ORIGINAL ARTICLE

Adverse events following immunization among children during primary immunizations in selected health facility of Himachal Pradesh

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ABSTRACT

Background: Vaccine related problems are commonly reported after immunizations and are a matter of concern for health care professionals. A study on the pattern and rate of incidences of vaccine related problems was conducted among children undergoing primary immunizations. **Materials and methods**: The study was conducted in Zonal hospital, Solan, Himachal Pradesh. 150 mothers and their children undergoing immunization were enrolled in the study using systematic random sampling and followed on every immunization event until nine months. Vaccine related problems were enquired at every immunization events namely birth, six weeks, ten weeks, fourteen weeks and nine months using a self-structured tool to assess vaccine related problems among children. **Results**: Pain at vaccination site, redness and swelling, excessive crying, fever, and sleep related problems, feeding problems and fever were common AEFIs reported by mothers among children. **Conclusion:** AEFIs are frequent and need to be reported. None of the child had any severe reaction or hospitalization after immunization.

KEYWORDS

Primary Caregiver; Primary Immunizations

INTRODUCTION

Immunization is an important event in a child's life. It provides protection from vaccine preventable diseases (VPDs) and gives lifetime immunity to a child. India despite being largest manufacturer of many vaccines falls behind global vaccination coverage of 81% and stands at 76% (1). Many VPDs are still claiming millions of lives worldwide due to low vaccination coverage. The vaccines are not without side effects. Some undesirable effects do occur in some percentage of children which makes vaccination troublesome and increases hesitancy among parents. Almost all vaccines can cause side effects. In most cases, there are minor reactions example, a sore arm or low-grade fever and that within a few days. However, not immunizing a child also involves risk and puts the child and others who come into contact with him or her at risk of contracting a potentially deadly disease.

A vaccine induces immunity by causing the recipient's immune system to react to the vaccine. Therefore, local reaction, fever and systemic symptoms can result as part of the immune response. In addition, some of the vaccine's components (e.g. adjuvant, stabilizers or preservatives) can lead to reactions (2). Like any medicine; vaccines can cause side effects such as a low-grade fever, or pain and redness at injection site. Mild reactions go away within a few days on their own. Severe, long lasting side effects are extremely rare. Vaccines are tested before marketing and administration to children. It ensures that they are safe and effective for children to receive at the recommended ages (3). The current involves study of vaccine related problems among children followed from birth till nine months of their primary vaccination.

MATERIAL & METHODS

Study area: The study was conducted among 150 mothers whose children undergoing primary immunizations at vaccination clinic of Zonal Hospital Solan (HP). Mothers and children attending vaccination clinic for first immunization after birth were enrolled. **Sampling technique:** The subjects were selected via systematic random sampling. A sampling interval of ten was selected based on the potential number of subjects in a month. The first subject was selected randomly between one and ten and thereafter every tenth subject was enrolled for study. The detail of subjects was obtained from the registration area of vaccination room. **Sample size:** a sample size of one fifty was obtained after randomization for over two months. The sample size was calculated by using the formula $n=Z\propto/2^2pq/l^2$) with a desired allowable error of 20% of 'p'where P was assumed 50% based on previous studies, q=1-p (50) and I (allowable error) =20% of p (10). The sample size was increased as per availability of time and subjects' interest. **Inclusion criteria:** Mothers who accompanied their child during vaccinations at birth who agreed to participate for till primary vaccination completed (i.e upto one year) and children who were born at term. **Exclusion criteria:** children who required additional care, child with any congenital anomaly. **Ethical approval:** Ethical clearance for the study was given by ethical committee of Swami Rama Himalayan University, Uttarakhand Reference no – SRHU/HIMS/ETHICS/2019/6. Written consent regarding the study was also obtained from the primary caregivers. Administrative permission regarding the study was obtained from the Director of health services, Shimla (H.P). **Tools used:** The tools for data collection consisted of part A that consisted of information regarding the mother and the child under study. Detail of attributes of children namely gender, birth weight and type of delivery was obtained. Part B consisted of follow up detail of vaccination of the children and vaccine related problems reported by the mothers. **Study duration:** The data was collected from February 2021 till February 2022. The mothers and the children enrolled at first immunization (at birth) were contacted telephonically after three days and vaccine related problems were enquired. Loss to follow-up occurred for various reasons at each vaccination event; the number of participants in the study was 150 at six weeks, 139 at ten weeks, 138 at fourteen weeks and 130 at nine months. The children received vaccination as per Government of India vaccination schedule. BCG, Hep B and OPV zero dose at birth, Pentavalent, rotavirus, OPV, PCV, FIPV at six weeks, Pentavalent, rotavirus, OPV at ten weeks, Pentavalent, rotavirus, OPV, PCV, FIPV at fourteen weeks and MR-1,booster PCV at nine months. This was done at subsequent vaccinations at six weeks, ten weeks, fourteen weeks and nine months. **Data analysis:** The data analysis was done using descriptive and inferential statistics. It was carried out manually using statistical package for social sciences (SPSS) version 23 and Microsoft Excel. Chi square was used to establish association of vaccine related problems with attributes of children.

