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Rotavirus gastroenteritis hospitalization rates and correlation with rotavirus vaccination coverage in Sicily

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Summary. *Background and aim of the works:* Rotavirus (RV) is considered the main cause of gastroenteritis in children from 0 to 59 months and vaccination represents the only strategy to prevent hospitalizations due to RV. In 2013 Sicilian Region introduced universal RV vaccination for all newborns. The present study aims to estimate the reduction rotavirus gastroenteritis (RVGE) hospitalization rates among Sicilian children and their relations with vaccination coverages of the nine Sicilian Local Health Units (LHUs). *Methods:* Were analyzed hospital discharge records including a diagnosis of RVGE occurred from January 2009 to December 2017 in hospitalized children aged 0 to 59 months, residents in Sicily. Were reported data on complete RV vaccination cycles among Sicilian children under 12 months of age (vaccination coverage). *Results:* A 49.2% overall reduction of RVGE hospitalization rates was reported after RV vaccination introduction. A more considerable reduction of hospitalization rates was observed among children aged 0 to 11 months (-61.4%), followed by children aged 12-23 months (-51.2%) and 24-35 months (-48.8%). In all the nine Sicilian Local Health Units (LHUs), a reduction of RVGE hospitalization rates was observed after RV vaccine implementation. *Conclusions:* This study demonstrated the significant impact of RV vaccination on RVGE hospitalization rates in Sicily, especially among children aged 0 to 23 months. The reduction in RVGE hospitalization rates observed in the Sicilian LHUs after universal vaccination program implementation, were generally higher or consistent with average vaccination coverage reported from 2013 to 2017. (www.actabiomedica.it)

Key words: rotavirus, gastroenteritis, rotavirus vaccination, hospital discharge records, hospitalizations rate, local health units, vaccination coverage

Introduction

Worldwide, rotavirus (RV) is the leading cause of childhood gastroenteritis and nosocomial infection in Paediatric units among children under five years (1). In industrialized countries morbidity and health costs associated with RV infection are considerable, while in developing countries, rotavirus gastroenteritis (RVGE) represents an health emergency, with 600,000 children killed every year by dehydration (1).

In Europe, before the introduction of the vaccines against RV, this viral infection was responsible annually for about 3.6 million cases of gastroenteritis among children 0-59 months, including 87,000 hospital admissions and about 700,000 medical consultations (2).

The availability of vaccines has greatly modified the incidence and the economic burden of RV infections worldwide (3).

Anti-RV vaccination actually represents the most effective strategy for reducing RVGE among children

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and the introduction of RV vaccines in immunization schedule is strongly recommended by international health authorities (4, 5).

Since 2006, several countries adopted universal RV vaccination in their immunization schedules, reporting high vaccine effectiveness in reducing RVGE hospitalizations and outpatient visits (6-8).

In Sicily, the Regional Health Department introduced the universal rotavirus vaccination program into the immunization schedule in January 2013, as the first Region in Italy (9). Right after the vaccine implementation, a decrease in the number of hospital admissions for RVGE was observed in Sicily among children aged 0-59 months (10).

Universal RV vaccination demonstrated a substantial cost reduction for the Regional Health System, but also a decreasing trend in the mean age of hospitalized children and a smaller peak of RVGE hospital admissions observed in late winter and early spring (11).

The present work aimed to assess the impact of vaccination coverage achieved in Sicily, on RVGE hospitalization rates among 0-59 months children, after a five-years period of RV universal vaccination programme, and to evaluate the reduction according to different age-groups and Provinces.

Materials and Methods

Data collection

A retrospective observational study on Hospital Discharge Records (HDRs) of Sicily, the fourth most populous region in Italy with 5 millions inhabitants, including a cohort of 45,000-50,000 newborns per year, was conducted (12).

The Sicilian Region is divided into 9 Provinces (Agrigento, Caltanissetta, Catania, Enna, Messina, Palermo, Ragusa, Siracusa and Trapani). Each Province corresponds to a Local Health Units (LHUs), health organisations responsible for inpatient and outpatient medical care of all residents.

