage also showed morphological features of hypertensive cardiovascular disease. In the gastrointestinal system & liver, most cases were from perforated typhoid enteritis (23.1%), and bleeding esophageal varices (23.1%) due to liver cirrhosis. Other gastrointestinal causes include; perforated duodenal ulcer (7.7%), bleeding hemorrhoids (7.7%), acute fulminant hepatitis (7.7%) and ruptured amoebic liver abscess (7.7%). Chronic glomerulonephritis (37.5%) and CKD/ CRF (37.5%) accounted for most of renal deaths followed by pyelonephritis (25.0%) [Table 2].

The most commonly seen cancer-related deaths were Hodgkin's lymphoma (22.2%) and pancreatic carcinoma (22.2%). Other cancer-related causes were; melanoma (11.1%), osteosarcoma (11.1%), hepatocellular carcinoma (11.1%), breast carcinoma (11.1%) and renal carcinoma (11.1%) [Table 2]. The cancer related cases were most commonly seen in males with a male to female ratio of 3.5:1 and in the 66-70 yrs age group [Table 3]. Diabetic ketoacidosis was the only cause identified in the

endocrine system, while in the miscellaneous group were one case each of ketamine anaphylaxis (50.0%) and eclampsia (50.0%) [Table 2].

Most SUNDs occurred in the 36-40yrs and 61-65yrs age groups with total of 14 (13.7%) cases each and a male to female ratio of 3: 1 and 3.7:1 respectively, followed by 51-55yrs (10.8%), 41-45yrs (9.8%), and 66-70yrs (8.8%) age groups [Table 3]. The youngest case of SUND was 18 years with dilated cardiomyopathy while the oldest was 80 years with subarachnoid hemorrhage.

Specific risk factors were identified in the course of this study from review of the clinical data in the deceased case notes as well as morphological features identified at autopsy. The non-infective risk factors 79 (77.5%) accounted for most of the identified risk factors compared with infective 23 (22.5%) risk factors. Hypertension 26 (25.5%), cancer 9 (8.8%), and nonspecific bacterial infections 9 (8.8%) were the most prevalent single risk factors identified, followed by Diabetes mellitus 7 (6.9%), and thromboembolism 7 (6.9%) [Table 4]. However, if all the infective risk factors were considered together, infection 23 (22.5%) would become the second prevalent risk factor behind hypertension 26 (25.5%), and followed by cancer 9 (8.8%). Within the infective category, nonspecific bacterial infections 9 (8.9%) and HIV/ AIDS 5 (4.9%) were the predominant identified risk factors. Other infective risk factors identified were tuberculosis 4 (3.9%), typhoid enteritis 3 (2.9%) and amoebiasis 1 (1.0%) [Table 4].

Tables:

Table 1

Table 1: Age and Sex Distribution of Adult Sudden Unexpected Natural Deaths

Age	Gender		Total (%)
	Female	Male	
18-20yrs	0	5	5 (4.9%)
21-25yrs	0	5	5 (4.9%)
26-30yrs	2	5	7 (6.9%)
31-35yrs	3	3	6 (5.9%)
36-40yrs	5	9	**14 (13.7%)**
41-45yrs	3	7	10 (9.8%)
46-50yrs	3	5	8 (7.8%)
51-55yrs	1	10	11 (10.8%)
56-60yrs	0	7	7 (6.9%)
61-65yrs	3	11	**14 (13.7%)**
66-70yrs	3	6	9 (8.8%)
71-75yrs	1	3	4 (3.9%)
76-80yrs	2	0	2 (2.0%)

Total (%)	**26 (25.5%)**	**76 (74.5%)**	102 (100.0%)

Table 2: System, Cause and Sex Distribution of Adult Sudden Unexpected Natural Deaths

