



Black Sea Journal of Health Science

Volume 8 | Issue 5



ISSN: 2619 - 9041


BS Journals



**BLACK SEA JOURNAL OF HEALTH SCIENCE
(BSJ HEALTH SCI)**


BS Journals

The Black Sea Journal of Health Science (BSJ Health Sci) is a double-blind, peer-reviewed, open-access international journal published electronically 6 times (January, March, May, July, September, and November) in a year since January 2018. BSJ Health Sci publishes, in English and Turkish, full-length original research articles, innovative papers, reviews, mini-reviews, conference papers, case reports, rapid communications, or technical notes by scientists on technical and clinical studies related to all health sciences.

ISSN: 2619-9041

Phone: +90 362 408 25 15

Fax: +90 362 408 25 15

Email: bsjhealthsci@blackseapublishers.com

Web site: <http://dergipark.gov.tr/bshealthscience>

Sort of Publication: Periodically 6 times in a year (January, March, May, July, September, and November)

Publication Date and Place: September 15, 2025 - Samsun, TÜRKİYE

Publishing Kind: Electronically

PUBLISHER

Karyay Karadeniz Yayımcılık Ve Organizasyon Trade Limited Company

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EFFECTS OF THYMOQUINONE ON OXIDATIVE STRESS AND BEHAVIOR IN MERCURY-EXPOSED RATS

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Abstract: Mercury (Hg) is widely used in nature. It is a substance that has toxic effects even in small amounts. Thymoquinone (TQ) is the main active phenolic compound obtained from the essential oil of *Nigella sativa* L. (black cumin) seed. The protective effects of TQ against diseases and toxic compounds have been studied for a long time. Aim: This study aimed to investigate the effect of TQ on oxidative stress and behavior in rats exposed to mercury. In this study, 24 adult male Wistar Albino rats weighing between 250±20 g were used. 5 mg/kg Hg and 10 mg/kg TQ were given via intragastric gavage for 21 days. Animals were randomly divided into four groups. Group 1 is the Control, Group 2 TQ (10 mg/kg), Group 3 Hg (5 mg/kg), Group 4 Hg (5 mg/kg) + TQ (10 mg/kg). Open field test and forced swimming test were performed to examine locomotor activity, anxiety, and depression-like behaviors in rats. At the end of the experiment, Malondialdehyde (MDA), total nitric oxide (NO), and reduced glutathione (GSH/RSH) levels were examined in cerebral cortex and plasma. In the open field test, Hg+TQ treatment increased the number of crossings and time spent in the center ($P<0.01$). In the forced swim test, Hg+TQ treatment increased the swimming and climbing time (respectively $P<0.01$, $P<0.001$) and decreased the immobility time ($P=0.001$). In cerebral cortex and plasma, TQ treatment decreased the increased MDA and NO levels ($p=0.01$) and increased the decreased GSH/RSH levels ($P<0.01$) as a result of Hg exposure. Mercury exposure increased oxidative stress in plasma and cerebral cortex, causing anxiety and depression-like behaviors. TQ is can be used to improve some behavioral changes and reduce oxidative stress in Hg-exposed rats.

Keywords: Mercury, Behavior, Oxidative stress, *Nigella sativa*, Rats, Antioxidants

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Received: May 14, 2025

Accepted: August 01, 2025

Published: September 15, 2025

Cite as: Kuzay Aksoy D. 2025. Effects of thymoquinone on oxidative stress and behavior in mercury-exposed rats. BSJ Health Sci, 8(5): 182-189.

1. Introduction

Mercury, which the World Health Organization (WHO) lists among the ten chemicals that cause significant public health concerns, causes damage to many tissues and organs and is considered the third most toxic element in terms of human health (Yavuz, 2020). Hg has been reported to cause behavioral and neurochemical changes in rats (Minj et al., 2012). It was also found to increase Reactive Oxygen Product (ROP) levels in cells (Zhang et al., 2021). Increased ROP in cells causes oxidative stress by disrupting the pro-oxidant/antioxidant balance. It has been determined that mercury at various doses decreases antioxidant weapons such as Glutathione (GSH) in cells and increases Malondialdehyde (MDA), which indicates lipid peroxidation in cells (Gstraunthaler et al., 1983; Nath et al., 1996; Fouda et al., 2008).

Thymoquinone (TQ) is the primary active ingredient of the essential oil obtained from black cumin seed (*Nigella sativa* L.). Studies have shown that TQ protects cells from inflammation and oxidative stress and has a neuroprotective effect (Fouda et al., 2008; Kuzay et al., 2022). TQ has been shown to have antioxidant effects against different toxic substances. (Akarsu and Çetin,

2022). Additionally, antioxidant and protective effects of TQ on kidney and liver tissue were demonstrated in rats exposed to mercury (Fouda et al., 2008; Owumi et al., 2025). However, in rats exposed to Hg, the oxidative stress levels and behavior of TQ in cerebral cortex and behavior were not examined. Therefore, in the present study, the oxidative stress levels and behavior of TQ in cerebral cortex and behavior were examined in rats exposed to Hg.

2. Material and Methods

In our study, 24 adult male Wistar Albino rats weighing 250±20 g (12-13 weeks old) were acquired from the Animal Experiment Laboratory. This study was supported by Institutional Scientific Research Projects. The Project number is TIP.A3.24.011.

2.1. Chemicals

HgCl₂ (Tekkim, Türkiye) and TQ (CAYMAN Chemical, USA) were used in this study.

2.2. Exposure to Mercury

Rats were given mercury (II) chloride (HgCl₂) by intragastric gavage at 5 mg/kg for three weeks. In their preclinical studies, Minj et al., reported that Hg caused neurologic impairment (Minj et al., 2021).



2.3. Experimental Design

The total duration of the study was 22 days. 5 mg/kg Hg and 10 mg/kg TQ were dissolved in tap water and administered via intragastric gavage for 21 days. Animals were randomly divided into four groups (n=6 for each group). Group 1 is the Control, Group 2 TQ (10 mg/kg), Group 3 Hg (5 mg/kg), Group 4 Hg (5 mg/kg) + TQ (10

mg/kg). The control group received only tap water to induce gavage stress. Chemicals were freshly prepared every day and administered in a total volume of 1 ml/kg (Fouda et al., 2008; Minj et al., 2021; Kuzay et al., 2022). TQ was given half an hour before Hg. The experimental protocol is summarized in Figure 1.

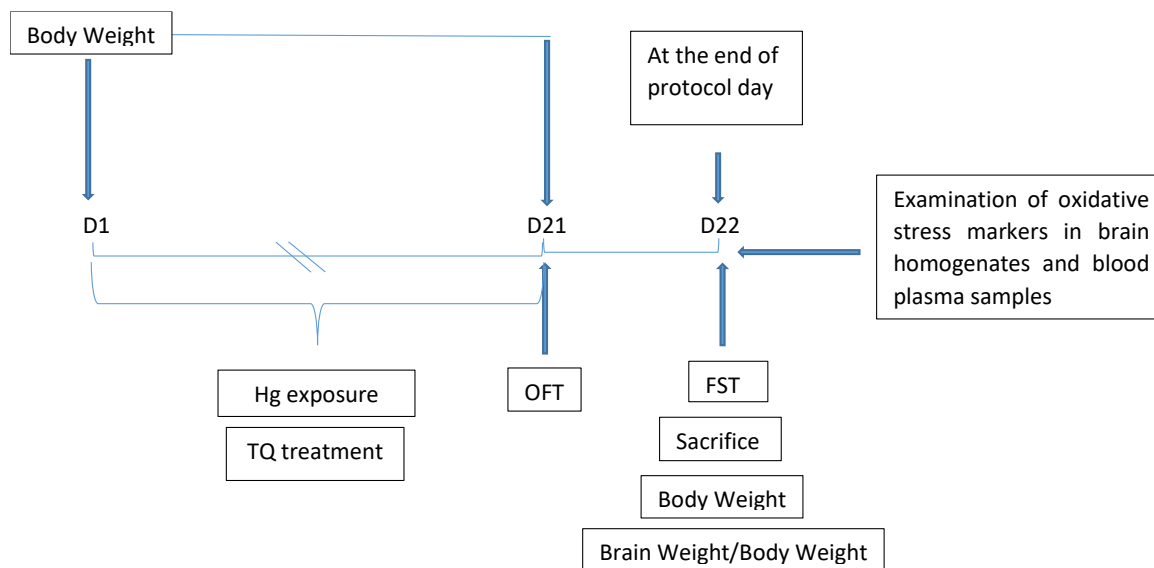


Figure 1. Timeline depicting the sequence of experimental events. D indicates day of experiment. Rats were tested in the forced swim test (FST) on day 22 and in the open field test (OFT) on day 21. Body weight was taken on day 1 and day 22. Brain weight / Body weight was taken on day 22.

2.4. Measurement of Body Weight

Rats were weighed on days 1 and 22 of the study.

2.5. Evaluation of the Relative Brain/Body Weight Ratio

Hg exposure can cause toxic effects on the brain. Therefore, on the 22nd day of the study, the brain weights of the rats were measured to establish a relationship between brain-body weight losses. To examine the change in absolute brain weight, the ratio of brain weight/body weight was calculated and this formula was used. Brain weight / Body weight x 100 (Shandilya et al., 2022).

2.6. Behavior Parameters

2.6.1. Forced swim test (FST)

FST was performed on day 22 to assess depression-like behavior in animals. It evaluates an animal's resilience to water stress. One day before, a 15-minute pre-test was performed to prevent acute stress in rats. After the pretest, rats were individually exposed to 30 cm of water at 25°C±1°C in cylindrical containers with a diameter of 15 cm and a height of 50 cm for 5 minutes. During the test period, swimming, climbing, and immobilization times were recorded with a video camera (Kuzay et al., 2022).

2.6.2. Open field test (OFT)

OFT was performed on the 21st day to assess locomotor activity and anxiety-like behavior in animals. In a 90 cm x 35 cm white Plexiglas arena divided into 24 units with a black strip on the floor, the individual movements of each rat were recorded by video camera for 5 minutes. The period spent in the center and periphery of the open field and the number of crossings were recorded (Brocardo et al., 2012). Two hours after the treatment, the behavioral tests of each rat were measured.

2.7. Evaluation of Oxidative Stress Markers

On day 22, all rats were sacrificed under im. 5mg/kg Rompun + 45mg/kg Ketamine anesthesia by removing blood from their hearts. The cerebral cortex separated from the rats were stocked at -80°C until the day of the study. The blood is centrifuged (at 2000-3000 RPM) for approximately 20 minutes at 4°C. (NUVE NF 800R, Türkiye). The supernatant is carefully collected and kept at -80°C until used.

2.7.1. Determination of plasma MDA levels

Plasma lipid peroxide levels were estimated by the method as per Kurtel et al. (1992). The supernatants were added into 1 ml of a solution with 15% (wt/vol) tricarboxylic acid, 0.375% (wt/vol) thiobarbituric acid, and 0.25 N HCL following the centrifugation of aliquots (0.5 ml). Protein precipitate was eliminated through

centrifugation and the supernatants were placed in glass test tubes with 0.02% (wt/vol) butylated hydroxytoluene with the aim of avoiding further peroxidation of lipids in the preceding steps. Next, the samples were heated at 100°C in a boiling water bath for 15 min, cooled, and centrifuged to eliminate the precipitant. The absorbance of each sample was decided at 532 nm. (Spectrostar Nano, Germany). The expression of lipid peroxide levels was achieved with regards to MDA equivalents by employing an extinction coefficient of $1.56 \times 10^5 \text{ mol}^{-1}$ (Kurtel et al., 1992).

2.7.2. Determination of plasma NO levels

NO levels were estimated by the method as per Miranda et al., The supernatants were deproteinized with 0.3 M NaOH and 5% (w/v) ZnSO₄, centrifuged at 14 000 rpm for 5 min, and supernatants were utilized for the assays. Experiments were carried out at room temperature. Nitrate standard solution was consecutively diluted. After loading the plate with samples (100 µl), vanadium III chloride (VCl₃) (100 µl) was added to each well and this was quickly followed by addition of Griess reagents, sulphanilamide (SULF) (50 µl) and N-(1-naphtyl) ethylenediamine dihydrochloride (NEDD) (50 µl). After incubation (usually 30-45 min), samples were measured at 540 nm by ELISA reader. (Miranda, Espey, Wink, 2001).

2.7.3. Determination of plasma RSH levels

The GSH levels were determined by the method as per Kurtel et al., 0.5 ml of each sample was blended with 1 ml of a solution with 100 mM Tris-HCl (pH 8.2), 1% sodium dodecyl sulfate, and 2 mM EDTA. Next, the mixture was incubated for 5 min at 25°C and centrifuged to eliminate any precipitant. 5,5-dithiobis (2-nitrobenzoic acid)/DTNB 0.3 mM was added to each reaction volume and incubated for 15 min at 37°C. The absorbance of each sample was 412 nm (Kurtel et al., 1992).

2.7.4. Determination of cerebral cortex MDA levels

Lipid peroxidation was quantified by measuring the formation of thiobarbituric acid reactive substances (TBARS). Samples were homogenized in ice-cold trichloroacetic acid (1 g tissue in 10 ml 10% trichloroacetic acid) in a tissue homogenizer (DAIHAN Scientific, Korea). Following centrifugation of the homogenate at 3,000 rpm for 10 min. 750 µl of supernatant was added to an equal volume of 0.67% (m/v) thiobarbituric acid and heated at 100°C for 15 min. The absorbances of the samples were measured at 535 nm. Lipid peroxide levels are expressed in terms of MDA equivalents using an extinction coefficient of $1.56 \times 10^5 \text{ mol/cm}$ (Casini et al., 1986).

2.7.5. Determination of cerebral cortex NO levels

NO levels were measured by Griess assay (Miranda, Espey, Wink, 2001). Prior to NO determination, the tissues were homogenized in five volumes of phosphate buffer saline (pH 7.4) and centrifuged at 2,000 g for 5 min. NaOH 0.25 ml, 0.3 M was added to 0.5 ml of the supernatant. After incubation for 5 min at room temperature, 0.25 ml of 5% (w/v) ZnSO₄ was added for

deproteinization. This mixture was then centrifuged at 14,000 rpm for 5 min and supernatants were used for the assays. A nitrate standard solution was serially diluted. After loading the plate with samples (100 µl), addition of vanadium III chloride (VCl₃) (100 µl) to each well was rapidly followed by addition of Griess reagents, sulphanilamide (SULF) (50 µl) and N-(1-naphtyl) ethylenediamine dihydrochloride (NEDD) (50 µl). After the incubation at 37°C (usually 30-45 min), samples were measured spectrophotometrically at 540 nm.

2.7.6. Determination of cerebral cortex GSH levels

The total GSH levels were determined by the Ellman method with some modifications (Aykaç et al., 1985). Briefly, samples were homogenized in ice-cold trichloroacetic acid (1 g tissue in 10 ml 10% trichloroacetic acid) in a tissue homogenizer. After centrifugation of the homogenates at 3,000 rpm for 10 min, 0.5 ml of supernatant was added to 2 ml of 0.3 M Na₂HPO₄ 2 H₂O solution. A 0.2 ml solution of dithiobisnitrobenzoate (0.4 mg/ml 1% sodium citrate) was added and after mixing, the absorbance at 412 nm was immediately measured using a spectrophotometer at room temperature.

2.8. Statistical Analysis

Comparisons between the groups were performed using a one-way analysis of variance followed by post hoc Tukey tests. Paired Samples T-test was used to compare the initial and final measurements of body weight in the same group. The data were examined using spss 29.0 software and presented as mean ± Standard Deviation (SD).

3. Results

3.1. Impact of TQ on Body Weight in Rats Exposed to Hg

On day 22, rats exposed to Hg showed significantly lower body weight compared to both the control and TQ groups ($P < 0.01$). However, co-administration of TQ with Hg (Hg+TQ group) partially reversed this weight loss, leading to a significant recovery compared to Hg-exposed rats ($P < 0.05$) (Figure. 2).

3.2. Impact of TQ on Relative Brain/Body Weight Ratio in Hg Exposed Rats

When compared with the control group, no statistically significant was determined in the relative brain/body weight ratio of the TQ group ($P = 0.3$). When compared with the control group and TQ group, there was a decrease in the relative brain/body weight ratio of rats exposed to Hg ($P < 0.01$). When compared with Hg-exposed rats, TQ treatment given together with Hg caused an increase in the relative brain/body weight ratio ($P < 0.05$) (Figure 3).

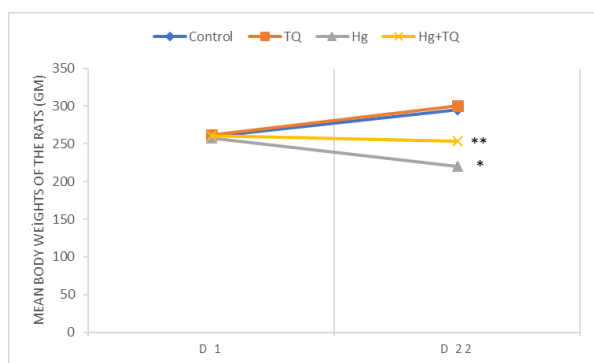


Figure. 2. Mean body weights of the rats (gm). D indicates day of experiment. Body weight was taken on day 1 and day 22. * $P < 0.01$ Significant differences with Control and TQ groups; ** $P < 0.05$ Significant differences with Hg group. C: No treatment was performed, TQ: Received TQ, Hg: Received Hg, Hg+ TQ: Received Hg and TQ.

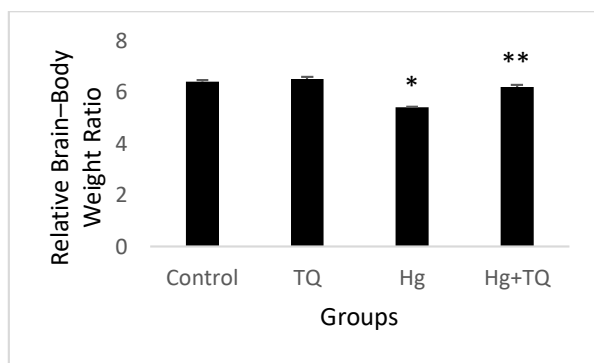


Figure. 3. Relative Brain/Body Weight Ratio. * $P < 0.01$ Significant differences with Control and TQ groups; ** $P < 0.05$ Significant differences with Hg group. C: No treatment was performed, TQ: Received TQ, Hg: Received Hg, Hg+ TQ: Received Hg and TQ.

3.3. Behavior Parameters

Effects of TQ on Locomotor Activity and Anxiety-like Behavior in Hg Exposed Rats

On the 21st day of the study, an OFT made to evaluate locomotor activity and anxiety-like behaviors. For appraise the locomotor activity in Hg-exposed rats, the number of passes was recorded as the number of crossings that the animals crossed with their four paws. When the control group and TQ group were compared, there was no statistically significant in the number of crossings ($P = 0.2$). When compared with the control and TQ groups, it was determined that there was a decrease in the number of crossings in rats exposed to Hg ($P < 0.001$). When compared with Hg-exposed rats, TQ treatment given together with Hg increased the number of crossings ($P < 0.01$).

The period spent in the center and periphery of the open field were examined to evaluate anxiety-like behaviors in rats exposed to Hg. When the control group and TQ group were compared, there was no statistically significant in the time spent in the center and periphery of the open field ($P = 0.3$). Compared with the control and

TQ groups, there was a decrease in the time spent in the center of the open field and an increase in the time spent in the periphery in rats exposed to Hg ($P < 0.001$).

When compared with Hg-exposed rats, TQ treatment given together with Hg caused an increase in the period spent in the center of the open field and a decrease in the time spent in the periphery ($P < 0.01$) (Figure 4A, 4B, 4C).

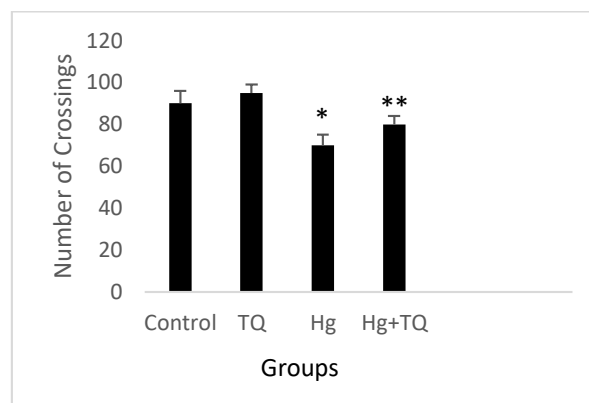


Figure. 4A. Number of crossings in the open field test. The values are means $\pm$ SD; $n = 6$. * $P < 0.001$ Significant differences with Control and TQ groups; ** $P < 0.01$ Significant differences with Hg group. C: No treatment was performed, TQ: Received TQ, Hg: Received Hg, Hg+TQ: Received Hg and TQ.

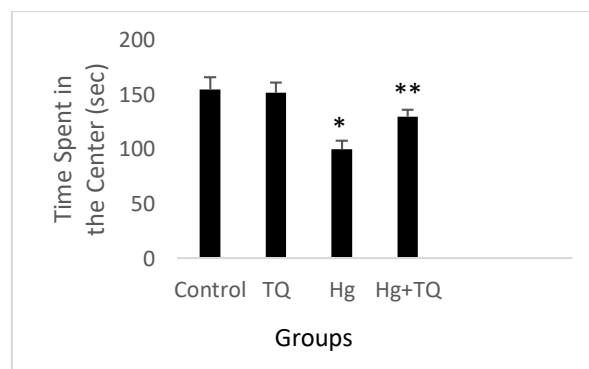


Figure. 4B. Time spent in the center (sec) in open field test. The values are means $\pm$ SD; $n = 6$. * $P < 0.001$ Significant differences with Control and TQ groups; ** $P < 0.01$ Significant differences with Hg group. C: No treatment was performed, TQ: Received TQ, Hg: Received Hg, Hg+TQ: Received Hg and TQ.

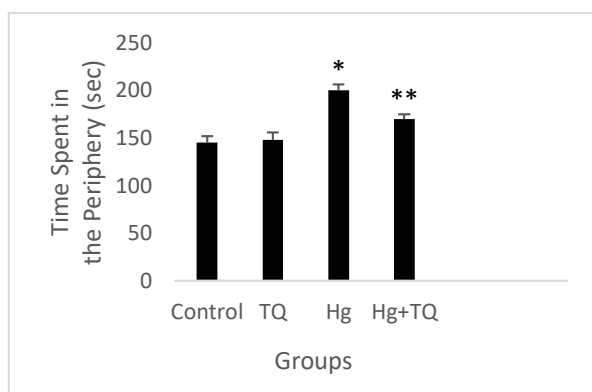


Figure 4C. Time spent in the periphery (sec) in open field test. The values are means $\pm$ SD; n=6. * P<0.001 Significant differences with Control and TQ groups; ** P<0.01 Significant differences with Hg group. C: No treatment was performed, TQ: Received TQ, Hg: Received Hg, Hg+TQ: Received Hg and TQ.

3.5. The Effect of TQ on Depression-Like Behavior in Hg-Exposed Rats

On the 22nd day of the study, a forced swim test was performed to assess depression-like behaviors. Swimming, climbing, and immobility times were recorded to examine depression-like or hopelessness behaviors. When the control group and TQ group were compared, there was no statistically significant in swimming, climbing, and immobilization times ($p=0.2$). When compared to the control and TQ groups, there was an increase in immobility time and a decrease in swimming and climbing time in rats exposed to Hg ($P<0.001$). When compared with Hg-exposed rats, TQ treatment given together with Hg caused a decrease in immobility times ($P<0.001$) and a rise in swimming and climbing times (Figure. 5A, 5B, 5C) (respectively $P<0.01$, $P<0.001$).

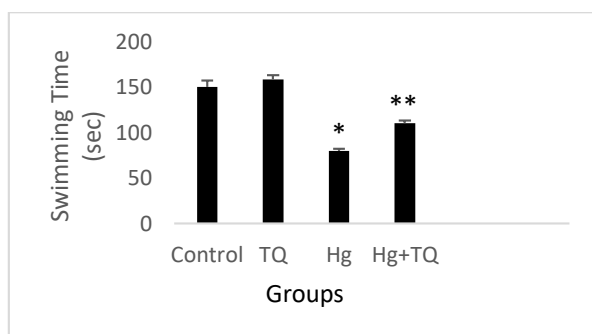


Figure. 5A. Swimming time (sec) in the forced swimming test. The values are means $\pm$ SD; n = 6. * P<0.001 Significant differences with Control and TQ groups; ** P<0.01 Significant differences with Hg group. C: No treatment was performed, TQ: Received TQ, Hg: Received Hg, Hg+TQ: Received Hg and TQ.