The Sicilian HDR database was established in 1994, including the complete data of patient hospitalized from both public and private regional hospital. Each HDR integrated demographic information (birthplace, residence, gender, and date of birth), admission and discharge dates, discharge status (categorized as "discharged/transferred" or "expired"), and up to six discharge diagnoses (one principal and five secondary diagnoses) coded according to International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM).

All HDRs included into the regional database with an ICD-9-CM diagnosis code of 008.61 as the first or other diagnosis position, corresponding to a diagnosis of "rotavirus gastroenteritis" occurred in children aged 0-59 months, from the 1st of January 2009 to the 31st of December 2017, were analysed.

Duplicate episodes of RVGE hospitalizations were considered unique if they occurred within 14 days between episodes, otherwise only the first episode was considered.

Statistical analysis

RVGE hospitalization rates observed in the pre-vaccination period (2009-2012) were compared with RVGE hospitalization rates of the post-vaccination period (2013-2017).

Vaccine coverages rates reported in the study correspond to the number of complete RV vaccination cycles per year on resident children younger than 12 months of age (birth cohort) and were obtained from the regional vaccination database, which is edited yearly according to the Italian Health Department recommendations.

The data of vaccination coverage reported for each Sicilian LHUs were intended as the average adherence data to RV vaccination in the first five years of vaccine implementation (from 1st January 2013 to 31st December 2017).

Quantitative variables (RVGE hospitalization rates, age class distribution) were evaluated during the pre (2009-2012) and post (2013-2017) vaccination periods and the corresponding percentage reductions were reported.

Hospitalization rates per 100,000 were calculated using the census population for children aged 0 to 59 months from 2009 to 2017 (12).

All statistical analyses were performed using the STATA v14.2 software package.

Results

RVGE hospitalization rates in Sicily, before (2009-2012) and after (2013-2017) the introduction of RV vaccination, are reported in Figure 1.

In particular, after the introduction of universal vaccination program, a decline in RVGE hospitalization rates among children aged 0 to 59 months was observed, decreasing from 394 per 100,000 in 2009-2012 to 200 per 100,000 in 2013-2017 (49.2% reduction overall).

In Figure 2, RVGE hospitalization rates documented in different age-groups, before and after RV vaccine introduction, were reported.

From 2013 to 2017, RVGE hospital admissions rates strongly decreased particularly among children aged 0-11 months (from 526 per 100,000 to 203 per 100,000; -61.4%).

A substantial reduction in RVGE hospitalizations rates was also observed among children between 11 and 23 months of age (from 657 to 321 per 100,000; -51.2%), followed by the age-groups 24-35 months (-49%), 36-47 months (-25.4%) and 48-59 months (-24%).

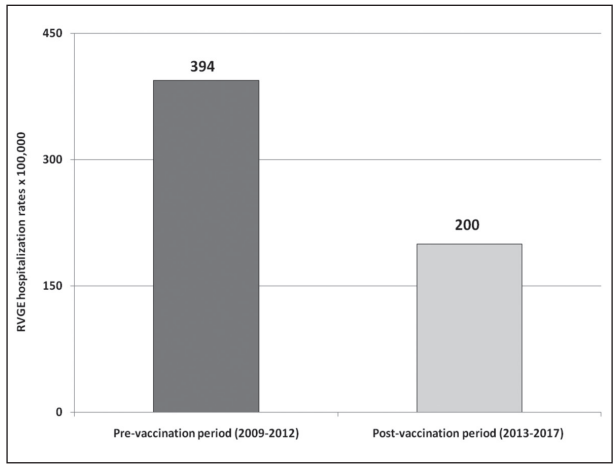

Figure 1. Average RVGE hospitalization rates (x 100,000) observed in Sicily among 0-59 months children before (2009-2012) and after (2013-2017) the introduction of RV vaccination

In Table 1, RVGE hospitalization rates observed in the 9 Sicilian LHUs before (from 2009 to 2012)

