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Serum B-type natriuretic peptide levels (BNP) can be used as a predictor of complications in patients undergoing non-cardiac surgery: a prospective observational study

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ABSTRACT

Objectives Worldwide, an estimated 10 million adults annually experience significant myocardial injury after non-cardiac surgery. Our aim is to assess whether preoperative and postoperative serum B-type natriuretic peptides levels (BNP) could be used as a predictor of postoperative complications in hypertensive and diabetic patients post non-cardiac surgery.

Design Prospective observational study.

Setting Single tertiary-care centre in northern India.

Participants This study included 260 adult participants with known hypertension and diabetes who were planned for elective non-cardiac surgery.

Interventions A preoperative BNP level (baseline BNP) was measured within 24 hours of surgery and another postoperative BNP level was measured within 24 hours of surgery.

Main outcome measures The primary outcome was the change in BNP levels (delta BNP) between the postoperative and the preoperative BNP levels (baseline BNP) with respect to the baseline BNP and the development of postoperative complications within 30 days of surgery.

Results The study established a correlation between delta BNP and baseline BNP (Pearson's correlation coefficient=0.60; p=0.01). Our study found an increased serum BNP both in the preoperative period and the postoperative period in the patient group that developed complications, respectively (152.02 pg/mL±106.56 vs 44.90 pg/mL±44.22; t=4.120; p≤0.001); (313.99 pg/mL±121.29 vs 83.95 pg/mL±70.19; t=7.73; p≤0.001).

Conclusions We found that an increased serum baseline and postoperative BNP is potentially important predictor for the development of postoperative complications. Serum BNP has the potential to emerge as a cost-effective test for risk-stratification for postoperative complications in patients undergoing non-cardiac surgery. It has promising prognostic advantages including modification of surgical procedures, deferral of surgery and the ability to tailor therapy postoperatively.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Preoperative serum B-type natriuretic peptides (BNP) is an independent predictor of perioperative cardiovascular complications.

WHAT THIS STUDY ADDS

⇒ Role of serum BNP as a predictive marker for post-operative surgical complications in non-cardiac surgery.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Serum BNP can substitute the existing array of expensive preoperative tests for risk-stratification of patients.

⇒ Need for further research with a larger population to elucidate the role of BNP in predicting surgical prognosis.

INTRODUCTION

Worldwide, an estimated 10 million adults annually experience significant myocardial injury after non-cardiac surgery.[1] To mitigate this risk, strategies are needed that provide appropriate preoperative medical and surgical measures with postoperative surveillance and management.[1] B-type natriuretic peptides (BNPs) are released from myocardial tissues in response to multiple physiological stimuli, including myocardial stretch, inflammation, myocardial ischaemia and other neuroendocrine stimuli. The 32-amino acid polypeptide BNP is secreted and attached to a 76-amino acid N-terminal fragment in the prohormone NT-proBNP (BNPT), which is biologically inactive. The biological half-life of BNP, however, is twice as long as that of atrial natriuretic peptide (ANP), making it a better target than ANP for diagnostic blood testing. The physiological actions of BNP

Table 1 Showing demographic data including BMI and ASA grade

	Gender		BMI (kg/m^2)		ASA	Class	Total no of patients
Age group (years)	Male	Female	18–24	>24	ASA-I	ASA-II	
40–49	2	2	4	0	4	0	4
50–59	38	29	50	17	40	27	67
60–70	114	75	104	85	84	105	189
Total	154	106					260

ASA, American Society of Anaesthesiologists; BMI, body mass index.

include a decrease in systemic vascular resistance and central venous pressure as well as an increase in natriuresis. The net effect of these peptides is a decrease in blood pressure. Additionally, the actions of BNP results in a decrease in cardiac output due to a reduction in blood volume that follows natriuresis and diuresis.

