Determinants of timeliness in early childhood vaccination among mothers with vaccination cards in Sindh province, Pakistan: a secondary analysis of cross-sectional survey data

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ABSTRACT

Objective Untimely vaccination refers to receiving the given dose before (early) or after (delayed) the recommended time window. The purpose of this study was to assess the extent of timeliness of childhood vaccinations and examine the determinants of vaccination timeliness in Sindh province, Pakistan.

Design Cross-sectional analysis of data from the 2013 and 2014 Maternal and Child Health Program Indicator Surveys.

Setting Community-based maternal and child health surveys.

Participants Among 10,200 respondents of Maternal and Child Health Program Indicator Surveys, 1143 women who had a live birth in the 2 years preceding the survey were included.

Outcomes At the participants' home, an interviewer asked mothers to show their children's vaccination cards, which contained information regarding vaccinations. Children's vaccination status was categorised into timely or early/delayed compared with vaccination schedule.

A logistic regression analysis using Firth's penalised likelihood was performed to identify factors associated with timeliness of vaccinations.

Results 238 children (20.8% of children who received a full set of basic vaccinations) received all vaccinations on schedule among children who received a full set of basic vaccinations. The percentages of timely vaccinations ranged from 2.3% for second measles vaccination to 89.3% for bacillus Calmette-Guérin. Child's age and place of delivery were associated with timely vaccinations. Older child age and institutional delivery were associated with decreased timely vaccination rate.

Conclusions Home-based vaccination record is a key tool to improve the timeliness of vaccinations. The redesigned vaccination cards, the new electronic registries for vaccination card information and the vaccination tracking system to remind the second/third vaccination visits may be helpful to improve timely vaccinations for children under 2 years old.

INTRODUCTION

Achieving high vaccination coverage is crucial in the control and prevention of childhood as well as older age infections. Currently, standard estimates of vaccination coverage are based on vaccination statuses at predefined ages, typically at 12 months, 24 months and 4–6 years. The most widely accepted indicator internationally is the proportion of children who have received recommended routine vaccinations by 24 months of age, as prescribed by the WHO. This indicator does not measure delays in the acquisition of immunity caused by late vaccination.

The timeliness of immunisations, that is, receiving vaccinations at the earliest appropriate age, is an important public health goal for several reasons. First, if children are vaccinated too early or if vaccinations are too closely spaced, it can significantly shorten the duration of protection or interfere with the body's immune response. Second, delayed immunisation potentially leads to prolonged exposure to vaccine-preventable diseases.
addition, timely vaccination heightens populations’ herd immunity levels, thereby protecting those who are too young to be vaccinated, those who have medical contraindications and those who do not produce an adequate immunological response. Despite the importance of the timeliness of childhood immunisations, vaccination delays are prevalent across lower income countries, including Pakistan. An analysis of the 2006–2007 Pakistan Demographic and Health Survey found substantial variations in the timeliness of vaccinations, including considerable delays in many cases.

Factors associated with lack of childhood vaccination have been studied extensively, and specific patterns have been identified. In contrast, less is known about factors associated with delayed vaccination and whether these factors follow the same patterns in different societies. Information about factors that influence the timeliness of childhood vaccination might be valuable for healthcare providers, programme managers and policymakers in identifying sub-populations at risk, which should be targeted with interventions and public health policies. The timeliness of childhood vaccination has received close attention in the USA and in Europe, but in-depth investigations in low-income countries have been limited, particularly in Pakistan. The purpose of this study was to examine the timeliness of childhood vaccination coverage and its determinants in Sindh province, Pakistan.

**METHODS**

**Data and subjects**

This study analysed a subset of data from the Maternal and Child Health Program Indicator Survey, which was conducted in June to October of 2013 and 2014 in 23 districts of Sindh province and Karachi in Pakistan. The survey was a cross-sectional study, and samples were selected using a stratified multistage sampling design. Survey respondents included 4000 women in 2013 and 6200 women in 2014 who had a live birth in the 2 years preceding the survey. Women answered questions about maternal and child health (MCH) related to their last live birth. The inclusion criterion of this analysis was the respondents who answered all variables of interest and who presented a vaccination card to the data collector. The vaccination card is a home-based record (HBR), which documents immunisation status in developing countries. It contains each child’s specific vaccination information, including child’s name, birthdate, type of vaccination and vaccination date. It is issued to each child at its first vaccination.

