

# Post-Surgical Stress Hyperglycaemia in Females

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## ABSTRACT

Twenty-eight female patients, who underwent elective cholecystectomy were studied for development of stress hyperglycaemia. Their insulin, growth hormone and cortisol levels were studied both before and after surgery. There was a significant elevation of blood glucose levels post-operatively which was associated with simultaneous increase in serum insulin, growth hormone and cortisol. While comparing the data with an earlier study on males (studied under similar conditions) it was found females having cholecystectomy as compared to males.

## INTRODUCTION

Stress has been described as a complex phenomenon of: (I) The characteristic of the environment, (ii) The response of the individual and (iii) the interaction of the individual's perception of the environment[1].

The neuro-endocrine responses to a variety of noxious influences are generally characterised by the stimulation of sympathetic neurons and the release of hormones which tend to elevate plasma glucose. Surgical and non-surgical injury initiates the release of stress hormones which stimulate a cascade of metabolic changes leading to substrate mobilisation (hyperglycaemia) with breakdown of carbohydrate, fat and protein stores[2].

The pathophysiology of stress hyperglycaemia continues to be a matter of debate. In our earlier study, we studied the phenomenon in adult males who underwent a major abdominal surgery in the form of cholecystectomy[3]. The present study was undertaken in adult females to evaluate the effect to evaluate the effect of elective cholecystectomy on glucose tolerance and on three major stress hyperglycaemia related hormones viz. Insulin, growth hormone and cortisol.

## MATERIAL AND METHODS

Twenty-eight female patients admitted in General surgery Department of the Institute of Medical Sciences, Srinagar (Kashmir), undergoing elective cholecystectomy were taken for this study. The age of the patients ranged from 28-45 years and the weight ranged from 42-58 Kg. Patients with diabetes mellitus (including those with history of gestational diabetes mellitus), renal disease or hypertension were not

included in the study. Patients who had been taking oral contraceptives were also excluded from the study.

## Sample collection

Two samples were taken: one prior to the surgery and second after surgery.

i. Pre-operative samples (24 hours before surgery) Samples A was taken at 9 AM in the fasting state for a fasting blood glucose, haemoglobin A 1c (HbA 1c), immunoreactive insulin (IRI), human growth hormone (hGH) and cortisol. Sample A also consisted of three more samples taken at an interval of 30 minutes, 60 minutes and 120 minutes as intra-venous glucose tolerance test (IVGTT) for blood glucose.

ii. Post-operative samples (24 hours after surgery). Sample B was taken at 9 AM in the fasting state and included a basal sample for blood glucose and hormone estimation and three more samples at 30 minutes, 60 minutes and 120 minutes interval for blood glucose during IVGTT.

On study days all feeding except for intravenous electrolyte infusion was omitted for 8-12 hours prior to blood sampling. All those patients with abnormal HbA1c before surgery were excluded from the study GTT was performed by an intravenous injection 50% glucose over a 3-minute period in an amount corresponding to 0.5 gm/kg body weight[4].

The blood glucose estimation was done on Hitachi 704 from Boehringer Mannheim, HbA1c was analysed on automatic HbA1c analyser from Kyota Japan. All hormone estimations were done by specific radio-immunoassay. Statistical evaluation of the data was performed by Students 't' test for paired data.

## RESULTS

Twenty-eight female aged between 28 to 45 (mean SD 35.28 4.20) and weighing between 42 to 58 Kg (mean SD 48.46 4.54) were studied. Comparison of pre-operative and post-operative GTT showed a highly significant elevation of blood glucose Levels post-operatively at all stages of estimation (Table 1). The pre-operative and the post-operative levels of IRI, hGH and cortisol showed a statistically significant elevation in all hormone levels post-operatively (Table 2). This was particularly pronounced in the case of IRI and cortisol.

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**Table 1****Mean Blood Glucose among females during .V.G.T.T. before and after elective surgery**

Time	Blood Glucose (mg/dl)		p	Statistical significance
	Pre-operative	Post-operative		
	Mean ± SD	Mean ± SD		
Fasting	74.36 ± 6.32	151.06 ± 11.66	< 0.001	HS
30 minutes	112.41 ± 6.59	177.03 ± 21.81	<0.001	HS
60 minutes	104.00 ± 5.62	159.01 ± 15.11	<0.001	HS
120 minutes	83.04 ± 7.47	149.32 ± 13.97	<0.001	HS

HS = Highly Significant

**Table 2****Effect of Surgery on hormones in females**

Hormone	Range	Pre-operative		Post-operative		P	Statistical Significance
		Mean ± SD	Range	Mean ± SD	Range		
IRI (uU/ml)	1.42-25.57	9.33±5.65	3.57-59.27	22.38±13.94		<.001	HS
hGH (ng/ml)	0.27-6.86	1.85±1.77	0.61-24.56	5.39±5.60		<.005	S
Cortisol (ug/dl)	2.53-16.99	9.04±4.15	10.29-42.00	22.46±8.88		<.001	HS

HS = Highly significant, S = Significant

We compared the results of this study with our earlier study[3] conducted on male patients and found:

The pre-operative blood glucose levels after IVGTT did not differ between the two sexes, whereas post-operative blood glucose levels after IVGTT were significantly higher in females at all stages of estimations (Table-3).