Multiple studies have demonstrated that elevated preoperative serum BNP concentrations are powerful independent predictors of perioperative cardiovascular complications like mortality, myocardial infarction (MI) and heart failure.[2 3] These are potentially avoidable causes of morbidity and mortality in patients undergoing non-cardiac surgery. The pre-existing data demonstrated that patients undergoing non-cardiac surgery with cardiac clinical risk factors should have preoperative NP testing as part of risk stratification.[4]

Hypertension and diabetes are risk factors for potential coronary artery disease. Thus, evaluation of the cardiovascular system in patients with hypertension is important to predict perioperative morbidity and mortality before undertaking non-cardiac surgery. At present, we lack a gold standard tool to effectively predict the perioperative or postoperative complications, length of hospital stay or mortality in hypertensive and patients with diabetes undergoing non-cardiac surgery. Preoperative evaluations of the cardiovascular system that use chest radiography, ECG, echocardiography and laboratory studies are limited. Furthermore, data on the relationship between preoperative and postoperative BNP levels and prognosis after non-cardiac surgery are scarce. The purpose of our study was to assess the role of BNP as predictors of postoperative complications in hypertensive and diabetic patients undergoing non-cardiac surgery.

METHODS

The study was conducted in the Department of General Surgery at Paras HMRI Hospital, Patna, India, from December 2019 to June 2021. In this prospective observational study, we included 260 adult patients less than 70 years with known hypertension and diabetes who were scheduled to undergo elective non-cardiac surgery. The exclusion criteria for recruiting the patients in the study protocol were age <18 years and >70 years, normotensive and non-diabetic patients, patients undergoing cardiac surgeries, patients undergoing emergency non-cardiac surgeries, patients with left ventricle dysfunction (ejection fraction <40%), patients with baseline troponin positivity and immunocompromised patients. We excluded patients over the age of 70 years, as old age is independently associated with adverse surgical outcomes.

Table 2 Showing type of surgeries

Surgery type	Frequency	Per cent
Open	169	65
Laparoscopic	87	33.5
Combined	4	1.5
Total	260	100

Collection of data

Each patient fulfilling the inclusion criteria was included in the study. Baseline BNP levels were measured preoperatively within 24 hours of non-cardiac surgery. The postoperative BNP levels were measured within 24 hours of the surgery. The measurement of BNP was performed in the same laboratory for all patients.

STrengthening the Reporting of OBservational studies in Epidemiology checklist for cohort reporting was completed.[5] The corresponding author had full access to all data in the study and takes responsibility for its integrity and the data analysis.

Outcome measures

The primary outcome was the change in BNP levels (delta BNP) between the postoperative and the preoperative BNP levels (baseline BNP) with respect to the baseline BNP and the development of postoperative complications within 30 days of surgery. We defined a postoperative complication as one or more of the following events

Table 3 Baseline BNP versus complications

Complications encountered	Frequency (no)	Mean of baseline BNP (pg/mL)	SD
Yes	17	**152.02***	106.56
No	243	44.90	44.22
Total	260	51.90	56.85

*BNP level (baseline BNP) was found to be markedly high
BNP, B-type natriuretic peptides.

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Table 4 Postoperative BNP versus complications

Complications encountered	Frequency	Mean of postoperative BNP (pg/mL)	SD
Yes	17	**313.99***	121.29
No	243	83.95	70.19
Total	260	98.99	93.58

*Postoperative BNP level (baseline BNP) was found to be markedly high
BNP, B-type natriuretic peptides.

Table 5 Correlation between preoperative BNP levels and delta BNP

		Preoperative BNP	Delta BNP
Preoperative BNP	Pearson correlation coefficient (N=260)	1.00	0.60
Delta BNP	Pearson correlation coefficient (N=260)	0.60	1.00

BNP, B-type natriuretic peptides.

like surgical procedure-related complications and cardiac complications. Surgical procedure-related complications include haemorrhage, shock, wound infection, sepsis, embolism, deep vein thrombosis, urinary retention or lung problems. Cardiac complications include death, congestive heart failure, MI, acute coronary syndrome, unstable angina, cardiac arrest, cardiac arrhythmia resulting in haemodynamic instability requiring urgent intervention.

Data management and statistical analysis

Statistical analysis was performed with the help of IBM SPSS software. All continuous variables were expressed as the mean±SD. The t-test was used to compare mean, while the Mann-Whitney U test was used for median. Categorical variables were expressed as frequencies with respective percentages. A p-value of 0.05 was considered statistically significant. The correlation between preoperative BNP levels and delta BNP was calculated using Pearson's correlation coefficient.

