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## **Association between sleep deprivation and fertility- a literature review**

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**Methods**

A literature review was conducted, based on the PubMed and Google Scholar databases, using keywords “sleep deprivation”, “fertility”, “hormonal homeostasis”, “infertility treatment”, “sleep hygiene”. The primary focus was on meta-analyses, double-blind studies, reviews pertaining to specific medical specialities, and research in basic sciences.

**Association between sleep deprivation and fertility- a literature review**

## **Abstract**

Infertility gained increasing importance throughout our life period in this fast pacing world as increasingly more couples struggle to conceive. Taking into account the cost of fertility treatment there is a good strategy to look into less high-priced options on increasing conception possibilities. In this article we are going to focus on one of them which is sleep. Sleeping hygiene is neglected by many of us as only 8% of polish population rate their sleeping as satisfactory. There are primary matters for instance regular sleep hours, sustaining a healthy diet to make a tremendous change in our mental and as well reproductive health. In the male population deprived sleep is blamed for lower sperm motility, as well as concentration, total count. There is a probability that Leydig cells function and count, cortisol secretion and testosterone levels can be affected but for now we have to conduct more research to rule it out or confirm. For women on the other hand sleep deprivation produces a huge hormonal dysregulation. Temporarily the impact of sleep deprivation is being inconsistent about estradiol, prolactin and melatonin. This article presents a meticulously collected data which shows the connection between sleep and punctuate need for further research.

Key words: sleep deprivation, sleep disorders, infertility, fertility.

## **Introduction**

Nowadays an increasing percentage of the population is having difficulty with conception. Looking at the research nearly 8-12 % couples are being diagnosed with infertility.[1]This produces a great cost on our mental health similar to influence on our financial budgets. As it was shown couples are prepared to pay even as much as 33% of their annual income to try to undertake an IVF procedure due to infertility. Its estimated that every IVF course of treatment is accounted for only 40 % probability in conception. [2] That plays a big role in infertility treatment accessibility to less well off couples . In our own country the cost of governmental infertility program was over 10,7 million EUR between the year of 2012 and 2020 and this not comprise the individual households out-of-pocket expenses which can be burden to many [3] . In this highly costly problem it is advisable to look for some low effort and low cost actions, which we can adjust to our daily lives to increase chances of conception. One of them is taking care of our sleeping hygiene. Sleeping in a lot of adults lives is highly disturbed by working

schedules and lifestyle. We define sleep hygiene as actions taken to enhance the quality and amount of sleep. To understand the topic better we should point out the basic assumptions of sleep hygiene which are: recurring resting timing, healthy daily habits as daily exercises and adequate diet, abstaining from alcohol and caffeine beverage, cognitive relaxation before rest. [4] In this research diagnosing sleep quality among Polish adults only 8 % were satisfied by it. [5]. Not only in our country we face that kind of problems ,nearly 14.71% of US adults suffer from sleeping disorders which show us the volume of its impact on considerable section of world's population [6].

In this article we are going to review in depth the influence of sleep deprivation on fertility in human population. As taking into account the tremendous cost of infertility treatment is really important for professional as well as general population to know the importance of basic necessity as undisturbed , high quality sleep on our fertility.

### **Influence of sleep depravation on men fertility:**

Men fertility relay on a handful of hormones which cooperate with each other making possible our reproductive system to work. The main hormonal axis is hypothalamo-pituitary-gonadal/testicular axis which produce the pulses of LH and FSH hormones. The hormones activate accordingly Leydig cells for testosterone production and Sertoli cells to help spermatogenesis. This hormones not only act on semen production but also determine to some extent men sexual behaviour [7].

As we all know sleep plays a huge role in our daily functioning. Lately more and more researchers got involved into detection of sleep deprivation and influence of it on men's fertility. The data says that in male subjects with sleep disorders there was decrease of sperm concentration, progressive mobility and total sperm count[8] This systematic review pointed out that there was no significant correlation between sleeping disorder and testosterone level. The authors will try to discuss this finding thoroughly in the incoming part of this article.

