



Prevalence and Risk Factor Analysis of Stroke after Coronary Artery Bypass Graft Surgery: A Retrospective Cohort Study

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Abstract

Background: Postoperative ischemic stroke is a major adverse effect following Coronary Artery Bypass Graft surgery (CABG). This study evaluates the prevalence, risk factors, and clinical outcomes of postoperative stroke patients undergoing CABG surgery in Bangladesh.

Methods: This current study evaluates the predictors of postoperative stroke (n=19, 1.72%) in 1100 consecutive patients who underwent CABG from July 2010 to June 2019 in single surgeon practice. Predictors of postoperative ischemic stroke were identified by logistic regression analysis.

Results: Risk factors analysis of stroke significantly correlates with recent MI (P=0.01), previous stroke or TIA (P<0.001), carotid artery stenosis (P<0.001), elderly age (P=0.008), hypertension (P<0.001), diabetes (P=0.001), atrial fibrillation (P<0.001), and severe left ventricular dysfunction (P=0.01). Moreover, postoperative ischemic stroke was significantly associated with longer postoperative stay (<0.001) as well as higher in-hospital mortality (P<0.001).

Conclusion: Ischemic stroke after CABG surgery is associated with a higher incidence of postoperative early morbidity and mortality. Furthermore, the prevalence of postoperative stroke following CABG can be predicted and managed by preoperative as well as postoperative early evaluation and risk factors management.

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Introduction

Coronary Artery Bypass Grafting (CABG) is associated with adverse neurological complications, of which stroke is the most debilitating and life-threatening complication, inducing a 3 to 6 times increased risk of death after cardiac surgery [1]. Surgical revascularization carries a higher procedural risk of stroke than PCI. However, CABG surgery may offer better long-term survival in certain subsets of patients [2]. Furthermore, the incidence of postoperative stroke is greater after CABG (1.4% to 3.8%) than after general surgery (0.08% to 0.7%) [2,3]. Neurological complications result in high economic costs worldwide each year for post-CABG stroke patients. Patients undergoing CABG often have atherosclerosis of multiple cerebral arteries as well as the carotid artery, which is regarded as an important risk factor for stroke [3-5].

The pathophysiology of stroke is multifactorial, but two variables are believed to play a significant role- cerebral atheroembolism from the ascending aorta and hypoperfusion during surgery. Preoperative screening and identifying high-risk stroke patients are paramount for the surgical decision-making approach and informed consent [4,6]. Several risk scoring systems like EuroSCORE and Syntax score were developed to stratify the hazard of stroke in patients undergoing CABG surgery, but identification of severe atherosclerosis of coronary artery, ascending aorta, and pre-existing cerebrovascular disease are key determinants for appropriate risk stratification and decision-making [5-8].

Preoperative proper screening as well as intraoperative measures that ensure adequate cerebral perfusion, minimize embolisation and improve systemic inflammatory response with hemodynamic performance appear mandatory to improve surgical outcomes following CABG surgery [2,7,8]. Better understanding of the prevalence of stroke and its sequela by both surgeons and patients may have important implications for choosing a particular surgical myocardial revascularization

strategy [7-9]. To systematically evaluate the incidence, predictors, and early clinical outcome of stroke following CABG surgery among the Bangladeshi population undergoing Off-pump coronary artery bypass graft surgery in a single surgeon's practice.

Patients and Methods

A total of 1,850 study patients undergoing isolated coronary artery bypass graft surgery in the year of January 2000 and June 2019 were evaluated in a single surgeon's practice. The study endpoint was a stroke, survival rate, and Major Adverse Cardiac and Cerebrovascular Events (MACCE). Strokes were classified as previous strokes when recorded before the CABG procedure. Information on comorbidities was collected during a hospital visit and or over a telephone interview. Written informed consent was obtained from all study populations. All patients were scheduled for isolated Off-Pump Coronary Artery Bypass Graft (OPCABG) surgery. Patients having clinically significant associated heart disease, either valvular or congenital heart disease, LV dysfunction (EF% <30%), Redo CABG surgery, Abnormal

coagulation profile, and systemic disease like hepatic and renal failure were excluded from the study.

