BENHA MEDICAL JOURNAL bmj

Print ISSN 1110-208X.

Online ISSN 2357-0016

Original article

Possible Role of Growth Hormone on Ovarian Reserve of Female Rats Exposed to Blue Light: Impact on IGF1/IGF1R Axis

Heba M. Nawar, Ola A. El Gohary, Mona A. Said,
Marwa H. Muhammad, Enas M Kasem

Physiology Department, Faculty of Medicine Benha University, Egypt.

Corresponding to:
Dr. Heba M. Nawar.
Physiology Department, Faculty of Medicine Benha University, Egypt.

Email:
hebanawar39@gmail.com

Received: 30-3-2026
Accepted: 24-4-2026

Abstract:

Background: Diminished ovarian reserve is increasingly reported in young women as well, it is an important cause of infertility. Widespread screen use and artificial lighting have increased exposure to blue light in the short-wavelength range, which may threaten ovarian reserve (OR). Growth hormone (GH) may counteract this injury by modulating the insulin-like growth factor-1/insulin-like growth factor-1 receptor (IGF-1/IGF-1R) axis. Aim: To evaluate the impact of blue light on OR and determine whether GH protects the ovary through IGF-1/IGF-1R restoration. **Methods:** After 7 days of acclimatization, twenty-four prepubertal female rats were randomized into four groups (n = 6) for a 10-day experiment: control (natural room light, saline subcutaneous (s.c.) once daily from day 4 to day 10); GH (natural room light, GH 1 mg/kg s.c. from day 4 to 10); blue light (450–480 nm for 12 h/night, 6:00 p.m.–6:00 a.m., from day 1 to day 10 plus saline s.c. from day 4 to 10); and blue light + GH (same light protocol plus GH 1 mg/kg s.c. from day 4 to 10). On day 11, estradiol, FSH, anti-Müllerian hormone (AMH), melatonin, oxidative-stress markers (Reduced glutathione (GSH), Malondialdehyde (MDA)), caspase-3, and serum and ovarian Insulin-like growth factor-1 (IGF-1) were determined, and ovarian IGF-1R immunohistochemistry with histopathology were performed. **Results:** Blue light significantly reduced estradiol, AMH, melatonin, serum and ovarian IGF-1, and GSH, while increasing MDA, caspase-3, and IGF-1R expression. GH co-treatment reversed these changes. **Conclusion:** Blue-light exposure impairs OR through oxidative and apoptotic mechanisms and disruption of the IGF-1/IGF-1R axis, while GH exerts a potent photoprotective effect.

Keywords: Blue light; ovarian reserve; IGF-1/IGF-1R axis; growth hormone; melatonin.

Introduction

The ovary is a highly sensitive organ to circadian disruption. Evidence suggests that short-wavelength light can alter gonadal function through both central and peripheral mechanisms, including suppression of melatonin, dysregulation of steroidogenesis, and direct oxidative damage to ovarian cells [1]. Importantly, the ovarian reserve (OR) reflects the pool of primordial and growing follicles particularly susceptible to oxidative stress, mitochondrial dysfunction, and apoptotic activation [2]. Anti-Müllerian hormone (AMH), a reliable indicator of ovarian reserve, is released from granulosa cells of pre-antral and tiny antral follicles, rendering it an indispensable biochemical indicator for the assessment of ovarian injury [3].

Among the pathways that influence ovarian survival, the insulin-like growth factor 1/ its receptor (IGF-1/IGF-1R) axis plays a central protective role. IGF-1 supports proliferation of granulosa cells, follicular development, mitochondrial stability, and anti-apoptotic signaling [4]. Growth hormone (GH) is an upstream regulator of IGF-1 synthesis and is also known to enhance ovarian steroidogenesis, promote antioxidant defense, and reduce apoptosis [5]. Several experimental and clinical studies demonstrate that GH supplementation increases AMH, improves follicular responsiveness and restores IGF-1 signaling. However, the potential role of GH in counteracting blue light–induced ovarian injury has not been comprehensively explored [6,7].

Exposure to artificial lighting has increased markedly with the global shift toward light-emitting diode (LED) illumination and prolonged screen use [8]. Blue light, particularly within the 450–470 nm spectrum, is biologically active and has been shown to disrupt circadian timing, suppress nocturnal melatonin secretion [9]. Melatonin, a key regulator of reproductive physiology, is essential in maintaining ovarian redox balance and supporting follicular survival; thus, its suppression renders the ovary vulnerable to damage. Excessive reactive oxygen species disturb ovarian redox homeostasis and trigger mitochondrial apoptotic signaling. Caspase-3 is a central executioner in this pathway and serves as a key marker of oxidative stress-induced apoptosis [10].

Despite increasing global exposure to blue light, especially among children and adolescents, data on its direct impact on OR remain limited, and the interaction between blue light, melatonin suppression, and IGF-1/IGF-1R dysregulation is poorly defined.

Therefore, the aim was to assess the effect of blue-light exposure on OR in prepubertal rats, with specific focus on hormonal profile, oxidative status, apoptosis, and IGF-1/IGF-1R signaling. Additionally, it also evaluated whether GH administration could mitigate blue-light–induced ovarian injury and improve hormonal, biochemical, and histopathological outcomes. This work provides mechanistic insights into the interplay between light exposure and ovarian health and explores a potential protective strategy of GH to counteract blue-light–induced reproductive dysfunction.

Materials and Methods

Experimental Animals

This prospective experimental study was conducted on 24 female albino rats, aged 21 days and weighing 55 ± 5 grams. The experimental rats were procured from Laboratory Animals Farm Unit, Faculty of Veterinary Medicine, Zagazig University. The rats were placed at suitable room temperature for 7 days acclimatization period before experiment started. The experimental procedure was done in the Physiology department, Benha University for 10 days from (7 to 16 November 2024). No rats died throughout the experiment .The committee of the ethics of animal experiments at the Faculty of Medicine, Benha University, revised and

authorised the experimental protocol (Approval No. MD7.4.2024). Following completion of study, animals were humanely sacrificed and incinerated at Benha University Hospital in accordance with ethical guidelines [11].

