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# Role of pharmacist during COVID-19 pandemic: A retrospective study focused on critically ill COVID-19 patients

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## ABSTRACT

**Background and aim:** During the Coronavirus 2019 (COVID-19) crisis, there has been a huge demand for medications and unprecedented utilization of intensive care unit (ICU) services that subsequently and profoundly impacted the quality of medical care provided to COVID-19 patients. This study aimed to shed light on the role of pharmacists on the health care provided to critically ill COVID-19 patients.

**Methods:** A retrospective study, was conducted in Diriyah hospital in Riyadh, Saudi Arabia on all COVID-19 patients admitted to the ICU between June 27th and August 15th, 2020 until patients were transferred to the medical ward, discharged, or deceased. All medication related interventions performed by pharmacists have been documented electronically, collected and subsequently categorized and analyzed.

**Results:** The mean age of patients was 58.8 years ( $\pm 12.98$  SD), with age of >64 years in approximately 37%. Four hundred and seventy interventions (470) were made by pharmacists of which 32%, 11.7%, 4%, 2.6%, 2.1% were due to error in dosing regimens, drug duplication, missing drug information, drugs requiring prior authorization, and missing critical information, respectively; while 40.6% were due to medication shortage of which 40.3% were substituted with alternative medications. Based on the analysis of drugs involved in interventions, medication groups that were mainly associated with interventions included antibiotics (16.8%), electrolytes/minerals (11.7%) and vitamins (9.4%).

**Conclusion:** During health crises such as COVID-19 pandemic, the role of pharmacists in the ICU services becomes extremely crucial for providing better patients' outcomes. Further studies should be conducted to follow up these findings in the context of COVID-19 pandemic.

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## 1. Introduction

Declaring Coronavirus 2019 (COVID-19) pandemic by the World Health Organization on March 11, 2020 (Tang et al., 2020; World

Health Organization), imposed a significant challenge on the global healthcare services and resources. During this crisis, there has been a huge demand for medications and unprecedented utilization of intensive care unit (ICU) services (World Health Organization, 2020), that has subsequently and profoundly impacted the quality of medical care provided to COVID-19 patients. Although respiratory distress and failure caused by SARS-CoV-2 is known to jeopardize the patients' lives, medication errors (MEs) and adverse drug events (ADEs) represent additional life-threatening factors.

All ICU cases are complicated in the sense that they require more parameters monitoring, multiple high-risk medications administration and are subjected to more frequent changes in therapeutic plans (Cullen et al., 1997; Moyon et al., 2008; Klopotoski et al., 2010). However, with COVID-19 pandemic, the situation has

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become more complex that consequently made the critically ill COVID-19 patients more vulnerable to MEs and ADEs.

Medication errors (MEs) represent a major concern globally. Early studies have estimated that MEs account for 7000 deaths annually in the United States (Phillips et al., 1998, 2001). Whereas recent reports have shown that the number is underestimated as MEs may account for up to 251,000 deaths a year in the U.S. (Makary and Daniel, 2016; Anderson and Abrahamson, 2017). Drug related mortality and morbidities have a major economic burden on the American health care system, as their cost was estimated to exceed \$177 billion annually (Ernst and Grizzle, 2001). This underlines the significant role that pharmacists can play to provide the most economically saving therapies and more importantly ensure patients' safety during the treatment process.

Pharmacists have a crucial role in emergency medical services (EMS), including the ICU, through participation in planning pharmacotherapies and decisions related to clinical parameters evaluation and drug monitoring (Kane et al., 2003). Their interventions represent the first line defense that prevents MEs and ADEs from occurring in the first place, ultimately improving the medication safety. Beyond this, their presence in the ICU and consultation with ICU physicians have shown to reduce the consumed quantities of drugs, which was correlated with a reduction in the cost of drug therapy (Aljbouri et al., 2013; Montazeri and Cook, 1994), and prevent inappropriate drug use or ADEs, thus avoiding their attributable cost (MacLaren et al., 2021; MacLaren and Devlin, 2019). More details regarding contribution of pharmacists in the ICU is discussed elsewhere (Preslaski et al., 2013).

