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Evaluation the health effects of low doses gamma irradiations on liver of obese rats

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ABSTRACT

***Background*:** Low-dose ionizing radiation has major health impacts in a variety of fields, including radiation therapy. However, all potential applications are currently subject to public interest. ***Aims*:** This study is an endeavor to evaluate the role of low dose gamma irradiation against the adverse effects of obesity in obese rats. ***Materials and Methods*:** Thirty-six rats were divided into 4 equal groups;"G1" is a normal control group; "G2" received a high-fat diet for 16 weeks to induce obesity; "G3" rats also received a high-fat diet for 16 weeks in addition to being exposed to 0.5 Gray γ- radiation for 2 weeks, two twice a week (accumulated dose =4×0.5=2 Gray); "G4" were normal rats, but also exposed to 0.5 Gray γ- radiation for 2 weeks, twice a week (accumulated dose =4×0.5=2 Gray). Rats were anaesthetized at the end of the experiment, and blood samples as well as liver tissues were collected for both biochemical and histological studies. ***Results*:** There are harmful effects on the liver of obese rats, which include elevated levels of liver weight, liver functions, Malondialdehyde and lipids and diminished glutathione, as well as increased levels of C reactive protein and lipase in "G2" compared to "G1". In contrast, low-dose fractionated gamma irradiation has a significant reduction in these harmful effects of obesity. ***Conclusions*:** The findings of the current study suggest that fractionated low-dose gamma irradiation plays a significant role against the harmful effects of obesity, and thus could augment and support the aim of current study by drawing attention to the health impacts of low-doses gamma irradiation.

INTRODUCTION

In today's society, ionizing radiation is quite significant. In affluent countries, every medium-sized hospital has a radiation therapy unit that treats a large number of cancer patients. As a result, ionizing radiation (similar to any other potentially hazardous factor) must be handled with care [1]. The main concern is whether low-dose radiation exposure, which may be utilized in medical fields or encountered by workers in radiation field and the public, has any harmful effects. According to several studies, biological responses to low-doses irradiation are substantially influenced by a variety of physical variables [2]. The total absorbed dose and dosage rate are clearly the most important factors (and in general, temporal patterns of radiation exposure). Also, the dispersion of radiation sources, as well as the structure and dimensions of biological targets, are further elements to consider [3].

DNA damages caused by low-doses radiation has been demonstrated to be far and less than that generated by oxidative processes in normal metabolism [4-6]. Low-dose radiation has also been found to have hormetic effects, which can equal for, or even over than, the harmful effects of reactive species, which are metabolic by-products [7]. Such responses are expected to aid in the prevention of a variety of negative environmental health consequences. The balance between the level of DNA damage (which increases linearly with dose) and the level of DNA repair, for example, can be used to determine the impact of low-dose irradiation on DNA repair. Different integrative end points, includes, tissue repair, compensatory of cell proliferation [8, 9], growth rate, adaptive as well as preconditioning responses, ageing pattern, and various several behaviors that can be induced or at least modulated by radiation and different environmental stimuli, all appear to influence these dose–response relationships [10]. Low-doses radiation also contain anti-oxidant capabilities, which are the primary mechanism of its anti-inflammatory impact [11]. Enzymatic and non-enzymatic processes protect cells from reactive oxygen species (ROS). The most essential intracellular antioxidants in the metabolism of ROS are superoxide dismutase (SOD): manganese SOD (MnSOD) and copper-zinc SOD (CuZnSOD), as well as Glutathione (GSH). Overproduction of reactive oxygen species (ROS) challenges the antioxidant enzymes [12]. *In-vitro* and *in-vivo* studies revealed that low-doses radiation induce these antioxidant

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processes, which has been associated with diminished lipid peroxidation in rats [13]. Moreover, Avti *et al.* (2005) [14] demonstrated that whole-body exposure to 25 cGy and 50 cGy gamma radiation altered the antioxidant defense system in both the liver as well as lungs of mice.

According to several reports, a high-fat diet (HFD) leads to obesity, dyslipidemia, cardiovascular disease, type II diabetes, non-alcoholic fatty liver, non -alcoholic steato-hepatitis (NASH), and cancer [15]. Oxidative stress is induced by HFD by increasing the amount of chylomicrons in the intestine [16]. When chylomicrons enter the bloodstream, they form free fatty acid (FFA) that is absorbed by the liver. These hepatic FFAs are either oxidized or esterified to generate triglycerides in mitochondria (TG). These TGs either form tiny droplets in hepatocytes or produce very-low- density lipoprotein (VLDL), which is then converted to low-density lipoprotein (LDL) [17].

