



# Missing the Dark: Malediction for the Environment and Human Health

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## **Author's contribution**

*The sole author designed, analysed, interpreted and prepared the manuscript.*

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## **ABSTRACT**

Modern civilization has flourished after the invention of electricity and eclectic lights for getting illumination at night. Initially, artificial light was a blessing for the civilization and mankind. Later, artificial-light-at-night (ALAN) appears as a serious problem in our modern world. Rapid urbanization and industrialization are the major causes of light pollution. Indeed, artificial light has several benefits, but it has negative impacts on the entire living system, including humans. Nighttime light exposure disrupts circadian clock activities and deregulates many rhythmic behaviors (sleep, hormone secretion, and others). Insects, fishes, frogs, turtles, birds, nocturnal mammals (bats and rats), and humans are facing serious problems. Light pollution alters behavioral functions, physical and physiological activities, feeding and nesting behavior, migration, and reproductive functions in different animals. Shift work, night work, and lit areas in the streets and residential areas make a serious issue for human exposure and may cause several pathologies. Thus ALAN affects entire ecosystems, and the present review focuses on the effects of light pollution on the different living systems.

**Keywords:** *Artificial-light-at-night; circadian rhythm; melatonin, behavioral changes; reproductive loss.*

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## 1. INTRODUCTION

The era of use of electric lights had been started after the invention of electric bulbs by Thomas Alva Edison in the year 1879. The journey of the evolution of electric lights has a long history. A series of electric lights appeared in the way of civilization. These include filament bulbs, fluorescent tubes, mercury vapor lamps, compact fluorescent bulbs, and recently light-emitted diode (LED) lamps. The powerful electric lights illuminate the office, streets, yards, parking lots, industrial areas, playgrounds, parks, hotels, restaurants, and nightclubs. Artificial light has given several benefits to our society, for instance, extending the length of working hours and productivity, increasing the facility of the medical system, expanding the facilities for teaching learning and research works, improving social life and security, road safety, and offering recreational activities. However, the uses of powerful lights in different sectors annihilate the darkness. Artificial outdoor lighting gradually starts light pollution. Urbanization in the civilization process has a great impact on light pollution and the urban areas are mostly affected. Environmentalists and medical researchers are assuming light pollution is a serious problem and is similarly detrimental to other forms of environmental pollution. However, people are not concerned about light pollution as they are serious about air, water, soil, pesticide and food pollution. Light pollution is not only harmful to human health but also affects wildlife, as well as ecological balance [1]. Light pollution occurs in different forms, including sky glow, light trespass, glare, and over illumination. Sky glow appears as an illuminated sky at night. It occurs mostly in urban areas due to scattering of artificial light at night. Light trespass occurs when floodlight or streetlight brightly illuminates the surrounding area during the night; otherwise, the area will remain dark. It creates unwanted illumination in localities or residential areas at nighttime. Glare occurs due to the horizontal dispersion of the bright light over the sky at night. Bright light from different sources in urban areas causes sky glare. Overillumination refers to the use of unnecessary excess light for the illumination of small area. The unnecessary uses of artificial light at night (ALAN) in office buildings and other public areas cause over illumination [2]. It is suggested that more than 80% world's population resides under the glowing sky [3], and the most affected areas are Europe, North

America, the Middle East, and Asia [4]. Developed countries are mostly affected by light pollution. In Europe, and North America, rapid industrialization, and urbanization caused excessive use of artificial light at night. Countries of the Middle East are the gate for communication with Europe, America, and Africa from Asian countries. So, many cities of the Middle East countries are facing light pollution due to huge pressure from aviation, surface transport, hotels, and restaurants. Moreover, countries of East Asia and Southeast Asia are also affected by light pollution due to industrialization, and urbanization.

The ecological impacts of ALAN were documented by several authors [2,5-7]. Exposure to ALAN for a long duration causes physiological and metabolic alteration in plants. Almost all animals, more specifically insects and birds are severely affected by light pollution (Table 1). Free-living animals are facing sleep disturbance, disorientation in regular activity, behavioral problem, suppression of melatonin secretion and reproductive loss [8-10]. Although certain steps of reproductive activity (egg laying and hatching) of sea turtles occur on sea beaches, they are suffering for reproductive success. Nocturnal mammals show irregular behavior and impaired physiological activities. Mammals are also affected by ALAN. Despite the different animals and plants, humans are seriously affected by light pollution. Shift work, night work, artificial light in the industrial area, and street lights in the residential area are the primary causes of light exposure at night. ALAN disrupts circadian oscillation and affects melatonin and other hormonal rhythm. Desynchronizations of circadian rhythm and melatonin output have negative impacts on human health. Light pollution promotes several health issues including, the disintegration of the sleep-wake cycle, poor physical performance, increased risk of metabolic disorders, neurodegenerative diseases, psychiatric problems, and suppression of melatonin secretion [11,12]. Low levels of melatonin decrease antioxidant profiles and increase oxidative stress, and inflammatory response, leading to cardiovascular disease, type II diabetes and induction of various types of cancers (breast, prostate, ovary and others) [13,14]. The present review focuses on the adverse effects of light pollution on the different living systems and their ecological impacts.

