

The 2009 influenza A virus - subtype H1N1 pandemic, a glance from Greece

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SUMMARY

The 2009 influenza A - subtype H1N1 pandemic tested the public health care systems all around the globe, infecting millions and leading to thousands of deaths. Greece became the epidemic centre of the 2009 flu pandemic due to the low compliance of the general population towards the vaccination programme, the resistance acquired against antiviral drugs and the economic scenario at the time. Our study, after a thorough research in the "Medline/PubMed, Scopus,

Google Scholars" medical databases, accompanied by a wide range search of medical literature from Greece, sought to have a closer look at the pandemic from a Greek perspective. Finally, we used as key words the terms: "2009, flu, influenza A - H1N1 virus, vaccine, pandemic, Greece".

Keywords: influenza A - subtype H1N1 virus, epidemiology, 2009 pandemic, vaccine, Greece.

INTRODUCTION

On April 25, 2009 the World Health Organization (WHO) due to serious influenza cases of the new virus strain influenza-A H1N1 2009 in Mexico and in the USA, announced with a formal declaration that it was a public health event with international impact. Gradually, in June 11, 2009 the scientific world underwent from the phase 3 of the pandemic vigilance, into the phase 6 pandemic alert, introducing the start of the 2009 influenza pandemic [1].

The 2009 flu outbreak in humans, known as "swine influenza", or influenza A - subtype H1N1, referred to an influenza A due to a new "H1N1" strain, also called swine-origin influenza virus A [2]. During April 2009, the emergence of a pandemic strain of influenza A H1N1 in North America was more than apparent. The virus was then predominant worldwide in human population and had become a significant public health problem with substantial

economic, social, psychological and health consequences. The virus contained a combination of genes from influenza viruses previously known to circulate in pigs, birds, and humans [3]. When the epidemic started, the scientific community wondered if this was a re-appearance of the Spanish flu pandemic [4]. However, this time the epidemic showed adequate dispersion among the population independently of whether they travelled or not [5].

This pandemic reserved for the Hellenic territory a significant role [1]. By June 10, 2010, more than 18.138 deaths were associated with the pandemic worldwide, while approximately 2.900 deaths were reported in the European continent. In Greece, the first laboratory confirmed case of the pandemic influenza was detected on May 18, 2009, while the first fatal case associated with the pandemic was reported on August 23 [6]. The epidemic wave furthered a decision to be announced on July 15, for the public health awareness in Greece, to be forwarded to a mitigation phase, which was communicated as "patient protection phase" [7]. During 2009-2010, 18.230 laboratory confirmed cases were registered in Greece depicting the country as the focal region of the virus spreading [1].

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With our study, we have tried to compose a Greek closer look for the 2009 pandemic. We have conducted a thorough search inside the “Medline/ PubMed, Scopus, Google Scholar” databases, combined with an extensive selection from the Hellenic literature of the time. As key words we used the terms “2009, flu, influenza A - H1N1 virus, vaccine, pandemic, Greece”.

The 2009 flu pandemic - Data from Greece

It was near the end of the usual influenza season in the Northern Hemisphere, when the first two cases of the swine-origin influenza A (H1N1) strain were identified in the United States, in California. The local “Centres for Disease Control and Prevention” confirmed that these cases were caused by a genetically similar strain to the swine virus that had not been previously identified in the United States. The genetic analysis of the strains showed that they were derived from a new re-assortment of six gene segments from the known triple re-assorting swine virus as well as two gene segments from the Eurasian influenza A - subtype H1N1 swine virus lineage [8]. Almost simultaneously the virus appeared in Mexico, to follow a worldwide outbreak, giving rise to the first pandemic in 40 years [9]. Europe was in the midst of the flu for more than two months from the first transmissions and outbreak of the 2009 pandemic when it affected the whole continent. The distribution of the transmission was highly heterogeneous between and within countries, with one country, the United Kingdom, experiencing the most cases and the highest transmission rates [10]. This new epidemic, the first of the 21st century, had affected during 2009 more than 290.000 patients and caused at least 3.486 deaths on 6 continents [11].

On April 27, 2009, the European Union Health Commissioner advised Europeans to postpone nonessential travel to the United States or Mexico. This announcement was followed by the discovery of the first confirmed case in Spain [12]. Europe was in alert to weaken the spread of the new influenza virus. In Greece, following Europe’s example, with the aid of KEELPNO (Greek: ΚΕΕΛΠΝΟ, Hellenic Centre for Disease Control and Prevention) a plethora of countermeasures twice in the same period to meet the epidemic wave, were taken. In the attempt to address the pandemic KEELPNO, in the period leading to

July 15 which was considered as the initial entrenchment phase, took a series of actions such as travellers surveillance, hospitals alert, public briefing. The “National Multiscientific Council Against the Epidemic” was immediately formed to manage and control the information flow and to announce the Pan-Hellenic strategy. Specially designated areas inside the largest hospitals and even to smaller General Health clinics were introduced, in an effort to isolate the infected patients. Special brochures to inform the public were printed and distributed throughout the whole Hellenic domain. The population was categorized into priority groups to receive the vaccine as soon as it was ready to be distributed. All clinical laboratories and health units were then put in high alert. Following July 15, the phase of limiting and logging of the effects of the pandemic started and Greece moved to a mitigation phase. Greece was fully participating in the European Mortality Monitoring (Euro MoMo) to register the infected as well as the diseased subjects [1].

