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# **Original article**

# Timing and Delay in Children Vaccination; Evaluation of Expanded Program of Immunization in Outskirt of Iranian Cities

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# **ABSTRACT**

**Background:** Most studies evaluated the vaccine coverage, but the time of vaccination is important as coverage. This study was conducted to evaluate the Expanded Program of Immunization (EPI) in outskirt of Iranian cities regarding to incidence of delayed vaccination among children less than 4 years.

**Methods:** This cross sectional descriptive study was conducted among children 24-47 months old, living in the suburbs of five metropolises of Iran. Totally, 3610 eligible children selected with proportioned cluster sampling method and data of vaccination card extracted after the interview with children's parents. Delayed incidence rate reported and predictive factors assessed by the Chi square test and Multivariate logistic regression.

Results: Overall, 56.6% to 93.2% vaccines were administered out of time. Delayed vaccination incidence with more than one-week delay varies from 5.5% to 74.9% of polio at birth and MMR2 at 18 months, respectively. Mother's educational level and birth order were the most important predictors of delayed vaccination. Incidence of delayed vaccination was enlarged by increasing birth order and decreased in lower educated mothers.

**Conclusions:** Incidence rate of delayed vaccination is more than expectation. Regarding to high coverage vaccines in Iran, health officers and health policy makers should attempt for ontime vaccination beside of high immunization coverage, especially in slum areas with more concentrated immigrants due to low literature and crowded families.

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# **Introduction**

he World Health Organization (WHO) established the Expanded Program of Immunization (EPI) in 1974, to protect all children around the world against more common vaccine preventable diseases at the first year of age<sup>1,2</sup>. Vaccination of children could prevent 2-3 million-child deaths annually<sup>3</sup>. Since immunization increased child survival besides its economic benefits<sup>4, 5</sup>, four core vaccines, including BCG, DTP, polio and measles vaccines among children defined as a basic index of vaccination program performance and also as scale for compliance of preventive medicine guidelines<sup>6</sup>. This index has increased from 20% in 1980 to 84% in 2013<sup>6-8</sup>.

Regarding to high coverage of vaccination in Iran and most countries<sup>9,10</sup>, timeliness of vaccination is equally important as vaccination coverage<sup>11</sup>. The delay time of vaccination for each EPI vaccine calculating from vaccination dates was noted on child health cards and recommended age of immunization guidelines <sup>5,12</sup>. Delayed vaccination is a risk

factor for childhood illness, including pertussis, measles and *Haemophilus influenza* type B as well as reduced survival and higher mortality<sup>5,13</sup>.

Studies on the timeliness of immunization, particularly among poor areas are rare and most studies focus on immunization coverage <sup>9,14</sup>. According to our search, only one study was conducted in Hamadan province and had shown that 42% to 67.6% of infant receive vaccine with delay despite of high coverage vaccination (>99.4%)<sup>15</sup>. Therefore, it is important to take attention to timeliness vaccination, especially in informal settlements, slum and poor urban areas that complexity of these informal settlements heightens the challenge of addressing missed or late vaccinations <sup>13,14</sup>.

This study aimed to assess delay or timing in all EPI vaccines and to evaluate this program in outskirt of five big cities of Iran. In addition, the influencing factors of delay in mumps-measles-rubella (MMR) vaccine assessed.

# **Methods**

A cross sectional descriptive study was carried out on the outskirt of Iran's big cities including Tehran, Esfahan, Arak, Mashhad and Zahedan. The target population was children 24-47 months old who lived in outskirt these cities in Jun 2013. Health experts in each city determined suburb area base on the social- economic and some other factors including the concentration of immigrant's population or noisy families. These areas defined as cluster and for enrollment of eligible children in the survey, proportioned cluster sampling was used. Children without vaccine card and the lower age child of twins were excluded from the study. More details of sampling and study protocol are described in other study<sup>9</sup>. Totally, 4502 children were assessed and those without an accessible vaccine card excluded from the analysis due to missed delay time. Accordingly, only 3610 children were enrolled who had a vaccination card, and 892 children were excluded because no vaccine card.

Data were collected by a WHO standard questionnaire 16. The interviewers were trained and the questionnaires were completed house to house. Study protocol approved by the Ethical Committee of Arak University of Medical Sciences.

