Research Article

Serum cortisol levels in critically Ill versus non-critically Ill patients

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Abstract

This case control study was undertaken to compare the early morning venous serum cortisol levels between 40 cases of critically ill (group A) vs non critically ill (group B) patients admitted to a tertiary teaching hospital for a duration of one year. It was found that there was significant increase in the serum cortisol levels among critically ill (mean 33.68 µg/dl ±15.93) as compared to non critically ill (mean 15.93 µg/dl ± 5.93) patients.

Key Word: f Serum cortisol.

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INTRODUCTION

Cortisol is a stress hormone, secreted by Zona - fasciculata which is a part of adrenal cortex, under the influence of ACTH. ACTH is released from anterior pituitary, the master gland, in pulsed manner whose peak reaches in the early morning at 6 AM, under the influence of CRH which is released from hypothalamus. Cortisol level in critically ill has always been a controversy as different studies have shown variable results. Prevalence of adrenal insufficiency has been estimated to be about 30% and this value rises to 50 to 60% in septic shock (Maxime *et al.*) [1, 6] There are other studies (Amir H *et al.*)[7] which support the view that, "Patients with critical illness have elevated glucocorticoid secretion marked by an increase in the serum total cortisol concentration". Above two studies from different authors stating contradicting results have been quoted as an example to show the lack of definite consensus about cortisol level in critically ill patients. We have undertaken this study to fill this lacunae by comparing, cortisol level in critically ill and non-critically ill patients in our institutional setting.

AIMS AND OBJECTIVES

To compare serum cortisol level in critically ill and non-critically ill patients.

MATERIAL AND METHODS

The present study was conducted in the general medicine and Intensive Care units of Medical college Hospital, Jaipur. Hospital based Case control study.Study was carried out over a period of one year (May2012 to Apr 2013). Sample size was calculated at 80% study power and 0.05 α-error, assuming incidence of adrenal insufficiency among critically ill and non critically ill patients to be 25% and 1% respectively.The sample size obtained was 38 in each group which was rounded off to 40 patients. Cases and controls were chosen randomly after matching and fulfilling inclusion and exclusion criteria.

Inclusion Criteria

Group A (Critically ill patients)

Patients admitted in Medicine department; with critical illness as defined by Van den *et al.*[11]. Patients who had not received steroids previously. Age>18yrs.

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Group B (Non-Critically ill patients)

Patients admitted in Medicine wards who were not critically ill, Age>18 years.

Exclusion Criteria

Those who were not willing to give informed consent. Those who had received steroid previously. Patients with serum albumin level < 2.5 mg/dl.Patients previously on drugs like Phenytoin, Ketoconazole, Phenobarbitone, and Rifampin. Pregnancy.

METHODOLOGY

After taking clearance from ethics committee of our tertiary care hospital, patients/relatives were explained about the study and given complete information regarding the procedures undertaken and written consent was taken in their local language.Patients were enrolled in to two groups after matching confounding factors like age, sex etc. Venous blood samples for serum cortisol were drawn under aseptic conditions at morning 8AM. Samples were transported in ice box to Advanced Immunology lab of SMS Hospital. Serum cortisol level was determined by Chemo Luminescent Immuno Assay (CLIA) (Immulite 2000).

Cortisol levels were then compared between group A and group B patients. Control group was categorized in to three groups based on cortisol levels : <15µg/dl (low cortisol), 15-34µg/dl (normal serum cortisol), >34µg/dl (abnormally raised cortisol). (Cooper *et al.*) [8, 9]..Later correlation between serum cortisol and outcome in these three groups was analyzed.

Outcome analysis: Data obtained from predesigned proforma was entered in to MS EXCEL sheets and thus master charts were prepared so as to find out statistical significance by unpaired t test or Chi-square test as per the character of data.

Defining critical illness: "Critical illness is any condition requiring support of failing vital organ systems without which survival would not be possible[11]".

This life-threatening condition, which may be evoked by trauma, extensive surgery or severe medical illnesses, is an ultimate example of acute, severe physical stress.

OBSERVATION AND RESULTS

From May2012 to Apr 2013. 80 patients admitted in Medical ICU and wards, who satisfied the inclusion criteria were enrolled in the study and were grouped in to group A (40 Critically – ill) and Group B (40 non Critically – ill) and were followed till discharge or death.

