



Seroprevalence for Measles Antibodies among Multi-Transfused Patients with Hemoglobinopathies: The Experience of a Thalassemia and Sickle Cell Department in Greece

Konstantinos Manganas^{1*}, Sophia Delicou¹, Myria Pougouka², Aikaterini Xydaki¹, Maria Liosi², Denis Gubini², Vasiliki Skandami²

¹Thalassemia and Sickle Cell Department, Hippocratio General Hospital, Athens, Greece

²Microbiology Laboratory Hippocratio General Hospital, Athens, Greece

ABSTRACT

Background: Infections are frequent in patients with hemoglobinopathies and in recent years have become a significant cause of morbidity and mortality in this group of patients.

Aims: The purpose of this study was to determine the immunity status to measles of patients with hemoglobinopathies due to the recent revival of measles in Greece.

Methods: 75 multi-transfused patients were studied. Serum measles IgG antibody titers were measured by an Enzyme linked immunosorbent assay to determine the measles immune status and document previous measles infection in individuals without a prior history of immunization.

Results: All but one of the 31 patients who were born before 1970, date of the introduction of nationwide vaccination, was antibody positive. Of the younger patients, 84% were antibody positive and 7 (6%) negative: of this group 72.7% had been vaccinated during childhood, while 11.8% had suffered measles. Of the vaccinated patients, 40.6% had received 2 doses of the vaccine while 59.4% received one. Of the non-immune patients 71.4% had not been vaccinated and the other two had been vaccinated with one dose of the vaccine. All were offered vaccination: 57.1% accepted and developed antibodies after one dose, while three refused.

Conclusion: Measles seropositivity was uniformly high among patients with hemoglobinopathies. Nearly both subgroups had evidence of measles seropositivity levels greater than the estimated threshold necessary to sustain measles elimination.

Keywords: Measles; Vaccinations; Hemoglobinopathies; Humoral immunity

DESCRIPTION

Infections are important cause of death in patients with hemoglobinopathies, on account of multiple transfusions, secondary hemochromatosis and iron overload, splenectomy, cellular and humoral immune deficiencies [1]. In such patients vaccination is necessary for the protection of from a potentially fatal infection like measles.

The recent measles outbreaks in Europe during the period 2016-2018 and the several deaths of people with underlying disease, challenged us to estimate the present prevalence of measles immunity among our patients with hemoglobinopathies by determining seroprevalence of IgG antibodies against measles.

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Corresponding author Manganas Konstantinos, Thalassemia and Sickle Cell Department, Hippocratio General Hospital, Greece; E-mail: kmagganas92@gmail.com

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MATERIALS AND METHODS

75 multi-transfused patients with hemoglobinopathies followed at our department were studied, 52 with β -thalassemia and 23 with sickle cell disease; they fell into two groups according to their birth date, those born before 1970 (n=31, median age: 56 years, range: 51-69 years old) and after 1970 (n=44, median age: 46 years, range: 21-50 years old). This classification was according to the National Immunization Programs [2], because the measles vaccine was released in Greece after 1970 and only those who had experienced measles had already acquired natural immunity.

The determination of IgG antibodies to measles was done by an Enzyme linked immunosorbent assay [3]; the sensitivity of the method is >99% and the specificity is 95%. The result is considered negative for measles immunity when IgG antibodies are less than 150 mIU/mL and positive when they are at levels >200 mIU/mL.

RESULTS

Out of the 31 patients who were born before 1970, all but 1 (96.7%) turned out to be immune. Of these, 8 had been vaccinated during adulthood.

Out of the 44 patients born after 1970, 37 (84%) were immune and 7 (6%) not; of the 37 immune ones, 5 (11.8%) had experienced measles and 32 (72.7%) had been vaccinated during childhood, with 2 doses in 13 patients (40.6%) and one dose in 19 (59.4%).

Of the 7 non immune patients born after 1970, 5 (71.4%) had not been vaccinated at all and the other two had been inoculated with one dose only; vaccination was recommended and offered to all 8 patients. 5 of them (62.5%) accepted and developed antibodies after one vaccine dose, while three refused vaccination.

Antibody titers were high in 41/67 (61%) of the immune patients, possibly indicating coexisting passive immunization from transfusions.

DISCUSSION

When the Morbillivirus entered a non-immunized, naive, population, 90%-100% of individuals develops the clinical symptoms of measles and acquires a lifelong immunity. After the introduction of compulsory vaccination, most incidents in the developed countries concerned the few non immune persons, who had escaped measles or had not been vaccinated properly.