Surgical technique

Coronary Artery Bypass Graft surgery (CABG) was performed through a standard median sternotomy on the off-pump beating heart technique, but a CPB (Cardiopulmonary Bypass) circuit was kept on standby for all cases. Heparin infusion was used just before completing LIMA harvest to maintain an ACT (Activated Clotting Time) of more than 350 seconds. Almost all the operations were performed off-pump CABG utilizing mechanical stabilizers like suction type and the compression type to immobilize the target coronary artery during grafting. However, a few cases required conversion to on-pump procedure with the assistance of a Cardiopulmonary Bypass (CPB) machine.

Furthermore, the coronary endarterectomy techniques have been published in detail elsewhere. A brief description was added in the methodology section [3]. However, we performed close

Table 1: Sociodemographic and Clinical characteristics of study population within 30 days following CABG surgery.

Variables	Stroke Group (n=34)	Non Stroke group (n=1816)	All patients (n=1850)
Age			
<50 years	1 (2.9%)	865 (47.6%)	866 (46.8%)
50 to 54 years	3 (8.8%)	356 (19.6%)	359 (19.4%)
55 to 59 years	4 (11.8%)	192 (10.6%)	196 (10.6%)
60 to 64 years	6 (17.6%)	169 (9.3%)	175 (9.5%)
65 to 69 years	9 (26.5%)	178 (9.8%)	187 (10.1%)
≥ 70 years	11 (32.4%)	56 (3.1%)	67 (3.6%)
Sex			
Men	25 (73.5%)	1465 (80.7%)	1490 (80.5%)
Women	9 (26.5%)	351 (19.3%)	360 (19.5%)
Comorbidity			
Prior stroke	8 (23.5%)	79 (4.4%)	87 (4.7%)
Hypertension	14 (41.2%)	464 (25.6%)	478 (25.8%)
Prior myocardial infarction	21 (61.8%)	939 (51.7%)	960 (51.9%)
Congestive heart failure	7 (20.6%)	212 (11.7%)	219 (11.8%)
Unstable angina pectoris	11 (32.4%)	425 (23.4%)	436 (23.6%)
History of atrial fibrillation	2 (5.9%)	195 (10.7%)	197 (10.6%)
Diabetes	9 (26.5%)	256 (14.1%)	265 (14.3%)
Renal impairment	2 (5.9%)	58 (3.2%)	60 (3.2%)
COPD	3 (8.8%)	102 (5.6%)	105 (5.7%)
Peripheral vascular disease	5 (14.7%)	114 (6.3%)	119 (6.4%)
Medication			
Beta blockers	26 (76.5%)	1785 (98.3%)	1811 (97.9%)
ACE inhibitors	17 (50.0%)	945 (52.0%)	962 (52.0%)
Clopidogrel and Aspirin	34 (100.0%)	1816 (100.0%)	1850 (100.0%)
Statins	34 (100.0%)	1816 (100.0%)	1850 (100.0%)
Calcium antagonists	14 (41.2%)	556 (30.6%)	570 (30.8%)
Digoxin	12 (35.3%)	346 (19.1%)	358 (19.4%)
Loop diuretics	17 (50.0%)	286 (15.7%)	303 (16.4%)
Spironolactone	15 (44.1%)	78 (4.3%)	93 (5.0%)
Warfarin	12 (35.3%)	129 (7.1%)	141 (7.6%)

COPD: Chronic Obstructive Pulmonary Disease; ACE: Angiotensin-Converting Enzyme

*Comorbidities registered from date of surgery and †Medication registered within 3 months of surgery