**Table 1. Summary of physiological and ecological impacts of light pollution on the different living systems**

<b>Living systems</b>	<b>Physiological and other effects</b>	<b>Cause</b>	<b>Impact</b>	<b>Reference</b>
Plants	Pressure in photosynthesis	Light induced-stress and pest attack	Ecological imbalance	[24]
	Changes in physiological functions	Changes in leaf functions, photosynthetic activity and plant respiration	Impaired seasonal variation	
	Impaired growth and reproduction		Disturbance in budburst, and flowering property	
	Increased pest attack		Reproductive failure Pressure in crop production yield	
Insects	Changes in physiological and locomotor activities	Circadian rhythm disruption	Imbalance in the food chain and ecological disproportion	[4]
	Imbalance in behavioral functions	Imbalance in hormone secretion	Imbalance in insect population	
	Disturbance in metamorphosis stage	Alteration in metabolic activities	Problems in pollination and crop production	
	Changes in reproductive activity			
	Impaired prey-predator relationship			
Fish	Changes in behavior and locomotor activity	Misalignment in circadian rhythm	Impacts on population, growth and production	[26]
	Problems in migration			
Turtle	Changes in behavior and movements	Circadian rhythm disruption	Ecological imbalance	[30]
	Problems in nesting, egg laying and hatching	Misalignment in navigation	Risk of attacks with other animals	
	Reproductive failure		Reduction in the young population	
Birds	Changes in behavior and daily activities	Circadian rhythm disruption	Impaired prey-predator activity and ecological imbalance	[34 -36, 38, 44]
	Changes in dawn and dusk singing	Impaired melatonin rhythm	Risk of collision	
	Problems in nesting and egg laying	Physiological stress	Impaired foraging activity	
	Sleep disturbance	Disturbance in neuroendocrine functions	Poor reproductive	

Living systems	Physiological and other effects	Cause	Impact	Reference
	Problems in mating and reproductive failure	Problems in the activity of the autonomic nervous system	activity and pressure in birds' population  Misleading in the navigation of migratory birds	
Bats	Changes in behavior and food searching  Problems in daily rhythm physiological functions	Circadian rhythm disruption  Disturbance in hormonal functions and the autonomic nervous system	Disturbance in the food chain and ecological imbalance  Impaired navigation and risk of collision  Disturbance in pollination and crop production	[68]
Human	Changes in behavior and daily activities  Sleep problems  Changes in neurological functions  Impaired daily rhythm (body temperature, heart rate, blood pressure, gastrointestinal functions, metabolic activities)  Hormonal imbalance and infertility	Circadian rhythm disruption  Impaired melatonin rhythm  Physiological and psychological stress  Disturbance in neuroendocrine functions  Problems in the activity of the autonomic nervous system	Poor physiological performance  Increased risk of metabolic (obesity, cardiovascular diseases, diabetes) and neurodegenerative diseases  Prone to psychiatric problems  High risk of cancer (breast, prostate, colorectal) development	[12,13]

## 2. CIRCADIAN CLOCK AND MELATONIN RHYTHM

The suprachiasmatic nucleus (SCN) is considered a circadian clock in the mammalian brain that regulates the circadian rhythms of central and peripheral tissues [15]. The SCN receives photic signals from the retina through the retinohypothalamic tract on exposure to light. Melanopsin containing non-visual intrinsic retinal ganglion cells (iRGCs) percept blue light (464–484 nm) and transmit the signal to the SCN [16,17]. The functions of SCN depend on the involvement of the core clock genes that are expressed under the control of the transcription-translation feedback loop (TTFL). The activity of TTFL is mediated by a complex network of positive control and a regulatory negative

