

Comparison of Impact of Single Dose and Multiple Dose Measles Vaccination Strategies on Measles Transmission Patterns

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Abstract: Background: Multiple dose measles vaccination intervention was applied in Gweru City, Zimbabwe, in 1990-96, following a single dose applied at 9 months of age during 1983-89. In the same periods in Bulawayo, only a single dose of measles vaccine was applied to children at 9 months of age. This study investigated the impact on measles transmission patterns of multiple dose measles vaccination strategy. Study design: Quasi-experimental community intervention applied in Gweru city with Bulawayo city as a control. The intervention included a single mass vaccination campaign carried out in 1990 targeted at children aged 12-119 months irrespective of their vaccination status or disease history. Children born after 1990 were vaccinated at 9 months of age plus another single dose applied at any point between ages of 12 and 23 months (revaccination). Subjects: Measles cases were identified in both cities through surveillance. Results: Mean coverage rates for measles vaccine applied at 9 months of age were in 1983-89 85.7% and 84.6% in Bulawayo and Gweru respectively, while in 1990-96 they were 89.0% and 89.7%, respectively. In both periods the vaccine coverage rates were not significantly different in the two cities ($p=0.464$). In the 12-23 months age group, Gweru measles vaccination coverage rate in 1990 was 83% for single dose and 82.4% for second dose in 1990-96. Measles incidence rates in 1983-89 in both cities significantly declined and were not significantly different ($p=0.898$). Median incidence rates of measles in 1990-96 were 131.0 and 19.0/100 000 population in Bulawayo and Gweru respectively and these were significantly different ($p=0.021$). Bulawayo had measles epidemics in 1992, 1993, 1994 and 1996. In Bulawayo in 1993-96 vaccinated measles cases accounted for a median of 58% of all reported cases aged 10-119 months. Median incidence rates of measles among vaccine failures aged 10-119 months in 1993-96 in Bulawayo and Gweru were 419.1 and 13.1/100 000 population respectively and these incidence rates were significantly different ($p=0.021$). In Bulawayo in 1993-96 cases aged 60-119 months accounted for a median of 56.5 % of all reported cases. Median incidence rates of measles among cases aged 60-119 months in 1993-96 in Bulawayo and Gweru were 869.9 and 26.9/100 000 population respectively and these rates were significantly different ($p=0.021$). Conclusion: Multiple dose vaccination strategies led to significantly reduced measles transmission in Gweru (compared to Bulawayo) in 1990-1996 by minimizing occurrence of vaccine failures and occurrence of cases in older children aged 60-119 months.

Keywords: Multiple Dose Vaccination Strategies, Measles Vaccine Failures, Measles Cases Aged 60-119 Months

1. Introduction

A study was carried out to determine the impact of single dose and multiple dose measles vaccination strategies on occurrence of measles. The study compared occurrence of measles in Gweru (population: 124 735) and Bulawayo (population: 620 936) cities in Zimbabwe in 1983-89 when both cities had a strategy that solely entailed applying measles vaccine at nine months of age and in 1990-96 when multiple

dose vaccination strategies were applied in Gweru while Bulawayo continued to apply measles vaccination to children aged 9 months.

2. Materials and Methods

2.1. Study Type

Application of multiple dose measles vaccination strategy

among children in the city of Gweru was a quasi-experimental community intervention with both internal and external comparisons.

(a) Internal comparison or “self-controlled” intervention (before and after) aspect of the study in Gweru has already been described.¹

(b) External comparison or external “control”: The purpose of this paper is to describe this aspect of the study by comparing measles transmission patterns in Gweru where the intervention was carried and Bulawayo, the “control”, where the intervention was not carried out.

2.2. Study Hypothesis

The hypothesis of the study was that: At high coverage rates of measles vaccine applied to children at nine months of age measles incidence rates would decline. Despite this decline, however, there would be an increase in occurrence of vaccine failures (occurrence of cases among vaccinated children) and a shift of disease to a school-going children population aged 60-110 months. High occurrence of vaccine failures in these older age groups would lead to accumulation of susceptibles who cause epidemics in the future. Multiple dose measles vaccination strategies could reduce occurrence of these susceptibles thus averting the occurrence of epidemics and maintaining low measles transmission.