RESULTS

The children enrolled were most mostly females i.e 64.7%. According to birth weight majority children ie 84.7% had birth weight more than 2500 gms, children with low birth

weight were 15.3% only. Most children were delivered normally i.e. 77.3%. (Table 1)

Table 1: Attributes of children enrolled for the study.

Variables	Categories	No of children (N=150)	
		N	%
Gender	Male	53	35.3
	Female	97	64.7
Birth weight (in gms)	≤2500	23	15.3
	>2500	127	84.7
Type of delivery	Normal	116	77.3
	Caesarean section	34	22.7

Both local reactions and systemic reactions were reported among children. Local reactions included redness, swelling, pain at vaccination site, nodule formation. Systemic problems observed among children were fever, restlessness, irritability, feeding problems, excessive crying. None of the children had any serious adverse reaction.

It was observed that pain at vaccination site, redness and swelling, excessive crying, restlessness& irritability and feeding problems were reported at every immunization event (Table 2) Pain was reported highest at six weeks(94%) followed by ten weeks. Fever 79.1%, redness & swelling 88% and nodule formation 82% were reported high among children from six weeks till fourteen weeks. Excessive crying was reported among all children at six weeks. Fever was reported among more than 75% children at six and ten weeks thereafter decreasing trend from fourteen weeks till nine months was observed with very few (5.4%) at nine months. Drowsiness /sleep disturbance was only observed at six weeks and fourteen weeks.

Table 2: Vaccine related problems at various immunization events.

Time of immunization event	Pain n(%)	Excessive crying n(%)	Redness & swelling n(%)	Nodule formation n(%)	Restlessness& irritability n(%)	Drowsiness / sleep disturbance n(%)	Feeding problems n(%)	Fever n(%)
Birth (BCG OPV Hep B)	77 (51.3)	33 (22)	120 (80)	-	21 (14)	-	49 (32.7)	-
6 weeks (Pentavalent, OPV,RV,FIPV,PCV)	141 (94)	150 (100)	132 (88)	123 (82)	72 (48)	63 (42)	66 (44)	113 (75.3)
10 weeks (Pentavalent, OPV,RV)	128 (92.08)	21 (15.10)	117 (84.2)	110 (79.1)	122 (87.8)	-	74 (53.2)	110 (79.1)
14 weeks (Pentavalent, OPV,RV,FIPV,PCV)	101 (73.2)	63 (45.7)	117 (84.8)	92 (66.7)	84 (60.9)	36 (26.1)	70 (46.4)	58 (42)
9 months (MR,PCV)	83 (63.8)	23 (16.9)	12 (9.2)	-	69 (50)	-	27 (20.8)	7 (5.4)

The chi-square test was used to assess the association between two categorical variables and $p < 0.05$ was considered statistically significant. Gender and birth weight of children were used to determine association as these have previously been found to be predictors of developing vaccine related problems.