The pre-operative and post-operative levels of IRI, hGH and cortisol did not differ between the two groups (Table-4).

**Table-3****Comparison of Pre-operative & Post-operative blood glucose (mg/dl) levels during I.V. glucose tolerance test between males and females**

Time	Mean Glucose (±SD)		p	Statistical significance
	Males	Females		
<b>PRE-OPERATIVE</b>				
Fasting	76.27 ± 7.16	74.36 ± 6.32	> 0.20	NS
30 minutes	114.82 ± 6.54	112.41 ± 6.59	<0.10	NS
60 minutes	104.09 ± 5.25	104.00 ± 5.62	>0.50	NS
120 minutes	87.09 ± 7.55	83.04 ± 7.47	>0.05	NS
<b>POST-OPERATIVE</b>				
Fasting	107.95 ± 9.93	121.06 ± 11.66	< 0.001	HS
30 minutes	145.73 ± 13.05	177.03 ± 21.81	<0.05	S
60 minutes	125.05 ± 7.49	159.01 ± 15.11	<0.01	S
120 minutes	111.50 ± 7.61	149.32 ± 13.97	<0.025	S

HS = highly significant, S = Significant, NS = Not significant  
Values for males are from an earlier publication.[3]

**Table-4****Comparison of Pre-operative & Post-operative hormone values between males and females**

Time	Males		Females		p	Statistical significance
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		
<b>PRE-OPERATIVE</b>						
IRI (μU/ml)	10.37 ± 7.84		9.33 ± 5.65		>0.50	NS
hGH (ng/ml)	1.90 ± 2.06		1.85 ± 1.77		>0.50	NS
Cortisol μg/dl	10.01 ± 5.15		9.04 ± 4.15		>0.40	NS
<b>POST-OPERATIVE</b>						
IRI (μU/ml)	19.94 ± 12.81		22.38 ± 13.93		>0.50	NS
hGH (ng/ml)	4.72 ± 4.28		5.39 ± 5.60		>0.50	NS
Cortisol μg/dl	18.69 ± 8.67		22.46 ± 8.88		>0.10	NS

NS = Not significant

Hormone values for males are from an earlier publication. [3]

The results indicate that stress hyperglycaemia was more pronounced females even though IRI, hGH and cortisol levels were comparable.

**DISCUSSION**

The metabolic response to stress is associated with a neuro-endocrine activation that would tend to elevate plasma glucose. A variety of traumatic, metabolic,

physiological and perhaps even psychic states can be associated with carbohydrate intolerance. If the injury is severe enough carbohydrate intolerance can be converted to overt hyperglycaemia. Stressful changes in the life circumstances and perhaps psychophysiological states of a person may conceivably lead to changes in levels of circulating hormones and deviations from normal blood glucose levels. Such hormones include cortisol, catecholamines, glucagon, growth hormone and beta-endorphins.[5]

The present study was undertaken to evaluate the effect of surgical stress on glucose intolerance on the first post-operative day in female patients undergoing cholecystectomy, and to study the hormonal response to this stress.

It was observed that post-operative blood glucose was significantly elevated in comparison to pre-operative blood glucose at all stages of estimation during IVGTT. Similar findings have been reported by Ross.[6] Markhu Aarimaa et al observed that GTT of all patients undergoing elective femoral osteotomy showed a diabetic pattern.[4] Post-operative IRI, hGH and cortisol were significantly elevated in comparison to pre-operative values. Similar hormonal alterations post-operatively have been reported by other workers. [3,6-13]

However, what was surprising in this study is the observation that when we compared the data with our earlier study performed on male subjects under identical conditions,[3] the blood glucose elevation post-operatively was more profound in female patients even though IRI, hGH and cortisol were comparable between the two groups. The factors responsible for this differential behaviour between the two sexes need further elucidation. Studies have shown that stress of surgery stimulates the release of cortisol, GH and prolactin in females.[13-15] The concentration of gonadotropins have been shown to decrease post-operatively in female patients. [13] the possible influence of sex steroids, prolactin and gonadotropins vis-a-vis stress-hyperglycaemia needs to be deciphered. Trying to establish a correlation between and individual hormone alone and this stress hyperglycaemia would not be justified.

To conclude, this study has brought forth that: (1) Females develop, significant post-surgical stress hyperglycaemia, (2) there is concomitant significant elevation of IRI, hGH and cortisol, (3) Females react to surgical stress adversely vis-à-vis males and (4) changes in IRI, hGH and cortisol do not account for this differential behaviour of two sexes to surgical stress.

It remains to be seen whether such a response to surgical stress is helpful or harmful in its ultimate dimension and what is the final cut off point in terms of duration of such a response.

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