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Perspective and Debates

Sudden and fulminant deaths of healthy children in Italy during the 2010-11 and 2011-12 seasons: results of an online study

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Significance for public health

Influenza is not only a disease that crowds the offices of general practitioners or a threat merely for the elderly and for those who belong to categories at risk. It can also cause severe illness and even death in young and perfectly healthy subjects. This was one of the lessons of the recent pandemic, as shown in the cases of sudden and fulminant death of otherwise healthy children reported in some countries, which would require more in-depth examination than is usually done in order to explain them. This study does not claim to prove the existence of this phenomenon, even in Italy, but rather proposes to reopen debate on this and other aspects that are now being considered outdated.

Abstract

The 2009 pandemic in Italy has been viewed as a false alarm, and it has not been properly understood based on historical precedents and more in-depth studies that have been conducted in other countries. Some of these studies have pointed to a phenomenon of sudden and fulminant death among healthy children, which is not the sole prerogative of pandemic influenza, but was, in 2009, a more frequent occurrence than in previous years. The purpose of this study is to gather such cases occurring during the 2010-11 and 2011-12 seasons. Google Search was used in order to find cases of children and teens with no reported preexisting conditions of relevance and who died suddenly and unexpectedly after exhibiting flu-like symptoms during the two seasons. During the 2010-11 season, 29 deaths were found to meet the above conditions, 18 of which were fulminant and 11 sudden. For the 2011-12 season, there were ten such cases: five fulminant and five sudden. Most of these cases occurred during the period of maximum circulation of the flu virus. Fulminant deaths were three times more frequent during 2010-11 season and involved children of a higher average age than the more recent season. It is not possible to come to any definite conclusions, but there is reason to suspect that the driver of this significant increase may be the A(H1N1)pdm09 virus. Regardless of how reading these results, it is advisable that the surveillance systems be strengthened and more recent study techniques be adopted in order to determine the causes of similar deaths in the future.

Introduction

The announcement, in June 2009, of the first pandemic of the 21st century raised a great deal of concern around the world due to the rapid worldwide diffusion of a novel reassortant strain of influenza A(H1N1)pdm09 containing swine, avian, and human elements. By season end, the official count was 17,700 victims.[1] This figure may seem insignificant when compared with pandemics of the past and even with normal seasonal flu epidemics and would appear to explain the great level of debate that has accompanied the interpretation of this pandemic.

In actual fact, many of the fatalities are overlooked in the official reports because the death certificates specify other causes, such as pulmonary and cardiovascular disease, which arise as a result of the infection.[2] In order to find out the true count for the season, it is necessary to await the publication of the mortality tables, which are then used for statistical calculations based on excess fatalities.[3] In many countries, such calculations may be done very quickly with the use of rapid indicators.[4]

During the 1957 pandemic, which resulted in two million to four million deaths, many of the fatalities were due to cardiovascular pathologies.[5] One phenomenon which came to light for the first time was that of fulminant deaths directly associated with the A(H2N2) virus or with bacterial superinfection, a number of cases of which were then studied.[6] Oseasohn describes 33 such cases, a portion of which died suddenly and unexpectedly, and documents the frequent myocardial involvement.[7]

In European countries, the 1968 pandemic was characterized by a more severe wave the following year. A similar phenomenon was also seen in a number of European countries in the 2010-11 season.[8,9] During the 1969-70 season in Italy, there was an excess of 20,000 deaths due to respiratory disease and of 57,000 deaths for all causes.[10]

In the US, where there is a rapid mortality surveillance system for all causes and for pneumonia and influenza covering 122 metropolitan areas, it has been determined that the actual number of victims in 2009 was at least six times greater than the official numbers indicate.[11] In Mexico, the ratio of confirmed deaths to calculated deaths is 1 to 7.[12] In the US, the risk of hospitalization and death for the pandemic virus was 5 to 12 times greater than for the seasonal virus in people younger than 65.[13] Having spared the elderly, who normally make a significant contribution to the overall mortality rate, the general mortality curves appeared to be in line with those of previous years, thereby masking the true impact of the 2009 pandemic.[14] In Italy, there is unfortunately no such surveillance system, so the only data currently available refers to cases in which there has been official confirmation of infection.

