Journal of Health, Medicine and Nursing
ISSN 2422-8419 An International Peer-reviewed Journal
Vol.54, 2018

Causes for Deficient Coverage of MMR Vaccine in the Balkan States and the Way Forward

Angjelka Jankulovska*
PhD Student, Medical Faculty, University Ss. Cyril and Methodius
Skopje, Republic of Macedonia, Bitola 7000, Republic of Macedonia

Katarina Mirchovska
Resident in Surgery, Medical Faculty, University Ss. Cyril and Methodius, Skopje, Republic of Macedonia

João M. Santos
[3] Instituto Universitário de Lisboa, Centro de Investigação e Intervenção Social, Lisboa, Portugal

Abstract
Objectives: To evaluate the causes for low MMR vaccination coverage in the 9 Balkan States, and provide solutions for this public health concern. *Methods:* Credible articles published 5 years ago, from 2012 up to date were sought for, to ascertain and analyze information on the cause for low MMR vaccine coverage in the Balkan States, and also to provide strategies for mitigation. These journals were sought for in the following reference libraries available online: PubMed, EMBASE, CAB Abstracts, the World Health Organization, the Cochrane Library, Popline, European Centre for Disease Prevention and Control, Centre for Disease and Control, and Google/Google Scholar. *Results*: This study evaluated MMR vaccinations in nine Balkan States (Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Macedonia, Montenegro, Slovenia, Serbia and Romania) from 2012 to 2016. While Albania ranked highest in maintaining the WHO recommended 95% vaccination coverage, other states fluctuated in their percentage of coverage with Bosnia and Herzegovina, Serbia, and Romania having the lowest coverage respectively. *Conclusion:* Socio-economic and Administrative factors have been the major challenge affecting MMR vaccination coverage in the Balkan States. Anti-vaccination movements recently increased their influence by encouraging the rejection of vaccination by parents. To curb these challenges, research institutes and governmental agencies should sensitize the society about the benefits of vaccination in children and further publicize clinical trials of vaccines in order to prove their safety and efficacy to the public.
Keywords: MMR vaccination, vaccine coverage, measles, public health.

Introduction

MMR vaccine is a live attenuated vaccine developed against Measles, Mumps, and Rubella diseases. It is given to children to protect them against these diseases, with the first dose being given at 12 months, and the second dose at a maximum age of 6. [1] When the dosage is completed, the vaccine is expected to offer long-lived immunity to about 98% of children who are immunized.[2] Measles, Mumps, and Rubella are viral infections of public health concern, as they have contributed immensely to the global burden of disease in children. The prevalence of these infectious diseases have risen and fallen over time. For instance, in Romania throughout the year 2012, the country experienced fluctuating cases of measles; between January and February there was 84.9% decrease (cases per million) in reported cases of measles in Romania, 488.18% increase in March, 51% decrease in April, 95.58% increase in May, and a decrease of 45.48% in June. [3] This decreasing trend continued until September, then in October, Romania recorded 155 measles cases, which was a 181.82% increase from September. [3] During this period, there was an outbreak of measles which affected children from <1 years old to 4 years. [4] This pattern has followed all the outbreaks in that region.[4]

Amongst other Balkan states that have witnessed measles outbreaks both in the past, and at present is Bulgaria. They had an outbreak from 2009 to 2011, which affected a total of 24,364, predominantly children <15 years old. [5] The major reason for this outbreak according to the report was low vaccine coverage which led to a backlog of children susceptible to measles virus. [5] Of children within the age of 1-14 years, immunization of MMR vaccine was achieved with only 70% of the population who received just a single dose, while 22% were unvaccinated. [5] It was also reported that different cities in Macedonia had measles outbreak between 2010 and 2011, despite the high MMR vaccine coverage in the region. [6] Skopje in Macedonia had the highest reported measles case, with 573 infected, followed by Strumica with 119 cases. [6] An accumulation of susceptible children between <1 to 4 years in Skopje were identified to be the prevalent factor that led to the outbreak. All these measles outbreaks have had more prevalence on children within this age group, which reveals that there is a lag in MMR vaccination, and in the completion of two doses in children from < 12 months old to 4 years.