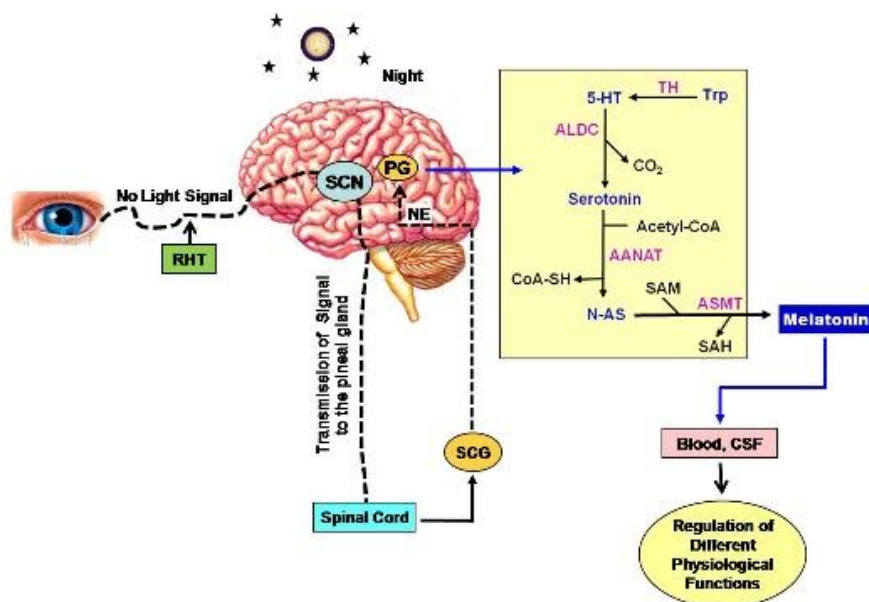
feedback loop [18]. In the mammalian system, a group of genes is listed in the core clock genes (ccg). Among these, the most concerned genes are 3 *Period* (*Per* 1-3), 2 *Cryptochrome* (*Cry* 1-2), *Brain and muscle aryl hydrocarbon receptor nuclear translocator-like 1* (*Bmal* 1), *Circadian locomotor output cycles kaput* (*CLOCK*), 3 *Retinoid-related orphan receptor* (*Rora*,  $\beta$  and  $\gamma$ ), 2 *Reverse-erythroblastosis* (*Rev-Erba* and  $\beta$ ), *Neuronal period-arylhydrocarbon receptor nuclear translocator single-minded 2* (*Npas2/Mop4*), *Aryl hydrocarbon receptor nuclear translocator like 2* (*Arntl2/Mop9*), *F-box/LRR-repeat 3* (*Fbxl3*), and *casein kinase 1* (*CK1 $\delta$* ) [11]. The rhythmic transcription of *Per* and *Cry* is modulated by a heterodimeric complex *CLOCK* and *BMAL1* proteins. Later, *CLOCK:BMAL1* complex also regulates the

expression of *Rora* and *Rev-Erba*. BMAL1-mediated induction of transcription is a positive effect, while PER and CRY are involved in a negative feedback process. PER and CRY accumulate in the cytoplasm and then translocates to the nucleus, where they form a heterodimer to inhibit the activity of CLOCK:BMAL1 complex, completing a negative loop [19]. The gene products of *Rora* and *Rev-Erb* have antagonistic effects. ROR $\alpha$  is responsible for the induction of *Bmal1* transcription, while REV-ERB $\alpha$  exerts negative effects [20]. Casein kinases 1 are involved in PER degradation and FbxL3 (E3 ligase- F-box protein) degrades CRY in the cytoplasm [11].

The pineal gland synthesizes and secretes melatonin. Synthesis of melatonin is very sensitive to light. Nighttime darkness induces melatonin synthesis, while bright daylight inhibits the process. Exposure to ALAN is very crucial to suppress melatonin synthesis. The synthesis of pineal melatonin is under the control of SCN activity. The SCN sends the photic signal to the pineal gland through a complex network, finally with the help of sympathetic innervation. The efferent nerves from SCN move downward to the superior cervical ganglion (SCG) of the spinal cord. The preganglionic nerves converge on the

sympathetic chain ganglia. The postganglionic adrenergic nerves move upward and terminate on the pineal parenchymal cells. Nighttime darkness activates this sympathetic connection and increases the release of noradrenaline as a neurotransmitter that stimulates melatonin synthesis (Fig. 1).

Any types of light exposure inhibit noradrenaline release and melatonin synthesis. The synthesis of melatonin is started from the amino acid tryptophan. The steps are like that: tryptophan  $\rightarrow$  5-hydroxytryptophan serotonin  $\rightarrow$  N-acetyl serotonin  $\rightarrow$  melatonin (Fig. 1). The last two steps are very vital and are mediated by arylalkylamine N-acetyl transferase (AANAT) and acetylserotonin O-methyltransferase (ASMT). Noradrenaline increases the tryptophan entry and the activity of AANAT in pinealocytes through a cAMP-mediated system [13]. Blood melatonin levels change with diurnal rhythm. Melatonin peak rises at midnight and remains low in the daytime due to exposure to light. Arendt reported that the activity of AANAT increases up to 7–150 folds at night. Therefore, light pollution significantly decreases melatonin synthesis [21].



**Fig. 1. Neural connection with eye, SCN and pineal gland, and steps of melatonin synthesis in the pineal gland**

SCN: Suprachiasmatic nucleus; RHT: Retinohypothalamic tract; SCG: Superior cervical ganglion; PG: Pineal gland; NE: Noradrenaline; TH: Tryptophan hydroxylase; ALDC: Aromatic L-amino acid decarboxylase; AANAT: Arylalkylamine N-acetyl transferase; ASMT: Acetylserotonin O-methyltransferase; N-AS: N-acetyl serotonin; SAM: S-adenosyl methionine; SAH: S-adenosyl homocysteine; CSF: Cerebrospinal fluid

### 3. EFFECT OF LIGHT POLLUTION

Natural light has a strong association with the daily and annual rhythms of every life, starting from bacteria to humans. ALAN has a great impact on the living system, both aquatic and terrestrial organisms. Light pollution disturbs the prey-predator relationship, nature of the habitat, locomotor activities, behavior of the animals, and reproductive functions. According to the ecological consequences, different species are present at different trophic levels, and their

activities are interlinked in the food web and energy flow.

