

# Sleep deprivation effect on concentration of some reproductive hormones in healthy men and women volunteers

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## ABSTRACT

The research aimed to explore the impact of sleep deprivation on some hematological parameters and concentration of some reproductive hormones in the serum of men and women volunteers. The study included 50 men and 50 women adult healthy volunteers aged between 20 to 45 years old suffering from sleep deprivation. Five ml of blood gathered from a cubical vein at 3-4 p.m. One ml was kept in EDTA tube for complete blood count test by Saw lab, while four ml in Jell tubes for separation of serum by centrifuge and kept in Eppendorf tubes at deep freeze till detection of hormones FSH, LH, testosterone and prolactin by VIDAS depending on enzyme-linked fluorescent assay. The results of the experiment recorded a significant decrease ( $p < 0.05$ ) in the concentration of Hb and % PCV and increase in MCV level in sleep-deprived men. While there was remarkable decline ( $P < 0.05$ ) in the level of LH and no significant alterations in testosterone hormone in sleep-deprived men, but significant increment ( $P < 0.01$ ) in the concentration of prolactin. On other hand sleep-deprived women recorded significant decline ( $P < 0.05$ ) in the concentration of prolactin and non-significant alterations ( $P > 0.05$ ) in other studied hormones. So we concluded that sleep deprivation have negative effects on some blood parameters and some reproductive hormones that may impact the health and fertility of individuals.

**Keywords:** Sleep deprivation, Reproductive hormones, Men volunteers, Women volunteers

## Introduction

Sleep is a rapid and reversible condition of behavioral immobility with great sensory responsiveness reduction and is related to the regulation of immune, autonomic and neuroendocrine systems that are important for reproduction [1].

During the day many deleterious and unwanted harmful toxic products, including free radicals, accumulate. While sleep is

very important for the elimination of toxic products, including all these excess accumulated products. Thus sleep increases endogenous antioxidant mechanism efficiency and plays a great role as an antioxidant [2].

The sleep-wake cycle is affected by the light and dark cycle. There is a nucleus in the hypothalamus known as the suprachiasmatic nucleus (SCN) that receives information of light and dark through retinohypothalamic fiber [3]. Neural and hormonal signals are sent from SCN that regulates the sleep-wake cycle via secretion of melatonin from the pineal gland antioxidant [2]. The pineal gland is influenced by light and dark; therefore, secretion of melatonin has a complex role in the alteration of ovulation and secretion of GnRH inhibition [4]. Melatonin is related to the circadian function that affects many biological functions including reproductive and fertility [3].

One of the consequences of an industrialized society that impacts individuals health is sleep deprivation which is a significant human being problem and contributed to several diseases [5], via its ability to change neurochemical, behavioral,

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and hormonal pathways [6]; besides, it creates stress and hence enhances the generation of oxidative stress that have adverse effects on the components of blood tissue [7, 8].

Sleep deprivation is related to several adverse physiological consequences such as disturbances of metabolic, immune, and endocrine function [9] with harmful stress that negatively affects the physiology of vital organs as the liver, kidneys, brain, and reproductive organs [10]. As a consequence of sleep deprivation is an increase in the level of stress factors that accelerates biological aging [11] and decreases serum testosterone concentration [12]. In healthy men, sleep deprivation has recorded a reduction in serum androgens including testosterone [10], which can hinder gonads function and greatly decline the fertility rate [13].

The impact of stress as a result of sleep deprivation promotes stimulation of hypothalamo-pituitary-adrenal axis (HPA axis), which elevates plasma corticosterone level and concomitant alteration in the level of testosterone [14] via alteration in LH pulses [11], and can exert adverse effects for different reproductive hormones [15]. So the study was carried out to explore the impact of sleep deprivation on the health and fertility states of individuals through evaluation of some blood and hormonal criteria.

## Materials and Methods

The study was carried out among adult healthy individuals of Kirkuk city aged between 20 to 45 years old including 50 men and 50 women suffering from sleep deprivation, the average sleep time/day=4-6 hours for at least during one year, while control subjects' average sleep period was 8 hours/day.

