



Review Article

An overview on the effects of power frequency electromagnetic field exposure on the female reproduction system, pregnancy outcome and fetal development

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KEYWORDS

Nonionizing radiation

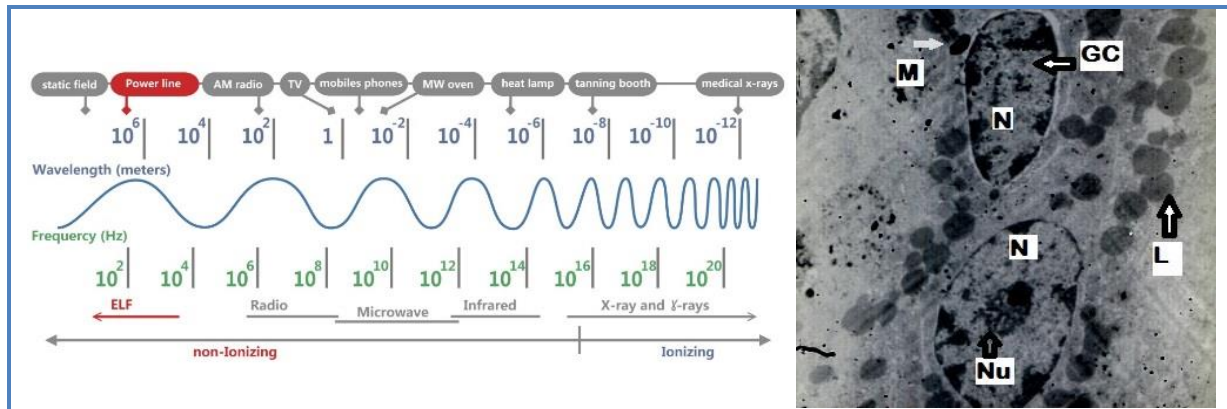
Electromagnetic field

Female infertility

ABSTRACT

This article presents a review of the published scientific studies on the potential adverse effects of power frequency electromagnetic field (50-60 Hz) from domestic and occupational sources and electric transmission lines on female reproduction system and pregnancy outcome. In this review, publications in English were searched in the ISI Web of Knowledge, PubMed databases and Google Scholar from January 2000 to December 2017 articles. For ascertaining the reliability of study, data were extracted independently and in duplicate by two investigators. According to some of the conducted studies, environmental exposure to power frequency EMF (electromagnetic field) exposure was found to adversely affect sex hormones, female genital system, embryonic development, pregnancy outcome and fetal and offspring development, while other studies reported no significant effect of power frequency EMF exposure on reproductive parameters and embryonic and fetal development. Overall, the results were not convergent and there was controversy regarding the findings. However, it can be concluded that a part of controversy can be attributed to differences in field strength and exposure time, the experiment condition in terms of in vivo and in vitro which had a significant impact on the observed results.

Graphical Abstract



Introduction

From the beginning of the 20th century, environmental exposure to electromagnetic fields from man-made devices is continuously growing. Biological effects of electromagnetic fields on the human body depend on several physical factors such as field intensity and frequency. In recent years, the chance of exposure to power frequency magnetic fields has increased as a result of increase in the use of electricity in human life. Rapid development of electronic equipment and steadily increasing of exposure to electromagnetic field is presumed to be involved in reproduction problems and infertility [1–4]. By definition, non-ionizing radiation is a type of energy emission which do not have enough energy to release electron from the atom of materials. Basically, non-ionizing part of electromagnetic field can be divided in to LF (Low Frequency) and Radio frequency electromagnetic fields [5]. See Figure 1 for more detailed information on EM radiation spectrum. Moreover, low frequency electromagnetic field is itself is composed of extremely low frequency (ELF) with frequencies up to 300 Hz, and intermediate frequency with frequencies between 300 Hz and 10 MHz. Induction-heating ovens, computers, compact fluorescent lamps, inductive metal heating and welding and anti-