2.3. Multiple Dose Measles Vaccination Strategy in Gweru

A two-pronged strategy was used in the provision of multiple doses of measles vaccine. The first variant of this strategy was that of a rapid and comprehensive “clean up” vaccination campaign targeted at all children aged 12-119 months (regardless of disease history or vaccination status) to clear this population of all susceptibles. This campaign was carried out over a two week period in early 1990. In the second variant of the strategy children who had had vaccination at 9 months of age at the city’s static health facilities were given another single dose (revaccination) at any point between ages of 12 and 23 months at the same facilities. This second strategy was implemented over the rest of the project period from immediately after the campaign.

2.4. Vaccination Records

In Gweru routine vaccinations are indicated on child health cards and data on vaccinations are compiled monthly. From 1990 revaccination were also indicated on child health cards and figures on revaccinations were also compiled monthly.

Vaccinations applied during mass campaign of 1990 were indicated on child health cards. Children that did not have child health cards had new ones issued to them on which the campaign vaccination was indicated. Records compiled after the campaign indicated the number of children vaccinated in age classes 12-23, 24-59 and 60-119 months.

2.5. Disease Surveillance

Gweru has had an active measles surveillance system since 1967. Measles cases are identified on the basis of a standard

clinical case definition that is available to staff at all healthcare facilities. There are personnel who are assigned to investigate occurrence of unreported infectious diseases (including measles cases) within communities (active case search). Measles surveillance/investigation forms which have been in use indicate age at infection, gender, presenting/clinical features of disease, need for hospitalization or lack of it, treatment regime, outcome of illness (alive or dead), and occurrence of any other cases in relation to the identified case (which would also be investigated). Indication of vaccination status of measles cases was added to the form in January 1980. When the multiple dose vaccination effort was commenced in 1990 a slot was added on the surveillance form to indicate whether a case had had revaccination either during the campaign of 1990 or routine revaccination that followed the campaign or none. Information from surveillance forms is compiled monthly.

2.6. City of Bulawayo, External Comparison for the Gweru City Multiple Dose Vaccination Project

Bulawayo city was selected to partner the city of Gweru as a “control” at the inception of the multiple dose measles vaccination project in Gweru in 1990 for several reasons. These included:

(a) Up till 1990 the vaccination practices in Bulawayo were similar to those of Gweru. Bulawayo city, like Gweru, had maintained high measles vaccination coverage rates for the vaccine applied at nine months of age and it had the capacity to maintain these rates during the project period 1990-96.

(b) Structures for measles disease surveillance and monitoring of measles vaccinations in Bulawayo are similar to those of Gweru.

(c) The age structure of the populations in Gweru and Bulawayo were similar and so were the living conditions of the two populations.

2.7. Comparison of Vaccination Performance and Occurrence of Measles Between Gweru and Bulawayo Cities

The following comparisons were carried out:

(a) Vaccination coverage rates for vaccine applied at nine months of age in Gweru and Bulawayo in the periods 1983-89 and 1990-96.

(b) Incidence rates of measles in Gweru and Bulawayo in the periods 1998-89 and 1990-96.

(c) Incidence rates of vaccinated cases (vaccine failures) among children aged 10-119 months in both Gweru and Bulawayo cities in the period 1993-96.

(d) Incidence rates of measles in children aged 60-119 months in both Gweru and Bulawayo in 1993-96.

2.8. Data Analysis

The following analyses were carried out:

(a) The student t test was used to compare means of normally distributed data.

(b) The Kruskal – Wallis test was used to compare medians of non-normally distributed data.

(c) The linear trend was determined using chi-square test for linear trend.

(d) 95% confidence intervals were computed in order to identify changes in the incidence rates.

(e) The cut off point for statistical significance was 5%.

3. Results

3.1. Vaccination Coverage Rates

In Bulawayo in 1983-89 vaccine coverage rates for the vaccine applied at nine months of age were 77.0-93.0% (mean= 85.7, SD=5.9) while in Gweru in the same period coverage rates were 72.0-92.0% (mean=84.6, SD 7.7). These coverage rates were not significantly different ($p=0.736$). In Bulawayo in 1990-96 vaccine coverage rates for the vaccine applied at nine months of age were 86.0-90.0% (mean=89.0, SD=1.8) while in Gweru in the same period they were 87.0-92.0% (mean=89.7, SD 1.7). These coverage rates were not significantly different ($p=0.464$).

In 1990-96 in Gweru coverage rates for the second dose of measles vaccine applied to children at 12-23 months were 81-87% (mean= 82.4, SD= 2.1). In the mass vaccination campaign of 1990 in Gweru children aged 12-23, 24-59 and 60-119 months had vaccine coverage rates of 83.0%, 87% and 89% respectively.

