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Evaluating Vaccination Delay in Infants during COVID-19 Outbreak in Yazd

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ABSTRACT

Background: One of the potential consequences of COVID-19 is the interruption of childhood vaccination. The aim of this study is to investigate the frequency of vaccination delay in children during the COVID-19 outbreak in Yazd, Iran.

Methods: In this cross-sectional study in 2020, 667 children living in Yazd were enrolled through multi-stage sampling method. Date of birth, vaccination dates of 2-, 4-, and 6- months of age, gender, family size, birth order and municipal area were extracted from the Integrated System Information Block (SIB) system. Data were analyzed using SPSS software version 22.

Results: among 667 infants, 322 (48.3%) were girls and 345 (51.7%) were boys. In total, 53.5% of children had delay in vaccination at 2-month of age, 54%, at 4-month, and 45% at 6-month regarding vaccination appointment. Moreover, the dangerous delay was 3% in vaccination rounds for 2-month-olds, 5.4% for 4-month-olds, and 1.7% for 6-month-olds**.** At all the three appointments, there was a statistically significant difference between both the family size (P-value: 0.025, 0.017 and 0.004, respectively) and birth order (P-value: 0.015, 0.007 and 0.013, respectively) regarding vaccination delay.

Conclusion: Despite the high frequency of one or more than one day delay for 2-, 4-, and 6-month-old infants regarding vaccination appointments, dangerous delay in the mentioned times was relatively infrequent. Meanwhile, family size and birth order were two influential factors respecting vaccination delay in children. It is essential to raise awareness among families, particularly those with larger size and higher number of children about the importance of timely vaccination.

Keywords: Vaccination, vaccination hesitancy, COVID-19, YAZD

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Introduction

COVID-19 pandemic was considered as the worst public health crisis of the century (1, 2). The disease began at first in Wuhan, a populous city in China in December 2019 (3-5), and rapidly spread from China to other parts of the world; 770,875,433 people were affected with this disease, and until 29 September 2023, the number of deaths reached 6,959,316 people(6). The accelerating spread of this ailment induced fear among public (7) as well as disturbance in established healthcare provisions, potentially impeding the management of additional and avoidable transmissible ailments (1, 8). The impact of this pandemic on routine immunization is of great importance (9) and can lead to an increase in morbidity and mortality from vaccine-preventable diseases (VPDs) such as measles and poliovirus in countries with weak vaccination coverage (1). The fear of disease contagion and the implementation of social distancing activities lead parents to postpone regular child vaccinations (10). At the same time, governments cannot take strict measures to improve vaccination in response to the COVID-19 pandemic (1). There is a serious concern about the emergence of rubella during COVID-19 pandemic, as the disease is highly contagious , and over 117 million children in 37 countries may not receive rubella vaccine due to the suspension of vaccination programs (11).

According to the report by World Health Organization (WHO), COVID-19 has caused an interruption in life-saving vaccinations around the world and has exposed millions of children - from rich to poor communities - to diseases such as diphtheria, polio and rubella (12). According to the WHO, VPDs are a serious threat to nearly 80 million children around the world due to health care systems disruption caused by the COVID-19 pandemic (13).

To date, limited information is available on the impact of the COVID-19 pandemic on childhood vaccination, especially in Iran (13). Therefore, the authors aimed to investigate the extent of delayed childhood vaccinations during the COVID-19 pandemic in Yazd, a city at the center of Iran, in 2020.

Methods

The current research was a descriptive cross-sectional study. After obtaining approval from the ethics committee, this study was conducted on infants covered by the comprehensive health center who were born during the first 3-4 months of COVID-19 emergence in Iran, and most of them were 6 months old in the fall and in the first month of winter in 2020 (born from February 20, 2020 to June 31, 2020) in Yazd**.**

In the present study, multi-stage sampling method was employed to select participants. Considering that Yazd city has 5 municipal districts, the names of comprehensive health centers in each municipal district were extracted, and one center was randomly selected from each municipal district. In this way, 5 comprehensive health centers were finally selected. Sampling was done in all comprehensive health centers and their affiliated health centers, and all the children from each center who turned 6 months old in the fall and first month of winter were included in the study**.**

The sample size was calculated based on the formula for estimating the proportion of a qualitative trait in a community using the results of a study conducted in Saudi Arabia (23.4% frequency of the delay of more than 1 month in child vaccination) (13). By considering the error of 0.047, the final sample size was calculated to be 309.

$$n = \frac{z^2_{1-\frac{\alpha}{2}} pq}{d^2}$$

In order to collect data, a form was designed based on the study variables, including date of birth, vaccination date of 2, 4, and 6 month ages for each infant, gender, household size, birth order, and municipal area; The needed data were extracted from the SIB system.

