Original article

# Seroprevalence of measles in Northern Greece

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## Summary

The aim of the present study was to determine the current status of measles immunity in northern Greece, in light of outbreaks in many European countries, while recently, there is an ongoing measles outbreak in our country, affecting mostly Northern Greece. For the 611 sera tested (collected during June 2014-January 2016, and age range 10 d. – 82 y.o.), the seropositivity rate to measles virus was found to be 82.07%, while the total vaccination rate was 41.85%. The highest rates of rubella seropositivity were found in the 41-50 year age group (100%) followed by the 51-60 year age group (98.8%). Since mass infant vaccination was introduced in Greece in the form of the National Immunization Program in 1989, it seems that most of these people acquired immunity through exposure to the wild virus. It also demonstrates that there is high rate of protection among older people. Moreover the high immunity rates in the age groups 4-6 indicates the high level of protection in individuals belonging to these groups, mostly acquired through vaccination. Since 2010, there has been no report from outbreaks in Greece, but sporadic cases are reported. It is essential to continue epidemiological and virological surveillance of measles in Greece to monitor the transmission pattern of the virus and the effectiveness of measles immunization, which will eventually lead to the achievement of the goal for elimination.

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Measles is a highly contagious viral disease and is one of the leading causes of vaccine-preventable deaths in young children globally.[1] It is caused by a virus that belongs to the paramyxovirus family and it is normally transmitted through direct contact and through air. The disease typically presents with fever and generalised rash, accompanied by cough, coryza and conjunctivitis. It is associated with a high risk of complications and in the worst case scenarios can result in mortality.[2] During the past years, outbreaks were reported in many countries in the western part of Europe, due to the accumulation of pockets of unvaccinated or insufficiently vaccinated susceptible individuals, which allows sustained transmission. Measles virus continues to spread across the European Continent leading to thousands of cases in people who are not immunized or not immunized on time, while outbreaks can be expected where coverage is below 95% for two doses of measles containing vaccine.[3] In 2015, there were 134.200 measles deaths globally – about 367 deaths every day or 15 deaths every hour.[1]

According to the Global Measles and Rubella strategic plan 2012-202o, WHO aims to achieve measles and rubella elimination in at least 5 WHO regions by year 2020.[1]

In Greece, measles is a notifiable disease, the European Union's case definition of 2008 is used.[4] The last measles outbreak occurred in 2010. During this outbreak, cases were mostly unvaccinated and mainly belonged to three groups: Roma population of Bulgarian nationality, Greek Roma population and Greek non-minority population.[3,5] Before that, outbreaks occurred in 2005-2006, affecting mostly Roma children 0-14 years old and unvaccinated or incomplete vaccinated immigrant families. Moreover, during that outbreak, older teenagers and young adults from the non-minority population were affected. This happened because they were either unvaccinated or had received only one dose of the measles containing vaccine.[6,7] Recently, there is an ongoing measles outbreak in our country, affecting mostly Northern Greece. According to Hellenic Centre for Disease Control and Prevention (HCDCP), cases are mostly Greek Roma population (unvaccinated children) and Greek non-minority adults, aged 22-44 years of age, who were either unvaccinated, or had received only one dose of the vaccine. The total number of notified cases till October the 3rd were 215, while no deaths have been recorded.[8]

According to the most recent data from ECDC, and for the period January 2016 to end of July 2017, more than 17 000 measles cases were reported by 30 EU/EEA countries, with 40 deaths attributed to measles. The highest number of cases was reported by Romania (5 067), Italy (4 544) and Germany (915), accounting for 41%, 37% and 7% respectively of the EU/EEA cases. Moreover, of all cases with known age, 90% had a known vaccination status and of these, 85% were reported as unvaccinated. In the target group for routine childhood MMR vaccination (1-4 year old children), 78% of all cases were unvaccinated.[9]

The aim of the present study was to determine the current status of measles immunity in northern Greece, in light of outbreaks in many European countries.