It was observed that gender and birth weight of the child were significantly associated with occurrence of vaccine related problems (Table 3-10). Gender was found significantly associated with pain at vaccination site at birth and ten weeks, excessive crying at birth, redness and swelling at birth, ten weeks, nodule formation at 14 weeks, irritability and restlessness at six and ten weeks, feeding problems at birth and fever at six weeks. According to birth weight, significant associations were found with pain at vaccination site at ten and fourteen weeks, excessive crying at birth, ten weeks and fourteen weeks, redness and swelling at birth, fourteen weeks and nine months, nodule formation at ten and fourteen weeks, irritability and restlessness at birth feeding problems at six weeks and nine months and fever at six weeks.

Table 3: Association of pain at vaccination site among children with their attributes.

Variables	Categories	Pain at vaccination site									
		At birth N=150		6 weeks N=150		10 weeks N=139		14 weeks N=138		9 months N=130	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Gender	Male	40	13	51	3	29	21	32	17	27	20
	Female	37	60	90	6	87	2	69	20	56	27
		χ2 19.115		χ2 0.154		χ2 36.637		χ2 2.405		χ2 1.306	
		p 0.000		p 0.694		p 0.000		p 0.120		p 0.253	
Birth weight (in gms)	≤ 2500	16	9	23	2	16	9	11	14	13	12
	>2500	61	64	118	7	100	14	90	23	70	45
		χ2 1.926		χ2 0.212		χ2 8.353		χ2 13.255		χ2 0.669	
		p 0.165		p 0.644		p 0.003		p 0.000		p 0.413	

Table 4: Association of excessive crying among children with their attributes.

Variables	Categories	Excessive crying									
		At birth N=150		6 weeks N=150		10 weeks N=139		14 weeks N=138		9 months N=130	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Gender	Male	16	37	53	-	11	39	23	26	10	37
	Female	17	80	97	-	22	67	40	49	12	71
		χ2 12.46		NA		χ2 0.130		χ2 0.051		χ21.245	
		p 0.000				p 0.717		p 0.138		p 0.10	
Birth weight (in gms)	≤ 2500	12	13	25	-	10	15	4	21	1	24
	>2500	21	104	125	-	23	91	59	54	21	84
		χ2 11.818		NA		χ2 4.450		χ2 10.819		χ23.678	
		p 0.000				p 0.034		p 0.001		p 0.055	

Table 5: Association of redness and swelling among children with their attributes.

Variables	Categories	Redness and swelling									
		At birth N=150		6 weeks N=150		10 weeks N=139		14 weeks N=138		9 months N=130	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Gender	Male	50	3	43	10	44	6	40	9	4	43
	Female	70	27	89	8	73	16	77	12	8	75
		χ210.533		χ2 3.660		χ2 9.184		χ2 0.584		χ2 0.045	
		p0.001		p 0.055		p 0.002		p 0.444		p 0.830	
Birth weight (in gms)	≤2500	15	10	15	10	19	6	17	8	5	20
	>2500	105	20	117	8	98	16	100	13	7	98
		χ27.5		χ2 22.27		χ2= 1.528		χ2 6.667		χ2 4.284	
		p0.006		p 0.000		p=0.216		p 0.009		p 0.038	

Table 6: Association of nodule formation among children with their attributes.

Variables	Categories	Nodule formation									
		At birth N=150		6 weeks N=150		10 weeks N=139		14 weeks N=138		9 months N=130	
				Yes	No	Yes	No	Yes	No		
Gender	Male	NA		43	10	42	8	39	10	NA	
	Female			80	17	68	21	53	36		
				χ2 0.0418		χ2 1.118		χ2 5.711			
				p 0.837		p 0.290		p 0.016			
Birth weight (in gms)	≤ 2500	NA		20	5	16	9	10	15	NA	
	>2500			103	22	94	20	82	31		
				χ2 0.081		χ2 4.230		χ2 9.769			
				p 0.775		p 0.039		p 0.007			

Table 7: Association of irritability and restlessness among children with their attributes.