Deaths that slip through traditional surveillance systems could include sudden (asymptomatic) and fulminant (within 72 hours of onset or preceded by minor symptoms) deaths of previously healthy children and young adults. The 1957 pandemic has already been mentioned, but sporadic reports can also be found in subsequent years,[15,16] which are at times associated with myocarditis.[17]

During the 2003-04 season, antigenically drifted variants of the A(H3N2) virus emerged, and in the US and UK a number of pediatric fatalities were recorded. A significant percentage (one-third in the US and fully half in the UK) were described as unexpected or fulminant and occurred within 48-72 hours of the onset of symptoms. Four children in the UK died without symptoms or within six hours of the onset of symptoms.[18,19] During the 2009 pandemic, 67 out of 270 children in the US dead after being infected with the H1N1 virus, died due to cardiac arrest prior to being admitted to the hospital.[20] In the UK, 16 out of 70 children were in cardiorespiratory arrest upon arrival to the emergency room. Within the subset of patients who died before reaching the hospital, there was a greater, statistically significant lack of risk factors or presence of only mild pre-existing disorders.[21]

The fact that fulminant death often involves otherwise healthy children is confirmed by a study of pediatric deaths in Japan. Of these deaths, 15 out of 47 were from unexpected cardiorespiratory arrest (13 before reaching the hospital) without presenting any risk factors. In addition, two reported deaths were from myocarditis, two for sepsis, and ten for encephalitis. For 34 children, death came within 48 h of the onset of symptoms.[22]

During the 2010-11 season in Italy, only the briefest of news reports in local newspapers made note of the severe illnesses and deaths recorded during that period, and this because of a general tendency to underestimate the threat presented by the pandemic virus. The markedly lower attention to the issue compared to 2009 may have had a negative impact on acknowledgement of the role played by the virus in cases such as those considered in this study. As such, an unconventional research method has been adopted, one based on an examination of news found online using Google Search. The Internet can be an innovative tool of great potential used along side, if not replacing, traditional monitoring systems in order to increase detection capabilities, particularly in countries where the monitoring tools have proven inadequate in documenting the true impact of epidemics related to traditional or emerging viruses.

The goal of this study is to use the Internet to gather news related to cases of unexplained sudden and fulminant deaths among otherwise healthy children and teens during the 2010-11 and 2011-12 seasons, while taking account of the different epidemiological development, with the first season being characterized by the A(H1N1)pdm09 virus and the second by the A(H3N2) virus.

Design and Methods

Study subject

Sudden unexpected or fulminant deaths among pediatric-aged (under 18) children with no reports of relevant pathologies and/or past predisposition and for whom it was not possible to reach a diagnosis. The study timeframe was from December 1st 2010 to March 31st 2011, and from December 1st 2011 to March 31st 2012.

Definitions

Sudden death shall be used to refer to rapid, natural, non-violent and unexpected death preceded by a loss of consciousness and which occurs within 1-6 h of the onset of symptoms. *Fulminant death* shall be used to refer to death occurring within 72 h of the onset of acute *flu-like* symptoms or which occurs later than 72 h after onset with a rapid and unexpected worsening of a preexistent, non-serious condition.

Exclusions

Not included in the study were children of less than one year of age who died without any signs of infection (SIDS), children younger than three months who suffered a fulminant death, and cases arising during or immediately after participation in a sporting activity.

Research tools

Figures regarding the epidemiological trends for the two flu seasons have been obtained from the web site of the Istituto Superiore di Sanità (ISS), including total influenza-like illness (ILI) rates and ILI rates by age group, percentages of positive tests for influenza and percentages of the virus types.

