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Effects of Measles Vaccine and Its Associated Risk Factors Among Children Presenting in a Tertiary Care Hospital, Rawalpindi/Islamabad

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Author`s Contribution

[1]Provided concept/research design and manuscript writing. [2,5]statistical analysis and manuscript writing, edit of manuscript and project management, [3]critical revision of the manuscript for important intellectual content, [4,6]responsibility and is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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ABSTRACT

Objectives: To identify risk factors associated with the development of measles among children under 12 years of age in a tertiary care hospital in Rawalpindi/Islamabad and to determine the effectiveness of measles vaccination in the study population.

Methodology: A retrospective case control study was done from January 2022 to January 2023 at the Department of Pediatrics, Holy Family Hospital (HFH), Rawalpindi & PAEC General Hospital, Islamabad. Total 600 children were included in the study. The hospital data record had children under the age of 12 with measles. Case controls were enrolled without measles at the same hospital, matched for age and sex. Study outcomes were analyzed by multivariant regression test adjusted with age and gender.

Results: The average age of the children was 32.24±14.58 months. Mothers with low education were mostly have measles [OR: 4.1, 95% CI: 1.9-6.5, for primary schooling and OR: 1.1, 95% CI: 0.7-2.0, for matriculation]. Children with measles were mostly not breastfed during the first 2 years of life [OR: 0.8, 95% CI: 0.5-1.4]. Cases were also more likely to have never been vaccinated [OR: 8.2, 95% CI: 5.5-15.0] and never vaccinated other children at home [OR: 6.5, 95% CI: 4.5-10.0].

Conclusion: The study concluded that breastfeeding and proper weaning practices are necessary to eradicate measles.

Keywords: Child; Immunization; Measles; Measles vaccine; Risk factors; Tertiary care hospital.

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Introduction

Pakistan is one of the 47 priority areas for measles control identified by the World Health Organization (WHO). Every year, 2.1 million children contract measles, and 19,000–20,000 die from measles. Measles kills 58 people every day in Pakistan.[1] The United Nations Millennium Development Goals aim in 2015 was to decrease two-thirds mortality of children. Consistent vaccination of measles campaign reduces the child mortality and achieve this goal.[2] There is a safe and cost-effective measles vaccine available that costs less than 1 US dollar, it is unfortunate that measles continues to be a leading cause of death among children in low-income countries.[3]

Measles vaccination is a part of the Expanded Program on Immunization (EPI) in Pakistan. While initiatives like additional immunization campaigns have been launched to improve vaccination coverage and control measles transmission, there are still challenges that need to be addressed, particularly related to low immunization coverage and the impact of floating populations.[4]

Malnutrition, low vaccine efficacy due to cold chain issues, and poor vaccination coverage are significant contributing factors that can make measles endemic in Pakistan.[5] In most industrialized countries, high vaccine coverage rates (≥ 80-90%), good disease surveillance systems, and a two-dose vaccine strategy have been instrumental in significantly reducing the burden of measles.[6]

Information on local risk factors for measles among children is crucial for effective service planning and implementing appropriate interventions to control the spread of the disease. Existing literature and global data provide valuable insights and general guidelines for addressing public health issues like measles. They help develop broad intervention models that can be applied in various settings. However, for the most effective and impactful interventions, local data and context-specific information are of utmost importance.[7]

Data on measles cases in Rawalpindi health facilities can provide valuable information for understanding the local burden of measles and designing effective interventions. Additionally, exploring variables that explain vaccination rates among measles cases and identifying local factors associated with the disease. So, the main objective of this study is to identify risk factors associated with the development of measles among children under 12 years of age in a tertiary care hospital in Rawalpindi/Islamabad, while the effectiveness of measles vaccination among the study population is defined as a secondary objective test of the rate of measles.

Methodology

A retrospective study was done from January 2022 to January 2023 at the Department of Pediatrics, Holy Family Hospital (HFH), Rawalpindi & PAEC General Hospital, Islamabad. These tertiary care hospitals are collaborating with the WHO measles surveillance cell and study included reported cases of measles by the surveillance system. After ethical approval by the hospital ethics committee, the study included a sample of 600 children. Data was matched by age and sex for cases and controls. Among the cases, parents who are residents of Rawalpindi/Islamabad for at least one year, up to 12 years old, aged 3 days or more, fever 101°F or more, cough, coryza, conjunctivitis presented in the hospital (OPD, ER or ward). Eligible controls were children under 12 years of age who presented to the pediatric outpatient department or were hospitalized without measles at same hospital setting. Match data was done by age and gender.