### Semen quality

Semen parameters check up is one of the first tests taken by infertile couples. We evaluate in this test many parameters including volume of ejaculate, liquefaction time, color and smell, viscosity, pH. Later semen is assessed by laboratory specialist for inspection where they determine the total number of sperm in 1 mm of semen, motility, viability and morphology of

sperm cell. [9] Semen quality is highly susceptible to sleeping disorders as research says. In the experiment male rats have been put under sleep restriction which led to decrease of sperm motility in experimental group.[10] Other research on healthy men group brought us to conclusion that in the group with shorter sleep duration total and progressive sperm motility was lower. The quality of sleep played as well a huge role. In the group with poor sleep quality the total sperm count and motility were decreased [11] In another experiment sleep deprivation was correlated with lower sperm concentration, lower sperm count and percent motile as well as the sperm being more commonly abnormal. [12]In another paper there was more variability but the sleep disorders still accounted for lower motility of sperm.[13] As we see not only the duration of sleep but also the quality of it plays a huge role in men semen features. The main quality which seem to be the most susceptible to changes, and were influence of sleep deprivation was repeatable confirmed ,is motility of sperm cells.

#### Leydig cells apoptosis

Leydig cells play a role in the production of testosterone stimulated by LH which is activated by hypothalamo-pituitary-gonadal axis [14]. LH binds with LH-receptors located on Leydig cells which start the intracellular cascade ending in testosterone production.

Some research says that lack of sleep can connect with lower count of Leydig cells and lower amount of testosterone. This could be connected to high susceptibility of Leydig cells to reactive oxygen species (ROS)[15]. Still more research has to be made to find out if this phenomenon is repeatable in the human population.

#### Corticosteroids secretion

The long periods of unrest produce increase of corticosteroids levels in plasma. Cortisol secretion has a circadian rhythm which means the hormone is released throughout a day with the biggest amount of secretion falling on the beginning of the day[16], [17] [18]. This cycle can be easily disturbed by inadequate sleeping pattern or sleeping hours variability. Some research shows that higher cortisol levels could play a role in male infertility. In the systematic review about this topic there were four experiments taken into account from which three determine significant correlation between higher level of cortisol in infertile men group. As they pointed out this subject is not definitely clear as infertile men are prone to higher levels of stress and depressive disorders[19].

## Testosterone secretion

We could not determine a clear connection between testosterone secretion and sleep deprivation. In the systematic review they only showed the connection between total sleep deprivation, therefore there were not connection between partial sleep depravation and testosterone levels [20]. In other research there was a significant difference between control and experimental group as the author said : “Daytime testosterone levels were decreased by 10% to 15% in this small convenience sample of young healthy men who underwent 1 week of sleep restriction to 5 hours per night”[21].In another paper there were no significant changes in testosterone concentration [22]. For now by taking into account accessible research on the connection between sleeping deprivation and testosterone levels was not definitely attested.

While sleep disruptions significantly affect men’s reproductive health, they also have notable effects on women’s fertility.

### **Influence of sleep depravation on women fertility:**

Sleep patterns in women going through her menstrual cycle differ significantly depending on the day of the cycle and the level of hormones which are released in this time.

During the luteal phase sleep quality is significantly poorer through all the women. That is attributed to progesterone effect on the female body. In women with severe premenstrual syndrome the quality of sleep in premenstrual and during menstrual phase is remarkably worse[23][24][25].This can make investigation on this topic even harder in this population group.

Women with irregular sleeping schedules are prone to lowered fertility levels and greater risk of pregnancy loss. In the investigation the percent of infertility was 9,9% in control vs 11,3% in experimental group which was constructed by female shift workers. As we can see the difference between this two group is significant [26]. The other paper pointed out that deprived sleeping can lead to hormonal dysregulation as LH, FSH, TSH, corticosteroid, melatonin secretion. The date about it is variable and i am going to explain this subject comprehensively in subsequent subsections [27].

## LH and FSH

Human gonadotropin group consist of luteinizing hormone (LH), follicle stimulating hormone (FSH) and chorionic gonadotrophin (hCG). Their role lies in encouraging follicular growth and stimulating ovulation [28].

Some experiments say that FSH is mainly required in the conception process as LH does not play equally an important role in it. In the research with two groups: long- time sleepers and short time sleepers we could see a significant 20% increase of FSH in the long-sleepers group. There was no notable connection between the period of sleep and LH secretion [29].

### Melatonin

Melatonin plays a important role in our circadian rhythm as it is mainly secreted during the night. Its secretion is stimulated by lack of light stimulation. Shift work, lack of sleep or lack of proper sleeping hygiene can deeply affect its secretion [30].

In the experiment during sleep deprivation time spans melatonin levels were notably higher but came back to baseline levels after recuperation of sleep [31]. They were not testing on long time sleep deprivation in women. The higher levels of melatonin are lowering the function of the anterior pituitary-ovarian axis which result in release of LH and FSH hormones. In group living in Arctic regions the pregnancy amount is lower through the winter period [32]. Still the connection between melatonin secretion, sleep deprivation and influence of it on woman fertility is staying unclear.