A systematic analysis of news reports was conducted using Google Search. The following are the search terms used: *morte autopsia* (death autopsy); *morte malore* (death illness); *morte febbre* (death fever); *morte improvvisa* (death sudden). These searches were run on a daily basis using the options *past 24 hours* and *sorted by relevance* and checked again at the end of each month using the options *past month* and *sorted by date*. Case-related information is limited to what was reported in the press, and no further research has been conducted. Over the ensuing weeks and months, news reports have been reviewed to find the outcome of any autopsies that may have been conducted.

Results

The ILI curve for the 2010-11 season began to rise rapidly by week 48 (Figure 1). The peak was reached during week 4 with 29.1 cases per thousand in the 0-4 age range and during week 5 with 30.4 cases per thousand in the 5-14 age range.[23] The highest percentage of positive tests for influenza was 43% during week 5. 72% of the isolated viruses were type A and 28% type B. Of the former, 86% were H1N1; 3%, H3N2, and 11% were not typed.[24]

For the 2011-12 season, the curve began rising during week 50, and the peak was reached during week 4 with 30.72 cases in the 0-4 age group and 17.90 cases in the 5-14 age group.[25] We do not yet have conclusive virological data, but the maximum level of isolation of the flu virus was reached during week 4 at 48.8%. The H3N2 virus accounted for nearly all of the viruses identified, along with rare cases of H1N1 and few type B viruses at the end of the season.[26]

There was a difference of one million cases, or roughly 20%, between the two seasons, with the greater number of cases in the first season: an estimated 5,913,000 cases occurred during the 2010-11 season, compared to 4,929,000 the following season. Among the pediatric-aged population, the 0-4 age group recorded 711,500 and 620,400 cases, respectively, for the two seasons, while the 5-14 age group recorded 1,110,000 and 708,250 cases. The total difference for these two groups was 470,000 cases with the first season exceeding the second by 35%.

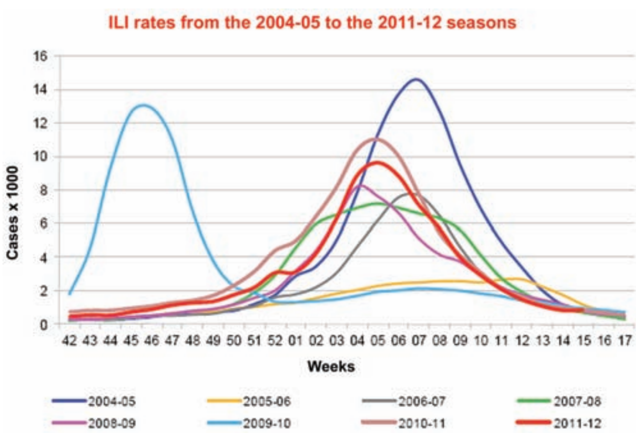

Figure 1. Influenza-like illness chart for most recent seasons in Italy. From the Influnet epidemiological report, week 15-2012.

Unfortunately, no data is available regarding the 15-18 age group as this is included in the 15-65 age group, although it can be assumed, lacking the actual numbers, that the difference in percentage terms was similar to that of the 5-14 age group.

During the 2010-11 season, of the 52 cases initially identified, 35 were found to meet the criteria described above (Figure 2). Of these, six were then eliminated when, weeks or months later, a diagnosis was reached that at least partially excluded any role played by influenza, and specifically: two for previous heart disease; two for cerebral hemorrhage; one case of pneumonia from streptococcus A; and one perforated ulcer.

Of the 29 remaining cases, 17 were among males and 12 among females, and the average age was 6.96 years (from 5 months to 18 years). Of the total, 18 were fulminant deaths and 11 were sudden (Table 1).