Exclusion criteria was; congenital anomalies and other surgical conditions because previous evidence shows that the mothers of children perceive that the benefits of child care differ from the general population. Other conditions like pertussis, poliomyelitis, and tuberculosis were also excluded due to prevention of possible transmission of measles.

Data were collected by questionnaire, anthropometric assessment and IgM levels measurement. The questionnaire has different items to ask about the socio-demographic characteristics of children and their parents, details of breastfeeding, vaccination status and vaccination administration, current nutritional status of children, symptoms of measles and the incidence of measles.

According to the recommendations, children weight and height were recorded. After that they are classified as malnourished or undernourished according to the Gomez Modified classification. IgM levels of measles were tested in a subset of cases to confirm the diagnosis. The Enzignost Kit (Germany) was used to test the case.

Data were entered into SPSS 23.0. and analyzed. Univariant regression test was conducted for estimation the odds ratio (OR) with CI;95%. A probability p-value ≤ 0.05 was considered uniformly significant. Statistically and biologically significant associations with the development of measles (outcome) were further evaluated in univariant analysis and multivariant regression test. Multicollinearity between independent variables was also tested. Biologically relevant effects were examined among several independent variables.

Results

Children with measles (n=300) and children with other medical conditions (n=300) were matched by age and sex. Average age of the children was 32.24±14.58 months. Statistics for age, sex, symptoms, signs, and diagnosis were measured for measles only (Table 1). A univariant analysis of odds ratio (OR) with CI;95% was measured for risk factors potentially associated with measles (Table II & III).

In multivariant regression test (Table 4), cases of measles are mostly in mothers with low education compared with controls [OR: 4.1, 95% CI: 1.9-6.5, for primary schooling and OR: 1.1, 95% CI: 0.7-2.0, for matriculation group, whereas the graduation group was a reference range. There is a significant association between household members and development of measles (p = 0.0001), as each 2

household members increases the risk of measles by 1.15 times [OR: 1.1, 95% CI: 0.9 - 1.4].

Measles was less likely to be breastfed children during first 2 years of life [OR: 0.8, 95% CI: 0.5-1.4], classified as underweight according to the modified Gomez classification [OR: 1.2, 95% CI: 1.0-2.0]. Also, not being vaccinated [OR: 8.2, 95% CI: 5.5-15.0] and having no other unvaccinated children in the household [OR: 6.5, 95% CI: 4.5-10.0].

The biological interaction between prenatal vaccination, place of birth, father's education, employment status, and maternal weaning and parenting was investigated. The criterion for detecting an interaction was set at $p \leq 0.05$, but a significant effect was found for maternal vaccination during pregnancy and weaning. Analysis of subgroup was done only for children whose parents reported being unvaccinated, including 135 measles cases and 280 controls.

Table-I: Descriptive statistics of measles cases. (n=300)

		N	%
Age (months)	≤ 9	40	13.33
	≤ 15-24	140	46.67
	25-60	50	16.67
	≥ 61	70	23.33
Gender	Male	145	48.33
	Female	155	51.67
Complications as per diagnosis	Measles	130	43.33
	Pneumonia	65	21.67
	Diarrhea	28	9.33
	Conjunctivitis	20	6.67
	Otitis	45	15.0
	Encephalitis	8	2.67
	Others (e.g., malaria)	4	1.33
Measles classification (IMCI)	Mild	125	41.67
	With complications	148	49.33
	Severe	27	9.0
Primary symptoms	Fever	290	96.67
	Rash	3	1.0
	Coryza	3	1.0
	Cough	4	1.33
Followed symptoms	Fever	24	8.0
	Rash	267	89.0
	Coryza	165	55.0
	Cough	114	38.0
	Conjunctivitis	30	10.0
Time to report	Immediate (within 24 hours)	75	25.0
	After 1 day	96	32.0
	After 2 days	24	8.0
	After 3 days	75	25.0
	≥ 3 days	30	10.0
Vaccine received at 9 months	Yes	180	60.0
	No	84	28.0
	Not applicable	36	12.0
Vaccine received at 15 months	Yes	27	9.0
	No	195	65.0
	Not applicable	78	26.0

