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Determinants of third dose of diphtheria–tetanus–pertussis (DTP) completion among children who received DTP1 at rural immunization centres in Pakistan: a cohort study

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Summary

OBJECTIVE—In Pakistan, a high proportion of children fail to complete third dose of diphtheria-tetanus-pertussis (DTP3) after having received the first dose (DTP1). A cohort study was conducted to identify the factors predicting three doses of diphtheria–tetanus–pertussis (DTP3) completion among children who have received DTP1 at six centres of Expanded Programme on Immunization (EPI) in rural Pakistan.

METHOD—We analyzed a cohort of mother–child pairs enrolled at DTP1 between November 2005 and May 2006 in the standard care group of a larger randomized controlled trial. Data were collected from mothers on a structured questionnaire at enrolment, and each child was followed up at clinic visits for 90 days to record dates of DTP2 and DTP3. Multivariable log-binomial regression analysis was performed to identify the independent predictors of DTP3 completion.

RESULTS—Only 39% (149/378) of enrolled children completed DTP3 during the follow-up period. After adjusting for the centre of enrolment in multivariable analysis, DTP3 completion was higher among children who were ≤60 days old at enrolment [adjusted risk ratio (Adj. RR) 1.39, 95% confidence interval (CI): 1.06–1.82], who were living in a household with monthly household income >Rs. 3000 (US$ 50) (Adj. RR 1.76, 95% CI: 1.16–2.65), and who were living ≤10 min away from EPI centre (Adj. RR 1.31, 95% CI: 1.04–1.66).

CONCLUSIONS—Interventions targeting childhood immunization dropouts should focus on bringing more children to EPI centres on-time for initial immunization. Relocation of existing EPI centres and creation of new EPI centres at appropriate locations may decrease the travel time to the EPI centres and result in fewer immunization dropouts.

Keywords

childhood immunization; Expanded Programme on Immunization; dropouts; determinants; cohort study; Pakistan

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Introduction

In most World Health Organization (WHO) member states, the Expanded Programme on Immunization (EPI) provides a series of childhood immunizations during the first year of life including vaccines for tuberculosis (Bacillus Calmette-Guérin; BCG), diphtheria–tetanus–pertussis (DTP), poliovirus (oral vaccine; OPV), hepatitis B virus (HBV) and measles. In Pakistan and many other WHO member states, the EPI schedule includes the administration of BCG/OPV vaccines at birth, three doses of DTP/OPV/HBV vaccines at 6, 10 and 14 weeks and measles vaccine at 9 months after birth. According to WHO, completion of three doses of DTP (DTP3) vaccine is a principal indicator of immunization coverage levels. Another indicator of immunization system performance is dropout rate between DTP1 and DTP3 coverage levels (WHO 2006).

Immunization coverage levels in Pakistan have been consistently lower than the socio-economically comparable WHO member nations of the eastern Mediterranean region and the southeast Asia region. In Pakistan from 2002 to 2005, the BCG coverage was recorded at 80–82% and DTP3 coverage at 65–72%. During that period, about 12–13% of children who received DTP1 did not complete DTP3 (WHO 2006). Dropouts from DTP1 to DTP3 immunization suggest that mothers/caregivers (henceforth simply referred to as ‘mothers’) are both motivated and resourceful enough to visit the EPI centres for DTP1. However, lower DTP3 and measles coverage indicates that a substantial proportion do not manage to complete the immunization schedule.

In developing countries, low adherence to immunization schedule has been found associated with parental socio-demographic characteristics (e.g. larger family size, lower parental education) and provider-based characteristics (e.g. longer distance of EPI centre from home) (Anandhi *et al.* 2000; Bhuiya *et al.* 1995; Lutwick 2000; Ughade *et al.* 2000). Behavioural factors (e.g. mothers’ lack of information and poor motivation) have also predicted both poor adherence to immunization recommendations and high risk of dropouts (Bhandari *et al.* 1990; Ray *et al.* 2004; Sokhey *et al.* 2001).