Chemical used:

Recombinant human growth hormone (somatropin 1.6 mg/4 IU inj., Lot No. 202310AK044) was procured from SEDICO Pharmaceuticals, Egypt. Estradiol kits (Lot No. MBS263466) and follicle-stimulating hormone (FSH) kits (Lot No. CEA830RA) were provided by Biodiagnostic, Egypt. Anti-Müllerian hormone (AMH) kits (Lot No. A79765) were obtained from Beckman Coulter, Ireland. Melatonin kits (Lot No. ab213978), malondialdehyde (MDA) kits (Lot No. ab118970), and caspase-3 kits (Lot No. ab39401) were supplied by Abcam Biochemicals, Cambridge, UK. IGF-1 ELISA kits (Lot No. DG100) were obtained from Quantikine, R&D Systems, Minneapolis, MN, USA. Reduced glutathione (GSH) assay kits (Lot No. K464-100) were obtained from KAMIYA Biomedical Company, Seattle, USA. Antibodies for immunohistochemical detection of IGF-1 receptor (IGF-1R) (Lot No. PA5-79444) were obtained from Thermo Fisher Scientific, Waltham, MA, USA.

Experimental design:

The female rats were allocated into four groups (6 rats in each group):

Group I (Control group): rats were maintained under natural standard surrounded lighting conditions without a specialized light-dark cycle for 10 days and received daily subcutaneous (S.C.) saline at a volume of (2 mL/kg/day) from day 4 to day 10**. Group II (GH group):** rats were maintained under natural standard surrounded lighting conditions without a specialized light-dark cycle for 10 days, while receiving daily S.C. injection of growth hormone (somatropin) (1 mg/kg), from day 4 to day 10 [12]. **Group III (Blue Light exposed group):** rats of this group subjected to blue light (450–480 nm) for 12 h/night (6 p.m.–6 a.m.) and standard light for 12 h/day for 10 days and concurrently received daily S.C. saline at a volume of (2 ml/kg/day) from day 4 to day 10 [13]. **Group IV (Blue light + GH):** rats were subjected to the same blue-light protocol as Group III and concurrently received S.C. injection of growth hormone (somatropin) (1 mg/kg/day) from day 4 to day 10.

Procedure of the experiment:

Protocol of blue light exposure

The blue light was obtained from light emitting diode (LED) lamp with wavelength of 460- 480 nm,10 WATT (manufactured in Korea, www.abusimbelmedical.com). The LED lamp was positioned 20 cm above the center of each cage in the blue light-exposed rats (Group III and Group IV), with each cage housing three rats to ensure equal exposure conditions [13,14].

Blood and Ovarian tissue sampling:

Rats were anaesthetized with thiopental sodium (40 mg/kg, i.p.) at the end of the experiment. Blood samples were obtained from the retro-orbital venous plexus, permitted to coagulate at room temperature, and thereafter centrifuged at 3000 rpm for 15 minutes The serum was separated and preserved at −80 °C for subsequent evaluation of FSH, oestradiol, AMH, melatonin, and IGF-1 levels. [15,16].

Following blood sampling, A 3-cm midline laparotomy was made along the linea alba, incising skin, fascia, and peritoneum. The animal was gently tilted ~45° to expose the ovary. Both ovaries were then removed [17]. Both ovaries were then rinsed in ice-cold saline. One ovary from each rat was stored at −80 °C for biochemical analyses, including GSH, MDA, caspase-3 activity, and ovarian IGF-1 levels, whereas for histopathological examination and immunohistochemical evaluation of IGF-1 receptor expression the contralateral ovary was fixed in 10% neutral-buffered formalin [18].

Statistical analysis:
The data were performed by Statistical package for social science (SPSS) version 23.0 (SPSS Inc., Chicago, IL, USA, 2000). In the statistical comparison among the different groups, the significance of difference was evaluated by one-way analysis of variance (ANOVA) after which Least Significant Difference (LSD) test for comparison among every two groups. The p-values < 0.05 were regarded as statistically significant.

Results

Impact of blue light & GH administration on serum AMH, melatonin, estradiol and FSH (Table 1).
Our study found that blue-light exposure significantly decreased AMH, melatonin and estradiol in comparison to control and GH groups ($p < 0.05$), whereas FSH remained unchanged ($p > 0.05$). Consistently, GH administration to blue light exposed rats significantly improved AMH, melatonin and estradiol relative to blue light group ($p < 0.05$). GH alone produced a non-significant change in these parameters when compared with the controls ($P > 0.05$).

Impact of blue light & GH administration on serum and ovarian IGF-1 and IGF-1R expression (Table 2, Figure 1).
Similarly, the blue light group had significantly reduced serum and ovarian IGF-1 levels in comparison to control and GH groups ($p < 0.05$). Conversely, GH co-treatment with blue light restored IGF-1 levels toward control values relative to the blue light group ($p < 0.05$). In the GH-only group, serum and ovarian IGF-1 expression non-significantly changed comparable to those of the control group ($p > 0.05$).
Regarding ovarian IGF-1R, immunohistochemical analysis showed normal expression in the granulosa and theca cells in the control and GH groups (Figure 1A, 1B respectively). On contrast, the blue light group showed stronger IGF-1 R immunoreactivity in granulosa cells compared to control and GH groups (Figure 1C). However, the blue light group that received GH exhibited moderate expression in granulosa and theca cells (Figure 1D).
Consistently, the semi-quantitative IGF1R immunohistochemical score was significantly higher in the blue light group than in the control and GH groups ($p < 0.05$), while GH administration to blue light exposed rats significantly reduced this score compared with blue light alone ($p < 0.05$). In the GH only group, IGF-1R expression score was non-significantly changed in comparison to the control group ($p > 0.05$).

Impact of blue light & GH administration on oxidative stress markers and caspase-3 (Table 3).
There was significant decrease in the antioxidant enzyme, GSH, while significant elevated in the MDA levels in blue light group in comparison to the control and GH group ($P<0.05$). On the other hand, GH administration to blue light exposed rats resulted in significant rise in GSH and significant decline in MDA levels compared to the blue light group ($P<0.05$).
Concerning the apoptotic protein, caspase-3, it was significantly augmented in blue light group versus the control and GH group($P<0.05$). Fortunately, GH administration to blue light exposed rats led to significant decrease compared to blue light group ($P<0.05$).
Furthermore, there was nonsignificant change in caspase-3 levels between GH and control groups.