theft systems at the exits of shops are examples of intermediate frequency electromagnetic fields sources [6, 7]. Also, it should be noted that the use and transmission of electricity in general generate the ELF- electromagnetic field (EMF) [8]. In the past three decades, exposure to environmental ELF-EMF is one of the major global concerns and matter of debate from the health and safety point of view [9]. In fact, we are surrounded with many sources of extremely low electromagnetic fields specially power lines, transformers and domestic and industrial devises that operate with 50-60 Hz power. Alternating Current power lines (Underground cables and overhead transmission power lines) and electronic devices are the main sources of ELF-EMFs called power frequency electromagnetic fields. The intensity of power frequency electromagnetic fields are stronger near the power lines and are decreased rapidly by distance. Magnetic field strength of household appliances is about 4 μ T EMF and is differed from 0.01 to 1 μ T inside and outside of house. It seems that residential long-term exposure to power frequency magnetic field of people living near the buildings where electric power transformers are installed can be extended to several tenths of μ T [6,10]. Electric and magnetic fields act independently in the range of power frequency electromagnetic fields. Therefore, effects of the external electric

and magnetic fields on the human body can be computed independently in this range. Direct interaction of extremely low frequency electromagnetic fields with body is done by inducing surface charge and electric fields inside the body that causes internal exposure and eddy currents within tissues which leads to increased oxidative-stress by reactive oxygen

species production. Orientation of the external field and the conductivity of tissues determine induced currents patterns [11, 12]. On the other hand, increased oxidative stress could cause, oxidative DNA damage and antioxidant system activity alternation leading to health risks [13, 14].

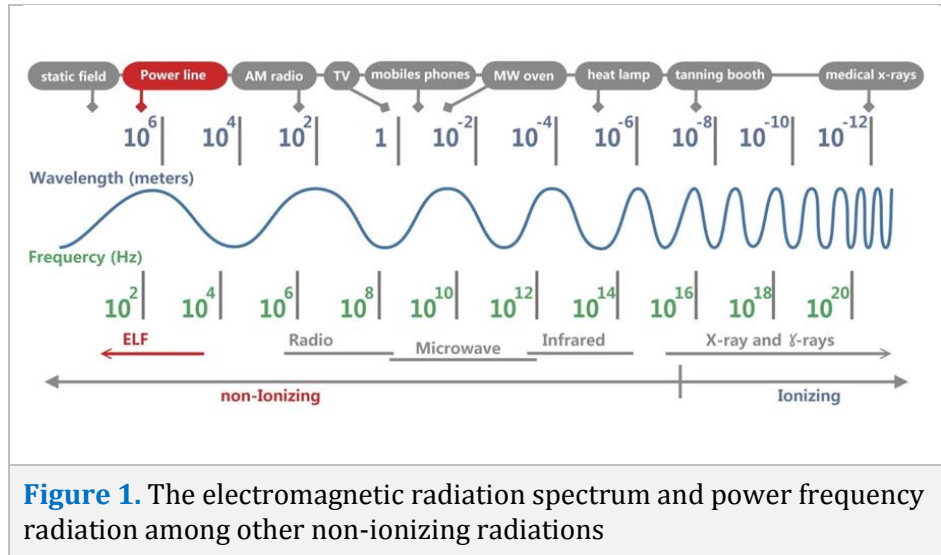


Figure 1. The electromagnetic radiation spectrum and power frequency radiation among other non-ionizing radiations

The magnetic field inside the body is the same as that of air because the permeability of tissue and air are the same for magnetic field. The electric field induced by external electromagnetic fields can be computed with the following equation (1): [15]