Also, the recent and ongoing measles outbreak which started in 2016 has affected all EU/EEA countries except Latvia and Malta. [7] The outbreak spread rapidly in the population affecting mostly children from below 1 years to 4 years of age. Bulgaria has recorded a total of 166 cases, Romania 5605, and Slovenia 6 as shown on

Table 1. Of the 13,724 reported cases with known age, 37% of children below five years were affected, and 336.2 cases per million children less than a year old were also affected, which is the highest incidence rate recorded so far. [7] Analyzing the prevalent circumstances for this outbreak, it was observed that it followed the same pattern as the previously recorded outbreaks. Children under the age of one had the highest unvaccinated rates - 96% - while 86% of children within one to four years were unvaccinated, and 11% were given one dose of MMR vaccination, while none completed the required two doses of the vaccination. [7] This reveals that there is a trend in the MMR vaccination in children that is yet to close up the immunity gap against measles. The purpose of this study is to analyze the reasons for the lapses in MMR vaccination coverage, through systematic study and evaluation of the available data. This report shall also discuss positive approaches that could be adopted to achieve the elimination goal of measles in the population.

Materials and Methods

A systematic review was conducted on peer-reviewed journals and credible articles published 5 years ago, from 2012 and up to the current year, to identify and analyze information on the cause for low MMR vaccine coverage in the Balkan States, and also to provide strategies for mitigation. This journals were sought for in the following reference libraries available online: PubMed, EMBASE, CAB Abstracts, the World Health Organization, the Cochrane Library, Popline, European Centre for Disease Prevention and Control, Centre for Disease and Control, and Google/Google Scholar. The journal descriptions and abstracts were examined and segregated according to the exclusion and inclusion criteria such that only resources valuable to this study were retrieved. Quantitative data obtained from different Balkan countries were evaluated using an ANOVA to determine if the same circumstance is responsible for low MMR vaccine coverage in the region.

The following exclusion criteria was applied on the journals retrieved during the search: journals published earlier than 2012, as well as those not specific to European region. While this study was specifically carried out to evaluate low coverage of MMR vaccination in some of the Balkan states, comparisons were made to other European countries. Also, MMR vaccination reported for adults, and its adverse reactions, were excluded from the analysis as they are not the focus of the present study.

Results

Statistical remarks

The data obtained from the nine Balkan states reflecting the MMR vaccination coverage and measles outbreaks were tested with an ANOVA procedure. To ascertain if the mean of the values is significantly different across the differing countries, with the goal of determining if the data are under similar influences, thus allowing inferences regarding the reported causes.

Table 1: ANOVA table

Country	Mean	Standard Deviation
BOSNIA and Herzegovina	88.2	25.7
ALBANIA	97.6	1.3
BULGARIA	93.7	3.7
CROATIA	91.2	34.7
MACEDONIA!	73	320
MONTENEGR	89.4	12.8
ROMANIA	86.6	12.8
SERBIA	86.6	3.6
SLOVENIA	93.8	1.2

F-Value = 0.0211
P-Value = 1.000
Confidence Level = 95%
Null Hypothesis = < P value
Null Hypothesis ≠ < P value

Profiles of MMR immunization coverage in the Balkan states.

Albania has maintained a steady optimum MMR immunization for children between the ages 12 – 23 months. From 2012 to 2016, Albania experienced 2% decrease from 2012 to 2016; however, the 95% sustainable level for MMR vaccine was exceeded throughout the five years under study. The highest MMR percentage coverage was observed in 2013, between 2012 and 2013 there was a percent increase, while 2014, 2015, and 2016 had a percent decrease preceding the following year (Table 2).

Macedonian is the second ranked Balkan State in this study that met the preferred coverage level for MMR

vaccination. The 95% target was met twice, in 2012 and 2013. At the end of 2016, the state experienced a reduced percentage coverage of 14.6% from 2012. Bulgaria met the target only once, in 2013, and had a total reduced coverage of 2.1% from 2012 to 2016. Slovenia, as of 2016, had 1.1% more reduced coverage when compared to Bulgaria.