# Data analysis

Data were analyzed with SPSS software (version 18). First, delay time for each vaccine was calculated based on dates on vaccination card and recommended age of vaccination according to the national immunization program. According to EPI in Iran oral polio vaccine (OPV), hepatitis B vaccine, BCG vaccine, DPT vaccine, and MMR are administered in accordance with the time schedule at birth, second, fourth, sixth, twelve and eighteen months after birth. The delay time categorized into four groups including: 1 week, 1-2 weeks, 2-4 weeks and more than 4 weeks. Due to, WHO and UNICEF reported the coverage of the first dose of measlescontaining vaccine (MMR1) annually as one of the immunization program monitoring indicators. Moreover the MMR1 coverage for children aged 1 year is one of the milestones for measles elimination programs by 2015<sup>17,18</sup>, the relationship between variables with time-delay in MMR1 vaccine was examined by chi-square test. Significance level considered at 0.05 and independent variables were child sex, parent's job, residence city, nationality, birth order and prior residency. Multivariate logistic regression was used to control the effect of covariates.

#### Results

From 3610 children 24-47 months were enrolled in this study, 1851 (51.3%) were boys and 3166 (87.7%) were Iranian. The mean age of children was 36.6±7.2 months. Among all vaccines between 56.6% to 93.2% were administered out of time. Delayed time more than a week varied from 5.5% to 74.9% of polio at birth and MMR2 at 18 months, respectively. Delay time incidence and more than 1-week delay in reception of vaccines given in Table 1 according to the time and type of vaccine. It showed that delay time increased by child age.

Table 1: Immunization delay (%) of infants at the birth, second, fourth, twelfth and eighteenth months

| Vaccine       | On time     | <1 week     | 1-2 weeks   | 2-4 weeks  | >4 weeks   | Cumulative<br>delay | Cumulative<br>delay >1 week | Not vaccinat-<br>ed |
|---------------|-------------|-------------|-------------|------------|------------|---------------------|-----------------------------|---------------------|
| At birth      |             |             |             |            |            |                     |                             |                     |
| OPV0          | 897 (24.8)  | 2441 (67.6) | 93 (2.6)    | 66 (1.9)   | 36 (1.0)   | 2636 (73.1)         | 195 (5.5)                   | 77 (2.1)            |
| HEP1          | 1498 (41.5) | 1842 (51.0) | 74 (2.1)    | 55 (1.5)   | 73 (2.0)   | 2044 (56.6)         | 202 (5.6)                   | 68 (1.9)            |
| BCG           | 1149 (31.8) | 2196 (60.8) | 97 (2.7)    | 62 (1.7)   | 41 (1.2)   | 2396 (66.4)         | 202 (5.6)                   | 65 (1.8)            |
| At 2th month  |             |             |             |            |            |                     |                             |                     |
| OPV1          | 1255 (34.7) | 1753 (48.5) | 298 (8.3)   | 147 (4.1)  | 93 (2.6)   | 2291 (63.5)         | 538 (15.0)                  | 64 (1.8)            |
| HEP2          | 1248 (34.6) | 1723 (47.8) | 290 (8.0)   | 138 (3.8)  | 137 (3.8)  | 2288 (63.4)         | 565 (15.6)                  | 74 (2.0)            |
| DTP1          | 1263 (34.9) | 1748 (48.4) | 299 (8.3)   | 149 (4.2)  | 81 (2.3)   | 2277 (63.2)         | 529 (14.8)                  | 70 (1.9)            |
| At 4th month  |             |             |             |            |            |                     |                             |                     |
| OPV2          | 896 (24.8)  | 1777 (49.2) | 462 (12.8)  | 246 (6.8)  | 157 (4.4)  | 2642 (73.2)         | 865 (24.0)                  | 72 (2.0)            |
| DTP2          | 904 (25.0)  | 1782 (49.3) | 460 (12.7)  | 245 (6.8)  | 145 (4.1)  | 2632 (72.9)         | 850 (23.6)                  | 74 (2.1)            |
| At 6th month  |             |             |             |            |            |                     |                             |                     |
| OPV3          | 649 (17.9)  | 1710 (47.4) | 602 (16.7)  | 300 (8.4)  | 263 (7.3)  | 2875 (79.8)         | 1165 (32.4)                 | 86 (2.3)            |
| HEP3          | 638 (17.7)  | 1715 (47.5) | 587 (16.2)  | 309 (8.6)  | 264 (7.3)  | 2875 (79.6)         | 1160 (32.1)                 | 97 (2.7)            |
| DTP3          | 638 (17.7)  | 1720 (47.7) | 592 (16.3)  | 310 (8.6)  | 259 (7.2)  | 2881 (79.8)         | 1161 (32.1)                 | 91 (2.5)            |
| At 12th month |             |             |             |            |            |                     |                             |                     |
| MMR1          | 572 (15.8)  | 1812 (50.2) | 518 (14.3)  | 298 (8.3)  | 307 (8.5)  | 2935 (81.3)         | 1123 (31.1)                 | 103 (2.9)           |
| At 18th month |             |             |             |            |            |                     |                             |                     |
| OPV4          | 91 (2.6)    | 677 (18.7)  | 1417 (39.2) | 760 (21.1) | 489 (13.5) | 3343 (92.5)         | 2666 (73.8)                 | 176 (4.9)           |
| DTP4          | 98 (2.7)    | 677 (18.8)  | 1401 (38.8) | 768 (21.3) | 487 (13.5) | 3333 (92.4)         | 2656 (73.6)                 | 179 (4.9)           |
| MMR2          | 64 (1.7)    | 661 (18.3)  | 1408 (39.1) | 760 (21.1) | 532 (14.7) | 3361 (93.2)         | 2700 (74.9)                 | 185 (5.1)           |