Based on the foregoing, the oxidative stress of HFD as well as the anti-oxidative properties of low doses gamma irradiation are summarized, therefore the current study was established to assess the health effects of fractionated low- doses gamma irradiation against obesity, in terms of decreasing inflammation effects as well as oxidative stress of obesity on liver of obese rats.

MATERIALS AND METHODS

Animals

Thirty-six male albino rats (weighing between 120- 130g - age of 10 weeks), were included in the present study. The experimental protocol was approved by the research ethics committee at Faculty of Science, Ain Shams University, Egypt (REC-FS, ref no. 00033). The animals were obtained from the Animal House of the Egyptian Atomic Energy Authority, Biological Applications Department. The animals were housed in cages with a standard diet and tap water *adlibitum* and acclimated for two weeks prior to the experiment.

Induction of obesity

Obesity was induced by feeding rats on a high fat-diet (HFD) providing 35 % calories from fat (butter oil) for 16 weeks, after several trials it turned out that a supply of 35% calories is the optimum ratio for the current study.

Irradiation procedure

Whole-body gamma-irradiation was performed at the Egyptian Atomic Energy Authority, Cairo, using a Gamma Cell-40 Carlo irradiator, cesium137 source. Animals were irradiated at a radiation dose level of 0.5Gray for 2 weeks, twice a week at a dose rate 0.74589 rad/sec.

Experimental groups

The rats were classified equally into 4 groups; each one consists of 9 rats.

Group 1: Normal (control) group (G1), normal rats were fed a normal diet.

Group 2: Obese group (G2), rats received a 35% high-fat diet (HFD) for 16 weeks.

Group 3: Normal rats (G4) were fed a normal diet and whole body was irradiated at 0.5 Gray for 2 weeks, twice a week (accumulated dose =4×0.5=2 Gray).

Group 4: Rats (G3) received a high-fat diet (HFD) for 16 weeks and whole body irradiation at a dose of 0.5 Gray for 2 weeks, twice a week (accumulated dose =4×0.5=2 Gray).

Every week for 16 weeks, body weight, liver weight, body length, and tail length were recorded, and Lee's index was determined using the following formula: Body mass index (BMI) was computed as body weight (g)/body length (cm2) and [Body weight (g) 1/3 × 1,000]/body length (cm) [18].

Blood sampling

Rats were anaesthetized by diethyl ether after 18 weeks. Blood samples were collected in heparin-treated tubes by cardiac puncture. Plasma was obtained at 3000rpm for 10 min by centrifugation and used for determination of C-reactive protein (CRP) and lipase.

Tissues (liver) sampling

Immediately after the animals were killed, the liver organs of each animal were quickly excised, weighed and washed with 0.9% saline and were ready for homogenization at phosphate buffer saline (PBS buffer) for the measurement of activity of GSH and levels of MDA in the homogenates of liver. The activity of GSH and levels of MDA was estimated by the methods of Beutler *et al.*, [19] and Ohkawa *et al.*, [20] respectively, by means of colorimetric enzymatic methods (Biodiagnostic kits). Moreover, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, gamma glutamle transferase (GGT), total protein (TP), albumin (Alb),globulin, total cholesterol (TC), total triglycerides (TG) and total lipids (TL) were measured calorimetrically using spectrophotometer (Milton Roy Spectronic 1201) and commercial kits purchased from Biodiagnostic Reagent Kits, Dokki, Giza, Egypt.

Histological studies

Histopathological studies were carried out to confirm the biochemical analysis. Liver samples were taken from animals, after killing, and placed in 10% neutral formalin, dehydrated in an ascending sequence of ethanol, cleared in xylol, and then

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embedded in paraffin. Six-micron-thick sections were prepared and stained with haematoxylin and eosin [21].

Statistical analyses

Data were expressed as means ± standard deviations. One-way (ANOVA) analysis of variance was performed among the mean values of the groups followed by Duncan's multiple range test, whenever necessary. The statistical difference is considered significant at $P<0.05$. All statistical analyses were performed using a computer program known as COSTAT- Program 3.03,1983, (CoHort Company Birmingham, UK).