Pakistani literature on barriers to childhood immunization is sparse and mainly reported from cross-sectional studies (Ahmad *et al.* 1999; Shaikh 2003). In these studies, children’s immunization status was primarily assessed by mother’s recall because of the unavailability of immunization cards at the time of interview. Such assessment of a child’s immunization status is liable to misclassification (Suarez *et al.* 1997; Valadez & Weld 1992), and thus the internal validity of these studies is questionable. On the other hand, review of childhood immunization records at EPI centres can provide estimates of DTP1–DTP3 dropout using accurate immunization status of children. However, absence of socio-demographic information in those records prohibits any analysis of determinants of immunization completion. To address these limitations, we used documented evidence of immunization status and conducted this cohort study to identify the determinants of DTP3 completion among children who have received their DTP1 at rural EPI centres in the peripheries of Karachi, Pakistan.

Methods

Study design

Within a larger randomized controlled trial, mother–child pairs were enrolled at DTP1 and randomized to three intervention groups and a standard care group. The objective of the trial was to assess the effect of substantially redesigned immunization card and centre-based education to mothers on DTP3 completion among children who received DTP1 at EPI

centres. For this follow-up study, only participants enrolled in the standard care group of the trial were analysed as a cohort of mother–child pairs.

Setting

The study was conducted at six rural EPI centres located at the periphery of Karachi. Study centres were selected from all rural centres around Karachi. For timely sample size completion, centres with highest volume of children vaccinated for DTP1 immunizations in the previous year were selected for this study. Housed in government dispensaries and basic health units, these centres provide primary health care to the rural population in their catchment areas. Mostly, infants from the lower and middle socio-economic tiers of the country received immunization at EPI centres. All immunizations provided by EPI are free.

Participants

Any child visiting the selected EPI centres for DTP1 was eligible to participate in the study, provided that the mother had been resident in the area for at least last 6 months. The 6 months residency requirement was used to exclude women temporarily living for a few weeks in their mother's home for the birth of the child. Such mothers were likely to change the immunization centre after DTP1 immunization. Given the low literacy rates among Pakistani women, a trained female interviewer read out the consent form to the mother of each eligible child. The interviewer and a witness signed the consent form for each consenting mother and completed enrolment.

After enrolment at DTP1, the mother was interviewed by a female interviewer and each study child was followed up at the visits to EPI centre for 90 days. By the EPI schedule, each DTP2 and DTP3 was scheduled at 30-day intervals after DTP1. Therefore, both DTP2 and DTP3 should have been completed ideally within 60 days after the DTP1 visit. During the study period, interviewers screened every child who visited a study centre and recorded DTP2 and DTP3 dates of study children.

Variables

A structured questionnaire, pre-tested at EPI centres not included in this study, was used at enrolment to record information from mothers on factors which have previously been associated with completion of immunization in published literature. The questionnaire included parents' attributes (parents' age at enrolment, mother's age at marriage and first conception, parents' education and occupation, monthly household income, ethnicity and family size), child's attributes (child's age at enrolment, child's sex and number of siblings) and mode of transport and travel time to reach the EPI centre. All these variables were assessed as independent variables in the analysis.

The study outcome was the immunization status of each child at the end of 90 days after enrolment. The immunization status was dichotomized into completion of both DTP2 and DTP3 (termed 'DTP3 completed') *vs.* completion of DTP2 only or neither immunization (termed 'DTP3 not completed').

Statistical methods

All analyses were performed using SAS® version 9.1 (SAS Institute, Inc., Cary, NC, USA). Overall distribution of participants' characteristics in the study cohort was described by computing their frequencies and percentages. The immunization status was the dependent variable. Because the study participants who had not returned to the centres for either DTP2 or DTP3 visits within 90 days of their DTP1 visit were considered DTP3 not completed, no study participant was considered lost to follow-up.