Despite the wealth of literature with the role of ICU pharmacists in general, there is a paucity of research on the role of pharmacists on the ICU admitted COVID-19 patients. This study aimed to explore the role of pharmacists in the ICU services provided to the critically ill COVID-19 patients. The overall goal of the study was to highlight the major types of pharmacists' interventions and MEs that pharmacists experience during caring for critically ill COVID-19 patients to draw the practitioners' attention to areas where they need to be more vigilant to warrant patients' safety during this pandemic.

## 2. Method

This retrospective study was conducted in Diriyah hospital in Riyadh, Saudi Arabia on all COVID-19 patients admitted to the ICU between June 27th and August 15th, 2020. Patients who were admitted before June 27th and after August 15th were excluded from the study. All patients' cases had been followed between June 27th and August 15th, until patients were transferred out of the ICU, i.e. transferred to the medical ward, discharged, or died. Baseline characteristics including demographic data, medical and disease history as well as pharmacists' interventions were collected by two on-duty pharmacists and two volunteering pharmacists with no need to informed consent from patients as the study was performed retrospectively. Ten out of twelve on-duty pharmacists provided therapeutic interventions during the study period. Pharmacist intervention in our study is defined as any action taken by the pharmacist on medications ordered to these patients that might have potential measurable impact on the quality of care provided to them during their stay in the ICU (Alderman and Farmer, 2001; Dooley et al., 2004; Mongaret et al., 2018). Following their collection, they were counted and classified according to the predefined types of interventions built into the utilized software at the hospital. Medication groups or classes corresponded to these interventions were determined. A designed collection sheet was utilized to gather all required information. Data related to pharmacists' interventions and medications would be reviewed by one

junior and 2 senior pharmacists, to ensure interventions align with the type or class provided by the software. Data were analyzed using Microsoft Excel 2019.

## 3. Results:

### 3.1. Baseline characteristics

During the study period, one hundred and nine patients were considered, of which thirty were excluded [9 admitted to the medical ward; 16 with inaccessible files since their transfer to Diriyah hospital was cancelled; 3 with inaccessible clinical notes; 2 patients with missing medication lists] that resulted in 79 patients to be included in the study. The mean age of patients was 58.8 years ( $\pm 12.98$  SD), with age of >64 years in approximately 37%, as shown in Table 1. Male patients represented 84.8% and all were non-Saudis. Diabetes and hypertension were the most prevalent comorbidities which were diagnosed in 59.5% and 58% of the

**Table 1**  
Clinical baseline characteristics of participants (N = 79).

Characteristic	Number (%)		
<b>Age [28 to 86; years]</b>			
< 55	34	(43.0)	
55-64	16	(20.3)	
> 64	29	(36.7)	
<b>Gender</b>			
Male	67	(84.8)	
Female	11	(13.9)	
NA	1	(1.3)	
<b>Nationality</b>			
Saudi	0		
Non-Saudi	79	(100)	
<b>BMI</b>			
Underweight (< 18.5)	0		
Normal (18.5 ≤ to < 25)	15	(19)	
Overweight (25 ≤ to < 30)	23	(29.1)	
Obese	30	(38)	
Class I (30 ≤ to < 35)	17	(56.7)	
Class II (35 ≤ to < 40)	8	(26.7)	
Class III (> 40)	5	(16.6)	
NA	11	(13.9)	
<b>Medical history</b>	Yes	No	NA
Diabetes	47	29	3
Hypertension	46	31	2
Anemia*	12	41	26
IHD	8	46	25
A-fib	3	52	24
CHF	1	52	26
Dyslipidemia	5	47	27
Chronic Kidney failure (CKD)	5	72	2
Asthma	2	36	41
COPD	2	37	40
Lung mass (Cancer or TB)	1	78	0
Peptic ulcer	1	12	66
Schizophrenia	1	78	0
Inflammatory bowel syndrome	1	59	19
Hypothyroidism	2	77	0
Pulmonary embolism	2	77	0
stroke	1	78	0
Acute renal failure	2	77	0
Hyperthyroidism	1	78	0
<b>Mechanical ventilation</b>			
Yes	71	(89.9)	
No	7	(8.8)	
NA	1	(1.3)	
<b>Sedation</b>			
Yes	69	(87.3)	
No	9	(11.4)	
NA	1	(1.3)	

NA: data is not available for this number of patients.