Impact of blue light & GH administration on ovarian histopathological changes (Figure 2).
Ovarian sections from the control and GH groups showed well-preserved architecture, with follicles at various developmental stages, intact oocytes, regularly arranged multilayered granulosa cells and normal stromal tissue, without evident edema or vascular congestion

(Figure 2A, 2B respectively). In contrast, the blue light group showed marked structural disruption, including extensive follicular atresia, thinning and disorganization of granulosa cell layers, oocyte degeneration, stromal edema and prominent vascular congestion (Figure 2C). On the other hand, ovaries from the blue light + GH group exhibited developing follicles with largely intact oocytes and granulosa layers, accompanied by only mild stromal congestion and focal atresia, indicating substantial structural preservation compared with blue light exposure alone (Figure 2D).

Correlation between ovarian IGF1and AMH, oxidative and apoptotic markers and IGF1R scoring (Figure 3).

Ovarian IGF-1 demonstrated a statistically significant positive correlation with serum AMH (r = 0.916) and ovarian GSH levels (r = 0.813). In contrast, ovarian IGF-1 was negatively correlated with IGF-1R immunohistochemical score (r = −0.851), ovarian caspase-3 activity (r = −0.793) and MDA levels (r = −0.814).

Table (1): Serum Melatonin, Estradiol, FSH and AMH levels in different experimental groups:

GROUP n = 6	**GROUP I (Control group)**	**GROUP II (GH group)**	**GROUP III (BL group)**	**GROUP IV (BL + GH group)**
Melatonin (ng/mL	179.3±8.04	179±4.56	101.5±5.46 [a,b]	133.16±4.02[a,b,c]
Estradiol (pg/ml)	29.3±1.31	30.15±0.36	19.56±1.26[a,b]	24.13±0.9[a,b,c]
FSH (ng/ml)	23±1.62	23.27±.91	22.58±1.04	23.7±0.25
AMH (ng/ml)	5.31±0.24	5.64±0.11	3.04±0.16[a,b]	4.18±0.23 [a,b,c]

Data are represented as mean ± standard deviation (SD). P < 0.05 is significantly tested by one way analysis of variance (ANOVA) and post hoc multiple comparison LSD method.

[a] P < 0.05 vs. control group; [b] P < 0.05vs. GH group; [c] P < 0.05 vs. BL group.

Abbreviations: BL; blue light, GH; growth hormone, FSH; Follicle-Stimulating Hormone, AMH; Anti-Müllerian Hormone.

Table (2): Serum and ovarian IGF1, in addition to IGF1R immunohistochemical scoring in different experimental groups:

Data are represented as mean ± standard deviation (SD). P < 0.05 is significantly tested by one way analysis of variance

GROUP n = 6	**GROUP I (Control group)**	**GROUP II (GH group)**	**GROUP III (BL group)**	**GROUP IV (BL + GH group)**
SerumIGF1 (ng/ml)	193±5.36	204±4.93	155.16±3.71 [a,b]	189.8±2.85 [c]
Ovarian IGF1 level (ng/mg)	9.8±0.34	10.33±0.53	7.63±0.41 [a,b]	8.46±0.48 [a,b,c]
IGF1R immunohistochemical scoring	1.5±0.14	1.6±0.14	3.3±0.14 [a,b]	2.55±0.11 [a,b,c]

(ANOVA) and post hoc multiple comparison LSD method.

a P < 0.05 vs. control group; b P < 0.05vs. GH group; c P < 0.05 vs. BL group.

Abbreviations: BL; blue light, GH; growth hormone, IGF1; Insulin-Like Growth Factor 1, IGF-1R; Insulin-like Growth Factor-1 Receptor.

Table (3): Ovarian GSH, MDA and Caspase-3 in different experimental groups:

GROUP n = 6	GROUP I (Control group)	GROUP II (GH group)	GROUP III (BL group)	GROUP IV (BL+ GH group)
GSH (nmol/gm tissue)	2.66±0.04	2.66±0.04	2.25±0.067 [a,b]	2.65±0.02 [c]
MDA (nmol/gm tissue)	9.95±0.49	9.9±0.4	12.95±0.5 [a,b]	11± 0.26 [a,b,c]
Caspase-3 (nmol/mg protein)	2±0.12	2±0.15	3.6±0.25 [a,b]	2.53±0.15 [a,b,c]

Data are represented as mean ± standard deviation (SD). $P < 0.05$ is significantly tested by one way analysis of variance (ANOVA) and post hoc multiple comparison LSD method.

[a] $P < 0.05$ vs. control group; [b] $P < 0.05$vs. GH group; [c] $P < 0.05$ vs. BL group.

Abbreviations: BL; blue light, GH; growth hormone, GSH; Reduced Glutathione, MDA; Malondialdehyde, Caspase-3; Cysteine-aspartic protease-3.