The distribution of DTP3 completion among children who received DTP1 was assessed by computing its percentage among the categories of independent variables. In univariate log-binomial regression analysis (SAS® PROC GENMOD), we computed crude risk ratio (RR) and 95% confidence interval (CI) to assess the association of each independent variable with DTP3 completion (Skov *et al.* 1998; Spiegelman & Hertzmark 2005; Wacholder 1986; Zocchetti *et al.* 1995). A multivariable log-binomial regression model (SAS® PROC GENMOD) was constructed to assess the association of independent variables with DTP3 completion adjusted for other variables. The variable indicating the EPI centre of enrolment was always kept in the model to adjust for centre to centre variation in DTP3 dropout. Adjusted RRs (Adj. RRs) and their 95% CIs were used for the interpretation of the final model.

Approval for this study was obtained from the Institutional Review Board of the University of Alabama at Birmingham and the Ethical Review Committee of The Aga Khan University, Karachi, Pakistan.

Results

Between November 2005 and May 2006, a total of 378 mother–child pairs were enrolled in the study from six EPI centres. The follow-up of the last study child was completed in August 2006. Child's age at DTP1 was not available for 12 children; therefore, data on 366 mother–child pairs were used for the multivariable analysis.

The majority (80%) of respondents in the study was mothers (Table 1). Prominent ethnic groups enrolled were Pashto (32%), Hindko (18%) and Mohajir (16%). Almost half of the study children were girls and 59% were ≤60 days old at enrolment. More than half of mothers never went to school and almost all were housewives. Fathers were better educated than mothers and were mostly labourers (42%), private employees (26%) or owned private business (20%). The majority (77%) of children lived in households with more than five members, and 84% of households had monthly income of >3000 Pakistani Rupees (50 US$). About half (47%) of study participants travelled ≤10 min to reach the EPI centre.

Univariate analysis

During the 90 days follow-up period, 60% (228/378) of enrolled children completed DTP2 and only 39% (149/378) of enrolled children completed DTP3. The proportion of children completing DTP3 ranged from 14% to 65% across study centres. In univariate analysis, children of Hindko (RR = 1.92; 95% CI = 1.20, 3.09) and Pashto (RR = 1.67; 95% CI = 1.07–2.68) ethnicity were more likely to complete DTP3 than Mohajir children (Table 1). Also, a higher proportion of children who were ≤60 days old at enrolment completed DTP3 (RR = 1.58; 95% CI = 1.19–2.09) than children who were >60 days old at enrolment. Similarly, more children from households with ≤5 members (RR = 1.40; 95% CI = 1.08–1.81) and monthly income of >Rs. 3000 (US$ 50) (RR = 1.72; 95% CI = 1.09–2.72) completed DTP3. DTP3 completion was also higher among children who travelled ≤10 min to reach the EPI centre (RR = 1.27; 95% CI = 0.99–1.63) than children who travelled >10 min to reach the EPI centre.

Multivariable analysis

The final multivariable model included centre of enrolment, child's age at enrolment, monthly household income and travel time to reach EPI centre. After adjusting for other variables in the model, DTP3 completion was higher among children who were ≤60 days old at enrolment (Adj. RR = 1.39; 95% CI = 1.06–1.82), who were living in a household with monthly household income >Rs. 3000 (US$ 50) (Adj. RR = 1.76; 95% CI = 1.16–

2.65), and who were living ≤10 min away from the EPI centre (Adj. RR = 1.31; 95% CI = 1.04–1.66) (Table 2).

Discussion

This study estimated that after having received DTP1 at six rural EPI centres in the peripheries of Karachi, a very low proportion (39%) of children completed DTP3 during 90 days of follow-up. The study also identified that a child's age at DTP1 immunization, monthly household income and travel time to reach the EPI centre were significant predictors of DTP3 completion.

