

A Study to Assess the Proportion of Hypocortisolemia among Patients Admitted in Medical Intensive Care Unit in a Tertiary Care Hospital in Central Kerala

Merlin Elizabeth Thomas¹, Geeta Panicker²

Department of General Medicine, Amala Institute of Medical Sciences, Thrissur, India
Corresponding Author Email: merlinelizabeth94[at]gmail.com

Abstract: ***Introduction:** Hypocortisolemia is a common complication that we come across in critically ill patients. Hence earlier diagnosis and adequate identification of this complication is warranted for planning early intervention. **Methods:** A cross sectional study was conducted among patients admitted in medical ICU under the Department of General Medicine, Amala Institute of Medical Sciences, Thrissur for a period of one year from March 2021 to February 2022. Consecutive consenting 231 patients were included in the study. Random serum cortisol level was assessed within 24 hours of admission to medical ICU. Patients with random serum cortisol level < 15µg/dl were considered to have hypocortisolemia, those with value between 15µg/dl - 34µg/dl were considered as normal and those patients with cortisol level > 34µg/dl were considered to have hypercortisolemia. Q - SOFA scoring was performed to assess the severity of illness. The requirement of vasopressors among the study population was noted. Patients were followed until the time of discharge from or death in medical ICU. **Results:** The proportion of hypocortisolemia in patients admitted to medical intensive care unit was 31.4%. The critically ill patients amongst the study population were found to have a significant association with low cortisol levels. **Conclusion:** Our study concluded that the proportion of hypocortisolemia among patients admitted in ICU was 31.4% with a male preponderance. Critically ill patients and those requiring a longer hospital stay were found to have a significant association with hypocortisolemia.*

Keywords: hypocortisolemia, critical illness, Q - SOFA

1. Introduction

Cortisol is the main adrenal glucocorticoid and plays a central role in glucose metabolism and in the body's response to stress (1). Adrenal cortisol production is regulated by adrenocorticotrophic hormone (ACTH), which is synthesized by the pituitary gland in response to hypothalamic corticotrophin - releasing hormone (CRH) (2, 3). Serum cortisol in turn inhibits the production of both CRH and ACTH (negative feed - back loop), and this system self - regulates to control the proper level of cortisol production. The coordinated stimulatory and inhibitory connections between CRH, ACTH, and cortisol are referred to as the hypothalamic - pituitary - adrenalaxis (4, 5).

The neuroendocrine response to critical illness consists primarily of activated anterior pituitary function, and inactivation of peripheral anabolic pathways. The HPA axis responds differently to both acute and chronic insults (6, 7).

Stimulation of HPA axis, resulting in an elevated plasma level of cortisol, is one of the most important hormonal reactions to severe insults (4, 8). Cortisol plays a vital role in maintaining the normal vascular tone and in potentiating vasoconstrictor action of catecholamines (1, 9). Glucocorticoids are both critical facilitators of adaptive response to stress and powerful immunosuppressive agents (10).

There is a prompt and sustained rise in both ACTH and cortisol in response to any form of stress. This is accompanied by a loss of circadian variability and ACTH

pulsatility. Cortisol concentrations have been found to be elevated in most severe illnesses. Hence plasma cortisol levels seem to reflect severity of illness (11, 12).

Some recent studies suggest that hypocortisolemia is associated with higher mortality. Early literature coats a wide range in incidence of hypocortisolemia in the critically ill (13). This may be attributed to different types of illnesses encountered from centre to centre. If the proportion of critically ill patients who end up in this state of adrenal exhaustion is large, the result may help in outlining policies for the role of temporary replacement of adrenal function with physiological doses of glucocorticoids.

Aim:

To assess the proportion of hypocortisolemia among patients admitted in medical intensive unit in Amala Institute of Medical Sciences, Thrissur.

Objectives:

Primary objective -

To determine the proportion of hypocortisolemia among patients admitted in medical intensive care unit in Amala Institute of Medical Sciences, Thrissur.

Methods:

Study Design:

Cross sectional study

Study Setting:

Volume 12 Issue 6, June 2023

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Department of General Medicine, Amala Medical College, Thrissur

Study Population:

Patients admitted to the medical intensive care unit of Amala Medical College, Thrissur

Duration of Study:

1 year from the date of approval by IRB.

