Potential drug-drug interactions and prescription errors in COVID-19 infected patients

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KEYWORDS
comorbidity, Bangladesh, COVID-19, drug-drug interaction, prescription error

Received: 28 December 2022, **Revised:** 27 April 2023, **Accepted:** 12 June 2023
Public Health Toxicol. 2023;3(2):9
https://doi.org/10.18332/pht/168246

ABSTRACT

INTRODUCTION Prescription errors can cause havoc during the pandemic, especially for comorbid patients with diabetes and hypertension identified as a risky population group for COVID-19. Therefore, the present study was designed to evaluate the prescription errors, including drug-drug interactions, among outpatients infected with COVID-19.

METHODS This study was carried out at the outpatient departments of different hospitals in Dhaka, Bangladesh, through a random sampling method between May and August 2021. Eighty prescriptions from COVID-19 patients were collected, among whom 44 had comorbidities. The Microsoft Excel 2016 program analyzed the prescriptions and online aiding tools, such as Drug Interaction Checker (Drugs.com), were used to identify potential drug-drug interactions.

RESULTS Among those 80 prescriptions, 44 cases (55%) contained moderate drug-drug interactions; Moxifloxacin and Remdesivir, the highest observed combination, were detected in 10 prescriptions (12.5%). A total of 7 prescriptions (8.75%) contained significant drug-drug interactions. The dose was not mentioned in 37 cases (46.25%), while the patient's history was not found in 21 cases (26%). Moreover, 6–10 drugs were found in 54 prescriptions (67.50%), while 11–15 drugs were prescribed in 19 prescriptions (23.75%).

CONCLUSIONS Prescription error and drug-drug interaction may implicate the disastrous situations more profoundly, especially for the comorbid patients. The prescription error, an avoidable occurrence, may be eradicated by awareness and tools with preventive measures.

INTRODUCTION

SARS-CoV-2 is a virus first reported in Wuhan, China, in December 2019 and later declared a pandemic by the World Health Organization (WHO) on 11 March 2020[1]. Specific comorbidities, such as diabetes, hypertension, asthma, and others associated with COVID-19, have been associated with increased mortality[2]. The unforeseen eruption of COVID-19, patient overflow, insufficient protective equipment, increased workload, stressful situations, and other factors may contribute to prescription error[3]. This results in misinformation being the cause of life-threatening situations, particularly for patients with underlying comorbidities suffering from COVID-19.

However, errors in prescriptions can be avoided. It has been reported that medication errors account for 70% of all written prescriptions[4]. Superscription, inscription, and subscription are the major prescription errors. Drug-drug interaction (DDI), toxicity, adverse drug reactions, and economic waste are the consequences of such prescription errors[5]. Polypharmacy is the main cause of DDIs and the majority of adverse drug reactions[6]. A prescription can contain DDI of major, moderate, and minor severity as well as in combination, which can give rise to a life-threatening condition[7]. According to a report, polypharmacy accounts for 5.33% medication use in Bangladesh[8].

SARS-CoV-2 leads to circulation disruption in different organs, forging vulnerability in comorbid patients[9]. Transmission of SARS-CoV-2 is enabled by prolonged

contact time and in connection with an infected individual in an poorly ventilated environment[10]. Living in a densely populated country like Bangladesh, people are more likely to become infected with COVID-19, as population density has been identified as a societal risk factor for SARS-CoV-2 transmission[11]. Although polypharmacy and DDIs are major drawbacks in patient care in Bangladesh, it has been a success story to vaccinate people against COVID-19 infections. The country obtained the 5th position in the world in the COVID-19 Recovery Index[12].

Earlier studies have indicated that COVID-19 patients with comorbidities should be closely monitored as they are more vulnerable. Patients with comorbidity and those who were older encountered severe forms of COVID-19, such as patients with underlying diabetes who were found to be hospitalized more than non-diabetic patients suffering from COVID-19. Higher morbidity and mortality had also been observed in those comorbid patients[13]. Likewise, patients with hypertension or any respiratory disease had also sustained severe forms of COVID-19[14,15]. Elderly patients with underlying comorbidities are classified as vulnerable to COVID-19 as they are at greater risk of suffering adverse outcomes while being administered numerous drugs as part of their clinical management. Prescription errors can lead to further catastrophic outcomes for this group of patients. Such errors can adversely affect patients' safety and the quality of the healthcare system. To counteract this outcome, priority should be given to ensuring the prescription is written correctly by trained and skilled health professionals, thereby minimizing adverse drug effects, polypharmacy, and, most importantly, DDI.