Five ml of blood samples gathered from all volunteers at 3-4 p.m. were from women at the luteal phase from the cubical vein by disposable syringes (5 ml capacity). One ml of blood kept in EDTA tubes for complete blood count tests by Automated blood analyzer SAW Lab (Sweden) including Red blood corpuscles count, the White blood cells count (WBCs), platelets count, differential leucocytes count (DLC), % of PCV, and concentration of hemoglobin (Hb), and mean corpuscles volume (MCV). While 4 ml of blood kept in jell tubes at R.T., serum was separated by centrifuge (Beckman) 5000 RPM for 10 minutes and kept in Eppendorf tubes in deep freeze (-20 c°) for hormonal assay.

For detection of reproductive hormones: Follicular stimulating hormone (FSH), Luteinizing (LH), prolactin, and testosterone in the serum of individuals were carried out with Biomerieux kits (France) by VIDAS instrument depending on the principle of Enzymes linked fluorescent assay techniques antioxidant [2].

### Statistical analysis

Data was analyzed by T-test, while means of differences assessed by multiple limited Duncan test were  $P < 0.01$  and  $P < 0.05$ .

## Results and Discussion

**Table 1** revealed that the impact of sleep deprivation on some blood parameters, were in men with a recorded significant decrease ( $p \leq 0.05$ ) in the Hb concentration ( $14.2 \pm 0.7\%$ ) gm/dl and % of PCV ( $41.1 \pm 0.7$ ) as compared to the control group ( $15.1 \pm 0.37$ ) g/dl, and ( $44.1 \pm 1.1$ ) respectively but significant increase was in MCV concentration ( $86.6 \pm 0.59$ ) fl as compared to control group ( $83.9 \pm 1.1$ ) fl. While there was no remarkable differences ( $p > 0.05$ ) in RBCs, platelets (PLTs), WBCs count, and DLC count including granulocytic leucocyte (GRAN), lymphocyte (LYM), and monocyte (MON) as compared to the control group.

**Table 1. The Effect of Sleep Deprivation on some Blood Parameters in Men**

Blood Parameters	Sleep deprivation group M $\pm$ SE	Control group M $\pm$ SE	Significance
<b>RBCs</b> ( $10^6$ corposcles/ $mm^3$ )	5.112 $\pm$ 0.085	4.944 $\pm$ 0.14	Ns
<b>Hb (g / dl)</b>	14.2 $\pm$ 0.23	15.1 $\pm$ 0.37	*
<b>PCV%</b>	41.1 $\pm$ 0.71	44.1 $\pm$ 1.1	*
<b>MCV fl</b>	86.6 $\pm$ 0.59	83.97 $\pm$ 1.1	*
<b>PLTs (<math>10^5</math> /<math>mm^3</math>)</b>	203.8 $\pm$ 6.4	220 $\pm$ 12	Ns
<b>WBCs (<math>10^3</math>cells/<math>mm^3</math>)</b>	8.67 $\pm$ 0.42	8.17 $\pm$ 0.43	Ns
<b>GRAN%</b>	5.46 $\pm$ 0.36	4.85 $\pm$ 0.30	Ns
<b>LYM %</b>	2.848 $\pm$ 0.14	3.07 $\pm$ 0.019	Ns
<b>MON %</b>	0.438 $\pm$ 0.024	0.412 $\pm$ 0.023	Ns

\*: refers to significant differences ( $p < 0.05$ )

Ns: refers to no significant differences ( $p > 0.05$ )

The results of the study on some blood parameters in women volunteers shown in **Table 2** recorded no remarkable differences ( $p > 0.05$ ) in studied blood parameters despite some alterations in sleep deprivation of women as compared to the control group.

**Table 2. The Effect of Sleep Deprivation on some Blood Parameters in Women**

Blood Parameters	Sleep deprivation group M $\pm$ SE	Control group M $\pm$ SE	Significance
<b>RBCs</b> ( $10^6$ corposcles/ $mm^3$ )	4.146 $\pm$ 0.14	4.293 $\pm$ 0.14	Ns
<b>Hb (g / dl)</b>	12 $\pm$ 0.37	12.43 $\pm$ 0.16	Ns
<b>PCV%</b>	35.23 $\pm$ 1.1	33.32 $\pm$ 1.7	Ns
<b>MCV fl</b>	84.50 $\pm$ 1.2	80 $\pm$ 3.3	Ns
<b>PLTs (<math>10^5</math> /<math>mm^3</math>)</b>	225 $\pm$ 13	240.9 $\pm$ 11	Ns
<b>WBCs (<math>10^3</math>cells/<math>mm^3</math>)</b>	9.35 $\pm$ 0.38	9.68 $\pm$ 0.26	Ns
<b>GRAN%</b>	6.05 $\pm$ 0.36	6.13 $\pm$ 0.30	Ns
<b>LYM %</b>	2.79 $\pm$ 0.17	3.24 $\pm$ 0.16	Ns
<b>MON %</b>	0.428 $\pm$ 0.019	0.424 $\pm$ 0.019	Ns

Ns: refers to no significant differences ( $P > 0.05$ ).