\* History of PRBCs transfusion in 8 patients (6 NA; 2 Yes).

patients, respectively. Obesity existed in 38% of the patients, while 29% of patients were classified as overweight. Most of the patients were sedated and mechanically ventilated (87% and 90%, respectively). Further details on baseline characteristics are provided in Table 1.

### 3.2. Classification of pharmacists' interventions based on their types

Four hundred and seventy interventions were made by pharmacists, as shown in Table 2. Of these interventions and based on the predefined types built into the software, 11.7%, 4%, 32%, 2.1% and

2.6% were due to drug duplication, drug information, error in dosing regimen, missing critical information about the patients and absence of prescriber's privilege, respectively. In addition, 40.6% of the interventions were related to medication shortage as they were out of stock or being nonformulary drugs, of which pharmacists suggested alternatives for 40%, while 60% were left without suggestions due absence of alternative medications, yet they were requested and supplied by the Saudi Ministry of Health (MOH) or other governmental hospitals falling under MOH umbrella. Interventions related to drug order rejection represented only 2%. Further analysis of the interventions under error in dosing

**Table 2**  
Classification of pharmacists' interventions during ICU admission of COVID-19 patients.

Interventions	Number of patients with this intervention	Example	Total number of interventions (%)
<b>Drug class duplicate</b>	<b>33</b>	Patient is on Vancomycin and prescribed Linezolid	<b>55 (11.7)</b>
<b>Drug information</b>	<b>14</b>	Patient is prescribed metronidazole without clear indication;	<b>19 (4.0)</b>
Missing drug information, direction of use, indication		Patient is prescribed phenytoin IV without choosing appropriate diluent	
<b>Error in dosing regimen</b>	<b>60</b>		<b>151 (32.13)</b>
Dose adjustment	38	Propofol was prescribed 500 mg/hr and maximum dose is 390 mg/hr (5 mg/kg/hr) for COVID19	80
		Favipiravir was prescribed 850 mg BID and corrected by pharmacist to 800 mg BID	
Frequency adjustment	23	Vancomycin was prescribed 1 gm daily, but corrected by pharmacist to BID	31
Duration adjustment	4	Enoxaparin was prescribed for 1 day only but extended by pharmacist for 3 days to be aptt after that.	4
Infusion rate adjustment	5	Potassium chloride is prescribed 80 mg over 6 hrs. However, potassium level was 3.35 WNR and based on hospital protocol it should be on 20 meq /200 ml over 2 hrs.	6
		Albumin 20% 100 ml was prescribed to infuse over 30 mins but adjusted by pharmacist to be over 4 hrs	
Route of administration Adjustment	6	Metoprolol 12.5 mg BID was requested as IV but adjusted by pharmacist to Oral form.	6
Dose and frequency adjustment	5	Colistin was prescribed 3 million units daily but based on Crcl (29.5 ml/min) dose should be 2.5 mu every 12 hrs as suggested by pharmacist	8
		Apixaban was prescribed 5 mg daily but patient had PE, so dose was adjusted by pharmacist to 10 mg Bid for 7 days then decreased to 5 mg BID	
Dose and infusion rate adjustment	1	MgSO4 50% dose and infusion rate were suggested by pharmacist	1
		20 mg/ml (2000 mg/100 ml) or 50 ml (40 mg/ml) over 4 hrs	
Infusion rate adjustment and missing diluents	1	Phenytoin 1 gm IV was prescribed and suggested by pharmacist to be in 100 ml D5W over 45 mins	1
Missing dose	7	Lactulose prescribed with no dose and 11 ml (11 gm prn) was recommended by pharmacist	8
Missing frequency	1	Dexamethasone prescribed without frequency	1
Missing infusion rate	2	Tranexamic acid 500 mg/5ml qid was prescribed without infusion rate	2
Missing dose and infusion rate	1	Magnesium sulfate was prescribed without dose and frequency and based on Mg level pharmacist recommended 2 gm\100 ml over 4 h	1
Missing route of administration	2	Sodium nitroprusside 50 mg prescribed without route of administration	2
<b>Medication is not available</b>	<b>69</b>		<b>191 (40.6)</b>
Medication is Not Available either out of stock or not in Formulary with no alternative suggestion	54	Beta-Sitosterol 0.25% ointment	114
Medication is Not Available either out of stock or not in Formulary but alternative suggested	39	Meropenem was not available and imipenem was recommended as an alternative	77
<b>Other: missing date, Time .. etc</b>	<b>9</b>		<b>10 (2.1)</b>
Missing patient data, lab values		Potassium chloride is prescribed, and K level was missed	
		Calcium gluconate was prescribed, and Ca level was missed	
		Amikacin was prescribed, and patient weight was missed	
<b>Reject drug order</b>	<b>6</b>		<b>9 (1.9)</b>
Reject drug order with justification	5	Acetazolamide 500 mg BID was rejected as based on pt. lab results no need to take this medication since bicarbonate and PH were within normal range	7
Reject drug order without justification	1	Cefotaxime was rejected by pharmacist with no clarification	2
<b>Re-Order Requested</b>	<b>10</b>		<b>17 (3.62)</b>
System error	10	-	14
Order entered by other-registered person	1	-	3
<b>Non-privileged prescriber</b>	<b>7</b>		<b>12 (2.6)</b>
None	<b>6</b>		<b>6 (1.3)</b>
Intervention description not entered	3	-	3
No intervention done during ICU stay	3	-	3