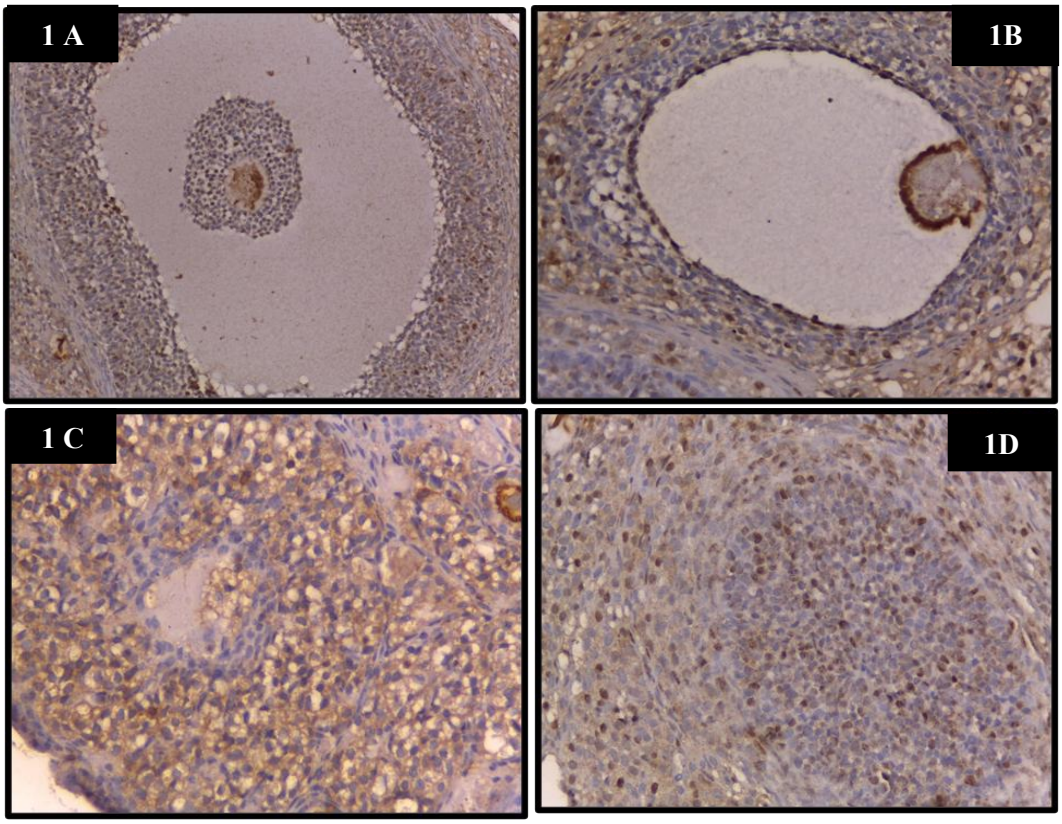

Figure 1. Representative photomicrographs of ovarian sections immunostained for IGF-1R expression in different experimental groups:
(1 A) Control: normal IGF-1R expression in granulosa cells; oocytes negative, (1 B) GH: normal expression, comparable to control, (1C) BL: marked overexpression in granulosa cells, (1 D) BL + GH: moderate expression. Scale bar: ×400.

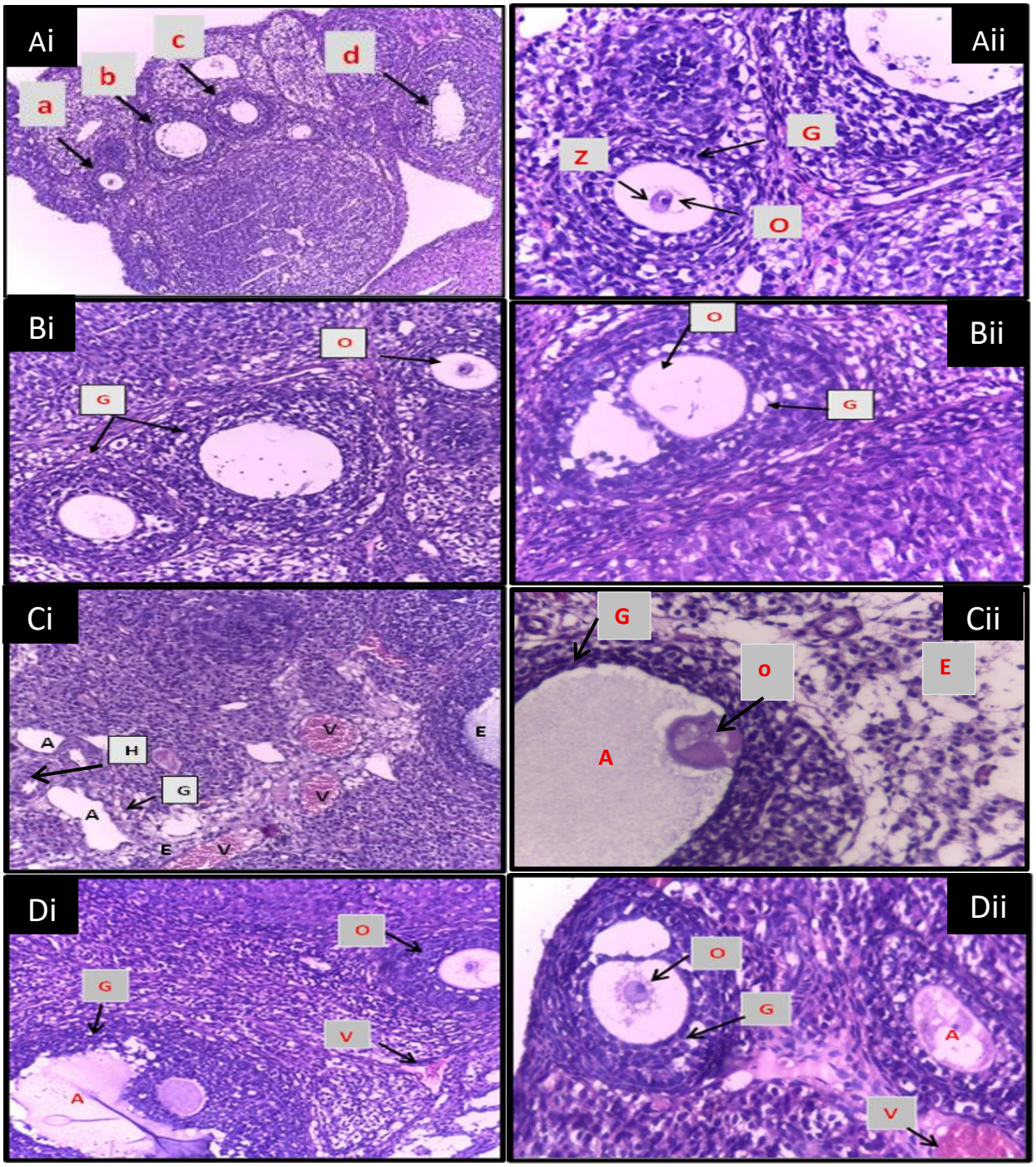

Figure 2. Representative photomicrographs of ovarian sections stained with hematoxylin and eosin (H&E) in the different experimental groups
Magnification: Ai (×100), Aii (×400), Bi (×200), Bii (×400), Ci (×200), Cii (×400), Di (×200), Dii. (×400)
Control group (A): Normal follicular architecture showing intact oocytes (O), organized granulosa cells (G), and clear zona pellucida (Z).GH group (B): Preserved ovaria). BLphology with developing follicles and intact stroma.BL group (C): Marked follicular atresia (A), disorganized granulosa cells (G), stromal edema (E), and vascular congestion (V). BL + GH group (D): Improved architecture with more organized granulosa cells (G) and reduced atresia (A).