3.4. The Effect of TQ on Oxidative Stress Markers in Rats Exposed to Hg

MDA, NO and GSH/RSH levels were analyzed to determine oxidative stress levels in cerebral cortex and plasma. When the control group and TQ group were compared, it was determined that there was no significant difference in MDA, NO and GSH levels in cerebral cortex ($p=0.3$). When compared to the control and TQ groups, it was determined that MDA and NO levels (respectively $P<0.001$, $P<0.01$) in the cerebral cortex of rats exposed to Hg increased, and GSH levels decreased ($P<0.01$). When compared with Hg-exposed rats, TQ treatment given together with Hg provided a significant improvement by increasing GSH levels in cerebral cortex and decreased MDA and NO levels ($P<0.01$) (Table 1).

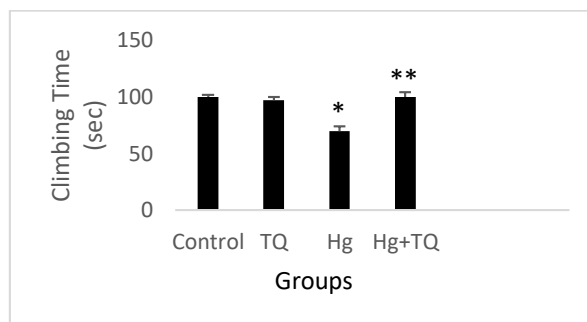


Figure 5B. Climbing time (sec) in the forced swimming test. The values are means $\pm$ SD; n = 6. * P<0.001 Significant differences with Control and TQ groups; ** P<0.001 Significant differences with Hg group. C: No treatment was performed, TQ: Received TQ, Hg: Received Hg, Hg+TQ: Received Hg and TQ.

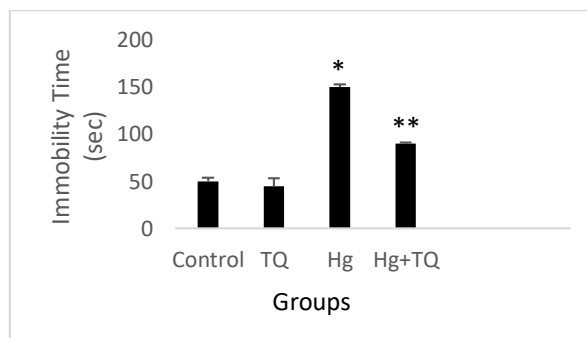


Figure 5C. Immobility time (sec) in the forced swimming test. The values are means $\pm$ SD; n = 6. * P<0.001 Significant differences with Control and TQ groups; ** P<0.001 Significant differences with Hg group. C: No treatment was performed, TQ: Received TQ, Hg: Received Hg, Hg+TQ: Received Hg and TQ.

In plasma, there was no statistically significant in MDA, NO and RSH levels when the control group and TQ group were confront ($P=0.8$). When compared to the control group and TQ group, MDA and NO levels rised, and RSH levels reduced in the plasma of rats exposed to Hg ($P<0.001$). When compared with Hg-exposed rats, TQ treatment given together with Hg provided a significant

improvement by increasing RSH levels in plasma and reduced MDA and NO levels ($P<0.01$) (Table 2).

Table 1. The results of Cerebral Cortex MDA, NO ve GSH levels

	Cerebral cortex		
	MDA Levels (nmol/g)	NO Levels (μ mol/g)	GSH Levels (nmol/g)
Control	4.43 $\pm$ 0.18 ^c	0.29 $\pm$ 0.03 ^c	4.2 $\pm$ 0.08 ^c
TQ	4.62 $\pm$ 0.21 ^c	0.27 $\pm$ 0.01 ^c	4.6 $\pm$ 0.2 ^c
Hg	7.5 $\pm$ 0.12 ^a	0.45 $\pm$ 0.02 ^a	2.7 $\pm$ 0.03 ^a
Hg+TQ	5.1 $\pm$ 0.093 ^b	0.3 $\pm$ 0.01 ^b	3.4 $\pm$ 0.19 ^b
	a: 0.001	a: 0.01	a: 0.01
P value	b: 0.01	b: 0.01	b: 0.01
	c: 0.03	c: 0.03	c: 0.03

The values are means $\pm$ SD; n = 6. $P<0.05$ statistically significant. There is statistical significance between mean values shown with different letters in the same column.

a: Significant differences with Control and TQ groups,

b: Significant differences with Hg group.

C: No treatment was performed, TQ: Received TQ, Hg: Received Hg, Hg+ TQ: Received Hg and TQ

Table 2. The results of plasma MDA, NO ve RSH levels

	Plasma		
	MDA Levels (nmol/ml)	NO Levels (μ mol/ml)	RSH Levels (nmol/ml)
Control	0.52 $\pm$ 0.006 ^c	8.2 $\pm$ 0.2 ^c	154.2 $\pm$ 3.81 ^c
TQ	0.47 $\pm$ 0.01 ^c	7.9 $\pm$ 0.4 ^c	150.6 $\pm$ 1.23 ^c
Hg	0.72 $\pm$ 0.009 ^a	11.6 $\pm$ 0.15 ^a	122.7 $\pm$ 1.37 ^a
Hg+TQ	0.59 $\pm$ 0.002 ^b	9.3 $\pm$ 0.3 ^b	138.4 $\pm$ 2.19 ^b
	a: 0.001	a: 0.001	a: 0.001
P value	b: 0.01	b: 0.01	b: 0.01
	c: 0.08	c: 0.08	c: 0.08

The values are means $\pm$ SD; n = 6. $P<0.05$ statistically significant. There is statistical significance between mean values shown with different letters in the same column.

a: Significant differences with Control and TQ groups,

b: Significant differences with Hg group.

C: No treatment was performed, TQ: Received TQ, Hg: Received Hg, Hg+ TQ: Received Hg and TQ

4. Discussion

Experimental studies show that Hg causes damage to brain tissue looking at the literature (Minj et al., 2021; Shandilya et al., 2022). In this study, body weight and brain/body weight rate were calculated; behavioral tests were used; the levels of some oxidative stress markers in the brain and plasma were investigated to determine whether TQ has healing effects in rats exposed to Hg.

Exposure to 5 mg/kg Hg for 21 days caused a decrease in body weight and brain/body weight ratio of rats, which is also supported by the studies in the literature. In rats given 5 mg/kg Hg for three weeks, a reduction in body weight and brain weight/body weight rate was observed. The investigators reported significant demyelination with a total decrease in brain weight and shrinkage and demyelination in the basal ganglia, cortex, and

hippocampus regions (Minj et al., 2021; Shandilya et al., 2022). In this study, 10 mg/kg TQ given with Hg for 21 days improved both body weight and brain/body weight ratio. In the literature, when postnatal body and brain weights were evaluated in fetuses exposed to lead in the womb, it was shown that 10 mg/kg TQ treatment produced a rise in body and brain weights. Researchers have reported that TQ is neuroprotective (Saleh et al., 2019). In rats with experimental Huntington's disease-like symptoms, 14 days of 40 and 80 mg/kg TQ suspension treatment caused a rise in body weight (Ramachandran and Thangarajan, 2016).

In this study, exposure to 5 mg/kg Hg for 21 days produced a decrease in the number of crossings in OFT, i.e., a decrease in locomotor activity in rats. In OFT, Hg exposure caused a reduction in the time spent in the center and a rise in the time spent in the periphery. This result suggests that Hg increases anxiety and causes neophobia in rats (Olczaka et al., 2011), which is in line with the studies in the literature. In rats exposed to 5 mg/kg Hg for three weeks, it was reported that there was a decrease in the number of crossings in OFT and locomotor activity and anxiety-like behaviors in rats (Minj et al., 2021; Shandilya et al., 2022). In the present study, 10 mg/kg TQ treatment increased the number of crossings and locomotor activity in OFT in rats exposed to Hg and caused improvement in anxiety-like behaviors. In 21-day-old infant rats with experimental attention deficit and hyperactivity disorder, it was found that 10 mg/kg TQ therapy for eight weeks increased locomotor activity in OFT (Abu-Elfotuh et al., 2023). TQ therapy with 5 mg/kg for three days before arsenic exposure increased locomotor activity in OFT, caused an increase in the period spent in the center of the open field and produced an anxiolytic effect (Firdaus et al., 2018). It was reported that 14 days of 40 and 80 mg/kg TQ suspension treatment increased locomotor activity in OFT in rats with experimental Huntington's disease model (Ramachandran and Thangarajan, 2018).

In this study, exposure to 5 mg/kg Hg for 21 days caused depression-like behaviors or hopelessness behaviors in rats by decreasing swimming and climbing times in FST and increasing immobility time. Studies in the literature support our results. In rats exposed to 5 mg/kg Hg for three weeks, a rise in immobility period in FST was reported (Minj et al., 2021; Shandilya et al., 2022). In the present study, in rats exposed to Hg, 10 mg/kg TQ treatment increased swimming and climbing times, decreased immobility time in FST, and caused improvement in depression-like behaviors. In rats in which experimental Huntington's disease-like symptoms were induced by Ramachandran and Thangarajan, (2016) 14 days of 10 and 20 mg/kg TQ therapy caused a reduce in immobility time in FST. In rats with an experimental depression model, 14 days of 10 mg/kg TQ treatment increased swimming and climbing and reduced immobility time (Kuzay et al., 2022). In another study in which an experimental depression model was

established, it was reported that TQ improved behavior and was effective as an antidepressant in FST (Aquib et al., 2015). These results related to behavioral tests support that TQ treatment shows neuroprotective effects by causing improvement.

Oxidative stress has been shown to play an important role in neurotoxicity caused by Hg exposure (Barber and Shaw, 2010). In this study, exposure to 5 mg/kg Hg for 21 days caused an increase in MDA and NO levels and a decrease in GSH levels in the cerebral cortex and plasma of rats. Our findings are consistent with previous studies showing that oxidative stress plays a major role in neurotoxicity caused by Hg exposure. In rats exposed to 5 mg/kg Hg for three weeks, an increase in MDA and NO levels and a decrease in GSH levels in brain tissue were reported (Minj et al., 2021; Shandilya et al., 2022). In the present study, 10 mg/kg TQ treatment caused a reduction in MDA and NO levels and a rise in GSH/RSH levels in cerebral cortex and plasma in rats exposed to Hg. This result shows that TQ acts as an antioxidant and may reduce the risk of oxidative damage. Studies in the literature also support this result. In rats exposed to 3 mg/kg mercury, 10 mg/kg TQ treatment decreased MDA levels in kidney tissue and increased GSH levels, and was observed to cause recovery (Fouda et al., 2008). In rats exposed to 20 µg mercury for 28 days, 5 mg/kg TQ treatment increased GSH levels in kidney and liver tissue and caused recovery (Owumi et al., 2025). Elevated MDA levels in the brain tissues of fetuses and pregnant rats exposed to lead were reduced following 10 mg/kg TQ treatment. Previous studies suggest that TQ acts as a potent free radical scavenger, preserving the activity of multiple antioxidant enzymes (Saleh et al., 2019). In the hippocampus of rats given 5 mg/kg TQ three days before arsenic exposure MDA levels due to arsenic exposure decreased, and decreased GSH levels increased. It has been reported that TQ reduces the general toxic environment in the cell thanks to its free radical scavenging mechanism (Firdaus et al., 2018).

5. Conclusion

In this study, it was investigated whether TQ has a neuroprotective effect in rats exposed to Hg. Although there are studies examining the antioxidant activity of TQ in liver, kidney and plasma in mercury exposure, there is no study examining its effects on cerebral cortex and behavior. Hg caused an increase in oxidative stress by increasing MDA and NO levels and decreasing GSH/RSH levels in cerebral cortex and plasma of rats. Hg decreased body weight and brain weight/body weight rate of rats. According to behavioral test results, Hg caused decreased locomotor activity, increased anxiety, and depression-like behaviors. In Hg-exposed rats, TQ treatment decreased Hg caused oxidative stress by reducing MDA and NO levels and increasing GSH/RSH levels. It increased body weight and brain/body weight rate and improved behavioral tests. TQ may be a hoping curative

drug candidate in improving behavioral and biochemical changes due to Hg exposure.

Author Contributions

The percentages of the author' contributions are presented below. The author reviewed and approved the final version of the manuscript.

	D.K.
C	100
D	100
S	100
DCP	100
DAI	100
L	100
W	100
CR	100
SR	100
PM	100
FA	100

C=Concept, D= design, S= supervision, DCP= data collection and/or processing, DAI= data analysis and/or interpretation, L= literature search, W= writing, CR= critical review, SR= submission and revision, PM= project management, FA= funding acquisition.

Conflict of interest

There is no conflict of interest.

Ethical Considerations

The experimental procedures were approved by the Local Animal Care and Ethics Committee of Kırşehir Ahi Evran University, (approval date: March 18, 2024, protocol code: 68429034/04).

Acknowledgments

This study was supported by Institutional Scientific Research Projects. The Project number is TIP.A3.24.011.

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SEDANTER YAŞAMDAN AKTİF YAŞAMA: HUZUREVİ SAKİNLERİ İLE ÜNİVERSİTE ETKİNLİĞİ

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Özet: Bu çalışmada, sanat ve spor etkinliklerin huzurevinde yaşayan bireylerin uyku ve yaşam kalitesi üzerine etkisi incelenmiştir. Ön test ve son test karşılaştırmalı randomize kontrollü deneysel bir çalışmadır. Araştırma, Ocak-Aralık 2023 tarihleri arasında bir huzurevinde yaşayan yaşlı bireylerle üniversite kampüsünde gerçekleşmiştir. Araştırmanın örneklemini, çalışmaya katılmaya gönüllü ve dâhil edilme kriterlerini karşılayan 60 yaşlı birey (müdahale grubu: 30, kontrol grubu: 30) oluşturmuştur. Müdahale grubundaki yaşlı bireylere 6 aylık süre boyunca sanat ve spor etkinlikleri yapılmıştır. Araştırmanın verileri; Tanıtıcı Bilgi Formu (TBF), Pittsburgh Uyku Kalitesi İndeksi (PUKİ) ve Yaşam Kalitesi Ölçeği (YKÖ) ile yüz yüze toplanmıştır. Gruplar ile yaş, kurumda kalma süresi, cinsiyet, medeni durum, eğitim, gelir durumu, sigara kullanımı, kronik hastalığa sahip olma, sürekli ilaç kullanımı, çocuk sahibi olma, kurumda kalma nedeni, aktivite varlığı, sosyal etkinliklere katılma durumu arasında istatistiksel olarak anlamlı ilişki yoktur ($P>0,05$). Gruplar belirtilen özellikler açısından bağımsız ve homojendir. Müdahale grubundakilerin ön test-son test PUKİ puanları açısından istatistiksel olarak anlamlı farklılık tespit edilmiştir ($P=0,00$). Yani sıra PUKİ ve YKÖ son test sonuçlarına göre, müdahale ve kontrol grupları arasında anlamlı bir farklılık elde edilmiştir (sırasıyla: $P=0,00$, $tb=-7,56$; $P=0,04$, $tb=2,08$). Ayrıca PUKİ ve YKÖ puanları arasında negatif yönde orta düzeyde güçlü bir ilişki tespit edilmiştir ($P=0,00$, $r=-0,57$). Bu çalışmadan elde edilen sonuçlar, huzurevinde yaşayan yaşlı yetişkinlere uygulanan 6 aylık etkinlik programının uyku ve yaşam kalitesini iyileştirmede etkili olduğunu göstermektedir.

Anahtar kelimeler: Sedanter yaşam, Aktif yaşam, Yaşlı sağlığı, Uyku, Yaşam kalitesi

From Sedentary to Active Living: University Event with Nursing Home Residents

Abstract: This study examined the effects of art and sports activities on the sleep and quality of life of individuals living in a nursing home. This is a pretest and posttest comparative randomized controlled experimental study. The study was conducted on a university campus with elderly individuals living in a nursing home between January and December 2023. The study sample consisted of 60 elderly individuals (intervention group: 30, control group: 30) who volunteered to participate and met the inclusion criteria. The elderly individuals in the intervention group participated in art and sports activities for a period of 6 months. Data were collected face-to-face using the Introductory Information Form (DIF), the Pittsburgh Sleep Quality Index (PSQI), and the Quality of Life Scale (WHOQOL-OLD). There was no statistically significant relationship between the groups and age, length of stay in the institution, gender, marital status, education, income, smoking, chronic disease, ongoing medication use, having children, reason for staying in the institution, activity status, or participation in social activities ($P>0,05$). The groups were independent and homogeneous in terms of the specified characteristics. A statistically significant difference was found in the pretest-posttest PSQI scores of the intervention group ($P=0,00$). Furthermore, according to the posttest results of the PSQI and WHOQOL-OLD scales, a significant difference was found between the intervention and control groups ($P=0,00$, $tb=-7,56$; $P=0,04$, $tb=2,08$, respectively). Furthermore, a moderately strong negative correlation was found between the PSQI and WHOQOL-OLD scale scores ($P=0,00$, $r=-0,57$). The results of this study indicate that the 6-month activity program implemented for older adults living in a nursing home was effective in improving sleep and quality of life.

Keywords: Sedentary lifestyle, Active lifestyle, Elderly health, Sleep, Quality of life

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Gönderi: 10 Temmuz 2025

Kabul: 08 Ağustos 2025

Yayınlanma: 15 Eylül 2025

Received: July 10, 2025

Accepted: August 08, 2025

Published: September 15, 2025

Cite as: Dağlı E, Uzun M, Karaaslan B. 2025. From sedentary to active living: University event with nursing home residents. BSJ Health Sci, 8(5): 190-196.

1. Giriş

Dünya Sağlık Örgütü, yaşlılığı “çevresel faktörlere uyum sağlayabilme yeteneğinin azalması” olarak tanımlamaktadır. Yaşlanma, önlenmesi mümkün olmayan kronolojik, sosyolojik, biyolojik ve psikolojik bir gerilemedir. Yaşlanma ayrıcalıksız her canlıda görülen, tüm işlevlerde azalmaya neden olan, süregelen ve evrensel bir süreçtir. Tüm dünyada yaşlı nüfusu giderek

artmaktadır (WHO, 2024). Nüfus projeksiyonlarına göre, Türkiye’de yaşlı nüfus oranı 2023 yılında %10,2 olup, 2030 yılında %12,9, 2040 yılında %16,3, 2060 yılında %22,6 ve 2080 yılında %25,6 olacağı öngörülmektedir (TUIK, 2024).

Yaşam süresinin uzaması ve yaşlı nüfus oranının artmış olması, ileri yaşlarda da sağlıklı kalmayı gündeme getirmiştir. Yaşlı bireylerin çoğu bağımsız olup kendi



evlerinde yaşamaktadır. Fakat bir grup yaşlı, bakım ihtiyaçları nedeniyle huzurevlerinde yaşamaktadırlar. Son yıllarda çekirdek aile yapısının benimsenmiş olması huzurevinde yaşayan bireylerin sayısında artışa neden olmuştur (Hallal vd., 2012; Copeland vd., 2015).

Huzurevinde yaşayan yaşlı bireylerin çevreyi tanıma ve denetleyebilme olanakları azalmakta ya da kaybolmaktadır. Sosyal bağları zayıflamış olan yaşlı bireyler izole biçimde yalnız ya da bakımevlerinde yaşamaktadırlar. Bu durum onların beden ve ruh sağlığını olumsuz etkileyerek daha az aktif bir yaşam tarzı oluşturmalarına neden olmaktadır (Altıparmak, 2009; Ardahan, 2010). Yanı sıra yaşamakta olduğumuz COVID-19 pandemisini kontrol altına almak için uygulanan sosyal izolasyon ve karantina, özellikle de ileri yaş grubunda fiziksel inaktivitenin daha da artmasına neden olmuştur. Bir yandan en fazla riske sahip yaşlı bireyler enfeksiyondan korunmaya çalışırken bir yandan da hareketsiz ve oturarak televizyon seyretme vb. sedanter davranışlar daha da artmıştır (Çelik vd., 2020; Aydın vd., 2021).

Yaşlanmayla birlikte sedanter yaşam, obezite, diyabet, hipertansiyon, kalp-damar hastalıkları, osteoartroz, osteoporoz ve bazı kanser çeşitleri artış göstermektedir. Depresyon, anksiyete ve bilişsel fonksiyonlarda gerileme de ortaya çıkmaktadır (Faghri vd., 2015). Uyku bozukluğu, çoğu bilişsel bozukluğu olan huzurevi ve destekli yaşam sakinlerinde sıklıkla görülmektedir (Liu et al, 2025). Yaş arttıkça egzersiz yapma oranı düşmektedir (Dahlan vd., 2020; Öcal vd., 2023).

Aktif yaşlanma, bireylerin yaşam kalitesi yüksek ve sağlıklı bir şekilde yaşlanması olarak tanımlanmaktadır. Sedanter yaşam, aktif yaşlanmanın önündeki en büyük tehdittir (Öcal vd., 2023). Bu nedenle Dünya Sağlık Örgütü (DSÖ) yaşam kalitesinin yükseltilmesini amaçlayan, aktif yaşlanmaya yoğunlaşmış ve aktif yaşlanmanın politikalarda yer alması gereken önemli bir konu olduğunu bildirilmiştir (Hijas-Gómez vd., 2020). Fakat çoğu yetişkin bireyler aktif yaşam tarzlarını benimsemekten uzaklaşmaktadır. Aktif yaşamın bireylere önemli faydalar sağladığı bilinmekte ve buna karşılık olarak sedanter yaşam tarzında sağlık açısından ciddi olumsuz sonuçlar doğurabileceği bilinmektedir (Öcal vd., 2023). Bireylerin sağlıklı bir biçimde yaşlanması yalnızca bireye ait olmayıp, toplumsal açıdan kendilerine sağlanacak psikolojik, sosyal, ekonomik ve fizyolojik destek hizmetleriyle yakından ilişkilidir. Yaşlılara öğrenmesi kolay, maliyetsiz ve vücut dayanıklılığını arttıran aerobik egzersiz yapması önerilmektedir. Ayrıca temiz, sakın, açık ve yeşil alanlarda gezerek egzersiz yapmak, güçlü olmasını sağlamanın yanı sıra psikolojik rahatlığı bakımından da yararlıdır. Fazla güneşte kalmadan temiz, açık, sakın ve güneşli havalarda ev dışına çıkmak, güneşin etkisiyle D vitamini yapıldığından kemiklerin yoğunluğunu ve direncini artırır. Özellikle yaşlıların birarada egzersiz yapmaları, ortak konularda konuşmaları, hobiler geliştirmeleri, sosyalleşmeleri yaşama bağlanmayı, uyku

ve yaşam kalitesini artırmaları açısından son derece yararlıdır (Soyguden vd., 2015; Akın, 2017; Dahlan vd., 2020; Hijas-Gómez vd., 2020; Öcal vd., 2023). Bu çalışmada, sanat ve spor etkinliklerinin huzurevinde yaşayan bireylerin uyku ve yaşam kalitesi üzerine etkisi incelenmiştir.

2. Materyal ve Yöntem

2.1. Araştırmanın tasarımı ve ortamı

Ön test ve son test karşılaştırmalı randomize kontrollü deneysel bir çalışmadır. Araştırma, Ocak-Aralık 2023 tarihleri arasında bir huzurevinde yaşayan yaşlı bireylerle bir üniversite kampüsünde yapılmıştır.

2.2. Evren ve örneklem

Araştırmanın evrenini Ocak-Aralık 2023 tarihleri arasında bir devlet huzurevinde yaşayan 286 yaşlı birey, örneklemi ise, çalışmaya katılmaya gönüllü ve dâhil edilme kriterlerini karşılayan 60 yaşlı birey oluşturmıştır. Örneklem büyüklüğünün hesaplanmasında G*Power uygulaması (version 3.1.9.3) kullanılmış olup, örneklem büyüklüğünü belirlemek için COHEN standart etki büyüklüğü alınmıştır. Cohen, .020'un "küçük" bir etki büyüklüğü; 0.50, "orta" bir etki büyüklüğü ve 0.80, "büyük" bir etki büyüklüğü olarak ifade etmektedir (Cohen, 1992). Bu çalışmada minimum örneklem büyüklüğünü hesaplamak için COHEN etki büyüklüğü 0.80 olarak varsayılmıştır. Bu etki büyüklüğü altında Tip I hata 0,05; testin gücü, 0.80 ($\alpha = 0.05$, $1-\beta = 0.80$, etki büyüklüğü = 0.80); ve minimum örneklem büyüklüğüne göre çalışma için 60 katılımcısının olması gerektiği saptanmıştır. Bu hesaplama doğrultusunda araştırmaya dâhil edilme kriterlerini karşılayan örnekleme 60 birey (müdahale grubuna 30, kontrol grubuna 30) alınmıştır.