In Greece, the measles vaccine was introduced in the 1970's, followed by the systematic application of the MMR vaccine from 1989, according to the compulsory National Immunization Programs. This led to a substantial reduction of measles incidence in the following years [4]. The next measles epidemic in Greece occurred in 1996 and from then since the autumn of 2005 there had been no recorded cases of measles [5]. More than 20,000 incidents across Europe (30 EU/EEA Member States) and 79 deaths (31 of which in 2018) have been recorded during the period 2016-2018. From May of 2017 until June of 2018, 3278 new cases of measles have been recorded in Greece, with a higher incidence in southern Greece and almost two-thirds of reported

cases belonged to the Roma population [6].

In the present study, most patients born before 1970 (23 out of 31%-74.1%) seem to have naturally acquired humoral immunity and 8 more (23.9%) have an artificially acquired immunity, as they had been vaccinated as adults.

In the current study, 32 of the 44 (72.7%) patients born after 1970 had been vaccinated during childhood: of these 32 vaccinated patients, two doses were administered to 13 (40.6%) and one dose to 19 (59.4%).

We found no measles antibodies in 7 patients born after 1970; of these, 5 (71.4%) had not been vaccinated, while two had received a single vaccine dose but did not develop antibodies due to conditions that caused them severe immunosuppression, as one patient suffered from chronic kidney disease and the other from diabetes mellitus with poor glycemic control [7]. Vaccination was recommended and offered to all 8 patients. 5 (62.5%) accepted and developed antibodies after one vaccination dose, while three refused vaccination due to social assertions (anti-vaccination movement) (Figures 1 and 2) [8]. Finally, during the measles epidemic, none of the patients became ill, or anyone from their contacts [9,10].

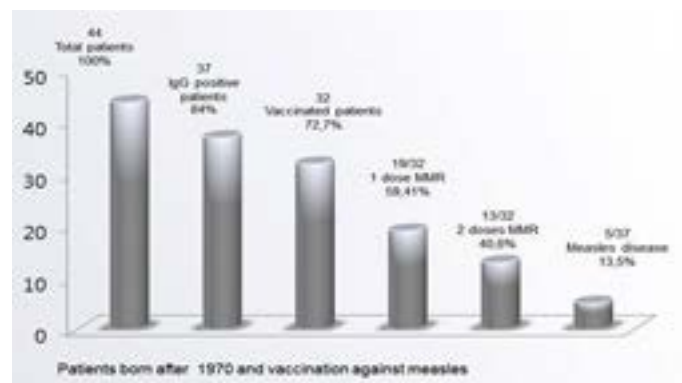


Figure 1: Prevalence of positive IgG antibodies against measles in all vaccinated and unvaccinated seropositive persons

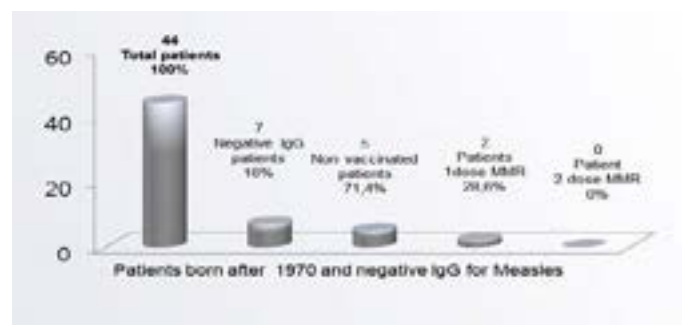


Figure 2: Prevalence of negative IgG antibodies against measles in all vaccinated and unvaccinated seropositive persons

CONCLUSION

Worldwide, vaccination has contributed in the interruption of the transmission of measles virus in the developed world by providing protection via herd immunity for unvaccinated individuals. Herd immunity must be preserved between 85%-95% to disrupt broad transmission. Groups at significantly increased risk for measles complications include immunocompromised patients, pregnant women, individuals with vitamin A deficiency or poor

nutritional status, and the elderly. In G Pardalos (1987) research the reduced T4/T8 ratio in beta-TM children was considered primarily due to T4+ cell decrease and was inversely correlated with patient age, amount of transfused blood units and, in particular, serum ferritin levels and the iron balance per annual basis. These data demonstrate that immune abnormalities in beta-TM patients seem to be acquired, correlated to transfusion, and associated with sufficient chelation therapy that is dependent on iron load. In some cases, the hypothesis may explain the observation of previous studies in thalassaemic patients who received the multivalent pneumococcal vaccine demonstrated attenuation of the antibody titers or non-response to the hepatitis B vaccine. We need further research and analyses on the response of the measles vaccination and natural immunity in this vulnerable patient population.

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AUTHOR DISCLOSURE STATEMENT

The authors report no conflicts of interest in this work.

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