In December 2020, the development and implementation of the COVID vaccine by the pharmaceutical industry came into use during this time of global emergency. The outcome of which has shown evident success in the prevention and transmission of the disease. Countries with low uptake of vaccination coverage are at a higher risk of transmission, leading to adverse outcomes in patients with comorbidities.

There is no doubt that polypharmacy and prescription errors can damage patients' safety profiles. There may be an increased risk of higher morbidity and mortality in COVID-19 infected patients. So, it is essential to evaluate the prescriptions with the aim of increasing patient safety through drug use management. Therefore, the present study was designed to evaluate prescription errors by looking at the types of drug-drug interactions comparing comorbid and non-comorbid COVID-19 infected patients.

METHODS

Study design

This study was carried out at the outpatient departments of different hospitals in Dhaka, Bangladesh, from May to August 2021. Both male and female patients suffering from COVID-19 with and without comorbidities were included in this study. The study's objectives were explained to the participants, and consent was obtained before collecting the prescription information. Confidentiality was maintained regarding sensitive personal information. There was no direct contact with patients, and information was gathered through the review of prescription scripts. Data were collected from participants who gave informed consent for the purposes of the study.

Data collection

A total of 80 prescriptions were randomly collected from the outpatient departments of different hospitals (Table 1).

Table 1. Prescription collection from different hospitals of Dhaka, Bangladesh, May to August 2021

Hospital	Number of prescriptions
Kurmitola General Hospital	39
Labaid Specialized Hospital	5
Square Hospital	1
Holy Family Red Crescent Medical College Hospital	1
Popular Medical College Hospital	26
Mugda Medical College Hospital	1
National Heart Foundation	1
TMSS Medical College and Hospital	1
Popular Diagnostic Centre	2
BGC Trust Medical College	2
South Apollo Diagnostic Complex Private Limited	1

Data analysis

The information from the prescription scripts was collected by taking explicit images of the scripts. The data retrieved from the prescription scripts were presented in a Microsoft Excel spreadsheet. After a complete list of medicines was compiled, the drug-drug interaction (DDI) was checked using an online drug information system, Drug Interaction Checker (Drugs.com). Drugs from each prescription were categorized by their generic names. Each drug prescribed on the prescription script was checked for DDI. The results obtained were ranked based on mild, moderate, and significant DDIs. Further preference was given to the major DDIs. A list of major generic pairs of drugs that were interacting was identified. Moreover, those interactions were evaluated in terms of their frequency of prescription. Following the subcategories, the prescription error was measured in terms of superscription, inscription, and subscription error. The research method was aligned with the Declaration of Helsinki.

RESULTS

A total of 773 drugs were found in 80 prescriptions. So, the number of medications encountered was 9.66 in each prescription. None of the patients was vaccinated against COVID-19.

Table 2 shows that 67.5% of prescriptions contain 6–10 medications per prescription; 11–15 medications per prescription were found in 23.8% of prescriptions; and 5% of prescriptions contained 16–20 medications per prescription. Only 2.5% of prescriptions had drugs ≤5, and 1.2% of prescriptions contained ≥21 medications.

Table 2. Number of drugs prescribed in prescriptions among COVID-19 patients, May to August 2021 (N=80)

Numbers of drugs per prescription	Number of prescriptions	%
0–5	2	2.5
6–10	54	67.5
11–15	19	23.8
16–20	4	5
≥21	1	1.2

Table 3 depicts cases of prescription errors, so one prescription may contain multiple cases or multiple prescription errors. From Table 3, superscription error was noticed in 11 cases for comorbid patients and 4 cases for non-comorbid patients. The prescription date was not mentioned in the prescriptions of 10 comorbid cases (12.5%). Overall, inscription errors were found in 76 cases out of 80 prescriptions, 47 cases out of 36 for non-comorbid, and 29 cases out of 44 prescriptions for comorbid. Dosage was not found in 9 prescriptions for comorbid instances (20.46%) and 28 non-comorbid cases (7.77%). The wrong strength of medicine was prescribed in 7.5% of prescriptions for comorbid patients. In 2 (4.54%) and 7 (8.8%) prescriptions for comorbid and non-comorbid cases, the improper dosage form was mentioned, respectively. Subscription errors were found in 35 cases for comorbid patients and 10 instances for non-comorbid patients.