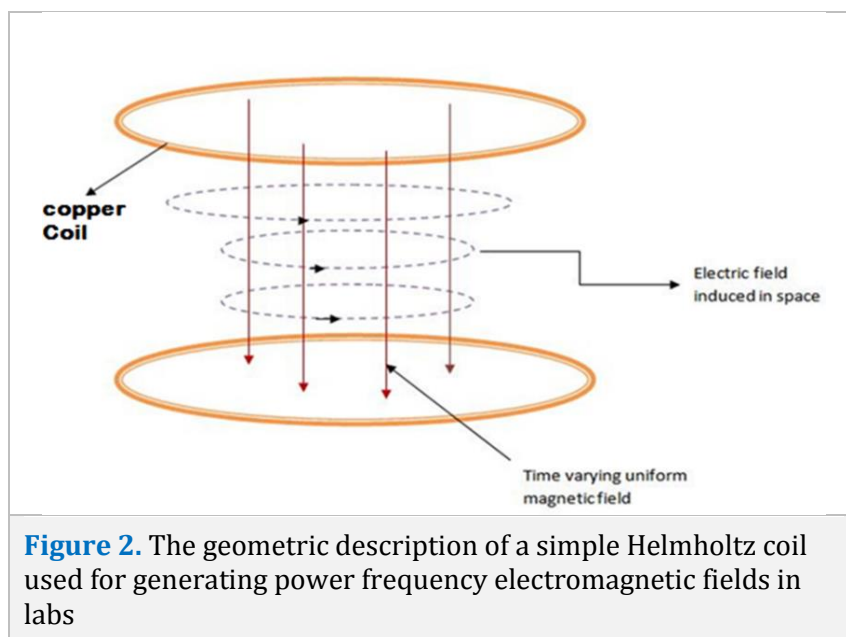
$$E_{normal,bio} = (\omega_{ELF} \cdot \epsilon_0 / \sigma_{bio}) E_{normal,air} \quad (1)$$

where $E_{normal,bio}$ and $E_{normal,air}$ are the normal components of the electric field in the human body and air, respectively, and ω_{ELF} , σ_{bio} , and ϵ_0 are the Alternating Current line frequency, whole body conductivity, and electrical permittivity of space, respectively. Most of performed studies about the effect of EMF on biological systems have been implemented by using instruments based on Helmholtz coils. A representation of EMF production in a simple Helmholtz coil is

represented by Figure 2. Studies show that the induced electric field is six or five times smaller than external power frequency electromagnetic field. The International Agency for Research on Cancer (IARC) has classified ELF-EMF as possible carcinogens to humans. Some recent epidemiologic studies have indicated the relationship between power frequency electromagnetic field exposure and increased incidence of health problems including children leukemia, Alzheimer, depression, birth defect, miscarriage and pregnancy and fetal growth problems among individuals exposed to ELF-EMFs occupationally or domestically [16, 17]. Reviewing the scientific journals shows that, in recent decades, concerns about declining fertility rates in the human population are growing. According to global statistics, an

average of one in six couples has fertility problems [18]. To date many in-vivo and in-vitro experiments have shown that ELF-EMF radiations are able to affect morphology and function of sperm [19–21], reproduction system [22, 23], sex hormones [11, 22, 24], estrous cycle, Follicular growth²⁵ and also can causes testicular germ cells apoptosis [26, 27], and changes in embryo development in human and animals. However, there are many studies

which have shown no significant biological damage to human and animal reproductive system. Finally, adverse effects of EMF on human and animal reproductive system function and fertility is still unknown and under debate [28, 29]. In the present review, the potential effects of power frequency electromagnetic field on female reproduction system and pregnancy outcome and fetal development are summarized.