Sample Size:

$$n = z^2 p (1 - p) / d^2$$

Here z =1.96 at 5% type 1 error (P<0.05); p is the expected prevalence; d is the absolute error of precision

Hence, n = 1.968×1.96×0.816 (1 - 0.816) /0.05×0.05 = 230.71

Inclusion Criteria:

Adult consenting patients in medical ICU requiring intensive care for more than 24 hours.

Exclusion Criteria:

- 1) Patients with a known disease of the HPA axis (itself causing adrenal insufficiency).
- 2) Current consumption of drugs interfering with the cortisol assay like glucocorticoids and spironolactone.
- 3) Patients with a known HIV infection.

2. Procedure

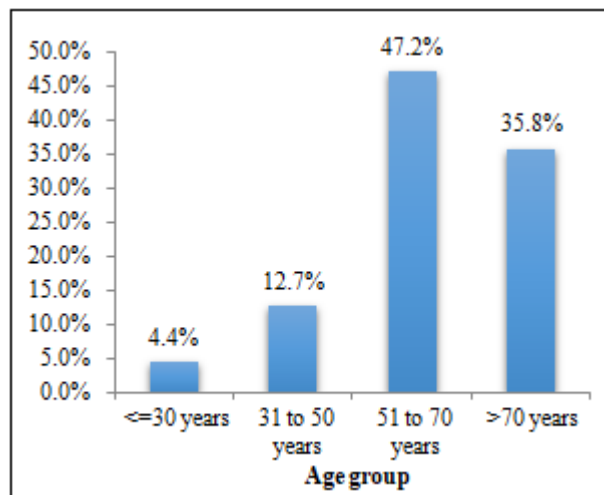
A cross sectional study was conducted among patients admitted in medical ICU under the department of general medicine, Amala Institute of Medical Sciences, Thrissur for a period of one year from March 2021 to February 2022. Consecutive consenting 231 patients were included in the study. On enrolment into the study, a complete history and physical examination was performed and a working primary diagnosis was obtained. Random serum cortisol level was assessed within 24 hours of admission to medical intensive care unit. Patients with random serum cortisol level less than 15µg/dl were considered to have hypocortisolemia and those patients exhibiting a value between 15µg/dl and 34µg/dl were considered as normal, those patients with cortisol level more than 34µg/dl were considered to have high cortisol level. Q - SOFA scoring was performed to assess the severity of illness. The requirement of vasopressors among the study population was noted. Patients were followed until the time of discharge from medical intensive care unit or death in medical intensive care unit and the final outcome was noted in all the study patients.

Patient data was maintained as confidential and was analyzed using SPSS 23 software.

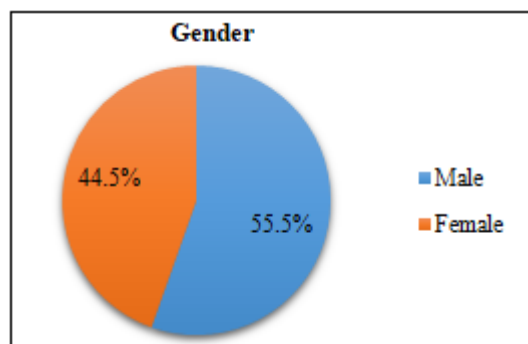
3. Results

The mean age of the study population was 64.15 years among which 4.4% were ≤30 years, 12.7% were between 31 to 50 years, 47.2% were between 51 to 70 years and 35.8% were >70 years.

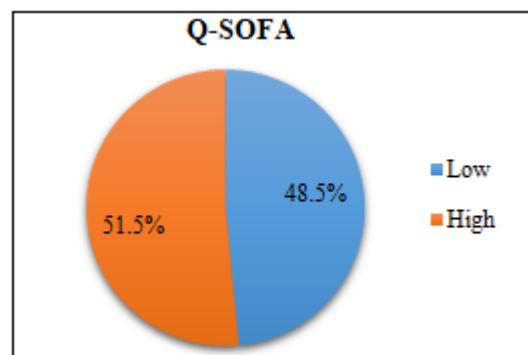
Age group	Frequency	Percentage
≤30 years	10	4.4%
31 to 50 years	29	12.7%
51 to 70 years	110	47.2%
>70 years	82	35.8%