Araştırmaya huzurevinde yaşayan, gönüllü olan ve etkinliklere katılmaya engel aktif bir sağlık sorunu olmayan yaşlı bireyler dâhil edilmiştir. Katılmaya gönüllü olmayan ve etkinliklere katılmaya engel aktif bir sağlık sorunu olan yaşlı bireyler araştırmaya dahil edilmemiştir. Araştırmanın sonlandırma kriterleri ise, anketlerin eksik doldurulması ve etkinliklere en az %80 devamlılığın sağlanamaması olarak belirlenmiştir.

2.3. Randomizasyon

Çalışmada basit randomizasyon tekniği kullanılmıştır ve bu süreç araştırmacılar dışındaki bir öğretim elemanı tarafından yürütülmüştür. Yaşlı bireyler basit bir rastgele sayı üretici yazılımı (www.random.org) kullanılarak müdahale ve kontrol gruplarına rastgele atanmıştır. Bu liste araştırmacılar tarafından isimsiz sadece numara olarak kayıt altına alınmıştır, numaraların son rakamları çift olanlar müdahale grubuna, son rakamları tek olanlar ise kontrol grubuna atanmıştır. Çalışmada yanlılığı önlemek amacıyla çalışmada kullanılacak formlar çalışmada yer almayan, bir öğretim elemanı tarafından doldurulmuştur. Veriler çalışmada yer almayan ve çalışma hakkında bilgisi olmayan bir analist tarafından değerlendirilmiştir.

2.4. Araştırmanın Uygulama Aşaması ve Verilerin Toplanması

2.4.1. Müdahale grubu

Müdahale grubundaki yaşlı bireylere 6 aylık süre boyunca aşağıda listelenen etkinlikler yapılmıştır. Bu gruptaki yaşlı bireylerin, Tanıtıcı Bilgi Formu (TBF), Pittsburgh Uyku Kalitesi İndeksi (PUKİ) ve Yaşam Kalitesi Ölçeği (YKÖ) ön test verileri toplanmıştır. Etkinlik sonrası PUKİ ve YKÖ ile son test verileri toplanmıştır.

Etkinlikler:

- ✓ Yürüyüş (her gün 30 dakika ya da haftada en az 3 kez)
- ✓ Bocce oyunu (ayda 1 kez)
- ✓ Müze/piknik gezisi (ayda 1 kez)
- ✓ Dans/müzik dinletisi (haftada 1 kez)
- ✓ Sinema gösterisi (ayda 1 kez)
- ✓ Aktif yaşlanma eğitimleri (ayda 1 kez)

2.4.2. Kontrol grubu

Kontrol grubundaki yaşlı bireylerin, TBF, PUKİ ve YKÖ ön test verileri toplanmıştır. Daha sonra PUKİ ve YKÖ ile son test verileri toplanmıştır. Kontrol grubundaki yaşlı bireylere etkinlikler yapılmamıştır.

2.5. Veri Toplama Araçları

Araştırmanın verileri; TBF, PUKİ ve YKÖ ile yüz yüze toplanmıştır.

2.5.1. TBF

Araştırmacı tarafından literatürden yararlanılarak hazırlanan bilgi formu, sosyo demografik ve yaşlı bireye özgü bazı tanımlayıcı özellikleri içeren 13 soru yer almaktadır.

2.5.2. PUKİ

Toplam 24 sorudan oluşmaktadır. Ölçekteki her bir madde 0 (hiç sıkıntı olmaması)-3 (ciddi sıkıntı) puan arasında bir değer almaktadır. Toplam PUKİ puanı ise 0-21 arasında değişmektedir. Toplam puanı 5 ve altında olanların uyku kalitesi "iyi" olarak değerlendirmektedir. Ölçeğin Türkçe geçerlilik ve güvenilirlik çalışması Buysse vd. (1989) ve Ağargün vd. (1996) tarafından yapılmıştır.

2.5.3. YKÖ

YKÖ Türkçe geçerlilik ve güvenilirlik çalışması, Eser vd. (2004) tarafından yapılmıştır. Ölçek cevapların beşli Likert ölçeği ile saptandığı 24 sorudan oluşmaktadır. Beşli likert ölçeği, 1: hiç, 2: çok az, 3: orta derecede, 4: çok fazla, 5: aşırı derecede şeklindedir. Her bir soru için olası en düşük puan 1, en yüksek puan 5'dir. Ölçekte alınabilecek en yüksek toplam puan 120, en düşük toplam puan ise 24'tür. Puan arttıkça yaşam kalitesi de artmaktadır (Power vd., 2005; Eser vd., 2005).

2.6. İstatistik Analiz

Araştırmadan elde edilen veriler, SPSS for Windows (versiyon 20.0) programı ile analiz edilmiştir. Araştırmada kullanılan ölçekler için iç tutarlılık Cronbach's Alfa güvenilirlik katsayısı ile değerlendirilmiştir. Verilerin dağılımı Skewness/Kurtosis değerlerine göre incelenmiş ve normal dağılıma uygun olduğu saptanmıştır. Araştırmadaki sürekli değişkenlere

ait istatistikler ortalama, standart sapma, minimum ve maksimum değerler ile gösterilmiştir. Kategorik değişkenlere ait tanımlayıcı istatistikler frekans, yüzde ve Ki kare testi ile incelenmiştir. Bağımsız grupların karşılaştırılmasında Bağımsız iki örneklem T testi kullanılmıştır. Bağımlı örneklemelerin ön test- son test karşılaştırılmasında Eşli İki Örnek T testi kullanılmıştır. Ölçekler arası ilişkiyi saptamak için Pearson korelasyon yapılmıştır. Araştırmada anlamlılık düzeyi için $P < 0,05$ alınmıştır. Bonferroni poc toc analizi için P değeri 0,01'in altı alınmıştır.

3. Bulgular

Katılımcıların sosyo-demografik ve diğer bazı özellikleri tablo 1'de incelenmiştir. Müdahale grubunun yaş ortalaması 72,53, kurumda kalma süresi ortalaması 8,33 yıl, kadınların oranı %56,7, erkeklerin oranı %43,3, evli olanların oranı %46,7, okuryazar olmayanların oranı %30,0, gelir durumu olanların oranı %63,3, sigara kullananların oranı %33,3, kronik hastalığa sahip olanların oranı %60,0, sürekli ilaç kullananların oranı %43,3, çocuk sahibi olanların oranı %70,0, "Hiç kimsesi olmayan" kurumda kalanların oranı müdahale grubunda %36,7, aktivite varlığı olanların oranı %63,3, sosyal etkinliklere katılanların oranı %43,3' tür. Kontrol grubunun ise kontrol grubunun yaş ortalaması 71,70, kurumda kalma süresi ortalaması 8,90 yıl, kadınların oranı %60,0, erkeklerin oranı %40,0, evli olanların oranı %60,0, okuryazar olmayanların oranı %40,0, gelir durumu olanların oranı %60,0, sigara kullananların oranı %23,3, kronik hastalığa sahip olanların oranı %53,3, sürekli ilaç kullananların oranı %46,7, çocuk sahibi olanların oranı %80,0, "Hiç kimsesi olmayan" kurumda kalanların oranı müdahale grubunda %33,3, aktivite varlığı olanların oranı %50,0, sosyal etkinliklere katılanların oranı %36,7' dir. Gruplar ile yaş, kurumda kalma süresi, cinsiyet, medeni durum, eğitim, gelir durumu, sigara kullanımı, kronik hastalığa sahip olma, sürekli ilaç kullanımı, çocuk sahibi olma, kurumda kalma nedeni, aktivite varlığı, sosyal etkinliklere katılma durumu arasında istatistiksel olarak anlamlı ilişki yoktur ($P > 0,05$) (Tablo 1).

Tablo 2, müdahale ve kontrol grubundaki katılımcıların PUKİ ön test ve son test puanlarının karşılaştırılmasını içermektedir. Tablo, her bir grubun ön test ve son test puan ortalamalarını ($\bar{X} \pm SS$), zaman içinde anlamlılık düzeylerini (P_{Zaman}), grup içi ve gruplar arası farkları değerlendirmek için kullanılan test istatistiklerini ve anlamlılık düzeylerini (P_{Grup}) göstermektedir. Müdahale grubunun ön test puanı ortalaması 8,5, son test puanı ortalaması ise 4,7'dir. Bu, müdahale grubunda zamanla anlamlı bir iyileşme olduğunu göstermektedir ($P_{Zaman} = 0,00$). Fa değeri 11,05'tir, bu da güçlü bir anlamlılık olduğunu göstermektedir. Kontrol grubunun ön test puanı ortalaması 8,4, son test puanı ortalaması ise 8,53'tir. Bu, kontrol grubunda zamanla anlamlı bir değişiklik olmadığını göstermektedir ($P_{Zaman} = 0,51$). Fa değeri 0,66'dir, bu da değişimin istatistiksel olarak

anlamli olmadigini gostermektedir (Tablo 2).
Ön test sonuçlarına göre, müdahale ve kontrol grupları arasında anlamlı bir fark yoktur ($P_{Grup}=0,87$, $t_b=0,17$). Ancak, son test sonuçlarına göre, müdahale ve kontrol

grupları arasında anlamlı bir fark vardır ($P_{Grup}=0,00$, $t_b=-7,56$). Bu, müdahale grubunun kontrol grubuna kıyasla önemli ölçüde daha fazla iyileştigini göstermektedir (Tablo 2).

Tablo 1. Katılımcıların sosyo-demografik ve diğer bazı özellikleri

Değişkenler (N=60)	Kategori	Müdahale grubu (n=30)		Kontrol grubu (n=30)		Test ist.	
		ort±ss		ort±ss		t*	P
Yaş		72,53 ± 3,08		71,70 ± 3,94		0,91	0,37
Kurumda kalma süresi		8,33±2,91		8,90±3,44		-0,69	0,49
		n	%**	n	%**	χ^2_{***}	p
Cinsiyet	Kadın	17	56,7	18	60,0	0,07	0,79
	Erkek	13	43,3	12	40,0		
Medeni durum	Evli	14	46,7	18	60,0	1,07	0,30
	Bekar	16	53,3	12	40,0		
	Okuryazar değil	9	30,0	12	40,0		
Eğitim durumu	Okuryazar	6	20,0	6	20,0	1,51	0,82
	İlköğretim	5	16,7	6	20,0		
	Ortaöğretim	5	16,7	3	10,0		
	Lisans ve üzeri	5	16,7	3	10,0		
Gelir durumu	Var	19	63,3	18	60,0	0,07	0,79
	Yok	11	36,7	12	40,0		
Sigara kullanma	Evet	10	33,3	7	23,3	0,79	0,39
	Hayır	20	66,7	23	76,7		
Kronik hastalığa sahip olma	Evet	18	60,0	16	53,3	0,27	0,60
	Hayır	12	40,0	14	46,7		
Sürekli kullandığı ilaç	Evet	13	43,3	16	53,3	0,60	0,44
	Hayır	17	56,7	14	46,7		
Çocuk sahibi olma	Evet	21	70,0	24	80,0	0,80	0,37
	Hayır	9	30,0	6	20,0		
	Özbakımını yapamamak	5	16,7	10	33,3		
Kurumda kalma nedeni	Hiç kimsesi olmamak	11	36,7	10	33,3	2,38	0,30
	Aileye yük olmamak	14	46,7	10	33,3		
Aktivite varlığı	Evet	19	63,3	15	50,0	1,58	0,46
	Hayır	11	36,7	15	50,0		
Sosyal etkinliklere katılma	Evet	13	43,3	19	63,3	2,41	0,12
	Hayır	17	56,7	11	36,7		
Toplam		30	100,0	30	100,0		

*Independent Sample T test, **Sütun yüzdesi alınmıştır ***Ki kare analizi

Tablo 2. Müdahale ve kontrol grubundaki yaşlıların PUKI puanlarının karşılaştırılması

Gruplar	Ön test	Son Test	Fa	P _{Zaman}
	X±SS	X±SS		
Müdahale Grubu*	8,5 ± 2,24	4,7 ± 1,73	11,05	0,00
Kontrol Grubu*	8,4 ± 2,33	8,53 ± 2,18	0,66	0,51
t _b	0,17	-7,56		
P _{Grup}	0,87	0,00		

*Grubun kendi içindeki zamanlar arasındaki anlamlı görülen ilişki. a: Paired- Samples T Test, b: Bağımsız Örneklem T Testi (Independent Samples T Test)

Tablo 3, müdahale ve kontrol grubundaki katılımcıların YKÖ toplam puanlarının ön test ve son test dönemlerinde karşılaştırılmasını içermektedir. Tablo, her bir grubun ön test ve son test puan ortalamalarını ($X\pm SS$), zaman içinde anlamlılık düzeylerini (P_{Zaman}), grup içi ve gruplar arası farkları değerlendirmek için kullanılan test istatistiklerini ve anlamlılık düzeylerini (P_{Grup}) göstermektedir. Müdahale grubunun ön test puanı ortalaması 46,33, son test puanı ortalaması ise 52,87'dir. Bu, müdahale grubunda zamanla anlamlı bir iyileşme olduğunu göstermektedir ($P_{Zaman}=0,00$). Fa değeri -10,95'tir, bu da güçlü bir anlamlılık olduğunu ifade eder. Kontrol grubunun ön test puanı ortalaması 44,2, son test puanı ortalaması ise 43,3'tir. Bu, kontrol grubunda zamanla anlamlı bir değişiklik olmadığını göstermektedir ($P_{Zaman}=0,14$). Fa değeri 1,49'dur, bu da değişimin

istatistiksel olarak anlamlı olmadığı ifade eder (Tablo 3).

Ön test sonuçlarına göre, müdahale ve kontrol grupları arasında anlamlı bir fark vardır ($P_{Grup}=0,04$, $t_b=2,08$). Son test sonuçlarına göre, müdahale ve kontrol grupları arasında çok daha büyük bir fark bulunmaktadır ($P_{Grup}=0,00$, $t_b=9,54$). Bu, müdahale grubunun kontrol grubuna kıyasla YKÖ puanlarında önemli ölçüde daha fazla iyileştiğini göstermektedir (Tablo 3).

Tablo 3. Müdahale ve kontrol grubundaki katılımcıların YKÖ puanlarının karşılaştırılması

Gruplar	Ön test	Son test	F ^a	P _{zaman}
	X±SS	X±SS		
Müdahale grubu*	46,33 ± 3,04	52,87 ± 3,29	-10,95	0,00
Kontrol grubu*	44,2 ± 4,72	43,3 ± 4,4	1,49	0,14
t _b	2,08	9,54		
P _{Grup}	0,04	0,00		

*Grupun kendi içindeki zamanlar arasındaki anlamlı görülen ilişki. a: Paired- Samples T Test, b: Bağımsız Örneklem T Testi (Independent Samples T Test)

Tablo 4. Müdahale ve kontrol grubundaki katılımcıların son test PUKİ ve YKÖ puanları arasındaki ilişki

Müdahale grubu n=30		YKÖ son test		
Kontrol grubu n=30		Müdahale grubu	Kontrol grubu	Toplam
Toplam N=60				
PUKİ son test	r	-0,16	0,04	-0,57**
	P	0,38	0,85	0,00

**0,01 düzeyinde anlamlı. Pearson korelasyon analizi ile incelenmiştir.

4. Tartışma

Dünya nüfusu yaşlanmaya devam ettikçe, yaşlılar arasında uyku bozukluklarının yaygınlığı artmakta ve önemli bir halk sağlığı sorunu oluşturmaktadır (Pappas vd., 2022). Yaşlı yetişkinler için genel sağlığı korumak ve yüksek bir yaşam kalitesi sağlamak için uyku kalitesini sürdürmek esastır (Liu vd., 2025). Bu çalışmada, grup içi karşılaştırmada, müdahale grubundaki katılımcıların PUKİ ön test puanı ortalaması 8,5, son test puanı ortalaması ise 4,7 elde edilmiştir, müdahale grubunda uyku kalitesinin daha fazla arttığını göstermektedir. Ayrıca gruplar arası karşılaştırmada da, müdahale grubundaki katılımcıların kontrol grubuna kıyasla uyku kalitesinin daha fazla artışı tespit edilmiştir. Bonab vd. (2022) çalışmasında egzersiz yapmanın yaşlıların uyku kalitesini iyileştirdiği bildirilmiştir. Benzer olarak Kelley vd. (2017) çalışmasında da etkinliklerin yaşlıların uyku kalitesini iyileştirdiği ve uyku sorunlarını ortadan kaldırmak ve uykuya dalmak için daha az uyku hapi kullanmalarına yol açtığı sonucuna varılmıştır. Yanısıra Du vd. (2015), Vanderlinden vd. (2020) ve Hatamipour vd. (2019) çalışmalarında da belirtildiği gibi aktiviteler yaşlıların uyku kalitesini iyileştirmiştir. Literatürdeki bu çalışmalar, mevcut çalışmanın bulgularını destekler

Tablo 4, müdahale ve kontrol grubundaki katılımcıların son test PUKİ puanları ile yaşam kalitesi ölçek puanları arasındaki ilişkiyi göstermektedir. Pearson korelasyon analizi kullanılarak incelenen bu ilişki, korelasyon katsayıları (r) ve anlamlılık düzeyleri (P) ile ifade edilmektedir. Müdahale grubunda PUKİ son test puanları ile YKÖ son test puanları arasında negatif yönde zayıf bir ilişki vardır ($r=-0,16$). Ancak, bu ilişki istatistiksel olarak anlamlı değildir ($P=0,38$). Kontrol grubunda PUKİ son test puanları ile YKÖ son test puanları arasında pozitif yönde çok zayıf bir ilişki vardır ($r=0,04$). Bu ilişki de istatistiksel olarak anlamlı değildir ($P=0,85$) (Tablo 4).

Tüm örneklemde (müdahale ve kontrol grupları birleştirildiğinde) PUKİ son test puanları ile YKÖ son test puanları arasında negatif yönde orta düzeyde güçlü bir ilişki vardır ($r=-0,57$). Bu ilişki istatistiksel olarak anlamlıdır ($P<0,001$). Bu bulgu, YKÖ puanlarının artmasıyla PUKİ puanlarının azalması arasında anlamlı bir ilişki olduğunu göstermektedir (Tablo 4).

niteliktedir. Amerikan Uyku Bozuklukları Derneği, egzersiz ve fiziksel aktiviteyi uyku sağlığının önemli bir parçası olarak görmektedir ve bunları uykuyu iyileştirmek için farmakolojik olmayan bir tedavi müdahalesi olarak sunmaktadır (Ramar vd., 2021). Uyku bozukluklarının yaşlı yetişkinler arasında yaygın olduğu ve sağlık, refah ve yaşam kalitesini derinden etkileyebileceği göz önüne alındığında, etkili müdahaleleri belirlemek oldukça önemlidir.

Nüfus yaşlanması dünya çapında önemli bir sorun haline gelmiştir ve yaşam kalitesini korumak yaşlanan toplum için birincil önceliktir (Yen vd., 2018). Mevcut çalışmada müdahale grubundaki katılımcıların grup içi ve gruplar arası karşılaştırmada müdahale grubundaki katılımcıların kontrol grubuna kıyasla yaşam kalitesinin daha fazla artışı tespit edilmiştir. Dahlan vd. (2015), yaşlıların 6 aylık sosyal aktivitelere katılımı ile, yaşam kalitesinin fiziksel, psikolojik ve sosyal alt ölçeklerinde anlamlı bir değişiklik görüldüğünü göstermiştir. Lvasseur vd. (2004) göre, yaşlıların yaşam kalitesi ve sosyal katılımı, fiziksel aktivite düzeyleriyle anlamlı şekilde ilişkilidir. Başka bir çalışmada da yapılandırılmış mesleki terapi müdahale programlarının yaşlı yetişkinler arasında aktif yaşlanmaya ve daha yüksek bir yaşam

kalitesine yol açtığı, hastalık, sakatlık ve bağımlılık durumlarını azalttığı bildirilmiştir (Portillo vd., 2023). Literatürdeki bu çalışmalar, mevcut çalışmanın bulgularını destekler niteliktedir.

Sedanter yaşam, aktif yaşlanmanın önündeki en büyük tehditlerdir. DSÖ, yaşam kalitesinin yükseltilmesini amaçlayan aktif yaşlanmaya yoğunlaşmış ve aktif yaşlanmanın politikalarda yer alması gereken önemli bir konu olduğunu bildirmektedir. Özellikle yaşlıların birarada egzersiz, aktivite yapmaları, sanat ve spor etkinliklerine katılmaları, hobiler edinmeleri, sosyalleşmeleri yaşama bağlanmayı ve yaşam kalitesini artırmaları açısından son derece yararlıdır (Faghri vd., 2015; Soygüden vd., 2015; Akın, 2017; Öcal vd., 2023; WHO, 2024).

5. Sonuç

Mevcut çalışmada, sanat ve spor etkinliklerin huzurevinde yaşayan bireylerin uyku ve yaşam kalitesi üzerine etkisi incelenmiştir. Bu çalışmadan elde edilen sonuçlar, huzurevinde yaşayan yaşlı yetişkinlere uygulanan 6 aylık etkinlik programının uyku ve yaşam kalitesini iyileştirmede etkili olduğunu göstermektedir.

Katkı Oranı Beyanı

Yazarların katkı yüzdeleri aşağıda verilmiştir. Yazarlar makaleyi incelemiş ve onaylamıştır.

	E.D.	M.U.	B.K.
K	100		
T	50	25	25
Y	50	25	25
VTI		50	50
VAY	50	25	25
KT	50	25	25
YZ	50	25	25
KI	80	10	10
GR	100		
PY	50	25	25

K= kavram, T= tasarım, Y= yönetim, VTI= veri toplama ve/veya işleme, VAY= veri analizi ve/veya yorumlama, KT= kaynak tarama, YZ= Yazım, KI= kritik inceleme, GR= gönderim ve revizyon, PY= proje yönetimi.

Çıkar Çatışması Beyanı

Yazarlar arasında herhangi bir çıkar çatışması bulunmamaktadır.

Etik Onay/Hasta Onamı

Araştırmanın etik kurul onayı bir devlet üniversitesinin Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu'ndan alınmış ve kurum izni alınmıştır (onay tarihi: 02 Aralık 2022 ve karar numarası: 69). Tüm prosedürler 1964 Helsinki İnsan Hakları Bildirgesi ve sonraki değişiklikleri veya karşılaştırılabilir etik standartlara uygun olarak gerçekleştirilmiştir. Katılımcılara istedikleri zaman araştırmadan ayrılabilirlikleri bilgisi verilmiştir, sözlü ve

yazılı onamları alınmıştır.

Teşekkür ve Bilgilendirme Beyanı

Bu çalışma, TÜBİTAK 2209-A Üniversite Öğrencileri Araştırma Projeleri Destek Programı kapsamında 1919B012202055 numaralı proje ile desteklenmiştir.

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IMPORTANCE OF β -CATENIN AND DRP-1 EXPRESSION IN HEPATOCELLULAR CARCINOMAS

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Abstract: Hepatocellular carcinoma (HCC) represents one of the most prevalent primary liver malignancies. The activation of the Wnt/ β -catenin signaling pathway is frequently observed in HCC, contributing to tumor progression. Dynamin-related protein-1 (DRP-1) is involved in apoptosis, tumor metastasis, and suppression of cell adhesion and migration. While DRP-1 and β -catenin have been reported in various tumors, their significance in HCC remains controversial. This study investigates the immunohistochemical (IHC) expression of β -catenin and DRP-1 in HCC. Thirty HCC cases diagnosed within the last 15 years at our institution were included. IHC staining with β -catenin and DRP-1 antibodies was performed on paraffin-embedded tumor and non-tumor tissue samples. Thus, the expressions of these proteins were analyzed. Among 30 cases, 25 had a cirrhotic background, while 5 were non-cirrhotic. IHC analysis revealed membranous β -catenin reactivity in tumor areas in 29 cases, with one case exhibiting both membranous and nuclear reactivity. Weaker immunoreactivity was observed in non-tumoral hepatocytes and biliary epithelium compared to tumor areas. DRP-1 expression was absent in non-tumoral hepatocytes, while cytoplasmic immunoreactivity was statistically strong in 16 cases (53%) ($P=0.0008$). No correlation was found between nuclear grade, lymphovascular invasion, serum AFP levels, necrosis, survival, and β -catenin or DRP-1 expression ($P>0.05$). Our findings suggest a potential role for DRP-1 in HCC pathogenesis. While no significant correlation with prognostic parameters was observed in our limited cohort, further multicenter studies with larger, heterogeneous patient groups are warranted.

Keywords: Hepatocellular carcinoma, DRP-1, β -catenin, Apoptosis

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Received: March 26, 2025

Accepted: August 21, 2025

Published: September 15, 2025

Cite as: Özmen S, Demirci E, Demirtaş R, Ceylan O, Ülke Esin K, Kara S, Aksungur N, Altundaş N, Alper F, Dursun H, Öztürk G, Karabulut İ, Selen R. 2025. Importance of β -catenin and DRP-1 expression in hepatocellular carcinomas. BSJ Health Sci, 8(5): 197-201.

