

Vaccination Coverage and Timeliness among Children Under 2 Years of Age in India: A Kaplan- Meier and Cox Regression Analysis

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Abstract: Child vaccination is important in significantly reducing child mortality and is seen as a cost-effective way of improving child health, especially for poor households located in highly disease-prone environments. In addition, evidence is available to determine that vaccine guards not just against a specific disease but can offer a wide variety of health benefits if given on time. Despite this evidence, vaccination coverage remains far from universal and, in particular, the scenario in developing countries is vulnerable. Though a number of studies on child vaccination have recently been conducted, but these are mostly focused on the determinants of full vaccination. However, to understand the timeliness of vaccination coverage, very limited studies have been conducted. In this context, this paper attempts to explore the timeliness scenario of age specific vaccines in India using District Level Household and Facility Survey 4 (DLHS 4) unit level data. The analysis of data shows that children face the highest risk of delayed vaccination in case of OPV3 followed by DPT3, Measles and BCG. However the scenario of delayed vaccination is not uniform across different states of the nation. Finding also shows that place of residence, religion of the child, education of mother, antenatal care, motivation, and social class are the determinants of delayed vaccination in India.

Keywords- Vaccination Coverage, Vaccination Timeliness, Cox-Regression, India

I. INTRODUCTION

Vaccination is generally regarded as the most successful and cost-effective public health intervention in today's world [1]. The widespread use of vaccines has led to the global eradication of smallpox, the elimination of OPV and measles from many countries, and a significant reduction in illness and death due to diseases such as diphtheria, tetanus, and whooping cough [2]. In addition, there is evidence that immunisation can not only protect against a specific disease, but can also provide a wide range of health benefits [3, 4] and thus make it a valuable measure of public health. Despite this evidence, immunisation coverage remains far from satisfactory in general, and the situation of the developing countries is vulnerable in particular [5]. The evolution of immunisation efforts in India is far more complex than can be imagined, the reluctance, opposition and slow acceptance of immunisation have been the hallmark of the history of immunisation in India and the chapters of numerous children's life losses especially from most of the preventable diseases cannot be removed from that history [6]. Despite the long-standing Universal Immunization Program of the government, which provides free vaccines for children, poor immunisation coverage has still been identified as one of India's leading causes of high infant mortality rates. Since 1978, the government of India has launched different immunisation programmes to prevent vaccine-preventable diseases. However, for protection against vaccine-preventable and life-threatening childhood diseases, mere initiation into the immunisation course is not sufficient, but completion of all doses of full vaccination during infancy is essential. The performance of vaccinations is often analysed by their spread and coverage [7-9], but studies have shown that timely vaccination is equally important in order to obtain the desired benefits, as the efficacy of vaccines largely depends on the timing of the vaccine. A noteworthy level of coverage for specific vaccines does not necessarily imply timely vaccination [10-12]. The current immunisation studies in India focus primarily on issues related to vaccination coverage and its determinants [13-15]. But studies are very rare at the national level on age-appropriate vaccination coverage. The only study that has been

conducted on the timeliness of vaccination coverage also suffers from a number of flaws¹ [16]. In this context, the present study is a modest attempt to identify the factors influencing the timeliness of age specific vaccination in India.

II. METHODS

2.1 Data Source-

We have used data from the latest District Level Household and Facility Survey (DLHS4) in India. The District Level Household and Facility Survey-4 (DLHS-4) is a nationwide survey covering 640 districts from 36 States and Union Territories of India. This is the fourth round of the district level household survey which was conducted during 2012-13. The Survey was funded by the Ministry of Health and Family Welfare, Government of India.

2.2 Measurement of Variables and Descriptive Statistics-

We have estimated the incidence of vaccination coverage and timeliness of vaccination of each vaccine in accordance with the national vaccination schedule. Up to date vaccination coverage in the country has been estimated among the children of 12-23 months of age based on the World Health Organization recommended schedule. In connection with the WHO guideline and as per the EPI schedule, vaccinations can be classified as “early” if they are administered 3 days prior to the recommended age. Vaccinations are defined as “delayed” if they are administered more than 28 days after the recommended age and the remaining vaccinations within these time frames were considered as “timely”. And in the present study, we have considered only two classifications, timely and delayed vaccination, where the category “early” is clubbed with timely vaccination. Time to event vaccination for each vaccine has been obtained from vaccination dates and dates of birth recorded in the DLHS 4 unit level file.