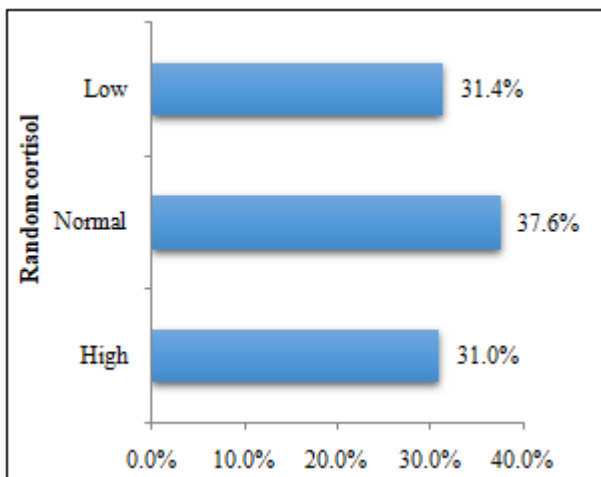
Among the 231 patients, 55.5 % were males and 44.5 % were females.



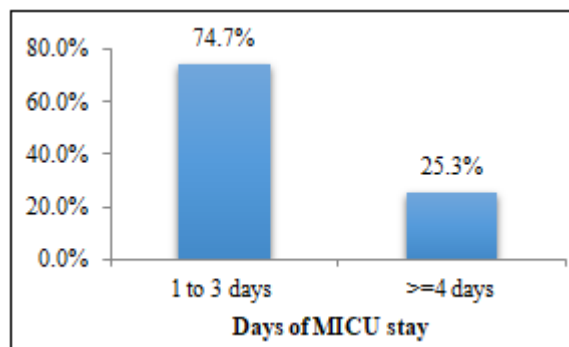
Gender	Frequency	Percentage
Male	129	55.5%
Female	102	44.5%



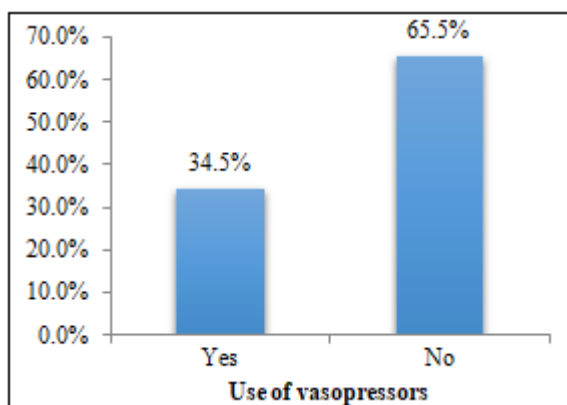
Q - SOFA	Frequency	Percentage
Low	113	48.5%
High	118	51.5%



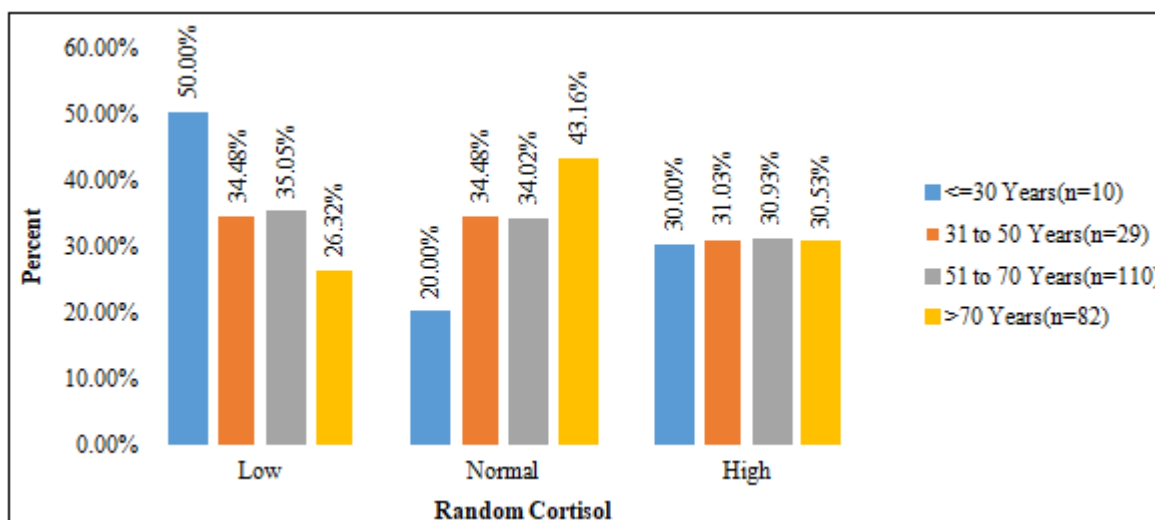
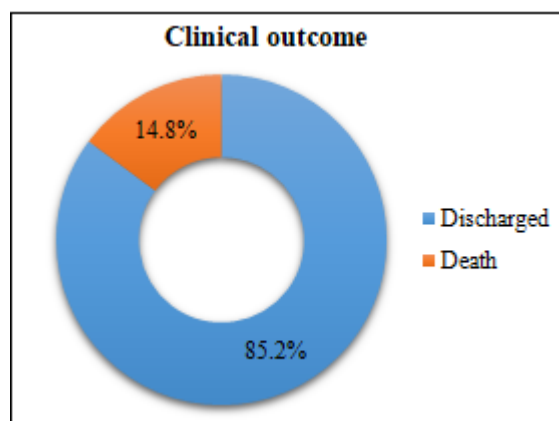
Random cortisol	Frequency	Percentage
Low	74	31.4%
Normal	86	37.6%
High	71	31.0%

