

# Comparative study of hemodynamic responses during laryngoscopy and endotracheal intubation with Dexmedetomidine and Esmolol



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## ABSTRACT

**Background:** Many drugs used to reduce the hemodynamic stress response during laryngoscopy and endotracheal intubation. The quest for ideal drugs and their dosage without major side effects is still pursued. Dexmedetomidine, an alpha-2 agonist, is emerging as a promising drug to counteract the catecholamine release. **Aims and Objectives:** This study is done to compare the effect of lower doses dexmedetomidine and esmolol in control of hemodynamic response and stability in cases undergoing laryngoscopy and endotracheal intubation during general anesthesia. **Setting and Design:** This was a prospective, randomized double-blinded comparative study. **Materials and Methods:** After approved by the Institute Ethics Committee, consent obtained from 60 patients (n=60) belonging to ASA I or II. Patients were equally divided into two groups (D and E). Group D patients (n=30) were infused with intravenous dexmedetomidine at 0.75 mcg/kg diluted in 20 ml with normal saline 10 min before induction. Group E patients (n=30) were infused with intravenous esmolol 0.75 mg/kg diluted in 20 ml of normal saline 2 min before intubation. After administration of drugs, SBP, DBP, MAP, HR, and SpO<sub>2</sub> were recorded, immediately after induction, after intubation at 1 min, 3 min, 5 min, and 10 min, respectively. **Results:** Data were entered into Microsoft Excel datasheet and were analyzed using SPSS 22 version software. In the study, there was a significant decrease in SBP, DBP, MAP, and HR from administration till 10 min after intubation in Group D compared to Group E. No severe hypotension or bradycardia was seen in any of the patients in either group, took part in our study. **Conclusion:** This study concludes low dose of dexmedetomidine (0.75 mcg/kg) was superior to low dose of esmolol (0.75 mg/kg) in maintaining of hemodynamic stability in response to laryngoscopy and tracheal intubation without any significant adverse effects even though both drugs were comparable in suppressing pressor response.

**Key words:** Dexmedetomidine; Esmolol; Hemodynamics; Laryngoscopy

## INTRODUCTION

Endotracheal intubation and laryngoscopy are core integral skills of anesthetic management in general anesthesia and critical care of the patient as first described by Rowbotham and Magill in 1921.<sup>1</sup> Laryngoscopy with further negotiation of endotracheal tube inside trachea stimulates the sympathoadrenal receptors releasing catecholamines in blood that transiently storms a pressor response characterized by the elevation of systolic blood

pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR). The response to laryngoscopy and tracheal intubation is a somatovisceral kind of reflex. It depends mainly on two factors such as duration and force of the procedure clinically. In pediatrics, such a response may lead to reflex vagal inhibition of the heart manifesting as bradycardia.

This pressor response manifests within 5 s and further elevates while endotracheal tube enters inside trachea.

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Average rise of SBP is 25–50 mmHg,<sup>2,6</sup> following a plateau at or above this peak pressure is sustained for 1–2 min. It takes about 5–10 min for the pressures to return to pre laryngoscopic value.<sup>7,8</sup> Such disturbances in hemodynamics are well withstood by normal individuals or the American Society of Anesthesiologist (ASA) 1 patients. Even, controlled hypertensives patients are more prone to elevations in pressures. Patients with limited cardiovascular reserve, coronary artery disease, cardiac dysrhythmia, cardiomyopathy, congestive heart failure, hypertension, limited intracranial compliance, and geriatric population may land to life-threatening complications such as myocardial ischemia, acute cardiac failure, and cerebrovascular hemorrhage.<sup>9,10</sup> Hemodynamic response to laryngoscopy and intubation in anesthetized persons was first reported by Donegan et al.<sup>11</sup> Since then, research works have been carried out to attenuate or prevent these responses and various measures such as shortening duration of laryngoscopy, smooth intubation, airway anesthesia by blocking superior laryngeal nerve, recurrent laryngeal nerve and topical lignocaine, beta-blockers, calcium channel blockers, and intravenous lignocaine.<sup>12-15</sup>

Various strategies with drugs and non-pharmacological techniques have been carried out for obtunding the stress response to laryngoscopy and intubation, including opioids, barbiturates, benzodiazepines, beta-blockers, calcium channel blockers, and vasodilators.<sup>16-20</sup>