The average age for the fulminant deaths was 4.11 years (from 5 months to 11 years), with 11 in the 0-4 and seven in the 5-18 age group. Six of the deaths occurred during hospital care, four en route to the

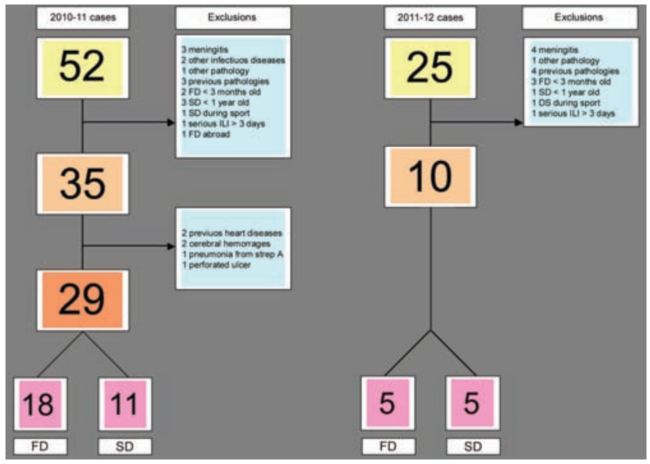

Figure 2. Research algorithm.

Table 1. Deaths during the 2010-11 season.

Case	Gender	Age (years, months)	Date	Type of death	Prior symptoms	Additional information
1	F	3 y	December 13	FD	Fever convulsions vomiting	Sepsis of unknown cause
2	M	16 y	December 19	SD	No	No
3	M	17 y	December 23	SD	No	No
4	F	2 y	December 28	FD	Ill for 2 days	No
5	F	9 y	December 28	FD	Fever respiratory symptoms for 2 days	No
6	M	11 m	December 30	FD	Fever respiratory symptoms for 2 days	Died in sleep pneumonia
7	M	17 y	December 31	SD	No	No
8	F	8 y	January 4	FD	Fever tonsillitis	Respiratory complications
9	F	7 y	January 6	FD	Fever abdominal pain for 1 day	Myocarditis
10	M	13 y	January 7	SD	No	No
11	M	11 y	January 11	FD	High fever	No
12	F	11 y	January 15	SD	No	No
13	M	8 y	January 15	SD	No	No
14	M	3 y	January 15	SD	No	Indeterminate heart pathology
15	M	1 y	January 16	FD	General malaise vomiting	No
16	F	3 y	January 17	FD	Fever for 2 days	No
17	M	3 y	January 18	SD	No	No
18	M	9 y	January 23	SD	No	No
19	M	14 y	January 24	SD	No	Died in sleep
20	F	7 y	January 27	FD	Vomiting abdominal pain	Pneumonia organ failure
21	F	10 m	January 28	FD	Three episodes of vomiting	No
22	M	7 y	February 8	FD	Rhinitis	No
23	M	11 m	February 11	FD	Minor intestinal symptoms	Excess blood salts ?
24	M	5 m	February 12	FD	Fever for 2 days	Premature
25	F	2 y	February 18	FD	Fever for 2 days	No
26	M	6 m	February 20	FD	No	Released from hospital the day before
27	F	9 y	February 27	FD	Fever for a few hours	Tonsils removed 5 days before
28	F	18 y	March 11	SD	No	No
29	M	13 m	March 22	FD	Vomiting abdominal pain for 3 days	No

FD, fulminant death; SD, sudden death.

hospital and eight not involving hospital care. Fever was the most frequent symptom (10 out of 17), followed by vomiting with or without diarrhea (6 out of 17). In two cases, death was preceded by a simple cold or other general malaise. In 12 cases, the symptoms had arisen within the previous 72 h. For five cases, there was no information given about the start of the illness. Of these, three entered the hospital with fairly minor symptoms, and then their condition precipitated within 24 h, while two died en route to the hospital. A six-month-old child died at home during the night after being released from the hospital after a five-day stay for bronchiolitis. The average age of the sudden deaths was 11.72 years (from 3 to 18 years), with two in the 0-4 and nine in the 5-14 age group.

During the 2011-12 season, of the 25 cases initially identified, 10 were found to meet the criteria described above (Figure 2), eight male and two female. The average age was 4.7 years (from 10 months to 17 years). Of the total, five were fulminant deaths and five were sudden (Table 2).

