Sudden unexpected non-violent death between 1 and 19 years in north Spain

Benito Morentin, Beatriz Aguilera, Pedro Manuel Garamendi, M Paz Suarez-Mier

Abstract

Aims—To study the epidemiological, clinical, and pathological characteristics of sudden unexpected non-violent deaths between 1 and 19 years.

Methods—Population based observational study of all sudden unexpected non-violent deaths between 1 and 19 years, from 1990 to 1997, in a north Spain county (Bizkaia). In each case, clinical information and circumstances of death were obtained and a complete forensic autopsy was performed.

Results—There were 34 sudden unexpected non-violent deaths. The mortality rate was 1.7 per 100 000 persons per year (representing 9% of the mortality rate of all non-violent deaths). In 10 cases the cause of death was cardiac, in 13 cases extracardiac, and 11 cases were unexplained. In 17 cases there were no pathological antecedents and in nine cases death occurred in patients with known disease processes. Syncopes prior to death were present in five cases. Exercise related deaths occurred in seven cases (mainly associated with cardiac causes). Eight cases were “death in bed”.

Material and methods

Sudden death is defined as an unexpected non-violent (natural) phenomenon in which death occurs instantaneously or within six hours of the onset of symptoms or collapse; in non-hospitalised individuals participating in their regular activities until the final event. Those cases surviving more than six hours with the help of life support systems and those with a non-serious known illness who died suddenly and unexpectedly were also included.

Bizkaia is an industrial county in the Basque Country (North Spain). Legislation requires a forensic autopsy to be performed (by the Forensic Anatomic Institute of Bilbao) in all violent deaths and in sudden unexpected non-violent deaths in non-hospitalised persons. All death certificates and all medicolegal autopsy reports are coded for principal cause of death, according to the rules of the International Classification of Diseases (ICD-9), by trained physicians of the Mortality Register of the Basque Country.

Postmortem records of the Forensic Anatomic Institute of Bilbao from 1990 to 1997 inclusive were examined. All sudden unexpected non-violent deaths occurring between 1 and 19 years of age (inclusive) were included. In all of them a complete gross and histological study (including cardiac conduction system), and toxicological and, occasionally, microbiological analysis were performed. Clinical information and circumstances of death were also reviewed.

Mortality rate was estimated overall as well as by gender and quinquennial age groups, on the basis of population data compiled by EUSTAT. From 1990 to 1997 the average population of Bizkaia between 1 to 19 years old was 245 109. Mortality rate for all non-violent deaths in those aged 1–19 years in the 1990–95 period (mortality register for 1996–97 period was not available) were obtained from computerised death certificate data compiled by the Mortality Register of the Basque Country. Violent deaths (external causes (E-code categories) of death of ICD-9) were excluded.

Keywords: sudden death; adolescence
Sudden unexpected non-violent death

EPIDEMIOLOGICAL AND DEMOGRAPHIC DATA

During the eight years studied, 299 cases of death in children and adolescents between 1 and 19 years old were investigated at the Forensic Anatomic Institute of Bilbao. A total of 253 (85%) were a result of violent causes and 46 (15%), non-violent (natural) causes. Twelve cases of non-violent deaths were excluded because of previous severe disease.

According to the selection criteria described above, there were 34 cases of sudden unexpected non-violent death in children and adolescents: 25 boys and nine girls. The median age was 16 years (25th centile 7.7 years; 75th centile 18 years). The quinquennial distribution showed that 19 were aged 10–14 year old groups, five between 10 and 14 years, and only two between 5 and 9 years. The mortality rate for sudden unexpected non-violent death in the 1–4 years old population was 1.7 per 100 000 persons per year (95% confidence interval (CI) 0.8 to 2.7). Mortality rate was higher for men (2.5 per 100 000 persons per year) than for women (0.9 per 100 000 persons per year). For quinquennial age groups, mortality rate was higher in the 1–4 and 15–19 year old groups (2.7 per 100 000 persons per year in both groups; fig 1).

