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Measles Susceptibility in Children in Karachi, Pakistan

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Abstract

Measles, despite being vaccine preventable is still a major public health problem in many developing countries. We estimated the proportion of measles susceptible children in Karachi, the largest metropolitan city of Pakistan, one year after the nationwide measles supplementary immunization activity (SIA) of 2007–08. Oral fluid specimens of 504 randomly selected children from Karachi, aged 12–59 months were collected to detect measles IgG antibodies. Measles antibodies were detected in only 55% children. The proportion of children whose families reported receiving a single or two doses of measles vaccine were 78% and 12% respectively. Only 3% of parents reported that their child received measles vaccine through the SIA. Among the reported single dose measles vaccine recipients, 58% had serologic immunity against measles while amongst the reported two dose measles vaccine recipients, 64% had evidence of measles immunity. Urgent strengthening of routine immunization services and high quality mass vaccination campaigns against measles are recommended to achieve measles elimination in Pakistan.

Keywords

Measles; Pakistan; vaccination; seroprevalence

Introduction

Measles elimination is one of the critical elements in achieving the Millennium Development Goal of reducing the child mortality by two thirds by the year 2015. Being a member of WHO EMRO region, Pakistan adopted a resolution in 1997 to eliminate measles by 2010 (1, 2). To eliminate measles, regional goal was to reduce the measles associated mortality by 90% by 2010 and to reduce the incidence of measles to 1 case per million (3). Although measles associated mortality has been reduced by 90% from 2000 to 2007 in the EMRO region (4), measles outbreaks continue to occur in Pakistan where the incidence of measles in 2007 was reported as 2 cases per thousand children less than 5 years of age (5).

In order to effectively control measles, routine measles vaccine coverage of >90% is required (6). Another key element of measles control is to ensure that every child receives at

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least two doses of measles vaccine, preferably after 1 year of age (7). Until 2007, a single dose of measles vaccine was being used in Pakistan's National EPI program at 9 months of age, and the coverage of this single dose was only 60% (8). Therefore, up to 2 million children were left unvaccinated against measles every year. Realizing the potential occurrence of major measles outbreaks, a nationwide one year measles vaccine supplementary immunization activity (SIA) was conducted in 2007–2008 (9). This campaign was reported to be the largest measles vaccine campaign in history and reportedly more than 66 million children aged 9 months to 13 years (97% of the target population) were vaccinated (9).

Despite this extensive supplemental immunization campaign, measles outbreaks have continued to occur in Pakistan. It is therefore important to determine the effectiveness of this measles SIA by determining what proportion of children is still seronegative for measles and hence susceptible to the disease. If a significant proportion of children are found to be susceptible, then a strong case for a repeat and more effective SIA against measles can be made.

Methodology

This study was done in Karachi, the largest metropolitan city of Pakistan located in the Sindh province at the coast of Arabian Sea. Karachi comprises of 18 towns (10) and approximately 7750 clusters. Children between the ages of 12 to 59 months were eligible for this study if they were living in Karachi for the past three months. Sampling frame was a complete line listing of 90 randomly selected clusters of Karachi which have the representation from all the towns of Karachi. Following the EPI 60 X 7 multi stage cluster sampling technique (11), 60 clusters were selected, and at least 7 children from each cluster were randomly selected from the given sampling frame. Data collectors checked for an eligible child in the randomly selected house hold. If an eligible child was not available at home after three attempts or if the house was locked, then the next randomly selected house was approached. Number of households approached and number of participant at each stage are shown in figure 1. If an eligible child was found and caretaker was present, then written informed consent was obtained from the caretaker. After consent, a questionnaire was administered to gather information of socio-demographic characteristics and education status of parents, child's vaccination status and past history of measles infection. Child's immunization cards were reviewed if provided and height and weight of each child was recorded for nutritional assessment.

Oral fluid was collected by Oracol® oral collection devices (Malvern Medical Developments, Worcester, UK) (12, 13). Sample was collected following manufacturer's protocol. Oracol® device was rubbed for one minute on the base of gums of both upper and lower jaws inside and out like a toothbrush (12). The collected oral fluid sample was transported in icepacks to the research laboratory at the Aga Khan University and stored at 2–8C (14) for analysis. We tested oral fluid specimens for antibodies to measles virus using Microimmune® IgG capture EIA kit (Microimmune Brentford, Middlesex, UK) (15). The accuracy of salivary measurements of measles IgG antibody as a marker of immunologic protection against measles has been previously validated (14). Sensitivity and specificity of EIA test for measles IgG detection using oral fluid is 93% and 98% respectively compared to the serum (16).