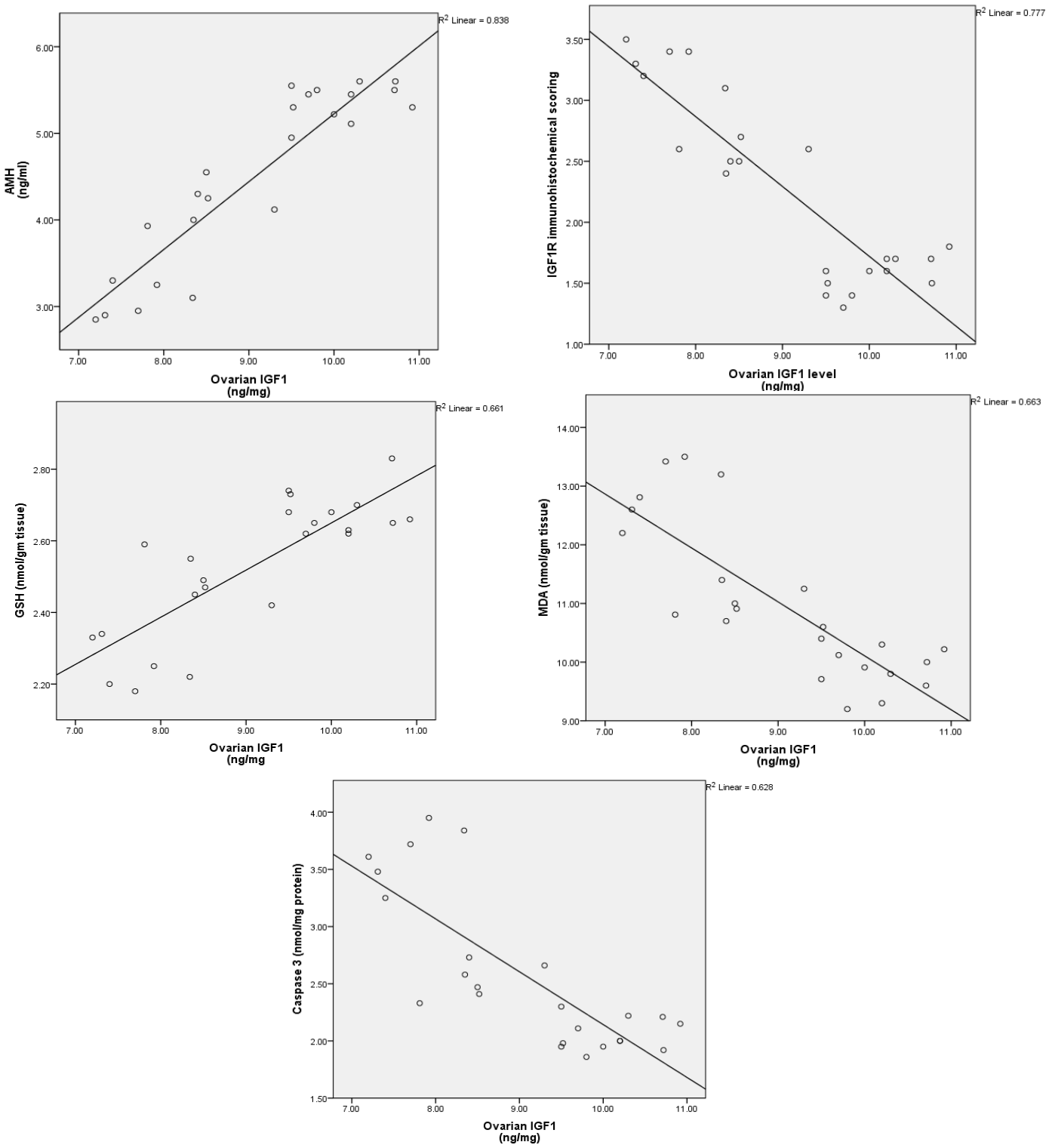

Figure 3. Scatter plots illustrate the correlations between ovarian IGF-1 levels and:(A) serum AMH, (B) IGF-1R immunohistochemical score, (C) ovarian caspase-3 activity, (D) Ovarian GSH and (E) Ovarian MDA.

It was analyzed using Pearson's correlation coefficient (r) 2-tailed test. A p value of less than 0.05 was considered statistically significant. AMH; Anti-Müllerian Hormone.

IGF1; Insulin-Like Growth Factor 1, GSH; Reduced Glutathione, MDA; Malondialdehyde, Caspase-3; Cysteine-aspartic acid protease-3.

Discussion

This study presents new experimental evidence demonstrating that blue-light exposure induces a significant decline in ovarian function in prepubertal female rats, affecting hormonal balance, oxidative status, apoptotic activity, and the IGF-1/IGF-1R axis. These findings support the growing body of literature indicating that artificial light at night acts as a potent endocrine disruptor capable of altering reproductive physiology.

In our study, blue-light exposure resulted in a profound suppression of melatonin, a key circadian hormone essential for normal ovarian steroidogenesis and follicular maturation. Consistent with earlier reports, blue light significantly suppressed serum melatonin, most likely through melanopsin-mediated activation of suprachiasmatic nucleus (SCN) pathways that inhibit pineal output [19,20]. This decline in melatonin was accompanied by a reduction in estradiol, in line with previous evidence that melatonin supports aromatase expression and protects granulosa cells from oxidative stress [21]. FSH levels, however, remained unchanged an observation that agrees with studies–on prepubertal rats exposed to short-duration blue light [22]. This stability is attributed to the immaturity of the GnRH/FSH axis and the non-cyclic hormonal pattern at this age. Longer exposure paradigms in adult animals have demonstrated FSH elevation, highlighting the influence of both age and exposure duration on gonadotropin response [23].

AMH, a sensitive marker of OR, was significantly reduced after blue-light exposure, reflecting early compromise of granulosa-cell function. Previous mechanistic data support this effect, showing that melatonin enhances AMH expression and protects granulosa cells from oxidative injury [24,25].

A major finding of this study is the pronounced suppression of serum and ovarian IGF-1 with concomitant upregulation of IGF-1R expression. This pattern is consistent with prior evidence that IGF1 ligand deficiency triggers compensatory receptor overexpression in an attempt to maintain signaling [26,27]. Notably, disruption of circadian light–dark cycling has been shown to alter GH secretory patterns, thereby limiting downstream IGF-1 availability [28]. The resulting disruption of IGF-1/IGF-1R balance may contribute to impaired follicular growth and steroidogenesis, as IGF-1 is essential for granulosa cell proliferation and the responsiveness to FSH [29].

Oxidative stress and apoptotic damage played a central role in mediating ovarian injury. Blue-light exposure significantly decreased GSH and elevated both MDA and caspase-3, indicating lipid peroxidation and exaggerated apoptosis. These outcomes are consistent with previous studies demonstrating that circadian disruption increases ROS generation [30,31] and activates caspase-dependent pathways in reproductive tissues [32].