The mortality rate for all non-violent deaths (according to the the Mortality Register data of the Basque Country) between 1 and 19 years old in the 1990–95 period was 18.7 per 100 000 persons per year. Nine per cent of all non-violent deaths were therefore sudden and unexpected. The percentage was highest in the group aged 15–19 years (14%) and lowest in the group aged 5–9 years (4%) (fig 1).

PATHOLOGICAL ANTECEDENTS, PRODROMES

In nine sudden death cases—three of cardiac origin (hypertrophic cardiomyopathy, tetralogy of Fallot, Wol–Parkinson–White syndrome) and in six of extracardiac origin (three asthmatic patients, one with epilepsy, one with neurofibromatosis, and one with mielomeningocoele Arnold–Chiari), the disease that caused their death had been diagnosed previously (table 2): tetralogy of Fallot (case 7), anomalous coronary origin (case 8), brain hemorrhage secondary to arteriovenous malformation (case 19), and Arnold–Chiari malformation (case 20). In four other cases the cause of death was infectious disease. Three were in patients younger than 9 years: laryngitis (case 14), bronchopneumonia (case 15), and fulminant meningococcaemia (case 23); in a 19 year old male the cause of death was myocarditis (case 9).

Table 1 summarises the main clinical and pathological findings of explained and unexplained deaths. In sudden cardiac deaths (10 cases), nine were males and eight were in the 15–19 years old group (table 2, fig 2). In six cases the cause of death was cardiomyopathy (three arrhythmogenic, two hypertrophic, and one dilated); all were in adolescents. Of deaths of extracardiac origin, the most frequent were those related to asthma and intracranial hemorrhage (three cases of each). The three cases of asthma were adolescent males (cases 11–13) and the three of intracranial hemorrhage were children aged 12–14 years (cases 17–19) (table 2).

In five cases there were antecedents of syncope prior to death, that appeared in
Figure 2  Distribution of the numbers of cases of sudden unexpected non-violent death classified by gender and quinquennial age groups, according to the cause of death (sudden cardiac death in black, sudden death of extracardiac origin in white, and sudden death of unexplained origin in grey portions).