Table-1 The Expanded Program on Immunizations (EPI) Schedule and Timeliness in India.

Diseases	Vaccine	Recommended Age	Early	Timely	Late
Childhood tuberculosis (TB)	Bacille-Calmette-Guerin (BCG)	At Birth/ 0 days	---	0-28 days	>28 days
Diphtheria/tetanus/pertussis	DPT1	42 days	<39 days	39-70 days	>70 days
	DPT2	70 days	<67 days	67-98 days	>98 days
	DPT3	98 days	<95 days	95-126 days	>126 days
Poliomyelitis	OPV1	42 days	<39 days	39-70 days	>70 days
	OPV2	70 days	<67 days	67-98 days	>98 days
	OPV3	98 days	<95 days	95-126 days	>126 days
Measles	Measles	275 days	<272 days	272-303 days	>303 days

Source: Compiled by the authors from National Vaccination Schedule (NIS) and the Expanded Program on Immunizations (EPI) schedule.

2.3 Statistical Analysis-

Time to event analysis has been used to analyze the age at administration and risk factors for delayed vaccination for the vaccine studied. Firstly, a non-parametric Kaplan – Meier survival analysis has been applied on DLHS 4 data to estimate the age-specific coverage rates. Survival analysis for assessment of delay in age-appropriate vaccination provides scientific and thorough information about the timeliness of vaccination coverage [17-19]. In our experiment, time-variable has been defined as the age (in days) a child has survived till the uptake of a specific dose of vaccine. Thus, the failure or event of interest is a positive event defined as the uptake of vaccine and the outcome variable is time (in days) to a particular event that is until a child received the vaccine. Secondly, risk factors for delayed vaccination have been identified by using Cox proportional hazard regression model. Since our data has a large number of missing observations, censoring occurred when the child still has not received the specified vaccine even if the observation period (0-23 months) ends. Hence, in the presence of such censoring and covariates, we do not know what particular distribution the used data actually follows. However, the real advantage of Cox Proportional Hazards regression is that we can still fit survival models without knowing or assuming the distribution. So it is very useful to

¹ The study is area specific and we have a doubt regarding their treatment of timeliness, as they did not consider the delay in immunization for specific doses. Further they also overlooked the importance of concomitant programs like ANC and place of delivery

have a technique that works well without needing a specific distribution and accordingly the model has been used. We estimated the Cox proportional hazards model of the following form (using Stata version 13).

$$h(t) = h_0(t)e(\beta_1x_1 + \beta_2x_2 + \dots + \beta_px_p) \dots \dots \dots \dots \dots 1$$

Where *t* is the time, *x_s* are the covariates, *β_s* the regression coefficients and *h₀(t)* is the baseline hazard function, i.e. the hazard function under *x=0*. Here our predicted hazard is the timeliness of age-specific vaccination.

2.4 Measurement and Descriptive Statistics of the Variables-

Following table contains a brief description of the variables chosen for the analysis

Table-2 Description of variables

Variables	Description of Variables	Mean	Standard Deviation
Locality	Takes 1 for rural and 0 otherwise.	0.6301	0.48280
Religion	Takes 1 for Muslim and or 0 otherwise.	0.1161	0.32036
Place of Delivery	Takes 1 for institutional delivery and 0 otherwise.	0.8347	0.37145
ANC3	Takes 1 for the mothers who have done all the three Antenatal checkups.	0.8772	0.32837
Education	Mothers' education.	9.4604	3.79073
Motivated	Takes 1 where eligible mothers have been motivated for vaccination or 0 otherwise.	0.8606	0.34632
Birth Order	Takes 1 for birth order of 2 or more; 0 otherwise.	0.2213	0.41515
Caste	Takes 1 for backward classes or 0 otherwise.	0.7997	0.40022
Number of observations - 21376			

Source: All data have been extracted from DLHS 4 and descriptive statistics are calculated by the authors.