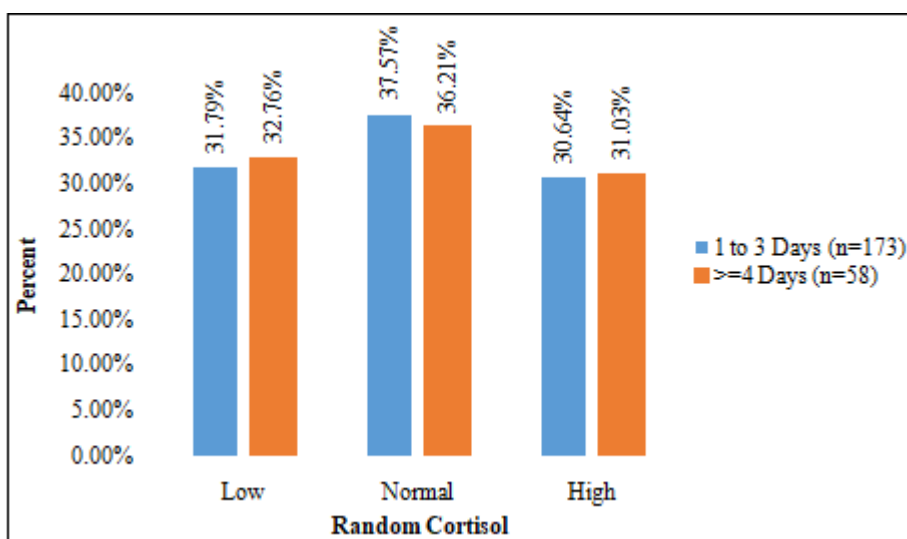
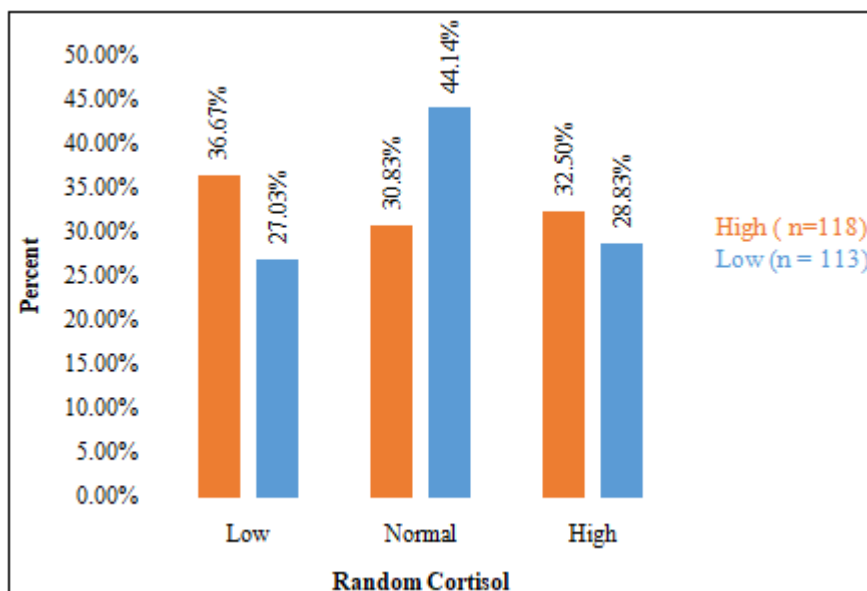
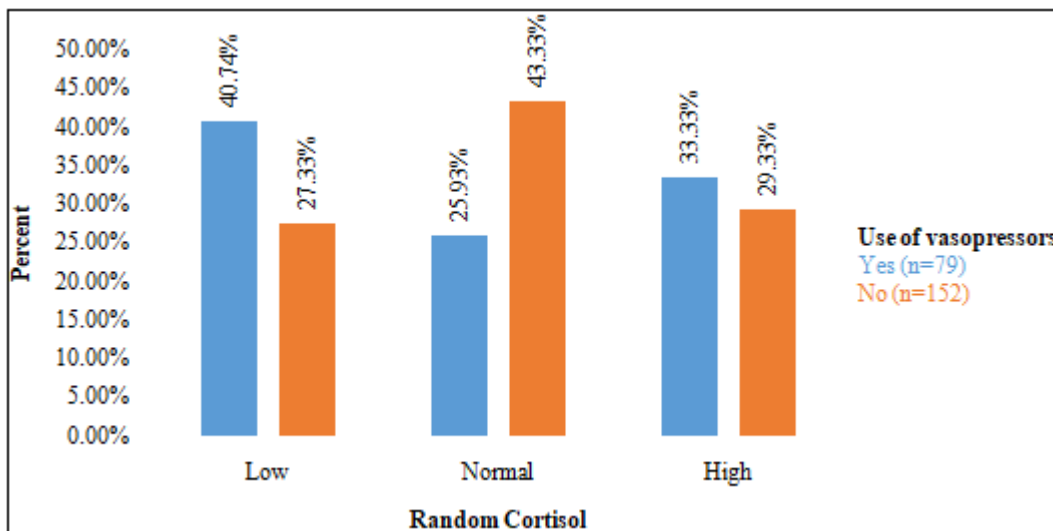