Esmolol is an ultra-short-acting, beta-adrenergic receptor blocker which has been proven efficacious clinically to provide hemodynamic control during laryngoscopy and intubation without severe side effects.<sup>16,17</sup>

Newer alpha-2 agonists such as clonidine and dexmedetomidine have been used currently for obtunding sympathoadrenal stimulation by tracheal intubation and surgery.<sup>18</sup> Dexmedetomidine blunts hemodynamic response and provides conducive hemodynamics during the placement of endotracheal tube.<sup>21,22</sup>

### Aims and objectives

The current study was done to compare the effect of lower doses of dexmedetomidine and esmolol for control of hemodynamic response and stability among cases undergoing laryngoscopy and endotracheal intubation during general anesthesia.

## MATERIALS AND METHODS

The current study was prospective, randomized controlled double-blinded study conducted after the approval of the Institutional Ethics Committee and registration in

Clinical Trials Registry India with registration number CTRI/2019/05/019172.

### Sample size

Sample size was calculated using OpenEpi software, version 3.0. by comparing with the previous studies<sup>14</sup> mean and standard deviation of mean arterial pressure (MAP) at various time intervals as  $77.4 \pm 10.1$ ,  $86.1 \pm 10.1$  for dexmedetomidine and esmolol, respectively, with probability of type 1 error ( $\alpha < 0.05$ ), 80% power, 95% confidence interval, and non-response rate of 10%. Sample size of 60 was calculated with 30 in each group.

### Inclusion criteria

The following criteria were included in the study:

1. Age group 18–60 years
2. Both genders
3. ASA Grade I or II
4. Modified Mallampati Grade 0/I/II.

### Exclusion criteria

The following criteria were excluded from the study:

1. Patients refusal
2. Pregnancy
3. Emergency surgeries
4. Patients with anticipated difficult airway
5. BMI > 30
6. Modified Mallampati Grade III/IV
7. Patients with ischemic heart disease, hypertension, and diabetes mellitus.
8. H/o chronic respiratory, hepatic, renal diseases, and on antipsychiatric medications.
9. H/o drug allergy
10. Laryngoscopy time > 20 s.

### Technique of anesthesia

All the study subjects underwent pre-anesthetic checkup and written informed consent was obtained. On the day of surgery, patients were shifted to the operating room and then standard monitors were connected and baseline parameters such as HR, SBP, DBP, and SpO<sub>2</sub> were recorded. Patients were pre-medicated with inj. glycopyrrolate 0.004 mg/kg iv, inj. midazolam 0.03 mg/kg iv, and fentanyl 2 mcg/kg iv.

Dexmedetomidine group (Group D) patients received single bolus infusion of dexmedetomidine 0.75 mcg/kg diluted in 20 ml 0.9% normal saline over 10 min. Esmolol group (Group E) patients received single IV bolus of esmolol 0.75 mg/kg diluted in 20 ml 0.9% normal saline over 10 min.

After the study, drug administration patients were pre-oxygenated and induced with inj. propofol 2 mg/kg iv. After confirming the feasibility to ventilation, inj. vecuronium

0.1mg kg<sup>-1</sup> supplemented to facilitate laryngoscopy and tracheal intubation. After 3min of giving vecuronium, using laryngoscope with Macintosh blade, intubation of the trachea was done with well lubricated appropriately sized cuffed endotracheal tube. Laryngoscopy and intubation time were kept minimum <20 s. The tube was fixed after confirmation of bilateral air entry. Anesthesia was maintained with N<sub>2</sub>O 66%, O<sub>2</sub> 33%, isoflurane 1–1.6%, in controlled ventilation. HR, SBP, DBP, mean arterial pressure (MAP), electrocardiogram, and SpO<sub>2</sub> were recorded immediately on arrival before administration of drugs, after administration of drugs, induction of anesthesia, 1min, 3 min, 5min, and 10 min after laryngoscopy and intubation, respectively. No surgical stimulus was allowed till 10 min post-intubation. After the completion of surgery, with return of respiratory efforts, residual neuromuscular blockade was reversed with inj. neostigmine 0.05mg kg<sup>-1</sup> and inj. glycopyrrolate 0.01mg kg<sup>-1</sup>. Patients were extubated after recovery from neuromuscular block and were shifted to post-operative ward.