The impact of power frequency electromagnetic field on female genital system

A significant number of studies have been published on the adverse effects of power frequency electromagnetic field (50-60 Hz ELF-EMF) on female reproduction system both in human and animals. The data was summarized in Table 1. The female genital system is composed of the uterus, ovaries, fallopian tubes, the released oocysts, and germ and somatic cells in their tissue. An ovarian follicle consists of oocyte and Granulosa cells which are essential for survival and maturity of ovary. It is

speculated that with increasing application of EMF in daily life, the reserved oocytes of females will decrease which leads to more infertility among human population. For example, in cows exposed to EMF with frequency of 60 Hz, estrous cycle was extended considerably [30]. Cao and colleagues was conducted a study on reproduction rate of female mice and embryo development (Cao et al., 2006). In their study, the EMF source had the frequency of 50 Hz and intensity of 1.2 mT and the mice were exposed to EMF 8 hours daily. Their results revealed increased miscarriage and fetal loss in mice exposed to Power frequency magnetic field. Additionally,

exposure to power frequency electromagnetic field during the developmental period could cause disruption of folliculogenesis process and oocyte differentiation and Granulosa cell alternation and morphologic changes of ovary [31]. Mansouri et al. worked on the FSH, LH and estrogen levels in rats exposed to 50 Hz EMF with intensity of 3 mT for 7 weeks exposure time, 4 hours daily. Their results showed reduced level of these hormones due to EMF

exposures [11]. A recent study showed that exposure to EMF may cause changes in the morphology and biochemistry of the rat ovarium [32]. Similarly, Aksen and coworkers showed that 50 Hz EMF with intensity of 1 mT can cause ultrastructure alternations of ovaries [12]. Also, Cecconi and colleagues reported that 50 Hz EMF has no impact on follicular growth but it influenced intensively the formation of antrum [27].

Table 1. The list of studies on the impact of power frequency electromagnetic field on female genital system

study	Power frequency EMF properties	Exposure properties	In-vivo/in-vitro	Result
Cao et al.	50 Hz, 1.2 mT	whole pregnant period (8 h/d) Long-term exposure	mice	Adverse effect
Roshangar et al.	50 Hz, 3mT	4hr/day during the pregnancy period of BALB/c mice Long-term exposure	BALB/c mice	Adverse effect
Elbetieha et al.	50 Hz, 25 μ T sinusoidal	90 days Long-term exposure	Adult male and female mice	No exposure-related adverse effect
Chung et al.	60 Hz, 0.5 mT	21 h/day from gestational day 6 through lactational day 21 Long-term exposure	female Sprague-Dawley (SD) rats	No exposure-related adverse effect
Kowalcakzuk et al.	50 Hz, 20 mT sinusoidal	day 0 to day 17 of gestation of CD1 mice Long-term exposure	Pregnant CD1 mice	No exposure-related adverse effect
Al-Akhras et al.	50 Hz, 25 μ T sinusoidal	90 days Long-term exposure	Sprague-Dawley rats	Adverse effect
Cecconi et al.	33 or 50 Hz,	5 day culture period Short-term exposure	in-vitro mouse pre-antral follicle	Adverse effect
Mansouri et al.	50 Hz, 3 mT	7 days/week for 6 weeks Long-term exposure	Wistar rats	Adverse effect
Rodrigues et al.	60 Hz 30 μ T Horizontal	16 h/day for 4 week Long-term exposure	lactating, pregnant Holstein cows	Adverse effect
Akdag et al.	50-Hz 1-mT	50 or 100 days Long-term exposure	Wistar albino rats	Adverse effect

EMF: Electromagnetic field

SD: Sprague-Dawley

CD1: The CD-1 mouse is a multipurpose research animal model that can be used in such fields as toxicology (safety and efficacy testing), aging and oncology.

The transmission electron micrographs of a rat ovary exposed to power frequency

electromagnetic field was shown in Figure 3. As it can be seen, there are marked changes in

ovary due to electromagnetic exposure. Shape of oocyte nuclei was changed and morphological change of zona pellucida and granulosa cell and lacking of lipid droplets are obvious in the ELF-EMF exposed tissue micrograph. However, there are studies which contradict the results of previously explained studies. A study by Aydin et al. was performed on female mature rat and the effect of 50 Hz EMF was assessed. They examined the hormonal variations, biochemical parameters

and histopathological status of uterus and ovaries. The results indicated lower activity of plasma catalase in the exposure group, while there was no effect on progesterone and beta estradiol levels as well as morphology and weight of uterus and ovaries [33]. Additionally, in another study, body and uterine weights were not affected in female mice exposed to 50 Hz field, but ovarian weight was significantly increased [16].

