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Original Research Article

Stress hyperglycemia after pancreatobiliary surgeries

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ABSTRACT

Background: Diabetes mellitus is a common problem and stress hyperglycemia occurring in patients undergoing surgery without history of diabetes mellitus has been shown to have a poorer clinical outcome. Effective glycemic control in the perioperative period results in marked improvement in clinical outcome.
Methods: This prospective study was conducted among 100 cases of the pancreatobiliary postoperative patients admitted in General Surgery Department, Government Medical College Kottayam during November 2015 to November 2016. The post-operative blood sugar values, age, sex, BMI, family history of diabetes mellitus, anemia, hypoproteinemia, intraoperative blood loss, intraoperative blood transfusion, duration of surgery, and type of surgery were studied with respect to occurrence of stress hyperglycemia.
Results: The total incidence was 35%. The incidence in pancreatic surgery (87.5%), other biliary surgeries (77.8%), open cholecystectomy (31.2%) and laparoscopic cholecystectomy (18%). Significant association was found in malnourished and obese persons, anemia, hypoalbuminemia, duration of surgery more than 3 hours, intraoperative blood loss of more than 500 ml and intraoperative blood transfusion and pancreatic surgery. Independent predictors of stress hyperglycemia were found to anemia, hypoproteinemia, duration of surgery more than 3 hours and underweight and obese individuals.
Conclusions: Stress hyperglycemia incidence in pancreatobiliary postoperative patients was found to be 35%. Independent predictors of stress hyperglycemia were anemia, hypoproteinemia, duration of surgery more than 3 hours and BMI <18.5 and >30. Hence correction of anemia, improving the nutritional status preoperatively and minimising the duration of surgery will improve the clinical outcome.

Keywords: Pancreatobiliary postoperative patients, Stress hyperglycemia

INTRODUCTION

The main role of the metabolic response to stress is to increase flux of substrates to tissues that need it.[1,2] The brain is the major user of glucose in the fasting state and its rate of utilization is not dependent on insulin. Therefore, maintenance of central glucose delivery depends solely on the plasma glucose concentration and adequate cerebral blood flow. Thus, stress hyperglycemia can be viewed as a means of ensuring adequate delivery of glucose to the brain during stress.[3-5] During conditions where there is normal cerebral blood flow, glucose uptake into the central nervous system (CNS) is sufficient if plasma glucose levels are above 70 mg/dl. Increased production of ketone bodies from the liver during a prolonged fast and their utilization by the brain can reduce its obligatory need for carbohydrate by approximately 50% without interfering with neuronal function. Any further reduction of brain, glucose uptake compromises of brain function and eventually results in neuronal death.

Stress hyperglycaemia (SH) is reported to occur in 50-85% of critically ill patients admitted to the intensive care unit (ICU) and is associated with poorer outcome in a variety of clinical settings (e.g. myocardial infarction, cardiothoracic surgery, stroke, and trauma).[6,7] Contributing factors leading to SH include inflammatory mediators, excessive release of counter-regulatory hormones, insulin resistance and medical interventions (e.g., administration of corticosteroids, vasopressors, dextrose solutions, enteral or parenteral nutrition, and dialysis). SH is also related to the severity of the underlying illness or injury.[8-10] A patient's predisposition [age, body mass index (BMI), family history of diabetes, beta cell reserve] may also play an important role in the development of SH. Although strict glycaemic control (80-110 mg/dl) is no longer advocated for most ICUs, there is a consensus that manifest hyperglycaemia should be treated and insulin induced hypoglycaemia should be avoided. The Society of Critical Care Medicine has recently published new guidelines that recommend a target range of 100-150 mg/dl.[11,12] A few studies have shown that post-operative blood sugar of >140 mg/dl is associated with increased incidence of adverse effects like surgical site infections, pneumonia, increase in morbidity and mortality and longer duration of stay at the hospital.

Objective

To find out the proportion of pancreatobiliary postoperative patients developing stress hyperglycemia and to identify the association with selected risk factors.