Table 4 depicts cases of drug-drug interaction (DDI), so one prescription may contain multiple DDI occurrences. The major DDIs were found in 6 cases out of 44 prescriptions of comorbid patients and in 1 case out of 36 cases of non-comorbid patients (Table 4). Moderate DDIs were found in 39 cases out of 44 prescriptions for comorbid patients and 5 cases

Table 3. Prescription errors in the studied population of COVID-19 patients, Dhaka, Bangladesh, 2021 (N=80)

Prescription error	Types of errors	Comorbid patients (N=44) n (%)	Non-comorbid patients (N=36) n (%)	Both groups (N=80) n (%)
Superscription	Age not mentioned	1 (2.28)	0 (0)	1 (1.25)
	Gender not mentioned	0 (0)	4 (11.11)	4 (5.00)
	Prescription date not mentioned	10 (22.72)	0 (0)	10 (12.50)
Inscription	Dosage not mentioned	9 (20.46)	28 (77.77)	37 (46.25)
	Dosage form not mentioned	0 (0)	0 (0)	0 (0)
	Wrong strength	6 (13.63)	0 (0)	6 (7.50)
	Spelling mistake in drug name	2 (4.54)	3 (8.33)	5 (6.25)
	Wrong dosage form	2 (4.54)	5 (13.88)	7 (8.80)
	Patient history/symptoms not mentioned	10 (22.72)	11 (30.55)	21 (26.00)
Subscription	Prescriber date not mentioned	28 (63.63)	10 (27.77)	38 (47.50)
	Prescriber signature not mentioned	7 (15.90)	0 (0)	7 (8.80)

Table 4. Major, minor, and moderate drug-drug interaction cases among the comorbid patients and non-comorbid patients with COVID-19, Dhaka, Bangladesh, 2021 (N=80)

Responsible drug-pair for drug-drug interaction	Severity of interaction	Comorbid patients (N=44) n (%)	Non-comorbid patients (N=36) n (%)
Palonosetron – Haloperidol	Major	1 (2.72)	0 (0)

Continued

Table 4. Continued

Responsible drug-pair for drug-drug interaction	Severity of interaction	Comorbid patients (N=44) n (%)	Non-comorbid patients (N=36) n (%)
Moxifloxacin – Dexamethasone	Major	2 (4.54)	1 (2.78)
Insulin Human – Moxifloxacin	Major	1 (2.72)	0 (0)
Ciprofloxacin – Methyl Prednisolone	Major	1 (2.72)	0 (0)
Voriconazole – Moxifloxacin	Major	1 (2.72)	0 (0)
Amlodipine – Rosuvastatin	Minor	1 (2.72)	0 (0)
Rosuvastatin – Moxifloxacin	Minor	1 (2.72)	0 (0)
Salbutamol – Budesonide	Minor	2 (4.54)	0 (0)
Bisoprolol Hemifumerate – Levothyroxine sodium	Minor	1 (2.72)	0 (0)
Dexamethasone – Diazepam	Minor	1 (2.72)	0 (0)
Clarithromycin – Linagliptin	Moderate	1 (2.72)	0 (0)
Insulin Human – Linagliptin	Moderate	1 (2.72)	0 (0)
Losartan potassium – Cefixime Trihydrate	Moderate	1 (2.72)	0 (0)
Haloperidol – Procyclidine HCl	Moderate	1 (2.72)	0 (0)
Ivabradine – Dexamethasone	Moderate	1 (2.72)	0 (0)
Moxifloxacin - Remdesivir	Moderate	7 (15.90)	3 (8.33)
Clarithromycin – Rivaroxaban	Moderate	1 (2.72)	0 (0)
Dexamethasone – Prazosin HCl	Moderate	1 (2.72)	0 (0)
Clopidogrel – Atorvastatin Calcium	Moderate	3 (6.81)	0 (0)
Atorvastatin – Esomeprazole	Moderate	1 (2.72)	0 (0)
Solifenacin – Nystatin	Moderate	1 (2.72)	0 (0)
Ceftriaxone – Moxifloxacin	Moderate	1 (2.72)	2 (5.56)
Paracetamol – Remdesivir	Moderate	1 (2.72)	0 (0)
Insulin Human – Dexamethasone sodium phosphate	Moderate	4 (9.09)	0 (0)
Dexamethasone sodium phosphate – Glycerin	Moderate	2 (4.54)	0 (0)
Clarithromycin – Insulin Glargine	Moderate	1 (2.72)	0 (0)
Nebivolol HCl – Insulin	Moderate	1 (2.72)	0 (0)
Insulin NPH – Clopidogrel bisulphate	Moderate	1 (2.72)	0 (0)
Amlodipine – Atenolol	Moderate	1 (2.72)	0 (0)
Bisoprolol Hemifumarate –Risperidone	Moderate	1 (2.72)	0 (0)
Piperacillin – Amikacin	Moderate	1 (2.72)	0 (0)
Mirtazapine – Clonazepam	Moderate	1 (2.72)	0 (0)
Formoterol – Salbutamol	Moderate	1 (2.72)	0 (0)
Ondansetron – Palonosetron	Moderate	1 (2.72)	0 (0)
Oxcarbazepine – Quetiapine Fumarate	Moderate	1 (2.72)	0 (0)
Gabapentin – Oxcarbazepine	Moderate	1 (2.72)	0 (0)
Bisoprolol Hemifumarate – Furosemide	Moderate	1 (2.72)	0 (0)