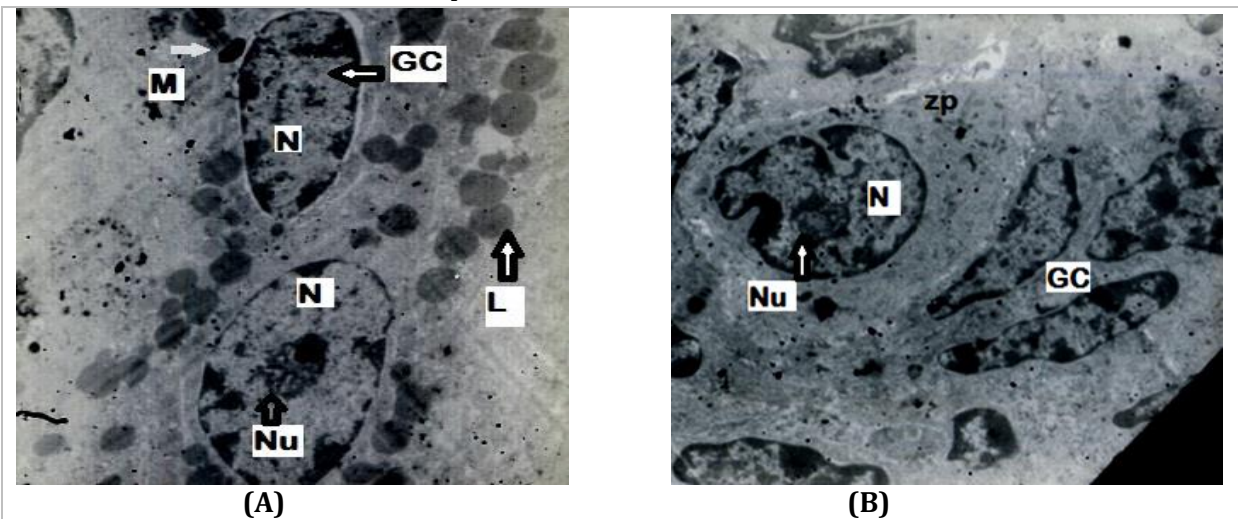


Figure 3. The transmission electron micrographs of a rat ovary. (A) Healthy ovary (B) exposed to power frequency electromagnetic field, 3 mT, 50 Hz. Granulosa cell (GC), zona pellucida (ZP), Mitochondria (M), Nuclei (N) and Nucleus (Nu) of oocyte, and lipid droplets (L) are visible. ($\times 4400$)

The effect of power frequency electromagnetic field on embryonic development and pregnancy success

The summary of studies performed on embryonic development and pregnancy success is seen in Table 2. Adverse pregnancy outcomes such as birth defects, low birth weight babies and congenital anomalies are significant public health concerns [27]. It seems that TV watching and using cellphones in the first semester of pregnancy increased the risk of birth defect and decelerated the growth rate of fetus especially in women with history of high risk pregnancy [34]. Also, another investigation revealed that

exposing of pregnant women to electromagnetic field during the first to 20th day of pregnancy reduced the percentage of living embryo in studied population. Moreover, a study by de Vocht and colleagues indicated that living in the vicinity of ELF-EMF sources during pregnancy could result in under-growth of uterus of embryo [35]. Similarly, in a study by Hug et al. the results revealed that for magnetic fields above 0.2 μ T there was no increased cancer risks in children whose fathers were occupationally exposed to EMF. Also, no evidence for a risk increase at magnetic field levels exceeding 1 μ T was reported. Additionally, there was no relation