Discussion

The aim of present study was to identify risk factors associated with developing measles among children under 12 years of age in a tertiary care hospital in Rawalpindi/Islamabad. In Pakistan, mostly studies were conducted previously in private hospitals. The diagnosis of measles, there are discrepancies in data used such as clinical and laboratory, and some trusted on the definition of clinical cases.[8,9] In the current study, only general hospital cases were analyzed based on data provided by the WHO measles surveillance cell. Management guidelines based on the WHO are used to accurately identify measles and prevent the severe and mild measles cases. These guidelines are diagnosed and classify measles in hospital and in the community.[10] Our study looked at caregivers' experiences of maternal immunization practices during pregnancy, breastfeeding and weaning, and foods commonly used in children with measles and compared with hospital matched controls. These outcomes were determined after household visits and discussions with pediatric physicians at the hospital. These outcomes were included for found the modified risk factors for prevention.

To interpret the results, we defined measles as ≤ 9 months, ≤ 15 months, 24 months, 25-60 months, and ≥ 61 months. These categories are based on recent recommendations of age for vaccination of measles in developing countries, with first dose at 9 months and booster dose at 15 months, and the group under 5 years of age remains the most vulnerable to measles in developing countries.[11] These data show the same incidence of measles in the South Asian region (20% to 22%), and (3.9% to 3.5%).[12] In our study, measles cases were mostly have low-educated mothers compare to controls [OR: 4.1, 95% CI: 1.9-6.5, for primary school and OR: 1.1, 95% CI: 0.7-2.0, for matric, and graduation was reference group]. Among the good studies that evaluate the effectiveness of education of mothers on child mortality, it has been determined a significant correlation in mortality and morbidity results, however levels of low education improve the survival prospects and health-related behaviors.[13,14] Research has shown that an increase in maternal education is associated with significant reductions (7-9%) in under-5 mortality rates. Tax benefits (i.e., income, water and sanitation facilities, housing quality, etc.) associated with education can play a significant role in explaining the general

relationship between maternal education and reduced morbidity and mortality of children.[15]

In our research, measles was mostly in households with more family members, as the presence of both family members was associated with measles [OR: 1.1, (0.9 to 1.4)]. Research in developing countries has shown that overcrowding can increase the risk of exposure to measles.[10] The data from rural Guinea-Bissau show that overcrowding and age can be important determinants of nutritional status.[16]

Some African and Asian community studies have shown overcrowding and high exposure to be found of measles

Table II: Association of risk factors of measles with demographic details of children (cases = 300, controls = 300)

		Cases (f & %)	Controls (f & %)	OR (CI;95%)	p value
Mother tongue	Punjabi	135 (45.0)	150 (50.0)	1.4 (0.7-2.1)	.087
	Pashtu	75 (25.0)	66 (22.0)	1.0 (0.9-1.5)	.072
	Hindku	30 (10.0)	39 (13.0)	0.7 (0.5-1.1)	.143
	Pothwari	45 (15.0)	21 (7.0)	0.8 (0.6-1.5)	.0001
	Others (Sindhi, Baluchi, Urdu)	15 (5.0)	24 (8.0)	0.3 (0.1-1.2)	.061
Education of mother	Primary	220 (73.3)	150 (50.0)	4.1 (1.9-6.5)	.0001
	Matric	65 (21.7)	120 (40.0)	1.1 (0.7-2.0)	.0001
	Graduation	15 (5.0)	30 (10.0)	2.5 (2.0-4.0)	.0001
Education of father	Primary	150 (50.0)	120 (40.0)	0.9 (0.5-1.4)	.0001
	Matric	120 (40.0)	135 (45.0)	0.6 (0.3-1.0)	.0001
	Graduation	30 (10.0)	45 (15.0)	1.5 (1.0-2.0)	.0521
Job status of father	Employed	30 (10.0)	30 (10.0)	0.6 (0.4-1.8)	.142
	Unemployed	270 (90.0)	270 (90.0)		
Job status of mother	House wives	280 (93.3)	279 (93.0)	0.95 (0.7-1.9)	.149
	Working	20 (6.7)	21 (7.0)		
Children under 12 years in home (median)		2 (1.0 - 4.0)	2 (1.0 - 3.0)	1.1 (0.9-1.4)	.151
No. of members in home (median)		8 (6.0 – 10.0)	7 (6.0 – 9.0)	0.99 (0.8-1.1)	.0001
Monthly income (PKR), median		18,000	20,000	-	-