**Table 3** showed that the effect of sleep deprivation on concentration of some hormones in men, recorded significant decline ( $P < 0.05$ ) in LH level ( $4.0 \pm 0.33$ ) mIU/ml and non-significant alterations ( $p > 0.05$ ) in the level of testosterone hormone ( $2.5 \pm 0.26$ ) ng/ml as compared to control group ( $5.08 \pm 0.44$ ) mIU/ml, and ( $2.28 \pm 0.35$ ) ng/ml, respectively. While prolactin recorded remarkable increment ( $P < 0.01$ ) in sleep deprivation of men ( $11.51 \pm 1.0$ ) ng/ml as compared to control group ( $7.95 \pm 0.73$ ) ng/ml. However, no significant alterations ( $p > 0.05$ ) were observed in FSH level between sleep-deprived men and control group.

**Table 3. The Effect of Sleep Deprivation on Concentration of FSH, LH, Testosterone, and Prolactin**

Hormones in Men			
Hormones	Sleep deprivation group M $\pm$ SE	Control group M $\pm$ SE	Significance
FSH ( $\mu$ IU/ ml)	$3.56 \pm 0.58$	$3.09 \pm 0.43$	Ns
LH ( $\mu$ IU/ ml)	$4.0 \pm 0.33$	$5.08 \pm 0.44$	*
Testosterone (ng/ml)	$2.5 \pm 0.27$	$2.28 \pm 0.35$	Ns
Prolactin (ng/ml)	$11.51 \pm 1.0$	$7.95 \pm 0.73$	**

\*: refers to significant differences ( $P < 0.05$ )

\*\*: refers to significant differences ( $P < 0.01$ )

Ns: refers to no significant differences ( $P > 0.05$ )

**Table 4** has shown that the concentration of hormones in the serum of sleep-deprived women volunteers recorded a significant decline ( $P < 0.05$ ) in prolactin level ( $11.73 \pm 1.6$ ) ng/ml as compared to the control group ( $15.9 \pm 1.7$ ) ng/ml. While, there was no significant changes ( $P > 0.05$ ) in activities of FSH, LH, and testosterone hormones as compared to the control group.

**Table 4. The Effect of Sleep Deprivation on Concentration of FSH, LH, Testosterone, and Prolactin**

Hormones in Women			
Hormones	Sleep deprivation group M $\pm$ SE	Control group M $\pm$ SE	Significance
FSH ( $\mu$ IU/ ml)	$5.92 \pm 0.51$	$6.19 \pm 0.73$	Ns
LH ( $\mu$ IU/ ml)	$4.44 \pm 0.7$	$4.486 \pm 1.6$	Ns
Testosterone (ng/ml)	$0.26 \pm 0.031$	$0.93 \pm 0.66$	Ns
Prolactin (ng/ml)	$11.73 \pm 1.6$	$15.9 \pm 1.7$	*

\*: refers to significant differences ( $P < 0.05$ )

Ns: refers to no significant differences ( $P > 0.05$ )

Components of the blood are considered as the most important and sensitive biophysiological indicators for body homeostasis [16]. Sleep disturbance hurts the biological clock, therefore affects different activities of vital organs and systems [17].

The results of the research in (**Table 1**) revealed a remarkable reduction ( $p < 0.05$ ) in Hb concentration and %PCV in sleep

deprivation subjects; this reduction was compatible with the results of [18], where Hb concentration decreased significantly in animals by exposure to light for long times as compared to exposure for short time.

Exposure of living organisms to light for long periods has negative effects from metabolic stress, so as a result, light stress causes exhaustion of large numbers of RBCs in addition to decreasing the processes of erythropoiesis in bone marrow [9]. Reduction of %PCV in sleep-deprived subjects as compared to control subjects attributed to adrenergic-spleno expansion at stress conditions [19]. While short-term exposure to light as in male rat recorded a significant increment in %PCV [20].