Our results were supported with histopathological changes revealing clear structural disruptions in ovarian morphology in the blue-light exposed group characterized by reduced healthy follicles, increased follicular atresia, granulosa cell disorganization These changes are in line with experimental evidence showing that light-at-night disrupt ovarian architecture through circadian dysregulation and oxidative stress–mediated follicular damage, ultimately promoting apoptosis and degenerative remodeling of ovarian tissue [13, 33].

Importantly, co-administration of growth hormone (GH) exerted a marked protective effect across nearly all evaluated parameters. GH significantly increased AMH, supporting its protective action on granulosa cells and preservation of OR, as

previously demonstrated in ovarian-injury models [34]. Histologically, GH co-treatment mitigated blue-light–induced architectural damage, showing reduced follicular atresia and improved granulosa-cell integrity, in line with reports that GH attenuates ovarian fibrosis and structural deterioration in various injury models [34,35].

Importantly, GH administration in the treated group resulted in elevation of serum and ovarian tissue IGF-1 concentrations, accompanied by moderate IGF-1R expression in granulosa cells, reflecting reactivation of the ovarian GH/IGF-1 axis. These outcomes are aligning with experimental evidence that GH enhances local IGF-1 synthesis and improves ovarian responsiveness to gonadotropins [36,37].

GH restored melatonin toward normal values, an effect likely mediated by activation of the GH/IGF-1 axis, which enhances pineal melatonin synthesis through upregulation of arylalkylamine N-acetyltransferase (AANAT), the key regulatory enzyme in melatonin synthesis [38].In a complementary bidirectional manner, accumulating evidence indicates that melatonin and GH mutually reinforce each other's secretion and endocrine actions, thereby supporting coordinated circadian and reproductive regulation [39].

Estradiol levels were elevated in the blue-light + GH cohort, indicating partial recovery of ovarian steroidogenic function, most likely mediated by GH-dependent the ovarian IGF-1/IGF-1R axis activation, which enhances granulosa-cell aromatase activity and estradiol synthesis, consistent with previous reports of GH and IGF-1-driven stimulation of ovarian steroidogenesis [12].

Moreover, GH markedly improved the redox profile by elevating GSH and reducing MDA, and lowered caspase-3 activity. This antioxidant and anti-apoptotic effect align with earlier studies demonstrating GH-induced activation of PI3K/Akt signaling, which strengthens antioxidant defenses and inhibits caspase-3–mediated apoptosis [35,40].

Correlation analysis further strengthened the mechanistic interpretation: ovarian IGF-1 showed a statistically significant positive correlation with serum AMH and ovarian GSH levels and these data were in line with Kim et al [35], Yücel et al [41]and Hayes et al [42]. Conversely, there was a negative correlation between ovarian IGF-1 and IGF-1R immunohistochemical scoring, ovarian caspase-3 activity, and MDA levels. These data were in line with Rieger and O'Connor [43] and Eckstein et al [44].

Taken together, the present data suggest that blue-light exposure disrupts ovarian function through multiple convergent mechanisms including hormonal suppression, IGF-1 deficiency, oxidative stress, and apoptosis, while GH provides partial but meaningful protection by restoring growth promoting and antioxidant pathways.

The proposed mechanisms underlying blue light–induced ovarian dysfunction and the modulatory role of growth hormone are illustrated **(Figure 4).**

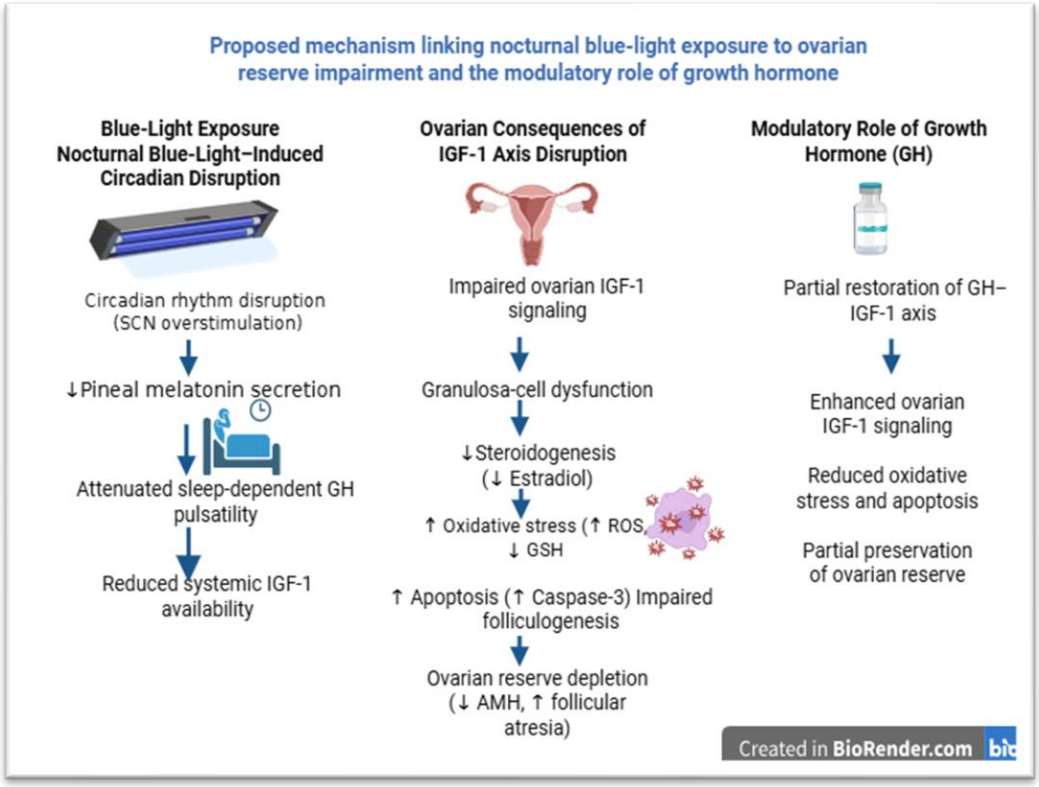

Figure 4. Proposed mechanism linking nocturnal blue-light exposure to ovarian reserve impairment and the modulatory role of growth hormone (GH). Created with BioRender.com.

Conclusion

Blue-light exposure for 10 days markedly impaired OR in prepubertal rats, as evidenced by reduced AMH, IGF-1, melatonin, estradiol and antioxidant capacity, together with upregulated IGF-1R expression and increased caspase-3 activity. Co-administration of GH maintained hormonal balance, improved oxidative status, reduced apoptosis, and prevented histological damage. These findings support the protective role of GH against nocturnal blue light–induced ovarian dysfunction through modulation of the IGF-1/IGF-1R axis.