RESULTS

Age versus sex distribution

In our study of 260 patients, the maximum number of cases was in the age group of 60–70 years in both male (74.02%) and females (70.75%) groups. The demographic data including body mass index and American Society of Anaesthesiologists (ASA) grade is shown in table 1.

In our study, 168 patients (64.6%) underwent surgery under general anaesthesia (GA), while 92 patients (35.4%) under spinal anaesthesia (SA). The open surgery was performed for 169 patients (65%), followed by laparoscopic approach in 87 patients (33.5%) and combined approach was employed in 4 patients only (1.5%) shown in table 2. The mean intraoperative duration was 1 hour with range from 30 min to 90 min. The intraoperative blood transfusion was done in seven patients only.

Baseline BNP levels versus complications

Postoperative complications were encountered in 17 patients (6.53%) . In these patients, the preoperative BNP level (baseline BNP) was found to be markedly high compared with those patients in whom complications were not seen (152.02 pg/mL±106.56 vs 44.90 pg/mL±44.22; t=4.120, p≤0.001) shown in table 3. To determine the significance of the difference in the mean, a t-test for independent samples was performed, which was significant (p≤0.001) at the 0.1% confidence level.

Postoperative BNP levels versus complications

Like baseline BNP, the postoperative BNP level was also found to be markedly high and statistically significant (p≤0.001) as compared with those patients in whom postoperative complications were not seen (313.99 pg/

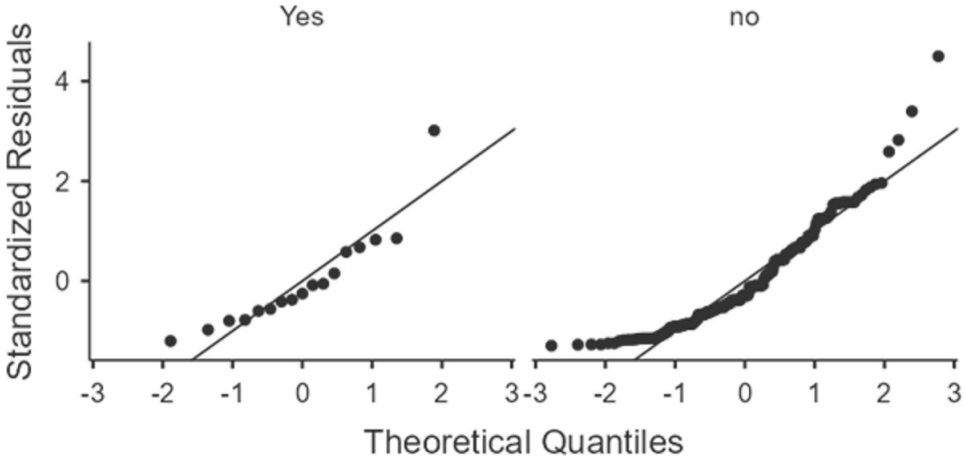

Figure 1 Q-Q Plot showing normality of baseline BNP across complication status. BNP, B-type natriuretic peptides.

Table 6 Baseline BNP across complication status (n=260)

Variable	Complication status (median (IQR))		P value*
	No (n=243)	Yes (n=17)	
Baseline BNP (pg/mL)	48 (31–85.8)	125 (88–214)	<0.001

*P value by Mann-Whitney U test.
BNP, B-type natriuretic peptides.

Table 7 Distribution of postoperative complications

Complication	No of patients	Percentage
Wound infection	11	65
Sepsis	4	24
Haemorrhage	3	18
Arrhythmia	2	12
Pneumonia	2	12
Atelectasis	1	6

mL±121.29 vs 83.95 pg/mL±70.19; t=7.73, p≤0.001), which has been shown in table 4.

Correlation between baseline BNP levels and delta BNP

To determine the relation between baseline BNP levels and Delta BNP, Pearson's correlation coefficient was computed. Using Pearson's correlation coefficient, it was concluded that baseline BNP levels and delta BNP were correlated. The value of Pearson's correlation coefficient was found to be 0.60, which was statistically significant (p=0.01) as shown in table 5.

The baseline BNP levels are not normally distributed across complication status as visually seen by Q-Q plot (figure 1). The median difference of 77 pg/mL in baseline BNP across two groups is statistically significant (p<0.001) as shown in table 6.