The average age for the fulminant deaths was 1.5 years (from 10 months to 2.5 years), all within the 0-4 age group and with a clear majority of children under two years of age. No deaths were reported among children older than four years of age. Four of the deaths occurred shortly after hospital admission, and one died at home. The most frequent symptoms were vomiting with or without diarrhea (4) and fever (3). Four of the deaths occurred within 48 hours of the onset of symptoms, and one had minor intestinal symptoms for a few days before a sudden worsening. The average age of the sudden deaths was eight years (from 10 months to 17 years), with one in the 0-4 and four in the 5-18 age group.

Discussion

The initial alarmist reaction in 2009 to the mere mention of the word *pandemic*, which is typically associated, in the public's mind, with catastrophe and terror, changed to accusations of conspiracy and false alarms when such a catastrophe failed to materialize. In Italy, the topic was written off as yet another misstep of the international surveillance system, coming in the wake of other *false* alarms, such as mad cow disease, SARS and the avian flu.

The final count for the 2009-10 season, with 260 deaths, 80% below the age of 65 and 5% children below the age of 14,[27] would seem to justify the critical behavior both among the general public and the medical community, as well. However, the rapid mortality indicators that made it possible for other countries to calculate a true mortality of up to seven times greater than the official cases, with a majority involvement (>80%) of individuals below the age of 65,[11,12] were not adopted in Italy.

This is a handicap that causes Italy to lag behind many other countries in the western hemisphere, including those, such as Portugal, that are certainly not more advanced that Italy in terms of health care and social services. The 1968 pandemic had a highly significant impact on mortality rates in all age groups in Italy, and on pediatric-aged children in particular, but this is something that has only been realized in recent years.[10] In the 40 years that have passed since then, we still have not developed the monitoring tools that would enable us to document the true impact of events such as the latest pandemic, so we are forced to await the delayed publication of statistical studies.

In countries where there is an active infant-death monitoring system, such as in the United States or Great Britain,[20,21] as well as in other countries such as Argentina,[28] the impact on the pediatric-aged population was significant. A retrospective Dutch study has pointed to higher mortality rates among small children compared to previous flu seasons, with an excess of 77 (from 61 to 93) deaths in the 0-4 age group, as opposed to an average of 16 in prior seasons (from 1999 on). A portion of these deaths has been attributed to myocardiopathy. In proportion to the population of Italy, that would correspond to an excess of 236 (from 194 to 285).[29]

For the 2009-10 season, a significant percentage of pediatric deaths reported in countries such as the US, England and Japan[20-22] concerned otherwise healthy children who died following the rapid onset of ultimately fatal conditions. Such deaths often occur prior to reaching a hospital or after being admitted to the hospital in cardiorespiratory arrest; therefore, the diagnoses require more in-depth examination using molecular techniques, not only routine postmortem testing.

In 2009, Italian news reports included the fulminant deaths of two otherwise healthy children, one 15-month-old from Catanzaro and one 11-year-old from Pompei, both of whom tested positive for the H1N1 virus. The cause of death of the older child was myocarditis.[30] There were no such reports for the 2010-11 season, which was also dominated by the A(H1N1)pdm09 virus, but which was not seen as being a particularly newsworthy season based on statements at the beginning of the season which called for a return to *normalcy*. The ILI index was quite high,[23] likely exacerbated by the very low level of vaccine coverage in 2009 in Italy, particularly among children, of just 0.3%, which placed Italy at the lowest levels among all western nations.[31] There were many cases of death or patients in intensive care that were only reported in the press because, unlike in other countries, no official bulletins were published. A significant presence of the B virus was also reported and accounted for more than one-fourth of all positive tests for

Table 2. Deaths during the 2011-12 season.