## RESULTS

Baseline demographic and clinical characteristics among the two groups are shown in Table 1.

The baseline demographic and the clinical characteristics among the two groups are shown in Table 1. Majority of the patients were in the age group of 21–40 years and were belonging to ASA Class I. There was equal representation of both genders. The distribution of all the characteristics was similar in both the drug groups (P>0.05).

SBP was significantly reduced after administration of the dexmedetomidine to 5 min post-intubation (P<0.001), as shown in Table 2.

Similarly, DBP was found to be significantly reduced after administration of dexmedetomidine to 10 min post-intubation (P<0.001) between two groups except at 1 min of intubation, as shown in Table 3.

MAP was significantly reduced after administration till 10 min post-intubation (p<0.001) in the dexmedetomidine group, as shown in Table 4.

HR was found to be significantly decreased in Group D 1 min after intubation to 5 min post-intubation with high statistical significance value (P<0.001) between two groups, as shown in Table 5.

The SBP, DBP, MAP, and HR of both dexmedetomidine and esmolol are shown in Figures 1–4, respectively. Figures indicate better maintenance of suppressed pressor response by dexmedetomidine from time of induction to 10 min post-induction. This study concluded that Group D dexmedetomidine at 0.75 mcg kg<sup>-1</sup> was superior compared to Group E (esmolol 0.75 mcg kg<sup>-1</sup>) at 1 min and 10 min post-intubation in attenuation of hemodynamic response.

## DISCUSSION

Laryngoscopy and endotracheal intubation are performed after induction with good will, it is not devoid of complications. On stimulation, laryngoscopy within 5 s activates sympathoadrenal reflex and propagates stress responses that suddenly surge catecholamines resulting in tachycardia and hypertension which can be withstood by normal patients. Such changes may unpleasantly result in myocardial ischemia, arrhythmias, raised intracranial pressure, raised intraocular pressure, laryngospasm, and bronchospasm in patients of limited cardiac reserve due to the disturbance of demand versus supply (oxygen)

**Table 1: Baseline demographic and clinical characteristics among the two groups (n=60)**

	Group D	Group E	P value
Age group, n (%)			
≤20 years	3 (10%)	3 (10%)	0.526*
21–30 years	10 (33.3%)	7 (23.3%)	
31–40 years	10 (33.3%)	14 (46.7%)	
41–50 years	6 (20%)	3 (10%)	
>50 years	1 (3.3%)	3 (10%)	
Gender, n (%)			
Female	14 (46.7%)	16 (53.3%)	0.606*
Male	16 (53.3%)	14 (46.7%)	
American Society of Anesthesiologist, n (%)			
I	24 (80%)	20 (66.7%)	0.245*
II	6 (20%)	10 (33.3%)	
Systolic blood pressure, mean (±SD)	125.3 (±8.1)	122.6 (±7.8)	0.199 <sup>^</sup>
Diastolic blood pressure, mean (±SD)	77.9 (±6.4)	78.1 (±6.4)	0.904 <sup>^</sup>
Mean arterial pressure, mean (±SD)	93.7 (±5.6)	93.0 (±4.8)	0.578 <sup>^</sup>
Heart rate, mean (±SD)	80.0 (±7.0)	77.3 (±5.6)	0.111 <sup>^</sup>

\*P value by Chi-square test; <sup>^</sup>P value by independent t-test

**Table 2: Mean SBP comparison among two groups at various intervals of follow-up**

SBP	Group						P value between groups
	Group D			Group E			
	Mean	±SD	P value within group	Mean	±SD	P value within group	
Baseline	125.27	8.06	-	122.60	7.83	-	0.199
After admin	113.87	7.37	<0.001*	121.53	7.84	0.002*	<0.001*
After induction	102.07	6.36	<0.001*	110.73	7.02	<0.001*	<0.001*
1 min	102.33	5.80	<0.001*	117.60	6.86	<0.001*	<0.001*
3 min	105.80	5.18	<0.001*	121.00	6.72	0.036*	<0.001*
5 min	111.67	5.61	<0.001*	119.07	7.52	<0.001*	<0.001*
10 min	118.00	5.63	<0.001*	119.60	6.90	<0.001*	0.329