Seven thousand eight hundred and forty (76.9% of total survey respondents) women were excluded due to not having vaccination cards or to missing information on their vaccination cards. An additional 107 women were excluded because they were missing information on the number of living children (n=1), woman’s education (n=6), husband’s education (n=15), household wealth (n=11) or antenatal care (ANC) visit (n=74). Women with children who did not receive a full set of basic vaccinations (n=1110) were also excluded. Finally, a total of 1143 women who had all the information needed for analysis and whose children received a full set of basic vaccinations were included in this study (figure 1). It was 11.2% of total survey respondents.

As female literacy is low in Sindh province, female interviewers obtained verbal informed consent from each respondent and then signed the consent form on behalf of the respondent.

**Patient and public involvement**

This research was done without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy.

**Measurement for timeliness in vaccination**

From the vaccination card, we collected information and then categorised each child’s vaccination status into timely or early/delayed. The definitions of timely and early/delayed vaccinations followed those used in Zaidi et al. The measles 2 schedule, which was not included in the study by Zaidi et al., was updated using a report by Khan and the WHO recommendation. Our definition of timely and early/delayed vaccination is shown in table 1.

Children who had received all appropriate vaccinations on schedule were put into the ‘timely’ vaccination group. If children received all appropriate vaccinations for their age, but one or more vaccinations were not administered on time, they were put into the ‘early or delayed’ group. We combined children who received vaccinations early and those who received vaccinations late into one group due to a small number, and both eventualities cause timely vaccination problems.

**Independent variables**

To identify the determinants of timely vaccination, our analysis included the following independent variables: child’s age, woman’s age, number of living children,
residence, woman’s education, husband’s education, wealth quintile, information source about MCH, number of ANC visits, assistance during delivery and place of delivery. Previous studies of a similar type conducted in Pakistan and other low/middle-income countries included the same variables.7 9 17

Categories of independent variables followed the Maternal and Child Health Program Indicator Survey report17. Wealth quintile was derived from household assets using a principal components analysis, as described previously.22. To identify MCH information sources, interviewers asked: ‘During the last 12 months, have you received any information about MCH from the following sources?’ . Sources were categorised as medical professionals (doctors, nurse/midwives and female health visitors), low-level health workers (Dai-traditional birth attendants, female health workers, homeopaths, Hakim-herbal medicine practitioners and outreach workers), relatives/friends and media (radio, TV, telephone helpline, text message on mobile phone, health education/ awareness session and print media). As multiple answers were permitted, answers per category were included in our model. The number of ANC visits was categorised into ‘1’ or ‘2, 3’ and ‘4+'. Assistance during delivery was categorised into traditional birth attendants, female health workers, homeopaths, Hakim-herbal medicine practitioners and outreach workers, low-level health workers (Dai-traditional birth attendants, female health workers, homeopaths, Hakim-herbal medicine practitioners and outreach workers), relatives/friends and media (radio, TV, telephone helpline, text message on mobile phone, health education/ awareness session and print media). As multiple answers were permitted, answers per category were included in our model. The number of ANC visits was categorised into ‘1’ or ‘2, 3’ and ‘4+'. Assistance during delivery was categorised into traditional birth attendants, medical professionals and no one/others. Place of delivery was categorised into home, private facility and public facility.

Statistical analysis

The χ² test was used to determine if a statistically significant relationship existed between each independent variable and timeliness of vaccination. Then, binary logistic regression analysis was performed to identify factors associated with timeliness of vaccination. A binary logistic regression analysis was conducted for early or delayed (reference) versus timely vaccination. Because the number of events were low, logistic regression using Firth’s penalised likelihood was conducted in this study.23

The criterion for significance was p≤0.05, two-tailed. ORs and 95% CIs were calculated. ORs were calculated after adjusting for all independent variables. All analyses were performed using SAS V.9.4.

RESULTS

The general characteristics of the study subjects are shown in table 2: 238 children (20.8%) received all vaccinations on schedule, while 905 children (79.1%) received all vaccinations, but some or all were early or delayed. The rate of early and delayed vaccinations increased as children got older, being 5.6% in children aged 0–5 weeks and increasing to 100.0% in the oldest children (12–23 months) (table 2). The timeline of vaccinations is presented in table 3. The percentage of children with timely vaccinations was 89.3% for bacillus Calmette-Guérin (BCG) and 87.7% for polio 0; all other rates of timely vaccinations were lower. Due to early vaccination, the number of subjects was more than the eligible number of subjects. The percentage of delayed vaccinations increased for polio 3 and penta 3 in children aged 14 weeks to 8 months. The percentage of delayed vaccinations for penta 3 was 43.4%, which was the highest among all vaccines. Over 90% of children in this study received measles 1–2 earlier than the recommended timeframe (table 3).