OPV: Oral Polio Vaccine, HBV: Hepatitis B Vaccine, BCG: Bacille-Calmette-Guerin Vaccine, DPT: Diphtheria-Pertussis-Tetanus Vaccine, MMR:Mumps-Measles-Rubella Vaccine

The relationship between delayed vaccination and studied variables were assessed by the chi square test and showed in Table 2. Living city and the delayed incidence relationship was significant (P<0.001). Arak with 25.4% and Zahedan by 53.4% have the minimum and maximum delayed incidence of more than a week, respectively. Delayed vaccination was higher in non-Iranians (P<0.001). Parents' education level showed a significant association with the delayed vaccine incidence. Therefore, children with high educated parents had lower vaccination rates (P<0.001). Housewife mothers vaccinated their children with more delay, but father's occupation, child gender and prior residence location have no effect on child's vaccination delay. There was a significant relationship between birth order and delay vaccination so that the higher birth order increases the likelihood of delayed vaccination (*P*<0.001).

Table 2: Distribution of MMR1 vaccine by various predictors using a chi-square test

|                     |            |                 |            |           |           | Cumulative    |         |
|---------------------|------------|-----------------|------------|-----------|-----------|---------------|---------|
| Variables           | On time    | 1 week          | 1-2 weeks  | 2-4 weeks | >4 weeks  | delay >1 week | P value |
| City                |            |                 |            |           |           |               | 0.001   |
| Tehran              | 291 (18.5) | 853 (54.3)      | 210 (13.4) | 109 (6.9) | 108 (6.9) | 427 (27.2)    |         |
| Isfahan             | 164 (17.2) | 483 (50.7)      | 137 (14.4) | 90 (9.5)  | 78 (8.2)  | 305 (32.1)    |         |
| Mashhad             | 83 (11.7)  | 344 (48.5)      | 133 (18.8) | 74 (10.4) | 75 (10.6) | 282 (39.8)    |         |
| Zahedan             | 14 (9.9)   | 52 (36.9)       | 14 (9.9)   | 21 (14.9) | 40 (28.4) | 75 (53.2)     |         |
| Arak                | 20 (14.9)  | 80 (59.7)       | 24 (17.9)  | 4 (3.0)   | 6 (4.5)   | 34 (25.4)     |         |
| Nationality         |            |                 |            |           |           |               | 0.001   |
| Iranian             | 518 (16.7) | 1642 (53.1)     | 458 (14.8) | 248 (8.0) | 229 (7.4) | 935 (30.2)    |         |
| Other nations       | 54 (13.1)  | 170 (41.3)      | 60 (14.6)  | 50 (12.1) | 78 (18.9) | 188 (45.6)    |         |
| Mother's education  |            |                 |            |           |           |               | 0.001   |
| Illiterate          | 45 (12.7)  | 140 (39.7)      | 53 (15.0)  | 46 (13.0) | 69 (19.5) | 168(47.5)     |         |
| Elementary          | 93 (14.4)  | 319 (49.4)      | 90 (13.9)  | 60 (9.3)  | 84 (13)   | 234(36.2)     |         |
| Middle school       | 106 (16.4) | 336 (52.2)      | 90 (14.0)  | 65 (10.2) | 48 (7.4)  | 203(31.6)     |         |
| High school         | 246 (17.5) | 778 (55.4)      | 223 (15.9) | 83 (5.9)  | 75 (5.3)  | 381(27.1)     |         |