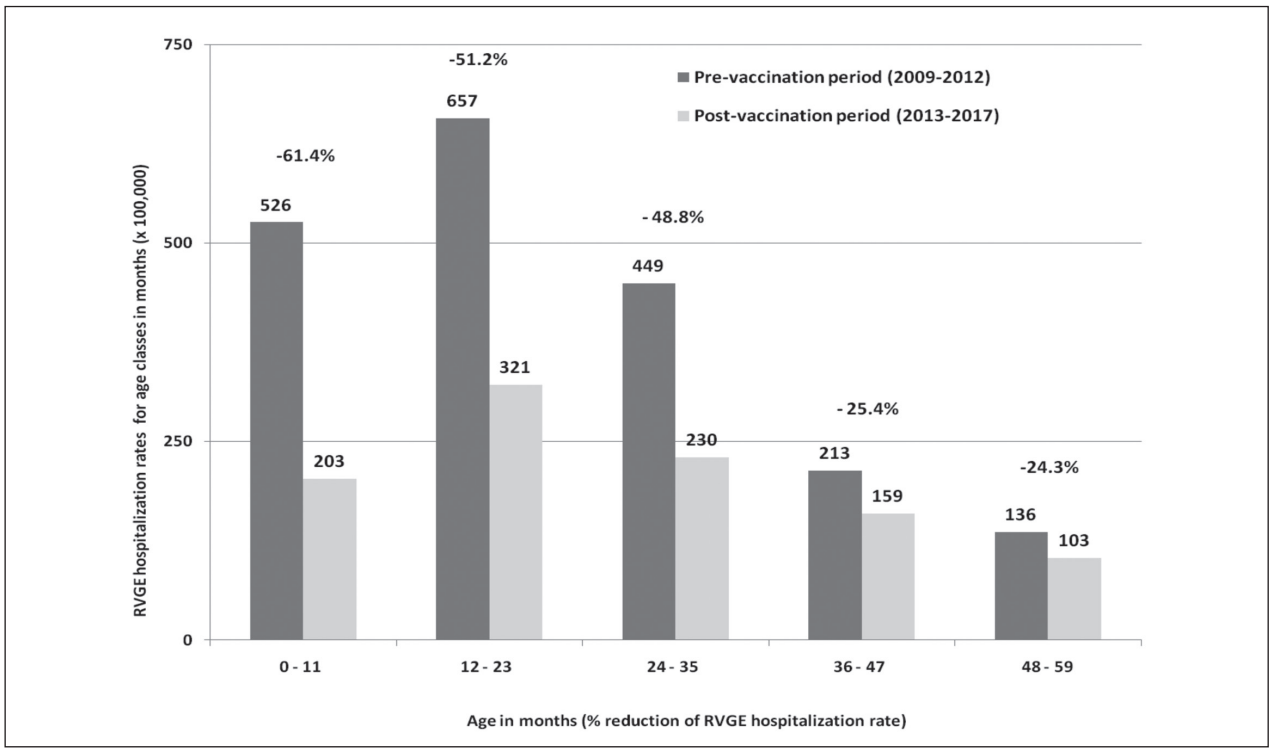

Figure 2. Average RVGE hospitalization rates (x 100,000) for age groups among 0-59 months aged children in Sicily, before (2009-2012) and after (2013-2017) the introduction of universal RV vaccination

Table 1. Average RVGE hospitalization rate observed in the nine Local Health Units (LHUs) of the Sicilian Region during pre (from 2009 to 2012) and post (from 2013 to 2017) vaccination period, and average RV vaccination coverage reported from 2013 to 2017

LHU	Prevaccination period (2009-2012) Average hospitalization rate	Postvaccination period (2013-2017) Average hospitalization rate	Difference (%)	Average vaccination coverage (2013-2017) (%)
Overall	394	200	-49.2	38.2
Agrigento	238	106	-55.5	48.1
Caltanissetta	239	194	-18.8	42.7
Catania	328	136	-59.5	30.6
Enna	461	226	-51	27.4
Messina	115	97	-15.7	19.1
Palermo	617	311	-46.6	51.5
Ragusa	451	243	-46.1	31.1
Siracusa	611	331	-45.8	34.1
Trapani	239	104	-56.5	58.6

and after (from 2013 to 2017) RV vaccination implementation and the average RV vaccination coverages, were reported.

Overall, the average RV immunization coverages from 2013 to 2017 among Sicilian children was 38.2% (range: 19.1%-58.6%; for Messina and Trapani, respectively).