METHODS

This was a prospective study conducted for a period of 1 year from November 2015 to November 2016 at the postoperative wards in the department of general surgery.

Sample size Calculated by the formula:

$$n = \frac{z\alpha^2 \times Q}{d^2}$$

zα is a constant 1.96, Q = 100-P = 65.72, d= relative precision- 20% of P= 6.9,

n= 34.28%

P is the prevalence of stress hyperglycemia among pancreatobiliary postoperative patients.[4]

Study procedure

A prospective study was carried out among 100 post pancreatobiliary surgery patients in the department of general surgery for a period of one year. Written informed consent from all patients was obtained after fully explaining the procedure and purpose of study was taken. Detailed history according to the proforma taking into account, age, sex, family history of diabetes mellitus, height and weight was taken. BMI was calculated using the formula weight in kg/height in meter. Hemoglobin value of <13 mg/dl in males and <12 mg/dl was taken as anemia. serum albumin level of <3.5 was taken as hypoalbuminemia. Intraoperative blood loss was calculated using modified Gross's formula using preoperative and post-operative hematocrit value.

Actual blood loss= blood volume ×[(initial hematocrit-final hematocrit)÷mean haematocrit]

Blood volume= body weight in kg × 70 ml/kg.

The duration of surgery was charted and the instances of blood transfusion were noted. Post operatively, immediate blood sugar value and fasting blood sugar value on the following day was noted.

A random blood sugar >140 or, fasting blood sugar value more than 126 was taken as stress hyperglycemia in my study.

Inclusion criteria

Patient undergoing elective pancreatobiliary surgical procedure, patients who give consent for the procedure and patients admitted in general surgery department in Government Medical College Kottayam.

Exclusion criteria

Patients undergoing emergency surgery, patients who are known case of diabetes mellitus, patients admitted for other elective surgical procedure and patients who do not give consent for the procedure.

Sampling method

Patients undergoing elective pancreatobiliary surgery in the department of General Surgery satisfying inclusion and exclusion criteria were selected.

Risk factors under study were age, sex, BMI, family history of diabetes, anemia, hypoproteinemia, intra operative blood loss, intraoperative blood transfusion, type of surgery and duration of surgery

Statistical analysis

SPSS v 16.0 software is used for analysis. The association between different risk factors and stress hyperglycemia was analysed using chi square test. The significant factors were analysed using multivariate analysis for independent predictors of stress hyperglycemia.

RESULTS

Age of the study population mean age of the study population was 49.21 years with the standard deviation 13.11 years minimum age of the study population was 19 years and maximum age, 81 years (Table 1).

Table 1: Distribution of study population based on the age and gender and incidence and distribution of stress hyperglycemia based on age group.

Age group (in years)	Frequency	Percentage	Male	Female	Stress hyperglycemia	
					Present N (%)	Absent N (%)
≤30	8	8.0	2	6	1 (12.5)	7 (87.5)
31 to 40	17	17.0	7	10	4 (23.5)	13 (76.5)
41 to 50	28	28.0	8	20	6 (21.4)	22 (78.6)
51 to 60	28	28.0	15	13	15 (53.6)	13 (46.4)
More than 60	19	19.0	10	9	9 (47.4)	10 (52.6)
Total	100	100.0	42	58	35 (35)	65 (65)

42% of the study population were males and 58% females (Table 1). 35% of the study population developed stress hyperglycemia while 65% were having euglycemic status post operatively.

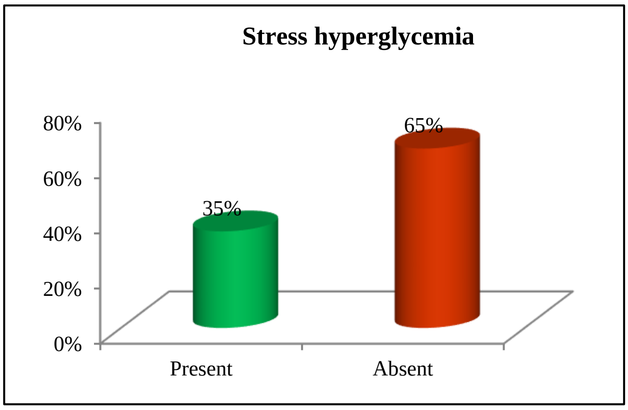

Figure 1: Incidence of stress hyperglycemia in the study population.