Days of stay in intensive care unit	Frequency	Percentage
1 to 3 days	173	74.7%
≥4 days	58	25.3%

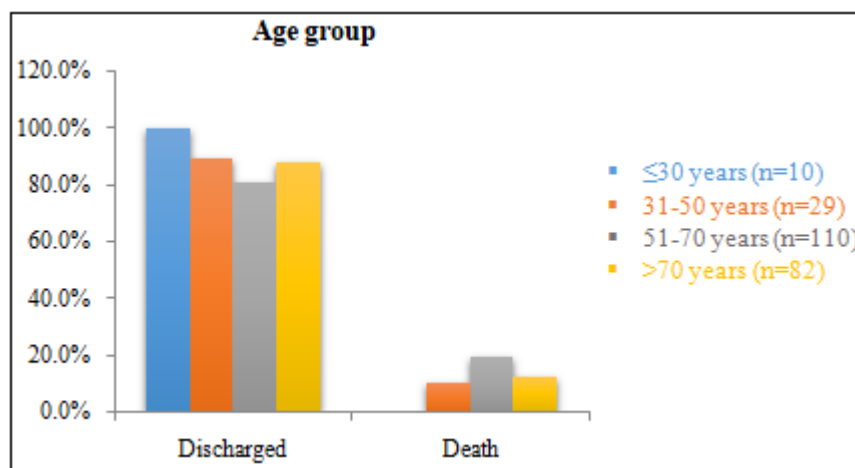
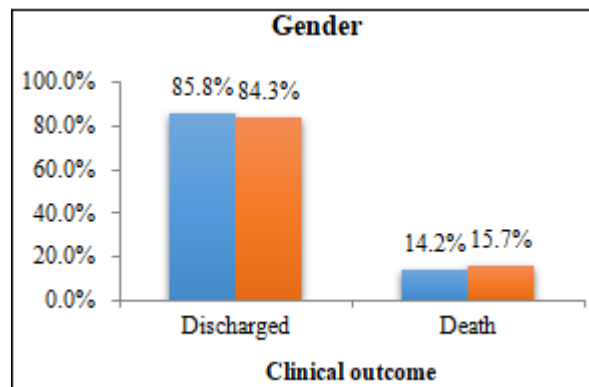