A reduction in RVGE hospitalization rates in children aged between 0 and 59 months was observed in all Sicilian LHUs (range: 15.7%-59.5%; for Messina and Catania, respectively).

Discussion

Rotavirus is the main responsible of moderate/severe acute viral gastroenteritis in neonatal and paediatric age. These findings were reported in several studies that demonstrated a RV aetiology in over 50% of children hospitalized for diarrhoea (13, 14).

From 2003 to 2012, in Sicily, RV was responsible for at least 950 hospital admissions per year in children aged from 0 to 59 months, with an average hospitalization rate higher than 370 per 100,000 (15).

All European countries that introduced RV vaccination as part of the routine childhood immunization schedule, reported a significant reduction of RVGE burden in hospital wards, emergency rooms and outpatient admissions (16).

However, the majority of countries where a significant reduction of RVGE hospitalizations was observed, achieved coverage rates ranging from 60% to 85%, as early as the first year of vaccine implementation (17-19).

Conversely, even tough Sicily was the first Italian Region that introduced universal RV vaccination for all newborns in January 2013, average vaccination coverage was lower than 40% after 5 years of active and free offer (9, 20).

Moreover, among different Sicilian LHUs inequalities in the vaccination offer and uptake emerged. In particular, RV vaccination coverages in the Western Sicily Provinces (Trapani: 58.6%; Palermo: 51.5% and Agrigento: 48.1%) were considerable higher than in the Eastern Provinces such as Messina (19.1%), Catania (30.6%), Ragusa (31.1%) and Siracusa (34.1%).

Unfortunately, confidence of some Sicilian paediatricians and healthcare workers to RV vaccination was erroneously conditioned by the withdrawal of a previous version of RV vaccine administered until 1999, which was suspected to be responsible for a possible association with intussusception among vaccinated children (21). Assumption that was recently retabled in Sicily by some authors and promptly rejected by Sicilian Public Health Authorities (22).

Nevertheless, in all Regional LHUs, a substantial decrease of RVGE hospitalization rates in post-

vaccination period (2013-2017) (-49.2% overall) was observed.

The greater hospitalization rates reductions were found especially among children aged between 0-11 and 12-23 months (-61.4% and-51.2% respectively), that represented the age groups at higher risk for serious RVGE clinical presentations, often requiring hospitalization (23, 24).

RVGE hospital admission rates in the LHUs of Messina, Palermo, Trapani showed consistent reductions in post-vaccination period (2013-2017), with the correspondent average vaccination coverage rates.

In the LHUs of Agrigento, Ragusa and Siracusa, hospitalization reductions observed (between 10% and 20% higher than average vaccine coverage observed) could be attributable to the herd effect of RV vaccination, that protected not only vaccinated children from infections, but could also lead to an overall reduction of seasonal circulation of the pathogen (25,26).

On the other hand, the decrease in RVGE hospitalization rate observed in the LHUs of Catania and Enna (-59.5% and -51% respectively), much higher than vaccination coverage (30% and 27.4% respectively), and the small reduction of RVGE hospital admission of Caltanissetta (18.8%) compared with vaccination coverage (42.7%), could be influenced by annual changes in rotavirus circulation, often associated to different factors apart from vaccination (27).

Conclusions

In Sicily, RV universal vaccination implementation resulted in a considerable reduction in RVGE hospitalization rates during the period 2013-2017 (-49.2%).

The impact of vaccination in reducing the burden of hospitalizations for RVGE, especially among children aged 0-23 months and in all the 9 Sicilian LHUs were encouraging.

Currently, the most important challenge for Sicilian Public Health Authorities will be the improvement of both knowledge and attitudes of health care workers on RV vaccination, that actually did not recommend the immunization to newborns.

Only a continuous increase of vaccination coverages over next years could lead to further reduction of RVGE hospital admission rates, overcrowding of paediatric departments during RV epidemic seasons and RVGE economic burden on Regional Health System (11).

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GlaxoSmithKline Biologicals SA was given the opportunity to review a preliminary version of this manuscript for factual accuracy but the authors are solely responsible for final content and interpretation.
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