Table 4 shows the factors associated with timely vaccination. As children aged, the timeliness of vaccination decreased. Children 70–97 days old were less likely to receive timely vaccinations (OR=0.12; 95% CI 0.04 to 0.36) compared with children 0–69 days old. The OR became 0.02 (95% CI 0.01 to 0.04) for children 98 days or older. With regard to place of delivery, compared with home deliveries, deliveries in both private facilities (OR=0.39; 95% CI 0.17 to 0.96) and public facilities (OR=0.34; 95% CI 0.14 to 0.89) showed significantly lower ORs for timely vaccinations (table 4).

DISCUSSION

In Pakistan, the vaccination rates for the full set of basic vaccines has been increasing due to the expanded programme on immunisation (EPI), but little is known about the vaccination timeliness and the determinants for early, timely and delayed vaccination. The present study aimed to assess the extent of timeliness of childhood

| Table 1 The definition of early, timely and delayed for each vaccine |
|---------------------------------------------------------------|
|                     | Recommended age (days) | Early (days) | Timely (days) | Delayed (days) |
|---------------------|------------------------|--------------|---------------|---------------|
| BCG, polio 0        | 0                      | –            | 0–28          | >28           |
| Polio 1, penta 1    | 42                     | <39          | 39–70         | >70           |
| Polio 2, penta 2    | 70                     | <67          | 67–98         | >98           |
| Polio 3, penta 3    | 98                     | <95          | 95–126        | >126          |
| Measles 1           | 273                    | <270         | 270–301       | >301          |
| Measles 2           | 365–455                | <Min (28 days from measles 1 or 362) | Min (28 days from measles 1 or 362) - 455 | >455          |

Authors edited this table with the articles of WHO,1 Zaidi et al7 and Khan19.
Table 2  General characteristics of the study population

| Variable                       | Category                  | Early/delayed, but complete vaccination (n=905) | Timely and complete vaccination (n=238) | Total (n=1143) |
|--------------------------------|----------------------------|-----------------------------------------------|----------------------------------------|----------------|
| Child’s age (days)             | 0–41                       | 4 (5.6)                                       | 63 (94.0)                              | 67             |
|                                | 42–69                      | 9 (22.0)                                      | 32 (78.1)                              | 41             |
|                                | 70–97                      | 10 (52.6)                                     | 9 (47.4)                               | 19             |
|                                | 98–272                     | 237 (64.6)                                    | 130 (35.4)                             | 367            |
|                                | 273–365                    | 226 (98.3)                                    | 4 (1.7)                                | 230            |
|                                | 365–                       | 441 (100.0)                                   | 0 (0)                                  | 441            |
| Woman’s age (years)           | 15–24                      | 294 (78.4)                                    | 81 (21.6)                              | 375            |
|                                | 25–34                      | 516 (79.9)                                    | 130 (20.1)                             | 646            |
|                                | 35+                        | 95 (77.9)                                     | 27 (22.1)                              | 122            |
| No of living children          | 1                          | 246 (78.9)                                    | 66 (21.2)                              | 312            |
|                                | 2                          | 246 (80.4)                                    | 60 (19.6)                              | 306            |
|                                | 3                          | 149 (77.6)                                    | 43 (22.4)                              | 192            |
|                                | 4                          | 105 (79.0)                                    | 28 (21.1)                              | 133            |
|                                | 5+                         | 159 (79.5)                                    | 41 (20.5)                              | 200            |
| Residence                      | Rural                      | 270 (82.6)                                    | 57 (17.4)                              | 327            |
|                                | Town/small city            | 319 (77.2)                                    | 94 (22.8)                              | 413            |
|                                | Large city                 | 316 (78.4)                                    | 87 (21.6)                              | 403            |
| Woman’s education              | No education               | 328 (79.4)                                    | 85 (20.6)                              | 413            |
|                                | Primary or middle school   | 267 (82.2)                                    | 58 (17.9)                              | 325            |
|                                | Secondary school or higher | 310 (76.5)                                    | 95 (23.5)                              | 405            |
| Husband’s education            | No education               | 195 (79.0)                                    | 52 (21.1)                              | 247            |
|                                | Primary or middle school   | 208 (83.2)                                    | 42 (16.8)                              | 250            |
|                                | Secondary school or higher | 502 (77.7)                                    | 144 (22.3)                             | 646            |
| Wealth quintiles               | First (poorest)            | 49 (83.1)                                     | 10 (17.0)                              | 59             |
|                                | Second                     | 99 (79.8)                                     | 25 (20.2)                              | 124            |
|                                | Third                      | 200 (80.7)                                    | 48 (19.4)                              | 248            |
|                                | Fourth                     | 243 (78.6)                                    | 66 (21.4)                              | 309            |
|                                | Fifth (richest)            | 314 (77.9)                                    | 89 (22.1)                              | 403            |
| MCH information source         | Medical professional       | No 367 (76.8)                                 | 111 (23.2)                             | 478            |
|                                |                            | Yes 538 (80.9)                                | 127 (19.1)                             | 665            |
|                                | Low-level health workers*  | No 805 (79.1)                                 | 210 (20.7)                             | 1015           |
|                                |                            | Yes 100 (78.1)                                | 28 (21.9)                              | 128            |
|                                | Relatives/friends          | No 363 (76.6)                                 | 111 (23.4)                             | 474            |
|                                |                            | Yes 542 (81.0)                                | 127 (19.0)                             | 669            |
|                                | Media                      | No 575 (79.2)                                 | 151 (20.8)                             | 726            |
|                                |                            | Yes 330 (79.1)                                | 87 (20.9)                              | 417            |
|                                | No of antenatal care visits| 1–2 132 (83.5)                                | 26 (16.5)                              | 158            |
|                                |                            | 3 128 (77.6)                                  | 37 (22.4)                              | 165            |
|                                |                            | 4+ 645 (78.7)                                 | 175 (21.3)                             | 820            |