Comparison between the preoperative and postoperative blood sugar value

Mean preoperative blood sugar value was found to be 108.07±26.941 standard deviation. Mean post-operative blood sugar value was found to be 137.25±35.51 standard deviation.

Table 2: Mean blood sugar values before and after surgery.

	Mean	N	Std. deviation	Std. error mean
Preoperative RBS	108.07	99	26.94183	2.70776
Post-operative RBS	137.25	99	35.51497	3.56939

This difference in mean was found to be significant with the paired t test with t value of 7.779 and p-value of <0.001 (Table 2).

Factors under study for association with stress hyperglycemia

Association of age group with incidence of stress hyperglycemia

The association with age group was found to be significant with χ^2 value of 10.553 and p-value of 0.032. Majority of patient who developed stress hyperglycemia belonged to the age group more than 51 years (Table 1).

Association of gender with incidence of stress hyperglycemia

Among males 47.6% developed stress hyperglycemia and among female 25.9% developed stress hyperglycemia. This difference in proportion was found to be statistically significant with χ^2 test (Table 3).

Table 3: Distribution of stress hyperglycemia based on gender.

Sex		Stress hyperglycemia		Total
		Present	Absent	
Male	Count	20	22	42
	% within sex	47.6	52.4	100.0
Female	Count	15	43	58
	% within sex	25.9	74.1	100.0
Total	Count	35	65	100
	% within sex	35.0	65.0	100.0

χ^2 value 5.069 and p-value 0.021.

Association of family history of type 2 diabetes mellitus with stress hyperglycemia

No significant association was found between family history of diabetes mellitus and incidence of stress hyperglycemia (Table 4).

Association of BMI with stress hyperglycemia

All patients who were underweight (BMI <18.5) or obese (BMI >30) developed stress hyperglycemia, and the association between extremes of BMI and stress hyperglycemia was found to be significant (Table 5).

Table 4: Distribution of stress hyperglycemia based on family history of diabetes mellitus.

Family history of T2DM		Stress hyperglycemia		Total
		Present	Absent	
Yes	Count	9	12	21
	Percentage	42.9	57.1	100.0
No	Count	26	53	79
	Percentage	32.9	67.1	100.0
Total	Count	35	65	100
	Percentage	35.0	65.0	100.0

χ^2 value 7.21 and p-value 0.274.

Table 5: Distribution of stress hyperglycemia based on BMI.

BMI		Stress hyperglycemia		Total
		Present	Absent	
<18.5	Count	2	0	2
	Percent	100.0	0.0	100.0
18.5-24.9	Count	22	47	69
	Percent	31.9	68.1	100.0
25-29.9	Count	8	18	26
	Percent	30.8	69.2	100.0
>30	Count	3	0	3
	Percent	100.0	0.0	100.0
Total	Count	35	65	100
	Percent	35.0	65.0	100.0

x^2 value 9.748 and p value 0.02

Association of anemia with stress hyperglycemia

68% of anemic patients developed stress hyperglycemia while only 24% of those who were not anemic developed stress hyperglycemia. This difference in proportion was found to be statistically significant (Table 6).

Table 6: Distribution of stress hyperglycemia based on anemia.

Anemia		Stress hyperglycemia		Total
		Present	Absent	
Present	Count	17	8	25
	% within Hb	68.0	32.0	100.0
Absent	Count	18	57	75
	% within Hb	24.0	76.0	100.0
Total	Count	35	65	100
	% within Hb	35.0	65.0	100.0

χ^2 value 15.97 and p-value<0.01.