Postoperative complication

In our study, the postoperative complications were wound infection, sepsis, haemorrhage, arrhythmia, pneumonia and atelectasis as shown in table 7 and figure 2 . The 10-point surgical APGAR score (considering the estimated blood loss, lowest mean arterial pressure and lowest heart) was used to predict the postoperative complications. On this score out of 260 patients, 5 patients had an APGAR score of 6 and 2 had score of 7. The raised BNP level was found in all these seven patients.

In our study, metabolic equivalent to task score more than 10 was seen in only 10 patients as shown in table 8 while cardiac risk factors of the participants has been shown in table 9. The Revised Cardiac Risk Index (Lee score) was also used. As per this index, 125 patients underwent high risk surgery, 45 patients with diabetes were on insulin, while 22 patients with diabetes on insulin underwent high-risk surgery with low risk in first two groups, and moderate risk in last group of patients, respectively, as shown in table 10.

DISCUSSION

Statement of principal findings

In our study, the average age of the patients ranged between 58 and 68 years out of 260 patients. Seventeen patients (6.53%) experienced postoperative complications, including surgical and cardiovascular. Our study found increased serum BNP levels both in the preoperative and the postoperative period in the patient group that developed complications. The decision-making tree according to the BNP level has been shown in figure 3. Interestingly, the delta BNP level was also observed to be related to complications in the patient population compared with the group that did not develop complications. In our study, we also demonstrated that delta BNP has a significant correlation with the baseline BNP level.

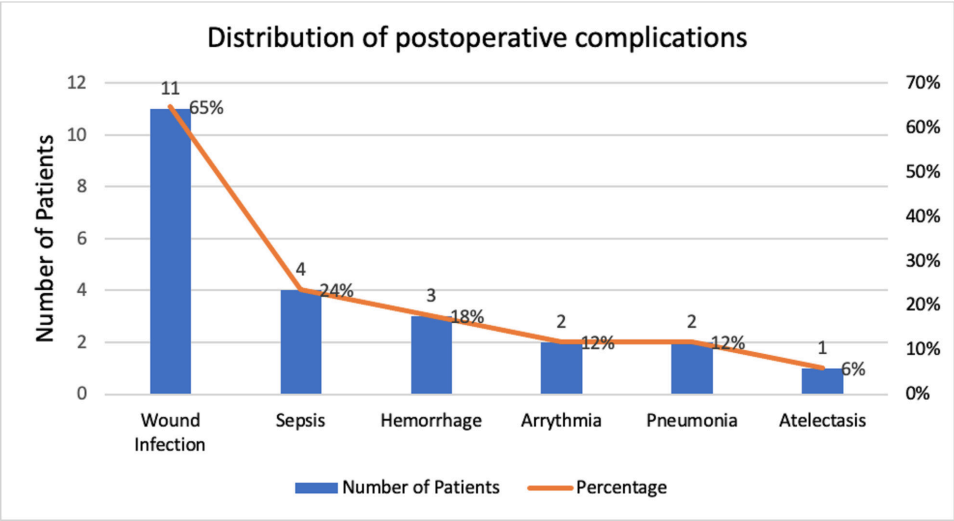

Figure 2 (Bar diagram) showing postoperative complications.

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Table 8 Showing MET score

Activity	MET score	No of patients
Sitting quietly at rest	1	190
Walking slowly on level ground, eat, dress, toilet, make bed	2	30
Doing light work around the house	3–4	20
Walking on level ground at brisk pace, light housework, golf, bowling	4	5
Climbing a flight of stairs, walking up a hill, sex, scrubbing of floors, moving furniture	4–5	2
Moderate recreational activity for example, dancing, double tennis	6	3
Strenuous sports for example, singles tennis, basketball, skiing	>10	10

MET, metabolic equivalent to task.

Strengths and weaknesses of the study

Strengths of the study

- The timing of the BNP sampling was kept uniform within 24 hours pre and post non-cardiac surgery.
- The measurement of BNP was performed in the same laboratory for all patients.
- The study was successful in obtaining individual-level data on 260 patients.
- Our study results are consistent with other similar studies conducted.

Weaknesses/limitations of the study

- First, the study was conducted on an adult population, thus it may not apply to the extreme age group (<18 years and >70 years).
- Second, our research was observational, thus we were able to show a correlation but not prove causality.
- Also, data collection by a single investigator may have been associated with investigator bias.
- The study was conducted in a single centre with a patient follow-up period for up to 30 days post non-cardiac surgery. Thus, the results may not be generalised to other centres.