Case	Gender	Age (years, months)	Date	Type of death	Prior symptoms	Additional information
1	M	10 y	December 5	SD	No	No
2	M	5 y	January 15	SD	No	A brother died of congenital cardiopathy
3	M	17 y	January 29	SD	No	No
4	M	2.5 y	February 4	FD	High fever, gastroenteritis	No
5	M	16 m	February 5	SD	No	Fulminant pneumonia
6	M	10 m	February 11	FD	Vomiting for 1 day	Prior hospital stay for asthma pneumonia
7	F	10 m	February 12	FD	Vomiting diarrhea for 1 day	Prior hospital stay for influenza
8	F	7 y	February 14	SD	No	No
9	M	13 m	February 15	FD	Fever vomiting for 2 days	No
10	M	20 m	February 16	FD	Fever for 1 day	No

FD, fulminant death; SD, sudden death.

influenza.[24]

In an attempt to document the impact on mortality rates despite the lack of tools for real-time, epidemiological research in Italy, an unconventional tool, Google Search, has been used that certainly leaves room for criticism, but which also has a great deal of potential. Online, what has been deemed to be a significant number of children and teens who died unexpectedly and unexplainably during the 2010-11 season have been found, and these have been compared with similar cases reported during the 2011-12 season, which was dominated by the seasonal A(H3N2) virus. It is interesting to note that, in both seasons, the greatest number of fatalities coincides with the prevailing period of circulation of the flu virus (Figure 1).

The 2010-11 season began about two weeks earlier than that of the previous year, and this is also reflected in the number of recorded cases, which began to rise during the last weeks of 2010. Whereas for the 2011-12 season nearly all of the cases occurred from the end of January to mid-February, *i.e.* the period from the 5th to the 7th week of the year and immediately following the peak in ILIs during week 4, for the 2010-11 season most of the cases (17 out of 29) occurred between week 2 and week 7, the period in which the ILI index was highest.

Lacking any *post-mortem* diagnoses, it is not possible to be certain of the causes of these fatalities, but the simultaneous events might suggest an involvement of the flu virus. Indeed, most of the deaths are concentrated in the weeks in which there were the greatest number of positive tests for the flu virus, which reached peaks of 43% in 2010-11 and of 49% in 2011-12 during weeks 4 and 5. Worth noting is also the frequency of gastrointestinal symptoms, which are often a distinctive characteristic of influenza, among the children who suffered fulminant death. Three children (two 10-month-old infants and one 9-year-old girl) died just a few days after being released from the hospital, and one six-month-old infant died just a few hours after leaving the hospital. Three of these were in the hospital for minor pathologies, and one (the 9-year-old girl) was in the hospital to have her tonsils removed. Such cases raise the issue of infections contracted in the hospital and, in the case of flu infections, of vaccinations for hospital staff, who need to be made more aware of the importance of such vaccinations. However, of particular note is the substantial difference in the number of cases between the two seasons, which was nearly three times greater in the 2010-11 season (29 *vs* 10), a difference which lessens only slightly when seen in relation to the ILI index, given that the first of the two seasons posted one million (20%) more cases.

The number of fulminant deaths was more than three times greater during the 2010-11 season (18 *vs* 5) and involved children with a higher average age. In the 0-4 age range, for which the ILI indexes were the same, in 2010-11 there were 11 fatalities as compared to 5 in 2011-12, while in the 5-18 age range, for which there was a difference of about 10 points per thousand in the ILI index (during its peak) in favor of the 2010-11 season, the fatalities numbered 7 and 0, respectively. Younger children, and particularly children under 24 months of age, are generally at greater risk than older ones, and the fact that it was the older children who were affected to a significantly greater extent in 2010-11 would appear to point to one or more pathogens that were more aggressive during the season.

Sudden unexpected deaths were two times greater (11 *vs* 5), but it should be noted that four sudden deaths during the 2010-11 season were eliminated because they were subsequently attributed to previous cardiac or cerebral defects. In addition, two deaths during the 2011-12 season are of doubtful relevance, one of which occurred in early December, *i.e.* before the ILI curve began to rise, and the other of which had another sudden death in the family (a brother) due to congenital heart disease. Unlike for the fulminant deaths, it is more difficult in these cases to point the finger at infective causes, although there is good reason to suspect that infections are at least a contributing factor, given the high rate of such deaths during this period. In other periods of the year, an average of one death per month among children under 18 (*unpublished figures*) has been found.