Association of hypoalbuminemia with stress hyperglycemia

90% of patients with hypoalbuminemia developed stress hyperglycemia while only 28.9% of patients with normal albumin level developed stress hyperglycemia. This difference in proportion was statistically significant with χ^2 test (Table 7).

Table 7: Distribution of stress hyperglycemia based on hypoalbuminemia.

Albumin		Stress hyperglycemia		Total
		Present	Absent	
<3.5	Count	9	1	10
	Percentage	90.0	10.0	100.0
>3.5	Count	26	64	90
	Percentage	28.9	71.1	100.0
Total	Count	35	65	100
	Percentage	35.0	65.0	100.0

χ^2 value 14.774 and p value<0.001.

Table 8: Distribution of stress hyperglycemia based on type of surgery and duration of surgery.

Type of surgery[a]	Total	Stress hyperglycemia		Duration (in minutes)[b]	Stress hyperglycemia	
		Present N (%)	Absent N (%)		Present N (%)	Absent N (%)
Lap cholecystectomy	61	11 (18.0)	50 (82.0)	60 to 120	5 (14.7)	29 (85.3)
Open cholecystectomy	16	5 (31.2)	11 (68.8)	12o to 180	7 (20)	28 (80)
Other biliary surgeries	9	7 (77.8)	2 (22.2)	More than 180	23 (74.2)	8 (25.8)
Pancreatic surgeries	14	12 (85.7)	2 (14.3)			
Total	100	35	65		35	65

[a]χ^2 value of 30.885 and p-value of 0.001; [b]$\chi2$ value: 30.549, p-value<0.00.

Association of type of surgery with stress hyperglycemia

Majority (87.5%) of those who underwent pancreatic surgery developed stress hyperglycemia while only 18%o of those who underwent laparoscopic cholecystectomy developed stress hyperglycemia. This difference in proportion was found to be statistically significant (Table 8).

Association of duration of surgery with stress hyperglycemia

Linear by linear association value: 24.329, p-value <0.001. When duration of surgery was more than 180 minutes, 74.2% of patients developed stress hyperglycemia and this association was found to be statistically significant (Table 8).

Association of intraoperative blood loss and stress hyperglycemia

54.2% of patients who had blood loss >500 ml developed stress hyperglycemia, while 28.9% of patients who had blood loss <500 ml developed stress hyperglycemia and this association was found to be significant (Table 9).

Association of intraoperative blood transfusion with stress hyperglycemia

84.6% of those who had intraoperative blood transfusion developed stress hyperglycemia while only 27.5% of those who did not have blood transfusion developed stress hyperglycemia and this association was found to be significant with p-value of <0.001 (Table 9).

Logistic regression analysis of factors associated with stress hyperglycemia

The factors that were found to be statistically significant in association with stress hyperglycemia in chi square test were analyzed using binary logistic regression. The dependent variable considered for analysis was stress hyperglycemia. This was analyzed with a set of independent variables and enter method of logistic regression was used.

Factors which were found to be independent predictors of stress hyperglycemia in logistic regression were presence of anemia, hypoalbuminemia, duration of surgery and BMI of <18.5 and >30.

Table 9: Distribution of stress hyperglycemia based on intraoperative blood loss and intraoperative blood transfusion.

Blood loss	Total	Stress hyperglycemia		Blood transfusion	Total	Stress hyperglycemia	
		Present N (%)	Absent N (%)			Present N (%)	Absent N (%)
<500 ml	76	22 (28.9)	54 (71.1)	**Given**	13	11 (84.6)	2 (15.4)
>500 ml	24	13 (54.2)	11 (45.8)	**Not given**	87	24 (27.5)	63 (72.5)
Total		35 (35%)	65 (65%)			35	65

[a]χ^2 test 5.099 and p-value of <0.02; [b]χ^2 value of 16.16 and p-value of <0.001.

DISCUSSION

Mean age of the study population was 49.21 years with standard deviation 13.11. Minimum age of the study population was 19 years and maximum age of the population was 81 years.