Continued
vaccinations and found two critical issues related to the reliable estimates.

In this study, 7840 (76.9%) women did not have vaccination cards or missed information on their vaccination cards in the dataset from the Maternal and Child Health Program Indicator Survey in 2013–2014, which might have overestimated or underestimated the vaccination status. Only 23.1% of total survey respondents were included in this analysis. According to the WHO guidance on vaccination coverage surveys, the survey can rely on HBRs as an important, effective, inexpensive source of documented evidence of vaccination history. A systematic review found that there was relatively good agreement between vaccination based on documented evidence in HBRs and that obtained from maternal/caregiver recalls, but comparatively poor agreement versus facility-based records. HBRs are a key tool to let families know when the child needs to go back for their next vaccine, however, in Pakistan, current HBR prevalence lies know when the child needs to go back for their next

Another issue in this study was that there is no global consensus on the definitions of timely, early and delayed vaccinations between governments, organisations and researchers. For example, recommended and minimum acceptable ages and intervals for routine vaccinations differed between the Centers for Disease Control and Prevention in the USA, the Pan American Health Organization and a study of Zaidi et al in Pakistan. Vaccine doses administered ≤4 days before the minimum interval or age are considered valid in the USA, whereas Zaidi et al defined ‘early’ if there were administered 3 days prior to the recommended age. The uniform global and national guideline for recommended and minimum ages and intervals between vaccine doses are required to enable consistent and comparable measurement of adherence to the guideline. One uniform guideline would improve timely complete immunisation of infants regardless of their country and would help infants to receive recommended vaccine doses, which may prevent side effects from overdose vaccination or reduce the risk of vaccine-preventable diseases from underdosing.

In this study, only 238 children (20.8%) received a full set of vaccinations on schedule in the Sindh province of Pakistan. Determinants for receiving timely vaccinations were the child’s age and the place of delivery. The proportion of children who had not received age-appropriate vaccinations increased with age, which was consistent with the findings of a previous study using 2006–2007 Pakistan Demographic and Health Survey data. In that study, the proportions of children who had early immunisations were 19.9% for the first vaccination for polio1 and penta, and these proportions progressively decreased by 11.2% in polio 3% and 11.4% in penta 3. Correspondingly, the proportions of delayed immunisations progressively increased by 42.6% in polio 3 and by 43.4% in penta 3. One possible reason for the early/delayed vaccination may be that the mothers were reminded of the importance of vaccinations for children due to the efforts by the EPI programme and the government of Pakistan and, as a result, had their children vaccinated at birth, but had difficulty remembering and/or complying to vaccination appointments over time due to other family/social activities, lost or misplaced vaccination cards and lack of an institutional vaccination monitoring system giving reminders for second/third vaccines. Therefore, a considerable proportion of children in Pakistan do not receive a timely, full set of vaccinations, placing them at risk of vaccine-preventable diseases such as meningitis, diarrheal disease and pneumonia as the main causes of death in children under 5 years old in Pakistan.