On the other hand, a significant increase ( $p < 0.05$ ) in MCV value in sleep-deprived individuals was compatible with the results of [21] that documented a significant decrease in male albino mice when injected S/C with  $25 \mu$ g melatonin twice a day. But the results were compatible with the results of the study by [9] that was carried out on male rabbits and recorded an elevation of MCV concentration in group exposure to a long period of light.

However, there was no significant changes ( $p > 0.05$ ) in total leucocytes count between groups (**Table 1**) because all individuals were healthy and at normal conditions, or maybe the volunteers were adapted to chronic sleep deprivation.

Sleep deprivation is physiological stress and considered a major problem in human beings [6]. The main regulators of stress response was activation of hypothalamo-pituitary-adrenocortical system and sympatho-adreno-medullary system [22], so alterations in the hormonal parameters in our study recorded a slight increase in the level of testosterone ( $p > 0.05$ ) in sleep-deprived men and were non-significant ( $P > 0.05$ ) in women that was compatible with the results of the study by [23]. Besides, slight alterations in the men's group were explained by stress factors [24].

Synthesis of testosterone depends on signals from the endocrine [3] and neuronal [25], which in turn are influenced by physiological conditions such as stress. Stress augments the secretion of several hormones such as CRH [26], ACTH [27], and corticosterone have an impact on HPG axis function.

Alterations of testosterone level associated with sleep deprivation may be in part due to serotonin-related inhibition of testosterone production [28]. Besides, both serotonin and serotonin receptors have been localized on Leydig cells isolated from the testes of golden hamsters; moreover, serotonin has been capable of suppressing of testosterone production. However, increment of corticosteroid concentration by stressful stimuli may inhibit the HPG axis leading to decrement of testosterone secretion [18]. Additionally, testosterone release may be related to activation of HPA axis inducing elevation in corticosteroids [29]. Exposure to stressful stimuli seems to alter testicular and plasma testosterone concentration [30]. However, there is some evidence that the inhibition of testicular androgen activity observed in chronic stress is associated with the reduction of GnRH and LH levels [31, 32].

In lab animals, sleep loss influences sexual hormones leading to increment of progesterone and glucocorticoids level but

decreases testosterone in male rats [33]. While in female rats it modulates the synthesis and secretion of ovarian hormones [9]. However, our study observed that the decrement of LH levels was associated with a slight decline of testosterone level in sleep deprivation individuals so agreed with the study results of [23]. In the present study, the levels of hormones FSH, LH, and testosterone except prolactin did not decline significantly ( $P>0.05$ ) in women subjects, that may be attributed to a long period of sleep deprivation that became harmful, or the volunteer women were better acclimatized to chronic sleep deprivation than men, so the results were compatible with those of Kao *et al.* (2017) in their study on rats. Moreover, Grant *et al.*, (2018) suggested that they may have suffered from adaptation through long-term exposure in case of chronic sleep deprivation. In addition, they may be attributed to the fluctuation of hormones during different phases of the menstrual cycle [23].

The study also recorded a remarkable decrease in the level of prolactin in sleep-deprived women ( $P<0.05$ ) suggesting the secretion of prolactin associated with duration of exposure to light and other factors. Prolactin secretion is affected by the dopamine-hypothalamo-pituitary axis, stress, light, temperature, etc. [34] which have a great role in lactation, puberty, maturity, and consequently with the fertility rate of women [18]. Sleep disturbance may modulate PRL secretion and thereby may lead to an irregularity concerning hormonal parameters [15]. Moreover, prolactin is inhibited by transient awakening and is profoundly suppressed by sleep deprivation [18].

Although prolactin in sleep-deprived men recorded a remarkable increase ( $P<0.01$ ) as a result of long-term exposure to light (Table 3), the elevated prolactin hurts fertility and fecundity of men through influences on testosterone secretion [35]. Moreover, prolactin has stimulatory effects on dopamine secretion via hypothalamo-prolactin, and prolactin secretion is related to the dopamine level in the serum [18].

## Conclusion

From the results of the study, it can be concluded that the impact of sleep deprivation has adverse effects on the health and fertility of human beings.

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