Table 9 Showing cardiac risk factors

Risk factors for cardiovascular diseases	No of patients
Smoking	63
High cholesterol levels	92
Obesity (BMI >24 Kg/m^2)	102
Family history of cardiac disease	22
Sedentary lifestyle	132

BMI, body mass index.

Table 10 Showing significant Lee score

Significant Lee score	No of patients	Risk as per Lee score
Patients undergoing only high-risk surgery	125	Low-risk
Diabetic patients on insulin	45	Low-risk
Diabetic patients on insulin undergoing high-risk surgery	22	Moderate-risk

Strengths and weaknesses in relation to other studies, discussing important differences in results

In our study of 260 patients, 17 patients (6.53%) experienced postoperative complications. A study by Cuthbertson *et al*[6] observed a cut-off point of 40 pg/mL for preoperative BNP levels as a predictor of perioperative death or acute myocardial injury in patients undergoing non-cardiac surgery. It differentiated patients with a sevenfold increased risk of cardiac events in the early postoperative period. A preoperative BNP level above this threshold was also associated with an increased postoperative hospital stay.[6] In our study, the mean baseline BNP was 152.02 pg/mL with SD 106.56 pg/mL (range: 45.46–258.58 pg/mL). A study by Karthikeyan *et al* included a total of 3281 patients, among whom 314 (9.5%) patients experienced a perioperative cardiovascular complication.[3] The decision threshold for BNP used in the study varied widely between 40 pg/mL and 189 pg/mL. The study demonstrated that a preoperative BNP measurement was an independent predictor of cardiovascular complications within 30 days of non-cardiac surgery. According to Goetze *et al*, the ability of BNP to predict outcomes in the peri-operative setting likely relates to its exquisite sensitivity to changes in ventricular function, both systolic and diastolic.[7] The potential for serum BNP measurement in preoperative risk stratification lies in its ability to integrate the impact of multiple preoperative pathophysiological processes into a single measurement.[8 9] Recent evidence also suggests that among patients with chronic stable coronary disease, serum BNP levels have the potential to reflect the presence and severity of the underlying cardiac pathology.[10] The NT-proBNP is also an alternative marker to predict the perioperative cardiac complications supported by many studies.[11 12] But in our set up especially in the low/middle-income countries such as India where cost is the major constraint and ease to get the result quickly, definitely BNP becomes a better option as compared to NT-proBNP. Previous meta-analyses suggest that a single elevated preoperative BNP level is highly predictive of serious cardiovascular complications after non-cardiac surgery and may be a better predictor of these events. Measuring BNP in adults undergoing major non-cardiac surgery thus significantly improves preoperative risk stratification and could easily be incorporated into clinical practice, particularly in patients undergoing major intraperitoneal, intrathoracic, orthopaedic or vascular surgery, and would allow