Table 1: Baseline Demographic data of patients according to age

AGE	Group A (CRITICALLY-ILL)		Group B NON CRITICALLY ILL	
	N+	Percentage	N	Percentage
0-20	3	7.5	2	5
21-40	10	25	11	27.5
41-60	15	32.5	14	35
61-80	10	25	10	25
>80	2	5	3	7.5
Mean	49.88	16-86 yrs. (Range)	51.4	17-82Yrs (range)

Mean age of patients in critically ill group and non critically ill group were 49.88 and 51.4 respectively. Most common age group among both was between 41 to 60 years. Age range among both groups was 16-86 and 17-82 among critically ill and non- critically ill groups respective**.**

Table 2: Comparison of mean age of two groups

	Group A (Critically ill)	Group B (Non-Critically ill)
N	40	40
Mean age	49.88	51.40
SD	18.22	19.71

t = 0.36, with degree of freedom being 78 and P=0.7204

Mean age of group A was 49.88 years while that of group B was 51.40 years. There was no significant difference in mean age of the two groups (p>0.05).

Underlying etiology for critical illness

Among critically-ill group, 23(57.5%) were male and 17 (42.5%) were females. Where as in non-critically ill group 25 (62.5%) were males and 15 (37.5%) were female. Out of 40 patients included in the Group A Pulmonary and neurologic illness were most common causes (25%) of critical illness followed by sepsis (20%), CAD (3%) and Malignancy (3%) were among least common etiology. Among the 40 patients enrolled in Group B Dengue (35%) and Malaria (75%) were most common cause of hospital admission.

Table 3: Comparison of Serum cortisol in critically- ill and non - critically ill

	Group A	Group B
Mean cortisol in (µg/dl)	33.68	15.94

Unpaired t test: t=6.047, P=0.001 highly significant.

In group A, mean cortisol level was 33.68µg/dl, and in group B mean cortisol level was 15.94µg/dl. And the difference was statistically significant p=0.001.

Table 4: Correlation of cortisol level (µg/dl) with survival

Serum cortisol level in µg/dl			
Out come	<15	15-34	>34
Survivors	1(6.6%)	12(80%)	2(13.33%)
Non-survivors	3(12%)	9(36%)	13(52%)

Chi square =5.9, with degree of freedom 1, p=0.03 statistically significant.

Among non-survivor's, 52% had increased cortisol (>34µg/dl), 36% had normal cortisol level (15-34%). Among survivors only 13.33% had increased cortisol (>34µg/dl), 80 % had normal cortisol level (15-34%). And the difference in increase in cortisol level among survivors and non survivors was statistically significant p<0.05. While 12% of non survivors had reduced cortisol (<15µg/dl), only 6% of survivors had reduced cortisol. However this difference in reduced cortisol level was not statistically significant p>0.05.

DISCUSSION

As described earlier there are no clear answers for question "what will be cortisol level in critically ill? Which has better prognosis; Cortisol of high value or a low value? Muzaffar *et al.*[7] in their study found that 58% of critically ill patients had cortisol above 34 µg/dl (i.e. Increased cortisol according to Cooper *et al.*[5]) and 66% patients who succumbed to death had increased cortisol level. Yang Y et[25] al in their study found that 40 % of critically ill patients had increased cortisol level, among non-survivor's 72% of patients had increased cortisol. Annae *et al.*[28] in their study they proposed a view that Cortisol level is an independent predictor of death and found that increased cortisol (>34 µg/dl) had a 28 day mortality of 67%. Schein R M *et al.*[27] in their study concluded that plasma cortisol concentrations were increased in patients with septic shock, but that the degree of increase was variable. While there are other groups who support the view that cortisol levels are decreased in critically ill for example - Winifried *et al.*[29] state that "cortisol response to severe stress has a wide variation, 56% of patients has a low cortisol level. Serial morning cortisol level may have prognostic significance since both low absolute levels and significance been shown to be associated with a significantly higher mortality (cortisol level less than 12.96 µg/dl." Jenn-yu *et al.*[8] highlighted in their study that the majority of acutely ill patients who remained in a critical condition had decreased serum cortisol levels. Depressed cortisol levels at follow up may lead to worse clinical outcomes. Amidst of this, recently there has been CORTICUS COHORT[32] (Lipiner *et al.*) trial which had a sample size of 477. In this study cortisol level was found to be increased in non survivors as compared to survivors and also noted that patients with cortisol level below 15 µg/dl were more likely to die, to have a longer duration of shock, and to have a shorter survival time. Thus this study potentiates the view that cortisol level either increased or decreased both have a dismal prognosis. In our study there was significant increase in cortisol level among critically ill (mean 33.68 µg/dl ±15.93) as compared to non critically ill (mean 15.93 µg/dl ± 5.93). It was also noted that Cortisol level was high (>34µg/dl) in 52 % of non-survivors as compared to 13.33% of survivors of critically ill group. 12% of non survivors had reduced cortisol level (<15µg/dl) while only 6.6% of survivors had reduced cortisol. However this was not statistically significant p>0.05. Thus our study supports the view that "cortisol level is increased in critically ill and this increased level is associated with increased mortality." And our study is comparable to findings of Muzaffar *et al.*[24].

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