42% of the study populations were males and 58% were females of the total study population, 61% underwent laparoscopic cholecystectomy, 16% underwent open cholecystectomy, 9% underwent other biliary surgeries and 14% underwent pancreatic surgeries.

The mean preoperative blood sugar value was found to be 108.07 with a standard deviation of 26.9 and mean postoperative blood sugar value was found to be 137.25 with a standard deviation of 35.5 and this difference in mean was found to be significant.

When the association of age group with stress hyperglycemia was studied, it was found that, 68.5% of those who developed stress hyperglycemia belonged to the age more than 51 years.

When the association of gender and incidence of stress hyperglycemia was studied, it was found that 47% of males developed stress hyperglycemia while only 25% of females developed SH and this was statistically significant.

Association of family history of diabetes mellitus and SH showed no significant association.

Association of BMI and stress hyperglycemia was studied and it was found that both underweight (BMK18.5) and obese (BMI>30) developed SH and this association was found to be significant.

Association of anaemia and SH was studied and found that 68% of anaemic patients developed SH while 24% of those who were not anaemic developed SH. This difference in proportion was found to be significant.

Association between hypoalbuminemia and SH was studied and found that, 90% of patients with hypoalbuminemia developed SH while 28.9% of patients who had normal levels of albumin developed SH. This difference in proportion was found to be significant.

Association of type of surgery and incidence of stress hyperglycemia was studied and found that 85.7% of those who underwent pancreatic surgery, 77.8% of those who underwent other biliary surgeries, 31.2% of those who underwent open cholecystectomy and 18% of those who underwent laparoscopic cholecystectomy developed stress hyperglycemia.

Association of duration of surgery and stress hyperglycemia was studied and found that when duration of surgery was more than 180 minutes, 74.2% developed SH. When the duration surgery was 60-120 minutes, 14.7% developed SH, when the duration of surgery was 121-180 minutes 20% developed SH. The study has found out that there is linear association between duration of surgery and development of SH.

Association between intraoperative blood loss and incidence of SH was studied and has found out that, 54.2% of those who had blood loss more than 500 ml developed SH, and this association was found to be significant.

Association between intraoperative blood transfusion and stress hyperglycemia was studied and found that 84.6% of those who had blood transfusion had developed stress hyperglycemia and this association was found to be significant.

Factors that were found to be independent predictors of stress hyperglycemia in logistic regression were, presence of anaemia, hypoalbuminemia, duration of surgery and BMI of less than 18.5 and more than 30.

Mean age of our study population was 49.21 mean age of the study by Shi et al was 54.86.[13] Among the 100 study population,42% were males and 58% were females.

Among the study population, 61% underwent laparoscopic cholecystectomy, 16% underwent open cholecystectomy, 9% underwent other biliary surgeries, and 14% underwent pancreatic surgeries. The incidence of stress induced hyperglycemia was found to be 18% in laparoscopic cholecystectomy, 31.2% in open cholecystectomy, 77.8% in other biliary surgeries and 85.7% in pancreatic surgery. In the study by Shi et al, simple cholecystectomy had 20.83% incidence, other biliary tract surgeries had 32.21% incidence and pancreatic surgery had 63.08% incidence of stress hyperglycemia.[13]

The incidence of stress hyperglycemia in the whole study population was 35% and in the study by Shi et al the incidence was 34.28%.[13]

In the study conducted 68% of the anemic patients developed stress hyperglycemia and in study by Shi et al, 65.5% of those with anemia developed stress hyperglycemia.

In the present study, 90% of patients with hypoalbuminemia developed stress hyperglycemia while, in the study by Shi et al, 75.25% developed stress hyperglycemia.[13]

In this study pancreatic surgery was found to have highest incidence of stress hyperglycemia 85.7% while only 18% patients who underwent laparoscopic cholecystectomy developed stress hyperglycemia.