between maternal occupational exposure and increased cancer risks. Finally, they concluded that the exposure of parents with electromagnetic field with frequency of 50 to 60 Hz before and during pregnancy could not play a crucial role in developing of cancers in children [36]. Some studies showed that power frequency electromagnetic field has harmful effects on the ovarian follicles and embryo development in offspring of exposed female rats. And, malformed fetus and fetal loss was reported. Also, a delay in testicular development of male offspring and reductions in the number, height, and volume of seminiferous tubules of male offspring were mentioned as adverse effects of exposure to power frequency electromagnetic field [29, 37–39]. In a histological study by Rajaei and co-workers, on the effect of ELF-EMF on reproduction system of female mice, it was shown a reduced number of flushed blastocysts as well as an increase in the height of epithelial cells of fallopian tubes [40]. In similar studies on ELF-EMF exposures, alternations in uterus and ovaries of rats, and changes in follicular growth and stereos cycle were observed. Moreover, it caused congenital abnormalities, abortion and birth defect (Cao et al., 2006). In a study by Roshangar and colleagues (2014), they used 30 pregnant BALB/c mice and exposed them to the EMF of 50 Hz and 3 mT, 4 hours daily for six weeks. Dams were studied histologically for possible damages. Their results showed that the nest of ovaries of dams was shrunk and irregular pattern was seen. Also, primordial follicles were seen shrunk and less heterochromatic and the cytoplasm was perforated. It was concluded that exposure to EMF during development period of fetus could

affect differentiation and folliculogenesis of ovary. Thus, it increases the probability of infertility by reducing oocyte reserve [31, 41]. It should be added that the literature review shows some different results with the above mentioned studies. For instance, in contrast to the previous studies, a study by Chung and colleagues was conducted on pregnant mice which exposed to 60 Hz magnetic field 0.5 mT during 6th to 20th days of pregnancy [42]. No biological effect was observed in embryos and off-springs. Also in another study, pregnant Wistar rats were exposed to low frequency EMF and no significant changes were seen in body weight and number of fetus [43]. In the study of Mizuno and co-workers on the effects of 50 Hz, (0.1–1 T), 0.5, 5 mT EMF on ICR mice, no major effects on reproduction and development were reported [44]. Also, no significant differences in number of live fetuses, sex ratio, live fetal weight, number of externally abnormal fetuses, and numbers of fetuses with skeletal and visceral anomalies were observed. In other studies, no exposure-related changes in pregnancy length were observed in rats exposed to power frequency magnetic field of 0.5 mT and no changes in Parameters of growth, behavior, and reproductive performance of first and second generations of rats exposed were seen [42]. Additionally, in other similar investigations, no abortion or congenital malformation following prenatal exposure to 50 Hz power frequency electromagnetic field was reported [45, 46]. Also, an epidemiological study that was conducted in 2017 showed no significant relationship between Maternal cumulative and exposure to ELF-EMF in pregnant women [47].

Table 2. The list of studies on the effect of Power frequency electromagnetic field on embryonic development and pregnancy success