out of 36 prescriptions for non-comorbid patients (Table 4).

DISCUSSION

In this study, moderate drug-drug interaction (DDI) was observed in 44 cases among the 80 prescriptions collected, indicating a higher risk of developing adverse outcomes as a result of prescription error in the studied population. This study showed a high incidence of drug-drug interactions (of any type), with 71.25% of cases affected. The study found a high frequency of moderate DDI in Moxifloxacin and Remdesivir when used in combination. There were 7 cases for comorbid patients and 3 cases for non-comorbid patients. Among the major DDIs, high numbers were seen with the Moxifloxacin and Dexamethasone combination, with 2 cases for comorbid patients and 1 case for non-comorbid patients. Polypharmacy was observed in 78 prescriptions (97.50% cases), which contained a total drug number of more than 6 per prescription. A total of 136 cases of prescription errors were found among 80 prescriptions, of which 15 were superscription errors, 45 were subscription errors, and the remaining 76 were inscription errors.

According to the prescribing indicator of the WHO, the leading health organization throughout the globe, the optimum number of drugs per encounter was directed at 1.6–1.8. In contrast, in this study, only 2 prescriptions (2.5%) were found to have the number of drugs prescribed below 5; the remaining 78 prescriptions (97.5%) were found to have a drug number greater than 5, indicating a substantial deviation from the standard guideline[16]. Earlier studies reported that inflated drug numbers prompted outpatient visits, elevated hospitalization rates, and an increase in medical costs[17]. A previous study on outpatients outlined that patients administering more than five medications concurrently had a 50% higher probability of an adverse drug reaction[18]. Moreover, patients taking more than five medications reported a diminishing ability to implement instrumental activities of daily living[19]. In 54% of patients prescribed more than 10 medications, cognitive impairment was observed[20]. A study on the eastern Indian population revealed that 87.5% of COVID-19 prescriptions contain drug-drug interactions, of which 20% are major drug-drug interactions and 77.14% are moderate drug-drug interactions[21]. We have also found different categories of DDIs in our study.

The drug-drug interaction may influence pharmacodynamic and pharmacokinetic effects. Simultaneous administration of medications can have a synergistic effect, which has a more significant impact than a summation of the administered drugs, and an additive effect, which is the sum of the co-administered drugs' influence. Pharmacokinetic interaction can alter the concentration of the co-administered drugs by interfering with pharmacokinetic parameters such as absorption, distribution, metabolism, and elimination. Several drugs commonly prescribed for COVID-19 patients, such as antiplatelet and anticoagulant combinations, were reported earlier to have toxicological consequences by increasing the risk of bleeding[22]. Patients' prescription errors can lead to fatal situations, especially for the comorbid population. A previous study conducted in the emergency outpatient department indicated that 54% of all medication errors were associated with prescription errors[23].

The communication gap between the prescribers and the patients and unethical medical product promotion were responsible for prescription error[24]. The prescription error was reported to be the reason for the economic burden for the patients; being a lower middle-income country, this incidence is much more fierce for the Bangladeshi population[25]. Polypharmacy; patients with comorbidity, primarily older people, requiring new medications for treatment of COVID-19 will have increased issues that will arise from this situation. This group of the population is at high risk of suffering from adverse effects due to prescription errors[26]. In our study, we found many medications in one prescription, which may lead to DDIs, thereby increasing the risk of vulnerability among COVID-19 patients. It has been reported that more than 250 million doses of COVID-19 vaccines have been administered in Bangladesh until May 2022[27]. That can have a positive impact on future episodes of COVID-19 infections in terms of DDIs.