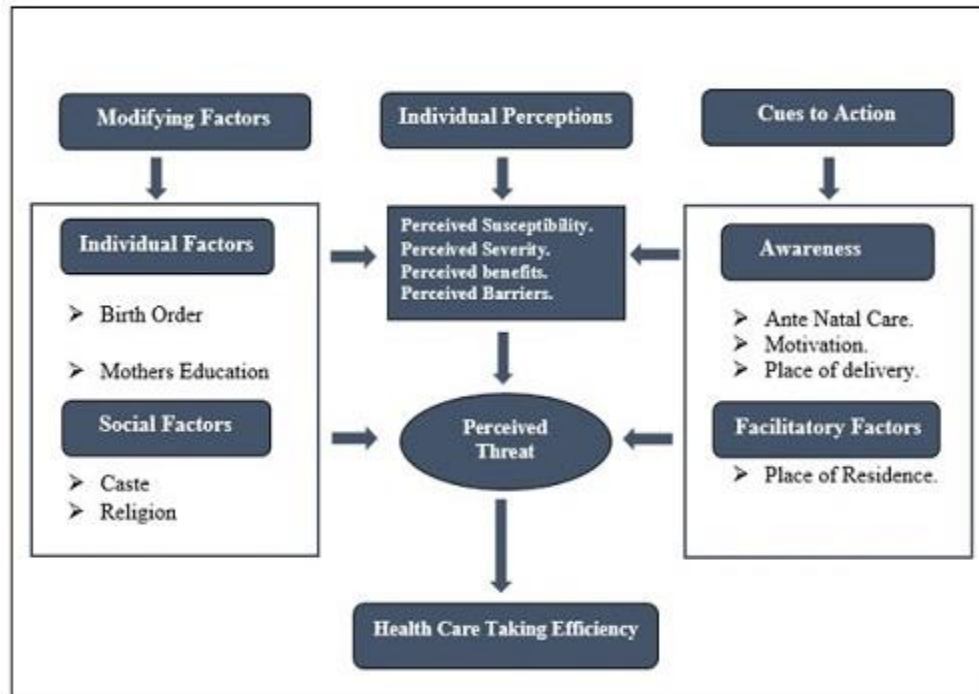
2.4 Theoretical and Conceptual Framework-

The model (Figure 1) contributes a framework for understanding the potential influences of an individual’s decision on the efficiency of health caretaking services. The model has been conceptualized based on two major conceptual models; Rosenstock’s (1990) health belief model and Tanahashi’s (1978) model on health service coverage. However, necessary modifications have been done in the line with the present study. The model represents the factors that are needed to consider for efficient utilization of health care services.

A set of constructs have been provided by the health belief model for the identification and understanding of the multiple factors that influence the demand and delivery of a vaccine. The health belief model, initially developed by the U.S. Public Health Service is one of the influential and widely used theoretical models. The key components used in the model are: firstly, the perception of threat, which is conceived as two components: perceived severity and susceptibility to an adverse outcome; secondly, perceived outcome expectations, which are examined as perceived benefits and perceived barriers to performing a protective behavior; and thirdly, modifiers, which influence the individual's response, such as socio-demographic factors and cultural beliefs. Modifiers such as demographic, socio-economic factors play an important in influencing the health outcome resulting from some action. People from backward classes have lower levels of education, less awareness, less motivated, and hence likely to have lesser utilization of all preventive health care services in general.

One of the main principles of the health belief model is the idea of perceived threat, which is the combination of an individual's perception of the severity of a health problem and that individual's perceived susceptibility of being affected by a potential health risk. The fourth construct of the model is cues to action. It is basically a facilitative mechanism and the factors included in the same can promptly influence a person’s protective behavior.

However, the health belief model did not determine the variables of cues to actions. Therefore, the Tanahashi health service coverage model concept has been used to express the extent of interaction between the health service and the concerned people.



Source: Adopted from Rosenstock, (1990) and Tanahashi (1978).
 Figure 1. Conceptual Framework.

III. RESULTS

3.1 Up To Date Vaccination Coverage-

Timeliness of vaccination coverage (Table 3) shows that for all the specific vaccines the percentage of delayed Vaccination coverage is more persistent than that of timely vaccination. In other words in all the specific vaccines, the timeliness of Immunization coverage is less followed in most of the states/UTs in India. The highest delayed vaccination coverage for BCG has been noticed in Manipur (89.70%), while the national average stands for 48.79%, for OPV 3 and DPT 3 the highest percentage is recorded at West Bengal as 90.10% and 90% against the national average of 77.69% and 78.02% respectively. Lastly, in the case of Measles, while the all India average of delayed vaccination stands for 65.08%, the highest percentage of delayed vaccination has been recorded at Tripura with 78.5%. The mentioned figures show that in the above-mentioned states the incidence of delayed vaccination is even higher compared to that of the national average. The table also reveals that the incidence of delayed vaccination coverage is more prone to North–Eastern states. While in the case of BCG only Sikkim has registered more than 60% timely vaccination coverage, the scenario of other states of the region is far from satisfactory. Pointing towards OPV 3, the highest timely vaccination coverage is merely 25.80% at Arunachal Pradesh and that of delayed vaccination coverage is 89% at Meghalaya. Similar to BCG and OPV 3, the timeliness of vaccination coverage in the region is quite unsatisfactory for both DPT 3 and Measles.