Overall immunization coverage is a function of the proportion of newborns that an immunization system brings in for the first immunization and the proportion of these children who eventually complete all immunizations recommended in the schedule. In our study, we enrolled children at DTP1 and followed them at EPI centres to estimate the proportion of these children completing DTP3. Therefore, this study only focused on those children who were already in the EPI system by having received DTP1. The factors identified in this study are the predictors of DTP3 completion among children who have already received DTP1 and should be differentiated from cross-sectional studies which compared fully or partially immunized children with not immunized children (children who never visited EPI centres). That may be the reason why factors such as mother's education (Adem *et al.* 2003; Altinkaynak *et al.* 2004; Cutts *et al.* 1991; Matthews & Diamond 1997; Minh Thang *et al.* 2007; Tiwari & Kulkarni 1999), family size, (Tiwari & Kulkarni 1999), child's sex (Tiwari & Kulkarni 1999) and number of siblings (Adem *et al.* 2003; Tiwari & Kulkarni 1999), identified frequently in low and middle income countries as predictors of immunization coverage using cross-sectional design, did not show significant association with DTP3 completion in this study. This may also indicate that factors predicting immunization completion may differ both within and among developing countries, particularly when rural areas are considered. Also, the possibility of differential misclassification of immunization status in cross-sectional studies cannot be ruled out; leading to false identification of many socio-demographic factors as predictor of immunization completion.

According to the EPI schedule, a 45-day-old child should be brought to the EPI centres for DTP1 immunization (WHO/UNICEF 2001). In this study, only 59% of the children were ≤60 days old at DTP1 visit. This may indicate that delay in receiving DTP1 is common in Pakistani rural areas. A higher proportion of younger children (≤60 days old at DTP1) completing DTP3 in our study suggested that if children received DTP1 in a timely manner, they were more likely to complete subsequent immunizations according to the schedule. Also, age appropriate immunization provides protection from illnesses at youngest possible age. Therefore, mothers should be encouraged to bring their children on time for their initial immunizations (e.g. DTP1). Not receiving DTP1 on time, on the other hand, might relate to much broader health-seeking behaviours of the population and needs further investigation.

Assessment of child's age at initial immunizations as a predictor of subsequent immunization has been rare in developing country settings. Most of the studies conducted in these settings used a cross-sectional study design and assessed immunization status primarily by mother's recall (Ahmad *et al.* 1999; Shaikh 2003). In these studies, child's age at specific immunizations was inherently difficult to document and therefore it was not possible to explore it as a predictor of follow-up immunization visits. However, because of the availability of immunization records in the United States and other developed countries, studies from these settings have reported significantly higher immunization coverage of subsequent immunizations among children who were up-to-date at 3 months of age (Daniels

et al. 2001; Rosenthal *et al.* 2004; Wood *et al.* 1995a,b). In another study from the United States, receiving DTP3 late was identified as a major risk factor for not completing DTP4 (Strine *et al.* 2003).

Monthly household income was the strongest predictor of immunization completion in the final model despite the fact that vaccines are provided free of cost at EPI centres. Children from households with monthly incomes > Rs. 3000 (US$ 50) were about 80% more likely to complete DTP3. Other studies have also suggested a positive association between socio-economic status and immunization coverage (Bardenheier *et al.* 2004; Bates & Wolinsky 1998; Cui & Gofin 2007).

In this study, 47% of participants travelled ≤10 min to reach the EPI centre for DTP1. These study participants were 30% more likely to complete DTP3 than those who travelled >10 min to reach the EPI centre. Close proximity to the immunization site is associated with a higher immunization uptake both in Pakistan (Hennessey *et al.* 2000; Reichler *et al.* 1997) and in other developing countries (Jamil *et al.* 1999; Perry *et al.* 1998a,b; Reichler *et al.* 1998; Tiwari & Kulkarni 1999). Spending more time to reach a health centre is a natural disincentive especially for childhood immunizations, which requires multiple visits to complete the series of doses. The reach of general population to EPI centres could be improved by setting up new EPI centres and geographical relocation of existing EPI centres based on population density.

For 2005 in Pakistan, the WHO-reported DTP1 (82%) and DTP3 (72%) coverage suggests that 88% (72/82*100) of children who received DTP1 went on to complete DTP3. However, no more than 39% of the children enrolled in our study completed DTP3 within 90 days follow-up (Table 2). Dropout rates in rural areas are expected to be higher because of lower socio-economic conditions than the country level estimates reported by the WHO. Also, our estimates are from a cohort of children followed at only six EPI centres of one province, whereas the WHO estimates were calculated using national DTP1 and DTP3 coverage. Therefore, comparison of these very differently calculated figures must be done with caution. Secondly, this study could not account for those children who did not return to the study centres but might have gone to other centres for subsequent immunizations and those who might have returned after 90 days follow-up period. Nonetheless, our stated reasoning might not fully explain the wide gap between the study and the WHO estimates.