Even though there has been no study to describe the reasons that children do not receive timely vaccinations in Pakistan, a systematic review indicated that out-of-hospital
Table 3  Vaccination status in children aged 0–23 months

|                  | BCG  | Polio 0 | Polio 1 | Polio 2 | Polio 3 | Penta 1 | Penta 2 | Penta 3 | Measles 1 | Measles 2 |
|------------------|------|---------|---------|---------|---------|---------|---------|---------|-----------|-----------|
| No of eligible subjects to be vaccinated | 1143 | 1143    | 1076    | 1035    | 1016    | 1076    | 1035    | 1016    | 649       | 419       |
| No of vaccinated subjects (N)         | 1143 | 1143    | 1088    | 1041    | 1021    | 1086    | 1040    | 1019    | 1010      | 938       |
| Early (%)                      | –    | –       | 19.9    | 13.9    | 11.2    | 19.9    | 14.9    | 11.4    | 92.9      | 94.8      |
| Timely (%)                     | 89.3 | 87.7    | 62.8    | 57.2    | 46.2    | 61.0    | 55.5    | 45.2    | 2.7       | 3.3       |
| Delayed (%)                    | 10.7 | 12.3    | 17.3    | 28.9    | 42.6    | 19.1    | 29.6    | 43.4    | 4.5       | 1.9       |

BCG, bacillus Calmette-Guérin; Polio, oral polio vaccine; Penta, diphtheria tetanus pertussis–hepatitis B–Haemophilus influenzae type b.
Table 4  Factors associated with timely vaccination

| Variable                              | Category          | Early/delayed (reference) versus timely |
|---------------------------------------|-------------------|----------------------------------------|
|                                       | OR    | 95% CI       |                                        |
| Child’s age (ref=0–69 days)           |       |              |                                        |
|                                       | 70–97 | 0.12         | 0.04 to 0.36                           |
|                                       | 98–272| 0.02         | 0.01 to 0.04                           |
|                                       | 273–365|            |                                        |
|                                       | 365–   |            |                                        |
| Woman’s age (ref=15–24 years)         |       |              |                                        |
|                                       | 25–34 | 1.20         | 0.79 to 1.84                           |
|                                       | 35+   | 1.29         | 0.63 to 2.61                           |
| No of living children (ref=1)         |       |              |                                        |
|                                       | 2     | 0.68         | 0.42 to 1.08                           |
|                                       | 3     | 0.98         | 0.58 to 1.65                           |
|                                       | 4     | 0.64         | 0.33 to 1.22                           |
|                                       | 5+    | 0.71         | 0.37 to 1.33                           |
| Residence (ref=rural)                 |       |              |                                        |
|                                       | Town/small city | 1.45     | 0.88 to 2.41                           |
|                                       | Large city      | 1.31     | 0.75 to 2.33                           |
| Woman’s education (ref=no education)  |       |              |                                        |
|                                       | Primary or middle school | 0.81 | 0.50 to 1.32 |
|                                       | Secondary school or higher | 0.98 | 0.58 to 1.65 |
| Husband’s education (ref=no education)|       |              |                                        |
|                                       | Primary or middle school | 0.76 | 0.44 to 1.32 |
|                                       | Secondary school or higher | 1.00 | 0.63 to 1.62 |
| Wealth quintiles (ref=first (poorest!))|      |              |                                        |
|                                       | Second      | 1.10         | 0.41 to 3.16                           |
|                                       | Third       | 1.37         | 0.54 to 3.78                           |
|                                       | Fourth      | 1.20         | 0.44 to 3.55                           |
|                                       | Fifth (richest) | 1.42 | 0.50 to 4.38 |
| MCH information source                |       |              |                                        |
| Medical professional (ref=no)         | Yes    | 0.99         | 0.67 to 1.48                           |
| Low-level health workers* (ref=no)    | Yes    | 1.02         | 0.56 to 1.83                           |
| Relatives/friends (ref=no)            | Yes    | 0.72         | 0.47 to 1.10                           |
| Media (ref=no)                        | Yes    | 1.15         | 0.79 to 1.66                           |
| No of antenatal care visits (ref=1–2) |       |              |                                        |
|                                       | 3      | 1.88         | 0.96 to 3.78                           |
|                                       | 4+     | 1.59         | 0.89 to 2.97                           |
| Assistance during delivery (ref=traditional birth attendant) | Medical professional | 2.22 | 0.86 to 5.42 |
| Place of delivery (ref=home)           |       |              |                                        |
|                                       | Private facility | 0.39 | 0.17 to 0.96 |
|                                       | Public facility   | 0.34 | 0.14 to 0.89 |