Taking into account the expected seroprevalence in measles in different age groups, according to previous serological studies conducted in Greece, as well as the current population of northern Greece (3.110.835 inhabitants), the minimum sample size for the present study was calculated to be 399 with a 5% error and 95% confidence interval[10] (http://www.statistics.gr/el/statistics/-/publication/SAM03/2011). A total of 611 residual serum samples were included in the study having been collected between June 2014 and January 2016, from patients presented to hospital for reasons unrelated to measles infection. The specimens belonged to 345 males and 266 females. The age range of the patients was 10 days to 82 years old and the samples were divided into ten age groups (Table 1). None of the patients included in the study was suffering from infectious diseases or any known

**Table 1** Age distribution of patients and their serpositivity and vaccination rates

| Age groups | Numbers | Seropositivity rate (%) | Vaccination rate (%) |
|---|---|---|---|
| GROUP1 0-6MONTHS | 34 | 47,1 | 0 |
| GROUP2: 7-15MONTHS | 28 | 17,9 | 10,7 |
| GROUP3: 16MONTHS-5YEARS | 81 | 87,7 | 98,7 |
| GROUP4: 6-10YEARS | 77 | 97,4 | 94,8 |
| GROUP5: 11-20YEARS | 80 | 92,5 | 98,7 |
| GROUP6: 21-30 YEARS | 56 | 92,9 | 100 |
| GROUP7: 31-40YEARS | 51 | 97,7 | 15,6 |
| GROUP8: 41-50YEARS | 44 | 100,0 | 0 |
| GROUP9: 51-60YEARS | 80 | 98,8 | 0 |
| GROUP10: >60YEARS | 80 | 88,7 | 0 |
| **Total** | **611** | **82,07** | **41,85** |

immunodeficiency syndrome. Of the 611 samples, 515 were collected from inhabitants of Thessaloniki and 96 from people living in other parts of northern Greece, while 73 of the patients were foreigners (mostly from Albania, countries of the former Soviet Union, mainly from Russia and from Turkey). Moreover, 301 out of 611 (49,2%) were vaccinated individuals, while the remaining 310 (50,8%) were unvaccinated. From the vaccinated group, 129 of them received 1 dose, while 149 received 2 doses of the vaccine.

For each individual, data pertaining to age, sex, ethnicity, place of residence and history of measles vaccination were obtained. For children, data regarding vaccination was obtained from the parents/caregivers, while adults provided this information themselves; all data obtained was cross-checked with the information in each individual's public health book, when available.

The method used to determine protective immunity was an enzyme immunoassay method, ELISA (KAPRMVG10 Measles IgG kit, DIAsource ImmunoAssay). An antibody titre of ≥1:20 was defined as protective seropositivity against measles.

Data analysis was conducted with IBM SPSS Statistics Version 23. Initially, Pearson's chi-square test for independence was implemented, to detect significant associations in the data. Adjusted Residuals were calculated, to observe how the associated data vary from what null hypothesis of independence predicts. Finally, statistical significance of associations was indicated by the Risk Factors, Ratio Risk and Odds Ratio, with Confidence Interval 95% (p-value < 0.05).

For the 611 sera tested, the seropositivity rate to measles virus was found to be 82.07%, while the total vaccination rate was 41.85%. The age-adjusted rates of measles seropositivity and vaccination are shown in Table 1. Among individuals aged 0-6 months, the seropositivity rate of 47.1% reflects maternal acquired immunity. The seropositivity rate for the next two groups (17.9% and 87.7%) follows the usual pattern of disappearing maternal antibodies and the appearance of vaccination-acquired immunity. The highest rates of rubella seropositivity were found in the 41-50 year age group (100%) followed by the 51-60 year age group (98.8%). Since mass infant vaccination was introduced in Greece in the form of the National Immunization Program in 1989, it seems that most of these people acquired immunity through exposure to the wild virus. It also demonstrates that there is high rate of protection among older people. Moreover the high immunity rates in the age groups 4-6 indicates the high level of protection in individuals belonging to these groups, mostly acquired through vaccination.

According to statistical analysis of the results, no evidence of association is shown between the presence of immunity and sex (OR=0.993, 95%CI[0.562, 1.549], p-value=0.79), while analysis also revealed that immunity is not statistically significant when it is associated with a patient's nationality (OR=0.776, 95%CI[0.378, 1.594], p-value=0.49). Thessaloniki residents represented 84.3% and the rest of Macedonia represented 15.7% the samples. The presence of im-

munity is independent of a patient's residence (OR = 0.779, 95%CI[0.408, 1.488], p-value=0.45).