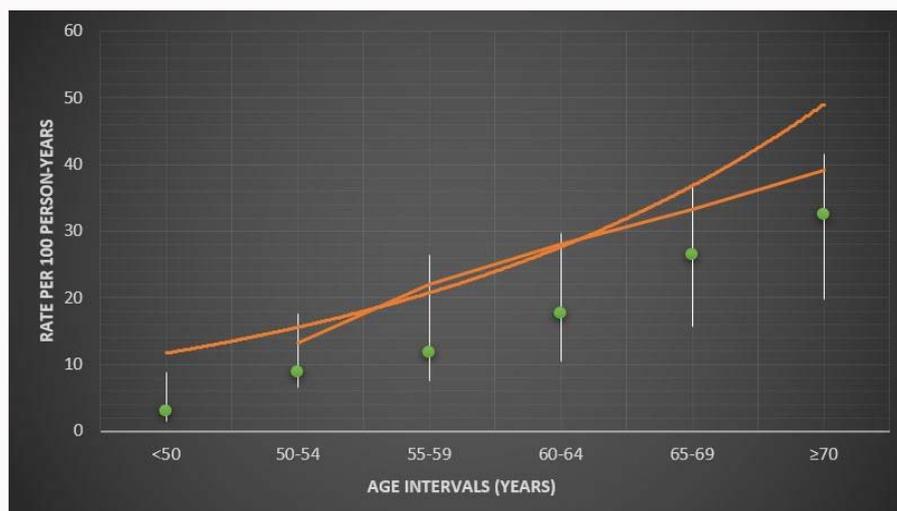


Figure 1: Stroke rate within 30 days of coronary artery bypass graft surgery.

technique endarterectomy by slow sustain and continuous traction of atheromatous plaque with delicate Forceps, and the arteriotomy incision was approximate 10 mm long. Moreover, the atheromatous plaque was carefully inspected for a smooth distal taper end to ensure complete expulsion and backflow of blood from the distal coronary artery following atherectomy is a consoling indication of adequate removal of plaque [3].

Statistical analysis

Analyses were performed using SPSS v25 software and logistic or Cox regression analysis was utilized to evaluate the impact of independent variables on stroke and mortality following CABG surgery. The cumulative risk of stroke was calculated, adjusting for competing risk. A $P \leq 0.05$ was considered significant, and all probability values reported were two-sided. The term Relative Risk (RR) refers to Odds Ratios (OR) in logistic models and Hazard Ratios (HR) in Cox models; Interaction terms are reported when significant.

Results

The sociodemographic and clinical variables study population after CABG surgery are demonstrated in Table 1. The overall incidence of postoperative stroke of 2.0% within 30 days after CABG surgery and 3.0% within one year after CABG surgery. The correlation between age and stroke and age in absolute, as well as relative, terms is illustrated in Figure 1 and 2, respectively. Figure 1 observed that the incidence of stroke increased from 9 per 100 person-years from age 50 to 31 per 100 person-years from 70 and older. Nevertheless, the incidence of stroke increased by a factor of 1.8 from RR, 1.7; 95% CI, 1.2 to 2.5 (P value 0.001) at the age of 50 years, to RR, 2.3; 95% CI, 2.0 to 3.8 (P value 0.001) at 60 years of age (Figure 2). At an age older than 70, the incidence and risk of stroke ceased to increase.

We analyzed the association between stroke and/or mortality and age, sex, associated comorbidities, and specific cardiac medication, as well as the relationship between these same covariates and mortality alone (Table 2). Dangers of stroke inside 30 days after medical procedure adjusted for age, sex, comorbidities, and medications included: 50 to 54 years: HR 1.6; 95% CI 1.2-2.5, 55 to 59 years: HR 2.3; 95% CI 1.6-3.4, 60 to 64 years: HR 2.5; 95% CI 2.0-3.7, 65 to 69 years: HR 2.6; 95% CI 2.1-3.8, >70 years: HR 2.9; 95% CI 1.7-4.8, prior stroke: HR 4.1; 95% CI 3.2-5.3, hypertension: HR 1.3; 95% CI 1.1-1.6,

diabetes: HR 1.3; 95% CI 1.0-1.6, renal failure: HR 1.8; 95% CI 1.2-2.6, peripheral vascular disease: HR 1.5; 95% CI 1.2-2.0, statins: HR 0.9; 95% CI 0.8-1.1, DAPT: HR 1.2; 95% CI 1.1-1.4. Besides, risks of mortality within 30 days after surgery was observed: 55 to 59 years (HR 1.6; 95% CI 1.2-2.1), 60 to 64 years (HR 2.2; 95% CI 1.7-2.9), 65 to 69 years (HR 3.1; 95% CI 2.3-4.2), >70 years (HR 4.9; 95% CI 3.2-6.9), prior MI (HR 1.3; 95% CI 1.1-1.6), CHF (HR 2.2; 95% CI 1.8-2.6), UA (HR 1.5; 95% CI 1.3-1.8), renal failure (HR 5.1; 95% CI 4.0-6.4), peripheral vascular disease (HR 1.6; 95% CI 1.3-1.9), Beta-blockers (HR 0.9; 95% CI 0.8-1.1), ACE inhibitor (HR 1.4; 95% CI 1.2-1.6), and statins (HR 0.9; 95% CI 0.7-1.0) were statistically significant ($P \leq 0.05$). Finally, Figure 3 illustrates the cumulative stroke incidence adjusted for risk during the year following CABG surgery within different age groups.