SBP: Systolic blood pressure

**Table 3: Mean DBP comparison among two groups at various intervals of follow-up**

DBP	Group						P value between groups
	Group D			Group E			
	Mean	±SD	P value within group	Mean	±SD	P value within group	
Baseline	77.93	6.44	-	78.13	6.41	-	0.904
After admin	68.93	6.16	<0.001*	77.53	5.89	0.240	<0.001*
After induction	61.00	6.07	<0.001*	72.87	5.53	<0.001*	<0.001*
1 min	60.67	5.76	<0.001*	61.33	4.85	<0.001*	0.630
3 min	61.33	5.54	<0.001*	66.60	5.01	<0.001*	<0.001*
5 min	63.87	5.48	<0.001*	71.60	4.88	<0.001*	<0.001*
10 min	66.40	6.04	<0.001*	75.53	5.14	0.002*	<0.001*

DBP: Diastolic blood pressure

**Table 4: Mean MAP comparison among two groups at various intervals of follow-up**

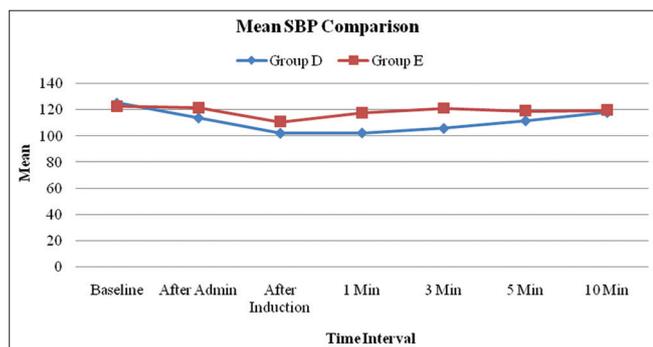
MAP	Group						P value between groups
	Group D			Group E			
	Mean	±SD	P value within group	Mean	±SD	P value within group	
Baseline	93.71	5.64	-	92.96	4.79	-	0.578
After admin	83.91	5.10	<0.001*	92.20	4.82	0.049*	<0.001*
After induction	74.69	4.90	<0.001*	85.49	4.89	<0.001*	<0.001*
1 min	74.56	4.59	<0.001*	80.09	4.42	<0.001*	<0.001*
3 min	76.16	4.26	<0.001*	84.73	4.62	<0.001*	<0.001*
5 min	79.80	4.34	<0.001*	87.42	4.60	<0.001*	<0.001*
10 min	83.60	4.69	<0.001*	90.22	4.59	<0.001*	<0.001*

MAP: Mean arterial pressure

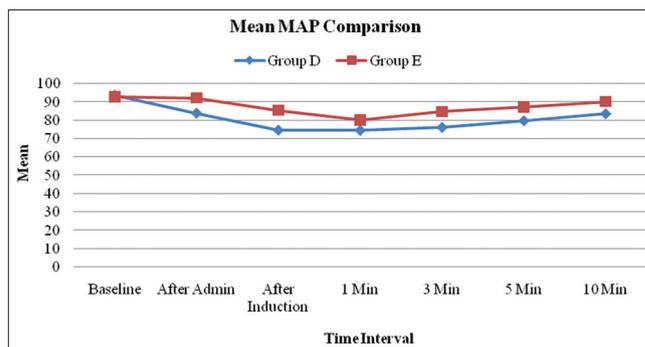
**Table 5: Mean HR comparison among two groups at various intervals of follow-up**

HR	Group						P value between groups
	Group D			Group E			
	Mean	±SD	P value within group	Mean	±SD	P value within group	
Baseline	80.00	7.05	-	77.33	5.62	-	0.110
After admin	75.60	6.73	<0.001*	75.47	5.82	<0.001*	0.935
After induction	69.33	5.79	<0.001*	71.27	4.25	<0.001*	0.146
1 min	66.13	4.42	<0.001*	81.47	5.38	<0.001*	<0.001*
3 min	68.73	4.83	<0.001*	85.00	5.25	<0.001*	<0.001*
5 min	65.27	4.15	<0.001*	70.33	3.79	<0.001*	<0.001*
10 min	69.27	3.13	<0.001*	68.47	3.63	<0.001*	0.364