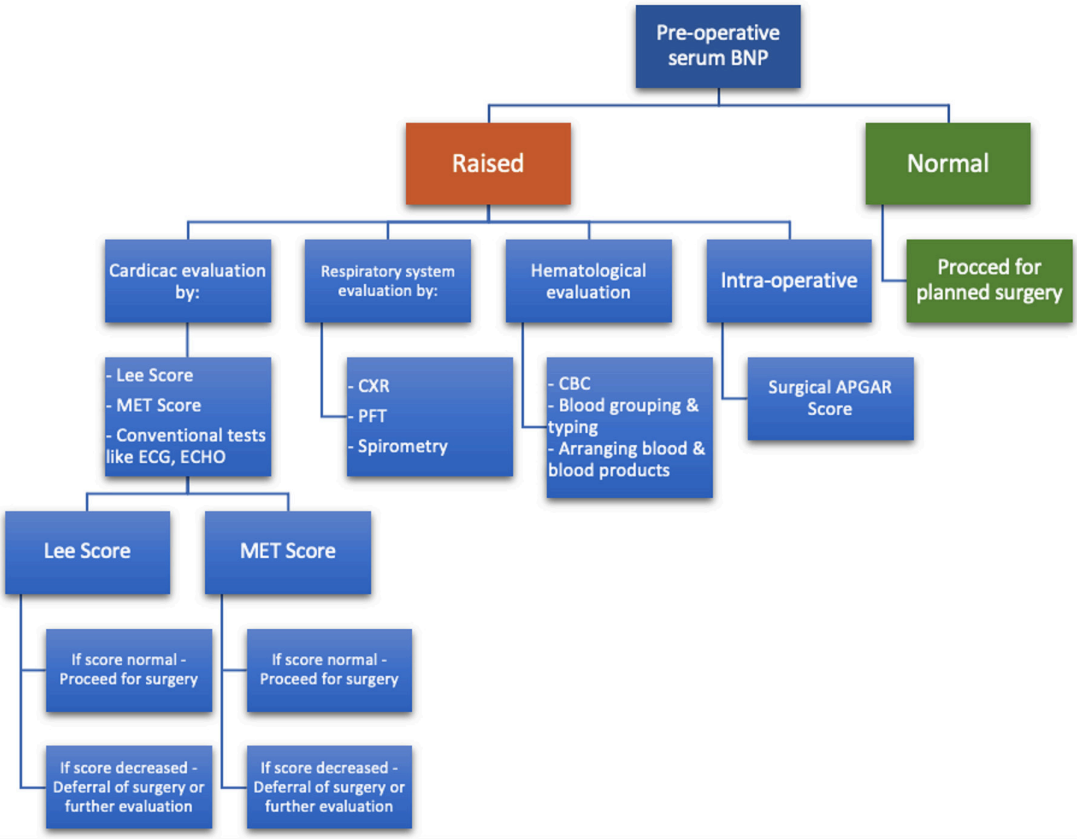

Figure 3 Showing the decision-making tree according to the BNP level. BNP, B-type natriuretic peptides; CXR, chest X-ray; CBC, complete blood count; ECHO, echocardiogram; MET, metabolic equivalent to task; PFT, pulmonary function test.

clinicians to strategise prophylactic measures in patients identified as high-risk patients. A preoperative BNP test might represent a cost-effective way of assisting in the identification of patients who would benefit from more intensive, and costly, preoperative testing and facilitate targeted interventions that may reduce morbidity and mortality.

Unanswered questions and future research

Further work is needed to determine the utility of BNP in combination with existing risk stratification tools. Research is needed to statistically establish BNP thresholds and to determine the cut-off point. This requires the evaluation of a large number of patients across the spectrum of perioperative risk undergoing a broad range of surgical procedures. Similarly, it is crucial to identify that the prognostic data obtained from the measurement of BNP remain imperfect. The predictive accuracy of existing methods might improve with more knowledge regarding BNP levels with further studies such that a strategy combining simple clinical parameters and BNP will be the most appropriate.

CONCLUSION

We found that an increased serum baseline and postoperative BNP is an independent predictor for the development of postoperative complications. Serum BNP has the potential to emerge as a cost-effective test for risk stratification for the postoperative complications in patients undergoing non-cardiac surgery. It has promising prognostic advantages including modification of surgical procedures, deferral of surgery and the ability to tailor therapy postoperatively. We can measure BNP preoperatively and postoperatively for every patients with hypertension and diabetes undergoing major surgery to pick up any silent pan-cardiac pathology, and also to risk-stratify patients deemed at high risk to develop surgical complications.

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Contributors AS, AK, AAH, MM, NT and PKS contributed to the conception or design of the work. All coauthors contributed to the acquisition, analyses or interpretation of data for the work. AK drafted the manuscript. All co-authors critically revised the manuscript. All gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy. The corresponding author (AK) had full access to all data in the study and takes responsibility for its integrity and the data analysis. AK acts as the guarantor, and accepts full responsibility for the work and conduct of the study, had access to the data and controlled the decision to publish.

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Competing interests None declared.

Patient consent for publication Consent obtained from parent(s)/guardian(s).

Ethics approval This study involves human participants and was approved by Scientific Research Committee, Paras HMRI Hospital, Patna.SRC/IEC/PHMRI/Faculty/139/2021 dated 27/08/2021Institutional Ethics committee Paras, HMRI Hospital for Biomedical and Health researchSRC/IEC/PHMRI/Faculty/140/2021 dated 28/08/2021. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

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