Table-3 Vaccination coverage and timeliness of administration for BCG, OPV3, DPT 3 and Measles vaccine across states in India

States	BCG		OPV3		DPT3		Measles	
	Timely	Delayed	Timely	Delayed	Timely	Delayed	Timely	Delayed
Himachal Pradesh	33.20	66.80	21.00	74.50	18.40	75.30	24.00	71.00
Punjab	47.00	53.00	19.90	77.80	19.50	78.60	33.50	61.40
Chandigarh	72.60	27.40	33.00	64.10	29.80	67.30	39.50	55.80
Haryana	31.50	68.50	13.10	84.00	14.50	82.90	29.90	66.80

Sikkim	63.20	36.80	23.50	74.10	23.60	74.60	40.60	56.90
Arunachal Pradesh	35.20	64.80	25.80	70.50	25.90	71.00	39.00	56.90
Nagaland	42.30	57.70	21.80	76.40	18.50	79.50	31.00	65.70
Manipur	10.30	89.70	11.80	86.60	11.20	87.00	26.80	69.40
Mizoram	12.20	87.80	18.90	76.40	18.60	76.80	36.60	60.80
Tripura	19.20	80.80	9.00	88.70	9.90	87.50	17.60	78.50
Meghalaya	39.00	61.00	10.70	89.00	9.70	89.80	27.20	68.80
West Bengal	50.90	49.10	8.70	90.10	8.80	90.00	23.60	74.30
Maharashtra	53.00	47.00	17.20	79.50	17.50	79.10	31.40	64.90
Andhra Pradesh	56.20	43.80	22.70	74.50	23.00	74.50	28.90	64.90
Karnataka	59.30	40.70	18.20	79.30	17.80	80.10	32.00	63.10
Goa	64.50	35.50	22.50	75.10	22.30	75.40	39.60	60.40
Kerala	76.30	23.70	22.40	75.40	23.20	75.40	26.50	70.40
Tamil Nadu	66.90	33.10	27.60	67.40	28.10	65.70	30.90	59.40
Pondicherry	70.10	29.90	24.90	71.60	23.40	71.90	24.60	69.00
And. & Niko	72.90	27.10	20.10	78.80	20.40	78.00	32.90	63.2
India	48.79	51.21	19.64	77.69	19.21	78.02	30.81	65.08

Source: Figures are estimated by the authors from DLHS 4

3.2 Vaccination by Age: Kaplan–Meier Analysis-

Estimates of age-appropriate vaccination coverage have been shown in figure 2. Panel A of the figure estimates the age-appropriate vaccination coverage for BCG, panel B is that of OPV3, panel C and D are for DPT 3 and Measles respectively. The Kaplan – Meier survival curve shows that 95% of the BCG vaccination coverage reached at 4 months of age. The same took approximately 10 months for OPV 3 and approximately 11 months for DPT 3 respectively. While in the case of Measles, the same level of vaccination coverage reached around 17 months of age.

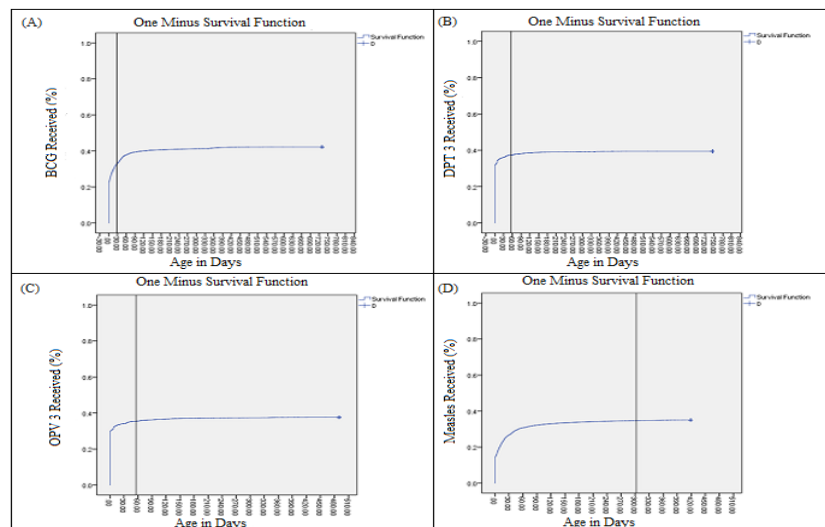


Figure 2. Age related coverage for specific vaccines
Source: drawn by the authors