Variables	Categories	Irritability and restlessness									
		At birth N=150		6 weeks N=150		10 weeks N=139		14 weeks N=138		9 months N=130	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Gender	Male	10	43	13	40	40	10	28	21	22	25
	Female	11	86	59	38	82	7	56	33	43	40
		χ2 1.616		χ2 18.090		χ2 4.391		χ2 0.443		χ2 0.299	
		p 0.204		p 0.000		p 0.036		p 0.505		p 0.598	
Birth weight (in gms)	≤2500	8	17	8	17	20	5	18	7	15	10
	>2500	13	112	64	61	102	12	66	47	50	55
		χ2 8.073		χ2 3.076		χ2 1.714		χ2 1.588		χ2 1.238	
		p 0.004		p 0.079		p 0.190		p 0.207		p 0.265	

Table 8: Association of feeding problems among children with their attributes.

Variables	Categories	Feeding problems									
		At birth N=150		6 weeks N=150		10 weeks N=139		14 weeks N=138		9 months N=130	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Gender	Male	10	43	23	30	28	22	25	24	9	42
	Female	39	58	43	54	46	43	39	44	18	65
		χ2 7.094		χ2 0.012		χ2 0.200		χ2 0.200		χ2 0.320	
		p 0.007		p 0.912		p 0.654		p 0.654		p 0.571	
Birth weight (in gms)	≤ 2500	6	19	6	19	12	13	12	13	10	15
	>2500	43	82	60	65	62	52	52	61	17	88
		χ2 1.024		χ2 4.870		χ2 0.335		χ2 0.324		χ2 6.956	
		p 0.311		p 0.027		p 0.562		p 0.172		p 0.008	

Table 9: Association of fever among children with their attributes.

Variables	Categories	Fever									
		At birth N=150		6 weeks N=150		10 weeks N=139		14 weeks N=138		9 months N=130	
				Yes	No	Yes	No	Yes	No	Yes	No
Gender	Male	NA		31	22	37	13	20	29	2	45
	Female			82	17	73	24	38	51	5	78
				χ2 2.152		χ2 0.027		χ2 0.045		χ2 0.184	
				p 0.144		p 0.867		p 0.830		p 0.667	
Birth weight (in gms)	≤ 2500	NA		13	12	18	7	12	13	1	24
	>2500			100	25	92	22	46	67	6	99
				χ2 8.878		χ2 0.940		χ2 0.446		χ2 0.116	
				p 0.003		p 0.332		p 0.503		p 0.73	

Table 10: Association of drowsiness/sleep disturbance among children with their attributes.

Variables	Categories	Drowsiness/sleep disturbance								
		At birth N=150	6 weeks N=150		10 weeks N=139		14 weeks N=138		9 months N=130	
			Yes	No	Yes	No	Yes	No	Yes	No
Gender	Male	NA	20	33	NA		11	38	NA	
	Female		43	54			25	64		
			χ2 0.612				χ2 0.522			
			p 0.102				p 0.126			
Birth weight (in gms)	≤ 2500	NA	8	15	NA		7	16	NA	
	>2500		55	72			29	86		
			χ2 0.581				χ2 0.271			
			p 0.139				p 0.173			