*Low-level health workers, including Dai-traditional birth attendants, female health workers, homeopaths, Hakim-herbal medicine practitioners and outreach workers.

†All independent variables were adjusted.

MCH, maternal and child health; ref, reference.

In many cases, children received vaccinations at the place they were born. When they deliver in facilities, mothers may try to have their babies receive all possible vaccines even if it is not the right time for vaccinations, due to limited access to healthcare services.

A previous study reported that institutional delivery was a positive determinant for full childhood vaccination; however, in the present study, children who were born in public and private facilities were less likely to receive timely vaccinations compared with those who were born at home.
to determine the reasons why institutional delivery was associated with early or delayed vaccination among children under 2 years old and to develop intervention programme to improve timely vaccination rates among children who are born in institutions.

This study has several limitations. First, it was restricted to one province, Sindh, in Pakistan, so the study findings might not be generalisable to all regions because there is a wide regional demographic variation in Pakistan. Second, study participants were limited to mostly women who had vaccination cards; therefore, the vaccination coverage rates and vaccination timeliness might have been overestimated in this study population compared with the general population, because they are more likely to have taken their children for vaccinations than other women who cannot present cards. However, as our variable of interest was vaccination status, we excluded those who did not have a vaccination card or who could not present a vaccination card. Reviewing the vaccination card is currently the only way to analyse children’s vaccination status and date in Pakistan. Also, most studies (49/62, 79%) used data from vaccination cards, according to the systematic review of vaccination status.28 Finally, other possible determinants of timely vaccination, such as the number of facility visits, previous experience of healthcare service use, and distance from a health facility or having transportation options/alternatives, were not included in this study.

Despite these limitations, this study is the first to identify the determinants of timely vaccination among children aged 0–23 months in Sindh Province, Pakistan. In this study, two-thirds of women did not have vaccination cards or missed information on their vaccination cards. Therefore, vaccination programme managers should monitor HBR prevalence and the causes which lead to women not having cards or missed vaccinations on the cards, and should identify solutions to increase current HBR prevalence. To improve timely vaccination rates, the redesigned HBRs, the new electronic collection formats and platforms to register HBRs information, and a vaccination tracking system for health workers that provides information about age-appropriate vaccinations and appropriate follow-up vaccinations for children under 2 years old may be helpful for women and children, to achieve herd immunity for vaccine-preventable diseases. In addition, it is necessary to conduct large nationally representative surveys about vaccination. To improve timeliness, it is necessary to not only understand factors associated with timeliness (or un-timeliness) well but also do a root-cause analysis and identify the evidence around interventions. Also, future investigators should determine the inhibiting factors for timely vaccinations and the factors related to the utilisation of follow-up vaccine doses, and develop intervention programme to improve timely vaccinations for children who were born in institutions.

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### Contributors

J-WN, Y-mk, YDK and JS conceptualised and designed the study. J-WN, Y-mk, NA, YDK and JS wrote up the results and revised the manuscript. J-WN and KBY cleaned and analysed the data and wrote sections of the manuscript. JC and JLJ reviewed the literature, interpreted the findings and wrote sections of the manuscript.

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### Competing interests

None declared.

### Patient consent for publication

Not required.

### Ethics approval

The study has been performed with approval of the Institutional Review Board at Johns Hopkins University School of Public Health (IRB00005002) and the National Bioethics Committee of Pakistan.

### Provenance and peer review

Not commissioned; externally peer reviewed.

### Data availability statement

No data are available.

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