Sample Size

According to official estimates, 97% children 9 months to 13 years of age received measles vaccine during the SIA campaign of 2007–08. Since the seroconversion rate after a

single dose of measles vaccine is 85%, we expected that 82% ($97\% \times 85\%$) of the children will have measles IgG. Keeping the 5% bound on the error of estimation for a 95% confidence interval, applying design effect of 2 to adjust for cluster sampling (17) and after inflating the sample size by 10% to account for non-responders, our estimated sample size was 499.

Statistical analysis

Data were double entered, checked and validated in Epi data version 3 and analyzed by SAS version 9.1 and SPSS version 17. Weighted analysis was done to adjust for cluster sampling (18). Categorical variables were compared by chi-square test and continuous variables by student's t-test. Multivariable analysis using multiple logistic regression was used to identify factors associated with presence of measles IgG antibodies and to adjust for potential confounders.

Results

A total of 504 randomly selected children from Karachi aged 12–59 months were enrolled in the study, Table 1 shows the baseline characteristics of study subjects. The mean age of study subjects was 34.7 months (SD 13 months) with almost equal distribution of male (251) and female (253) children. Mean age of children receiving first dose of measles vaccine was 9 months and 15 months for second dose of measles vaccine.

Saliva samples for serological analysis were available for all of the 504 study subjects. Overall, 276 (55%) children had IgG antibodies against measles in their saliva. Caretakers of 394 (78%) children reported the receipt of at least a single dose of measles vaccine, and it was confirmed by vaccination card in 143 (36%) subjects. History of second dose of measles vaccine was reported by 62 (12%) children and vaccination card documenting the same was provided by 34 (55%) subjects. Non routine / extra dose of measles vaccine given by SIA was reported by 16 (3%) subjects. History of past measles infection was present in 37 (7%) children. Among these 37 children, 25 (68%) were found to have serologic immunity. Wasting was present in 67 (13%), 197 (39%) were stunted and 151 (30%) were underweight.

Presence of serologic immunity against measles was associated with increasing age of the child, and with the history of measles vaccination. Children with card verified information of single dose measles vaccination were more likely to have serologic immunity against measles compared to children who had not received the measles vaccine (adjusted odds ratio [OR] 2.67, 95% CI 1.39– 5.10). Verbal report alone of receipt of one dose of measles vaccine was not associated with measles seropositivity. Card-verified receipt of two doses of measles vaccine was also associated with increased measles seropositivity (76%) with adjusted OR of 1.85 (0.64, 5.32). However, there were only 34 children with card-verified receipt of two doses. Verbal report of receipt of two doses showed no association with seropositivity. No difference in presence of immunity was found if child was well-nourished or wasted. (Table: 2).

Discussion

Our study showed that after one year of a reportedly successful nationwide measles vaccine SIA, only 55% of 12 to 59 months children in Karachi were protected against measles. This seroprevalence was considerably less than the expected seroprevalence of 82%, which was calculated by using reported measles vaccine coverage of 97% in the SIA (19). The proportion of children reportedly vaccinated through the SIA was surprisingly only 3%. We feel that it is highly unlikely that parents would be unaware if their child received a non-

routine additional dose of measles vaccine as it is an injectable vaccine. There can be several reasons for this disparity in official estimates and our results. A likely reason is that official estimates at the district or province level were exaggerated to show campaign success, as has been reported for polio vaccine campaigns. Another reason could be that 97% coverage was the overall estimated figure from the whole country and our study was done only in one city. Efforts may have been more focused on vaccinating children in under-served areas than to vaccinate children in urban areas like Karachi. Large metropolises such as Karachi present unique challenges for vaccinators because of high-rise apartment complexes, security fears, and higher rates of refusals from middle and high-income households. However, most parents reported no knowledge about the measles SIA campaign. This may be because of lack of aggressive advertisement campaigns, publicity or mass messaging through electronic or print media.