Although the study findings clearly suggest a greater severity of the pandemic virus in comparison to the seasonal virus, they should be interpreted cautiously owing to the use of an unconventional tool of investigation, not validated by scientific literature and limited to just two years. Accordingly, they require further confirmation from methodologically sound investigations. We should also not underestimate the impact of the B virus, which was documented in 28% of the positive tests for influenza, given that a recent study has pointed to the significant role of this virus in pediatric deaths in the last ten years in the US.[32] In several experimental and clinical trials, the A(H1N1)pdm09 virus has been shown to be more dangerous than the seasonal virus.[33] This would explain its greater impact on the mortality rates among young people, with death occurring mainly as a consequence of major respiratory distress, but possibly also of rapidly occurring fatal events that are not usually attributed to the presence of the virus. Among the elderly, the seasonal flu virus is known to play a role in triggering cardiovascular conditions,[34] but one could also speculate that the new virus's direct (*e.g.* myocarditis and heart attack) or indirect (fatal arrhythmia) cardiac involvement could be the cause of sudden and fulminant death among young people. Myocarditis is a known cause of both sudden unexpected death (in 10% of cases involving non-athletes under the age of 35)[35] and fulminant death. Several studies published in the last three years have associated the pandemic virus with fulminant myocarditis,[36] which is something that cannot be explained by an increase in interest alone. Three broad pediatric case studies have documented the presence of myocarditis in severely ill children and/or child fatalities due to the A(H1N1)pdm09 influenza virus and have pointed to a variable incidence, depending on the study, ranging from 1.3% to 5%.[37-39] One case has been described involving a young person infected with the H1N1 flu virus who died of myocardial infarction without any coronary artery disease.[40] For type B viruses as well, a recently published study has shown frequent myocardial involvement in child fatalities.[32] However, sepsis and fulminant pneumonia directly associated with the virus[22] or secondary to coinfection with bacteria such as multi-resistant staphylococcus, pneumococcus or others, which the influenza virus often helps to penetrate the lower airways,[39] may also be the cause of sudden and unexpected fatalities.

The results of this study are not to be seen as incontrovertible proof that the A(H1N1)pdm09 virus is responsible for the greater number of deaths recorded during the 2010-11 season, as other interpretations of the results are possible, but this does appear to be one plausible interpretation. In any event, the study may provide points for further, reasoned consideration of the meaning and impact of the latest pandemic, which has been too quickly written off as a misstep by the global surveillance system.

It is true that its evolution fell below expectations, but the frequent use of extreme intensive care techniques (*e.g.* ECMO) and the deaths resulting from severe multi-organ failure, which have involved young people in particular, testify to how dangerous the virus is. It is not just a question of rehashing an event that is now only a part of the past, because the H1N1 virus will be faced in the years to come, as well. It may take as many as four or five years for a recently emerging virus to assume the characteristics typical of a seasonal virus.[41] Last season, there was a recurring wave in Mexico, after a year of respite, resulting in an unofficial count of 229 victims.[42]

It is hoped that this study can also shed light on little-known aspects of influenza in all its forms. Influenza is typically seen as more of an illness that crowds the offices of general practitioners than as a problem that puts patients' lives at risk, except when the patient has other preexisting pathologies. In other countries, such as the US and the UK, where there have been systems for monitoring unexplained child fatalities for years and where more advanced molecular analysis techniques are used systematically, it has been possible to find answers for a portion of these tragic deaths. In Italy, there is a lack of awareness that such dramatic events can also happen to perfectly healthy people, which means that cases such as those described above are not adequately studied, and the victims' families are denied a diagnosis that could, if not ease their pain, at least promote an acceptance of the loss without feeling a need to place blame where often there is none.