regimens type revealed that 53% and 21% were associated to dose and frequency adjustments, respectively. Additional information related the types of interventions, corresponding number of recipients and example for each intervention are provided in Table 2.

3.3. Classification of pharmacists' intervention based on the pharmacological category of involved medications and their numbers

Many pharmacological groups were associated with the interventions. However, antibiotics (16.8%), electrolytes/minerals (11.7%) and vitamins (9.4%) are considered the most involved categories. Further details are provided in Table 3.

Regarding the number of interventions per patient, it ranged between none in 3 patients to 22 interventions in 1 patient, while many had 3 to 4 interventions, as shown in Table 4.

3.4. Health complications in COVID-19 patients during ICU stay and patients' survival

Cardiovascular and respiratory complications were found the most common in this cohort (25.5% and 26%, respectively), as shown in Table 5.

Patients were also categorized based on their survival. Unfortunately, 74.7% (59 patients) died, while only 20.3% (16 patients) survived at the end of the study. Interestingly, when BMI was

**Table 3**  
Classification of pharmacists' interventions based on the pharmacological category of involved medications.

Interventions in Drugs categories	Total number of medications	Number of involved cases (%)
Antibiotic	19	79 (16.8)
Electrolytes & Minerals	8	55 (11.7)
Vitamin	5	44 (9.4)
Laxative	10	26 (5.5)
Antihypertensive	10	21 (4.5)
Antipsychotic	3	19 (4.0)
Anticoagulant	4	18 (3.8)
Antifungal	8	16 (3.4)
Antiulcer	2	15 (3.2)
Analgesic	6	11 (2.3)
Wound healing drop/ ointment	3	10 (2.1)
Antiplatelet	2	7 (1.5)
Colloid	1	7 (1.5)
Vasopressor	3	7 (1.5)
Antiepileptic	3	6 (1.3)
Antidiabetic	2	5 (1.1)
Antihemorrhagic	2	5 (1.1)
Antiviral	1	5 (1.1)
Steroid	3	5 (1.1)
Diuretic	3	4 (0.9)
Sedative and anxiolytic	3	4 (0.9)
Antiasthmatic	1	3 (0.6)
Antiasthmatic-COPD	1	3 (0.6)
Hemostatic agent	1	3 (0.6)
Antiallergic	2	2 (0.4)
Antidote	2	2 (0.4)
Antiseptic	1	2 (0.4)
Sedative and analgesic	1	2 (0.4)
Antiarrhythmic	1	1 (0.2)
Antibiotic/Steroid	1	1 (0.2)
Antidepressant	1	1 (0.2)
Antihyperthyroidism	1	1 (0.2)
Lubricant	1	1 (0.2)
Neuromuscular blocker	1	1 (0.2)
Sedative and anesthetic	1	1 (0.2)
Vasodilator	1	1 (0.2)
Others	-	76 (16.2)