1. Introduction

Hepatocellular carcinoma (HCC) is among the most common primary hepatic malignancies, accounting for approximately 85-90% of primary liver cancer cases (El-Serag et al., 2007). Over the last three decades, its incidence has been on the rise. So, early detection and surveillance become crucial for achieving curative

treatment. Major risk factors for HCC include chronic hepatitis B and C infections, excessive alcohol consumption, metabolic liver diseases and exposure to dietary carcinogens such as aflatoxins (Yang et al., 2019). Hepatocellular carcinoma may develop in a cirrhotic or a rarer non-cirrhotic liver. While ongoing hepatocyte damage and hepatocyte proliferation generally occur in the cirrhotic background, some molecular changes begin



to accumulate in hepatocytes. Some of the cirrhotic nodules progress to the stages of dysplastic nodule, early hepatocellular carcinoma and advanced hepatocellular carcinoma. The process in HCC development is “low-grade dysplastic nodule → high-grade dysplastic nodule → early hepatocellular carcinoma → advanced hepatocellular carcinoma” and occurs due to the buildup of molecular changes (Nault et al., 2014).

Key molecular changes include telomere shortening, activation of TERT, and inactivation of cell cycle checkpoint inhibitors (Schulze et al., 2015). The molecular basis of HCC carcinogenesis has not been clearly defined. Among the molecular signaling pathways involved in HCC pathogenesis, the Wnt/ β -catenin signaling pathway is one of the most frequently activated. Understanding this pathway's role in HCC and its potential as a therapeutic target is therefore a major area of research.

In many cancers, including HCC, mitophagy is essential for cellular homeostasis. Mitophagy is a form of autophagy that eliminates damaged mitochondria, thus ensuring the continuity of cellular homeostasis (Ma et al., 2020). The control mechanism in the fission process, which is the first stage of mitophagy, depends significantly on DRP-1 (Eisner et al., 2018). DRP-1, a member of the death-associated protein kinase (DAPK) family in various tumors, has been shown to play an important role in promoting apoptosis and suppressing cell adhesion and migration and is involved in tumor metastasis.

DRP-1 and β -catenin protein expressions are monitored in various human tumors, including HCC. However, only a limited number of studies have investigated their expression in HCC and their importance is still controversial. Our aim in this study is to immunohistochemically examine the relationships of DRP-1 and β -catenin expression with prognostic parameters in HCC.

1.1. Structural Patterns in HCC

Hepatocellular carcinoma (HCC) exhibits four fundamental growth patterns: trabecular, pseudoglandular, solid and macrotrabecular. In 50% of cases, a combination of these patterns is observed, with the macrotrabecular pattern being linked to a poorer prognosis. Additional histological characteristics include the absence of a portal triad within the tumor, a reduction in the normal reticulin framework, expansion of hepatocyte plates and increased arterialization with unpaired arteries or arterioles (Yang et al., 2019).

1.2. Pathological Diagnosis

Since the classification of liver cancer is based on morphological parameters, histopathological diagnosis is the gold standard in defining HCC and its differential diagnoses. Histopathological diagnosis of HCC is based on World Health Organization (WHO) classification criteria (Bosman et al., 2010). The sensitivity of HCC diagnosis based on liver biopsy depends on the location,

differentiation and size of the lesion, the experience of the person who makes the biopsy and the pathologist. Pathological diagnosis is generally more difficult for nodules smaller than 2 cm in size (Roskams et al., 2010) because these lesions are often well-differentiated tumors (Forner et al., 2008).

Histopathological criteria for malignancy in hepatocellular tumors, namely significant cytological and histological atypia and interstitial and vascular invasion, may be missed by biopsy specimens. Therefore, the diagnosis of early and well-differentiated HCC should be further supported by immunohistological analyses for markers associated with malignant transformation of hepatocytes (Di Tommaso et al., 2007).

It is important to increase the sensitivity of these panels by identifying new markers associated with malignant transformation. Immunohistological markers are important to distinguish well-differentiated tumors from moderately/poorly differentiated tumors (Durnez et al., 2006).

2. Materials and Methods

This study analyzed the expression and topological distribution of DRP-1 and β -catenin in 30 HCC cases using immunohistochemical methods. The relationship between protein expression and clinicopathological features such as tumor size, histological grade, vascular invasion, lymph node metastasis and background liver status was also evaluated.

The cases included patients who underwent surgery for HCC at the Department of General Surgery, Ataturk University Faculty of Medicine Hospital, between 2005 and 2021. Of the 30 cases, 26 were male and 4 were female. The study material consisted of 19 liver explant specimens from transplanted patients and 11 partial liver resection specimens from non-transplanted metastatic HCC cases.

Tissue slides and pathology reports were retrieved from the hospital automation system and re-evaluated to confirm key histopathological parameters. Immunohistochemical staining was performed to assess the expression of β -catenin (Figure 1) and DRP-1 (Figure 2). The results were statistically analyzed in relation to relevant clinicopathological variables.

The normality of data distribution was evaluated using the D'Agostino-Pearson test. Variables that did not follow a normal distribution were reported as median values. Comparisons of DRP-1 and β -catenin expression between infiltrative regions and adjacent non-tumorous tissue were performed using the chi-square test. Associations between DRP-1 and β -catenin expression and prognostic indicators were analyzed with Spearman's rank correlation test. A two-tailed P value of less than 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics.

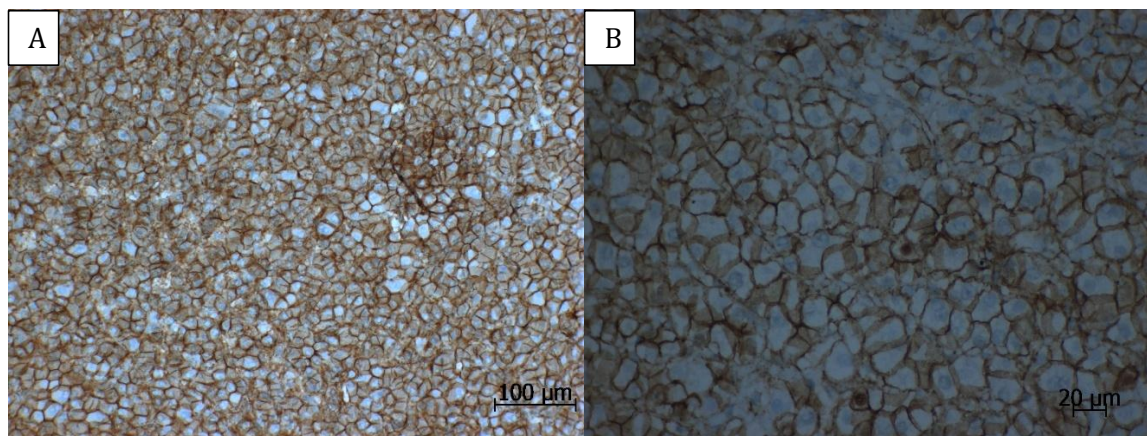


Figure 1: A- Cytoplasmic reactivity with β -catenin, B- Membranous and nuclear immunoreactivity with β -catenin.

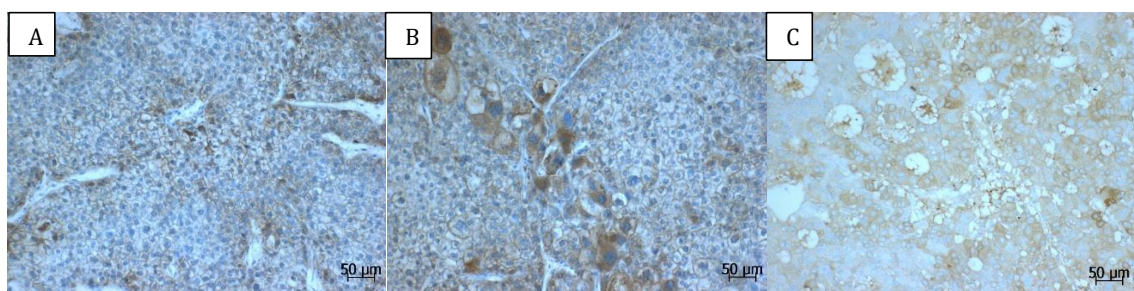


Figure 2: A- Cytoplasmic reactivity in tumoral cells with DRP-1, B- Strong cytoplasmic reactivity in tumoral cells with DRP-1, C- Weak cytoplasmic reactivity in tumor cells with DRP-1.

3. Results

The findings obtained from 30 HCC cases, 26 males and 4 females, were as follows: According to hospital records, 13 patients had died by the time of data collection. The tumor diameter was between 2.5 cm – 15 cm, and the average diameter was calculated as 8.75 cm. Trabecular, solid and steatotic patterns coexist in 14 cases. 5 cases consist of solid pattern only. Solid and acinar patterns were observed together in 5 cases. 5 cases consist of acinar pattern. One case was diagnosed as the fibrolamellar variant of HCC. The background liver tissue was cirrhotic in 25 cases and non-cirrhotic in 5 cases.

In the grading made according to cytological atypia,

abundant cytoplasm and minimal nuclear atypia were evaluated as Nuclear Grade 1 in 3 cases (no relationship was observed between nuclear grade and patterns). 4 cases had prominent nucleoli, hyperchromasia, nuclear irregularity and were evaluated as Grade 2 with mild nuclear atypia. 14 cases had moderate nuclear atypia characterized by nuclear hyperchromasia and nuclear irregularity and were evaluated as Grade 3. 9 cases were evaluated as Grade 4 with significant nuclear pleomorphism, nuclear hyperchromasia and the presence of anaplastic giant cells (Table 1). The presence of necrosis was observed in 15 cases.

Table 1. Grading of the cases according to their cytological atypia

Grade 1: 3 cases	Grade 2: 4 cases	Grade 3: 14 cases	Grade 4: 9 cases
Abundant cytoplasm and minimal nuclear atypia	Contains prominent nucleoli, hyperchromasia, nuclear irregularity, and mild nuclear atypia	Moderate nuclear atypia characterized by nuclear hyperchromasia and nuclear irregularity	Significant nuclear pleomorphism, nuclear hyperchromasia, presence of anaplastic giant cells

In the immunohistochemical study, beta-catenin showed membranous reactivity in 29 cases, and 1 case showed membranous and nuclear reactivity. Cytoplasmic positivity with DRP-1 is observed in 18 cases. While 11 of these cases showed reactivity with a prevalence of over 50%, DRP-1 showed reactivity with a prevalence of less than 50% in 7 of the cases according to the extent of DRP-1 staining in the tumoral areas. These 7 cases

showing low reactivity were generally cases with low and moderate nuclear grade.

Biliary epithelium was also observed to be faintly immunoreactive with DRP-1. No statistically significant relationship was observed between the important prognostic parameters nuclear grade, lympho-vascular invasion, serum AFP value, necrosis, survival and β -catenin and DRP-1 expression ($P>0.05$).

DRP-1 expression was classified as either strong or weak according to the intensity of immunostaining. While no immunoreactivity with DRP-1 was observed in non-tumoral hepatocytes, statistically strong immunoreactivity was observed in tumoral areas in 16 (53%) cases ($P=0.0008$). Weak immunoreactivity was

present in two cases.

Membraneous expression of beta catenin was found to be associated with a high degree of cancer differentiation and lymph node metastasis ($P<0.05$). Nuclear expression was observed together with membranous expression in only one case (Table 2).

Table 2. P values for the relationship between β -Catenin and DRP-1 expression and prognostic parameters

Prognostic Parameter	β -catenin (p)	DRP-1 (p)
Nuclear Grade	> 0.05	> 0.05
Lympho-vascular Invasion	> 0.05	> 0.05
Serum AFP level	> 0.05	> 0.05
Presence of Necrosis	> 0.05	> 0.05
Survival	> 0.05	> 0.05
Tumoral vs. Nontumoral Areas	-	0.0008
Lymph Node Methastasis	< 0.05	> 0.05

4. Discussion

DRP-1 overexpression was noted in 58% of HCC cases. DRP-1 overexpression was not observed in all dysplastic nodules and also in non-neoplastic hepatocytes. Only eight out of 30 cases (26%) were positive for both DRP-1 and β -catenin. In our study, no significant relationship was found between DRP-1 and β -catenin expression and prognostic parameters.

Many studies report that DRP-1 plays important roles in cancer cellular processes, including mitochondrial dynamics and apoptosis. However, there are also studies showing that the expression and prognostic effect of DRP-1 is different in various tumors (Zhao et al., 2013; Qian et al., 2013; Lima et al., 2018).

DRP-1 expression varies across cell types and is influenced by physiological and pathological conditions. (Hu et al., 2017). Reports from lung cancer studies showed that DRP-1 expression is controversial. Kim et al. found that DRP-1 levels were significantly decreased in lung cancer tissues, but Rehman et al. showed the opposite (Kim et al., 2018; Rehman et al., 2012). Immunohistochemical data showed that DRP-1 was higher in lung cancer than in normal lung tissues, but there was no correlation between DRP-1 expression and histological differentiation, tumor size, tumor location, age, gender, T stage and N stage. All these results suggested that DRP-1 gene may participate in tumorigenesis and growth. DRP-1 may be a molecular marker for lung cancer diagnosis (Lima et al., 2018; Shen et al., 2018). Increasing evidence shows that DRP-1 protein level is associated with cell cycle progression, genome instability, cell proliferation, migration, invasion and apoptosis in different cancer cells, including lung cancer cells (Lima et al., 2018; Hu et al., 2017; Shen et al., 2018).

In a study conducted by Ma et al., it was shown that suppression of mitophagy via cisplatin increased cell apoptosis by inhibiting DRP-1 in HCC (Ma et al., 2020). In a study conducted by Zhao et al., the downregulation of DRP-1 by aerobic exercise in a mouse model of HCC was

examined (Zhao et al., 2021). Since the effects of DRP-1 on HCC and its target modality have not been fully determined, its effects on other cancers are also being studied. There are also studies showing that DRP-1 expression is low in colon cancer (Hu et al., 2017). Zhai et al. showed in their study that DRP-1 expression is decreased in squamous cell carcinoma of the esophagus and they associated this situation with the progression of tumorigenesis (Zhai et al., 2014).

The results suggest that DRP-1 overexpression may play a role in tumor differentiation. Simultaneous analyses of DRP-1, β -catenin, AFP expression levels may be useful to determine the malignancy and metastatic potential of HCC. New studies are required to elucidate the complex interaction and coordination between DRP-1 and HCC. Our results suggest that DRP-1 expression may play a role in tumor pathogenesis in HCC. Although our study with a limited number of cases did not find a significant relationship between prognostic parameters and DRP-1 and β -catenin expression, we believe that multicenter studies with larger and heterogeneous patient groups should be conducted. In conclusion, DRP-1, β -catenin and AFP expression levels in HCC can be attributed to the development and progression of HCC.

Author Contributions

Percentages of the authors' contributions is present below. All authors reviewed and approved final version of the manuscript.

	S.O	E.D.	R.D.	O.C.	K.U.E.	S.K.	N.A.	N.A.	F.A.	H.D.	G.O.	I.K.	R.S.
C	20	10	10	10	10	10	10	10	10				
D	30	10	10	20	10	10				10			
S	20	20	20	20							20		
DCP	10	10	10	10	10	10	10	10	10	10			
DAI	30			70									
L	20	10		20	10							20	20
W												50	50
CR	70			30									
SR	20											30	50
PM						10	10	20	20	20	20		
FA	100												

C= concept, D= design, S= supervision, DCP= data collection and/or processing, DAI= data analysis and/or interpretation, L= literature search, W= writing, CR= critical review, SR= submission and revision, PM= project management, FA= funding acquisition.

Conflicts of Interest

We wish to state that there are no known conflicts of interest regarding this publication.

Ethical Considerations

The study was approved by the Clinical Research Ethics Council of Ataturk University (approval date: June 18, 2023, protocol code: B.30.2.ATA.0.01.00/681).

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THE PROTECTIVE ROLE OF CROCIN IN THE FEMALE REPRODUCTIVE SYSTEM

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Abstract: Saffron is a highly valuable spice derived from the dried stigmas of *Crocus sativus* L., a plant species belonging to the Iridaceae family. Although saffron production is predominantly concentrated in Iran, significant quantities are also produced in countries such as Türkiye, India, France, Greece, Spain, and Morocco. The primary bioactive compounds in saffron include crocin, quercetin, and safranal. Additionally, saffron contains a range of essential nutrients, including vitamins, sugars, proteins, amino acids, vital minerals, flavonoids, and other chemical constituents. Saffron extract contains a variety of carotenoids, including crocin (crocin di-gentiobiose ester), crocetin, crocetin di-glucose ester, and crocetin gentiobiose-glucose ester. Beyond its widespread use as a food additive, saffron extracts, which contain crocin, are utilized in traditional medicine as natural healing agents for the treatment of diseases. The therapeutic effects of crocin include antioxidant, hypolipidemic, anti-inflammatory, antifibrotic, and anticancer properties. The existing literature encompasses a substantial body of research that demonstrates the protective and therapeutic effects of crocin on the female reproductive system, employing contemporary scientific methodologies. This review offers a detailed summary of the use of crocin, a key component of saffron, which is also cultivated in the Western Black Sea region of Türkiye, within the context of traditional medicine. Furthermore, the review will present modern scientific evidence derived from both preclinical and clinical studies regarding the application of crocin in the treatment of disorders affecting the female reproductive system.

Keywords: Saffron, Crocin, *Crocus sativus*, Fertility, Female reproductive system

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Received: April 16, 2025

Accepted: July 12, 2025

Published: September 15, 2025

Cite as: Şimşek R, Akpolat Ferah M, Keçeci M. 2025. The protective role of crocin in the female reproductive system. BSJ Health Sci, 8(5): 202-211.

1. Introduction

Infertility is a health issue with familial and societal impacts. It is noted that fertility in women is highest in their twenties and thirties, while in men it remains high until their forties. In healthy fertile couples, pregnancy typically occurs after an average of 8 months of regular intercourse (Knez, 2016). Infertility is characterized as the inability to conceive after one year of consistent, unprotected sexual intercourse (Vander Borgh and Wyns, 2018). Globally, fertility rates are declining due to various factors, primarily environmental ones, among other influences (Starc et al., 2019).

Sex hormone therapies (such as human chorionic gonadotropin, follicle stimulating hormone (FSH), etc.), tubal reconstructive surgery and in vitro fertilization (IVF) are conventional treatments for infertility. However, the interventions are associated with unavoidable side effects and potential negative consequences. For instance, hormone therapy may result in ovarian hyperstimulation syndrome (OHSS) or contribute to mental health concerns (Freeman et al., 2013; Rashidi et al., 2015). The prolonged, physically demanding, and financially burdensome nature of these treatments often drives individuals to explore complementary and adjunctive approaches (Öztürk et al., 2021). A study indicated that 65% of women utilized

complementary and supportive therapies as part of their infertility treatment (Çelik and Kırca, 2018). Another study found that 47.3% of 150 women undergoing infertility treatment reported using alternative medicine methods alongside conventional therapies (Kurt and Arslan, 2019).

Saffron is derived from the dried stigma of the saffron flower (*Crocus sativus* L.), a plant from the Iridaceae family, and is cultivated in countries such as Iran, Morocco, India, Greece, Türkiye, Spain, and France. This plant contains orange-colored pigments and is commonly used as a spice with coloring and aromatic properties in various cuisines, baked goods, confectionery products, and perfumes. In addition to its widespread use as a dietary supplement, saffron has historically been used as a therapeutic agent for a variety of ailments, including depression, mental disorders and cancer (Schmidt et al., 2007; Bathaie and Mousavi, 2010). Saffron is a source of carbohydrates, proteins, anthocyanins, as well as various vitamins and minerals (Petersen et al., 2008). Saffron also contains over 150 volatile aromatic compounds, and its value comes from these distinct phytochemical compounds (Deniaud et al., 2008). The majority of these compounds are carotenoids, including lycopene, zeaxanthin, vitamin A, and β -carotene. Saffron is



composed of three primary components: crocin, picrocrocine, and safranal (Figure 1). Crocin, a carotenoid pigment, is responsible for the characteristic color of saffron, comprising more than 10% of its dry weight. Picrocrocine contributes to the distinctive bitter aroma of saffron, while safranal, the primary volatile oil compound, is chiefly responsible for its unique flavor profile.

Crocin exhibits antioxidant, hypolipidemic, anti-inflammatory, antifibrotic, and anticancer properties, and there are studies that suggest its potential use in infertility research. This review will summarize current scientific findings from studies investigating the effects of crocin, a key component of the saffron plant, on the female genital system.

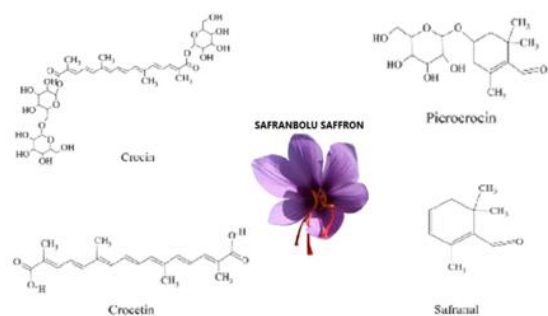


Figure 1. The main structural components of saffron are crocin, picrocrocine, crocetin and safranal, which are also instrumental in determining the quality and aroma of the substance (Giaccio, 2004).

2. Effects of Crocin on the Female Genital System

Oogenesis and follicle development in the female genital system are regulated hormonally in the ovary. The follicular structure consists of an oocyte and the surrounding granulosa and theca cells. Within the follicle, the growth of the oocyte and the development of granulosa and theca cells occur in a coordinated manner. This balance influences the fertilization potential of the ovum after ovulation and its subsequent embryonic development (Matur and Solmaz, 2010).

In the literature, a study was found to examine the effects of crocin, a bioactive compound found in saffron, on the hormonal regulation of the female reproductive system. It is noteworthy that this study focused significantly on its effect on ovarian function and oocyte development. In a study conducted by Maleki et al., the impact of crocin and saffron extract on murine oocytes were examined through the collection of cumulus-oocyte complexes from ovarian tissues. The retrieved oocyte complexes were subsequently cultured in the presence of aqueous saffron extract and crocin. The saffron extract was introduced into the culture medium at concentrations of 5, 20 and 40 µg/ml, while crocin was administered at concentrations of 50, 100 and 400 µg/ml. The research yielded findings that indicated the significant enhancement of in vitro oocyte

maturation (IVM) and IVF rates by aqueous saffron extract and crocin. This finding suggests that these substances may have the potential to modulate reproductive processes (Maleki et al., 2014).

Chen et al. (2019) conducted a comparable study in which porcine oocytes aspirated from the ovaries of female pigs were cultured in a medium supplemented with 0, 300 µg/ml, 400 µg/ml, or 500 µg/ml of crocin. Following IVM, a range of parameters were evaluated, encompassing IVM rates, levels of reactive oxygen substances (ROS) and glutathione (GSH), and the kinetics of major antioxidant enzymes including superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx). Furthermore, the protein levels of apoptosis-regulating genes, like Bcl-2, Bcl-2-associated X protein (BAX) and caspase-3, were analysed together with the subsequent embryonic cleavage rates. The results demonstrated that oocytes cultured with 300 µg/ml and 400 µg/ml of crocin exhibited a significant upregulation in SOD and CAT activity, while those treated with 300 µg/ml, 400 µg/ml, and 500 µg/ml of crocin displayed a notable increase in GPx levels and IVM rates. The highest IVM rate was recorded in the 400 µg/ml crocin-treated group. Furthermore, a significant downregulation of caspase-3 expression was shown in the 400 µg/ml and 500 µg/ml groups alongside a substantial alteration in the Bcl-2/BAX mRNA expression ratio in these treatment groups. These findings suggest that crocin exerts a dose-dependent influence on IVM, oxidative stress regulation and apoptotic gene expression, potentially enhancing in vitro developmental competence (Chen et al., 2019).

A research was carried out by Zohrabi et al. in Wistar albino rats to investigate the effects of crocin on ovarian function and hormone regulation. In this experiment, crocin was administered intraperitoneally (IP) at doses ranging from 100 to 200 mg/kg, administered every other day, for a period of 30 days. Following the treatment, the serum hormone levels were quantified from blood samples and ovarian tissues were subjected to histopathological analysis. The findings indicated that the administration of 200 mg/kg crocin led to a remarkable decrease in the number of atretic follicles. Furthermore, treatment with 100–200 mg/kg crocin led to a significant decrease in estradiol (E₂) and progesterone concentrations in comparison with the control group, while FSH and luteinizing hormone (LH) levels remained unaltered. These results suggest that crocin may influence ovarian follicular dynamics and steroidogenesis without altering gonadotropin levels (Zohrabi et al., 2018).