Table 2  Sudden death: main clinical and pathological findings

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Gender</th>
<th>Location of death</th>
<th>Activity at death</th>
<th>Time*</th>
<th>Previous symptoms or clinical diagnosis</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19/M</td>
<td>DOA</td>
<td>Exercise</td>
<td>&lt;15 min</td>
<td>Asymptomatic</td>
<td>Arrhythmogenic cardiomyopathy</td>
</tr>
<tr>
<td>2</td>
<td>18/M</td>
<td>DOA</td>
<td>Exercise</td>
<td>&lt;15 min</td>
<td>Ventricular tachycardia. Syncope during exercise</td>
<td>Arhythmogenic cardiomyopathy</td>
</tr>
<tr>
<td>3</td>
<td>18/M</td>
<td>OH</td>
<td>Exercise</td>
<td>&lt;15 min</td>
<td>Syncope during exercise</td>
<td>Arhythmogenic cardiomyopathy</td>
</tr>
<tr>
<td>4</td>
<td>19/F</td>
<td>DOA</td>
<td>Sedentary</td>
<td>&lt;15 min</td>
<td>Frequent headache</td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>5</td>
<td>18/M</td>
<td>OH</td>
<td>Sedentary</td>
<td>&lt;15 min</td>
<td>Hypertrophic cardiomyopathy. Mild mitral insufficiency. Family history of SD</td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>6</td>
<td>19/M</td>
<td>OH</td>
<td>Death in bed</td>
<td>&lt;15 min</td>
<td>Morbid obesity. Psychiatric antecedents</td>
<td>Dilated cardiomyopathy</td>
</tr>
<tr>
<td>7</td>
<td>1/M</td>
<td>DOA</td>
<td>Sedentary</td>
<td>&lt;15 min</td>
<td>Tetralogy of Fallot. Palliative operation months earlier</td>
<td>Tetralogy of Fallot</td>
</tr>
<tr>
<td>8</td>
<td>9/M</td>
<td>DOA</td>
<td>Exercise</td>
<td>&lt;15 min</td>
<td>Physiological heart murmurs 5 years before death</td>
<td>Anomalous origin of LAD coronary</td>
</tr>
<tr>
<td>9</td>
<td>19/M</td>
<td>DOA</td>
<td>Sedentary</td>
<td>&lt;15 min</td>
<td>Asymptomatic</td>
<td>Wolf-Parkinson-White syndrome</td>
</tr>
<tr>
<td>10</td>
<td>15/M</td>
<td>DOA</td>
<td>Exercise</td>
<td>&lt;15 min</td>
<td>WPW during first year of life, later asymptomatic</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>16/M</td>
<td>OH</td>
<td>Sedentary</td>
<td>&lt;15 min</td>
<td>Asthma. Cardiac arhythmias with normal ECG</td>
<td>Unexpected SD in asomatic</td>
</tr>
<tr>
<td>12</td>
<td>18/M</td>
<td>OH</td>
<td>Exercise</td>
<td>&lt;15 min</td>
<td>Asthma. Physiological heart murmurs</td>
<td>Unexpected SD in asomatic</td>
</tr>
<tr>
<td>13</td>
<td>18/M</td>
<td>ER</td>
<td>Sedentary</td>
<td>15–60 min</td>
<td>Asthma. Upper airway infection prior to death</td>
<td>Unexpected SD in asomatic</td>
</tr>
<tr>
<td>14</td>
<td>1/F</td>
<td>DOA</td>
<td>Death in bed</td>
<td>&lt;15 min</td>
<td>Fever. Treated with antipyretics and antibiotics</td>
<td>Acute viral laryngitis</td>
</tr>
<tr>
<td>15</td>
<td>9/M</td>
<td>ER</td>
<td>Sedentary</td>
<td>15–60 min</td>
<td>Asymptomatic</td>
<td>Bronchopneumonia</td>
</tr>
<tr>
<td>16</td>
<td>18/M</td>
<td>ER</td>
<td>Sedentary</td>
<td>1–6 h</td>
<td>Neurofibrinosis in lungs. Arterial hypertension due to bilateral renal artery stenosis surgically corrected at 12 years</td>