In this study, we considered the three mentioned vaccine rounds because it was intended to examine the children who were born during the COVID-19 pandemic (from early 2020) on the one hand, and

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to collect all the necessary data until the end of 2020, on the other hand. Therefore, the authors needed infants who were 6 month old at the time of data gathering and only received these three vaccine rounds. Moreover, the three rounds had to be about one infant. The reason was that each vaccine round must be provided for the infant of 60 days old until the next one. If an infant visits earlier than 60 days between 2-4 month and 4-6 month vaccination rounds- even if the vaccination date of that appointment is completely correct based on his/her date of birth - the SIB system does not allow registration of that vaccine round and obliges the caregiver to observe an interval of at least 60 days between two appointments. Because in the national vaccination table, some vaccination appointments are related to each other, and the delay in one appointment is determined based on the date of the previous one and not the child's birth date, therefore we decided to include three rounds of the vaccine in one person for more accuracy.

Because it was possible that the day considered for the child's visit was a holiday or some months were 31 days, the 62-day interval between two vaccination appointments without delay was considered. Therefore, time interval of more than 62 days between two appointments was considered as delay, and more than 62 days was regarded as delay time. In addition, dangerous vaccination delay was considered to be 15 days or more for infants of 2 and 4 months of age(14) and 30 days or more for infants of 6 months of age with respect to vaccination rounds (15)

Statistical analysis

Data were collected and entered into SPSS software version 22 and analyzed. Then, mean/standard deviation and frequency/percentage were extracted and compared within qualitative variables through independent sample T-test. In addition, the relationship between qualitative variables was evaluated using chi-square test**.**

Results

Totally, 667 infants were included in the study, with 322 (48.3%) females and 345 (51.7%) males. The results of the study on the frequency of vaccination delay in 2, 4 and 6-month vaccination rounds showed that 53.5% of the children were delayed at 2months of age, 54% at 4 month of age, and 45% at 6 month months of age regarding vaccination rounds. In addition, the average time of vaccination delay was 4.12 ± 6.97, 8.81 ± 4.62, and 7.81 ± 4.10 days at 2, 4 and 6-month vaccination rounds, respectively**.**

In this study, the frequency of vaccination delay at three vaccination rounds was investigated according to the gender, number of family members, birth order, and municipal area. The results of the analysis with the chi-square test showed that in all the three rounds, there was a statistically significant relationship between vaccination delay, the number of family members (P-value: 0.025, 0.017 and 0.004, respectively), and birth order (P-value: 0.015, 0.007 and 0.013, respectively); so that with the increase in the number of family members and birth order, the probability of vaccination delay in each vaccination round increased significantly. Also, a significant relationship was observed between vaccination delay and the 2-month-old infant regarding appointment place (not for other two ones). The results of this analysis are shown in Tables 1 to 3.

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Table 1. Frequency (percentage) of infants' delayed vaccination at the two-month appointment according to the study variables

Variable		Delay in 2-month-old infant vaccination (N (%)) No	Yes	P-value
Gender	Female	147 (45.7)	175 (54.3)	0.680
	Male	163 (47.2)	182 (52.8)	
Family size	3	123 (52.1)	113 (47.9)	0.025
	4	125 (46.5)	144 (53.5)	
	> 4	62 (38.3)	100 (61.7)	
Birth order	1st child	124 (51.5)	117 (48.5)	0.015
	2nd child	129 (47.6)	142 (52.4)	
	3rd child and over	57 (36.8)	98 (63.2)	
Municipal area	1	66 (36.1)	117 (63.9)	0.001
	2	71 (48.6)	75 (51.4)	
	3	99 (55.3)	80 (44.7)	
	4	43 (54.4)	36 (45.6)	
	5	31 (38.8)	49 (61.2)	

Table 2. Frequency (percentage) of infants' delayed vaccination at the four-month appointment according to the study variables

Variable		Delay in 4-month vaccination (N(%)) No	Yes	P-value
Gender	Female	140 (43.6)	181 (56.4)	0.230
	Male	166 (48.3)	178 (51.7)	
Family size	3	125 (53.4)	109 (46.6)	0.017
	4	115 (42.8)	154 (57.2)	
	> 4	66 (40.7)	96 (59.3)	
Birth order	1st child	129 (54)	110 (46)	0.007
	2nd child	116 (42.8)	155 (57.2)	
	3rd child and over	61 (39.4)	94 (60.6)	
Municipal area	1	79 (43.2)	104 (56.8)	0.288
	2	68 (46.6)	78 (53.4)	
	3	92 (51.7)	86 (48.3)	
	4	37 (46.8)	42 (53.2)	
	5	30 (38)	49 (62)	