A research paper was published by Nili-Ahmadabadi et al., which evaluated the impact of saffron aqueous extract and crocin on FSH, LH, progesterone and E₂ levels in pregnant rats. The saffron aqueous extract was administered via oral gavage at doses of 500, 1000, and 2000 mg/kg, while crocin was administered at doses of 150, 300, and 600 mg/kg. Reproductive hormone levels were assessed during the early, mid-, and late stages of pregnancy. Female rats were mated, and the presence of vaginal plugs

was designated as gestational day 0. The animals were then assigned to experimental groups, with the study comprising 21 groups, each consisting of six rats. While control groups received oral saline, the experimental groups were administered saffron aqueous extract or crocin at the specified doses. On days 9, 13 and 22 of gestation, the rats were sacrificed and blood samples, ovaries, uteri and fetuses were sampled for analysis. On day 9 of gestation (early pregnancy), no statistically significant effect on FSH levels was observed between the groups. However, on days 13 (mid-pregnancy) and 22 (late pregnancy), FSH levels in the group receiving 2000 mg/kg saffron aqueous extract were significantly elevated compared to the control group. Conversely, the administration of 600 mg/kg of crocin led to a substantial increase in FSH levels exclusively during the late stages of pregnancy, with no significant alterations observed in the earlier stages. Additionally, a significant reduction in serum progesterone levels was observed across all stages of pregnancy in the groups receiving saffron aqueous extract at all doses. However, in the crocin-treated groups, a significant decrease in progesterone levels was detected only in late pregnancy. In the initial phase of pregnancy, a substantial decline in serum E₂ levels was observed among subjects administered 2000 mg/kg of saffron aqueous extract, in contrast to the control group. During mid-pregnancy, E₂ levels remained comparable to the control group, whereas in late pregnancy, E₂ levels were again significantly lower in the saffron-treated group. Furthermore, saffron aqueous extract administration resulted in a dose-dependent elevation in serum LH levels during early pregnancy, whereas no significant alterations were observed in the mid- or late-gestational stages. Conversely, crocin treatment led to a significant increase in serum LH levels exclusively during late pregnancy. The study also demonstrated that high doses of saffron and crocin were associated with a reduction in fetal count. In the high-dose groups, increased incidences of small embryo formation, embryonic degeneration, placental resorption, and fetal resorption were observed, along with occasional occurrences of decidual bleeding (Nili-Ahmadabadi et al., 2022). The findings indicate that saffron and crocin exert dose-dependent effects on reproductive hormone levels and fetal development during pregnancy.

In a research by Sadoughi et al., the protective effect of crocin was investigated in a letrozole-induced rat model of polycystic ovarian syndrome (PCOS). Crocin was administered IP to rats for 28 days, after which serum levels of LH, FSH, testosterone, and E₂ hormones were measured, and histological examination of the ovaries was conducted. The results indicated that crocin significantly reduced LH, testosterone, and E₂ levels in the PCOS rats, while FSH levels were significantly increased. Histopathological analysis showed a significant increase in the number of preantral and antral follicles, as well as corpora lutea in the treated group. These findings suggest that crocin may be effective in addressing hormonal

imbalances and ovarian cysts associated with PCOS in rats (Sadoughi, 2017).

In another study, PCOS was induced in rats by administering letrozole via oral gavage for 21 days, followed by crocin treatment at a dose of 50 mg/kg via IP for a period of six weeks. The results of this study showed that rats treated with letrozole had elevated levels of testosterone, FSH, and LH and reduced levels of E₂. Crocin treatment restored normal hormonal parameters and eliminated cystic formations in the ovarian cortex. These findings suggest that crocin may have significant therapeutic potential in the treatment of PCOS (Elham et al, 2019).

In a clinical trial by Rahimi et al., the study population comprised women suffering from PCOS. The study sample was partitioned into two groups (n = 25 each). The first group was administered crocin (15 mg, twice daily), while the second group received a placebo. After 12 weeks, a comprehensive assessment was conducted to evaluate the changes in the patients' lipid profiles, fasting blood glucose levels, fasting insulin, as well as inflammatory markers such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α). These assessments were conducted before and after the administration of the treatment. The results demonstrated that the crocin-treated group exhibited significant improvements in lipid profile and fasting glucose levels in comparison to the placebo group. Furthermore, the administration of crocin resulted in a substantial decrease in serum levels of the inflammatory cytokines IL-6 and TNF- α . These results indicate that crocin may serve as a promising therapeutic agent for the treatment of PCOS (Rahimi et al., 2022). The results of the animal and clinical studies indicate the possible therapeutic value of crocin in the management of PCOS.

Some drugs used in cancer treatment cause adverse side effects on ovarian follicles and folliculogenesis (Spears et al., 2019). There is a paucity of research on the use of crocin to treat side effects arising from cancer therapies in the female genital system (Wang et al., 2022). Khanmohammadi et al. showed in a study in which crocin was given together with Cyclophosphamide (CP), which is frequently used in cancer therapies, that the administration of crocin together with CP in 6-8 week old female mice caused an increase in the number of follicles in all developmental stages and a significant decrease in mast cells. In the same study, it was shown that crocin positively changed the oxidative stress parameters due to CP administration and caused a significant decrease in malondialdehyde (MDA) level and a significant increase in total antioxidant capacity (TAC) and SOD levels. These favourable changes in redox balance were also reflected in hormonal parameters and significant increases in LH, FSH and E₂ levels were shown in subjects given crocin together with CP (Khanmohammadi et al. 2021).

In other study conducted by Shams et al. (2024), the potential protective effects of crocin against CP-induced ovarian damage were examined. The study included 24 female Wistar albino rats weighing 160–180 grams, which

were assigned to four groups. The control group received only saline, while the second group received 30 mg/kg CP. The third and fourth groups were administered 30 mg/kg CP combined with 100 mg/kg or 200 mg/kg crocin, respectively. Treatments were administered IP three times per week. In the CP treated group, the number of primordial follicles and the diameter of primary follicles were reduced compared to the control group. However, both crocin-treated groups exhibited an increase in these parameters relative to the CP group. Furthermore, the number of atretic follicles was markedly elevated in the CP group when compared to the control group, whereas it exhibited a profound and statistically significant reduction in the 200 mg/kg crocin group in comparison to the CP group (Shams et al., 2024). In conclusion, the study by Khanmohammadi et al. and Shams et al. indicate that crocin may exert protective effects on ovarian follicles and enhance redox balance in females exposed to CP, potentially mitigating the detrimental side effects of cancer therapies on ovarian function.

As reported by Chen et al. (2021), Gestational hypertension (pre-eclampsia) was induced in female pregnant Sprague-Dawley rats by administering nitro-arginine methyl ester hydrochloride (L-NAME) at a dose of 50 mg/kg/day by oral gavage on days 14-19 of pregnancy, and rats treated with crocin at a dose of 50 mg/kg, 100 mg/kg and 200 mg/kg by oral gavage on days 10-19 of pregnancy were sacrificed on day 20 of pregnancy and placental tissue and serum samples were collected. Enzyme Linked Immunosorbent Assay (ELISA) was performed to determine whether crocin treatment could ameliorate abnormal changes in placental growth factor (PIGF) and soluble fms-like tyrosine kinase (sFlt-1). Treatment with 200 mg crocin decreased the circulating level of sFlt-1 but increased the circulating level of PIGF and significantly decreased the serum sFlt-1/PIGF ratio in hypertensive rats. In L-NAME-induced hypertensive rats, crocin treatment at a dose of 200 mg was found to improve the clinical signs of systolic high blood pressure and proteinuria. Both placental and serum levels of TNF- α , IL-6 and IL-1 β (interleukin-1 beta) cytokines were detected by ELISA quantitative real-time polymerase chain reaction (RT-PCR). TNF- α , IL-1 β and IL-6 inflammatory cytokine levels were significantly reduced in hypertensive rats treated with 200 mg crocin. Placental MDA, hydrogen peroxide (H₂O₂), SOD, CAT, GPx and GSH antioxidant parameters were measured in rats in which pre-eclampsia was induced. While MDA and H₂O₂ levels were very low, SOD, CAT, GPx and GSH parameters were found to be very high in rats treated with a dose of 200 mg of crocin. Levels of heme oxygenase-1 (HO-1) and nuclear factor-erythroid 2-like 2 (Nrf-2) were analysed by Western blot in rats with a pre-eclampsia model, and both HO-1 and Nrf-2 levels were significantly raised in the group of hypertensive rats treated with a dose of 200 mg of crocin. In the assessment of fetal weight and fetal survival rate, it was also observed that fetal weight and fetal survival rate were significantly elevated in crocin-treated hypertensive rats (Chen et al.,

2021).

In an experimental study, Liu et al. (2017) sought to ascertain the potential therapeutic properties of crocin on endometriosis-associated infertility and inflammation in a mouse model. Endometriosis was induced in 7-week-old female BALB/c donor mice through IP administration of estradiol benzoate. One week post-injection, uterine tissues were harvested, and the endometrial layer was meticulously isolated and suspended in sterile saline solution. The collected endometrial tissue was then fragmented into pieces smaller than 1 mm, homogenized, and introduced into the peritoneal cavity of 30 recipient mice via laparoscopy to establish endometriotic lesions. Following the induction of endometriosis, the recipient mice were randomly allocated into three groups (n=10 per group). Group 1 was designated as the control group and received no intervention. Group 2, the sham group, was administered IP saline injections. Group 3 was treated with crocin at a dose of 25 mg/kg IP for 20 consecutive days. On the 21st day of the study, the animals were euthanised. Their uterine tissues and serum samples were then examined for further histological and biochemical analysis. The results demonstrated a statistically significant size and weight reduction of endometriotic lesions in the crocin-treated group compared to both the control and sham groups. Histopathological assessments supported these findings. Further immunohistochemical analysis demonstrated that administration of crocin led to a substantial reduction in the levels of vascular endothelial growth factor (VEGF) and proliferating cell nuclear antigen (PCNA). Furthermore, a marked reduction in serum levels of pro-inflammatory cytokines, including TNF- α , IL-6, interferon-gamma (IFN- γ) and VEGF, was observed in the crocin-treated group compared with the control and sham groups. These findings suggest that crocin may exert therapeutic effects by attenuating inflammation and suppressing endometriotic lesion development in an experimental endometriosis model (Liu et al., 2017).

A substantial body of studies has been conducted using various experimental models, which collectively indicate that crocin exerts a beneficial effect on the ovaries by modulating hormonal balance and ameliorating symptoms associated with conditions such as endometriosis, PCOS and gestational hypertension. Furthermore, the incorporation of crocin into oocyte culture media has been demonstrated to significantly enhance IVM and fertilization IVF outcomes. Crocin has been demonstrated to exert a protective effect against ovarian toxicities induced by cancer treatment, to alleviate oxidative stress, and to have anti-apoptotic and anti-inflammatory properties. Crocin administration at different doses has been found to regulate hormonal levels, particularly by altering the concentrations of LH, FSH, E₂ and progesterone during pregnancy.

3. Effects of Saffron Compounds on the Estrus Cycle

Rodents, particularly rats, are frequently utilized in reproductive and infertility research due to the similarity of their estrous cycle to the human menstrual cycle. These cycles are commonly referred to as the estrous cycle (Auta et al., 2016). In female rats, puberty typically begins after the fourth postnatal week, which is marked by a surge in LH (Ekambaram et al., 2017). The estrous cycle in rodents is a dynamic process, during which ovulation can be monitored, and fluctuations in the levels of E₂ and progesterone secreted by the ovaries mirror the cyclical changes in various ovarian cell types, which become prominent and recede throughout the cycle. This cycle typically recurs every 4-5 days, unless disrupted by conditions such as pregnancy, pseudopregnancy, or anestrus. The cycle is divided into four distinct phases: proestrus, estrus, metestrus, and diestrus (Byers et al., 2012; Cora et al., 2015). The proestrus phase lasts approximately 12 hours, estrus lasts between 12 to 24 hours, metestrus lasts 6-8 hours, and diestrus lasts 52-60 hours (Petroianu et al., 2005). During the proestrus and estrus phases, follicular development occurs in the ovaries, ovulation typically occurs around the midpoint of estrus, and corpus luteum formation follows ovulation. The diestrus phase serves as a resting phase for the reproductive system (Hubscher et al., 2005).

Vaginal cytology is a non-invasive and relatively cost-effective method commonly employed to assess the stages of the estrous cycle (Sahoo et al., 2014). This technique is typically performed using two methods. In the vaginal smear technique, a cotton swab moistened with saline at room temperature is inserted into the vaginal opening and

gently rotated to collect cells from the vaginal wall. These cells are then spread onto a microscope slide, air-dried, fixed, and stained (Barret et al., 2018). In the vaginal lavage technique, a sterile pipette is carefully inserted into the vaginal canal for several millimeters. A volume of 100 µl of phosphate-buffered saline, distilled water or isotonic serum is slowly administered into the vagina and subsequently aspirated. This procedure should be repeated 4-5 times using the sterile latex balloon. It is important to position the rubber pipette at the entry of the vaginal canal and not to enter the vaginal opening. The cell suspension, including a few drops of liquid, is then placed on a microscope slide, air dried, and properly dyed and analyzed (Auta et al., 2016).

In vaginal cytology, the determination of the estrous phase after staining is based on the distribution and density of various cell types. During the proestrus phase, the presence of small and large round nucleated cells, which are homogeneous in appearance and size, is characteristic of this stage. These cells may be observed individually or in clusters. There may also be a small number of anucleated, keratinized epithelium cells. Early proestrus may also show few neutrophils. In the estrus phase, a high number of anucleate keratinized epithelial cells is observed. The cytoplasm of these cells appears granular, and the cells exhibit irregular shapes, with very few nucleated epithelial cells occasionally seen. The metestrus phase is marked by the presence of numerous leukocytes and a few large, granule-free, anucleate keratinized epithelial cells, as well as some nucleated epithelial cells in the late metestrus phase. In the diestrus phase, prominent leukocytes, nucleated epithelial cells, and rare keratinized cells may be detected (Figure 2, Table 1) (McLean et al., 2012; Auta et al., 2016; Barret et al., 2018).

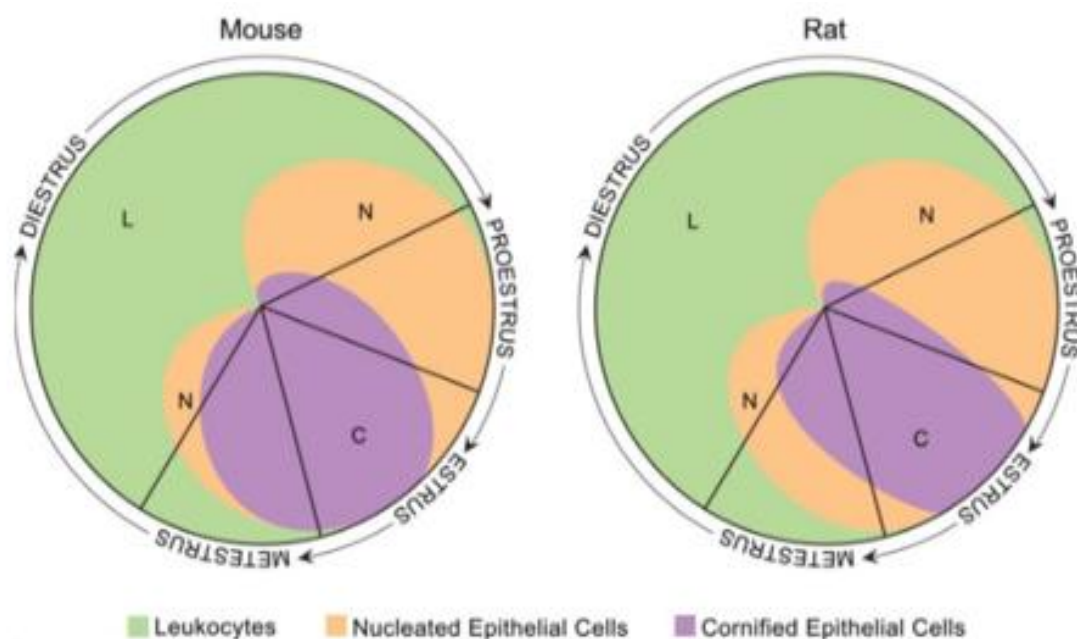


Figure 2. The fundamental principle for determining the stage of the estrous cycle is to know the predominant cell type for each stage (Ajayi and Akhigbe, 2020).

Table 1. Phases of the estrous cycle based on the density of vaginal smear cell types (Cora et al., 2015)

Stage	Neutrophils	Small Nucleated Epithelial Cells	Large Nucleated Epithelial Cells	Anucleated Keratinized Epithelial Cells	Relative Cell Density
Proestrus	0 to +	++ to +++	0 to +	0 to +	Low to moderate
Estrus					
Rat	0 to +	0 to ++	0 to ++	++ to +++	Moderate to high
Mouse	0 to +	0 to +	0 to +	++ to +++	Moderate to high
Metestrus					
Rat	+ to +++	+ to ++	+ to ++	+ to +++	Moderate to high
Mouse	+ to +++	0 to +	0 to +	++ to +++	Moderate to high
Diestrus	++ to +++	+ to ++	+ to ++	0 to +	Low to moderate

0 = none; + = few; ++ = moderate; +++ = high.

Cellat et al. (2024) examined the protective effects of safranal, a compound derived from saffron, against letrozole-induced PCOS in Wistar albino rats. At the start of the study, estrous cycles were monitored in 50 rats, with 44 of them showing a normal cycle duration of 4 to 5 days. From these, 32 female rats were selected at random and allocated to one of four groups, with each group consisting of eight rats. Group 1 received 1.2 ml/kg of 1% carboxymethylcellulose, group 2 received 1 mg/kg of letrozole, group 3 received safranal at a dose of 200 mg/kg, and group 4 received a combination of letrozole (1 mg/kg) and safranal (200 mg/kg) for 21 days via oral gavage. Throughout the study, vaginal lavage was performed to monitor the estrous cycle and assess its length. Irregular estrous cycles were monitored in 7 rats in the letrozole group, while regular estrous cycles were monitored in 8 rats in control group, 8 rats in safranal group, and 6 rats in letrozole + safranal group. The results indicated that while safranal alone did not alter the estrous cycle length, it effectively reversed the prolonged estrous cycle induced by letrozole (Cellat et al., 2024).

In their study, Bashir et al. (2022) investigated the impact of saffron extract on the onset of temporary infertility and the estrous cycle in Wistar albino rats. Female rats with a regular estrous cycle were randomly assigned to either the control group (12 rats) or the experimental group (12 rats), which received 1 g/kg of saffron extract for 12 days. Vaginal smear samples were collected from days 13 to 43, and the Giemsa staining protocol was used for analysis. Monitoring of the estrous cycle through Giemsa staining revealed that the saffron-treated group exhibited disruptions in their estrous cycles. In addition, the number of offspring born to mated rats between days 44 and 60 was remarkably lower in the group treated with saffron

versus the control group. These results suggest disruption of the estrous cycle by saffron extract, which may have a negative effect on fertility (Bashir et al., 2022).

Hu et al. (2018) induced PCOS in female mice offspring by administering 250 µg/kg dihydrotestosterone (DHT) subcutaneously on days 16-18 of pregnancy. This study evaluated the impact of crocetin, a component of saffron, on the length of the estrous cycle in 36 female offspring with PCOS. The study's control group comprised 18 female offspring without induced PCOS. Of the 36 PCOS-induced offspring, 18 were treated with 40 mg/kg of crocetin for a period of 4 weeks. The results indicated that in the PCOS group, the duration of diestrus was extended, while the durations of other estrous cycle phases remained normal. Conversely, the administration of crocetin to the PCOS treated group restored the diestrus to its normal duration (Hu et al., 2018).

The authors of this review comprehensively report on the modulatory effects of crocin, a pharmacologically active compound derived from saffron, on the regulation of the estrous cycle in female Wistar albino rats between 8 and 12 weeks of age. In the study, estrous cycle monitoring and cycle length were determined after 20 days of treatment with crocin at a dose of 100 mg/kg/day by IP injection. In our study, vaginal lavage samples were collected continuously for 10 days. After drying and fixation, H&E and toluidine blue staining were performed. It was observed that crocin, when administered alone, did not alter the estrous cycle length, as confirmed by H&E and toluidine blue staining of the vaginal lavage samples. The samples were analyzed using a light microscope, and the estrous phase was identified. Photographs of the crocin and control groups, captured at 20X magnification, are presented in Figure 3.

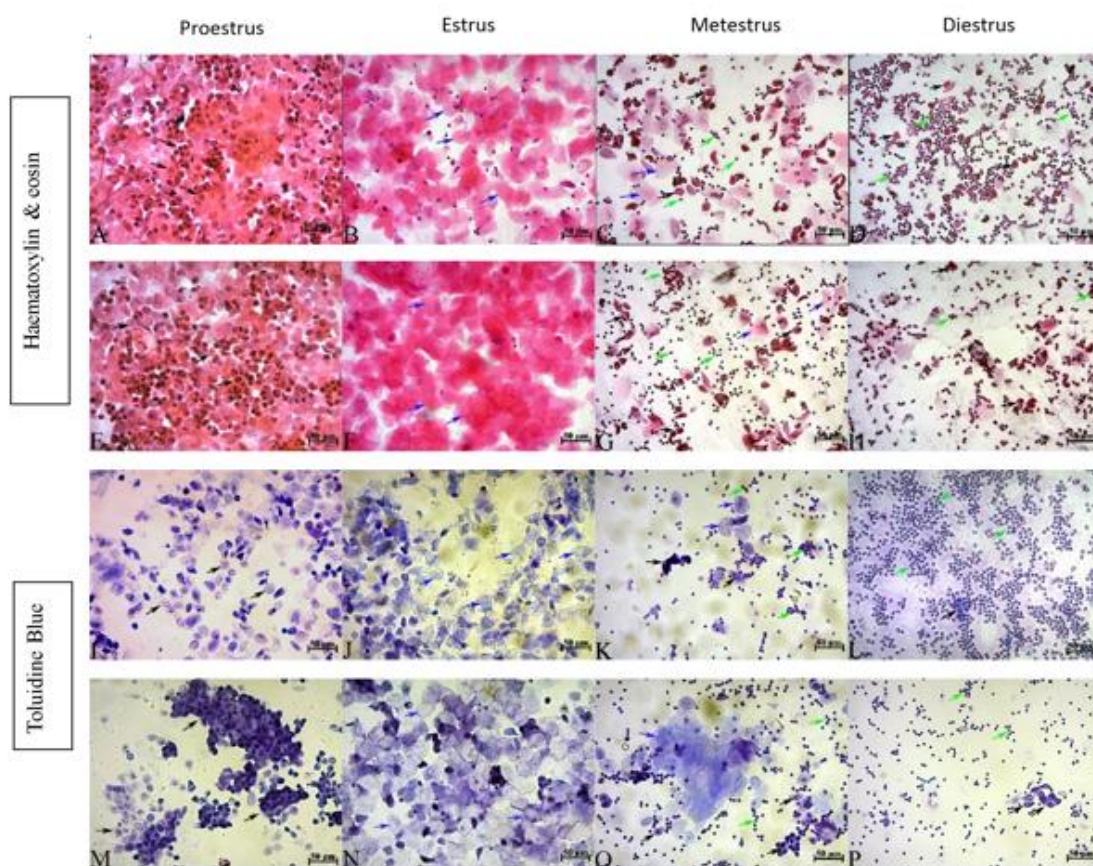


Figure 3. A, B, C, D, I, J, K, L; control, E, F, G, H, M, N, O, P; crocin. Black arrow: Nucleated Epithelial Cells, blue arrow: cornified epithelial cells, green arrow: neutrophils. Scale bar: 50 μ m. (Ramazan ŞİMŞEK Archive).

4. Discussion

The World Health Organization (WHO) asserts that traditional medicine, encompassing practices derived from plants, minerals, and animals, is utilized either as a standalone modality or in conjunction with other therapeutic approaches for the management of diseases and the promotion of health and well-being (Hoenders et al., 2024). According to the WHO, approximately 80 percent of the global population uses traditional medicine for their health care needs. (Kamboj, 2008). In many developing countries, traditional medicine is regarded as a complementary aspect of modern medical practice, with numerous natural remedies having been used for centuries in Asia. A scientific framework is needed to integrate such remedies into modern medical care (Agarwal et al., 2007). Numerous studies have demonstrated the successful use of conventional treatments together with traditional therapies, and have provided evidence of their benefit through modern approaches.

Environmental chemicals, genetic factors, and the side effects of cancer treatments can induce various histopathological changes and hormonal regulation disorders in the female reproductive organs, which may impact the estrous cycle and lead to infertility (Pan et al., 2024) Environmental pollutants and chemicals have the

potential to adversely affect folliculogenesis, oogenesis, female reproductive hormones, and the regulation of oxidative stress, thereby playing a significant role in the pathogenesis of female infertility (Yao et al., 2023).