3.2. Measles Incidence Rates

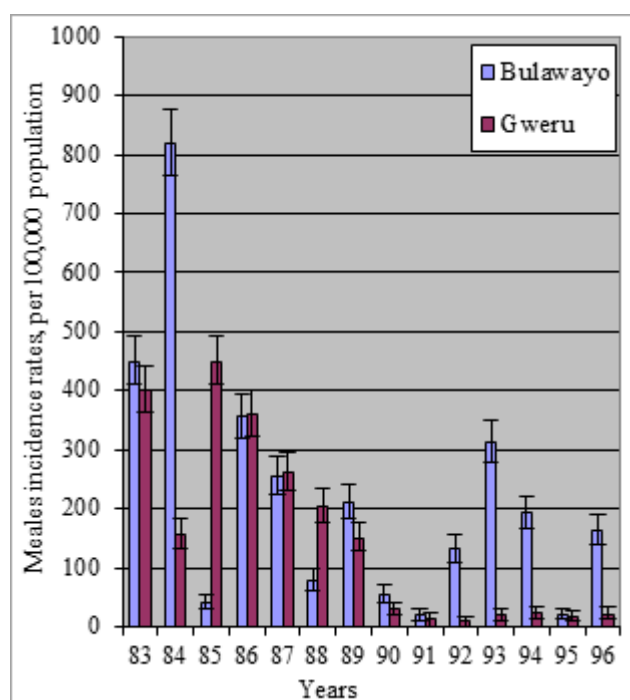


Figure 1. Comparison of measles incidence rates in Gweru and Bulawayo cities in 1983-1996.

In Bulawayo in 1983-89 measles incidence rates were 41.0-820.0/100 000 population (median= 254.0, $Q_1= 79.0$, $Q_3=450.0$) while those in Gweru in the same period were 151.0-450.0/100 000 population (median = 261.0,

$Q_1=156.0$, $Q_3=400.0$). The incidence rates in the two cities were not significantly different ($p=0.898$). Incidence rates in both Bulawayo and Gweru in 1983-89 significantly declined (Bulawayo: X^2 for linear trend=446.04, $p<0.001$ and Gweru: X^2 for linear trend = 88.83, $p<0.001$) – see fig 1.

In 1990-96 measles incidence rates in Bulawayo were 19.0-313.0/100 000 population (median=131.0, $Q_1=20.0$, $Q_3=193.0$) while those in Gweru were 9 to 29.0/100 000 population (median=19.0, $Q_1=13.0$, $Q_3=22.0$). These incidence rates were significantly different ($p=0.021$).

Bulawayo city had measles epidemics in 1992, 1993, 1994 and 1996 – see figure 1.

3.3. Occurrence of Vaccinated Measles Cases Among Children Aged 10-119 Months

The 121-2004 cases of measles (median=1069.0, $Q_1=550.0$, $Q_3=1581.5$) aged 10-119 months reported in Bulawayo city in 1993-96 accounted for 98.6-99.9% (mean 99.1, SD 0.6) of all cases measles cases reported in that period. Of these cases some 58.0-64.0% (median=58.5) had had vaccination against measles. In the same age group in the same period in Gweru 22-30 cases of measles (median=25.5, $Q_1=23$, $Q_3=28.5$) were reported of whom 5-11 cases (median 10.0) had had measles vaccination at 9 months of age.

Incidence rates of vaccinated measles cases in the age group 10-119 months in Bulawayo in 1993-96 were 46.4-836.7/100 000 (median=419.1, $Q_1=224.3$, $Q_3=636.3$) while in Gweru these rates were 7.3-21.8 (median=13.1, $Q_1=8.1$, $Q_3=19.5$). The incidence rates of vaccinated cases in the age group 10-119 months in the two cities were significantly different ($p=0.021$).

3.4. Occurrence of Measles Among Children Aged 60-119 Months

In 1993-96 in Bulawayo 67-1167 cases of measles (median=656.5, $Q_1=340.5$, $Q_3=933.0$) were reported in age group 60-119 months and these accounted for 53.0-71.0% (median=56.5, $Q_1=54.0$, $Q_3=64.5$) of all reported cases of measles. Of these cases some 55.0-67.2% (median=57.9) had been vaccinated while the rest were not. In Gweru in the same age group in the same period 9-13 cases (median=10.5, $Q_1=9.5$, $Q_3=12.0$) were reported of whom 3-7 cases (median=4.5) had been vaccinated at 9 months of age while the rest were not.