Duration of surgery was found to have linear association with stress hyperglycemia. When duration of surgery was more than 3 hours, incidence of stress hyperglycemia was found to be 74.2%, duration of one to two hours was 14.7% and two to three hours, incidence was 20%. The study by Shi et al also showed that duration of surgery was an independent predictor for stress hyperglycemia.[13]

In the present study 54% of patients, who had intraoperative blood loss of more than 500 ml that required blood transfusion was associated with stress hyperglycemia.

The independent predictors of stress hyperglycemia in the present study was found to be anemia, hypoproteinemia, duration of surgery, and extremes of BMI, which was comparable to the study by Shi et al.[13]

The causes of stress hyperglycemia include the presence of excessive counter regulatory hormones (glucagon, growth hormone, catecholamine, and glucocorticoid, either endogenous or exogenous), high circulating or tissue levels of cytokine [in particular tumor necrosis factor-a (TNα) and interleukin-1].[14] This metabolic milieu results in failure of insulin to suppress hepatic gluconeogenesis despite hyperglycemia; in addition, insulin-mediated glucose uptake into skeletal muscle is impaired. Patients given excessive nutritional support, especially by the intravenous route, are particularly likely to encounter hyperglycemia.

The results of this study show that stress hyperglycemia incidence for pancreatobiliary postoperative patients was 35%, of which stress hyperglycemia incidence of pancreatic surgery, other biliary surgery, and laparoscopic cholecystectomy patients was 85.7%, 77.8% and 18%, respectively. Compared with other studies, the stress hyperglycemia incidence of pancreatic surgery patients was higher than acute stroke, sepsis and acute myocardial infarction (42.3% and 50%, respectively), which may be associated with that insulin hormone being only one hormone to lower blood sugar in the body and insulin secreted by pancreatic P cells, reduced insulin secretion by pancreatectomy or tissue damage.[15,16] However, stress hyperglycemia incidence of simple cholecystectomy patients is relatively low; most of bile duct stones patients had a certain degree of preoperative liver dysfunction, affecting gluconeogenesis and glycogen synthesis and decomposition process. In addition, Podell et al also reported that a positive correlation between the blood sugar level and disease severity.[17] In this study, gallbladder resection was not severe and stress hyperglycemia incidence was relatively low.

This study found that, long duration of surgery, anemia hypoproteinemia and extremes of BMI were stress hyperglycemia risk factors, suggesting that for the patients suffering from anemia and hypoproteinemia, long operation, extremes of BMI were prone to stress hyperglycemia, such patients should be paid attention to. The reasons may be prolonged operative time enhanced the body's stress response, resulting in a serious nutrient and energy metabolism disorders in the body; anemia patients can produce insulin resistance, studies have shown that recombinant human erythropoietin corrected anemia and may be an useful way to reverse cardiovascular disease and insulin resistance; hypoproteinemia patients often had reduced protein synthesis, and proteins are composed of amino acids, and many amino acid can be converted into glucose.[18,19] Due to the decrease in protein synthesis, gluconeogenesis increases and thus, the patient's blood sugar is elevated.[13]

CONCLUSION

Incidence of stress hyperglycemia in the study population was found to be 35%. Association between factors like age more than 51 years, male sex, extremes of BMI, anemia, hypoalbuminemia, pancreatic surgery, duration of surgery more than 3 hours, amount of blood loss more than 500 ml during surgery, and intraoperative blood transfusion were found to be statistically significant with incidence of stress hyperglycemia.

These variables were assessed using logistic regression method, and anemia, hypoalbuminemia, duration of surgery and extremes of BMI were found to be independent predictors of stress hyperglycemia.

Preoperative correction of anaemia, hypoalbuminemia, and correction of nutrition status will improve the clinical outcome in postoperative patients. Patients who are at risk of developing hyperglycemia can be predicted on the basis of intra operative factors like, duration of surgery, blood loss >500 ml and intraoperative blood transfusion and such patients can be monitored closely and hyperglycemia can be prevented thereby reducing the morbidity and mortality associated with stress hyperglycemia.

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