This review focuses on the potent antioxidant, anti-apoptotic, and anti-inflammatory properties of saffron extract and its key component, crocin, and their effects on hormone regulation and the female reproductive system in experimental and clinical studies. Specifically, it examines the effects of crocin on the female reproductive system, including its influence on estrous cycle length, oocyte maturation and antioxidant activity in embryo cultures. It also sheds light on crocin's potential to mitigate the side effects of cancer treatments, diabetes, gestational hypertension, endometriosis and PCOS (Table 2). However, the teratogenic impact of crocin on embryos and developing foetuses has not yet been scientifically investigated in detail. Therefore, further in vivo and in vitro research is necessary to ensure its safety for human use and to gain a more sophisticated understanding of its potential effects on fertility and fetal development.

Table 2. Effects of crocin on the female reproductive system

Study type	Inducer	Inducer type	Crocin treatment dose	Duration	Effect of crocin	Referenses
<i>In vitro</i> / Mouse Oosit	No	No	50, 100 and 400 µg/mL Crocin	6 days	IVM ↑ IVF ↑	Maleki et al., 2014
<i>In vitro</i> / Swine Oosit	No	No	0, 300, 400 veya 500 µg/mL Crocin	22 hours	IVM ↑ IVF ↑ SOD ↑ CAT ↑ GSH ↑ GPx ↑ Bcl-2/BAX ↑ Caspase-3 ↓	Chen et al., 2019
<i>In vivo</i> / Female Pregnant Rat	No	No	150, 300 and 600 mg/kg Crocin (Oral)	22 Day	FSH ↑ LH ↑ progesterone↓ Number of fetuses ↓	Nili- Ahmadabadi et al., 2022
<i>In vivo</i> / Female Rat	No	No	100-200 mg/kg/ every other day Crocin (IP)	30 days	Atretic follicles ↓ E ₂ ↓ Progesterone ↓	Zohrabi et al., 2018
<i>In vivo</i> / Female Rat	Letrazole	PCOS	50 and 100 mg/kg Crocin (IP)	28 days	FSH ↑ LH ↓ Testosterone ↓ E ₂ ↓ Atretic follicles ↓ Cystic follicles ↓ Developing Follicles ↑	Sadoughi et al, 2017
<i>In vivo</i> / Female Rat	Letrazole	PCOS	50 mg/kg/day Crocin (IP)	46 Days	FSH ↓ LH ↓ Testosterone ↓ E ₂ ↑ Atretic follicles ↓ Cystic follicles ↓	Elham et al., 2019
<i>In vivo</i> / Women	Patients wiht PCOS	No	15 mg / day Crocin (Oral)	90 days	IL-6 ↓ TNF-α ↓	Rahimi et al., 2022
<i>In vivo</i> / Female Mice	Cyclophosphamide	Anticancer Medicine	200 mg/kg/day Crocin (IP)	21 days	MDA TAC ↑ SOD ↑ LH ↑ FSH ↑ E ₂ ↑ Number of follicles ↑ Mast cells ↓	Khanmohammadi et al., 2021
<i>In vivo</i> / Female Rat	Cyclophosphamide	Anticancer Medicine	100, and 200 mg/kg,Crocin (IP)		Atretic follicles ↓ Primordial follicles ↑ Primary follicles ↑	Shams et al., 2024
<i>In vivo</i> / Female Rat	L-NAME	Gestational Hypertension	50, 100, and 200 mg/kg/day,Cro cin (Oral)	10 days	sFlt-1/PIGF ↓ IL-1β↓ IL-6 ↓, TNF-α ↓ MDA ↓ H ₂ O ₂ ↓ SOD ↑CAT ↑ GPx ↑ GSH ↑ Nrf-2 ↑ HO-1 ↑ Fetal survival rates ↑ Fetal weight ↑	Chen et al., 2020
<i>In vivo</i> / Female Mice	Estradiol benzoate	Endometriosis	25 mg/kg Crocin (IP)	21 days	VEGF ↓ PCNA ↓ TNF-α ↓ IL- 6↓ IFN-γ ↓	Liu et al. 2017
<i>In vivo</i> / Female Rat	No	No	1g/Kg Saffron extract (Oral)	80 Days	Irregular estrous cycle	Bashir et al., 2022
<i>In vivo</i> / Female Mice	DHT	PCOS	40 mg/kg Crocin (Oral)	30 Days	Cured prolonged diestrus phase	Hu et al.,2018
<i>In vivo</i> / Female Rat	Letrazole	PCOS	200 mg/kg Safranlal	21 days	Cured Irregular estrous cycles	Cellat et al., 2024

↓= Statistically significant decrease, ↑= Statistically significant increase, Bcl-2/BAX= B-cell lymphoma 2 / Bcl-2 associated X protein, CAT= catalase, DHT= dihydrotestosterone, E₂= estradiol, FSH= follicle-stimulating hormone, GPx= glutathione peroxidase, GSH= glutathione, HO-1= heme oxygenase-1, H₂O₂= hydrogen peroxide, IFN-γ= interferon gamma, IL-1β= interleukin-1 beta, IL-6= interleukin-6, IVF= in vitro fertilisation, IVM= in vitro oocyte maturation, L-NAME= Nω-Nitro-L-arginine methyl ester, LH= luteinizing hormone, MDA= malondialdehyde, Nrf-2= nuclear factor erythroid 2-related factor 2, PCNA= proliferating cell nuclear antigen, PCOS= polycystic ovary syndrome, SOD= superoxide dismutase, sFlt-1/PIGF= soluble fms-like tyrosine kinase-1 / placental growth factor, TAC= total antioxidant capacity, TNF-α= tumor necrosis factor-alpha, VEGF= vascular endothelial growth factor.

Author Contributions

The percentages of the authors' contributions are presented below. All authors reviewed and approved the final version of the manuscript.

	R.Ş	M.A.F	M.K
C	40	30	30
D	50	25	25
S	50	25	25
DCP	70	10	20
DAI	70	10	20
L	80	10	10
W	65	10	25
CR	60	20	20
SR	70	15	15

C=Concept, D= design, S= supervision, DCP= data collection and/or processing, DAI= data analysis and/or interpretation, L= literature search, W= writing, CR= critical review, SR= submission and revision, PM= project management, FA= funding acquisition.

Conflict of interest

The authors declare that they have no conflicts of interest related to this study.

Limitations of the study

The heterogeneity of the included studies, particularly in terms of species (humans, rats, and mice), as well as variations in crocin dosage, duration of administration, and routes of delivery, may limit the external validity and generalizability of the review's findings.

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EFFECTIVENESS OF EXTRACORPOREAL SHOCK WAVE THERAPY AND HIGH-INTENSITY LASER THERAPY IN SHOULDER REHABILITATION: A NARRATIVE REVIEW

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Abstract: Shoulder disorders are among the most prevalent musculoskeletal conditions, often resulting in pain, limited mobility, and reduced quality of life. In recent years, non-invasive modalities such as Extracorporeal Shock Wave Therapy (ESWT) and High-Intensity Laser Therapy (HILT) have gained recognition in physiotherapy for their potential to accelerate tissue healing and provide symptomatic relief without the risks of pharmacologic or surgical intervention. This article presents a narrative review of peer reviewed literature published between 2020 and 2025, selected using structured searches in PubMed, Scopus, Web of Science, and Google Scholar. Studies were included based on predefined inclusion and exclusion criteria, with a focus on clinical outcomes, therapeutic mechanisms, and safety across various shoulder pathologies. The findings indicate that both ESWT and HILT show considerable promise in managing conditions such as rotator cuff tendinopathy, calcific tendinitis, adhesive capsulitis, and subacromial impingement. However, variability in treatment parameters, study quality, and outcome measures continues to hinder the development of standardized clinical guidelines. This review offers practical insight for clinicians and identifies critical gaps in the literature that should inform future research priorities, including protocol optimization and comparative effectiveness studies.

Keywords: Shoulder disorders, Extracorporeal shock wave therapy, High intensity laser therapy, Rehabilitation

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Received: August 07, 2025

Accepted: August 26, 2025

Published: September 15, 2025

Cite as: Karaca İ. 2025. Effectiveness of extracorporeal shock wave therapy and high-intensity laser therapy in shoulder rehabilitation: A narrative review. BSJ Health Sci, 8(5): 212-217.

1. Introduction

The shoulder joint is one of the most mobile structures in the human body. This mobility, while essential for daily function, also makes it vulnerable to a wide range of musculoskeletal disorders. Conditions such as rotator cuff tendinopathy, subacromial impingement, calcific tendinitis and adhesive capsulitis are commonly seen and often result in pain, stiffness, and loss of mobility, which can interfere with both work and daily activities (Xue et al., 2024).

Standard treatment approaches typically include rest, medication, physical therapy modalities, and exercise. Although many patients respond well to these methods, a considerable number continue to report pain and functional limitations. In such cases, exploring alternative or complementary therapies becomes necessary (Salem et al., 2024).

Among the recent developments in non-invasive treatment, extracorporeal shock wave therapy (ESWT) and high intensity laser therapy (HILT) have gained interest. These modalities are thought to reduce pain and promote tissue repair, without the risks associated with surgery or long term drug use (Aldardour et al., 2025). Even so, it is still unclear which patient groups benefit

most, how frequently these therapies should be applied, and how they compare with each other. The limited number of high-quality clinical studies that directly compare ESWT and HILT makes it difficult to establish consistent treatment guidelines. This uncertainty can be challenging for clinicians when deciding how to apply these methods in practice (Liao et al., 2025).

Due to the heterogeneity of available studies and variations in clinical protocols, a narrative review format was chosen to provide a flexible yet structured synthesis of the literature. This format is particularly appropriate when the existing evidence is insufficiently homogeneous for meta-analysis, and when clinical context and mechanistic insights need to be integrated across study types.

There remain important research gaps, including: lack of standardized treatment protocols for both ESWT and HILT; limited data on long-term outcomes; and few high quality, head to head comparative trials (Aldardour et al., 2025; Liao et al., 2025). These gaps hinder the development of clear clinical guidelines and complicate patient specific treatment planning.

Therefore, the objective of this narrative review is to critically synthesize recent literature (2020–2025) on the



physiological mechanisms, clinical effectiveness, and comparative outcomes of ESWT and HILT in shoulder rehabilitation. It also aims to highlight key knowledge gaps, identify patient-specific indications, and offer practical recommendations for clinicians and researchers.

2. Review

2.1. Search Strategy and Selection Criteria

This review was conducted using electronic databases including PubMed, Scopus, Web of Science, and Google Scholar. The keywords used in the search were: “*shoulder disorders*,” “*extracorporeal shock wave therapy*,” “*high-intensity laser therapy*,” and “*physiotherapy*.” Boolean operators (AND/OR) were utilized to refine search sensitivity.

Inclusion criteria were as follows:

- Articles published between 2020 and 2025
- English language full text availability
- Studies designed as randomized controlled trials (RCTs), systematic reviews, or comparative clinical studies

Exclusion criteria included:

- Case reports, opinion pieces, editorials, or non peer reviewed sources
- Non English publications
- Studies not directly related to shoulder rehabilitation

After applying these criteria, a total of 12 studies were selected for final synthesis.

2.2. Narrative Review Approach

Given the heterogeneity of study designs, populations, treatment protocols, and outcome measures, a narrative synthesis methodology was adopted rather than meta-analysis. This approach facilitates integration of diverse types of evidence and emphasizes clinical interpretation over statistical aggregation (Liao et al., 2025).

Included studies were analyzed thematically based on their focus: (1) physiological mechanisms of action, (2) clinical outcomes related to pain relief, function, and mobility, and (3) comparative effectiveness of ESWT and HILT across shoulder disorders.

The review prioritized findings that reported standardized outcome metrics such as *the* Visual Analog Scale (VAS), Shoulder Pain and Disability Index (SPADI), and *the* Constant-Murley Score (CMS). Additionally, mechanistic outcomes (e.g., tissue perfusion, neovascularization, nerve modulation) were synthesized to understand therapeutic underpinnings.

A structured data extraction sheet was developed to capture key details including sample size, patient population, treatment modality, frequency and dosage, and short and long term outcomes.

3. Mechanisms of Extracorporeal Shock Wave Therapy

ESWT has been used in musculoskeletal medicine to treat soft tissue injuries and chronic pain conditions. Its exact biological mechanisms are still being investigated, but several theories have been proposed based on clinical and experimental data.

One key effect of ESWT is its ability to stimulate cellular activity in injured tissues. The mechanical pulses generated by the shock waves may cause microtrauma, which triggers a healing response. This process is thought to promote neovascularization, increase local blood flow, and support tissue regeneration (Mazin et al., 2023). Additionally, ESWT appears to influence pain perception. It may help to desensitize nerve endings or modulate pain related neurotransmitters, resulting in an analgesic effect. Some studies suggest that ESWT also disrupts the pain spasm cycle, which is common in shoulder pathologies (Xue et al., 2024).

Another important factor is its mechanical action on calcific deposits. In conditions such as calcific tendinitis, shock waves may help fragment and dissolve calcium buildup, improving shoulder mobility and reducing inflammation (Demirel et al., 2021; Lee et al., 2022).

While these effects seem promising, the clinical outcomes can vary depending on treatment intensity, frequency, and patient-specific factors. Despite this variability, ESWT has become a popular non invasive option in physical therapy for shoulder conditions.

4. Mechanisms of High-Intensity Laser Therapy

HILT has emerged as a promising treatment in the management of musculoskeletal conditions, particularly for pain relief and functional recovery. Its therapeutic effects are primarily related to photothermal and photomechanical processes, which influence both cellular and tissue level responses.

One of the primary mechanisms is increased tissue perfusion. The high energy laser penetrates deep into the tissues, generating localized heat that leads to vasodilation. This enhanced blood flow supports oxygenation and nutrient delivery to damaged areas, accelerating the healing process (Abdelhakiem et al., 2024).

HILT is thought to stimulate mitochondrial activity. By enhancing adenosine triphosphate (ATP) production, it boosts cellular metabolism, which contributes to tissue repair. The laser energy may influence inflammatory mediators, helping to reduce swelling and sensitivity in the affected region (Hao et al., 2024). Pain reduction is another key effect of HILT. It may suppress nociceptor sensitivity and modulate the transmission of pain signals through the nervous system. This contributes to a notable decrease in pain perception in patients with chronic shoulder conditions (Ismail et al., 2025).

In clinical applications, HILT has shown potential not

only in pain modulation but also in restoring range of motion and improving muscular function. However, treatment parameters such as dosage, frequency and wavelength vary widely across studies, making standardization an ongoing challenge (Aldardour et al., 2025).

5. Findings

A total of 12 studies were included in this review. These studies investigated the application ESWT and HILT in various shoulder pathologies, including rotator cuff tendinopathy, calcific tendinitis, adhesive capsulitis, and subacromial impingement syndrome.

- Most ESWT studies reported improvements in pain reduction, range of motion (ROM), and functionality, particularly in cases of calcific tendinitis and chronic tendinopathies (Demirel et al., 2021; Lee et al., 2022).
- HILT studies showed significant benefits in terms of short term pain relief, inflammation reduction, and quicker recovery, especially in adhesive capsulitis and subacromial impingement syndrome (Abdelhakiem et al., 2024; Salem et al., 2024).
- Several comparative studies emphasized ESWT's advantage in long term functional improvement, while HILT was more effective for rapid symptom control (Aldardour et al., 2025).
- However, substantial variation in treatment parameters (e.g., dosage, frequency) and patient characteristics (e.g., chronicity, comorbidities) made direct comparisons between interventions methodologically difficult (Ranjithkumar et al., 2025).

The most frequently reported outcome measures included the Visual Analog Scale (VAS) for pain, the Shoulder Pain and Disability Index (SPADI), and the Constant Murley Score (CMS) for functional assessment. Despite general consistency in outcome domains, inconsistent reporting standards, variable follow up durations, and differing treatment protocols limited the feasibility of performing a quantitative meta analysis.

To enhance clarity and improve clinical applicability, a comparative summary table outlining each study's design, shoulder condition targeted, sample size, intervention modality, and outcome measures is provided in Table 1.

6. Clinical Applications and Outcomes of ESWT and HILT in Shoulder Physiotherapy

6.1. Applications and Outcomes of ESWT

ESWT has demonstrated significant clinical utility, particularly in cases where conservative treatment has failed. Evidence suggests ESWT offers sustained pain relief and functional improvement through both mechanical disruption of pathological tissue and neuromodulatory effects.

It is particularly effective in managing calcific tendinitis, where it facilitates calcium resorption and improves

shoulder joint mobility (Demirel et al., 2021; Lee et al., 2022). Clinical gains are especially evident in chronic degenerative cases with calcification and fibrosis. Additionally, ESWT is beneficial in rotator cuff tendinopathies, supporting neuromuscular activation and vascularization (Xue et al., 2024). Notably, patients' refractory to conventional physiotherapy protocols showed meaningful long term analgesia and reduced need for pharmacologic agents following ESWT application (Ranjithkumar et al., 2025).

ESWT is particularly suitable for patients who are contraindicated for surgery or prefer minimally invasive interventions.

6.2. Applications and Outcomes of HILT

HILT has also shown robust results in treating shoulder dysfunctions, especially in conditions dominated by acute inflammation and joint stiffness, such as adhesive capsulitis. Clinical studies report accelerated pain relief and enhanced joint mobility when HILT is used adjunctively with traditional physiotherapy (Salem et al., 2024).

HILT facilitates deep tissue penetration, promoting mitochondrial activity and vascular perfusion, which aids muscle regeneration and functional recovery in rotator cuff pathologies (Abdelhakiem et al., 2024). Its analgesic and anti inflammatory mechanisms also make it effective in managing neuralgia and post surgical pain syndromes, such as post mastectomy intercostobrachial neuralgia (Ismail et al., 2025).

6.3. Protocol Limitations and Patient Variability

Despite their promise, both modalities suffer from a lack of protocol standardization, complicating evidence-based application in diverse clinical contexts. HILT outcomes are influenced by parameters such as laser energy output, wavelength, and treatment site, while ESWT effectiveness depends on pulse frequency, pressure, and chronicity of the condition (Hao et al., 2024).

6.4. Comparative Insights and Integration Potential

When analyzed comparatively, ESWT appears superior in managing chronic, degenerative shoulder disorders, particularly calcific tendinitis, due to its capacity to fragment deposits and promote tissue regeneration. In contrast, HILT shows greater effectiveness in acute, inflammatory, or neurogenic pain presentations, offering faster symptomatic relief with higher patient tolerability (Aldardour et al., 2025).

There is growing interest in the sequential or combined use of both modalities. For example, HILT may be used initially to reduce inflammation and pain, followed by ESWT to enhance mechanical tissue remodeling. Such integrative strategies could enhance overall rehabilitation efficiency and warrant further clinical investigation.

7. Comparative Analysis of Extracorporeal Shock Wave Therapy and High-Intensity Laser Therapy

7.1. Clinical Effectiveness in Different Conditions

Although both ESWT and HILT have gained significant attention in musculoskeletal rehabilitation, direct comparisons between them remain limited. Available evidence, however, points to differential strengths depending on the pathology and clinical presentation. ESWT appears particularly beneficial in chronic degenerative conditions such as calcific tendinitis and long-standing tendinopathies. Its mechanical action facilitates the breakdown of calcium deposits and promotes localized tissue regeneration, making it highly suitable for managing chronic shoulder disorders (Lee et al., 2022). HILT, on the other hand, is more commonly applied in acute or subacute conditions due to its deep tissue penetration and photothermal effects. It is often favored for managing acute pain and inflammation, particularly in adhesive capsulitis and post operative pain syndromes (Hao et al., 2024). This divergence in clinical applicability reflects the different physiological mechanisms underlying each modality, and underscores the importance of diagnosis specific treatment planning.

7.2. Comparative Study Outcomes

Clinical studies that have directly compared the two modalities suggest nuanced differences in outcomes. In a randomized controlled trial by Aldardour et al. (2025), both ESWT and HILT significantly improved pain scores and shoulder mobility in patients with subacromial impingement syndrome. However, ESWT was associated with better long term functional maintenance, while HILT produced faster short-term relief. These findings underscore that the timing and chronicity of the condition may influence which modality yields more effective outcomes in clinical practice. Yet, the limited number of well powered comparative trials prevents firm conclusions and highlights the need for more methodologically robust research.

7.3. Patient Tolerability and Clinical Decision-Making

Beyond clinical efficacy, patient tolerability plays a critical role in treatment selection. ESWT, due to its mechanical pulse delivery, may cause discomfort in sensitive anatomical regions, potentially affecting patient adherence. In contrast, HILT is generally well tolerated, which can enhance compliance during multi-session protocols and broaden its applicability across a wider patient population (Abdelhakiem et al., 2024). These differences highlight the importance of patient-centered decision-making, where individual tolerance, condition severity, and therapeutic goals are taken into account.

7.4. Integration Potential and Research Gaps

Although both treatments demonstrate promising outcomes, standardized protocols are still lacking, and the heterogeneity in study design, patient populations, and outcome measures limits the generalizability of findings. The sequential or combined application of

ESWT and HILT has been proposed as a potentially superior rehabilitation strategy, especially in complex or refractory cases. For example, HILT may be used in the early phase to reduce inflammation and pain, followed by ESWT to stimulate mechanical repair processes. However, this integrative approach remains underexplored in the literature and requires validation through prospective, controlled trials (Ranjithkumar et al., 2025). To advance clinical decision making, future research should prioritize comparative randomized studies, long-term outcome tracking, cost effectiveness analysis, and the inclusion of patient reported measures such as quality of life and treatment satisfaction.

8. Discussion

The findings of this review support the potential of ESWT and HILT as effective non-invasive modalities in the treatment of shoulder disorders. Both therapies demonstrated measurable benefits in reducing pain, improving range of motion, and enhancing functional performance across a range of shoulder pathologies. These results align with the current literature and reinforce the clinical relevance of these interventions.

However, these encouraging findings must be interpreted with caution, particularly given the variability in methodological quality and treatment protocols across studies. One of the most prominent limitations is the inconsistency in parameters such as treatment intensity, session frequency, and patient selection criteria. This heterogeneity compromises comparability and complicates the development of standardized clinical guidelines. Moreover, the limited number of direct, head-to-head trials between ESWT and HILT significantly restricts the ability of clinicians to make condition-specific, evidence-based decisions.

In this context, the development of standardized protocols is not merely a research aspiration but a clinical necessity. Without uniformity in application, the reproducibility and scalability of these therapies remain uncertain. Clinicians must also consider patient-specific variables such as pain chronicity, comorbidities, and treatment history to optimize therapeutic outcomes.

This narrative review also has limitations inherent to its design. The inclusion of heterogeneous study types without quantitative synthesis introduces potential interpretive bias. Additionally, many of the included studies lacked long term follow up or robust blinding, increasing the risk of outcome overestimation. Publication bias and language restrictions may have further influenced the synthesis.

From a health system perspective, both ESWT and HILT offer non-invasive, potentially cost-saving alternatives to pharmacological and surgical treatments. Their application in outpatient rehabilitation settings could reduce healthcare utilization for chronic musculoskeletal conditions. For patients with persistent shoulder dysfunction unresponsive to conventional physiotherapy,

these modalities offer additional clinical tools that are generally well tolerated and associated with minimal adverse effects.

Of particular interest is the emerging rationale for combining ESWT and HILT into sequential or multimodal rehabilitation protocols. For example, HILT may be applied in early inflammatory stages to modulate pain and vascular response, while ESWT can later facilitate tissue regeneration and remodeling in chronic stages. Such integration could improve patient outcomes by leveraging the complementary mechanisms of both modalities, though clinical evidence for this strategy remains limited.

Looking ahead, future research should address critical gaps through rigorous and methodologically sound trials. There is a strong need for high quality randomized controlled studies that directly compare ESWT and HILT using standardized treatment protocols and homogeneous populations. Additionally, patient reported

outcomes such as treatment satisfaction, return to function rates, and quality of life should be prioritized to enhance clinical relevance.

Key future research priorities include the standardization of ESWT and HILT protocols across different clinical settings, the implementation of well designed head to head randomized controlled trials with sufficient sample sizes and extended follow up periods, and the development of combination therapy models that explore both sequential and integrated applications. In addition, future studies should place greater emphasis on patient reported outcome measures (PROMs) to capture functional and quality of life improvements, and conduct cost effectiveness analyses to inform broader health policy and resource allocation decisions.

By addressing these priorities, the clinical integration of ESWT and HILT can become more precise, personalized, and evidence driven.