Thus, any pressure from the anthropogenic activity may induce the remodeling in the trophic levels that disturb the entire ecosystem [22,23]. Moreover, ALAN also affects the involvement of the non-trophic interacting species that have great importance in pollination, seed dispersal, and crop protection from pests. Therefore, light pollution is critically detrimental to the entire living system (Fig. 2).

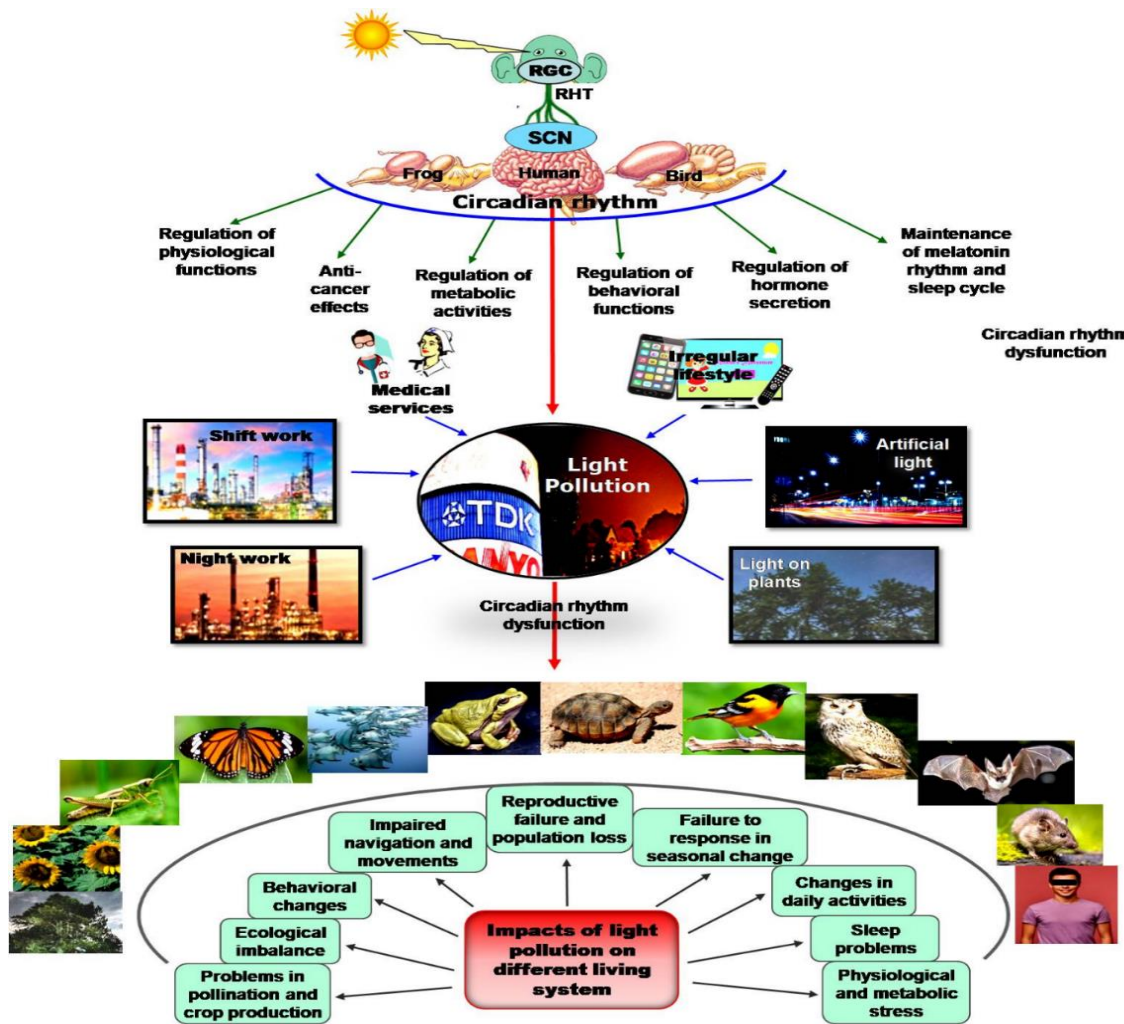


Fig. 2. Anthropogenic activity, sources of artificial light at night and effects of light pollution on living systems

RGC: Retinal ganglion cells RHT: Retino-hypothalamic tract;  
SCN: Suprachiasmatic nucleus

**Plants and insects:** Light exposure at night affects the physiological activities of plants. The effects are more prominent in urban and suburban areas, and that was illustrated by Bennie et al. [24]. The trees show maladjustment in seasonal variations, flowering activity, and reproductive functions. Exposure to artificial light at night on plants changes the photosynthetic activity and alters budburst activity, flowering property, leaf coloring and abscission. Deciduous trees in lit areas may concern with the retention of leaves. Changes in the leaf functions and flowering activity significantly affect the plants' physiology, growth, and reproductive functions. Artificial light affects the diatoms population and its variations by lowering the respiratory activity and redistribution of sedimentary microbial populations. These effects increase carbon accumulation in sediments [5].