Discussion

The purpose of this study was to recognize independent risk factors for stroke in ischemic heart disease patients going through coronary artery bypass graft surgery at BSMM University. By recognizing hazard factors, we plan to lessen the stroke rate during coronary activity and reduce postoperative morbidity and mortality. A stroke following cardiac surgery is a devastating and debilitating complication that increases the mortality risk and decreases the postoperative health-related quality of life.

Previously published studies have found the incidence of stroke to be 2% to 5% after CABG surgery which is comparable with this current study [1-5]. The etiology of stroke is thought to be multifactorial, and this study observed perioperative risk factors associated with postoperative stroke after CABG, including the influence of sociodemographic, clinical, and surgical techniques on postoperative outcomes [8-12]. A study by McKhann et al. [13] reported that hypertension, increasing age, diabetes, and prior stroke all correlated with a higher incidence of stroke. Prolonged cardiopulmonary bypass time was related to a greater risk of stroke, which resembles other study findings [14-18]. Furthermore, several published studies have identified three common independent preoperative risk factors using multiple logistic regressions: Older age, diabetes, and previous history of stroke [4-7,15-21]. In the present study, older age has been identified as a risk factor for postoperative stroke. However, the effect of age is likely to be a moderator as it is associated with many

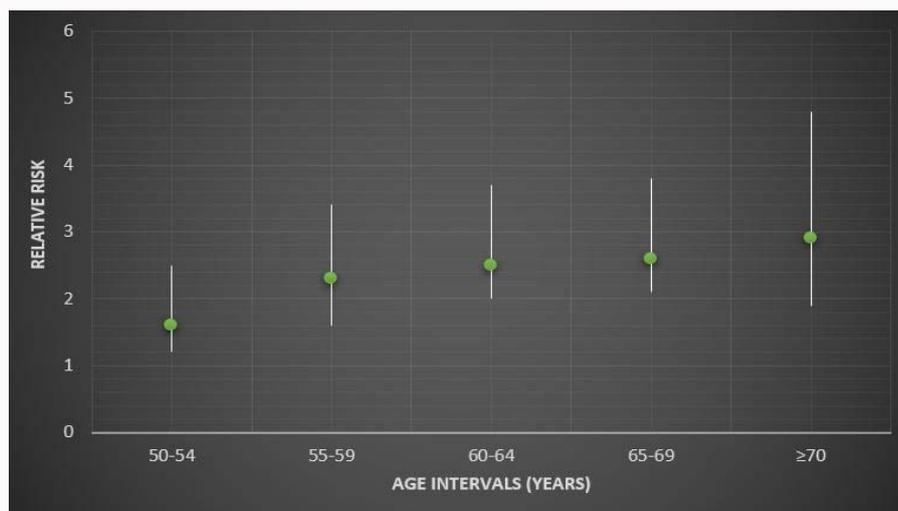


Figure 2: Risk of stroke within 30 days of coronary artery bypass graft surgery. Baseline group: patients 50 years of age.