Table 1. Comparative summary table of 12 studies

Author (Year)	Condition	Sample Size	Modality	Outcome Measures	Key Findings	Study Type
Demirel et al. (2021)	Calcific tendinitis	60	ESWT	VAS, CMS	Significant pain and functional improvement	RCT
Lee et al. (2022)	Supraspinatus tendinitis	78	ESWT	VAS, SPADI	Better outcomes vs. injection therapy	RCT
Salem et al. (2024)	Diabetic frozen shoulder	50	HILT vs. ESWT	VAS, ROM	HILT faster relief; ESWT better long-term	RCT
Abdelhakiem et al. (2024)	Hemiplegic shoulder dysfunction	40	HILT	VAS, SPADI	Improved shoulder function and pain	RCT
Hao et al. (2024)	Subacromial impingement	92	HILT	VAS, ROM	Effective in reducing inflammation and pain	Systematic Review
Ismail et al. (2025)	Post-mastectomy neuralgia	30	ESWT	VAS	Effective pain relief in neuralgia	RCT
Ranjithkumar et al. (2025)	Rotator cuff tendinopathy	66	ESWT, LLLT, US	VAS, SPADI	ESWT superior to LLLT and US	Comparative Trial
Xue et al. (2024)	Rotator cuff tendinopathy	105	ESWT	VAS, CMS	Effective in chronic tendinopathy	Systematic Review
Aldardour et al. (2025)	Impingement syndrome	84	ESWT vs. HILT	VAS, ROM	ESWT better long-term; HILT faster short-term	RCT
Sharahili & Alzahrani (2025)	Adhesive capsulitis	56	ESWT + PT	VAS, SPADI	Combined therapy showed significant benefit	RCT
Mazin et al. (2023)	Muscle injuries	70	ESWT	VAS	ESWT supports tissue regeneration	Systematic Review
Liao et al. (2025)	Hemiplegic shoulder pain	Narrative	ESWT & HILT	n/a	Overview of mechanistic and clinical rationale	Narrative Review

9. Conclusion

This review highlights the clinical relevance of ESWT and HILT as valuable additions to the physiotherapeutic management of shoulder disorders. Their distinct yet complementary mechanisms of action provide clinicians with versatile tools for addressing both chronic degenerative and acute inflammatory conditions. ESWT's mechanical and regenerative effects make it particularly suited to calcific and long-standing tendinopathies, while HILT offers rapid symptomatic relief in acute presentations through its neuromodulatory and vascular benefits.

Despite promising findings, the lack of protocol standardization and the heterogeneity across studies limit their clinical generalizability. To bridge this gap, upcoming research should not only focus on refining therapeutic parameters but also clarify which intervention best suits specific patient subgroups and stages of rehabilitation.

Ultimately, improving methodological rigor and integrating patient centered outcomes will be key to translating current evidence into reliable clinical guidelines. As the field evolves, these modalities hold considerable potential for optimizing outcomes in both routine and complex shoulder rehabilitation cases.

Author Contributions

The percentages of the author' contributions are presented below. The author reviewed and approved the final version of the manuscript.

	İ.K.
C	100
D	100
S	100
DCP	100
DAI	100
L	100
W	100
CR	100
SR	100

C=Concept, D= design, S= supervision, DCP= data collection and/or processing, DAI= data analysis and/or interpretation, L= literature search, W= writing, CR= critical review, SR= submission and revision.

Conflict of Interest

The author declares no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

Acknowledgments

The author would like to thank the institutional library resources and all researchers whose works were cited in this review for their valuable contributions to the field.

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TELEPSİKİYATRİ HEMŞİRELİĞİ VE PSİKİYATRİ HEMŞİRELİĞİNDE DİJİTAL UYGULAMALARIN YERİ

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Özet: Bu derleme, sağlık hizmetlerinde dijitalleşmenin hemşirelik uygulamalarına etkisini incelemekte ve özellikle telehemşirelik ile telepsikiyatri hemşireliği alanlarını güncel literatür ışığında analiz etmektedir. Dijital sağlık teknolojileri, COVID-19 pandemisi ve doğal afetler gibi kriz durumlarıyla birlikte hemşirelik hizmetlerinin sunum biçiminde köklü değişimlere yol açmış; hemşirelerin uzaktan bakım, izlem, danışmanlık ve psikoeğitim gibi rolleri dijital ortamda yeniden tanımlanmıştır. Telehemşirelik, hem bireysel hem de toplum sağlığına yönelik hizmetlerde erişilebilirlik ve süreklilik sağlarken, telepsikiyatri hemşireliği özellikle ruh sağlığı hizmetlerinde terapötik iletişim, kriz müdahalesi ve psikososyal destek işlevlerini güçlendirmiştir. Bu dönüşüm, hemşirelik mesleğinde yalnızca teknolojik entegrasyonla sınırlı kalmayıp, aynı zamanda etik sorumluluklar, profesyonel sınırlar ve dijital yeterlilikler açısından da yeni paradigmlar ortaya koymaktadır. Literatürde hasta memnuniyetinin yüksek olduğu, hizmet kalitesinin arttığı ve hemşirelerin dijital becerilerinin geliştiği saptanmış; ancak altyapı eksiklikleri, dijital eşitsizlik, veri güvenliği ve mevzuat boşlukları gibi çok boyutlu sorunların da sürdürülebilirlik açısından risk oluşturduğu belirtilmiştir. Bu bağlamda, hemşirelik hizmetlerinin dijital dönüşüm sürecinde etkin, güvenli ve etik bir çerçevede yürütülebilmesi için kapsamlı politika geliştirme, eğitim reformları ve teknolojik altyapı yatırımlarına ihtiyaç duyulmaktadır. Dijital hemşirelik, yalnızca bir adaptasyon süreci değil, aynı zamanda sağlık hizmetlerinin geleceğini şekillendiren stratejik bir dönüşüm alanı olarak değerlendirilmelidir. Derleme, sağlık hizmetlerinin dijitalleşme sürecinde hemşirelik uygulamalarında meydana gelen dönüşümleri kapsamlı biçimde incelemeyi; özellikle telehemşirelik ve telepsikiyatri hemşireliği bağlamında, dijital teknolojilerin mesleki rollere, etik sorumluluklara ve hizmet kalitesine etkilerini literatür temelli olarak analiz etmeyi amaçlamaktadır. Aynı zamanda, mevcut uygulamalardaki yapısal, teknolojik ve eğitsel eksiklikleri ortaya koyarak alandaki literatür boşluklarına dikkat çekmekte ve dijital hemşirelik pratiklerinin geliştirilmesine yönelik kanıta dayalı öneriler sunmayı hedeflemektedir.

Anahtar kelimeler: Dijital sağlık hemşireliği, Telehemşirelik, Telepsikiyatri hemşireliği, Hemşirelik bilimi

Telepsychiatry Nursing and the Integration of Digital Applications in Psychiatric Nursing

Abstract: This review examines the impact of digitalization in healthcare on nursing practices, with a particular focus on the fields of telenursing and telepsychiatric nursing, analyzed through the lens of current literature. Digital health technologies, especially during crisis situations such as the COVID-19 pandemic and natural disasters, have led to fundamental transformations in the delivery of nursing services. Nurses' roles in remote care, monitoring, counseling, and psychoeducation have been redefined within digital environments. Telenursing enhances accessibility and continuity in both individual and public health services, while telepsychiatric nursing has strengthened functions such as therapeutic communication, crisis intervention, and psychosocial support in mental health care. This transformation is not limited to technological integration in the nursing profession; it also introduces new paradigms in terms of ethical responsibilities, professional boundaries, and digital competencies. Literature indicates that patient satisfaction is high, service quality has improved, and nurses' digital skills have developed. However, multifaceted challenges such as infrastructure deficiencies, digital inequality, data security issues, and regulatory gaps pose risks to sustainability. In this context, comprehensive policy development, educational reforms, and investments in technological infrastructure are needed to ensure that the digital transformation of nursing services is conducted within an effective, safe, and ethical framework. Digital nursing should be regarded not merely as an adaptation process but as a strategic transformation area that shapes the future of healthcare services. This review aims to comprehensively examine the transformations occurring in nursing practices during the digitalization process of healthcare. Specifically, it seeks to analyze, based on literature, the effects of digital technologies on professional roles, ethical responsibilities, and service quality within the contexts of telenursing and telepsychiatric nursing. Additionally, by identifying structural, technological, and educational deficiencies in current practices, it highlights gaps in the literature and aims to offer evidence-based recommendations for the development of digital nursing practices.

Keywords: Digital health nursing, Telenursing, Telepsychiatric nursing, Nursing informatics

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Gönderi: 21 Haziran 2025

Kabul: 09 Eylül 2025

Yayınlanma: 15 Eylül 2025

Received: June 21, 2025

Accepted: September 09, 2025

Published: September 15, 2025

Cite as: Ceviz R. 2025. Telepsychiatry nursing and the integration of digital applications in psychiatric nursing. BSJ Health Sci, 8(5): 218-226.



1. Giriş

21. yüzyılın ikinci on yılından itibaren, sağlık hizmetlerinin dijitalleşmesi sağlık sistemleri açısından kaçınılmaz ve zorunlu bir dönüşüm alanı olarak değerlendirilmiştir. Bu dijital dönüşüm sürecinde; bilgi ve iletişim teknolojileri sağlık ortamlarına entegre edilmiş, hasta bakımının izlenmesi ve yönetimi sağlanmış, klinik karar destek sistemleri uygulanmış ve sağlık çalışanlarının rolleri yeniden yapılandırılmıştır (Christoforou vd., 2020). Elektronik sağlık kayıtları, mobil sağlık uygulamaları, uzaktan izleme sistemleri ve özellikle uzaktan sağlık hizmetlerinin (tele-sağlık), modern sağlık sistemlerinin vazgeçilmez bileşenleri arasında konumlandırıldığı belirtilmiştir. Bu süreçte hemşirelerin, dijitalleşmenin hem uygulayıcısı hem de taşıyıcısı olarak konumlandığı vurgulanmıştır (Stone, 2025).

COVID-19 pandemisiyle birlikte, dijital sağlık teknolojilerinin sağlık sistemlerine entegrasyonu kaçınılmaz bir gereklilik olarak değerlendirilmiştir. Pandemi sürecinde sağlık hizmeti sunumundaki fiziksel etkileşim önemli ölçüde sınırlandırılmış; bulaş riskini azaltma amacıyla yüz yüze temasın asgariye indirilmesiyle birlikte, uzaktan sağlık hizmetlerinin kullanımının zorunlu hâle geldiği belirtilmiştir. Bu doğrultuda, hasta ile sağlık profesyonelleri arasındaki mesafenin azaltılmasına olanak tanıyan tele-sağlık uygulamaları, sağlık sistemlerinin sürdürülebilir işleyişinde kritik bir unsur olarak konumlandırılmıştır (Zhang vd., 2023). 6 Şubat 2023 tarihinde meydana gelen Kahramanmaraş merkezli depremler sonrasında sağlık altyapısında oluşan ciddi hasarın, dijital sağlık çözümlerine olan ihtiyacı belirgin biçimde artırdığı gözlemlenmiştir. Bu bağlamda, e-Nabız gibi dijital platformlar ve tele-sağlık hizmetlerinin, afet mağdurlarının sağlık hizmetlerine hızlı ve etkin bir biçimde erişiminde önemli katkılar sunduğu ortaya konmuştur (Al Mandhari, 2023; Rubayyi vd., 2024).

Dijitalleşme dalgasının hemşirelik üzerindeki etkilerinin, özellikle telehemşirelik uygulamaları üzerinden belirginleştiği ifade edilmiştir. Telehemşirelik, hemşirelerin bilgi ve iletişim teknolojileri aracılığıyla uzaktan bakım, izleme, danışmanlık ve eğitim hizmetleri sunmasını sağlayan bir uygulamadır. Uzaktan hastane bağlantılı cihazlarla yapılan vital bulgu ölçümleri, online danışmanlıklar ve dijital hasta takip sistemleri, hemşirelik bakımının sınırlarını genişletmiştir (Chankiniené ve Augulé, 2024). Özellikle kronik hastalık yönetimi, yaşlı bakımı ve ruh sağlığı gibi uzun süreli izlem gerektiren alanlarda telehemşireliğin etkinliği artmıştır (Kahn vd., 2019).

COVID-19 pandemisi döneminde telehemşireliğin kullanım oranı dramatik biçimde artmış; hemşireler, fiziksel ortama gitmeden hastaları telefon, video görüşmeleri ve mobil uygulamalar üzerinden izlemiş, bilgilendirmiş ve yönlendirmiştir. Sağlık hizmetine erişimin kısıtlandığı dönemlerde bu uygulamaların kritik öneme sahip olduğu ve sağlık sisteminin dayanıklılığının

bu yolla artırıldığı belirtilmiştir (Mohammed vd., 2025).

Psikiyatri hemşireliği ise, hemşirelik disiplinleri arasında duygusal emek ve iletişim becerileri açısından en yüksek yoğunluklu alanlardan biridir. Şizofreni, bipolar bozukluk, depresyon, anksiyete gibi ciddi ruhsal hastalıklarla çalışan psikiyatri hemşireleri; kronikleşen vaka yapısı, hasta-hemşire ilişkilerinin yoğunluğu ve şiddet riski gibi sorunlarla karşı karşıya kalmaktadırlar (Imkome ve Imkome, 2022).

Pandemi süreci, psikiyatri hemşireliğinde de hizmet sunumunu yeniden şekillendirmiştir. Ruh sağlığı hizmetlerine fiziksel erişim azaldıkça, psikiyatrik destek ihtiyacı artmış; bu ikili dinamik, telepsikiyatri hemşireliğini gündeme getirmiştir. Telepsikiyatri hemşireliği, ruh sağlığı hizmetlerinin dijital araçlarla sürdürülmesini sağlayan bir model olup görüntülü görüşmeler, dijital terapi platformları ve online izlem sistemleri aracılığıyla hastalara destek olmaya devam etmiştir (Ciccolini vd., 2022). Bu model, hemşirelerin hasta güvenliğini artırmakta, fiziksel şiddet riskini azaltmakta ve esnek çalışma sistemine geçişte kolaylık sağlamaktadır.

Telepsikiyatri hemşireliği ayrıca psikiyatrik tedaviye uyumu artırma, hasta ile sürekli ve yapılandırılmış bir ilişki kurma ve empatik iletişimi sürdürme gibi yönleriyle de avantaj sağlamaktadır. Uygulamalı çalışmalarda, telepsikiyatri hizmetlerinin hasta memnuniyetini ve hizmet kalitesini artırdığı; özellikle genç yetişkin bireyler arasında daha yüksek katılım oranlarına neden olduğu saptanmıştır (Chan vd., 2015). Bununla birlikte, bu alandaki uygulamaların henüz standartlaşmamış olması, teknolojik altyapı eksiklikleri ve veri güvenliği gibi konular hâlâ çözüm bekleyen sorunlar arasındadır.

Bu derlemenin amacı; dijitalleşme sürecinin hemşirelik uygulamaları üzerindeki etkilerini ortaya koymak, özellikle telehemşirelik ve telepsikiyatri hemşireliği uygulamalarının güncel durumunu literatür temelli analiz etmektir. Aynı zamanda psikiyatri hemşireliğinde karşılaşılan zorluklara dikkat çekilerek, dijital teknolojilerin bu sorunlara nasıl çözüm olabileceği değerlendirilecektir. Böylece, hemşirelik eğitimi, sağlık hizmet planlaması ve politika geliştirme süreçlerinde dijital dönüşümün etkisi bağlamında kapsamlı bir bakış açısı sunulacaktır.

2. Sağlıkta Dijitalleşme ve Hemşirelik Uygulamalarına Yansıması

Hemşirelik mesleğinde dijitalleşme, klinik uygulamalardan eğitime, karar destek sistemlerinden hasta takibine kadar çok yönlü dönüşümleri beraberinde getirmiştir. Bu dönüşüm, yalnızca araçların değil, aynı zamanda uygulayıcıların bilgi, beceri ve karar mekanizmalarının da yeniden yapılanmasını zorunlu kılmıştır. Bu bağlamda dijital altyapılar hemşireliğin sistematik uygulamalarını dönüştürmekte; veri odaklı ve hasta merkezli bir yaklaşıma zemin hazırlamaktadır.

Öncelikle Elektronik Sağlık Kayıtları (ESK), hemşirelik

belgelerinin dijitalleştirilmesiyle birlikte veri yönetimini ve hasta bakımını daha sistematik hale getirmiştir. Bu sistemler, yalnızca kayıt tutmakla kalmayıp aynı zamanda klinik karar destek sistemleriyle entegre olarak hemşirelerin hızlı ve doğru karar almasına olanak sağlamaktadır (Jonathan, 2025). Kleib vd. (2024), bu dijital yapıların hemşirelik eğitiminde vaka yönetimi ve klinik karar verme süreçlerine olumlu katkı sunduğunu ifade etmektedir.

Bu sistematik dijitalleşmenin bir diğer bileşeni olan mobil sağlık (mHealth) uygulamaları, özellikle kronik hastalık yönetiminde hemşirelerin eğitimsel ve izleyici rollerini güçlendirmiştir. Bu uygulamaların hemşire-hasta etkileşimini artırdığını ve bireyselleştirilmiş sağlık hizmetlerinin önünü açtığını belirtmektedir. mHealth, veri akışını kolaylaştırarak hem hasta hem de hemşire için zamandan tasarruf sağlamak ve takip süreçlerini daha etkin kılmaktadır (Ceviz ve Özden, 2025).

Dijital dönüşüm yalnızca kayıt ve takip sistemleriyle sınırlı kalmamış; aynı zamanda yapay zekâ tabanlı karar destek mekanizmalarıyla da hemşirelik uygulamalarına yeni bir boyut kazandırmıştır. Yapay zekânın yapılandırılmamış verileri analiz edebilme kapasitesi hemşirelikte tanı ve değerlendirme süreçlerine ciddi katkı sunmaktadır (Harmon vd., 2021). Bu sistemler, risk değerlendirmesi, komplikasyon öngörüsü ve bakım planlamasında daha nesnel kararlar alınmasını kolaylaştırmakta; bu sayede hemşirelerin yükünü azaltmakta ve hasta güvenliğini artırmaktadır.

Bu teknolojik dönüşüm, doğal olarak hemşirelik eğitiminin de dijital tabanlı yeniden yapılandırılmasını beraberinde getirmiştir. Sanal gerçeklik (VR) ve artırılmış gerçeklik (AR) gibi simülasyon teknolojileri, öğrencilerin klinik becerilerini risksiz bir ortamda geliştirmesine olanak tanımaktadır. Dicheva vd. (2023)'nın sistematik incelemesi, bu teknolojilerin öğrenci başarısı, karar verme yetisi ve iletişim becerileri üzerindeki olumlu etkilerini ortaya koymaktadır.

Dijitalleşme, hemşirelik uygulamalarında yalnızca teknolojik entegrasyon değil; aynı zamanda kültürel, pedagojik ve etik boyutlarıyla bütünsel bir değişim yaratmakta, mesleğin yapısal dinamiklerini yeniden şekillendirmektedir.

3. Telehemşirelik

Telehemşirelik, sağlık hizmetlerinin dijitalleşmesi sürecinde hemşireliğin temel işlevlerini yeni bir bağlamda yeniden tanımlayan bir yaklaşımı temsil etmektedir. Bu model, yalnızca hemşirelik uygulamalarını teknolojiyle desteklemekle kalmayıp, hemşirelik epistemolojisinin de dönüşümünü içermektedir. Özellikle COVID-19 pandemisiyle birlikte hız kazanan dijitalleşme eğiliminin, hasta merkezli bakım anlayışını sanal platformlara taşımış, dijital teknolojilerin danışmanlık, eğitim ve izlem gibi hemşirelik işlevleriyle bütünleşmesini sağlamıştır (Prathiba vd., 2025).

Bu dijital dönüşümün başarısı, yalnızca klinik bilgiye değil aynı zamanda güçlü bir teknolojik altyapıya da

dayanmaktadır. Elektrik ve internet ağına dayalı altyapı sistemleri, elektronik sağlık kayıtları, karar destek yazılımları ve güvenli görüntülü görüşme araçları gibi bileşenler telehemşirelik uygulamalarının omurgasını oluşturmaktadır. Ancak birçok bölgede internet erişimi ve dijital okuryazarlık düzeyi hâlâ istenen düzeyde değildir. Yustikasari vd. (2025), özellikle kırsal bölgelerde bu eksikliklerin hemşirelerin uzaktan hizmet sunumunu sınırladığını ortaya koymuştur.

Telehemşirelik yalnızca bireysel hasta bakımı ile sınırlı kalmayıp, kronik hastalık yönetimi, bulaşıcı hastalık takibi, yaşlı bakımı ve psikiyatrik destek gibi geniş uygulama alanlarına yayılmıştır. Febrianti vd. (2025), özellikle tüberküloz gibi bulaşıcı hastalıkların dijital sistemlerle izlenmesinin hemşirelik bakım kalitesini artırdığını ve hastalık kontrolünü kolaylaştırdığını vurgulamaktadır. Benzer şekilde, David-Olawade vd. (2024), dijital sistemlerin doğru ve bilinçli kullanımıyla hem klinik sonuçların iyileştiğini hem de hastaların hizmete erişiminin kolaylaştığını göstermiştir.

Bu gelişmelerin doğal bir sonucu olarak hemşirelik rollerinde köklü değişiklikler ortaya çıkmıştır. Dijital cihazların ve yazılımların kullanımı, hemşirelerin bilişim yetkinliklerini geliştirmelerini ve sağlık teknolojilerini klinik karar süreçlerine entegre etmelerini zorunlu kılmıştır.

Bu kapsamlı dönüşüm, hemşirelik mesleğinin geleceğine dair önemli ipuçları vermekte, dijital becerilerin yalnızca birer destekleyici unsur değil, hemşirelik uygulamalarının asli birer bileşeni haline geldiğini göstermektedir. Bu değişim yalnızca teknik becerilerle sınırlı kalmamış, aynı zamanda hemşirelik uygulamalarında yeni hizmet modellerinin ortaya çıkmasına da zemin hazırlamıştır.

4. Telepsikiyatri

Telepsikiyatri, ruh sağlığı hizmetlerinin uzaktan sunumunu sağlayan ve hemşirelik uygulamalarını dijitalleştiren önemli bir yaklaşımdır. Bu model; değerlendirme, danışmanlık, tedavi planlaması ve izlem gibi temel psikiyatrik süreçlerin, bilgi ve iletişim teknolojileri aracılığıyla gerçekleştirilmesini mümkün kılmaktadır. Özellikle COVID-19 pandemisi ile birlikte, telepsikiyatri uygulamalarının benimsenme oranı artmış; hemşirelerin rolü, dijital ortamda ruh sağlığı hizmeti sunumu açısından kritik hâle gelmiştir. Dijital sağlık teknolojileri psikiyatri hemşireliği pratiklerinde dönüşüme yol açmış ve hemşireler bu dönüşümde merkezi bir aktör olmuştur (Clement David-Olawade vd., 2024).

Bu teknolojik modelin hemşirelik pratiğine entegrasyonu, özellikle erişimi kısıtlı bölgelerde ruh sağlığı eşitsizliklerinin azaltılması açısından stratejik bir değer taşımaktadır. James ve Kushwah (2024), telepsikiyatrik hizmetlerin yalnızca bireysel müdahalelerle sınırlı olmadığını; aynı zamanda uzaktan izleme, kriz yönetimi ve dijital tabanlı terapi girişimleri ile genişletilebileceğini belirtmektedir.

Bu çerçevede, telepsikiyatri hemşireliğinin uygulama alanları da çeşitlenmiş ve bireysel danışmanlıktan grup terapilerine, aile temelli psiko eğitimlerden psikososyal destek gruplarına kadar geniş bir yelpazeye yayılmıştır. Mueser vd. (2022) tarafından yürütülen çalışmada, şizofreni tanılı bireylerin ailelerine yönelik grup temelli dijital eğitimlerin, hastalıkla başa çıkma becerilerini olumlu etkilediği ortaya konmuştur.

Bu kapsamlı hizmetlerin sürekliliğini sağlayan en önemli bileşenlerden biri, dijital platformlar üzerinden yürütülen psikiyatrik izlem sistemleridir. Teleizlem, yalnızca semptom takibini değil, aynı zamanda ilaç uyumu, davranışsal değişim süreçlerinin takibi ve geribildirim mekanizmalarının işletilmesini de içermektedir. Tian vd. (2025)'nin genç bireylerde yürüttüğü çalışmada, yapay zekâ destekli sistemlerin hemşirelerin değerlendirme ve müdahale sürecini kolaylaştırdığı ve terapötik sonuçları olumlu etkilediği gösterilmiştir. Hasselberg ise, dijital davranışsal sağlık modellerinin, hemşirelerin hasta ile sürekli ve yapılandırılmış bir iletişim kurmasına imkân verdiğini, bunun da özellikle kronik psikiyatrik hastalıkların yönetiminde etkili olduğunu ifade etmektedir (Sasangohar vd., 2020).