### Prolactin

Prolactin have an important role during human pregnancy. It prepares the body for the production of breast milk by being a source of stimulus for mammary glands to increase its volume. In the other hand increased levels of prolactin prevent production of different sex hormones [33].

The level of prolactin in a group of infertile women are markedly higher [34]. Sadly the research made on humans studying the influence of sleep deprivation on prolactin level was mainly focused on men. The research focused on women showed decreased in prolactin after partial sleep deprivation which is showing us an unclear picture of this problem. As the experimental group consisted of only 10 women, more research has to be conducted to show a clearer view on this matter [35].



## TSH

TSH production is stimulated by the TRH. This hormone stimulates likewise the production of prolactin. Elevated TSH levels are connected with oligomenorea and other menstrual cycle interruption [36].

Higher TSH levels are shown through infertile women as well as higher levels of prolactin. The connection between TSH and sleep deprivation was found in the conducted research. It produces the increase of TSH hormones in human organism [37][38].

## Estradiol

Estradiol function is really broad but here we are going to focus on its involvement in female fertility. Estrogens and one of them in particular, estradiol play a crucial role in reproductive system. Estradiol in uterus stimulates muscle proliferation, enhances secretion of cervical mucus together with relaxation of the muscular membrane of the cervix. All of this helps the process of fertilization. With all of this positive role it also lowers the secretion of FSH which correlates with absence of ovulation [39]. As the research says regular sleep plays a role in lowering the level of estradiol by 60% [40].

## Irregular cycles

Regular menstrual cycle should last between 21 and 35 days. The average duration of menstruation should be between 3 and 7 days [41][42]. We can try to connect irregular cycles to irregular sleeping schedules. Women who are subjected to sleeping less than 5 h a day were exposed to higher risk of period irregularity [43]. The other study says that shift workers are more prone to period irregularities [44]. In one of the newest cohort study results were not repeated. We need more investigation to clarify this matter as it can change our minds in the future about this subject [45][46].

## **Sleep quality impact on couples undergoing infertility treatment**

Infertility is described as absence of pregnancy after 12 months or more of unprotected intercourse [47]. The research which focussed on women population proved that women with better quality of sleep were more likely to become pregnant. From the group of women having

more than 5 points in evaluation using The Pittsburgh Sleep Quality Index (PSQI) only one in five become pregnant. In comparison the group with better quality of sleep ended with fertilization level of 36% [48][49][50]. In another research where the connection between chronotype and fertility was observed women with shorter sleep than 7 hours were more likely to become pregnant. It was important that the sleep happen before 4AM [51]. Focusing on men, we could present another paper where participants were separated into two groups using PSQI: group with PSQI <5 and group with scoring  $\geq 5$ . Men with notably better quality of sleep ended up fertilizing in 67,36%, in comparison with the second group with fertilization level placed at 60,13% [52]. Some investigations were focusing on both genders and the influence of sleep patterns in couples. There was a confirmed association between longer sleep and higher chances of conception [53]. Research unanimously speaks of a positive impact of high quality of sleep on fertilization chances during infertility treatment [54].

## **Conclusion**

In this article we discussed research information about the link connecting sleep deprivation and fertility. We focused on the female group, male group and couples undergoing infertility treatment. In all three groups we found significant correlation. To summarise in men group there is a clear connection between sleep deprivation and sperm motility level which is significantly lower. Influence of sleep deprivation can be seen as well in testosterone level, Leydig cells count and corticosteroid levels but the results are not unanimous. Taking into consideration women population there were a significant connection between decrease of FSH, increase of TSH and sleep deprivation. Both corresponded with decreased fertility. The connection of estradiol levels, melatonin secretion in sleep deprived patients as its impact on fertility was not consistent. As we can see there is still a lot of research to be done in some topics whereas in others the connection between sleep deprivation and decrease of fertility is clearly recognizable. Developing healthy sleeping habits can be a relatively easy matter to incorporate in our lives to increase chances of conception. Taking into account a tremendous cost of fertility treatment this could be a new path of approach in this problem.

## **Disclosure**

### **Author's contribution:**

Conceptualisation: AF, AK

Methodology: WF, AD

Software: AD, BU

Check: JRD, JL

Formal analysis: AM, MJ

Investigation: MN, AK

Resources: BU, JL

Data curation: MJ, WF

Writing-rough preparation: JRD, AF

Writing review and editing: AD, AM

Visualisation: MN, BU

Project administration: AD, AK

All authors have read and agreed with the published version of the manuscript.

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