A substantial variation in DTP3 completion across study centres was recorded in this study. This might have been because of different geographical location of EPI centres with respect to the socio-demographics characteristics of the population living in their catchment areas. The contribution of centre characteristics as a predictor of immunization completion should be evaluated in future studies.

We chose RRs over odds ratios (ORs) to assess the strength of association between the predictors and DTP3 completion. Crude and Adj. RRs as well as their 95% CIs were estimated using proc genmod in SAS® by log-binomial regression (Skov *et al.* 1998; Spiegelman & Hertzmark 2005; Wacholder 1986; Zocchetti *et al.* 1995). The study outcome, i.e. the proportion of children completing DTP3 was not rare and reporting OR would have been an overestimation of actual effect size.

There are limitations in our study. Because of limited time and resource constraints, the childhood immunization cohort was followed from DTP1 to DTP3. A follow-up from DTP1 to measles would have given us a full extent of immunization completion and an opportunity to explore the predictors of full immunization schedule completion. Another limitation was that the follow-up of study children for return visits took place only at the study centres. There is a chance that some study children might have visited non-study EPI centres for

DTP2 and DTP3, leading to underestimation of DTP3 completion in our study. However, limiting to mothers living in the area for at least 6 months should have minimized switching to non-study centre after enrolment. Finally, our follow-up of each study child for no more than 90 days after enrolment (at DTP1) means that we may have lost some children who returned for DTP3 later. However, the survival curve of days to DTP3 (data not shown) indicated a plateau at around 80 days of follow-up and it was not expected to have a large number of children returning for DTP3 after 90 days. In future studies, in-depth interviews of mothers not returning for subsequent immunization visits might provide additional information on the reasons for dropouts. This study was conducted at six high-volume rural EPI centres at the periphery of Karachi, and its results may not be generalizable to all rural settings of Pakistan.

In conclusion, this study provides strong evidence that a very low proportion of children who received DTP1 at selected rural EPI centres in Pakistan returned to complete DTP3. Efforts to improve DTP3 coverage among children who received DTP1 in Pakistan should target the predictors of DTP3 completion identified in this study. In addition, interventions found effective in improving childhood immunization completion in Pakistan (Usman *et al.* 2009) and elsewhere (Barton & Schoenbaum 1990; Nichol *et al.* 1990; Pierce *et al.* 1999; Waterman *et al.* 1996) should be considered for large scale implementation in the EPI system. Studies exploring the factors influencing child's age at DTP1 are needed. We also recommend studies to investigate the issue of distance to EPI centre using geographic information systems (GIS). Such GIS-based studies should aim at evaluating the geographical locations of existing EPI centres with reference to the population density. Based on such studies, appropriate relocation of existing EPI centres and creation of new EPI centres may reduce the travel time to the EPI centres and result in higher immunization completion.

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Table 1

Association of factors with three doses of DTP (DTP3) completion shown by crude risk ratios (RRs) and their 95% confidence intervals (CIs) (Pakistan, 2005–2006)