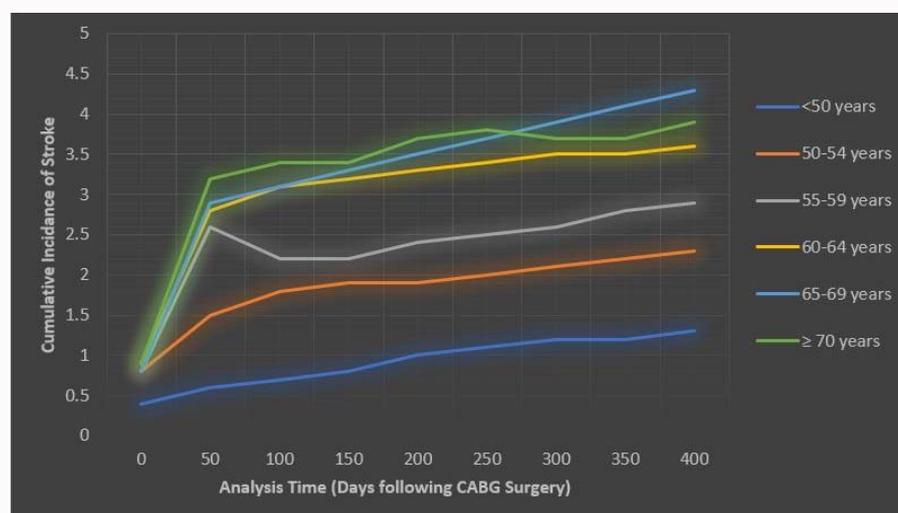


Figure 3: Cumulative risk of stroke after Coronary Artery Bypass Grafting (CABG).

other risk factors, including an increased incidence of carotid and aortic disease, systemic atherosclerosis, cerebrovascular disease, and cognitive decline [10-15,18-21].

The current study also identified that twenty-three per cent of stroke patients had a prior history of stroke, which has been supported in most previous analyses [4-6,13-16]. Although previous strokes were a risk factor for early postoperative stroke after CABG surgery but not a predictor of 30-day mortality [8-12,20-25]. Moreover, McKhann et al. [13] and Cernaianu et al. [22] have shown that preoperative hypertension was an independent risk factor for postoperative cerebrovascular accidents. Consistent with other studies, we found previous stroke, hypertension, diabetes, renal impairment, and peripheral vascular disease as significant risk factors for stroke within 30 days after CABG [10-16,22-25]. In general, patients with postoperative stroke had significantly higher mortality rates than patients without this complication which concord with current study results [7-10,17-22].

Previous research has identified carotid bruits and stenosis as significant predictive factors for post-CABG stroke [21,22]. In a

recent study, Ranjan et al. [24] identified a preoperative prevalence rate of carotid stenosis of 10%, leading to an almost fourfold excess risk of operative stroke for those with carotid bruit compared with those without CAS. A recent study by Puskas et al. [25] found that advanced age, tobacco use, left main CAD, extensive peripheral vascular disease, and history of previous stroke or TIA correlate with carotid disease, which is a fundamental cause of postoperative stroke. Nonetheless, modifying surgical techniques like using a single cross-clamp to the ultrasound-guided application of aortic cross-clamp, avoiding aortic clamping and alternative sites of arterial cannulation are similar to other study results [12-15,22-26]. Also, the preprocedural TOE evaluation of the aorta may allow the surgeon to appropriately individualize surgical techniques to reduce the incidence of stroke due to atheroembolism in high-risk patients, which is impossible with limited resources in Bangladesh [20-25].

Albeit the study analyzed a large sample size, we need to acknowledge a few limitations. Due to a lack of appropriate logistic support, we could not retrieve the complete data set on the lesion site or type of stroke. Moreover, this study lack data on the severity of aortic atherosclerosis, and carotid artery stenosis, as preoperative

Table 2: Risk factors analysis for stroke, combined stroke and mortality, and mortality within 30 days after CABG†.