<td>Lung haemorrhage secondary to neurofibrinosis</td>
</tr>
<tr>
<td>17</td>
<td>14/M</td>
<td>ER</td>
<td>Sedentary</td>
<td>&lt;15 min</td>
<td>Asymptomatic. Headache 24 hours before death</td>
<td>Subarachnoid haemorrhage</td>
</tr>
<tr>
<td>18</td>
<td>12/M</td>
<td>DOA</td>
<td>Sedentary</td>
<td>&lt;15 min</td>
<td>Urinary infection a month before</td>
<td>Subarachnoid haemorrhage</td>
</tr>
<tr>
<td>19</td>
<td>12/F</td>
<td>DOA</td>
<td>Sedentary</td>
<td>&lt;15 min</td>
<td>Migraine with an aura</td>
<td>Brain haemorrhage secondary to AVM</td>
</tr>
<tr>
<td>20</td>
<td>2/M</td>
<td>DOA</td>
<td>Sedentary</td>
<td>1–6 h</td>
<td>Myoelmenincoocele lumbar with derivative valve</td>
<td>Arnold-Chiari malformation</td>
</tr>
<tr>
<td>21</td>
<td>19/F</td>
<td>OH</td>
<td>Death in bed</td>
<td>1–6 h</td>
<td>Epilepsy</td>
<td>Unexplained SD in epileptic</td>
</tr>
<tr>
<td>22</td>
<td>4/M</td>
<td>ER</td>
<td>Sedentary</td>
<td>1–6 h</td>
<td>Asymptomatic</td>
<td>Diabetic coma</td>
</tr>
<tr>
<td>23</td>
<td>2/M</td>
<td>ER</td>
<td>Sedentary</td>
<td>1–6 h</td>
<td>Asymptomatic</td>
<td>Fulminant meningococcaemia</td>
</tr>
<tr>
<td>24</td>
<td>4/M</td>
<td>OH</td>
<td>Death in bed</td>
<td></td>
<td>Diarrhoea 2 days before death</td>
<td>SD of unexplained origin</td>
</tr>
<tr>
<td>25</td>
<td>13/F</td>
<td>DOA</td>
<td>Unknown</td>
<td>&lt;15 min</td>
<td>Three episodes of vagal syncope and bradycardia</td>
<td>SD of unexplained origin</td>
</tr>
<tr>
<td>26</td>
<td>14/M</td>
<td>DOA</td>
<td>Sedentary</td>
<td>&lt;15 min</td>
<td>Asymptomatic</td>
<td>SD of unexplained origin</td>
</tr>
<tr>
<td>27</td>
<td>1/F</td>
<td>DOA</td>
<td>Death in bed</td>
<td></td>
<td>Asymptomatic</td>
<td>SD of unexplained origin</td>
</tr>
<tr>
<td>28</td>
<td>2/M</td>
<td>DOA</td>
<td>Death in bed</td>
<td></td>
<td>Asymptomatic</td>
<td>SD of unexplained origin</td>
</tr>
<tr>
<td>29</td>
<td>18/F</td>
<td>DOA</td>
<td>Death in bed</td>
<td></td>
<td>Asymptomatic</td>
<td>SD of unexplained origin</td>
</tr>
<tr>
<td>30</td>
<td>16/M</td>
<td>DOA</td>
<td>Sedentary</td>
<td>&lt;15 min</td>
<td>Asymptomatic</td>
<td>SD of unexplained origin</td>
</tr>
<tr>
<td>31</td>
<td>16/F</td>
<td>OH</td>
<td>Sedentary</td>
<td>Unknown</td>
<td>Recent trip. Antimalarial treatment</td>
<td>SD of unexplained origin</td>
</tr>
<tr>
<td>32</td>
<td>19/M</td>
<td>DOA</td>
<td>Exercise</td>
<td>&lt;15 min</td>
<td>Growth retardation treated with growth hormone. Salbutamol on requirement. Syncope during exercise and near syncope</td>
<td>SD of unexplained origin</td>
</tr>
<tr>
<td>33</td>
<td>17/M</td>
<td>DOA</td>
<td>Sedentary</td>
<td>&lt;15 min</td>
<td>Acne on retinoic acid treatment. Surgery of ureter stenosis when 1 year old</td>
<td>SD of unexplained origin</td>
</tr>
<tr>
<td>34</td>
<td>17/F</td>
<td>DOA</td>
<td>Death in bed</td>
<td></td>
<td>Probable syncope considered as seizures with normal neurological examination</td>
<td>SD of unexplained origin</td>
</tr>
</tbody>
</table>