Systems [N (%)]	Causes of death (% per system)	Gender		(% of Total) N=102
		Male (76)	Female (26)	
Cardiovascular N = 27 (26.5)	**Hypertensive heart disease (63.0)**	**12**	**5**	**17 (16.7)**
	Coronary artery disease (7.4)	2	0	2 (2.0)
	Dilated cardiomyopathy (7.4)	1	1	2 (2.0)
	Hypertrophic cardiomyopathy (7.4)	2	0	2 (2.0)
	Constrictive pericarditis (3.7)	1	0	1 (1.0)
	Mitral valve endocarditis (3.7)	0	1	1 (1.0)
	Ruptured aortic aneurysm (7.4)	2	0	2 (2.0)
Central nervous (CNS) N = 17 (16.7)	**Subarachnoid hemorrhage (35.3)**	**4**	**2**	**6 (5.9)**
	Intracerebral hemorrhage)17.6)	2	1	3 (2.9)
	Cerebral infarction (23.5)	3	1	4 (3.9)
	Cerebral abscess (5.9)	1	0	1 (1.0)
	Meningitis (17.6)	2	1	3 (2.9)
Respiratory N = 22 (21.6)	Saddle pulmonary embolism (18.2)	1	3	4 (3.9)
	Pulmonary tuberculosis (13.6)	3	0	3 (2.9)
	Pneumonia (31.8)	**5**	**2**	**7 (6.9)**
	Bronchial asthma (9.1)	2	0	2 (2.0)
	Aspiration pneumonitis (27.3)	**5**	**1**	**6 (5.9)**
Gastrointestinal & liver N = 13 (12.7)	Perforated typhoid enteritis (23.1)	3	0	3 (2.9)
	Perforated duodenal ulcer (7.7)	1	0	1 (1.0)
	Bleeding peptic ulcer (23.1)	2	1	3 (2.9)
	Bleeding esophageal varices (23.1)	3	0	3 (2.9)
	Bleeding hemorrhoids (7.7)	0	1	1 (1.0)
	Acute fulminant hepatitis (7.7)	0	1	1 (1.0)
	Ruptured amoebic liver abscess (7.7)	1	0	1 (1.0)
Renal N = 8 (7.8)	Chronic glomerulonephritis (37.5)	3	0	3 (2.9)
	Pyelonephritis (25.0)	2	0	2 (2.0)
	CKD/ CRF (37.5)	2	1	3 (2.9)
Cancer related N = 9 (8.8)	Melanoma (11.1)	1	0	1 (1.0)
	Osteosarcoma (11.1)	1	0	1 (1.0)
	Hepatocellular carcinoma (11.1)	1	0	1 (1.0)
	Hodgkin's lymphoma (22.2)	2	0	2 (2.0)
	Breast carcinoma (11.1)	0	1	1 (1.0)
	Renal carcinoma (11.1)	1	0	1 (1.0)
	Pancreatic cancer (22.2)	1	1	2 (2.0)
Endocrine / Diabetic complications N = 4 (3.9)	Diabetic ketoacidosis (100)	3	1	4 (3.9)
Miscellaneous N = 2 (2.0)	Ketamine anaphylaxis (50.0)	0	1	1 (1.0)
	Eclampsia (50.0)	1	0	1 (1.0)

Age (years)	CVS	CNS	Resp.	GIT & liver	Renal	Cancer related	Endocrine/ Diabetic	Miscellaneous	Total (%)

18-20yrs	1	0	1	1	1	1	0	0	**5 (**4.9)
21-25yrs	2	0	2	0	0	1	0	0	**5 (**4.9)
26-30yrs	2	0	0	1	2	1	0	1	**7 (**6.9)
31-35yrs	1	1	1	1	0	1	0	1	**6 (**5.9)
36-40yrs	1	5	4	2	2	0	0	0	**14 (13.7)**
41-45yrs	6	0	1	1	0	0	2	0	**10 (**9.8)
46-50yrs	3	1	2	1	0	0	1	0	**8 (**7.8)
51-55yrs	2	3	2	1	1	1	1	0	**11 (**0.8)
56-60yrs	3	0	1	1	1	1	0	0	**7 (**6.9)
61-65yrs	3	4	3	3	1	0	0	0	**14 (13.7)**
66-70yrs	3	0	4	0	0	2	0	0	**9 (**8.8)
71-75yrs	0	2	1	1	0	0	0	0	**4 (**3.9)
76-80yrs	0	1	0	0	0	1	0	0	**2 (**2.0)
Total	27	17	22	13	8	9	4	2	**102 (**100.0)

Table 3: Age Distribution of Causes of Adult Sudden Unexpected Natural Deaths by Systems