In the USA about the 19.6% of the population was infected, while the mortality rate was worldwide 0.5%. In Greece, according to the last KEELPNO epidemiological report on May 26, during the time period 2009-2010 were registered 18,230 laboratory confirmed cases. Greece became the epicentre of the H1N1 pandemic in the European continent. The average age for the Greek infected part of the population was 21 years old [1]. It is almost a certainty, that these numbers significantly underestimated the true incidence of the new influenza pandemic in Greece, as in most cases the symptomatology was milder, and therefore had never been laboratory confirmed, as patients addressed their family physicians to treat simply the flu. The epidemic peak was between the 48th-49th week, with an estimation of 750-1,500 new cases for every 100,000 people per week [13]. The difference between the pre-pandemic and the pandemic peak in Greece was hugely increased, reaching the 100% in percentage increase. Therefore, Greece experienced an increase in the total cases’ number compared with the pre-pandemic years that were much larger than those seen elsewhere [14]. It is estimated that the clinical infection index was higher for children aged between 5 and 19 years (range 27-54%), while it was lower for people aged over 64 years of age (range 0.65-2.2%). Almost 19.7% of the entire Hellenic population was infected (range

13.3-26.1%), while it is estimated that 15 episodes per 1000 were hospitalized. The fatality rate was 6.3 per 100,000 infections. A sero-epidemiological study conducted by the University of Athens and KEELPNO, noted an antibody prevalence that was slightly higher, *i.e.* 28.5% (95% Confidence Interval 25.6-31.3%). Despite the fact that the new flu pandemic was considered moderate, eventually in Greece 149 deaths were recorded (average age 53 years), while during the course of the pandemic there had been progressively recorded a higher death rate among the older aged [1, 13, 15]. Among the victims that died from the flu epidemic, almost half of them had been also suffering from underlying secondary diseases, while a strong relationship emerged between serious influenza cases with obesity and pregnancy [16]. The most commonly reported underlying conditions were chronic cardiovascular diseases and immunosuppression. These findings were taken into consideration when vaccination strategies were deployed in Pan-Hellenic domain [6, 17].

The first specialized anti-influenza vaccines were approved during September 2009, while the vaccination effort in global level has not had the expected success and the results varied in countries all over the world. In Greece two vaccines were released including the newest immuno-amplifying serum. Whereas for example in the USA by the end of 2009, 20% of the population was vaccinated, in Greece a small percentage of approximately 3% of the entire population, one of the lowest rates in the European Union, had decided to proceed with the new vaccine, as the majority relied on the previous one.

It was typical for the period that parents were utterly negative towards the vaccination program, with only 1.18% being willing to accept it. From their perspective, a significant barrier to H1N1 vaccination was the concern about the vaccine's safety [18]. Among the health care workers, the percentage (17%) was relatively low, too [19]. Minimal side effects were emerged globally by the end of the pandemic vaccination, with only a negligible incident, the display of narcolepsy caused by the circulating vaccines in the Scandinavian region [1]. When talking for cost-saving, isolating the importance of human lives, the vaccination program in Greece at its completion produced a negative cost-benefit assessment [20]. Unfortunately, the vaccine disaster in Greece was

added to the economic turmoil, which seemed to have a significant impact on the infectious disease dynamics. It is essential to safeguard and even boost budgetary allocations, both to the state and to the public health sectors, in order to alleviate both the burn out of the medical staff and to detain further resources loss [21].

On August 10, 2010 WHO announced that the new influenza virus strain A H1N1 had passed to the post-pandemic phase. In many countries, Greece included, the predominant new influenza strain continued the epidemic phase until the season 2010-2011 with a significant morbidity. Unfortunately, to those waves previous cases were involved of the Hellenic populations in relation to the period 2009-2010 [22, 23]. The 2009-2010 pandemic waves were very mild and the seroprevalence rates remained low after this first new influenza virus season resulting in the exclusive detection of the pandemic strain during the 2010-2011 during the second influenza season. A large number of infected patients were hospitalised with severe influenza complications, presenting a high level increase of resistance towards the antiviral treatment [24, 25]. Regarding the antiviral treatment, during the beginning of the pandemic, all patients received oseltamivir, soon after the confirmation of pandemic H1N1 2009 infection, only but 21% of the cases were treated from the beginning of the symptoms. After the widespread transmission within the country, patients no longer received antiviral treatment unless necessary [26].