Study limitations

This study has many weaknesses. There may be doubts regarding the use of Google Search in conducting the research. There are examples in the literature of using the Internet for monitoring purposes. One is HealthMap, developed by Harvard Medical School pediatricians and epidemiologists and led by John Brownstein, a site bonding online gathered data (*e.g.* news, forums and the contributions of individual users) with data from official sources in order to create a health map that users can access online at HealthMap.org.[43] The use of special algorithms with the Google search engine makes it possible to monitor flu epidemics more quickly and so correlates well with traditional surveillance systems based on sentinel physician networks.[44] The *Istituto Superiore di Sanità* (Superior Health Institute), also ISS, has recently conducted a survey of cases of drowning in Italy based on news reports found in the press.[45] For both seasons, the same research methods have been used; however, there may be a difference in the level of *sensitivity* of the search engine from one year to the next or in the media's attention on the events studied. Nonetheless, this is believed to be unlikely given that the cases studied are of great emotional impact in that they involve the unexpected deaths of young people under highly noteworthy conditions and are often followed by legal action, meaning that they typically attract the attention of multiple local and national news sources. It should also be noted that, during the 2010-11 season, the attention paid to the pandemic virus declined significantly compared to the previous season, since it was no longer being seen as a threat. Objections could also be made about the study being based on the work of a single person, but all of the cases described are documented and verifiable (by way of links to the news reports, which can be provided), and the field of study is freely accessible to anyone wishing to take up the research. Most of the cases may be found on the international forum FluTrackers, of which the author is an active member and which has proved to be an invaluable support platform.

The evidence regarding the various cases has been taken solely from the news reports, so it is possible that information regarding the patients' symptoms and history and development of the illness is not entirely accurate. However, in most cases there were multiple sources of information from various time periods, both immediately after the event and over time, so it has been possible to compare the information provided. It is also possible that a significant number of cases have escaped detection both due to the intrinsic limitations of the research method and because not all of the cases of this nature end up in the news, particularly online. Nonetheless, it is important to note that the primary purpose of this study is not to determine the frequency of such events, but to make a comparison between the two seasons using the same detection system. However, it is more likely that a number of cases slipped through during the first season, given that only retrospective study was conducted for the first few weeks. Daily monitoring did not begin until mid-January.

The deaths could be attributable to multiple causes, such as fulminant leukemia, other tumors, sepsis, congenital defects, malformations, thromboembolism, and so on, but significant differences in the frequency of such events from one season to the next are unlikely. There may have been other pathogens that circulated more during the first season than in the second, such as parainfluenza viruses, the respiratory syncytial virus, adenoviruses, or others, but there have been no reports of anomalous circulations of these germs. In any event, any differences would be unlikely to explain such a marked increase, particularly during the period in which the influenza virus is dominant, reaching peaks of nearly 50% of all virus tests. This study is limited to just two seasons, so it is possible that the results are a mere fluctuation in fatality rates over the years. However, it is believed to be unlikely that such a considerable number of unexplained deaths among children and teens could have occurred in previous seasons without anyone becoming aware of the phenomenon. The impression given by the research data is that every year, becouse of the combination of pediatrics deaths reported on the web and the high circulation of influenza virus reported by the influnet network, many flu-related deaths are likely to slip. The lack of an adequate surveillance of flu-related deaths can result in an understimation of the severity of the disease, expecially that caused by the pandemic virus, as suggested by other authors. In any case, it is the author's hope that Italy, too, implements a national system for monitoring such events and that common guidelines are established and applied in all research institutes for more detailed diagnostics. In the same way, it is hoped that Italy follow in the footsteps of other countries that are adopting more modern tools of epidemiological research, so as to be better prepared to deal with future circumstances that may be even more serious than this latest pandemic.

Conclusions

Should the figures presented here be confirmed by future statistical studies, we certainly cannot consider the pandemic of the A(H1N1)pdm09 virus a catastrophe, but this data can help to better contextualize it within the scope of other similar events throughout history. It is also hoped that this study can help shed light on less known and rarely considered aspects of the influenza virus and its impact on young people.

This study represents a starting point for further studies designed to provide knowledge about the real impact of influenza on mortality, particularly among the pediatric population and in both pandemic and inter-pandemic periods.

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