3.3 Determinants of Vaccination Delay: Cox Proportional Hazard Regression Analysis-

As a first step, we identify the factors affecting vaccination delay in India. In the literature, several variables have been considered as influencing vaccination delay. Here, we shall discuss the potential linkage between vaccination and the socio-economic, demographic, and other factors. Place of residence is an important factor that determines the survival of children. The rural-urban differences might be attributed to different health care services, including the number of

health institutions and centers, access to health care services, especially vaccination services [20]. Moreover, significant differences have also been found in vaccination coverage with respect to the place of residence in previous studies [21-22]. Religion also plays an important role in vaccination coverage. Various socioeconomic, cultural, behavioral and other such factors of different religious groups might be attributed to this. People belonging to different religions are actually having different perceptions of vaccination resulting in a significant influence on the completion of vaccination [23]. Women who utilized institutional delivery service, might also, be more confident in utilizing preventive services like child vaccination. Also, the administration of the BCG vaccine quickly after childbirth and vaccination counseling at a health facility can increase the chances of children being fully immunized. Moreover, previous studies have also revealed that children born at a health facility were more likely to be fully immunized [24, 25]. Parental education, specifically mother's education is a key factor which is found to be directly correlated with better health care and timeliness of vaccination [26]. But then, these parents have to know about the facility of child vaccination and its benefits. There are studies that point out that lack of awareness among parents has been a dominant reason for not immunizing the child. [27] ANC visits provide an opportunity to promote health care utilization, including institutional delivery, Post Natal Check-up, vaccination, and family planning [28]. Moreover, ANC visits provide a platform for making mothers aware of child vaccination [30]. Motivated mothers are generally more aware of the importance of available health and vaccination services, and tend to better utilize available services. Recommended ANC visits, motivate pregnant women to give birth in a health facility. During the institutional delivery, a woman receives, not only skilled care but also counseling and education to use the postnatal care and vaccination services, which eventually is more likely to result in higher compliance towards the recommended vaccination schedule [29]. Existing literature has revealed that children in bigger families had a lower probability of receiving full vaccination [30, 31]. As the number of children in a family increases, the mother becomes busier in fulfilling her children's needs. Furthermore, a mother's attention is divided between children if she has many children [32] Thus, birth order is an important determinant of child vaccination. Parents, more importantly mothers, from lower socioeconomic classes had a lower level of education and less awareness, motivation, and utilization of all preventive health services in general. Furthermore significant influence of socioeconomic class on the vaccination status of children has also observed in previous studies [24, 33]. After identifying the probable factors for vaccination delay, we conducted Cox Proportional Hazard regression analysis. Here we found a place of residence, religion, institutional delivery, antenatal care, birth order, and caste as the determinants of age specific vaccination delay in India. The regression results are reported in table 4.

Table-4 Cox Proportional Hazard Regression

Indicators	BCG		OPV3		DPT3		Measles	
	Coefficient	HR	Coefficient	HR	Coefficient	HR	Coefficient	HR
Locality	-0.059 (5.20)**	0.942	-0.082 (9.15)***	0.921	-0.062 (5.38)**	0.940	-0.058 (4.17)**	0.944
Religion	0.056 (1.94)	1.058	0.188 (18.84)***	1.207	0.201 (22.44)***	1.223	0.164 (13.37)***	1.178
Place of delivery	-0.159 (12.05)***	0.853	-0.126 (6.87)***	0.882	-0.149 (9.83)***	0.862	-0.113 (4.96)**	0.893
Education	-0.009 (7.18)***	0.991	-0.002 (.33)	0.998	-0.004 (1.51)	0.996	-0.004 (.96)	0.996
ANC3	-0.275 (43.04)***	0.759	-0.298 (44.70)***	0.742	-0.294 (45.41)***	0.745	-0.351 (54.98)***	0.704
Motivate	-0.209 (25.57)***	0.811	-0.193 (19.62)***	0.825	-0.225 (27.26)***	0.798	-0.238 (26.74)***	0.789
Birth Order	0.128 (13.64)***	1.136	0.098 (7.33)***	1.103	0.107 (9.06)***	1.113	0.127 (11.04)***	1.135
Caste	0.093 (10.11)***	1.097	0.099 (10.58)***	1.104	0.110 (13.81)***	1.117	0.158 (25.56)***	1.171
Diagnostic Statistics	-2loglikelihood-125596.7		-2loglikelihood-115091.0		-2loglikelihood- 119559.3		-2loglikelihood- 106853.3	
	Chi-Square-126.134***		Chi-Square-128.167***		Chi-Square-145.264***		Chi-Square-151.473***	