Use of vasopressors	Frequency	Percentage
Yes	79	34.5%
No	152	65.5%





Gender	Clinical Outcome		P - value
	Discharged	Death	
Male (n=129)	111 (85.8%)	18 (14.2%)	0.749
Female (n=102)	86 (84.3%)	16 (15.7%)	



50% of those patients aged ≤ 30 years were found to have a low random serum cortisol value as against 20% with normal random serum cortisol and 30% with high random serum cortisol values. Amongst those patients aged between 31 to 50 years, 34.48% had low random serum cortisol values, 34.48% had normal random serum cortisol values and 31.03% had high random serum cortisol values. 35.05% of patients had low random serum cortisol values among those patients aged between 51 to 70 years with 34.02% and 30.93% of the remaining patients belonging to that age group having normal and high random serum cortisol levels respectively. Of those patients belonging to age group above 70 years in the study population, 26.32% had low random serum cortisol levels, 43.16% had normal random serum cortisol values and 30.53% had high random serum cortisol values.

The random serum cortisol values were found to be low in 31.4 % of the study population. 37.6 % of the 231 patients had a normal value of random serum cortisol. A high random serum cortisol value was observed in 31% of the patients. Of the patients with hypocortisolemia, 36.5% were males and 63.5% were females. 44.59% of patients with hypocortisolemia required vasopressor support as compared to 24.42% of patients with normal serum cortisol values and 38.03% of patients with high serum cortisol values.

51.5 % patients amongst the 231 were critically ill which was determined using the Q - SOFA scoring system as against 48.5 % of the study sample who were not critically ill. In patients who had a high Q - SOFA score in the study population, 36.67% were recorded to have a low serum cortisol value, 30.83% had normal random serum cortisol

and the rest 32.5% had a high random serum cortisol value. In a study conducted by Shy - Shin Chang et al which included 30 critically ill patients in a tertiary care hospital in Taiwan, the prevalence of hypocortisolemia was 43% (14) . In comparison to this, our study showed a 36.67% prevalence of hypocortisolemia among critically ill patients. The need for vasopressors was observed in 34.5% of the 231 patients while 65.5 % of them did not require the use of vasopressors. 40.74 % of the subjects requiring vasopressors in the study population expressed a low random serum cortisol value. 25.93% of the same population exhibited normal random serum cortisol values. High random serum cortisol values were observed in 33.33% of those patients requiring vasopressors. Amongst those patients that were not on any vasopressor support, 27.33% had a low random serum cortisol value, 43.33% showed a normal value of random serum cortisol and the rest 29.33% had a high random serum cortisol value. In the SHIPS study which looked at patients in intensive care unit on vasopressor support, the prevalence of relative adrenal insufficiency was found to be 81.6% (13).

74.7% of the subjects remained in the intensive care unit for a period ranging between 1 and 3 days whereas 25.3 % amongst the 231 patients stayed at least or beyond 4 days. Low random serum cortisol levels were observed in 31.79% of the 173 patients in the study population who required to stay in the intensive care unit from 1 - 3 days. 37.57 % of them had normal random cortisol values whereas the rest 30.64% of the 173 patients who remained in intensive care unit for a duration of 1 - 3 days had high levels of random serum cortisol. Of the 58 patients who required to be in the intensive care unit for a duration of 4 days and above,

32.76% had low random serum cortisol values, 36.21 % had normal random serum cortisol values and high random serum cortisol values were seen in 31.03%.

85.2% of the study population were discharged from the intensive care unit while 14.8% expired during stay in the intensive care unit. All patients ≤ 30 years were discharged from intensive care unit with no death reported amongst them. Among those aged 31 - 50 years, 89.7 % were discharged from the intensive care unit and 10.3% died during stay in the intensive unit. 19.4% died during stay in the intensive care unit with 80.6% having been discharged from the intensive care unit among those patients aged 51 to 70 years. Death was observed in 12.2% among patients aged >70 years and 87.8 % were discharged from the intensive care unit.

4. Discussion

The proportion of hypocortisolemia in patients admitted to medical intensive care unit was 31.4%. Among the various age groups that were included in the study population, the presence of low cortisol levels was observed in those patients between 51- 70 years. Hypocortisolemia was predominant amongst the male population in the study. The critically ill patients amongst the study population were found to have a significant association with low cortisol levels.