ALAN attracts insects, and they scatter at the lit area. In certain cases, light activity decreases food intake and hampers metabolic and physiological activities. On the other hand, light pollution increases foraging activity in spiders (*Eriophorabi apicata*) [25]. Artificial light exposure accelerates the maturation process but decreases the body size of the developing spiders. Light also affects the sexual activity of moths and spiders due to disruption in attraction behavior between males and females [4].

**Fish:** Nighttime lighting affects the behavior of coastal and fresh water fishes. The locomotor activity, energy expenditure, nesting behavior, and parental care are affected by various spectrums of light [26]. A case study report by Riley et al. indicated that light disrupted the migrating behavior of Atlantic salmon (*Salmo salar*), leading to a reduction of fitness and increased risk of predation [27]. ALAN has diverse effects on fish reproduction. It affects the hypothalamic-gonadal axis. Different experiments showed assorted results. Light pollution decreases LH and FSH expression, as well as melatonin secretion in Perch (*Percafluviatilis*). In contrast, artificial exposure accelerates estradiol expression and gonadal maturation in *Chrysiptera parasema* (dwarf fish) and *Carassius auratus* (goldfish) [4].

**Frogs:** ALAN has an impact on ecological balance and changes the behavior of the prey-predator relationship. Nighttime lighting increases the vulnerability of the frogs

because of their exposure to the nocturnal predators. Light pollution hampers the mating behavior of frogs and decreases their reproductive success. Touzot et al. reported that ALAN altered the metabolic activity in common male toads (*Bufo* spp.) during the breeding season, which might be the cause of poor reproductive success [28]. Artificial light exposure accelerates the steps of metamorphosis and decreases the growth of the offspring of the American toad (*Anaxyrus americanus*) [29].

**Turtles:** Sea turtles are facing serious problems in choosing particular locations for nesting and egg-laying. Moreover, newly hatched turtles become disoriented and do not navigate the sea direction due to light pollution in beach areas, resulting in serious impacts on the turtles' population [30]. Disturbance in hatching, and population loss were also reported by Truscott et al. for Green turtles (*Chelonia mydas*) [31]. Brei et al. reported that light pollution accelerated the extinction process of several sea turtles: Green turtle, Hawksbill turtle (*Eretmochelys imbricate*), and Leatherback turtle (*Dermochelys coriacea*) [32].

**Birds:** The physiological and behavioral activities of birds are maintained by natural photoperiodism. Seasonal variation and natural environmental cycles regulate the normal biological functions of the birds [7,33]. ALAN deregulates many physiological rhythms of birds that are associated with seasonal changes. Birds are suffering from habitat, sleep problems, behavioral changes and reproductive activity [34-36]. ALAN advances the onset of the daily activity of the birds. Songbird species start their dawn and dusk singing before the onset of natural timings. Reports are available on different species: European robin (*Erithacus rubecola*) [37,38], American robin (*Turdus migratorius*) [39], common blackbird (*Turdus merula*) [37,38,40], great tit (*Parus major*) [37,38], song thrush (*Turdus philomelos*) [38] and the blue tit (*Cyanistes caeruleus*) [37,38]. ALAN also creates sleep problems, increases sleep latency and decreases sleep duration. Artificial light deregulates the circadian rhythm and advances awakening time before the onset of dawn. Raap et al. reported that artificial light influences the early wake-up of birds, and they stay less time in their nest [36]. Moreover, experimental birds showed delayed entry to

the nest and took more time to fall asleep in comparison to the control group.

Molenaar et al. reported that black-tailed godwits (*Limosalimos*) moved away from artificial street lights for their breed [41]. Reproductive functions of birds are associated with seasonal variability and get maximum success when environmental conditions are most favorable for both parents and offspring. Several factors are involved in the light-induced advancement of reproductive activity. These include higher environmental temperature, scarcity of habitat and social stimulation, availability of sufficient food (anthropogenic supply), poor sleep quality, and decreased anti-gonadal effects of melatonin. Artificial electric light extends the breeding season of urban birds. Both males and females are reproductively active for a longer time due to the advanced onset of reproductive activity. Both male and female urban population of European blackbirds (*Turdus merula*) exhibits their gonadal activity three weeks before from the normal breeding period [42]. Poultry birds were kept in longer periods of light to stimulate reproductive behavior [43]. Inappropriate light exposure disrupts circadian rhythm and stimulates luteinizing hormone secretion that stimulates gonadal activity [7]. Experimental evidence revealed that light exposure advanced reproductive functions. Exposure to low-intensity light (0.3 lux) on experimental birds (blackbirds- *Turdus merula*) promotes the development of functional testis 26 days earlier than the control birds. The experimental birds increase testosterone secretion earlier than the control group. Additionally, testicular activities continue for extra 12 days [44]. In the same experiment, the authors also reported that the birds residing in city areas started their reproductive activity earlier than the natural forest birds of the same species, and the city birds continued their reproductive functions for a longer time. Partecke et al. reported that the number of birds, living in urban areas showed an earlier breeding activity in comparison to similar species in rural areas [42]. ALAN affects the circadian clock, pineal function, and melatonin secretion in the avian system, more specifically in the urban population [45]. In birds, the pineal gland plays a much more important role than it does in mammals. The pineal gland receives non-visual light stimuli through the retinohypothalamic tract [46]. Cassone and Menaker suggested that the