DISCUSSION

Immunization is an important intervention related to child health. Although vaccine are safe but not without side effects or problems. The present study focuses on vaccine related problems occurring among children after vaccination during primary immunizations as reported by their primary caregivers. The study consisted of children born as normal terms new-borns enrolled at their first vaccination (at birth). Majority children under study were females i.e 64.7%. Most children (84.7%) in the study had normal birth weight (ie. > 2500gms) and had a normal delivery (77.3%). It was also observed that most local and systemic problems appeared within the same day of vaccination and recovered within the same week. Mittal S et al also conducted a study in northern state of India and reported similar pattern of appearance of AEFIs after immunization of children (4). Karami M et al observed that the incidence of vaccine related problem among children was, 15.8% for swelling, 10.9% for redness, 44.2% for pain, 12.6% for mild fever, 0.1% for high fever, 20.0% for drowsiness, 15.0% for loss of appetite, 32.9% for irritability, 4.6% for vomiting and 5.5% for persistent crying(5). Sebastian J et al found that apart from fever having the highest incidence (10.9%) of vaccine side effect, other were followed by persistent crying (0.24%) and diarrhoea (0.17%)(6). The current study observed pain at vaccination site (51.3%), redness and swelling among 80% children, excessive crying was seen in 22% children and feeding problems was reported by 32.7% at first vaccination event. Redness and swelling at immunization site was seen at all events. It was among most children (80%) at birth and was maximum at nodule formation after Pentavalent vaccination was a common occurring among all children.

Fever is known to be associated with pertussis component of Pentavalent vaccine. It was reported among more than 80% children. Contrary to previous study done by Sebastian et al that reported a decrease in fever incidence at successive Pentavalent vaccine administration (6), current study did not observe same pattern. It occurred around 6 - 14 weeks of immunization mainly. Pentavalent vaccine and BCG have long been majorly implicated for AEFIs among children(6). Results from researches conducted in other countries by Hu Y et al in China and Sharafi et al in Iran, also report mild fever and injection site reaction after Pentavalent vaccination(7,8). Drowsiness/sleep disturbance was observed only at 6 weeks and 14 weeks. The current study reports more diverse and higher incidences of AEFIs as compared to previous studies that mainly report fever, redness swelling and excessive crying (9-11). While most others studies have observed AEFIs at single immunization event, present study reports vaccine related problems during primary immunizations among the children followed through and up to nine months.

In the majority of cases, AEFI shows a temporal association between vaccination and adverse events and not a causal relationship between the two. Although most adverse events are minor (e.g. pain, swelling, redness at the

injection site, fever), more serious reactions (e.g. seizures, anaphylaxis) can occur, though at a very low frequency. No significant association was found of AEFI with age and gender ($p > 0.05$) (4). However, Sebastian J et al in his study indicated age (neonate) and low birth weight as predictors of AEFIs in children irrespective of the vaccine administered (6).
The investigator in the current study observed that pain at vaccination site was significantly associated with gender at birth and with birth weight at six and fourteen weeks (Table 3). Excessive crying significantly associated with gender at birth and with birth weight at fourteen weeks (Table 4). Redness and swelling was not influenced by gender but was found to be influenced by birth weight at all immunization events except at ten weeks (Table 5). Nodule formation was found among children from six to fourteen weeks. While gender was found associated significantly with redness and swelling, birth weight was found significantly associated at six weeks and fourteen weeks (Table 6). Irritability and restlessness was found significantly associated with birth weight at birth and ten weeks (Table 7). Feeding problems associated with gender at six weeks only (Table 8). Fever was present at all vaccination events except at birth and was found to be associated with birth weight at six, ten and fourteen weeks (Table 9). None of the child's attributes was found to influence drowsiness /sleep disturbance among children (Table 10).

Although the incidence of AEFI reported was high, all of them were minor and no serious AEFI was identified in our study, while others, like Joshi et al., reported 0.7% AEFIs to be serious (12) and Arora et al. reported 365 hospitalizations and 17 deaths during four-week follow-up (13).

Conclusion

AEFIs were studied among one fifty children enrolled at birth and followed till nine months. Vaccine related problems (AEFIs) were reported by mothers at every vaccination event however all the reported vaccine related problems were mild /non serious reactions. Pain, redness & swelling, excessive crying and fever were the main problems. Feeding problems were also reported at every immunization event. None of the child had the serious adverse reaction nor needed any hospitalization due to vaccine related problems.