Prescription error is an avoidable occurrence and may be eradicated by awareness, aiding tools, and some preventive measures. A study reported that more than 60% of prescription-related mistakes could be avoided by employing computer software[28]. Moreover, clinical pharmacists and hospital pharmacists may play a crucial role in reducing prescription error-related adverse effects. This is lacking in Bangladesh, as graduate pharmacists have little scope to work in clinical or hospital settings.

Limitations

The limitations of this study include a small sample size due to the urgency of the situation and certain restrictions during sample collection.

CONCLUSIONS

Prescription error is a global problem, but its consequences may have led to fatalities during the pandemic. Compliance with prescribed medications ensures a successful treatment outcome, provided the prescription is free of error. Policymakers in the health sector and experts need to emphasize the issue of prescription errors to secure adequate health safety for patients. Strict rules and regulations should be implemented by policymakers and those in power to reduce prescription error.

REFERENCES

1. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed. 2020;91(1):157-160. doi:10.23750/abm.v91i1.9397

2. Ejaz H, Alsrhani A, Zafar A, et al. COVID-19 and comorbidities: deleterious impact on infected patients. J Infect Public Health. 2020;13(12):1833-1839. doi:10.1016/j.jiph.2020.07.014
3. Khatun MF, Parvin MF, Rashid MM, et al. Mental health of physicians during COVID-19 outbreak in Bangladesh: a web-based cross-sectional survey. Front Public Health. 2021;9:592058. doi:10.3389/fpubh.2021.592058
4. Patel S, Patel A, Patel V, Solanki N. Study of medication error in hospitalised patients in tertiary care hospital. Indian J Pharm Pract. 2018;11(1):32-36. doi:10.5530/ijopp.11.1.6
5. Ragam AS, Acharya S, Holla R. Assessment of drug use pattern using World Health Organization prescribing indicators in a tertiary care hospital in Mangalore: a cross-sectional study. Natl J Physiol Pharm Pharmacol. 2017;7(10):1026-1030. doi:10.5455/njppp.2017.7.0413713052017
6. Magro L, Arzenton E, Leone R, et al. Identifying and characterizing serious adverse drug reactions associated with drug-drug interactions in a spontaneous reporting database. Front Pharmacol. 2021;11:622862. doi:10.3389/fphar.2020.622862
7. Day RO, Snowden L, McLachlan AJ. Life-threatening drug interactions: what the physician needs to know. Intern Med J. 2017;47(5):501-512. doi:10.1111/imj.13404
8. Rasu RS, Iqbal M, Hanifi S, et al. Level, pattern, and determinants of polypharmacy and inappropriate use of medications by village doctors in a rural area of Bangladesh. Clinicoecon Outcomes Res. 2014;6:515-521. doi:10.2147/CEOR.S67424
9. Sardu C, Gambardella J, Morelli MB, Wang X, Marfella R, Santulli G. Hypertension, thrombosis, kidney failure, and diabetes: is COVID-19 an endothelial disease? A comprehensive evaluation of clinical and basic evidence. J Clin Med. 2020;9(5):1417. doi:10.3390/jcm9051417
10. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel Coronavirus-infected pneumonia. N Engl J Med. 2020;382(13):1199-1207. doi:10.1056/NEJMoa2001316
11. Alam MZ. Is population density a risk factor for communicable diseases like COVID-19? A case of Bangladesh. Asia Pac J Public Health. 2021;33(8):949-950. doi:10.1177/1010539521998858
12. UNB. Bangladesh 5th in world in Covid Recovery Index, top in South Asia. The Daily Star. May 7, 2022. Updated May 7, 2022. Accessed April 27, 2023. https://www.thedailystar.net/health/disease/coronavirus/news/covid-recovery-index-bangladesh-tops-south-asia-5th-world-3018306
13. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: prevalence, pathophysiology, prognosis and practical considerations. Diabetes Metab Syndr. 2020;14(4):303-310. doi:10.1016/j.dsx.2020.04.004
14. Zhang J, Wang X, Jia X, et al. Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China. Clin Microbiol Infect. 2020;26(6):767-772. doi:10.1016/j.cmi.2020.04.012