*Interval between onset of symptoms to death.

AVM, arteriovenous malformation; DOA, death on arrival to emergency room; ER, death in emergency room; LAD, left anterior descending; OH, outside hospital death; SD, sudden death.
festation of illness. This percentage was higher in sudden deaths of unexplained origin (64%).

CIRCUMSTANCES OF DEATH
 Concerning the activities carried out at the moment of death, in 18 cases sudden death took place at rest or performing routine activities; in eight cases sudden death occurred in bed; and in seven during or immediately after physical exercise. In one case the circumstances of death were unknown. Of those dying in relation to physical exercise, six were adolescent males, and in five a cardiac cause was shown (cases 1, 2, 3, 8, and 10; table 2). Of the eight deaths in bed, five were women; four were in the 1–4 years old group (representing in this group 50% of total deaths); five were of unexplained origin, and one other was an unexplained sudden death in an epileptic.

Of those with a known period of time since the onset of symptoms to death (excluded death in bed), in 19 cases death occurred within 15 minutes of the onset of symptoms (virtually instantaneous). All cardiac and unexplained deaths presented within 15 minutes or were dead in bed. Most cases (62%) were dead on arrival at the hospital, 21% deaths occurred outside hospital, and 17% died in the emergency room.

Discussion
SUDDEN DEATH OF UNEXPLAINED ORIGIN
 One of our main findings is the high percentage (32%) of unexplained sudden deaths, higher than the 5–20% reported in other series of sudden death in the young.3–17 This discrepancy might be a result of the diagnostic criteria used in our series: mild or moderate heart hypertrophy (probably related to sport activity), mild coronary stenosis, or focal lymphocytic infiltration of the myocardium were not considered sufficient cause of death. Furthermore, according to our and other authors’ experiences,24–26 most of the lesions reported in the cardiac conduction system in unexplained sudden deaths, are so frequent in the normal population (controls) that they cannot be considered the cause of death without electrocardiogram abnormalities.

Another factor behind the many unexplained deaths in our series is the interval of time between symptoms and death. Most deaths in our series occurred in a few minutes or the patient was found dead in bed, whereas in other series the interval considered is 24 hours.3–7–15–17 Studies with young survivors of sudden cardiac arrest support the idea that unexplained sudden death is not exceptional.25–29

Sudden unexplained deaths are found in all age groups but are a major component of mortality both in infancy (sudden infant death syndrome) and early childhood,30–33 and in a smaller proportion of older children and adolescents. In three of the group aged 1–4 years in our series, the cause of death was unknown. Moreover, two of them (cases 27 and 28) were 1 year old (22 months) and 2 years old (24 months) respectively. The upper limit of age for sudden infant death syndrome definition is arbitrary37 and it is possible that these two cases fit with sudden infant death syndrome, as they were found dead in bed and no cause of death was found after a complete autopsy and examination of the medical reports.

In our series five of eight “sudden death in bed” cases were unexplained, a circumstance very similar to sudden infant death syndrome and sudden death of southeast Asian young men.35–39 This similarity may mean that the three entities share a common aetiopathogenic mechanism. Whereas in sudden infant death syndrome and sudden death in southeast Asian young refugees, males are more often affected,41–45 in our series unexplained deaths were more frequent in females (56% versus 24%); however the low number of cases of this series do not permit definite conclusions concerning gender.

It is well known that some unexplained deaths can be related to arrhythmias which can produce sudden death in patients with hearts without structural abnormalities, and usually in patients who have had no previous electrocardiogram investigations.46 Scientific researchers have focused mainly on QT long syndrome, Wolff–Parkinson–White syndrome, Brugada syndrome, and idiopathic ventricular fibrillation.47

Scientific research on epidemiology, aetiology, pathogenesis, or circumstances surrounding unexplained deaths in the young, as has been performed in sudden infant death syndrome, is necessary; it may be possible to define a category of sudden unexplained death syndrome in the young as has been proposed.37

OTHER CAUSES OF SUDDEN DEATH
 In contrast to sudden death in adults where atherosclerotic coronary disease is clearly predominant, sudden death in children and adolescents is the result of many causes.48–52 Our series showed a similar diversity. Among the 23 sudden explained deaths, we found 17 different diseases (table 1) and no one was observed in more than 10% of the cases. Because of this diversity the prevention of sudden death in the young is very difficult.

In our series, sudden cardiac death constituted the most frequent group (29% of the total), especially in males and adolescents. In childhood (1–14 years old) extracardiac sudden deaths were more frequent.