We used oral fluid collected by using a swab to detect measles serology. This method is now widely used to assess population immunity levels against measles and has a sensitivity of 93% and specificity of 98%, compared to serum antibody (16). With this non invasive, easy to use technique, evaluation of measles serologic immunity should be incorporated in measles elimination programs for highly endemic countries as a tool to measure the effectiveness of both routine and supplementary measles immunization activities.

Routine vaccination with a single dose of measles vaccine was reported by 78% of the caretakers of study subjects in our study. This was higher than the Pakistan Demographic and Health Survey (PDHS) estimate of measles vaccine coverage, which reports that 50.7% children of 12–23 months were vaccinated against measles in Sindh province (8). One reason for more vaccinated children in our sample was the broader age group (12 to 59 months) compared to the age group in PDHS (12 to 23 months). Another reason could be that in the PDHS data, the proportion of vaccinated children is a combined estimate of Sindh urban and rural areas while our study was limited to urban areas only.

Among the single dose measles vaccine recipients in our data, vaccine history of only 36% children could be confirmed by card and remaining children had no documentation of measles vaccine although caretakers recalled their child as receiving the vaccine. Our results showed that card retention was associated with the presence of serologic immunity and verbal report alone of child's vaccination was not associated with the presence of immunity. Different studies have assessed the reliability of verbal report of vaccine receipt versus verification by card or other written records. Some studies suggested that verbal information can be a reliable source of information for vaccine surveys (20). Others showed that verbal information gives incorrect estimates of vaccine recipients (21). Our study shows that verbal report was an unreliable predictor of vaccination status in children residing in Karachi.

Caretakers of only 12% of the children reported receiving the second dose of measles vaccine. Second routine dose of measles vaccine was included in Pakistan's EPI in 2009 but second dose was been given at private sectors in combination with mumps and rubella (MMR). As MMR vaccine is not accessible to the vast majority, so this low proportion of second dose recipients is not unexpected. Among card verified two-dose vaccine recipients, 76% demonstrated serological immunity; however small sample size resulted in wide confidence intervals (Adjusted OR 1.85, 95% C.I 0.64, 5.32). Of note, measles antibody could not be detected in 24% of children with card confirmed receipt of two doses of measles vaccine. Although the sample size was small (only 34 children received two doses of measles vaccine verified by card documentation), possible explanations for vaccine failure are first dose of vaccine given before 9 months of age (22) with the potential for interference from maternally-acquired antibody (23). Other known reasons for vaccine failure are improper administration or improper cold chain maintenance of vaccine (24).

Maternal education showed an increasing trend with measles immunity. This finding was consistent with other studies as well (25). No trend was observed for father's education.

Presence of serologic immunity was not different in children who were well nourished compared to wasted children. This finding was consistent with the existing literature which suggests that malnutrition does not affect the development of measles antibodies after vaccination (26). There have been misconceptions about measles vaccine causing immune-suppression in malnourished children, and this sometimes leads to reluctance of vaccinating malnourished children against measles by health providers and parents (26). Malnourished children therefore become even more vulnerable to measles infection, which is most severe in this population. Malnourished children should therefore be a high priority group for measles vaccination in order to decrease measles morbidity and mortality.

Our study had some limitations. We had to rely on the verbal report of caretakers regarding vaccination status for a large proportion of our study children. We were not able to verify this verbal information from local EPI centers or any other written records. We visited few EPI centers to get vaccination information but record keeping was inconsistent and we failed to find the required information. However, our data show that verbal report of vaccination does not associate with measles immunity, but card verified reports do correlate with immunity. Another limitation was the participation refusal rate of almost 26% which could have biased study population selection and resulted in an under or over-estimate of measles immunity in population. The major reason for refusal was the poor law and order situation in the city, due to which many mothers were reluctant to interact with strangers.

In conclusion, our study showed that even after one year of mass measles vaccination campaign, only 55% children in Karachi had detectable measles serologic immunity. This shows that a large proportion of the under 5 year population in Karachi is still susceptible and future measles outbreaks are likely. In addition to urgent strengthening of routine immunization, immediate mass level high-quality measles vaccination campaign is required. Also monitoring and evaluation of vaccination campaigns by assessment of measles serologic immunity on national scale should be done regularly and vaccination strategies should be refined on basis of serologic immunity estimates to effectively control and eliminate measles from this country, specially as Pakistan recovers from the unprecedented floods of 2010.