Characteristics	Stroke			Combined Stroke and Mortality			Mortality		
	HR	P	95% CI	HR	P	95% CI	HR	P	95% CI
Age									
50 to 54 years	1.6	0.005	1.2 to 2.5	1.4	0.002	1.0 to 1.8	1.2	0.172	0.8 to 1.6
55 to 59 years	2.3	0.001	1.6 to 3.4	2	0.001	1.6 to 2.5	1.6	0.001	1.2 to 2.1
60 to 64 years	2.5	0.001	2.0 to 3.7	2.5	0.001	2.0 to 3.1	2.2	0.001	1.7 to 2.9
65 to 69 years	2.6	0.001	2.1 to 3.8	3.2	0.001	2.5 to 4.0	3.1	0.001	2.3 to 4.2
>70 years	2.9	0.001	1.7 to 4.8	4.2	0.001	3.3 to 5.8	4.9	0.001	3.2 to 6.9
Male	0.8	0.15	0.8 to 1.1	0.6	0.001	0.5 to 0.7	0.5	0.001	0.4 to 0.6
Comorbidity									
Prior Stroke	4.1	0.001	3.2 to 5.3	2.1	0.001	1.8 to 2.6	1.1	0.517	0.9 to 1.3
Hypertension	1.3	0.002	1.1 to 1.6	1.1	0.011	1.1 to 1.4	1	0.81	0.8 to 1.5
Prior myocardial infarction	1.2	0.23	1.0 to 1.5	1.3	0.007	1.3 to 1.5	1.3	0.01	1.1 to 1.6
Congestive heart failure	1.4	0.11	1.2 to 1.7	1.8	0.001	1.5 to 2.1	2.2	0.001	1.8 to 2.6
Unstable angina pectoris	1	0.512	0.9 to 1.3	1.2	0.001	1.0 to 1.4	1.5	0.001	1.3 to 1.8
Prior atrial fibrillation	1.1	0.845	0.7 to 1.3	1.1	0.985	0.9 to 1.3	1.1	0.895	0.9 to 1.3
Diabetes	1.3	0.017	1.0 to 1.6	1.1	0.011	0.9 to 1.2	1.3	0.175	1.1 to 1.5
Renal impairment	1.8	0.015	1.2 to 2.6	3.3	0.001	2.7 to 4.1	5.1	0.001	4.0 to 6.4
COPD	1.1	0.985	0.9 to 1.3	1.1	0.845	0.7 to 1.3	1.1	0.34	0.8 to 1.4
Peripheral vascular disease	1.5	0.001	1.2 to 2.0	1.5	0.001	1.2 to 1.8	1.6	0.001	1.3 to 1.9
Concomitant medication									
Beta blockers	1.1	0.865	0.9 to 1.2	1	0.05	0.7 to 1.1	0.9	0.015	0.8 to 1.1
ACE inhibitors	1	0.825	0.7 to 1.2	1.1	0.089	1.1 to 1.4	1.4	0.019	1.2 to 1.6
Combined Clopidogrel and Aspirin	2.2	0.055	1.1 to 4.0	1.7	0.146	0.9 to 3.0	2.3	0.554	1.3 to 3.5
Statins	0.9	0.05	0.8 to 1.1	0.9	0.001	0.9 to 1.0	0.9	0.003	0.7 to 1.0
Calcium antagonists	1.2	0.022	1.1 to 1.4	1.2	0.225	1.1 to 1.4	1.1	0.786	0.9 to 1.3
Digoxin	0.9	0.285	0.7 to 1.1	1.1	0.565	0.8 to 1.5	1.4	0.098	1.1 to 1.9
Loop diuretics	1.1	0.415	0.8 to 1.3	1.2	0.165	1.1 to 1.4	1.3	0.275	1.2 to 1.8
Spironolactone	0.8	0.756	0.5 to 1.4	0.9	0.225	0.7 to 1.3	0.9	0.145	0.6 to 1.2
Warfarin	1.3	0.215	0.9 to 2.1	1.2	0.123	1.0 to 1.5	1.2	0.335	0.9 to 1.8

CABG: Coronary Artery Bypass Grafting; COPD: Chronic Obstructive Pulmonary Disease; ACE: Angiotensin-Converting Enzyme

*The model was adjusted for calendar years without significant findings. †Reference groups: age-50 years; sex-female

TOE studies of the great vessels were not routinely performed in Bangladesh. The EuroSCORE risk scoring system is widely used among cardiothoracic surgeons in EU countries; however, this scoring system is not validated among the Bangladeshi population.

Conclusion

Proper use of risk scoring systems like EuroSCORE in selecting suitable candidates for CABG surgery helps reduce the prevalence of stroke among elderly patients to a constant rate. Age is not an independent predictor of stroke following CABG but is a consequence of the burden of comorbidities like diabetes, hypertension, previous stroke, renal failure, and peripheral vascular disease. Higher risk group patients may benefit from considering off-pump CABG procedures and minimally invasive surgery utilizing Internal mammary & radial artery 'Y' graft.

Author Contributions

Ranjan R: Data curation; Conceptualization; Formal analysis; Investigation; Methodology; Resources; Visualization; Writing-original draft; Writing-review & editing; and Final approval of the

version to be published.

Barman S: Data curation; Resources; Writing-original draft; Writing-review & editing; and Final approval of the version to be published.

Adhikary D: Data curation; Formal analysis; Methodology; Resources; Writing-original draft; Writing-review & editing; and Final approval of the version to be published.

Adhikary AB: Conceptualization; Methodology; Resources; Visualization; Supervision; Validation, Writing-review & editing; and Final approval of the version to be published.

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