| College             | 82 (18.1)  | 236 (52.2)      | 61 (13.5)  | 42 (9.3)  | 31 (6.9)  | 134(29.7)     |         |
| Father's education  | ` '        | ` ,             | ` '        | ` /       | ` '       | ` ,           | 0.001   |
| Illiterate          | 37 (14.1)  | 97 (36.9)       | 42 (16.0)  | 37 (14.1) | 50 (19.0) | 226 (49.1)    |         |
| Elementary          | 94 (13.1)  | 360 (50.3)      | 107 (15.0) | 70 (9.8)  | 84 (11.7) | 537 (75.1)    |         |
| Middle school       | 158 (17.4) | 458 (50.4)      | 153 (16.9) | 76 (8.4)  | 63 (6.9)  | 292 (32.2)    |         |
| High school         | 182 (16.4) | 628 (56.6)      | 148 (13.3) | 76 (6.8)  | 76 (6.8)  | 300 (26.9)    |         |
| College             | 98 (19.7)  | 264 (53.0)      | 65 (13.1)  | 38 (7.6)  | 33 (6.6)  | 136 (27.3)    |         |
| Mother's occupation | , ,        | ()              | ,          | ,         |           |               | 0.002   |
| Housewife           | 521 (15.7) | 1737 (52.3)     | 493 (14.8) | 281 (8.5) | 290 (8.7) | 1064 (32.0)   |         |
| Employed            | 47 (26.9)  | 73 (41.7)       | 23 (13.1)  | 15 (8.6)  | 17 (9.7)  | 55 (31.4)     |         |
| Father's occupation | (===,      | , ( ( , , , , ) | ()         | (0.0)     | (>)       | 22 (221.)     | 0.080   |
| Unemployed          | 8 (10.8)   | 41 (55.4)       | 10 (13.5)  | 3 (4.1)   | 12 (16.2) | 25 (33.8)     |         |
| Employed            | 561 (16.4) | 1766 (51.6)     | 507 (14.8) | 294 (8.6) | 292 (8.5) | 1093 (31.9)   |         |
| Birth order         | ( )        |                 | 207 (2110) | _, (0.0)  |           | 10,10 (01.0)  | 0.001   |
| 1st                 | 243 (18.6) | 700 (53.7)      | 203 (15.6) | 84 (6.4)  | 74 (5.7)  | 361 (27.7)    | 0.001   |
| 2nd                 | 231 (16.4) | 744 (52.7)      | 205 (14.5) | 123 (8.7) | 108 (7.7) | 436 (30.9)    |         |
| 3th                 | 63 (12.7)  | 249 (50.3)      | 66 (13.3)  | 56 (11.3) | 61 (12.3) | 183 (36.9)    |         |
| 4th or more         | 35 (12.1)  | 114 (39.3)      | 43 (14.8)  | 34 (11.7) | 64 (22.1) | 141 (48.6)    |         |
| Child's gender      | 33 (12.1)  | 111 (37.3)      | 13 (11.0)  | 51(11.7)  | 0. (22.1) | 111 (10.0)    | 0.227   |
| Female              | 259 (15.3) | 878 (51.8)      | 268 (15.8) | 137 (8.1) | 153 (9.0) | 558 (32.9)    | 0.227   |
| Male                | 313 (17.3) | 930 (51.5)      | 249 (13.8) | 161 (8.9) | 154 (8.5) | 564 (31.2)    |         |
| Original City       | 313 (17.3) | 750 (51.5)      | 247 (13.0) | 101 (0.7) | 154 (0.5) | 307 (31.2)    | 0.091   |
| City                | 540 (16.3) | 1732 (52.1)     | 481 (14.5) | 285 (8.6) | 285 (8.6) | 1051 (31.7)   | 0.071   |
| Rural               | 19 (16.1)  | 51 (43.2)       | 26 (22.0)  | 8 (6.8)   | 14 (11.9) | 48 (40.7)     |         |

Logistic regression showed that birth order and mother education were most important predictors of delayed MMR vaccination. Therefore, second birth to forth birth increase delayed vaccination compared to the first birth as RR; 1.27, CI95%: 1.06-1.5, RR; 1.7, CI95%: 1.3-2.2 and RR; 2.5, CI95%: 1.8-3.5. Furthermore, college educated mothers were significantly less delay for children vaccination as RR; 0.79, CI95%: 0.62-0.99 (*P*<0.001).