Table 4: Sex Distribution of Major Risk Factors of Adult Sudden Unexpected Natural Deaths

Risk factors	Gender		Total	Percent (%)
	Male	Female		

Non-infective N = 79 (77.5%)	**Hypertension**	**18**	**8**	**26**	**25.5**
	Diabetes mellitus	**6**	**1**	**7**	**6.9**
	Cardiomyopathy	3	1	4	3.9
	Atherosclerosis	3	0	3	2.9
	Peptic ulcer disease	3	1	4	3.9
	Chronic glomerulonephritis	4	0	4	3.9
	Thromboembolism	**3**	**4**	**7**	**6.9**
	Bronchial asthma	2	0	2	2.0
	Liver cirrhosis	2	0	2	2.0
	Cancer	**7**	**2**	**9**	**8.8**
	Obstructive uropathy	1	1	2	2.0
	Hemorrhoidectomy	0	1	1	1.0
	Unconsciousness	4	1	5	4.9
	Pregnancy	0	1	1	1.0
	Alcoholism	1	0	1	1.0
	Ketamine anaesthesia	1	0	1	1.0
Infective N = 23 (22.5%)	HIV/ AIDS	3	2	5	4.9
	Hepatitis b virus infection	0	1	1	1.0
	Typhoid enteritis	3	0	3	2.9
	Tuberculosis	4	0	4	3.9
	Nonspecific bacterial infections	**7**	**2**	**9**	**8.8**
	Amoebiasis	1	0	1	1.0
Total		**76**	**26**	**102**	**100.0**

Discussion:

Sudden unexpected natural deaths in adults remain an important form of presentation and indication for autopsy at our hospital, constituting 13.6% of all autopsies done in our hospital's Morbid Anatomy Department during the twelve years period under review. The causes of SUNDs mirror major causes of mortality in our environment [14] with cardiovascular (26.5%), respiratory (21.6%) system and central nervous systems (16.7%) diseases constituting the major causes of SUNDs in our study which altogether account for more than half (64.8%) of all our SUND cases. This finding

is in agreement with reports from other regions in Nigeria [19-21] as well global indices [16, 22-24]. Though most cardiovascular deaths in the western world were associated with coronary heart disease [1-3], we found that hypertensive cardiovascular heart disease was the most prevalent cause of SUNDs in adults in our region constituting 16.7% and 63% of all cases and cardiovascular cases respectively. This was followed by pneumonia 6.9%, subarachnoid hemorrhage 5.9%, and aspiration pneumonitis 5.9%. The finding of higher hypertensive cardiovascular deaths is not unexpected bearing in mind that hypertension and its complications are the most common noncommunicable diseases in Nigeria and amongst Africans [25], causing significant noncommunicable disease mortality [14, 26]. The importance of hypertension as a cause of SUND further extends into the central nervous system since all cases of subarachnoid hemorrhage (5.9%) and intracerebral hemorrhage (2.9%) in our study also showed morphological features of hypertensive cardiovascular disease. Nevertheless the low level of awareness, treatment and control of hypertension amongst Nigerians [7, 27] with the attendant high burden of its related complications entails that hypertension is a silent killer whose insidious features come to light only with its complications or sudden death [28]. Although coronary artery disease is still relatively uncommon among Nigerians [19], the finding of 2 (2.0%) cases of coronary artery disease in our study may suggest that its incidence may be increasing within the Nigerian population, contrary to previously held views [7, 29, and 30].

The respiratory system accounted for 21.6% of SUND cases in our study with the major causes being; pneumonia (31.8%), aspiration pneumonitis (27.3%), and saddle pulmonary embolism (18.2%). While this is in agreement with reports from most developing countries [5, 16, 19], it is however at variance with studies conducted in the north central Nigeria [6] and South West Nigeria [20] that reported pulmonary thromboembolism as the commonest cause in the respiratory system.

Disorders of the gastrointestinal system & liver accounted for 12.7% of SUND cases in our study, most of which were from perforated typhoid enteritis (23.1%), and bleeding esophageal varices

(23.1%) due to liver cirrhosis. These are conditions that can either be treated or prevented thus underlying the importance of appropriate healthcare interventions in preventing SUNDs.