study	Power frequency EMF properties	Exposure properties	subject	Result
Ohnishi et al.	50 Hz, (0.1–1_T), 0.5, 5 mT	9 weeks, 22.7hr/day female mice, 2 weeks 23.0hr/day male mice before mating-Long-term	ICR mice	No exposure-related adverse effect
Chung et al.	60 Hz, 0.5 mT	21h/day from gestational day 6 through lactational day 21 Long-term exposure	female Sprague-Dawley rats	No exposure-related adverse effect
De et al.	50-Hz, 35.6 μ T (sinewave) and 15.0 μ T (sawtooth)	Day 0 to day 20 of pregnancy for 24 h/day until necropsied on day 20. Long-term exposure 22 h/day on gestational	140356 singleton live births between 2004-2008	No exposure-related adverse effect
Cecconi et al.	60 Hz, 5, 83.3, or 500 μ T	day 6–20 in Sprague Dawley (SD) rats Long-term exposure 13 weeks (3 weeks	in-vitro mouse pre-antral follicle	No exposure-related adverse effect
Khaki et al.	50 Hz, 3 mT	intrauterine +10 weeks after birth) Long-term exposure day 0 to day 17 of gestation of CD1 mice	Wistar rats	Adverse effect
Kowalczuk et al.	50 Hz, 20 mT sinusoidal	Long-term exposure whole pregnant period (8 h/d)	Pregnant CD1 mice	Adverse effect
Cao et al.	50 Hz, 1.2 mT	Long-term exposure 4hr/day during the pregnancy period of BALB/c mice	mice	Adverse effect
Roshangar et al.	50 Hz, 3mT	Long-term exposure 3times/day (30 min), between the 13th day of gestation and the 21st postnatal day	BALB/c mice	Adverse effect
Tenorio et al.	60 Hz, 1 mT	Short-term exposure 50 or 100 days	Wistar rats	Adverse effect
Akdag et al.	50-Hz 1-mT	Long-term exposure	Wistar albino rats	Adverse effect
Aydin et al.	50 Hz 48.21 +/- 1.58 Mili- Gauss	24 hr for 3month Long-term exposure	adult Wistar female rats	Adverse effect
Huuskonen et al.	50-Hz 35.6 μ T	from day 0 to day 20 of pregnancy for 24 h/day until necropsied on day 20	Han:Wistar-strain rats	No exposure-related adverse effect
Hug et al.	ELF-EMF above 0.2 μ T	Case control study	No exposure-related adverse effect

Conclusions and perspectives

In the current paper, we reviewed studies on the effect of environmental exposure to power frequency EMF on reproductive systems, pregnancy outcome and embryonic development. Totally, there were no conclusive results in terms of delivered damage and harmful effects of power frequency (50-60 Hz) EMF. In other words, some studies found adverse effects on sex hormones, female genital system, embryonic development, pregnancy outcome and fetal and offspring development, while other studies reported no significant effect of power frequency EMF exposure on the above mentioned complications. But, considering the reviewed papers we would be able to reach to an approximate conclusion. It means that, in most of animal studies with field strength higher than 0.5 mT and long exposure time, the results showed adverse effect of EMF of female reproductive system, pregnancy and fetus development. However, in other studies which reported no adverse effects, lower field strength and short exposure time were applied. Comparing the studies indicates that the exposure time plays an influencing role in observed damages in animal studies. Additionally, it should be noted here that in some of in vitro studies, harmful effects have been reported for lower field intensities such as 30 μ T and short exposure time. While, as far as we reviewed in this work, epidemiological studies on human population with field strength of less than 0.5 mT have not reported any adverse effect of EMF on female reproductive system so far. Thus, it can be assumed that in addition to field strength and exposure time, the experiment condition in terms of in vivo and in vitro have a significant impact on the observed results. The authors think that a part of the controversies seen in the results of different studies can be attributed to

the differences in the experiment set up and exposure parameters such as exposure duration and intensity of EMF. Thus, to have reproducible, reliable and conclusive results, more organized studies should be conducted with a similar experiment setup and avoiding confounding factors which affect the results. Also, it seems that the in vivo and in vitro conditions may influence the results because of the different condition of the cells in these two biological statuses. However, we know that experiments in in vivo conditions are more tedious and cumbersome to be implemented, but their results would be more reliable due to the similarities to the condition of living cells. Finally, a problem which exists in the most of animal studies is that their results cannot be simply generalized to the human because of differences between human biological response and their response to EMF exposure. It seems that further researches should be done in order to clarify the effects of power frequency EMF on human reproductive system, pregnancy outcome and fetal development.

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Conflict of interest

The authors declare no conflict of interests.

Disclosure statement

No potential conflict of interest was reported by the authors.

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