Source: Estimated by the author from DLHS 4

Note: (1) Values in the parenthesis indicate Wald Statistic; (2) ** & *** represents significant at 5% & 1% respectively; (3) HR represents the Hazard ratio

Before we interpret the result it is important to note that the various diagnostic test statistics justify the appropriateness of the model. Moving on with the analysis, the Cox Proportional Hazard regression shows that the hazard of BCG

vaccination delay for rural children is 0.058 times less than that of urban children. The incidence of vaccination delay for other age-specific vaccines also follows a similar trend. In the case of OPV 3, rural children are 0.079 times, for DPT3, 0.060 times and for measles 0.056 times less than that of urban children. The impact of religion has been found to be negligible for the BCG vaccine. However, in the case of OPV 3, DPT 3, and Measles the impact of religion on vaccination delay has been found to have a positive impact. More specifically, the risk of vaccination delay is more for children belonging to the Muslim religion. In the case of the OPV 3 vaccine, Muslim children are found to be 0.207 times more prone to delayed vaccination. Similar to OPV3, children belonging to the Muslim religion are 0.223 times and 0.178 times more likely to delayed vaccination for DPT3 and Measles respectively. The regression result also shows that the risk of delayed vaccination for institutional deliveries and babies born to mothers who have done all the three recommended antenatal checkups is less as against non-institutional deliveries and incomplete antenatal checkups respectively. With respect to institutional delivery, the risk of vaccination delay has been found to be 0.147 times less for BCG, 0.118 times less for OPV 3, 0.138 times less for DPT 3, and 0.107 times less for Measles. Pointing towards the significance of mother's education, it has been found to be positive and statistically significant for BCG only. More precisely, for each additional unit of education the hazard of delayed vaccination decreases by 0.09%. The risk of vaccination delay of children whose mothers have been motivated by health professionals or by family members is also found to be lower than those who are not motivated. Looking at the figures for the birth order of the children, it is clear from the table that the hazard of vaccination delay is 0.136 times for BCG, 0.103 times for OPV 3, 0.113 times for DPT 3, and 0.135 times more for the children of higher birth order. In addition to this, the regression result also shows that the risk of vaccination delay for backward classes is 0.097 times more for BCG, 0.104 times more for OPV 3, 0.117 times more for DPT 3, and 0.171 times more for Measles. In other words, children belonging to other classes are found to be less prone to delayed vaccination.

IV. CONCLUSION

Timeliness of vaccination coverage in India varies for specific vaccines as well as across states / UTs. The incidence of delayed vaccination has been experienced to a larger extent across various states/UTs in India compare to schedule or timely vaccination. The finding is also supported by the annual report of UNICEF, 2010. Pointing towards the state-level scenario, the North - Eastern States are found to be in a more vulnerable position compared to other states. Sikkim is the only state of the region where the incidence of timely mannered vaccination coverage has been found to be slightly better as against the performance of other states o the region. The above findings are also validated by the survival curve analysis. The Kaplan – Meier curve also shows that maximum coverage for all the age specific vaccines are experienced very lately than that of the scheduled time. The regression result identifies the place of residence, religion, and caste as responsible factors for delayed vaccination. The said findings are also supported by the empirical findings of [34, 35] who also observed that socio-economics factors like locality, religion, caste, etc are the major factors responsible for delayed vaccination. Higher birth order is also found to be positively related to delayed vaccination in India [36]. Healthcare provisioning arrangements like babies registered with Institutional deliveries are found to be negatively related with delayed vaccination. That is the hazard of delayed vaccination is found to be less with institutional deliveries [37]. Finally, in our data analysis, we have found a conflicting result: children residing in rural areas are less prone to vaccination delay than those from urban habitations, which has to be further examined before making any comment.

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