RESULTS

The data of the present study showed significant harmful effects of obesity on liver biochemical parameters as well as histopathology studies, meanwhile, a fractionated low-dose gamma irradiation decreases these harmful effects which will be covered in detail.

Effects of obesity on body and liver weight

There was a significant increase in the body as well as liver weigh (456±88.6, 11.58±0.9), respectively, in the "G2" obese group as compared to the normal control group "G1" by (344.8±22.8, 8.91±0.4), respectively.

Meanwhile, there was a significant decrease in low-dose irradiation"G3" in addition to the obesity + irradiation group "G4" obesity group as compared to the obese group, with a change percentage of -17.63 and -18.8%.

Furthermore, there was a significant increase in both Lee index and body mass index (BMI) in the obese group as compared to the normal group with a change percentage of 13.26 and 40 %, respectively. While a low-dose gamma irradiation in the obesity + irradiation group "G4" showed a significant decrease as compared to the obese group "G2" with a change percentage of -9.9 and -19.04 %, respectively as shown in table 1.

Effect of obesity in lipid content of liver tissue

There was an elevated substantial increase (in total lipid, TC and TG) in the obese group"G2" as compared to the "G1" normal group by a change percentage of 159.9%, 406% and 140.28 %, respectively. However, the "G4" obesity + irradiation group showed a significant decrease in the lipid profile as compared to "G2" by a change percentage of -50.48, -50.47 and -38.44% as shown in table 2.

Effect of obesity on Glutathione "GSH" and Malondialdehyde "MDA" of liver tissue

The current study showed that there are significant increases in (MDA) in the obese group "G2" as compared to the normal group"G1" with a change percentage of 153.7%. However, the obesity + irradiation"G4" showed a significant decrease in (MDA) as compared to "G2" to the change percentage of -53.5%. Meanwhile, there is a significant decrease in GSH in "G2" compared to "G1" with a percent of change (-37.37%), nonetheless, there was a significant increase in GSH in "G4" as compared to "G2" in terms of the change percentage (23.19%) as shown in table 2.

Effect of obesity in liver functions

The data of the present study postulated that a high-fat diet has a harmful effect not only on liver weight, but also on liver functions as there was a significant increase in the levels of Alt, AST, ALP, GGT and total Bilirubin with change percentages of 121, 89.9, 207.6, 120 and 69.38 %, respectively, when compared to the normal group G1. Moreover, there was a significant decrease in total protein and albumin in the obese group "G2" by -67.2 and -75.22 % as compared to the normal control group. Meanwhile, there was a significant decrease in liver enzymes (ALT, AST, GGT and total Bil.) in the obesity + irradiation" G4" group with change percentages of -51.45, -51.02,-45.88, -14.45 %, respectively, as compared to "G2".

In addition, there was a significant increase in total protein and albumin in "G4" as compared to "G2", with change percentages of 152.5 and 237.03% as shown in table 3.

Effect of obesity on Lipase and inflammatory agent C Reactive protein (CRP)

There was a significant increase in the levels of both Lipase as well as CRP in the obese group "G2" as compared with the normal group"G1", while the obesity + irradiation "G4" showed a significant decrease in both lipase and CRP as compared to "G1", as shown in figure 1.

Effect of different treatments on macroscopic liver appearance

The obesity group showed detrimental effects on the macroscopic appearance of the liver, which was manifested by the change in both color and external shape of liver tissues. The "G2" obese group showed a rough and irregular surface as well as the presence of lipid tissues as compared to the normal group. On the contrary, the irradiation group "G3 and the obesity + irradiation group G4" showed normal liver color and with regular smooth surface as compared to the control group as shown in figure 2.

Effect of different treatments on histological study of liver tissue

Histological examinations of liver tissues with hematoxylin and Eosin stains in the different studied groups confirmed the biochemical study in all the studied groups, as shown in figure 3. In the normal

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group, "A" liver showed a normal hepatic parenchyma; normal hepatocytes, blood sinusoids, and central veins were noticed. However, in the obese group "G2", the liver showed Glycogen infiltration; vacuolated hepatocytes with peripheral nucleus were noticed. Meanwhile, in the irradiation group"G3" liver showed slight portal tract changes. In the obesity + irradiation group "G4", a fractionated low dose radiation decreases the harmful effects of obesity as shown in figure3, in which liver shows normal hepatic parenchyma, and normal hepatocytes, blood sinusoids, and central veins were observed (H&E X200).