Limitation

The study included children vaccinated in a Government hospital. Self- reported vaccine related problems were recorded. Any concurrent illness among children was not taken into account. Direct observation was not done.

Authors Contribution

All authors have contributed equally.

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Nil

Conflict of Interest

There are no conflicts of interest.

References

1. Summan A, Nandi A, Schueller E, Laxminarayan R. Public health facility quality and child immunization outcomes in rural India: A decomposition analysis. Vaccine. 2022;40(16):2388-98.
2. Revised AE. Guidelines: Executive Summary, MoHFW. Accessed on Dec 24, 2023. Available at https://main.mohfw.gov.in/sites/default/files/Revised%20AEFI%20Guidelines%20Execute%20Summary.pdf
3. Lane S, MacDonald NE, Marti M, Dumolard L. Vaccine hesitancy around the globe: Analysis of three years of WHO/UNICEF Joint Reporting Form data-2015–2017. Vaccine. 2018;36(26):3861-7.
4. Mittal S, Rawat CM, Gupta A, Solanki HK, Singh RK. Adverse Events Following Immunization Among Children Under Two Years of Age: A Prospective Observational Study From North India. Cureus. 2023;15(4): e38356.
5. Karami M, Ameri P, Bathaei J, Berangi Z, Pashaei T, Zahiri A, Zahraei SM, Erfani H, Ponnet K. Adverse events following immunization with pentavalent vaccine: experiences of newly introduced vaccine in Iran. BMC immunology. 2017;18(1):1-7.
6. Sebastian J, Gurumurthy P, Ravi MD, Ramesh M. Active surveillance of adverse events following immunization (AEFI): a prospective 3-year vaccine safety study. Ther Adv Vaccines Immunother. 2019 Nov 21;7:2515135519889000
7. Hu Y, Li Q, Chen Y. Timeliness of childhood primary immunization and risk factors related with delays: evidence from the 2014 Zhejiang provincial vaccination coverage survey. International journal of

environmental research and public health. 2017;14(9):1086.
8. Sharafi R, Mortazavi J, Heidarzadeh A. Comparison of complications of pentavalent and DTP vaccination in infants aged 2–6 months in Anzali, Iran. Iran J Neonatology IJN. 2016;7(2):1–6.
9. Barański K, Gajda M, Braczkowska B, Kowalska M. Parental declaration of adverse event following immunization in a cross-sectional study in Poland. International Journal of Environmental Research and Public Health. 2019;16(20):4038.
10. Lombardi N, Crescioli G, Bettiol A, Tuccori M, Rossi M, Bonaiuti R, Ravaldi C, Levi M, Mugelli A, Ricci S, Lippi F. Vaccines safety in children and in general population: a pharmacovigilance study on adverse events following anti-infective vaccination in Italy. Frontiers in pharmacology. 2019;10:948.
11. Maizare HI, Tsiga-Ahmed FI, Jibo AM, Adamu AL, Jalo RI, Magaji A, Ibrahim UA, Gajida AU. Prevalence and patterns of adverse events following immunisation among children less than 24 months attending immunisation clinics in Kano, Nigeria. Annals of African Medical Research. 2021;4(1).
12. Pattern of adverse events following immunization in an Indian teaching hospital. Joshi N, Prajapati H, Solanki K, et al. https://www.bibliomed.org/mnsfulltext/67/67-1344319073.pdf?1682877925 Int J Med Sci Public Health. 2013;2:62.
13. Arora NK, Das MK, Poluru R, Kashyap NK, Mathew T, Mathai J, Aggarwal MK, Haldar P, Verstraeten T, Zuber PLF; INCLEN Vaccine Safety Study Group. A Prospective Cohort Study on the Safety of Infant Pentavalent (DTwP-HBV-Hib) and Oral Polio Vaccines in Two South Indian Districts. Pediatr Infect Dis J. 2020 May;39(5):389-396.