Also, under the period of study, MMR vaccination coverage in Bosnia and Herzegovina declined from 2012 to 2016. A 11.7% decrease was observed from 2012 to 2016, with the lowest percentage coverage being observed in 2015, a 6% decrease from 2014. Bosnia and Herzegovina, as well as Romania, Montenegro, and Serbia never met the 95% sustainable level for MMR vaccination coverage (Table 2).

Generally, all of the identified Balkan States had a decline in MMR vaccination for children between 12 to 23 months from 2012 to 2016. The resultant effect of this decreasing coverage is seen in the number of measles cases reported in these states (Table 3). Romania and Bulgaria recorded the highest number of measles cases between 2012 and 2016, while Albania had the fewest recorded measles cases. Montenegro had no official data on measles cases in this time period [8].

Table 2: % of Children Immunized Between the Age of 12 – 23 Months from 2012 – 2016 [9]

YEAR COUNTRY	2012	2013	2014	2015	2016
Albania	98	99	98	97	96
Bosnia and Herzegovina	94	92	89	83	83
Bulgaria	94	95	93	92	92
Croatia	95	94	94	93	90
Macedonia	96	96	93	89	82
Montenegro	90	88	76	64	47
Romania	94	92	89	86	86
Serbia	87	92	86	86	82
Slovenia	95	94	94	94	92

Table 3: Measles cases in the Balkan States from 2012 to 2016 [10]

YEAR COUNTRY	2012	2013	2014	2015	2016	TOTAL
Albania	9	0	-	-	16	25
Bosnia and Herzegovina	22	0	3000	1677	133	4832
Bulgaria	1	14	0	219	1	235
Croatia	2	1	18	206	4	231
Montenegro	-	-	-	-	-	-
Romania	3843	1159	59	7	2432	7500
Serbia	0	1	37	383	11	432
Slovenia	2	1	52	18	1	74

Note: Albania lacks reported data for years 2014-2015, while Montenegro lacks reported data for all years from 2012-2016.

Discussion

The trend noticed in the immunization rates of the MMR vaccine across the Balkan states suggests a central cause. There is no particular trend detected in the other European countries regarding MMR vaccination. For instance, Germany, Hungary, and Spain have maintained more than the recommended 95% target with no net decrease from 2012 to 2016. Hungary maintained 99% coverage throughout the five years under study, as well as Germany with 97%, and Spain with 97%. Although Spain had a 2% decrease in 2013 from 97%, it still didn't fall below the 95% MMR coverage level recommended by WHO [9] [11]

ANOVA was utilized at a 95% confidence level to statistically establish the existence of significant differences in the data for deficient coverage of MMR vaccine in the Balkan states (Table 1). The calculated p values were > .05, therefore, the null hypothesis was not rejected. It demonstrated that there are no statistically significant differences among the groups of data. This indicates that a set of common causes have led to a steady decline in MMR vaccination. The examination of MMR coverage in the individual states revealed varying

exposition.

Albania established their routine MMR vaccination in 1971, and they have since then managed to stay true to the plan; hence, the low number of measles outbreaks in the country. From 2012 to 2016, the region had few reported measles cases; however, this study shows that they had a reduced vaccine coverage of 2% from 2012 to 2016. [12] This is a slight decrease, which can be attributed to a negligible cause. According to the research work by Pojani et al, [13] one of the early challenges Albania encountered in MMR immunization coverage was an insufficient supply of the vaccine, such that it wasn't enough to immunize the children within the age group. This led to a national coverage below the 95% recommended level. [13] Also, Nelaj et al, observed reduced vaccination coverage in Albania from 2009 – 2010. [14] They reported that the major cause for the low vaccination coverage is the poor statistical data available in the region, existence of remote areas, and the high migration rate such that children fail to get vaccinated as scheduled. [14]