The press during the crisis went wild, terrifying the general population for both the new vaccine and the intensity of the pandemic. The "fear" virus infected almost all, as a journal article noted at the time [27]. Headlines like "Autumn scenarios for huge hospitalization", "The decade of fear", "The pandemic's peak during Christmas day", caused the public to have serious concerns for the vaccine and for the state's plans to confront the pandemic alike [28-30]. At the end of the second wave during 2010, more than 2.6 million vaccines were left in storage [31].

■ DISCUSSION

The most important conclusion of the WHO Committee of External Experts was that the world was still unready for an integrated re-

sponse to a severe influenza pandemic or any similar global persistent and threatening for the public health emergency incident. The Committee had recommended further improve on vigilance by promotion of specialized research, health systems strengthening, economic growth in countries of low and average economic level and finally an overall improvement of the health status worldwide [32]. In Greece high mortality rates were reasoned by the KEELPNO by its reference towards two important factors; firstly, the non-direct use of antiviral drugs at the first sign of serious clinical symptoms and secondly the failure to immediate introduction to the ICU (Intensive Care Unit) of the hospital [33]. As for a secondary reason, the low compliance towards immunization of both the general population and the scientific staff was indicated [1]. Although the majority of the General Practice physicians recommended measures and vaccination to be administered since the first phases of the pandemic, low rates of vaccine uptake have been observed during the national immunisation campaign against the 2009 pandemic in Greece [34-35]. Small percentages (0.35%-1.53%) of the parents were positive to vaccinate their children [36]. Overall, in Greece only 350,735 individuals (3% of the general population) had been vaccinated until December 24, 2009 [37]. The only group that achieved high rates (87% compliance) was the population of children with cancer treated at a paediatric oncology department during the pandemic season [38]. Influenza A - subtype H1N1 infected one fifth and caused symptomatic infection in up to 15% of the Hellenic population. Although individuals older than 65 years were the least affected age group in terms of attack rate, they had between 55 and 185 times higher risk of ICU admission and case fatality rate, respectively [39]. Wide spatial differences in seroprevalence rates were noted across Greece, with the highest burden of infections being recorded in the Ionian Islands and the district of Epirus (North-western Greece) and the lowest in Thessaly (Central Greece) [13]. Recourses to confront the higher cost of a hospitalized patient infected by the subtype H1N1 virus should have been distributed in such a way to be possible even to the Greek province Health Care Units to treat the patients in order for the time period between the diagnosis and the hospitalization to be shortened [13, 40]. The

vaccine distribution should also have presented in ratio, balancing the availability in all Hellenic districts for the general population, especially the high risk groups to be vaccinated [41].

The press emphasized the state's failure, by provoking public hysteria, causing a misperception of risk, capturing the readers in a scaremongering mood, to increase sales and readership, as modern media techniques prefix [42]. During the two year (2009-2010) flu pandemic in Greece, the absence of experts from the written press became obvious. The excess of vaccines that remained inside the state's storehouses intensified the economic loss during a difficult period for Greece [31].

All studies supported the importance of surveillance of the influenza viruses, both at epidemiological and molecular level, for the further strengthening of the recording and monitoring mechanisms [43]. While influenza constitutes a zoonosis of pigs, first recognized during the Spanish influenza pandemic of 1918-1919, the emergence of yet another serious global health threat from an animal source highlighted the critical need for the deeper understanding of the zoonotic viruses. *In vivo* studies of pathogenesis in animals, field epidemiologic studies and surveillance in animal populations, alongside with the development of computational models, need to be carefully organized and executed. The worldwide spread of the new combined AH1N1 strain of influenza virus showed the critical importance of international collaboration in efforts to predict and control future pandemic threats [8,44].

■ CONCLUSION

Influenza A - subtype H1N1 during 2009-2010 brought out the inefficiency of the health care systems to confront a pandemic globally. In Greece, while the immunisation coverage was proposed to be the only way to eliminate uncertainties about future waves, vaccination campaign was a disaster, presenting low rates of compliance. It seems that Greece was a Trojan horse for the second wave in the region during 2010. In the country of philosophers and orators, both journalists and state officials failed to produce a structured and informative speech, both to familiarize and to calm the public for the existing health threat. The

economic crisis, youth obesity, parent resistance and fear towards the new vaccine, created a need for new strategies. Influenza A viruses are notorious for their continuous in-field genetic interplay among avian species, swine, and human, leading to an endless variety of new viruses and the unpredictable onset of new pandemics. Thus, it requires the highest alertness during the flu season from both private and the state public health care systems. The general Hellenic population should adopt higher rates of confidence towards those strategies.

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