Table 3. Frequency (percentage) of infants' delayed vaccination at the six-month appointment according to the study variables

Variable		Delay in 6-month vaccination (N(%)) No	Yes	P-value
Gender	Female	177 (55.5)	142 (56.4)	0.808
	Male	186 (54.5)	178 (51.7)	
Family size	3	147 (63.4)	85 (36.6)	0.004
	4	140 (52.4)	127 (47.6)	
	> 4	76 (47.2)	85 (52.8)	
Birth order	1st child	148 (62.4)	89 (37.6)	0.013
	2nd child	140 (52)	129 (48)	
	3rd child and over	75 (48.7)	79 (51.3)	
Municipal area	1	107 (58.5)	76 (41.5)	0.109
	2	71 (49.3)	73 (50.7)	
	3	106 (60.2)	70 (39.8)	
	4	36 (45.6)	43 (54.4)	
	5	43 (55.1)	35 (44.9)	

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The results of the study on the frequency of dangerous vaccination delay in three mentioned rounds showed that the delay rate of 15 days or more was 3%in the 2-months rounds and 5.4% in the 4-month appointments. Also, the delay rate of more than30 days was reported as 1.7% regarding the 6-month vaccination appointment**.**

Discussion

The results of the present study revealed that 53.5% of the infants at 2 months, 54% at 4 months, and 45% at 6 months of age showed delay in vaccination. In addition, the average time of vaccination delay at 2, 4 and 6 months was 4.45, 4.62 and 4.10 days respectively. In a study conducted in Saudi Arabia, about 23.4% of parents reported more than 1 month of delay in their children vaccination (13). Another research in the eastern region of this country revealed that almost one third of the children did not receive routine vaccines during the pandemic (16).In a study conducted in Pakistan, a 52.5% reduction in the average daily vaccination rate was observed during quarantine period compared to the baseline. The highest reduction was related to the BCG vaccination (40.6%). Per day, about 8,438 children did not go for vaccination during quarantine (1). The results of Din's study also showed that during the COVID-19 pandemic, Pakistan experienced a delay in vaccination against poliovirus. From December 2019 to April 2020, about 40 million children did not receive polio vaccination due to the cessation of the national vaccination campaign. Interruption in vaccination programs can have long-term adverse effects and increase the prevalence of poliovirus in this country (17). The results of another study conducted in the United States revealed that during the first 4 months of 2020, the vaccination rate of children ≤ 18 years old decreased by 21.5%, and in infants of ≤ 24 months old by 15.5% compared to the same period in 2018 and 2019. According to other studies, the prescription rate of vaccines, including the rubella- containing vaccine, was lower in April and March 2020, compared to the same period in previous years (11). Bramer conducted a study in the United States and found that vaccination coverage, except hepatitis B vaccine at birth, decreased for the mentioned ages. In addition, vaccination coverage of 5-month-old infants decreased to 49.7% and 16-month-old infants to 70.9% in May 2020. Meanwhile, the vaccination rate of infants less than 24 months of age during January-April 2020 was 15% lower than the same period in 2018-2019 (18). The results of a study in Nigeria also revealed that the COVID-19 pandemic had a negative impact on vaccination activities in Nigeria which was considered a threat with regard to controlling preventable diseases (19). It seems that one of the negative effects of the COVID-19 pandemic is an increase in the risk of vaccine-preventable diseases in low-income countries, where vaccination programs had been temporarily suspended to prevent the spread of the disease. Of course, the need for COVID-19 vaccine could improve people's adherence to vaccination after the end of the pandemic, and this would be one of its positive effects (20). In general, the COVID-19 pandemic had a significant impact on preventive measures including vaccination all over the world, especially in developing countries.