Bosnia and Herzegovina didn't meet the recommended 95% coverage in the period under study. In 2012, 94% MMR vaccination coverage was achieved, which reduced measles cases in the population. [15] Nevertheless, in subsequent years a lower vaccination coverage was noted, leading to more recorded outbreaks of measles. In 2014, 3000 measles cases were reported in the region, which is also the same year where a reduced MMR vaccination coverage of 5.3% occurred. Bosnia and Herzegovina nosedived from 94% in 2012 to 83% in 2016, and during this downward transition, a major measles outbreak occurred from 2014 to 2015. [15][16] Hukic et al's report on this outbreak made known that majority of the outbreak affected the unvaccinated population of the country, which amounted to 70% of the population, while 20% of the affected population had unknown vaccination status. [17] [18] The rationale for low MMR vaccination in the region was connected to the war effects, as well as parental influence in preventing their children from MMR vaccination. [19] Due to the recent controversies of developmental disorders surrounding MMR vaccination, parents hesitated to take their wards for immunization, thus contributing to low MMR vaccination in the region. [20] [21]

The lifestyle of the population in Bulgaria and Romania is a predisposing factor to low vaccination coverage. [22][23] The technical report of ECDC grouped the population as nomadic, comprising of the highest population of Roma people. [24] Romania and Bulgaria have the highest population of Roma people, 8.32% and 10.33% respectively, and this group of people have been the most susceptible to measles outbreaks. [24] An outbreak of measles from March to August 2017 in Bulgaria, as reported by the National Measles Surveillance system, affected mostly the Roma population. Out of the 204 reported cases, 80.9% of which representing 165 children below 9 years, resulted in the death of one child. [25] It was discovered that 41% of the reported cases were unvaccinated. [25] Their frequent travelling and migration makes it challenging to obtaining information on their vaccination and health status. In addition, these lifestyles cause difficulties in their access to health care which would benefit Roma children needing MMR vaccinations. In a study done to evaluate the effects of this health gap, it was observed that there is an evidently large difference in vaccination coverage between the Roma population and the non-Roma groups. [26] Roma children are less likely by 38.6% to be vaccinated with the MMR vaccine, which is explained to an extent by their socio-economic status. [26] It was affirmed that an increase to health care facilities will improve their immunization status. Also, the geographical settlements of these groups in rural areas are lacking healthcare providers. Other challenges that have contributed to low MMR vaccination coverage in the region are the poor health infrastructures, illiteracy (over 30% of Roma youths can't read, write or speak Bulgarian well enough), administrative barriers seen in the low registration of Roma children with health facilities due to lack of identity documents and access to primary health care.

Conclusion

In this study, we examined the coverage rate of MMR vaccination in the Balkan states, incidence rates of measles cases, and attempted to ascertain possible causes for the low coverage. It was possible to determine that some of these causes leading to low MMR vaccination coverage are related to the existence of remote areas, lack of centralized information, ongoing wars in the region, and the nomadic lifestyle of the population. Statistical analysis suggests that these causes are common across countries in the region.

Furthermore, recent controversies related to the side effects of MMR vaccinations have increased the low coverage of MMR vaccine in the Balkan states. These controversies resulted from a perceived lack of proper testing of vaccines to ascertain their safety and efficacy in humans. [27] The development of an anti-vaccination movement in Europe had a negative impact on parents' attitude to MMR immunization. Their opinions on vaccinations are not proven, and they continue to misinform parents with several side effects of vaccinations. [28] Since humans generally depend on each other for personal experiences and information when it concerns infectious disease, the influence of these anti-vaccination movements have greatly affected the coverage of MMR vaccination in most Balkan states.[28] Based on recent research [29], educational programs aiming to improve the knowledge of parents in regards to immunization have led to significant and positive changes in terms of knowledge. Although research on this topic is still ongoing, it is a promising avenue of intervention to mitigate the impact of anti-vaccination movements. Furthermore, training doctors on their specific approaches towards immunization has also

been shown to be an effective strategy – specifically, by recognizing the parents' concerns, respecting their attitudes, and only afterwards attempting to correct their misconceptions regarding vaccination [30].