5. Conclusion

This study was done to see the prevalence of hypocortisolemia among patients admitted in intensive care unit of a tertiary care center in central Kerala. This study was conducted among 231 patients admitted to medical intensive care unit over a period of one year.

The proportion of hypocortisolemia in patients admitted to medical intensive care unit in our tertiary care center was 31.4%. Among the various age groups that were included in the study population, the presence of low cortisol levels was observed in those patients between 51 - 70 years. Hypocortisolemia was predominant amongst the male population in the study. The critically ill patients amongst the study population were found to have a significant association with low cortisol levels.

References

- [1] Sam S, Corbridge TC, Mokhlesi B, Comellas AP, Molitch ME. Cortisol levels and mortality in severe sepsis. *ClinEndocrinol (Oxf)*.2004 Jan; 60 (1): 29–35.
- [2] Dhillon WS, Kong WM, Le Roux CW, Alaghband - Zadeh J, Jones J, Carter G, et al. Cortisol - binding globulin is important in the interpretation of dynamic tests of the hypothalamic–pituitary–adrenal axis. *European Journal of Endocrinology*.2002 Feb; 146 (2): 231–5.
- [3] Ghulam A, Vantighem MC, Wemeau JL, Boersma A. Adrenal minerlocorticoids pathway and its clinical applications. *ClinChimActa*.2003 Apr; 330 (1–2): 99–110.
- [4] Spiga F, Walker JJ, Terry JR, Lightman SL. HPA axis - rhythms. *Compr Physiol*.2014 Jul; 4 (3): 1273–98.
- [5] Stephens MAC, Wand G. Stress and the HPA Axis. *Alcohol Res*.2012; 34 (4): 468–83.
- [6] Everitt BJ, Hökfelt T. Neuroendocrine Anatomy of the Hypothalamus. In: Pickard JD, Cohadon F, Antunes JL, editors. *Neuroendocrinological Aspects of Neurosurgery*. Vienna: Springer Vienna; 1990. p.1–15.
- [7] Liyanarachchi K, Ross R, Debono M. Human studies on hypothalamo - pituitary - adrenal (HPA) axis. *Best Practice & Research Clinical Endocrinology & Metabolism*.2017 Oct 1; 31 (5): 459–73.
- [8] Buckley TM, Schatzberg AF. On the Interactions of the Hypothalamic - Pituitary - Adrenal (HPA) Axis and Sleep: Normal HPA Axis Activity and Circadian Rhythm, Exemplary Sleep Disorders. *The Journal of Clinical Endocrinology & Metabolism*.2005 May 1; 90 (5): 3106–14.
- [9] Hawley JM, Owen LJ, Lockhart SJ, Monaghan PJ, Armston A, Chadwick CA, et al. Serum Cortisol: An Up - To - Date Assessment of Routine Assay Performance. *Clinical Chemistry*.2016 Sep; 62 (9): 1220–9.
- [10] Dickmeis T. Glucocorticoids and the circadian clock. *J Endocrinol*.2009 Jan; 200 (1): 3–22.
- [11] Ospina NS, Al Nofal A, Bancos I, Javed A, Benkhadra K, Kapoor E, et al. ACTH Stimulation Tests for the Diagnosis of Adrenal Insufficiency: Systematic Review and Meta - Analysis. *The Journal of Clinical Endocrinology & Metabolism*.2016 Feb; 101 (2): 427–34.
- [12] Jurney TH, Cockrell JL, Jurney TH, Lindberg JS, Lamiell JM, Wade CE. Spectrum of Serum Cortisol Response to ACTH in ICU Patients: Correlation with Degree of Illness and Mortality. *Chest*.1987; 92 (2): 292–5.
- [13] Chacko S, John G, Thomas N, Nellickal A. Subclinical hypocortisolemia in patients with sepsis in a medical intensive care unit in India (The SHIPS Study). *Indian Journal of Critical Care Medicine*.2004 Jan 1; 8.
- [14] Chang SS, Liaw S, Bullard M, Chiu T, Chen J, Liao H. Adrenal Insufficiency in Critically Ill Emergency Department Patients: A Taiwan Preliminary Study. *Academic emergency medicine : official journal of the Society for Academic Emergency Medicine*.2001 Jul; 8: 761–4.