15. Zhao Q, Meng M, Kumar R, et al. The impact of COPD and smoking history on the severity of COVID-19: a systemic review and meta-analysis. J Med Virol. 2020;92(10):1915-1921. doi:10.1002/jmv.25889
16. Atif M, Azeem M, Sarwar MR, et al. WHO/INRUD prescribing indicators and prescribing trends of antibiotics in the Accident and Emergency Department of Bahawal Victoria Hospital, Pakistan. Springerplus. 2016;5(1):1928. doi:10.1186/s40064-016-3615-1
17. Mangin D, Bahat G, Golomb BA, et al. International Group for Reducing Inappropriate Medication Use & Polypharmacy (IGRIMUP): position statement and 10 recommendations for action. Drugs and Aging. 2018;35(7):575-587. doi:10.1007/s40266-018-0554-2
18. Sherman JJ, Davis L, Daniels K. Addressing the Polypharmacy Conundrum. US Pharmacist. June 16, 2017. Accessed April 27, 2023. https://www.uspharmacist.com/article/addressing-the-polypharmacy-conundrum
19. Crentsil V, Ricks MO, Xue QL, Fried LP. A pharmacoepidemiologic study of community-dwelling, disabled older women: factors associated with medication use. Am J Geriatr Pharmacother. 2010;8(3):215-224. doi:10.1016/j.amjopharm.2010.06.003
20. Jyrkkä J, Enlund H, Lavikainen P, Sulkava R, Hartikainen S. Association of polypharmacy with nutritional status, functional ability and cognitive capacity over a three-year period in an elderly population. Pharmacoepidemiol Drug Saf. 2011;20(5):514-522. doi:10.1002/PDS.2116
21. Manjhi PK, Kumar R, Priya A, Rab I. Drug-drug interactions in patients with COVID-19: a retrospective study at a tertiary care hospital in Eastern India. Maedica (Bucur). 2021;16(2):163-169. doi:10.26574/maedica.2021.16.2.163
22. Shatzel JJ, Olson SR, Tao DL, McCarty OJT, Danilov AV, DeLoughery TG. Ibrutinib-associated bleeding: pathogenesis, management and risk reduction strategies. J Thromb Haemost. 2017;15(5):835-847. doi:10.1111/jth.13651
23. Poornima P, Reshma P, Ramakrishnan TV, et al. Medication reconciliation and medication error prevention in an emergency department of a tertiary care hospital. J Young Pharm. 2015;7. doi:10.5530/jyp.2015.3.15
24. Patel N, Desai M, Shah S, Patel P, Gandhi A. A study of medication errors in a tertiary care hospital. Perspect Clin Res. 2016;7(4):168. doi:10.4103/2229-3485.192039
25. Janković SM, Pejčić AV, Milosavljević MN, et al. Risk factors for potential drug-drug interactions in intensive care unit patients. J Crit Care. 2018;43:1-6. doi:10.1016/j.jcrc.2017.08.021
26. Busa G, Burlina A, Damuzzo V, Chiumente M, Palozzo AC. Comorbidity, polytherapy, and drug interactions in a neurological context: an example of a multidisciplinary approach to promote the rational use of drugs. J Pharm Pract. 2018;31(1):58-65. doi:10.1177/0897190017699138
27. United Nations International Children's Emergency Fund. Bangladesh's COVID-19 Vaccination Rate Has Soared in a Year. UNICEF; 2022. Accessed April 27, 2023. https://www.unicef.org/stories/bangladesh-covid-19-vaccination-rate-

has-soared
28. Lainer M, Mann E, Sönnichsen A. Information technology interventions to improve medication safety in primary care: a systematic review. Int J Qual Heal care J Int Soc Qual Heal Care. 2013;25(5):590-598. doi:10.1093/INTQHC/MZT043

ACKNOWLEDGEMENTS
The authors are thankful to Nafiza Anwar, Lead Maternal Medicine Midwife, NHS North East London, for critically revising the language of this manuscript.

CONFLICTS OF INTEREST
The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none was reported.

FUNDING
There was no source of funding for this research.

ETHICAL APPROVAL AND INFORMED CONSENT
The study was approved by the Ethical Committee of Department of Pharmacy of East West University, (Approval number: EWU-ERCDOP-00001; Date: 15 May 2021). Participants provided informed consent.

DATA AVAILABILITY
The data supporting this research is available from the following source: https://doi.org/10.21203/rs.3.rs-2411752/v1

AUTHORS' CONTRIBUTIONS
SRT, HAS and TK: data collection, writing of original draft. NH: editing, supervision. MR: writing, supervision. AK: data collection. SI: conceptualization, project administration. All authors read and approved the final manuscript.

PROVENANCE AND PEER REVIEW
Not commissioned; externally peer reviewed.