Incidence rates of measles in age group 60-119 months in Bulawayo in 1993-96 were 95.5-1660.6/100 000 (median=868.9, $Q_1=469.0$, $Q_3=1278.0$) while those in Gweru were 7.3-49.5/100 000 population (median=26.9, $Q_1=10.8$, $Q_3=44.6$). Incidence rates of measles in the age group 60-119 months age group in the two cities were significantly different ($p=0.021$).

4. Discussion

This study has shown that in 1983-89 both Gweru and Bulawayo maintained similar levels of high coverage rates of

measles vaccine applied at nine months of age and that under this vaccination regime both cities experienced a decline in measles incidence rates. It has also been shown that in 1990-96 both cities maintained similar levels of high coverage rates for vaccine applied at nine months of age.

In this latter period, however, Bulawayo had higher incidence rates of measles than Gweru and had epidemics

Occurrence of epidemics after low transmission, as experienced in Bulawayo in 1992-96, has been described in some developing countries with moderate to high measles vaccine coverage rates for measles vaccine that is applied at nine months of age.^{2,3} These countries or areas include Latin America and Caribbean countries³, Harare in Zimbabwe⁴, Muyinga in Burundi⁵, Lesotho⁶, Swaziland⁶ and Cape Town in South Africa⁷. These epidemics have partly been due to accumulation of vaccine failures.^{3,7} Occurrence of vaccine failures is blamed on a vaccine of less than 100% efficacy^{3,8,9} or waning immunity in immunized persons^{3,5,7,8}. In the current study it has been shown that vaccine failures played an important role in the high measles transmission experienced in Bulawayo in years 1993, 1994 and 1996. In Gweru in 1993-96 occurrence of vaccine failures may have been minimized on account of revaccination either during the campaign of 1990 or routine application of second dose of vaccine to children aged 12-23 months that followed this campaign. Revaccination is known to improve vaccine efficacy thereby reducing the occurrence of vaccine failures.¹⁰⁻¹²

Epidemics described above have also partly been due to a high occurrence of measles in older children and adults, persons outside the primary target age group of the Expanded Programme on Immunization.^{2,3,6} These epidemics have involved both vaccine failures and unvaccinated persons.³ The explanation for the high occurrence of cases among older children and adults has been that for vaccine applied in infancy, vaccination of large proportion of the community reduces the chances of susceptibles being exposed to the infectious agent in infancy such that they would be exposed at an older age leading to an increase in the average age at infection.^{2,3,6} In this study it has been shown that epidemics that occurred in Bulawayo in 1992-96 could partly be blamed on high transmission among vaccinated older children and to a lesser extend unvaccinated older children. Epidemics that have mostly involved vaccinated older children, as observed in Bulawayo, have been described in Cape Town (South Africa)⁷ and Jordan¹³. Unlike Bulawayo that relied solely on a vaccination programme that applied the vaccine at 9 months of age, Gweru may have avoided high occurrence of cases among older children aged >60 months on account of the vaccination campaign of 1990 which covered these children who were either revaccinated if they had had vaccination in infancy or received vaccination for the first time if they had not had vaccination before.

Although vaccination coverage rates for the vaccine applied at nine months of age were as high in Gweru as in Bulawayo in 1990-96, thus minimizing occurrence of unvaccinated cases in both cities in this period, the mass vaccination campaign of 1990 gave Gweru an opportunity to reach many susceptibles

in the various age groups that were included in the campaign. This could partially explain the low measles transmission that occurred in Gweru and not in Bulawayo where a similar campaign was not carried out.

5. Conclusion

In 1983-89 in both Gweru and Bulawayo, at high vaccination coverage rates of single dose measles vaccine applied at nine months of age, measles transmission declined. Bulawayo, despite maintenance of high coverage rates of vaccine applied at nine months of age in 1990-96, had accumulation of vaccine failures in children aged 10-119 months and susceptibles (both vaccine failures and unvaccinated children) among older children aged 60 months and over that gave rise to epidemics after a period of declining and low transmission. In Gweru in 1990-96 application of multiple dose measles vaccination regime led to low level of measles transmission (compared to Bulawayo) by minimizing vaccine failures and cases among older children aged 60 months and over.

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