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Figure 1.
Flow chart of participants

Table 1

Baseline clinical and socio-demographic characteristics of study subjects

Variables		Frequency (%)
		n=504
Age in months	12 ≤ 24	126(25)
	>24 ≤ 36	128(25)
	> 36 ≤ 48	143(28)
	> 48 ≤ 59	106(21)
Mean (SD)	34.7(13)	
Sex	Female	251(50)
	Male	253(50)
Mother's education *	No formal education	150(30)
	≤ 10 years	202(40)
	11 to 14 years	132(26)
	≥ 14 years	19(4)
Father's education *	No formal education	109(22)
	≤ 10 years	216(43)
	11 to 14 years	147(29)
	≥ 14 years	30(6)
Socio-economic status [¶]	Low	211(42)
	Middle	154(31)
	High	135(27)
History of 1st dose measles vaccine	No	110(22)
	Yes	394(78)
	Card verified	143(36)
	Verbal	251(64)
History of 2nd dose measles vaccine	No	442(88)
	Yes	62(12)
	Card verified	34(55)
	Verbal	28(45)
History of vaccine through SIA	No	488(97)
	Yes	16(3)
Past measles infection [✓]	No	467(93)
	Yes	37(7)
Wasting [†] (Weight for height)	No	437(87)
	Yes	67(13)
Stunting [†] (height for age)	No	307(61)
	Yes	197(39)
Under weight [†] (weight for age)	No	353(70)
	Yes	151(30)

* Information about a mother and father's education was missing.

[¶]Information of 4 participants were missing. This variable was constructed by using household items like telephone /mobile, television, refrigerator, air conditioner, motor cycle, car, washing machine, VCR / DVD player and generator / UPS.

[§]Diagnostic criteria was age of child > 5 months and history of fever and maculopapular rash or history of cough, coryza or conjunctivitis or peeling of skin was present.

[†]Using Z score of < -2 SD

Table 2

Factors associated with presence of measles serologic immunity in oral fluid among children in Karachi (n=504)

Variables	Measles antibodies present Frequency (%)	Measles antibodies absent Frequency (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Overall	276(55)	228(45)		
History of 1st dose measles vaccine				
No (n=109)	47(43)	62(57)	1	1
Card verified (n=140)	92(66)	48(34)	2.56(1.44, 4.53)	2.67(1.39, 5.10)
Verbal (n=253)	137(54)	116(46)	1.58(0.98, 2.54)	1.64(0.97, 2.79)
History of 2nd dose measles vaccine				
No (n=442)	236(53)	206(47)	1	1
Card verified (n=34)	26(76)	8(24)	2.94(1.29, 6.73)	1.85(0.64, 5.32)
Verbal (n=28)	14(50)	14(50)	0.85(0.37, 1.96)	0.71(0.27, 1.88)
Wasting				
Yes (n=67)	32(48)	35(52)	1	1
No (n=437)	243(56)	194(44)	1.33(0.81, 2.18)	1.46(0.82, 2.61)
Mother's education				
No formal (n=150)	75(50)	75(50)	1	1
≤ 10 years (n=202)	107(53)	95(47)	1.13(0.74, 1.73)	1.18(0.65, 2.15)
11–14 years (n=132)	78(59)	54(41)	1.43(0.90, 2.28)	1.52(0.68, 3.41)
>14 years (n=19)	13(68)	6(32)	2.42(0.75, 7.77)	2.17(0.48, 9.66)
Father's education				
No formal (n=109)	62(57)	47(43)	1	1
≤ 10 years (n=216)	111(51)	105(49)	0.79(0.50, 1.24)	0.61(0.34, 1.10)
11–14 years (n=147)	82(56)	65(44)	0.94(0.57, 1.55)	0.58(0.27, 1.27)
>14 years (n=30)	20(6)	10(33)	1.42(0.62, 3.24)	0.69(0.24, 1.94)
Age in months				
12 ≤ 24 (n=126)	52(41)	74(59)	1	1
>24 ≤ 36 (n=128)	60(47)	68(53)	1.24(0.76, 2.01)	1.34(0.78, 2.28)
>36 ≤ 48 (n=143)	89(62)	54(38)	2.34(1.44, 3.78)	2.84(1.62, 5.00)
>48–59 (n=106)	74(70)	32(30)	3.25(1.88, 5.61)	3.82(2.15, 6.77)