In this study, one or more than one day delay were more frequent, and in vaccination appointments regarding 2- and 4-months' infants, more than half of the infants had experienced this type of delay. However, the important question was whether this level of delay could cause any problem in immunity and affect the health of children? And basically, how much delay could bring risks for children (dangerous vaccination delay)? According to the reviewed literature and based on a study by Gras et al. in France on 37 experts in the vaccination field, it was concluded that delays of 15 days or more in the first and second rounds of vaccination, including diphtheria, tetanus, pertussis, polio, and hemophilus influenza type B vaccines can be dangerous. The same study also pointed out that in areas where these vaccines were administered in three doses, the experts needed to decide on the level of risk and dangerous

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duration for the third dose delay (14). Based on a study by Kiely et al. on 7183 children from 2006 to 2016 in Canada, the delay in vaccination was 5.4% at 2 months of age, 13.3% at 4 months of age, 23.1% at 6 months of age, and 23.6% at 12 months of age; furthermore, a delay of more than 30 days was considered dangerous in the third round of vaccination in children (15) .Accordingly in the present study, the dangerous delay in the third round of vaccination was considered to be more than 30 days. In current study, the rates of dangerous delay, defined as15 days and more in the 2-month and 4-month-old infants vaccination appointments were 3% and 5.4% respectively. In addition, dangerous delay of more than one month of window time was 1.7% among 6 months infants. Most of the research conducted had evaluated missed vaccination appointments or vaccination rate decline during COVID pandemic (21-24) and some had assessed the vaccination delay. However, they had considered vaccination delay as nearly or more than one month of window time between the expected to the observed time of vaccination (definition of dangerous delay); accordingly, they had reported significant proportion of children with delay. For example, in Saudi Arabia, nearly one fourth of children experienced more than one month of delay in their routine vaccination (13). In addition, in Canada, the frequency of delayed/no vaccination time was 14-47% in some age groups (25). Meanwhile, according to Hull BP et al.'s study, in Australia in 2006, ,long delays (more than 6 months) occurred in 1 to 2% of the indigenous and 5 to 12% of non-indigenous children (26).It seems that dangerous delay in this study was not as significant as previous studies, and most of the parents were careful with routine vaccination despite COVID-19 pandemic in Yazd.

Regarding the factors affecting the frequency of vaccination delay, the results of the present study demonstrated that there was a significant association between the frequency of vaccination delay in all the three cases of 2-, 4- and 6- month-old infants and in families with more members. The results of Alsuhaibani's et al. study showed that the most common reason for delayed vaccination was the fear of contracting COVID-19 (60.9%). The large size of the household and lack of insurance were other risk factors for delay in vaccination (13), which was consistent with the results of this study regarding the impact of the family dimension. Besides, birth order was another factor with significant association with vaccination delay, in which children with higher birth order showed more delay in vaccination. This finding was also consistent with other studies regarding the important factors affecting vaccination timeliness (27, 28). These similar findings might be due to decreasing parental sensitivity towards timely vaccination after first child (29). Parents may feel that since their first child was vaccinated on time and did not experience any adverse effects, they could delay or skip vaccinations for their subsequent children. Meanwhile, with the demands of caring for multiple children, parents may forget to schedule appointments for vaccinations or may not prioritize them as well as they did for their first child.

Strengths and limitations

This was the first and maybe the only study in evaluating routine vaccination delay in Iran as an important subject. However, there were some limitations that should be considered when interpreting the results:

- A relatively short observation window: the study only had a 6-month period observation during the COVID-19 pandemic. This limited timeframe may not capture the full extent of the vaccination delay and its long-term consequences.
- Local context: The study focused on Yazd city in Iran, which might not be representative of other cities or provinces, and the findings might not be generalizable to a broader population.
- Lack of vaccine supply constraints: This article did not provide information on the availability of vaccines in Yazd, which could impact the vaccination delay.
- Potential confounding factors: The study did not account for other factors that may have contributed to the vaccination delay, such as parental attitudes towards vaccines or healthcare

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system capacity. These factors could influence the results and should be considered when interpreting the findings.

- The type of study: the type of study was also cross-sectional and causality could not be investigated.

Conclusion

Based on the results of this study, families with more members and the higher birth order were two influential factors on vaccination delay in children. It is essential to increase awareness among families, particularly those with more children regarding the importance of timely vaccination. Despite high frequency of one or more than one day delay at 2-, 4- and 6-months of age, vaccination appointments and dangerous delays in the three periods are relatively infrequent. However, it is highly recommended to perform similar studies in other cities and provinces to further confirm that the dangerous delay is frequent in other parts of Iran as well.

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Conflict of interest

The authors declared no conflict of interests.

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Ethical considerations

The proposal of this research was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

This study was conducted in accordance with relevant guidelines of the institution.

Code of ethics

IR.SSU.MEDICINE.REC.1399.256 (available at: https://ethics.research.ac.ir/ProposalCertificateEn.php?id=173029&Print=true&NoPrintHeader=true&NoPrintFooter=true&NoPrintPageBorder=true&LetterPrint=true).

Authors' contributions

All the authors contributed to writing, editing, and reviewing of the manuscript.

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