Moreover, 49.3% of the tested individuals are vaccinated, while 50.7% of them are unvaccinated. From those who are vaccinated, 92.4% display immunity and 7% do not display. From those who are not vaccinated, 85.2% display immunity and 14.8% do not. Odds ratio shows evidence that it is more possible for vaccinated patients to display immunity than from patients that are not vaccinated. (OR=2.1 95%CI[1.2-3.6], p-value=0.005). From the 538 Greeks, 263 are vaccinated (48.9%) and 275 are not vaccinated (51.1%). From those who are vaccinated, 242 display immunity (92.0%) and 21 do not display immunity (8.0%). From those that are not vaccinated, 237 display immunity (86.2%) and 38 do not display immunity (13.8%). The results shows that is statistical significant that Greek vaccinated patients to display immunity from those that are not vaccinated. (OR=1.85 95% CI[1.053, 3.242], p-value=0.03). From the vaccinated group, 110 received 1 dose (45.5%) and 132 received 2 doses (54.5%). The number of doses that a Greek patient receives is not statistically significant associated with the presence of immunity. (OR=0.417 95% CI[0.162, 1.069], p-value=0.06).

Additionally, from the vaccinated patients, 145 received 1 dose (48.2%) and 156 received 2 doses (51.8%). From those that received 1 dose, 89.0% display immunity and 11% do not display. From those that received 2 doses, 95.5% display immunity and 4.5% do not display. The presence of immunity in a patient does not statistically associated with the number of doses received (OR = 0.379 95% CI[0.151, 0.949], p=0.004).

A cross-sectional study that was conducted in order to determine the prevalence of mumps and measles antibodies in the general population in Northern Greece in 2004-2007 revealed that the great majority were protected against measles and the total protection rate against mumps was significantly less (87% versus 72%, respectively; p<0.01). Moreover, protection rates against measles seem to be lower than expected in certain age groups, such as infants and young adults, something that was not found in the present study which was conducted almost 10 years later and several outbreaks in between.[11]

The high seroprevalence rates of the study were in accordance with a similar cross-sectional vaccination coverage study in preschool children conducted in 2016, in which a coverage of more than 95% was found.[12]

On the other hand, in a healthcare students groups which were tested for measles antibodies, the susceptibility rate was 20,5%.[13]

In conclusion, it is essential to continue epidemiological and virological surveillance of measles in Greece to monitor the transmission pattern of the virus and the effectiveness of measles immunization, which will eventually lead to the achievement of the goal for elimination.

# Περίληψη

## Η επιδημιολογία της ιλαράς στην Βόρειο Ελλάδα

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Ο σκοπός της παρούσας μελέτης ήταν ο προσδιορισμός του ανοσολογικού επιπέδου της ιλαράς στον πληθυσμό της Β. Ελλάδος, σε περίοδο εμφάνισης ενός σημαντικού αριθμού επιδημιών σε αρκετές χώρες της Ευρώπης. Εξετάστηκαν συνολικά 611 δείγματα ορών (ηλικίας από 10 ημερών έως 82 ετών), τα οποία συλλέχθηκαν την περίοδο Ιούνιος 2014-Ιανούαριος 2016 και διαχωρίστηκαν σε 10 ηλικιακές ομάδες. Το συνολικό ποσοστό ανοσίας ανέρχεται στο 82.07%, ενώ το ποσοστό εμβολιασμού των υπό εξέταση ατόμων ήταν 41.85%. Τα υψηλότερα ποσοστό ανοσίας ανευρέθησαν στα άτομα ηλικίας 41-50 ετών (100%) καθώς και στην ηλικιακή ομάδα των 51-60 ετών (98.8%). Φαίνεται ότι τα άτομα των ανωτέρω ηλικιακών ομάδων απέκτησαν ανοσία κατόπιν επαφής με το άγριο στέλεχος του ιού της ιλαράς, μια και ο υποχρεωτικός εμβολιασμός έναντι του ιού της ιλαράς ξεκίνησε στην χώρα μας το 1989. Παράλληλα, τα υψηλά ποσοστά ανοσίας στις ηλικιακές ομάδες 4-6 οφείλονται κυρίως στον εμβολιασμό αυτών των ατόμων. Η τελευταία επιδημία ιλαράς στην χώρα μας έχει σημειωθεί το 2010, ενώ έκτοτε έχουν καταγραφεί μόνο σποραδικά κρούσματα. Είναι επομένως απαραίτητη η συνεχής επιδημιολογική και ιολογική επιτήρηση της νόσου στην χώρα μας, προκειμένου να επιτευχθεί ο έλεγχος της αλλά και τελικός στόχος του Παγκόσμιου Οργανισμού Υγείας που αφορά στην εξάλειψή της.

***Λέξεις κλειδιά***
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