			DTP3 completed during 90 days follow-up		
Variables	***n* = 378**	**Column (%)**	**Row (%)**	**Crude RR**	**95% CIs**
Enrolment centre					
A	93	(25)	(45)	1.09	(0.76, 1.58)
B	73	(19)	(14)	0.33	(0.17, 0.63)
C	20	(5)	(65)	1.57	(1.02, 2.44)
D	112	(30)	(46)	1.12	(0.79, 1.61)
E	17	(4)	(35)	0.86	(0.42, 1.74)
F	63	(17)	(41)	1.00	
Relationship of respondent with child					
Mother	304	(80)	(39)	0.93	(0.68, 1.25)
Others	74	(20)	(42)	1.00	
Ethnicity					
Hindko	69	(18)	(52)	1.92	(1.20, 3.09)
Pashto	120	(32)	(46)	1.67	(1.07, 2.68)
Punjabi	41	(11)	(41)	1.53	(0.88, 2.66)
Sindhi	41	(11)	(37)	1.35	(0.75, 2.41)
Others	48	(13)	(21)	0.77	(0.38, 1.53)
Mohajir	59	(16)	(27)	1.00	
Child’s age at enrolment (*n* = 366)					
≤60 days	215	(59)	(47)	1.58	(1.19, 2.09)
>60 days	151	(41)	(30)	1.00	
Child’s sex					
Boy	186	(49)	(40)	1.02	(0.79, 1.31)
Girl	192	(51)	(39)	1.00	
Total number of living children					
≤2	185	(49)	(43)	1.21	(0.94, 1.55)
>2	193	(51)	(36)	1.00	
Mother’s age at enrolment (years)					

			DTP3 completed during 90 days follow-up		
Variables	***n* = 378**	**Column (%)**	**Row (%)**	**Crude RR**	**95% CIs**
≤19	31	(8)	(26)	0.73	(0.38, 1.40)
20–29	257	(68)	(42)	1.19	(0.87, 1.63)
>29	90	(24)	(36)	1.00	
Mother's age at first conception (years)					
≥18	252	(67)	(42)	1.19	(0.90, 1.58)
<18	126	(33)	(35)	1.00	
Mother's years of formal schooling					
>0	170	(45)	(42)	1.11	(0.87, 1.43)
0	208	(55)	(38)	1.00	
Mother's occupation					
House wife	372	(98)	(39)	0.78	(0.35, 1.76)
Others	6	(2)	(50)	1.00	
Father's years of formal schooling					
>10	51	(13)	(49)	1.41	(0.98, 2.05)
1–10	20	(54)	(40)	1.15	(0.86, 1.55)
0	12	(33)	(35)	1.00	
Father's occupation					
Unemployed	9	(2)	(44)	1.04	(0.48, 2.26)
Government servant	37	(10)	(49)	1.14	(0.75, 1.74)
Private employee	97	(26)	(41)	0.97	(0.68, 1.38)
Labourer (unskilled worker)	160	(42)	(34)	0.81	(0.57, 1.13)
Owned private business	75	(20)	(43)	1.00	
Number of household members					
≤5	87	(23)	(51)	1.40	(1.08, 1.81)
>5	291	(77)	(36)	1.00	
Monthly household income (Pak Rs.)					
>3000	317	(84)	(42)	1.72	(1.09, 2.72)
0–3000	61	(16)	(25)	1.00	
Mode of transport to EPI centre					
Public bus system	23	(6)	(35)	0.70	(0.35, 1.37)

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			DTP3 completed during 90 days follow-up		
Variables	***n* = 378**	**Column (%)**	**Row (%)**	**Crude RR**	**95% CIs**
On foot	329	(87)	(39)	0.78	(0.52, 1.17)
Privately owned or rented vehicles	26	(7)	(50)	1.00	
Travel time to reach EPI centre					
≤10 min	178	(47)	(44)	1.27	(0.99, 1.63)
>10 min	200	(53)	(35)	1.00	

EPI, Expanded Programme on Immunization.

Table 2

Multivariable analysis of the factors associated with three doses of DTP completion shown by adjusted risk ratios (Adj. RRs) and their 95% confidence intervals (CIs) (Pakistan, 2005–2006) (*n* = 366)

Variables	Adj. RR*	95% CIs
Child's age at enrolment (days)		
≤60	1.39	(1.06, 1.82)
>60	1.00	
Monthly household income (Pak Rs.)		
>3000	1.76	(1.16, 2.65)
0–3000	1.00	
Travel time to reach EPI centre		
≤10 min	1.31	(1.04, 1.66)
>10 min	1.00	

EPI, Expanded Programme on Immunization.

*Adjusted for the centre of enrolment, child's age at enrolment, monthly household income and travel time to reach EPI centre.