avian retina, pineal gland, and SCN could produce self-generating oscillation in the presence of the photic or endocrine signal [47]. Melatonin is the hormone of the dark. The secretion of melatonin starts in the evening and reaches the maximum peak at midnight. Melatonin has several physiological functions and also suppresses gonadal activity. A minimum of light (0.3 lux) can suppress melatonin secretion [44,48]. Recently, several authors reported the ALAN-induced suppression of melatonin release in different birds, such as Eurasian tree sparrow (*Passer montanus*) [9], European blackbirds (*Turdus merula*) [49]. Dominoni et al. also reported that low levels of melatonin might be associated with the early onset of daily activity [49]. Normally, melatonin promotes the release of the gonadotropic-inhibitory hormone (GnIH) from the avian hypothalamus and regulates seasonal breeding [50]. Low levels of melatonin can not maintain the inhibitory effect on gonadotropin releases, resulting in early secretion of LH (luteinizing hormone) and FSH (follicular stimulating hormone) that stimulate gonadal functions [51,52]. Light pollution advances the egg-laying date of urban birds. The urban population of European blackbirds showed early gonadal development and the advanced peak of reproductive hormones. Studies were also conducted on Florida scrub jays, Albert's towhee (*Melospiza aberti*), and Curve-billed thrasher (*Toxostoma curvirostre*) [53]. De Jong et al. reported that experimentally exposure to artificial light at night in different forests of the Netherlands, the great tits showed 5 days of advancement in the egg-laying process [54]. The role of melatonin was also established by Greives et al. [55]. They reported that exogenous administration of melatonin in wild great tits (*Parus major*) delayed the duration of the egg-laying. Caro et al. suggested that the egg-laying date is not only dependent on photoperiodism but also influenced by environmental temperature and food abundance [56]. Early reproductive activity sometimes causes reproductive loss because, owing to seasonal advancement, there is a chance of food scarcity, lack of energy, and failure to fulfill metabolic costs. ALAN increases the abundance of prey for the nocturnal predatory birds, such as European nightjars (*Caprimulgus europaeus*) and burrowing owls (*Athene cunicularia*). The abundance of forage changes the site selection for nesting, which may increase the



vulnerability of the nocturnal birds, as well as reproductive loss [57,58]. Migratory birds show disorientation of movements and alter migration patterns at night due to confusion. Light pollution also increases the risk of collision with skyscrapers, high-rise buildings, and communication towers as the birds are confused during passing the buildings that are illuminated with bright lights [35,59,60].

The circadian clock, melatonin levels and sleep quality have significant effects on cognitive performance in both avian and mammals. ALAN enhances nocturnal activity in domestic pigeons (*Columba livia domestica*) and southern lapwing (*Vanellus chilensis*) for the availability of foraging opportunities and excess feeding activity [61,62]. ALAN-induced nocturnal activity disrupts the circadian rhythm, melatonin pulse, and sleep cycle. These effects alter behavioral activity, mood, cognitive functions, and performance of learning, and memory [63-65]. ALAN alters the expression of core clock genes, like *Clock*, *Bmal1*, *Per*, and *Cry* along with the expression of different cytokines (pro-inflammatory: interleukin 1 $\beta$ , IL 6; IL12, IL 17, IFN- $\gamma$ , TNF- $\alpha$ , and anti-inflammatory IL 10). Evidential proof indicated that light pollution affects the behavioral activity, rest cycle, and dawn and dusk singing in different birds such as Eurasian blackbird (*Turdus merula*), great tits (*Parus major*), zebra finches (*Taeniopygia guttata*), house crows (*Corvus splendens*), European robin (*Erithacus rubecula*), song thrush (*Turdus philomelos*), blue tits (*Cyanistes caeruleus*), chaffinch (*Fringilla coelebs*), American robins (*Turdus migratorius*), and Indian peafowl (*Pavo cristatus*) (see review Taufique 2022) [10]. Light pollution affects neural activity in the hippocampus (HP), caudal nidopallium (NC), substantia nigra (SN) and ventral tegmental area (VTA). SN and VTA contain huge numbers of dopaminergic neurons. ALAN decreases the activity of tyrosine hydroxylase (TH) and the activity of the dopaminergic system [63]. Taufique et al. reported that light-associated phenomena diminish neurogenesis, dendritic complexity, and neural plasticity in the HP and NC of house crows [66]. Light-induced activity modulates the activity of histone deacetylase-4, affects histone H3 acetylation near the *bdnf* gene, resulting in a low level of expression of BDNF (brain-derived neurotrophic factor) [67].