Table 1. Effects of different treatments on liver and body weight of all studied groups.

Groups		Body weight (g)	Lee index	Body mass index (BMI)	Liver weight (g)
Normal "G1"group	Mean ±SD	344.8±22.8^{b}	294±3.9^{b}	0.60±0.04^{b}	8.91±0.4^{b}
	%change	-----	-----	-----	-----
Obesity"G2"	Mean ±SD	456±88.6^{a}	333.12±22.4^{a}	0.84±0.15^{a}	11.58±0.9^{a}
	%change	32.25%	13.26%	40%	29.9%
Normal rats + Irradiation"G3"	Mean ±SD	342.4±47.1^{b}	290.8±13.5^{b}	0.60±0.08^{b}	9.0±0.6^{b}
	%change	-24.9%	-12.9%	-28.57%	-22.27%
Obesity + Irradiation "G4"	Mean ±SD	375.6±30.8^{b}	300.2±8.6^{b}	0.68±0.05^{b}	9.4±0.4^{b}
	%change	-17.63	-9.9%	-19.04%	-18.8%

Table 2. Effects of different treatments on lipid content of liver, Glutathione "GSH" and Malondialdehyde "MDA" of all studied groups.

Groups		Total lipid (mg/g tissue)	Cholesterol (mg/g tissue)	Triglyceride (mg/g tissue)	Glutathione liver (mg/g tissue)	Malondialdehyde liver (nmol/g tissue)
Normal "G1"group	Mean ±SD	60.94±4.3^{bc}	18.77±1.5^{c}	16.68±2.15^{c}	22.58±2.1^{a}	128.16±10.16^{c}
	%change	-----	-----	-----	-----	-----
Obesity "G2"group	Mean ±SD	158.39±21.9^{a}	95.01±18.9^{a}	40.08±4.68^{a}	14.14±0.85^{c}	325.26±24.51^{a}
	%change	159.9%	406.1%	140.28%	-37.37%	153.7%
Normal rats + Irradiation "G3"	Mean ±SD	58.34±13.9^{c}	18.96±0.88^{c}	17.23±0.74^{c}	24.41±2.9^{a}	120.94±5.6^{c}
	%change	-63.1%	-80.04%	-57.01%	72.63%	-62.81%
Obesity + Irradiation "G4"	Mean ±SD	78.7±10.5^{b}	47.05±2.6^{b}	24.67±0.48^{b}	17.42±0.7^{b}	151.28±11.3^{b}
	%change	-50.48%	-50.47%	-38.44%	23.19%	-53.5%

The numerical data were expressed as mean ± SD., of number = 9, and values with small different letters in the shown columns are significantly different and similar letters are not significantly different ($p<0.05$) in various groups.

Table 3. Effects of different treatments on liver function tests of all studied groups.

Groups		ALT(U/g)	AST(U/g)	Gamma GT. (U/g)	Alkaline P. (U/g)	Bilirubin (mg/g)	Albumin (mg/g)	Total protein (mg/g)
Normal "G1"group	Mean ±SD	97.5±3.2^{c}	41.2±8.9^{b}	7.7±1.9^{b}	221.1±41.7^{b}	0.49±0.03^{c}	1.09±0.21^{a}	1.8±0.36^{a}
	%change	-----	-----	-----	-----	-----	-----	-----
Obesity "G2"group	Mean ±SD	215.9±7.4^{a}	78.2±12.2^{a}	17.0±0.89^{a}	679.9±58.9^{a}	0.83±0.08^{a}	0.27±0.15^{b}	0.59±0.17^{b}
	%change	121%	89.8%	120%	207.6%	69.38%	-75.22%	-67.2%
Normal rats +Irradiation "G3"	Mean ±SD	101.7±1.9^{c}	40.5±7.9^{b}	8.7±1.63^{b}	226.4±46.8^{b}	0.51±0.04^{c}	1.01±0.17^{a}	1.65±0.55^{a}
	%change	-52.89%	-48.2%	-48.8%	-66.7%	-38.55%	274.07%	179.66%
Obesity + Irradiation "G4"	Mean ±SD	104.8±2.7^{b}	38.3±5.6^{b}	9.2±1.33^{b}	673.5±89.5^{a}	0.71±0.05^{b}	0.91±0.32^{a}	1.49±0.47^{a}
	%change	-51.45	-51.02%	-45.88%	-0.94%	-14.45%	237.03%	152.5%

Numerical data were expressed as mean ± SD., of number=9, values with small different letters shown in columns are significantly different and similar letters are not significantly different ($p<0.05$) in various groups.