As suggested by most research, the total elimination of measles will occur through the process of herd immunity. Thus, measles must be eradicated in all countries according to the global eradication programme through continuous immunization by means of the MMR vaccine. This should involve implementing strategies that will closely keep track of the yearly scheduled vaccination for measles, such that the complete doses will be available based on the surveyed data for new births. Also, efforts should be made towards vaccinating children who are unvaccinated to close up every opportunity through which measles can re-infect the population. To close up the susceptible groups in the Balkan community, more efforts should be directed to improve the retrieval of data in the Roma population, and health policies should solve the challenge of proper education, housing and socio-economic status. One way to achieve this would be through the creation of vaccine registration systems which would send reminders on the vaccination schedule, while also providing immunization services in specialized medical stations, or, alternatively, by integrating health networks – to achieve this, civil society organizations can play a pivotal role by divulging information through underrepresented channels such as blogs and social media, acting as intermediaries between the experts and the general public [31]. Finally, to further curb these challenges, research institutes and governmental agencies should sensitize the society about the benefits of vaccination in children and further publicize clinical trials of vaccinations to prove its safety and efficacy to the public.

References (numerical)

1. The Centre for Disease Control and Prevention. Vaccines and preventable diseases. 2016, https://www.cdc.gov/vaccines/vpd/mmr/public/index.html.
2. Strebel PM, Papania MJ, Parker Fiebelkorn A, Halsey NA. Measles vaccine. In: Plotkin SA, Orenstein WA, Offit P. Vaccines. 6th ed. Elsevier Saunders, 2013:352–87.
3. European Centre for Disease Prevention and Control. Measles and rubella monitoring – December 2012, Stockholm. ECDE; 2012.
4. European Centre for Disease Prevention and Control. Ongoing outbreak of measles in Romania, risk of spread and epidemiological situation in EU/EEA countries – 3 March 2017, Stockholm. ECDE; 2017.
5. Muscat M, Marinova L, Mankertz A et al. The measles outbreak in Bulgaria, 2009 – 2011: An epidemiological assessment and lessons learnt. Euro Surveill. 2016;21:9:30152.
6. Kondova T.I, Milenkovic Z., Marinkovic PS. Measles outbreak in Macedonia: Epidemiological, clinical and laboratory findings and identification of susceptible cohorts. PLoS One. 2013; 8:9.
7. European Centre for Disease Prevention and Control. Monthly measles and rubella monitoring report – December, 2017 Stockholm. ECDE; 2017.
8. Laušević D, Tiodorović B, Begić S. The impact of a'chosen'physician on immunization coverage with MMR vaccine. Acta medica Medianae. 2015;54(2):56-62.
9. The World Bank. Immunization Measles (% of Children Ages 12- 23 Months). World Bank Group, 2017. https://data.worldbank.org/indicator/SH.IMM.MEAS?locations=BA-AL.
10. European Centre for Disease Prevention and Control. Annual Surveillance Data for Measles. ECDE; 2018. https://ecdc.europa.eu/en/measles/surveillance-and-disease-data/annual-surveillance-data.
11. WHO. Eliminating measles and rubella and prevention congenital rubella infection, WHO European region strategic plan 2005–2010 http://www.euro.who.int/__data/assets/pdf_file/0008/79028/E87772.pdf. Accessed 04 January 2018
12. Albania: WHO and UNICEF estimates of immunization coverage. July 4, 2017. https://data.unicef.org/wp-content/uploads/country_profiles/Albania/immunization_country_profiles/immunization_alb.pdf.
13. Pojani R., Nelaj E., and Ylli Alban. An insight into the immunization coverage for combined vaccines in Albania. European Scientific Journal. 2017; 13:3: 1857 – 7881.
14. Nelaj E., Bino S., and Preza I. Albania vaccination coverage 2009 – 2010. Institute of Public Health. 2011. https://ecdc.europa.eu/sites/portal/files/media/en/eurovaccine/Documents/Eurovaccine%202011/Eurovaccine_2011_Nelaj.pdf.
15. HukicM, HajdarpasicA, RavlijaJ, LerZ, BaljicR, DedeicLjubovicA, et al.Mumps outbreak in the Federation of Bosnia and Herzegovina with large cohorts of susceptibles and genetically diverse strains of genotype G, Bosnia and Herzegovina, December 2010 to September 2012.Euro Surveill. 2014;19:33:20879. http://dx.doi.org/10.2807/1560-7917. ES2014.19.33.20879 PMID:25166347
16. Robert H., and Damien J. International measles incidence and immunization coverage. J Infec Disease. 2011; 204:1: 158 – 163. doi:10.1093/infdis/jir124.
17. Hukic M, Ravlija J, Karakas S, Mulaomerovic M, Dedeic Ljubovic A, Salimović-Besic I, Seremet M, Ahmetagic S, Comor A, Feric E. An ongoing measles outbreak in the Federation of Bosnia and Herzegovina, 2014 to 2015. Euro Surveill. 2015;20:9:21047. Available online:

http://www.eurosurveillance.org/ViewArticle. aspx?ArticleId=21047
18. CDC Course Textbook Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book, Measles module. May 2012;12: 173-193.
19. World Health Organization. Measles immunization coverage. Global Health Observatory (GHO). 2016.
20. Kaic B, Gjenero-Margan I, Kurecic-Filipovic S, Muscat M. A measles outbreak in Croatia, 2008, Euro Surveill, 2009.http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19083. Accessed 04 January 2018.
21. Muscat Mark. Who gets measles in Europe? The Journal of Infectious Diseases. 2011; 204 :S353 – S365. https://doi.org/10.1093/infdis/jir067.
22. Santibanez S, Prosenc K, Lohr D, Pfaff G, Jordan Markocic O, Mankertz A. Measles virus spread initiated at international mass gatherings in Europe, 2011. Euro Surveill. 2014;19:35:20891. http://dx.doi.org/10.2807/1560-7917. ES2014.19.35.20891 PMID:25210982
23. SantibanezS, HübschenJM, MullerCP, FreymuthF, MosqueraMM, MamouMB, et al.Long-term transmission of measles virus in Central and continental Western Europe. Virus Genes. 2015. [Epub ahead of print]. http://dx.doi.org/10.1007/s11262-015- 1173-1 PMID:25663095.
24. Technical Report. Review of outbreaks and barriers to MMR vaccination coverage among hard to reach populations in Europe. Venice II Consortium – Sep. 2012. ECDC.
25. Kurchatova A., Krumova S., Vladimirova N., Nikolaeve-Glomb L., Stoyanova A., Kantardjiev T., and Gatcheva N. Preliminary findings indicate nosocomial transmission and Roma population as most affected group in ongoing measles B3 genotype outbreak in Bulgaria, March to August 2017. Euro Surveill. Sep 2017; 22:36: 30611. doi: 10.2807/1560-7917.ES.2017.22.36.30611.
26. Duval L., Wolff F.C., McKee M., and Roberts B. The Roma vaccination gap: Evidence from twelve countries in Central and South- East Europe. Vaccine November 2016; 34:5524 – 5530. https://doi.org/10.1016/j.vaccine.2016.10.003.
27. Karafillakis E., Dinca I., Apfel F., Cecconi S., Wurz A., Takacs J., Suk J., Calentano L.P., Kramarz P., and Larson HJ. Vaccine hesitancy among healthcare workers in Europe: A qualitative study. Vaccine. September 2016; 34: 41: 5013 – 5020. https://doi.org/10.1016/j.vaccine.2016.08.029.
28. Barbacariu C.L. Parents refusal to vaccinate their children: An increasing social phenomenon which threatens public health. Procedia-Soc and Behavioural Sciences. September 2014;149:84-91. https://doi.org/10.1016/j.sbspro.2014.08.165.
29. Awadh AI, Hassali MA, Al-Lela OQ, Bux SH, Elkalmi RM, Hadi H. Does an educational intervention improve parents' knowledge about immunization? Experience from Malaysia. BMC pediatrics. 2014 Dec;14(1):254.
30. MSc CPD HA, HVCert RG. Parents' difficulties with decisions about childhood immunisation. Community Practitioner. 2008 Oct 1;81(10):32.
31. Gostin LO. Law, ethics, and public health in the vaccination debates: politics of the measles outbreak. Jama. 2015 Mar 17; 313(11):1099-100.