Table-III: Association of risk factors of measles with disease characteristics and birth, nutrition, and weaning status of children (cases = 300, controls = 300)

		Cases (f & %)	Controls (f & %)	OR (CI;95%)	p value
Birth order (median)		3 (1.0 - 5.0)	3 (1.0 - 4.0)	2.2 (1.8-2.5)	.011
During pregnancy mother vaccine	Yes	150 (50.0)	200 (66.7)	1.1 (0.9-2.0)	.0001
	No	150 (50.0)	100 (33.3)		
Delivery place	Home	100 (33.3)	70 (23.3)	0.9 (0.8-1.5)	.051
	Hospital	200 (66.7)	230 (76.7)		
Delivery mode	NVD	270 (90.0)	250 (83.3)	1.1 (0.9-2.0)	.0001
	C-section	30 (10.0)	50 (16.7)		
Birth weight	≤ normal	35 (11.7)	25 (8.3)	1.6 (0.9-2.8)	.212
	Normal	265 (88.3)	275 (91.7)		
After birth problems	Any illness	110 (36.7)	80 (26.7)	0.9 (0.7-2.0)	0.12
	No	190 (63.3)	220 (73.3)		
Breast feeding	Yes	260 (86.7)	270 (90.0)	0.8 (0.5-1.4)	0.075
	No	40 (13.3)	30 (10.0)		
Weaning	3 months	100 (33.3)	150 (50.0)	3.0 (2.0-4.0)	.0001
	6 months	140 (46.7)	75 (25.0)		
	≥ 7 months	60 (20.0)	75 (25.0)		
Modified Gomez classification	Low	140 (46.7)	70 (23.3)	1.2 (1.0-2.0)	.0001
	Normal	160 (53.3)	230 (76.7)		
Bitot's spots	Yes	10 (3.3)	8 (2.7)	3.1 (2.6-5.5)	0.075
	No	290 (96.7)	292 (97.3)		
Any other vaccine received	Yes	165 (55.0)	20 (6.7)	8.2 (5.5-15.0)	.0001
	No	135 (45.0)	280 (93.3)		
Vaccine other children	Yes	120 (40.0)	220 (73.3)	6.5 (4.5-10.0)	.0001
	No	155 (51.7)	60 (20.0)		
	Can't say	25 (8.3)	20 (6.7)		

mortality. Therefore, sociocultural factors that increase the number of vulnerable children at home also increase the mortality of measles.[17] Children with measles can face difficulties with breastfeeding, especially in the first two years of life [OR: 0.8, (0.5-1.4)]. It can also explain the lower prevalence of weight loss between cases and controls. Numerous studies have documented the protective effect of breastfeeding in the context of measles and other infectious diseases.[18] Evidence has found a negative association between breastfeeding for more than 3 months and the diagnosis of clinical measles infection, even after adjusting for various factors such as population, social class, measles vaccination, parity, and gender, 0.69 (0.60-0.81).[19]

Measles can be classified as low weight according to the modified Gomez classification [OR: 1.2, (1.0-2.0)]. Underweight is a major cause of early childhood infections. Previous large-scale studies have shown that 52.5% deaths occurred in young children due to malnutrition, which leads to weak immunity and high exposure of childhood infections. It is also proven that among malnourished children, 44.8% of deaths due to measles and 60.7% of deaths due to measles are due to diarrhea.[20] These cases are more likely to have never been vaccinated [OR: 8.2, (5.5-15.0)] and no other children in the household have been vaccinated [OR: 6.5, (4.5-10.0)]. The literature has shown that vaccination of measles is strongly associated with a lower risk of measles (OR: 0.14).[21]

One of the most important limitations of the study is controls including from hospital setting. Sick children who are admitted to the hospital may have different characteristics, risk factors, or disease severity compared to healthy children who are not hospitalized. Previous studies that have compared findings from hospital controls with those from community or environmental controls have shown similar results.[20] In additionally, verbal report of birth weight and vaccination status by parents or guardians. However, because hospital setting was selected and data was obtained from parents of sick children. It is very possible that parents remember the different vaccination record compare to controls.

Conclusion

The results of this study support that to improve measles control in the twin cities of Rawalpindi/Islamabad, according to WHO guidelines, the immunization capacity should be reduced in all health facilities. In addition, breastfeeding and proper weaning techniques are essential to increase the child's immunity against diseases. It is a need for coordinated efforts to increase the spread of local and global vaccination to prevent the burden of measles in children.

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