According to other reports in adolescents and young adults,12–14 38–40 cardiomyopathies are the most frequent causes of sudden cardiac death. We observed cardiomyopathy in six of 10 cardiac causes of death (tables 1 and 2), arrhythmogenic cardiomyopathy being the most frequent, similar to a series studied in northern Italy.15–19

Intracranial haemorrhages and those associated with asthma were the most frequent extracardiac causes of death (table 1). Intracranial haemorrhages were observed in 9% of the cases, a value similar to those reported elsewhere.3–7–9–15 Two of the patients had suffered headache before death, which is especially common.3–9
Unexplained deaths in asthmatics occur mainly in adolescents and young adults, and can be associated with severe or moderate disease. In our series we observed this in three adolescents, two of which were treated with salbutamol and inhaled corticosteroids (one had been hospitalised previously because of severe attacks). The third was treated with salbutamol only during bronchospasm episodes.

The other causes of sudden death in our series, both cardiac and extracardiac, are well known causes of sudden death in children and adolescents. In contrast to cardiac deaths, infectious diseases causing sudden death are rarely instantaneous and occur mainly in younger children. As previously reported by Molander, it is striking that an infection that lead to death had such a discrete manifestation in life. In the group of sudden death of non-cardiac origin there were three patients with diseases that only exceptionally are associated with sudden death: Arnold–Chiari malformation, diabetes mellitus, and intrathoracic haemorrhage by neurofibromatosis.

Epidemiological and demographic factors

The present observational study analysed sudden unexpected non-violent death in childhood and adolescence during an eight year period in a well defined geographical area. The series of a non-selected, non-referred general population was based on forensic autopsies. This type of sample avoids the inconvenience of reference and selection biases characteristic of other studies regarding sudden death in the paediatric population. The epidemiological data on sudden death in children and adolescents obtained in our series are difficult to compare with the small number of other published studies because selection criteria are different.

Sudden death is an uncommon event outside the infant period. Mortality rate in this series was 1.7 per 100 000 persons per year (fig 1), similar to that in previous reports on sudden death in children and adolescents based on the general population. Mortality rate in the Driscoll and Edwards series was 1.3 per 100 000 persons per year, and in the Molander series was 1.1. Neuspiel and Kuller reported an incidence of 4.6, and Kennedy and Whitlock a 2.4–8.5 incidence, but the time interval from onset of symptoms to death in both studies was 24 hours, whereas in our series it was six hours.

In this study sudden unexpected non-violent death represented 9% of all non-violent deaths. In other series, sudden death in the young population represented 2.3%, 8.2%, and 21.8% of all natural deaths. According to Spanish legislation, sudden deaths in children and adolescents—non-violent (natural) or violent—must be investigated through a forensic autopsy. These figures are therefore an accurate representation of the true incidence of sudden death in the population studied.

In our series mortality rate in males was 2.5 times higher than in women, a figure similar to that pointed out in previous studies. In agreement with other reports, males are at increased risk for sudden unexpected non-violent death.

Sudden death is much more frequent during the first years of childhood (1–4 years old group) and during adolescence (15–19 years old group) than from 5–14 years of age (fig 1). This result is similar to that reported in the Neuspiel and Kuller series where mortality rate was 9.3 per 100 000 persons per year for children (1–4 years old) and 5.7 per 100 000 persons per year for adolescents (14–21 year olds), whereas mortality rate was 2.0 per 100 000 persons per year for children aged 5–13 years. Mortality rate of sudden unexpected non-violent death in relation to all non-violent deaths varied according to age group (fig 1), being more frequent in adolescents than in children.

Pathological antecedents

One of the main findings of the present study, according with other series, is that sudden death is frequently the first manifestation of the disease. In sudden cardiac death it is known that underlying disease is usually a clinically silent cardiovascular disorder that may not have been diagnosed or even suspected during life. In contrast to cardiac deaths, most non-violent deaths occurred in five of 21 who died as a result of cardiac disease or unexplained sudden death, and was more frequent during exercise. It has been recommended that patients with exercise related syncope and recurrent unexplained syncope should be submitted to early and detailed cardiovascular evaluation in order to identify persons with a potentially lethal pathology.

In 21% (7/33) of our series sudden death were exercise related. In other series the percentage was similar, from 15% to 30%. Most exercise related sudden deaths are cardiac deaths, mainly cardiomyopathies.

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Sudden unexpected non-violent death


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