**Bats:** A large number of mammalian populations belong to bats. ALAN disturbs the activity, food searching, and feeding pattern in bats. Bats have multiple species diversity. Most bats are insectivores. Some are vegetarian, eating fruits, flowers, or nectar. Thus, bats are involved in the regulation of insect populations, pest control, pollination, and seed dispersal. Their regular activity, movements, and behavior vary from species to species. The activities of some bats are advanced by light, while others prefer complete darkness. Light pollution affects the nesting behavior (delay or advance to leave the nest) sexual activity, flight speed and pathways. Sometimes, illumination increases the risk of collision with obstacles [4,68]. All these effects have negative impacts on the bats' population, as well as ecology.

**Rat:** Rats and other free-living nocturnal mammals decrease their physical activity and food searching on exposure to ALAN to minimize the risk of attack from predators. Contrastingly, light pollution increases the physical activity and movements for food searching in diurnal and crepuscular animals (insect feeding) [69]. Light pollution alters food intake, metabolism, glucose concentration, lipid accumulation, as well as leptin and corticosterone levels in rats (*Rattus norvegicus*) [70], which may affect the reproductive activity. Ikeno et al. conducted a well-established study on Siberian hamsters (*Phodopus sungorus*) [71]. This animal shows poor gonadal activity, reduced body mass, and fewer numbers of spermatogonia in the winter season. However, Exposure to ALAN affects these types of adaptive changes and also alters the expression of some specific genes, such as *Per1*, *TSH*, *gonadotrophin inhibiting hormone*, and *gonadotrophin releasing hormone*. Torres-Farfan et al. suggested that ALAN had a serious threat to rats, non-human primates, and sheep, as light pollution causes shorter pregnancy periods, poor fetal development, and low birth weight of the newborn, resulting in poor metabolic and physiological activities, ensuring long-term effects [72].

**Human:** In our modern society humans are involved in different activities at night. These include medical services, electric power generation, transport services, satellite operations, industrial work, security services, and military activities. To operate these functions, humans are involved in shift work

and night work, and they are severely exposed to ALAN. Moreover, modern lifestyle, rapid urbanization, industrialization, and the application of bright light in residential areas also increase nighttime light exposure in common people. Night-time light pollution desynchronizes the circadian rhythm and also disrupts the melatonin rhythm. Circadian clock dysfunction deregulates different rhythms (melatonin ACTH/cortisol, body temperature), and metabolic activities. Besides these, circadian clock disruption and low levels of melatonin are associated with many health problems, such as sleep disorders, cardiovascular diseases, metabolic disorders, infertility, neurodegenerative diseases, psychiatric problems, and cancers [12]. Light-induced circadian clock dysfunction decreases alertness, cognitive behavior, mental stability, and physical performance that sometimes increase the probability of accidents at late night in the transportation system, industrial area, and power plants [73].

Light pollution, shift work, and circadian rhythm disorders promote sleep disorders. The American Academy of Sleep Medicine classifies these disorders into different classes: advanced sleep phase disorder/syndrome (ASPD/ASPS), delayed sleep phase disorder/syndrome (DSPD/DSPS), free-running disorder (FRD), and irregular sleep-wake rhythm (ISWR) [74]. Melatonin has a role in sleep physiology. This indolamine inhibits the activity of the SCN and induces the onset of sleep because SCN has tried to maintain a waking state. Do Amaral and Cipolla-Neto reported that melatonin supplementation in human subjects reduces sleep latency and improves sleep quality [75].

Circadian dysfunction increases the formation and accumulation of misfolded or mutant protein-aggregates in common neurodegenerative diseases, such as  $\beta$ -amyloid plaque and tau in Alzheimer's disease,  $\alpha$ -synuclein in Parkinson's disease, and huntingtin in Huntington's disease [76]. The circadian clock regulates the expression of several genes that are involved in protein processing, transport, and removal of misfolded proteins. Circadian misalignment increases the risk of formation of misfolded proteins in neurodegenerative diseases. Sleep disorders, oxidative stress (OS) and low levels of melatonin also advance this process. Melatonin is a potent antioxidant that controls

OS, mitochondrial functions, cellular activities, and inflammation [14]. Low levels of melatonin increase OS, mitochondrial dysfunctions and neuroinflammation, resulting in the advancement of neurodegenerative diseases.

ALAN affects the natural light-dark cycle that influences the occurrence of seasonal affective disorder (SAD). Circadian dysfunction-associated sleep disorder and low levels of melatonin are linked with the development of different psychological disorders, such as SAD, bipolar disorder (BD), unipolar depression, schizophrenia, autism spectrum disorder (ASD), and attention deficit hyperactivity disorder (ADHD) [77]. Sun et al. reported the importance of melatonin (pharmacological dose) in the improvement of psychiatric disorders [78].