Acknowledgment

The author gratefully acknowledges the staff of the animal house for their invaluable help in animal care and handling throughout the experimental period. Sincere thanks are also extended to the Histology and Biochemistry Departments, Faculty of Medicine, Benha University, for their support in sample processing and laboratory analyses. The author expresses gratitude to colleagues who offered valuable scientific guidance during the development of this work.

Conflict of Interest

There is no conflict of interest

Funding

This research received no external funding and was fully supported by the author.

Abbreviations:

AANAT; arylalkylamine N-acetyltransferase**,**
AMH; Anti-Müllerian hormone,
FSH; Follicle-stimulating hormone,
GH; Growth hormone,
GSH; Reduced glutathione,
IGF-1; Insulin-like growth factor-1,
IGF-1R; Insulin-like growth factor-1 receptor,
LED; light-emitting diode,
MDA; Malondialdehyde,
OR; ovarian reserve,

S.C.; subcutaneous,
SCN; suprachiasmatic nucleus.

References

1. Bora G, Önel T, Yıldırım E and Yaba A. Circadian regulation of mTORC1 signaling via Per2 dependent mechanism disrupts folliculogenesis and oocyte maturation in female mice. J Mol Histol.2023;54(3):217-229.
2. Ammar OF, Massarotti C, Mincheva M, Sharma K, Liperis G, Herraiz S., et al. Oxidative stress and ovarian aging: from cellular mechanisms to diagnostics and treatment. Hum Reprod. 2024 ;39(7):1582-1586.
3. Vale-Fernandes E, Moreira MV, Rodrigues B, Pereira SS, Leal C, Barreiro M, et al. Anti-Müllerian hormone a surrogate of follicular fluid oxidative stress in polycystic ovary syndrome? Front Cell Dev Biol. 2024; 12:1408879.
4. Baumgarten SC, Armouti M, Ko C and Stocco C. IGF1R Expression in Ovarian Granulosa Cells Is Essential for Steroidogenesis, Follicle Survival, and Fertility in Female Mice. Endocrinology.2017;158(7):2309-2318.
5. Wang J, Wu J, Zhang Y, Zhang J, Xu W, Wu C., et al. Growth hormone protects against ovarian granulosa cell apoptosis: Alleviation oxidative stress and enhancement mitochondrial function. Reprod Biol.2021;21(2):100504.
6. Yang P, Wu R and Zhang H. The effect of growth hormone supplementation in poor ovarian responders undergoing IVF or ICSI: a meta-analysis of randomized controlled trials. Reprod Biol Endocrinol.2020; 18(1):76.
7. Guo Q, Liu P, Zhou W, Xia M, Li J, Lu J, et al. Growth hormone supplementation ameliorates blastocyst euploidy rates and improves pregnancy outcomes in women undergoing preimplantation genetic testing for aneuploidy cycles. Front Endocrinol (Lausanne). 2023; 14:1117706.
8. Bedrosian TA and Nelson RJ. Timing of light exposure affects mood and brain circuits. Transl Psychiatry.2017; 7(1): e1017.
9. Tosini G, Ferguson I and Tsubota K. Effects of blue light on the circadian system and eye physiology. Mol Vis.2016; 22:61-72.
10. Sun TC, Liu XC, Yang SH, Song LL, Zhou SJ, Deng SL., et al. Melatonin Inhibits Oxidative Stress and Apoptosis in Cryopreserved Ovarian Tissues via Nrf2/HO-1 Signaling Pathway. Front Mol Biosci .2020.; 7:163 .
11. National Research Council. Guide for the Care and Use of Laboratory Animals. 8th ed. Washington, DC: The National Academies Press;2011.
12. Mahran YF, El-Demerdash E, Nada AS, El-Naga RN, Ali AA and Abdel-Naim AB.Growth Hormone Ameliorates the Radiotherapy-Induced Ovarian Follicular Loss in Rats: Impact on Oxidative Stress, Apoptosis and IGF-1/IGF-1R Axis. PLoS One.2015;10(10): e0140055.
13. Kılınç Uğurlu A, Bideci A, Demirel MA, Take Kaplanoğlu G, Dayanır D, Gülbahar Ö., et al. Effects of Blue Light on Puberty and Ovary in Female Rats. J Clin Res Pediatr Endocrinol. 2023;15(4):365-374.
14. Ahmed AF, Madi MA, Ali AH and Mokhemer SA. The ameliorating effects of adipose-derived stromal vascular fraction cells on blue light-induced rat retinal injury via modulation of TLR4 signaling, apoptosis, and glial cell activity. Cell Tissue Res.2024; 398(3):207-225.
15. Ferrua B and Masseyeff R.Immunoassay of melatonin with enzyme-labeled antibodies.J Immunoassay. 1985;(1-2):79-94.
16. Ivan D, Brabant G and Kann PH. German KIMS Board. Applicability of recently established reference values for serum insulin-like growth factor 1: a comparison of two assays—an automated chemiluminescence immunoassay and an enzyme-linked immunosorbent assay. Clin Lab.2005; 51(7-8):381-7.
17. Khajuria DK, Razdan R and Mahapatra DR. Description of a new method of ovariectomy in female rats. Rev Bras Reumatol. .2012;52(3):462-70. English, Portuguese. PMID: 22641600.
18. Fischer AH, Jacobson KA, Rose J and Zeller R. Hematoxylin and eosin staining of tissue and cell sections. CSH Protoc. 2008 May 1;2008:pdb. prot4986.
19. Zeng Y, Rong R, You M, Zhu P, Zhang J and Xia X. Light-eye-body axis: exploring the network from retinal illumination to systemic regulation. Theranostics.2025; 15(4):1496-1523.
20. Rai S and Ghosh H. Modulation of human ovarian function by melatonin. Front Biosci (Elite Ed).2021;13(1):140-157.
21. Cheng JC, Fang L, Li Y, Wang S, Li Y, Yan Y., et al. Melatonin stimulates aromatase expression and estradiol production in human granulosa-lutein cells: relevance for high serum estradiol levels in patients with ovarian hyperstimulation syndrome. Exp Mol Med.2020; 52(8):1341-1350.
22. Uğurlu AK, Bideci A, Demirel AM, Kaplanoğlu GT, Dayanır D, Gülbahar Ö., et al.