Though cancer and renal deaths accounted for 8.8% and 7.8% cases of SUNDs in our study, while most cancer related deaths were from Hodgkin's lymphoma (22.2%) and pancreatic carcinoma (22.2%), most renal deaths were from chronic glomerulonephritis (37.5%) and chronic renal failure (37.5%) respectively. The inclusion of these conditions which are largely non acute conditions as causes of SUNDs could be due to the modes of death. [19].

Most cases of sudden unexpected death in adults were largely males (74.5%) compared to females (25.5%), giving a male to female ratio of 2.9: 1. This is in agreement with studies from other Nigerian regions [6, 19, 20] as well as those from other developing countries [31] as well as developed countries [32]. This gender disparity could be due to cardioprotective effects of oestrogen on the cardiovascular system [32].

The age range of this study was from 18 years to 80 years, and the mean age was 48.2 years ± 16.0 SD. This mean age incidence is about a decade younger than what was observed in similar previous studies done many years earlier in other Nigerian regions [7, 20, 33] as well as other developing countries [31], but is in agreement with recent study in south west Nigeria [19]. This has led some authors to suggest an earlier affectation of environmental impacts of urbanization and shift toward Western lifestyle [19].

Most of the SUNDs in our study occurred within the middle age group with a bimodal peak distribution of 13.7% in the 36-40yrs and 61-65yrs age groups and a male to female ratio of 3: 1 and 3.7:1 respectively. The middle age is the period of life when most subjects in our environment are married and hence the added social responsibilities that come with it. The role of these social and environmental factors in SUND need to be further evaluated. The youngest case of SUND in our

study was 18 years with dilated cardiomyopathy while the oldest was 80 years with subarachnoid hemorrhage.

The finding of more married (77.5%) cases in our study is at variance with reports from developed countries that report a better health for married [34] and a higher incidence of SUND amongst unmarried [35]. Thus further research is also required to determine if social factors such as sexual intercourse contributed adversely in our cases of sudden deaths as have been reported both locally [36] and internationally [37-40]. Sex-related deaths in men have been reported to be commoner with men in extra-marital relationships and occur often in locations outside the matrimonial homes [36]. This is because of the interplay of known trigger factors and modifiable lifestyle behaviours in susceptible people [36]. Early identification of susceptible subjects and counselling could help in reducing the incidence of SUNDs.

Specific risk factors were identified in the course of this study from review of the clinical data and record of morphological features identified at autopsy. Non-infective (77.5%) risk factors accounted for most of the identified factors compared with infective (22.5%) risk factors. Hypertension (25.5%) was also the most prevalent single risk factor identified in our study which is in agreement with previous studies [35, 41]. Thus reducing the incidence of hypertension and other identified major risk factors such as cancer (8.8%), nonspecific bacterial infections (8.8%), Diabetes mellitus (6.9%), and thromboembolism (6.9%) will go a long way in reducing the overall incidence of SUNDs in our environment. Also if all the infective risk factors were to be considered together as infection (22.5%), it would become the second major risk factor behind hypertension 26 (25.5%), and followed by cancer 9 (8.8%). Since most of the infective agents involve in SUNDs can be treated or controlled by antimicrobial agents, effective medical intervention could as such prevent these cases of SUNDs.

Study limitations:

The authors hereby acknowledge that the conclusions drawn from this study may not be representative of the general population because the study was based on cases on which autopsies were performed to the exclusion of those for which autopsy was not performed. Also the absence of toxicological evaluation in these cases, would mean that the possible effect of drugs and poisons in the death processes were not assessed.

Conclusion:

Cardiovascular, respiratory, and central nervous system disorders are the major group causes of adult SUNDs in southeastern Nigeria with hypertensive heart disease, pneumonia, subarachnoid hemorrhage and aspiration pneumonitis being the predominant specific causes occurring mostly in middle aged married men. Identifying those with high risk factors especially hypertension could allow for timely interventions and prevention of sudden death.

Consent:

The authors declare that written informed consents were obtained from the next of kin of dead before autopsies were carried out on them.

Ethical Approval:

Approval for the study was obtained from the Institutional Review Board, Nigerian Institute of Medical Research, Lagos, Nigeria.

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