Heart rate, blood pressure, blood catecholamine, cortisol, platelet aggregation, and other humoral factors are under the control of circadian rhythm. Light pollution-mediated-circadian misalignment affects sympathetic activity and secretion of catecholamines, cortisol, and aldosterone that can advance cardiovascular diseases (CVD). Moreover, peroxisome proliferators activated receptor  $\gamma$  (PPAR $\gamma$ ) signaling, impaired lipid metabolism, and nitric oxide (NO) signaling alter the activity of endothelial cells during circadian dysfunction and promote hypertension and CVD.

Obesity, hyperglycemia, type 2 diabetes, and dyslipidemia are common metabolic disorders that are characterized by alteration in blood triglyceride levels, high-density lipoprotein concentrations, blood glucose content, as well as inflammatory markers, like C-reactive protein, TNF- $\alpha$ , IL-6, and plasminogen activator inhibitor type 1 [79]. Light-induced circadian dysfunction alters the activity of several nuclear receptors, including PPAR $\alpha$ , PPAR $\gamma$ , retinoic acid orphan receptor  $\alpha$ , hepatocyte nuclear factor 4 $\alpha$  (HNF4 $\alpha$ ), thyroid hormone receptor  $\alpha$  (TR $\alpha$ ), and nuclear receptor-related 1 (NURR1); the result is inductive pressure of development of metabolic disorders, as these receptors are associated with lipogenesis, lipid storage, ketogenesis, hepatic fatty acid oxidation and others [80].

Circadian events regulate the expression of core clock genes: *Clock*, *Bmal1*, *CK 1 $\epsilon$* , *Cry1*–

2, *Npas2*, *Per1–3*, *Rora*,  $\beta$ , and  $\gamma$ , *Rev-Erba* and  $\beta$ . The clock components are essential for the regulation of the cell cycle, DNA repair, metabolism, redox homeostasis, and inflammatory response. The circadian activity also controls the release/expression of cytokines, hormones, neurotransmitters, tumor-specific metabolites, oncogenic proteins, and tumor suppressor factors. Exposure to ALAN disrupts circadian functions, leading to the deregulation of cellular activities and the progression of cancer development [81]. Another important factor is melatonin, which is crucial in the regulation of OS, cell cycle, DNA repair, activity of nuclear receptors, inflammatory response, and tumor growth. Nighttime light exposure suppresses melatonin release and lowers the melatonin peak. Low levels of melatonin increase the risk of cancer development [14]. The people of modern society are exposed to bright light at night due to their professional burden, resulting in a misalignment of the circadian rhythm. According to International Agency for Research on Cancer (IARC) shift work is “carcinogenic to humans (Group 2A)” [82]. Shift work and night work can enhance the risks of breast, ovarian, prostate, colorectal, hepatocellular, and other cancers [11,12]. Although melatonin is associated with several essential functions, the deregulation of melatonin rhythm promotes breast cancer [83,84], ovarian cancer [85], prostate cancer [86], colorectal cancer [87], hepatocellular [88], endometrial cancer [89], and lung cancer [90].

#### 4. CONCLUSION

Natural light is the primary source of power. However, illumination through artificial electric light at night causes light pollution. Indeed, artificial light improves economic development, regular activities, working duration, social security, and recreational activities, but it creates serious threats to health issues and ecological balance (Table 1). Light changes the behavior, daily activities, foraging, and reproductive functions of insects. Fishes show their behavioral changes and feeding pattern. Sea turtles are mostly affected because they are facing problem in searching their habitat for egg laying, leading to reproductive loss. Birds are facing varieties of problems. ALAN deregulates the sleep cycle, behavior, physical movements, and

reproductive pattern. Bats and rats are also facing different problems. Humans are mostly affected by light pollution. Exposure to ALAN promotes sleep disorders, hormonal imbalance, neurodegenerative diseases, psychological problems, metabolic disorders, CVD, and cancers. Melatonin has several protective functions in humans and other animals. ALAN decreases melatonin secretion at night and lowers its peak. Although light pollution is directly associated with anthropogenic activities, it affects the entire ecosystem. To establish the molecular basis of physiological and behavioral changes related to light pollution, more research is needed, and there must be multidimensional approaches. Survey-based ecological studies and cross-sectional studies will be helpful to establish the impacts of light pollution on various animals. Biochemical and the study of molecular genetics can explore the mechanism of effects of light pollution for the alteration of physiological and behavioral functions. Finally, it can be said that natural darkness is an essential part of our living system that should be maintained in a scientific way to sustain the ecological balance. Restricted use of light at residential places, highways, sea beaches, and forest areas can be the preventive measures. Plantation of trees in residential areas, highways, and sea beaches can decrease the effects of light pollution. Moreover, increased public awareness about the effects of light pollution will give the benefits in the near future.

#### DATA AVAILABILITY

This review article is prepared on the basis of literature survey. So, no new data has been generated.

#### COMPETING INTERESTS

Author has declared that no competing interests exist.

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