Is blue light exposure a cause of precocious puberty in male rats? Front Endocrinol (Lausanne). 2023;20; 14:1190445.
23. Li Y, Cheng S, Li L, Zhao Y, Shen W and Sun X. Light-exposure at night impairs mouse ovary development via cell apoptosis and DNA damage. Biosci Rep2019; 39(5): BSR20181464.
24. Wu M, Yao Y, Chen R, Fu B, Sun Y, Yu Y., et al. Effects of Melatonin and 3,5,3'-Triiodothyronine on the Development of Rat Granulosa Cells. Nutrients. 2024;16(18):3085.
25. Feng J, Ma WW, Li HX, Pei XY, Deng SL, Jia H, et al. Melatonin prevents cyclophosphamide-induced primordial follicle loss by inhibiting ovarian granulosa cell apoptosis and maintaining AMH expression. Front Endocrinol (Lausanne).2022; 13:895095.
26. Hiramoto K, Kubo S, Tsuji K, Sugiyama D, Hamano H. et al. Melatonin inhibits oxidative stress and apoptosis in cryopreserved ovarian tissues via Nrf2/HO-1 signaling pathway. Frontiers in Molecular Biosciences. 2020; 7:163.
27. Grzywa-Czuba R, Trojanek JB, Michałkiewicz J, Kubiszewska I, Obrycki Ł, Wierzbicka-Rucińska A., et al. Association between Expression of Insulin-like Growth Factor-1 (IGF-1), IGF-1 Receptor (IGF-1R), and Hypertension-Mediated Organ Damage (HMOD) Parameters in Leukocytes and Plasma of Children/Adolescents with Primary Hypertension. Journal of Personalized Medicine 2024;14(3):255.
28. Wang W, Huang Z, Huang L, Tan C, Chen W, Roelfsema F et al. Rotating Day and Night Disturb Growth Hormone Secretion Profiles, Body Energy Metabolism, and Insulin Levels in Mice. Neuroendocrinology.2022.;112(5):481-492.
29. Afradiasbagharani P, Hosseini E, Allahveisi A and Bazrafkan M. The insulin-like growth factor and its players: their functions, significance, and consequences in all aspects of ovarian physiology. Middle East Fertility Society Journal.2022;27(1):27.
30. Sun TC, Liu XC, Yang SH, Song LL, Zhou SJ, Deng SL., et al. Melatonin inhibits oxidative stress and apoptosis in cryopreserved ovarian tissues via Nrf2/HO-1 signaling pathway. Frontiers in Molecular Biosciences. 2020; 7:163.
31. Li JY, Zhang K, Xu D, Zhou WT, Fang WQ, Wan YY, et al. Mitochondrial fission is required for blue light-induced apoptosis and mitophagy in retinal neuronal R28 cells. Frontiers in Molecular Neuroscience.2018; 11:432.
32. Xu, G., Dong, Y., Wang, Z., Ding, H., Wang, J., Zhao, J., et al. Melatonin Attenuates Oxidative Stress-Induced Apoptosis of Bovine Ovarian Granulosa Cells by Promoting Mitophagy via SIRT1/FoxO1 Signaling Pathway. International journal of molecular sciences, 2023;24(16), 12854.
33. Chu W, Zhai J, Xu J, Li S, Li W, Chen ZJ, et al. Continuous light-induced PCOS-like changes in reproduction, metabolism, and gut microbiota in Sprague-Dawley rats. Frontiers in microbiology.2020; 10:3145.
34. Hong Z, Zhou L, Ji H, Xu C, Yang D, Yang X., et al. Growth hormone protects oocytes from premature ovarian failure by alleviating apoptosis. Research Square [Preprint]. 2022.
35. Kim SM, Yoo JY, Hong YH, Lee J, Kim JH and Lee JR. The effect of growth hormone on ovarian function recovery in a mouse model of ovarian insufficiency. Frontiers in Endocrinology. 2023; 14:1184977.
36. Ipsa E, Cruzat VF, Kagize JN, Yovich JL and Keane KN. Growth hormone and insulin-like growth factor action in reproductive tissues. Frontiers in endocrinology.2019; 12; 10:777.
37. Lewitt MS and Boyd GW. The role of insulin-like growth factors and insulin-like growth factor–binding proteins in the nervous system. Biochemistry insights.2019.;12:1178626419842176.
38. Wang W, Duan X, Huang Z, Pan Q, Chen C and Guo L. The GH-IGF-1 Axis in Circadian Rhythm. Front Mol Neurosci.2021; 14:742294.
39. Askar MM and Zaaen AY. Effect of melatonin on body weight and hormones in male rats. Pharmakeftiki. .2025;7;37(2).
40. Liu Z, Feng C, Li C, He T, Wu G, Fu C., et al. IGF-I protects porcine granulosa cells from hypoxia-induced apoptosis by promoting homologous recombination repair through the PI3K/AKT/E2F8/RAD51 pathway. The FASEB Journal.2024; 38(1): e23332.
41. Yücel GS, Ahn S, Ecemiş T, Keskin M, Arslanca T and Atik A. P-655 Insulin like growth factor-1 levels in follicular fluids of patients with poor ovarian response undergoing in vitro fertilization. Human Reproduction. .2022;1;37(Supplement_1): deac107-604.
42. Hayes E, Winston N and Stocco C. Molecular crosstalk between insulin-like growth factors and follicle-stimulating hormone in the regulation of granulosa cell function. Reproductive Medicine and Biology.2024.;23(1): e12575.
43. Rieger L and O'Connor R. Controlled signaling—insulin-like growth factor receptor endocytosis and presence at intracellular

compartments. Frontiers in Endocrinology.2021; 11:620013.
44. Eckstein N, Servan K, Hildebrandt B, Pölitz A, Jonquières GV, Wolf-Kümmeth S, et al. Hyperactivation of the insulin-like growth factor receptor I signaling pathway is an essential event for cisplatin resistance of ovarian cancer cells. Cancer research. 2009;69(7):2996-3003.

To cite this article: Heba M. Nawar , Ola A. El Gohary, Mona A. Said, Marwa H. Muhammad, Enas M Kasem. Possible Role of Growth Hormone on Ovarian Reserve of Female Rats Exposed to Blue Light: Impact on IGF1/IGF1R Axis. BMFJ XXX, DOI (in press): 10.21608/bmfj.2026.479667.2993.