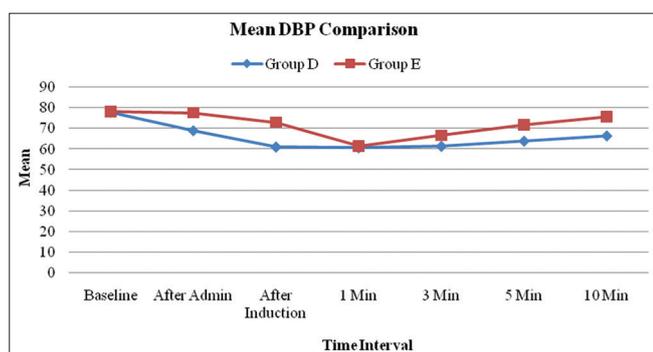
HR: Heart rate



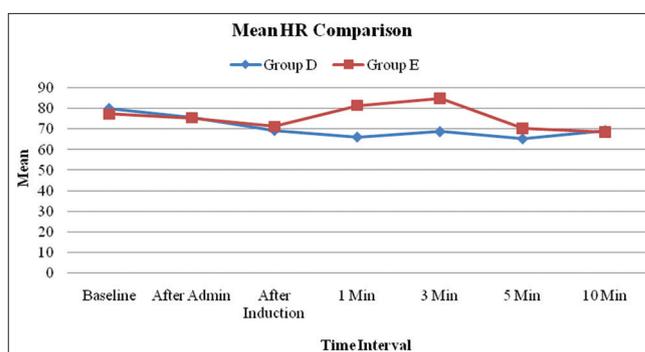
**Figure 1:** Line diagram showing mean systolic blood pressure comparison among two groups



**Figure 3:** Line diagram for mean arterial pressure comparison among two groups



**Figure 2:** Line diagram showing mean diastolic blood pressure comparison among two groups



**Figure 4:** Line diagram for mean heart rate comparison among two groups

mismatch. The magnitude of response further escalates, peaks around 1–2 min, and returns to pre-laryngoscopy level by 5–10 min.

Recently, many studies are being carried out with newer  $\alpha_2$  agonists such as dexmedetomidine and beta-blockers like esmolol at different dosage in attenuation of hemodynamic response.

Dexmedetomidine is a highly selective alpha-2 agonist having clinically favorable prospects such as sedation with very easy arousal, sympatholysis, neuroprotection, analgesia, and anesthetic sparing effect with wide safety margin. In relation to the attenuation of hemodynamic stress response, dexmedetomidine decreased central sympathetic outflow, reducing serum epinephrine, and norepinephrine levels proportional to the dose. Therefore, dexmedetomidine causes dose-dependent reduction in arterial blood pressure and HR. At lesser dose, 0.25–0.5 mcg kg<sup>-1</sup> dexmedetomidine only decreases blood pressure while at higher dose 1–2 mcg kg<sup>-1</sup>, there was transient raise in blood pressure followed by hypotension and bradycardia. Hence, in our study, we selected dexmedetomidine 0.75 mcg kg<sup>-1</sup>.

Esmolol, a Class II antiarrhythmic agent, is a highly selective beta-1 receptor blocker with favorable properties such as controlling tachyarrhythmias, myocardial oxygen

demand, coronary perfusion, restriction of infarct size, and improved rate pressure product. Esmolol inhibits the action of catecholamines on beta-receptors, thereby preventing the cardiovascular response due to laryngoscopy and endotracheal intubation. In the study by Miller et al., injection esmolol 1.5 mg kg<sup>-1</sup> and 3 mg kg<sup>-1</sup> were used and they observed adverse effects like hypotension while using higher dose of esmolol during induction and found optimal results with lesser dose.<sup>23</sup> This was basis for using smaller dose of 0.75 mg kg<sup>-1</sup> in this study.

Anish Sharma compared clonidine (3 mcg kg<sup>-1</sup>) and dexmedetomidine (1 mcg kg<sup>-1</sup>) in his study and observed that dexmedetomidine at 1 mcg kg<sup>-1</sup> was more efficacious in attenuating the pressor response and also found that patients among clonidine group developed profound hypotension.<sup>24</sup> In a study by Fernandez-Galinski et al., comparing effects of alfentanil (3 mcg kg<sup>-1</sup>), esmolol (1 mg kg<sup>-1</sup>), and clonidine (3 mcg kg<sup>-1</sup>) in attenuating cardiovascular response to endotracheal intubation, esmolol at 1 mg kg<sup>-1</sup> gave conducive hemodynamics.<sup>25</sup> Hence, based on the above studies, this study was carried out with dexmedetomidine and esmolol.