## **Discussion**

According to our results, the percent of unvaccinated children was low and changed from 1.8% to 5.1% at birth to eighteen-month age. However, delayed vaccination incidence is high in the outskirts of big Iranian cities. The delayed incidence regarding to more than one-week delay varied from 5.5% for at birth OPV to 74.9% for MMR2. The coverage of three doses of DTP vaccine (DTP3) is the most important indicators of public health. A global coverage estimate of 84% in 2013 also for the first time in 2013 global coverage of the second dose of MMR vaccine 35% was estimated. Our results showed that both of these indicators are much higher than the average global coverage (97.3% for DTP3 and 94.8 for MMR2). These findings reflect the successfulness of the Iran immunization program\_to increase vaccination coverage even in outskirt areas. Despite high vaccination coverage, 56.6% (for HEP1) to 93.2% (for MMR2) of children have been vaccinated with delay more than one day according to vaccine type. This rate is higher than 42%-67.6%, reported in another study conducted in Hamadan province of Iran<sup>15</sup>. One cause for the difference is that our study was conducted in poor areas. The outskirt areas of big Iranian cities are including high percent of immigrant and low socioeconomic people. However, the study population of the current study was different to Hamadan study.

Delayed vaccination rate increased with increasing child age, so that the maximum delayed rate occurred in booster doses especially in booster dose of MMR. The same results obtained in other studies<sup>1,15</sup> due to parental attention to children vaccinations have lost by increasing of child age.\_So, it is necessary that in each vaccination turn health workers emphasize to parents for the importance of late vaccination regarding to reduced survival and mortality<sup>5,13</sup>. Moreover, it is recommended that date of future return noted on vaccination card. Because the MMR vials were 10 doses, this vaccine was injected only on a certain day. It is essential to prepare a single dose of MMR vaccine.

Chi square test showed a significant difference between cities in vaccination delay time. Zahedan City located\_in southeastern Iran\_had the maximum amount of vaccine delay. It may be due to low levels of socio-economic status, some

cultural issues and large population of immigrants particularly from Afghanistan. On the other hand, the lowest delay time was in Arak City in central of Iran since it is near the capital with higher living standards of the people, lower population and following health care centers is easier. Long distance from the health center is effective on the increasing possibility of the delayed vaccination 15. Several studies also have shown the geographical differences in vaccination <sup>2,13,19</sup> Delay was more among foreigners due to the most Afghans immigrants immigrated to Iran and concentrated in slum are-

Multivariate analysis showed that higher levels of parent's education associated with less delay in vaccination. This has been confirmed in other studies <sup>5,7,20</sup>-22 since educated parents are have understood better importance of vaccination. Housewives had more delays in vaccinating children. Wiysong et al study showed that children of mothers who are not employees were vaccinated with more delay in comparing to employed mothers <sup>22</sup>. It is perhaps for this reason that mothers who are employed generally have higher levels of education. Besides, a significant relationship was observed between birth order and delayed vaccination and with increasing birth order of children's vaccines delay also increased. The probability of delayed vaccination increased from 27% from the second birth to 70% for third birth and up to 150% for the forth or higher birth. These findings are similar to other studies that the sensitivity of the parents to the ontime vaccination decreases after the first child. 13,23,24. However, our results did not show a significant relationship between delayed vaccination and child sex, former location (city or rural) as well as father's education and job. Gender inequality has been observed in some studies in health care utilization<sup>25,26</sup> that delay or non-vaccination was greater in girls because of the son preference in some developing countries.<sup>4,27</sup>.

The current study has some limitations. A low percent of children did not access to vaccine card at the interview time and these children were excluded. In addition, vaccines can be delayed or omitted because of some other factors, including minor illness, past history of febrile convulsion or family history of epilepsy. Due to increasing recall bias and also using WHO standard questionnaire for immunization coverage, these factors did not assess in a vaccination delay time.

## **Conclusions**

Despite the low percent of unvaccinated children, the delayed vaccination incidence is higher in the suburbs of big Iranian cities. The coverage of indicators vaccines is much higher than the average global coverage and reflects the successfulness of the Iran immunization program to increase vaccination coverage even in outskirt areas. Furthermore, health officers and health policy makers should attempt for on-time vaccination beside of high immunization coverage especially in slum areas. The educational intervention should focus on areas with high concentrated immigrants and crowded families with low education.

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# **Conflict of interest statement**

The authors declare no potential conflicts of interest.

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