**Table 4**  
Patients classification based on the number of interventions implemented by pharmacists.

Interventions	Number of patients
0 intervention	3 (3.8)
1 intervention	8 (10.1)
2 interventions	4 (5.1)
3 interventions	11 (13.9)
4 interventions	14 (17.7)
5 interventions	5 (6.3)
6 interventions	5 (6.3)
7 interventions	8 (10.1)
8 interventions	5 (6.3)
9 interventions	3 (3.8)
10 interventions	3 (3.8)
11 interventions	2 (2.5)
13 interventions	1 (1.3)
14 interventions	2 (2.5)
16 interventions	2 (2.5)
18 interventions	1 (1.3)
19 interventions	1 (1.3)
22 interventions	1 (1.3)

**Table 5**  
Medical complications in patients during their ICU admission.

Complications	Number of patients with each complication	Total number of cases (%)
<b>Cardiovascular system</b>		<b>139 (25.5)</b>
Tachycardia	21	
Bradycardia	22	
Hypertension	13	
Hypotension	30	
Septic shock	22	
Others	31	
<b>Respiratory system</b>		<b>142 (26%)</b>
Tachypnea	14	
Pneumonia	32	
ARDS	23	
Others	73	
<b>Urinary system</b>		<b>53 (9.7)</b>
Oliguria	20	
Acute Kidney injury	16	
Others	17	
<b>Gastrointestinal system</b>	26	<b>26 (4.8)</b>
<b>Central nervous system</b>	37	<b>37 (6.8)</b>
<b>Dermatological system</b>		<b>18 (3.3)</b>
Bed sore or skin ulcers	15	
Other	3	
<b>Others</b>		<b>131 (24%)</b>
Fever	12	
Hyperkalemia	24	
Hypernatremia	12	
Hypomagnesemia	11	
Other	72	
<b>No complications</b>	2	<b>2 (0.35)</b>

compared between patients who survived and discharge (12 patients) vs. those who died (51 patients), no significant difference was observed (mean BMI 30.30 kg/m<sup>2</sup> vs. 31.2 kg/m<sup>2</sup>, respectively), as provided in Fig. 1. It is worth to mention that a total of 16 patients from the cohort were excluded from this analysis because of missing BMI and/or survival data (4 patients), missing BMI data only (10 patients) or being transferred to another hospital where survival data could not be obtained (2 patients).

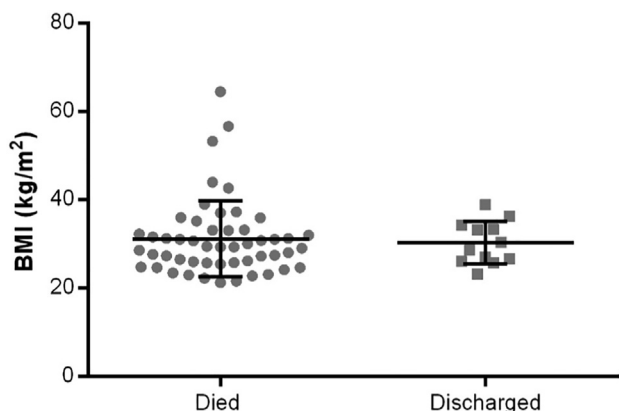


Fig. 1. Body mass index (BMI) comparison between deceased and survived critically ill COVID-19 patients.

#### 4. Discussion

Many studies have been conducted investigating the essential services delivered by pharmacists during COVID-19 pandemic. Pharmacists had the likely to show a superior role during this pandemic in multiple aspects, such as providing drug information for healthcare providers (Dhahri et al., 2020; Louiselle et al., 2020), patients counseling (Meng et al., 2020), suggestion alternative therapy (Ong et al., 2020), therapeutic drug monitoring (Mongaret et al., 2018), drug supply administration (Ong et al., 2020; Tan et al., 2020) and safety measures for infection control (Ong et al., 2020; Zuckerman et al., 2020). This study sheds light on the services provided by pharmacists to the critically ill COVID-19 patients in Riyadh, Saudi Arabia.

Since the beginning of this pandemic, researchers all over the world started searching different aspects of this novel disease. As the available peer reviewed literature regarding the services of pharmacists provided to COVID-19 patients in the ICU setting has been scarce, it has become of our interest to assess that during the pandemic. Understanding how pharmacists have contributed in providing services to the critically ill COVID-19 patients would highlight their achievements and more importantly expose any gap in their practice giving ample opportunity for future improvements.