Bu doğrultuda, telepsikiyatri hemşireliği hem hizmet kapsamını hem de mesleki rollerin yeniden tanımlanmasını içeren çok katmanlı bir dönüşümü temsil etmektedir. Bu dönüşüm, hemşirelerin uzaktan terapötik ilişki kurma biçimlerini, dijital ortamda empati geliştirme stratejilerini ve çok disiplinli dijital sağlık ekipleriyle etkileşim modellerini yeniden şekillendirmektedir.

5. Telepsikiyatride Hemşirelerin Rolü ve Sorumlulukları

Telepsikiyatride hemşirelerin görev tanımları, yalnızca teknik uygulamalarla sınırlı kalmamakta; aynı zamanda psikososyal destek, iletişim yönetimi ve dijital platformlarda terapötik sürecin liderliğini içerecek şekilde genişlemektedir. Özellikle terapötik ittifak kurma süreci, bu dijitalleşmenin merkezinde yer almaktadır.

Terapötik ittifak, psikiyatri hemşireliği açısından etkili müdahale süreçlerinin temelini oluşturmaktadır. Geleneksel yüz yüze uygulamalardan farklı olarak, dijital ortamlarda bu ittifakı kurmak daha fazla bilişsel dikkat ve iletişim uyumu gerektirmektedir. Finley vd. (2024)'nin çalışmasına göre, video tabanlı telepsikiyatri seanslarında hemşireler, duygusal bağ kurmakta zorluk çekmemekte; ancak bu sürecin sürdürülebilirliği iletişim becerileri, ekran üzerinden empati gösterme kapasitesi ve teknik altyapı ile doğrudan ilişkilidir.

Bu bağlamda, dijital psiko eğitim ve danışmanlık uygulamaları hemşirelerin sorumluluk alanlarını genişletmektedir. Özellikle depresyon, anksiyete bozuklukları ve psikotik semptomlar gibi durumlarda, hemşireler hasta ve ailelere yönelik bilgi temelli destek sağlayarak tedaviye katılımı artırmakta ve farkındalık geliştirmektedir. James ve Kushwah, dijital psiko eğitimin,

bireylerin hastalıklarını anlama, tedaviye uyum sağlama ve kriz dönemlerini yönetme becerilerini anlamlı düzeyde artırdığını belirtmektedir (James ve Kushwah, 2024).

Dijital terapötik süreçte hemşirelerin sahip olması gereken en önemli becerilerden biri de dijital empati kurabilme yetisidir. Yüz yüze etkileşimde kullanılan sözel olmayan ipuçlarının eksikliği, hemşireleri yeni iletişim stratejileri geliştirmeye yönlendirmektedir. Abou Hashish (2025), dijital empatiyi hemşirelik bağlamında analiz ettiği çalışmasında, bu becerinin sadece teknik değil, aynı zamanda etik ve duygusal boyutlar içerdiğini belirtmektedir. Kalia ve Narikuzhy (2024) ise, empatik iletişimin dijital platformlarda yapılandırılmış öğrenme süreçleriyle geliştirilebileceğini ve bu eğitimin müfredatın bir parçası olması gerektiğini savunmaktadır. Bu kapsamda hemşirelerin rolü sadece bireysel ilişkilerle sınırlı kalmayıp aynı zamanda çok disiplinli dijital sağlık ekiplerinin organizasyonunda ve işleyişinde de belirleyici hâle gelmektedir (Troncoso ve Breads, 2021).

Bu bağlamda dijital sağlık ortamlarında hemşirelerin terapötik süreçteki konumları yalnızca uygulayıcı değil; aynı zamanda koordinatör, eğitimci ve duygusal destek sağlayıcı olarak çok boyutlu bir yapıya evrilmiştir. Bu dönüşüm, sistematik olarak hemşirelik uygulamalarının altyapısına entegre edilen dijital sistemlerle birlikte daha görünür hale gelmektedir.

6. Telepsikiyatri Hemşireliğinin Sağlığa Etkileri

Telepsikiyatri hemşireliği, dijital sağlık teknolojilerinin hızla gelişmesiyle birlikte, psikiyatri hemşirelerinin ruh sağlığı hizmetlerini daha erişilebilir, etkili ve sürdürülebilir biçimde sunmasına olanak tanımaktadır. Son beş yılda yapılan çalışmalar, bu alanın özellikle COVID-19 pandemisiyle ivme kazandığını ve hem hasta hem de sağlık çalışanı memnuniyetinin arttığını göstermektedir (Zhang vd., 2023). Telepsikiyatri hizmetlerinin etkililiği, klinik sonuçlar, hastaların memnuniyeti ve tedaviye erişim olanakları açısından olumlu değerlendirilmektedir. Bir sistematik derlemede, hastaların büyük kısmı telepsikiyatri hizmetlerinden memnun olduğunu, tekrar kullanmak isteyeceğini ve gizlilik, zaman tasarrufu gibi avantajlardan faydalandığını belirtmiştir (Sharma ve Devan, 2021). Benzer şekilde, COVID-19 hastalarıyla yapılan bir randomize kontrollü çalışmada telepsikiyatri müdahalelerinin anksiyete düzeyini anlamlı biçimde azalttığı ve katılımcıların %78'inin hizmetten memnun kaldığı bildirilmiştir (Tokell vd., 2021).

Bu olumlu sonuçlar, uygulamada kullanılan yöntemlerin çeşitliliğini de gündeme getirmiştir. Telepsikiyatri hemşireliği kapsamında yaygın olarak senkron (canlı görüntülü görüşme) ve asenkron (önceden kaydedilmiş değerlendirmeler) modeller tercih edilmektedir. Senkron model hasta ile doğrudan etkileşim sağlayarak terapötik ilişkinin güçlenmesine katkı sunarken, asenkron model

özellikle kırsal veya altyapı sorunu yaşanan bölgelerde esneklik sağlamaktadır (Chan vd., 2015). Bu yöntemlerin etkinliği hemşirelerin rolleriyle de doğrudan ilişkilidir. Nitekim bazı çalışmalarda hemşirelerin danışmanlık, ilaç uyumu izleme ve psikoeğitim görevlerini üstlendikleri bildirilmektedir. Hindistan'da önerilen üçlü model (doğrudan bakım, telekonsültasyon, işbirlikçi bakım) bu bağlamda dikkat çekicidir (Ghosh vd., 2020).

Klinik uygulamalar ve vaka raporları ise uygulamadaki başarıyı etkileyen faktörleri açığa çıkarmaktadır. Avustralya'da yapılan bir kapsamlı derleme, özellikle metropol dışı bölgelerde telepsikiyatri uygulamalarının yaygınlaştığını ancak vaka bazlı sonuç ölçütlerinin henüz yeterince sistematik toplanmadığını göstermektedir (Woon vd., 2024). Öte yandan bazı özel gruplarda (örn. LGBTQ+ bireyler) teknolojiye aşinalığın memnuniyeti artırdığı; ancak teknik problemler, önyargılar ve iletişim engellerinin hizmet kalitesini düşürebildiği gözlenmiştir (Mishkin vd., 2022).

Bu bulgulara rağmen telepsikiyatri hemşireliği ile ilgili literatürde belirli boşluklar göze çarpmaktadır. Çocuklar, yaşlılar ve ağır psikotik bozukluğu olan bireyler üzerindeki etkiler henüz yeterince araştırılmamıştır. Ayrıca ekonomik analizler ve uzun vadeli etkilerin değerlendirildiği kapsamlı çalışmalar oldukça sınırlıdır (Gutiérrez-Rojas vd., 2023). Bu noktada hasta deneyimlerinin niteliksel biçimde derinlemesine analiz edilmesi büyük önem taşımaktadır. Eğitimin sistematik hale getirilmesi gerekliliği ise başka bir araştırma alanı olarak karşımıza çıkmaktadır (Alotabi vd., 2024). Literatürdeki bu boşluklar, telepsikiyatri hemşireliğinin daha kapsayıcı, etkili ve sürdürülebilir bir biçimde uygulanabilmesi adına yeni araştırmalara olan ihtiyacı ortaya koymaktadır.

Kriz durumları, özellikle pandemi ve doğal afetler, dijital sağlık hizmetlerinin önemini ve gerekliliğini daha görünür hâle getirmiştir. COVID-19 pandemisi, fiziksel erişimin kısıtlandığı bir dönemde hemşirelerin uzaktan psikiyatrik destek sağlama becerilerini test etmiş; bu süreçte telepsikiyatri hemşireliği, giderek artan biçimde uygulanan etkili bir müdahale modeli olarak öne çıkmıştır. Schroeder, (2022), dijital psikiyatri uygulamalarının yalnızca geçici bir çözüm olmadığını; aksine, kalıcı bir dönüşümün başlangıcını oluşturduğunu ve gelişmiş hemşirelik uygulamaları açısından yeni fırsatlar sunduğunu belirtmektedir. Buna ek olarak, Čosić vd. (2020), dijital psikiyatri araçlarının –yapay zekâ, telepsikiyatri sistemleri ve bilgisayar destekli mental sağlık uygulamaları dâhil olmak üzere– özellikle afet sonrası dönemlerde hem bireysel hem de toplumsal düzeyde ruh sağlığının izlenmesinde yüksek potansiyel taşıdığını vurgulamaktadır. Krizlerde yaşanan psikolojik travmaların dijital destek yoluyla takibi, hemşirelerin bireylere hızlı ve etkili bir şekilde ulaşmasını mümkün kılmıştır. Pandemiyle başlayan bu dijital dönüşüm, yalnızca bulaşıcı hastalıklarla sınırlı kalmayıp, deprem gibi doğal afetler sonrasında da devam etmiştir.

James ve Kushwah (2024), ruh sağlığı hemşirelerinin

dijital ortamda kriz yönetimi konusunda eğitilmeleri gerektiğini ve özellikle acil hizmetlere erişim, hızlı değerlendirme ve yönlendirme alanlarında dijital teknolojilerin destekleyici bir rol üstlendiğini ifade etmektedir. Benzer şekilde, Augusterfer vd. (2020) düşük kaynaklı ve afet sonrası ortamlar için tele-konsültasyon ve tele-denetim gibi hemşirelik pratiklerinin geliştirilmesinin, sağlık hizmetlerinin sürekliliği açısından kritik olduğunu ileri sürmektedir. Bu bağlamda dijital sağlık çözümleri, yalnızca kriz dönemlerinde değil, aynı zamanda afet sonrası yeniden yapılanma süreçlerinde de sürdürülebilir hizmet sunumuna katkı sağlamaktadır. Telepsikiyatri sistemlerinin krizlere hazır hâle getirilmesi ise ayrıca önem arz etmektedir. Smith vd. (2020), telepsikiyatri hizmetlerinin afetlere özgü senaryolar çerçevesinde yapılandırılması gerektiğini; bu kapsamda, klinik rehberlerin güncellenmesinin, uygulamalarda tutarlılığı sağlayarak afetlere hazır ve dijital olarak donanımlı hemşirelerin yetişmesini destekleyeceğini ifade etmektedir. Tüm bu gelişmeler, dijital ruh sağlığı hizmetlerinin yalnızca mevcut ihtiyaçlara yanıt vermekle kalmayıp, geleceğe yönelik güçlü bir bakım modeli oluşturduğunu ortaya koymaktadır.

7. Telehemşirelik ve Telepsikiyatri Hemşireliğinde Karşılaşılan Güçlükler

Dijital sağlık teknolojilerinin hemşirelik uygulamalarına entegrasyonu, yalnızca hizmet sunum biçimini değil, aynı zamanda etik, yasal ve profesyonel sınırların nasıl tanımlandığını da radikal biçimde dönüştürmüştür. Bu dönüşüm özellikle telehemşirelik bağlamında mahremiyetin korunması, veri güvenliği, dijital profesyonellik ve mevzuat uyumu gibi çok boyutlu konular etrafında şekillenmektedir.

Telehemşirelikte ilk dikkat çeken etik meselelerden biri, dijital ortamda iletilen hasta verilerinin korunmasıdır. Telemedikal platformların yaygınlaşmasıyla birlikte hasta bilgilerinin güvenliği, hemşirelerin doğrudan sorumluluğu altına girmiştir. (Clement David-Olawade vd., 2024). Mohammed vd. (2025), dijital hemşirelik uygulamalarında hasta gizliliğinin korunmasının, yalnızca teknik önlemlerle değil, hemşirelerin eylemlerinde göstereceği özenle sağlanabileceğini belirtmiştir. Ancak dijital mahremiyetle sınırlı olmayan etik dönüşüm, aynı zamanda hemşirelik davranışlarının dijital bağlamda yeniden tanımlanmasını da zorunlu kılmaktadır. Geleneksel etik ilkeler olan şeffaflık, dürüstlük ve gizlilik; dijital sağlık ortamlarında dijital etik protokoller, dijital profesyonellik normları ve sınır yönetimi stratejileri ile bütünleşerek yeni bir etik çerçevenin oluşmasına zemin hazırlamaktadır. Medina Martin vd. (2023), bu yeni bağlamda etik karar verme süreçlerinin hemşireler açısından daha karmaşık hale geldiğini ve dijital profesyonellik eğitimlerinin kurumsal düzeyde desteklenmesi gerektiğini vurgulamaktadır.

Dijitalleşmenin beraberinde getirdiği bir diğer önemli

sorun alanı ise yasal düzenlemelerdir. Hızla gelişen teknolojik altyapılar karşısında mevcut mevzuatın yetersiz kalması, hemşirelerin görev tanımları ve sorumluluk alanlarını belirsizleştirmektedir (Brown vd., 2020).

Bu etik ve yapısal karmaşanın merkezinde ise profesyonel sınırların dijital bağlamda yeniden çizilmesi gerekliliği yer almaktadır. Dijital ortamlarda terapötik ilişkilerin sürdürülebilmesi, hemşirelerin empatik yaklaşımlar ile profesyonel mesafe arasında hassas bir denge kurmalarını zorunlu kılmaktadır (Brown vd., 2020). Medina Martin vd. (2023), dijital iletişimin sürekliliği ve kolay erişilebilirliğinin terapötik sınırları bulanıklaştırabileceğini ve bunun meslekte etik erozyona neden olabileceğini belirtmektedir. Bu nedenle, hemşirelerin dijital ortamlarda mesleki rollerini sürdürülebilir biçimde tanımlayabilmeleri kritik bir öneme sahiptir.

Tüm bu veriler, telehemşireliğin yalnızca teknik değil; aynı zamanda etik, yasal ve mesleki boyutlarıyla da yeniden yapılandırılması gerektiğini ortaya koymakta ve hemşirelik uygulamalarının bu çok katmanlı dönüşüm bağlamında değerlendirilmesini zorunlu kılmaktadır. Telepsikiyatri uygulamaları, dijitalleşmenin sunduğu avantajlara rağmen çeşitli yapısal, teknolojik ve insani engeller nedeniyle sağlık hizmetlerinde kesintisiz, adil ve etkili sunum açısından sınırlamalarla karşı karşıyadır. Bu engeller özellikle hemşirelerin görev alanlarında önemli uygulama zorlukları doğurmakta, sistemsel sorunların klinik sonuçlara yansımalarına neden olmaktadır.

İlk olarak, teknik altyapı eksiklikleri telepsikiyatri hizmetlerinin en temel sınırlayıcılarından biri olarak öne çıkmaktadır. Özellikle kırsal alanlarda yetersiz internet bağlantısı, düşük bant genişliği ve donanım eksiklikleri, hizmetin sürekliliğini doğrudan etkilemektedir. James ve Kushwah (2024), dijital altyapının sınırlı olduğu bölgelerde hizmet sunumunun düzensizleştiğini ve bu durumun hemşirelerin iş yükünü artırdığını vurgulamaktadır. Benzer biçimde, pandemi sonrası dönemde dijital hizmet erişiminde yaşanan eşitsizliklerin sağlıkta adaletsizlikleri daha da derinleştirdiği belirtilmektedir (Zemlak vd., 2024).

Bu teknik yetersizliklerin yanı sıra dijital okuryazarlık eksikliği de önemli bir bariyer oluşturmaktadır. Hemşirelerin dijital sistemlere aşinalık düzeyi hizmet kalitesini belirleyen temel unsurlar arasında yer almaktadır. Gajarawala ve Pelkowski (2021) dijital yetkinliğin geliştirilmesinin, yalnızca bireysel beceri değil, aynı zamanda kurumsal sorumluluk olduğunu vurgulamaktadır.

Öte yandan, hastaların dijital hizmetlere adaptasyonu da süreci doğrudan etkileyen bir başka faktördür. Dijital sağlık hizmetlerine karşı güvensizlik, mahremiyet endişesi ve teknolojik cihazlara duyulan yabancıklık, özellikle yaşlı bireyler ve düşük sosyoekonomik gruplarda daha yaygın gözlemlenmektedir. James ve Kushwah (2024) bu dirençlerin aşılması için kültürel açıdan duyarlı iletişim stratejilerinin ve hasta merkezli

eğitim programlarının kritik olduğunu belirtmektedir.

En karmaşık zorluklardan biri ise uzaktan kriz müdahalesi süreçlerinde ortaya çıkmaktadır. Özellikle akut psikiyatrik ataklar, intihar riski taşıyan bireyler ya da ani davranışsal değişiklikler söz konusu olduğunda, hemşirelerin uzaktan müdahale kapasitesi sınırlı kalmaktadır. Cowan vd. (2019), bu tür durumlarda hemşirelerin hızlı karar verme yükü altında kaldığını ve çoğu zaman hukuki ve etik sorumluluklar arasında sıkıştığını ifade etmektedir. Kriz yönetimi konusunda standart protokollerin eksikliği ve yeterli mevzuat desteğinin olmaması hem hizmet sunucuları hem de hastalar açısından riskleri artırmaktadır.

Bu güçlüklerin sistematik biçimde ele alınması, yalnızca hizmet sunumunun kalitesini değil, aynı zamanda hemşirelerin iş doyumu, hasta güvenliği ve toplum ruh sağlığına olan katkısı da doğrudan etkileyecektir.

8. Gelecek Perspektifi: Dijital Teknolojilerle Güçlenen Hemşirelik

Dijital teknolojiler, hemşirelik pratiğinde yalnızca bir araç değişimi değil, aynı zamanda yapısal bir paradigma dönüşümünü beraberinde getirmektedir. Bu dönüşümün merkezinde yer alan yapay zekâ destekli karar sistemleri, hemşirelerin hasta bakımında daha hızlı ve doğru kararlar almasını sağlamaktadır. Özellikle derin öğrenme algoritmalarına dayanan karar destek yazılımları, hasta kayıtlarını analiz ederek olası klinik riskleri önceden tahmin edebilmekte ve hemşirelik müdahalelerini bu doğrultuda yönlendirebilmektedir. Božić (2024), bu sistemlerin yalnızca iş verimliliğini artırmakla kalmadığını, aynı zamanda mesleki sorumlulukların dijital ortamlara taşınmasını da zorunlu hâle getirdiğini ifade etmektedir. Auf vd. (2025) ise, yapay zekâ destekli karar sistemlerinin özellikle ruh sağlığı hizmetlerinde olumlu terapötik etkiler yarattığını göstermektedir. Buna karşılık, Lukkahatai vd. (2025), yapay zekâ sistemlerinde görülen veri önyargılarının sağlık hizmetlerinde eşitsizlik oluşturabileceğine dikkat çekmekte ve bu nedenle etik denetim mekanizmalarının gerekli olduğunu vurgulamaktadır.

Bu çerçevede dijital dönüşüm, yalnızca klinik uygulamalarla sınırlı kalmamakta, aynı zamanda ruh sağlığı hemşireliğinde kullanılan araçları da çeşitlendirmektedir. Sanal gerçeklik (VR) ve artırılmış gerçeklik (AR) uygulamaları, özellikle travma, fobi ve sosyal kaygı gibi durumlarda tedavi sürecine entegre edilmektedir. Bu dijital terapötik yöntemler, hem hasta memnuniyetini artırmakta hem de hemşirelerin sanal ortamda klinik becerilerini geliştirmelerine olanak tanımaktadır (Lukkahatai vd., 2025). Park vd. (2025), VR ve AR uygulamalarının hemşirelerin karar verme süreçlerini desteklediğini ve hasta-hemşire etkileşimini güçlendirdiğini belirtmektedir. Teknolojik dönüşüm yalnızca uygulama alanlarıyla sınırlı kalmamakta, hemşirelik eğitiminde de önemli bir yeniden yapılanmayı beraberinde getirmektedir. Özellikle yapay zekâ ve

simülasyon teknolojilerinin kullanımı ile dijital hemşirelik eğitimi daha etkileşimli ve bireyselleştirilmiş bir yapıya kavuşmuştur.

Tüm bu dijital gelişmelerin mesleki ortamlara sağlıklı bir şekilde entegre edilebilmesi için insan merkezli dijital sağlık politikalarına olan ihtiyaç giderek artmaktadır (Irwin vd., 2025). Bu noktada Ruksakulpiwat ve Thorngthip (2024), yapay zekânın hasta bakımına entegrasyonunun hemşire-hasta ilişkisini yeniden şekillendireceğini ve bu sürecin yalnızca teknolojik değil, aynı zamanda etik ve politik boyutlarda da düzenlenmesi gerektiğini vurgulamaktadır. Skuban-Eiseler vd. (2023) ise dijitalleşmenin, hemşirelikte yalnızca teknolojik bir uyum süreci olmadığını; aynı zamanda bireylerin öznel deneyimlerine, kimlik temelli gereksinimlerine ve bakım ilişkilerinin duygusal yönlerine duyarlı, insan merkezli bir mesleki kimliğin yeniden şekillenmesini içerdiğini ileri sürmektedir. Bu bağlamda, dijital sistemlerin etik duyarlılık, eşit erişim ve kapsayıcı iletişim ilkeleriyle bütünleşmesi; hemşirelik mesleğinin toplumsal adalet ve hasta hakları temelinde yeniden konumlandırılmasını gerekli kılmaktadır.

9. Sonuç

Dijital sağlık teknolojilerinin hemşirelik pratiğine entegrasyonu, yalnızca hizmet sunumunun biçimini değil, aynı zamanda mesleki rol ve sorumlulukların tanımını da köklü biçimde dönüştürmüştür. Bu dönüşümün en belirgin yansımaları, telehemşirelik ve telepsikiyatri hemşireliği uygulamaları üzerinden gözlemlenmiştir. Özellikle COVID-19 pandemisi ve doğal afetler gibi kriz dönemlerinde, hemşirelerin dijital ortamlar aracılığıyla sağlık hizmeti sunması zorunlu hale gelmiş; bu süreç, dijital yetkinliklerin artırılması, etik sınırların yeniden tanımlanması ve yapısal altyapıların güçlendirilmesi gerekliliğini beraberinde getirmiştir.

Literatürden elde edilen veriler doğrultusunda, dijital hemşirelik uygulamalarının hasta memnuniyeti, hizmet kalitesi ve erişilebilirlik gibi parametrelerde olumlu etkiler yarattığı görülmektedir. Telepsikiyatri hemşireliği özelinde, terapötik iletişim, kriz müdahalesi ve psikoeğitim süreçlerinde dijital çözümler etkin biçimde kullanılmakta; ancak bu alandaki standartlaşma eksikliği, teknik altyapı sorunları ve dijital eşitsizlik gibi faktörler, sürdürülebilirliğe yönelik risk unsurları oluşturmaktadır. Bu bağlamda, dijitalleşmenin hemşirelik alanındaki etkilerinin bütüncül olarak değerlendirilmesi ve uygulamaların daha güvenli, etik ve erişilebilir hale getirilmesi için politika düzeyinde kapsamlı reformlara, eğitim müfredatlarının dijital yeterlilik ekseninde yeniden yapılandırılmasına ve altyapı yatırımlarının artırılmasına ihtiyaç duyulmaktadır. Ayrıca, özel gruplar (örneğin yaşlı bireyler, çocuklar, düşük sosyoekonomik gruplar) üzerindeki etkilerin değerlendirilmesi, hasta deneyimlerinin niteliksel analizlerle derinleştirilmesi ve kriz dönemlerine özgü dijital hemşirelik rehberlerinin geliştirilmesi, alana yapılacak katkıyı daha da derinleştirecektir.

Sonuç olarak, dijital hemşirelik yalnızca geçici bir uyum süreci değil; aynı zamanda hemşirelik mesleğinin geleceğini şekillendiren stratejik bir dönüşüm alanı olarak görülmeli ve bu dönüşüm süreci, hem teorik hem de pratik düzlemde disiplinler arası iş birlikleriyle desteklenmelidir.

Katkı Oranı Beyanı

Yazarın katkı yüzdeleri aşağıda verilmiştir. Yazar makaleyi incelemiş ve onaylamıştır.

	R.C.
K	100
T	100
Y	100
KT	100
YZ	100
KI	100
GR	100

K= kavram, T= tasarım, Y= yönetim, KT= kaynak tarama, YZ= Yazım, KI= kritik inceleme, GR= gönderim ve revizyon.

Çıkar Çatışması Beyanı

Yazarın herhangi bir çıkar çatışması bulunmamaktadır.

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