

UNIVERSITI TEKNOLOGI MARA

**DETERMINATION OF REFERENCE
INTERVAL FOR MIDNIGHT
SALIVARY CORTISOL AMONG
HEALTHY ADULTS IN KINTA
VALLEY REGION**

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ABSTRACT

Cortisol has been well established as an assessment of adrenocortical function. Cortisol levels are elevated in Cushing's syndrome and the levels are low in adrenal insufficiency such as Addison's disease. The Endocrine Society Guidelines has recommended that screening for Cushing's syndrome in adults includes assessment of Urinary Free Cortisol (UFC) , overnight dexamethasone suppression test and midnight salivary cortisol. Measurement of midnight salivary cortisol is the most sensitive, specific and non-invasive method for screening of Cushing's syndrome. This study aims to establish reference interval of midnight salivary cortisol in healthy adults in Kinta Valley region. This cross-sectional study involving 125 participants, 86 (68.8%) females and 39 males (31.2%), median age = 19 (19-19) and median BMI = 21.62 (19.40-24.77). Participants were refrained from teeth brushing, eating or drinking 1 hour prior to samples collection. Midnight salivary samples were taken using Saliva Bio Oral Swab (SOS) equipped with an insert containing oral swab for the analysis of midnight salivary cortisol on the Roche Cobas e620-analyzer (Germany) via electrochemiluminescence immunoassay (ECLIA). The midnight salivary cortisol presented a non-Gaussian distribution with median [IQR] 2.2 (1.55, 3.45), 2.5th percentile (90 % CI); 1.5 (1.5-1.5), 97.5th percentile (90 % CI); 12.6 (8.4-15.8). Our study showed no association between gender and MSC [(n=125); $p > 0.05$, 90 (%) CI]. Spearman's rank correlation analysis indicated that midnight salivary cortisol levels were significantly correlated with body mass index although it was a poor correlation ($\rho=0.224$, $P < 0.05$). Using the same statistical analysis, there is no correlation observed between midnight salivary cortisol levels and age ($\rho=0.106$, $P=0.239$). These findings contribute toward establishing the laboratory's reference range for midnight salivary cortisol which can provide to the national's reference range program.

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CHAPTER ONE

INTRODUCTION

1.1 Definition of Cortisol and Its Functions

Cortisol is an endogenous glucocorticoid hormone (Turpeinen and Hamalainen 2013) secreted by the adrenal glands (Turpeinen and Hamalainen 2013). The secretion is regulated by adrenocorticotrophic hormone (ACTH) from the anterior pituitary gland (Oakley and Cidlowski 2013). Cortisol secretion is pulsatile, exhibiting maximum secretion in early morning and minimum at midnight (11pm - 2am) (Yorke et al. 2017, Nieman et al. 2008). Cortisol plays a central role in the body's response to stress and glucose metabolism (George T Grifing et al 2014). In addition, cortisol exerts anti-inflammatory effect (Cruz-Topete and Cidlowski 2015) and is critical for maintaining energy homeostasis (Magomedova and Cummins 2016) by regulating protein metabolism in skeletal muscle, giving rise to catabolic effect (Bodine and Furlow 2015).

1.2 Cortisol as an Assessment of Adrenocortical Function

Serum cortisol levels are elevated in Cushing's syndrome (CS) as a result of various causes, including cortisol-secreting adrenal tumour, pituitary adenoma (Cushing's disease) and ACTH-secreting tumours (Noralkairys, Ari Schwell 2017). Furthermore, high serum levels have been reported in stress, psychiatric diseases, obesity, diabetes, alcoholism and pregnancy rendering diagnostic challenges in patient with Cushing disease (Androulakis II et al 2015). Low cortisol levels are seen in adrenal insufficiency, for example in Addison's disease (Sadaf Munir, Muhammad Waseem 2017).

1.3 Cortisol as a Screening Test for Cushing's Syndrome

Globally, CS has an incidence of 0.2 – 5 per million/ year and a prevalence of 39 – 79 per million in various population (Yorke et al. 2017). The Endocrine Society