Only one study conducted on 22 ICU-admitted COVID-19 patients in China investigating this topic and was published recently by Wang et al. (2021). Wang et al. (2021) have shown that drug discontinuation was the most common recommendation (31.5%; 35 out of 111) while dose adjustment accounted for 15.3%. Despite the slight difference in type of interventions at drug level compared to our study, most of the recommendation based on their observation were related antibiotics (57.7%) which aligns with the current reported results (16.8%; 79 of 470) in spite of the lower rate. As studies discussing this matter are rarely reported (Wang et al., 2021), it becomes challenging to compare our findings to additional studies. Nevertheless, a quick glance on types of interventions made by pharmacists on the critically ill COVID-19 patients revealed some similarities with their interventions at different critical care units. For instance, a study focused on the impact of pharmacists' interventions with respect to drug-related problems (DRPs) in the ICU has shown 28.9% and 14.3% were related to wrong dosing regimen and no indication for drug use, respectively (Al-Jazairi et al., 2008). Additional study assessing the role of clinical pharmacy services in the oncology ward showed that 26.6%, 21.5% and 10.3% of pharmacist's interventions were related to drug discontinuation, drug dosing adjustments, and

therapeutic drug monitoring (Delpeuch et al., 2015). Further findings from the oncology ward revealed 27.1%, 20.0%, 6.2%, 5.1% of the pharmacist interventions were secondary to drug dosing modifications, therapy discontinuations, recall of the treatment, and replacement of a drug with another one, respectively (Moukafih et al., 2021). Another study conducted by Faqeer and colleagues on identifying DRPs in the oncology ward, showed that addition of medications (38.7%), then discontinuation of medications (25%) were the most common types of interventions followed by dose adjustment secondary to wrong dose (3.7%) (Faqeer et al., 2021). In the internal medical ward, Abunahlah and colleagues showed that inappropriate drug use (44.79%), inappropriate dose (27.61%), and inappropriate medication treatment procedures (21.47%) were the most common interventions identified by the clinical pharmacists (Abunahlah et al., 2018). Although Molino and colleagues' study was conducted in the outpatients' setting, they reported similar rate of our interventions related to drug duplication (11.29%), and lower rate of those associated to dose adjustment (20.05%) (Molino Cde et al., 2014).

Comparing with the current literature, our results are in agreement with the type of ICU pharmacists' interventions seen in the current pharmacy practice in hospitals, reiterating the notion that more attention should be directed towards errors in the prescribed regimens that are mainly attributed to wrong dose and/or frequencies. Our results also showed approximately 60% of the interventions associated to medication shortage were left with no alternative suggestions (117 of 191). Despite that, these medications were requested and supplied by MOH, either directly or via other MOH-operated hospitals.

Our results showed that antibiotics (16.8%) were the most common drug classes associated with interventions, which goes hand on hand with previous studies (Wang et al., 2021; Faqeer et al., 2021; Babelghaith et al., 2020; Hajjar et al., 2021). This was followed by electrolytes/minerals (11.7%) and vitamins (9.4%).

By looking at the complications that COVID-19 patients developed during ICU admission, respiratory complications were found to be the most prominent (26%) among which pneumonia, tachypnea, ARDS, hypoxia, and metabolic acidosis which were more frequent, followed by the cardiovascular complications (25.5%), which were mainly hypotension, septic shock and bradycardia/tachycardia. These results are in agreement with Hajjar et al study that was focused on the intensive care management of COVID-19 patients (Hajjar et al., 2021). Finally, and unexpectedly, when BMI was compared between the survived and deceased patients, there was no significant difference between the two groups.

#### 5. Conclusion

Our findings highlight that pharmacist's attention should be amplified towards errors in dosing regimens and drug duplications throughout caring of critically ill COVID-19 patients. In addition, with medication shortage that potentially occur during the pandemic, pharmacist as a medication expert should be proactive in providing information about drugs and their alternatives, if necessary, for healthcare providers. Studies focused on significance of pharmacists' interventions on health outcomes of critically ill COVID-19 patients and their acceptance by physicians should be conducted to follow up these findings.

#### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Authors' contributions

Conception and design: AW, AR, SO, and SA; Data collection, analysis, and interpretation: AW, AR, SO, SA and SW; Writing the manuscript: AW, AR, SO, SA, SW and SB. All authors reviewed the manuscript.

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