Dexmedetomidine 0.75 mcg kg<sup>-1</sup> and esmolol 0.75 mg kg<sup>-1</sup> were compared in the present study in attenuating hemodynamic response to laryngoscopy and

endotracheal intubation as a single dose, administered intravenously. The SBP, DBP, MAPs, and HR were inferred to be decreased with high statistical significance from administration of both study drugs till 10 min post-intubation. On core analysis of the study, it was revealed that Group D had complete attenuation of hemodynamic response to tracheal intubation compared to Group E. The above findings concluded that dexmedetomidine obtunds pressor response effectively following laryngoscopy and intubation.

Srivastava *et al.*, compared (Group C) 20 ml 0.9% normal saline, dexmedetomidine (Group D) 1 mcg kg<sup>-1</sup>, and group esmolol (Group E) 1.5 mg kg<sup>-1</sup>. Their study concluded that dexmedetomidine 1 mcg kg<sup>-1</sup> was more efficacious than esmolol 1.5 mg kg<sup>-1</sup> for blunting hemodynamic stress response.<sup>26</sup> Reddy *et al.*, conducted a study to evaluate the effect of intravenous dexmedetomidine (1 mcg kg<sup>-1</sup>) infusion, esmolol (2 mg kg<sup>-1</sup>) intravenous infusions, and placebo on attenuation of pressor response to laryngoscopy and tracheal intubation. The study concluded that dexmedetomidine 1.0 mcg kg<sup>-1</sup> proved to be dominant when compared to esmolol 2 mg kg<sup>-1</sup> in providing a consistent and reliable blunting of sympathoadrenal response.<sup>27</sup> The results of the above studies are in corroboration with the results of the present study.

However, in contrary to our study results, Gogus *et al.*, concluded in their study that esmolol at 2 mg kg<sup>-1</sup> was more competent in maintaining stable hemodynamics compared to dexmedetomidine at 1 mcg kg<sup>-1</sup> during laryngoscopy and endotracheal intubation.<sup>28</sup>

In the present study, dexmedetomidine was administered slowly as an infusion over 10 min at dose of 0.75 mcg kg<sup>-1</sup> and no patient in this study developed severe bradycardia, hypotension, post-operative sedation, fall in SpO<sub>2</sub>, or needed oxygen supplementation.

There are limited studies that analyzed esmolol at dosage of 0.75 mg kg<sup>-1</sup> infused 2 min before intubation on pressor response. Therefore, this study has tried to fill the gap in literature and established the potential benefit of esmolol at 0.75 mg kg<sup>-1</sup> on attenuation of hemodynamic response. From time of administration till 10 min post-intubation, there is a high statistical significant attenuation of hemodynamic response with no serious side effects or adverse outcomes in any participant. Hence, this study also analyzed the minimal effective dose for attenuation of intubation response among both the study drugs.

However, this study could not infer on the performance of both drugs in attenuating hemodynamic response to extubation, post-operative extubation standards with

extubation scale, post-operative sedation, and post-operative analgesic requirements which extend the scope for future research.

### Limitations of the study

The present study didn't have any Control group for comparing the characteristics. Plasma catecholamine, cortisol, insulin levels were not analyzed which could have been more informative and as well as confirmative of stress response due to cost factor and non-availability of resources. Assessment of post-operative requirement of analgesics was not done as it was not part of the present study.

## CONCLUSION

This study concludes that both dexmedetomidine (0.75 mcg kg<sup>-1</sup>) and esmolol (0.75 mg kg<sup>-1</sup>) have statistically significant attenuation of hemodynamic stress response to laryngoscopy and tracheal intubation without any adverse effects. Although, the study drugs have favorable reduction in hemodynamic response, dexmedetomidine has better maintenance of hemodynamics following intubation.

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VRH-Concept and design of the study, prepared first draft of manuscript; VC-Interpreted the results, reviewed the literature, and manuscript preparation; and RN-Concept, coordination, statistical analysis and interpretation, preparation of manuscript, and revision of the manuscript

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