Table 4. Correlation coefficient between body weights and biochemical parameters in liver and blood plasma.

		Liver	parameters		
Parameters	Liver ALT	Liver AST	Liver ALP	Liver GGT	Liver T-Bilirubin
Body weight	0.7092	0.6438	0.4751	0.6787	0.5578
		Liver	parameters		
	Liver TP	Liver Alb.	Liver GSH	Liver MAD	Weight liver
	-0.4932	-0.6156	-0.67515	0.71576	0.69981
		Lipids	in liver		
Parameters	Liver TC	Liver TG	Liver TL		
Body weight	0.641373	0.838413	0.634671		
Parameters	Serum Lipase	Serum CRP			
Body weight	0.706807	0.581626			

Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), total bilirubin, Gamma glutamle transferase (GGT), Total protein (TP), Albumin (Alb), globulin, total cholesterol (TC), total triglyceride (TG) and total lipids (TL), Glutathione "GSH" and Malondialdehyde "MDA. All parameters have a significant correlation with body weight at $p<0.01$.

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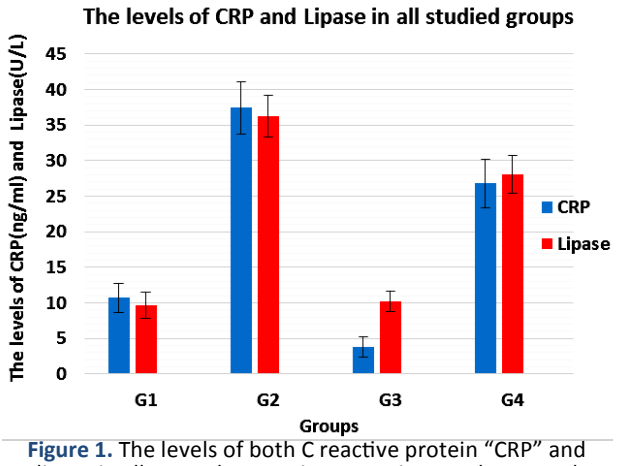


Figure 1. The levels of both C reactive protein "CRP" and lipase in all treated groups in comparison to the normal control group"G1", showing significant increases in both CRP and Lipase in the obese group "G2" compared with all groups.

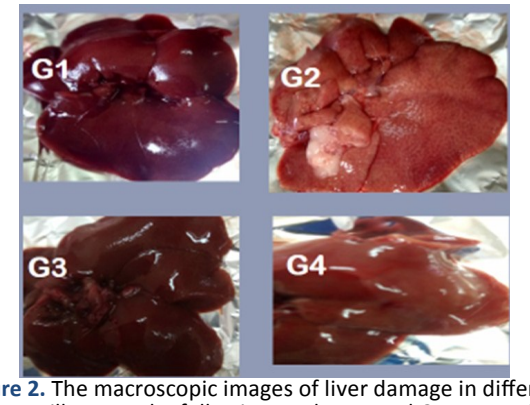


Figure 2. The macroscopic images of liver damage in different groups illustrate the following: In the normal G1 group, the liver is completely normal. Meanwhile, the obese group "G2" had a change in both color and external shape of the liver tissues, showing a rough and irregular surface as well as presence of lipid tissue as compared to the normal group. In contrast, both the irradiated group "G3" and obesity + irradiation group "G4" showed normal liver tissues, as there were regenerative effects of a low dose irradiation in the obesity + irradiation group"G4" as compared to the obese group "G2".

DISCUSSION

In recent years, significant progress has been made in understanding the mechanism of action of low-doses ionizing radiation in biological systems. Low doses of ionizing radiation have been found to have favorable benefits in epidemiological and experimental research [22-24].The present study investigated the effects of the exposure to a fractionated low-dose of gamma-rays against the harmful effects of high fat diet in the liver tissues of obese rats.

The current study showed that a high-fat diet had significant increases in both body and liver weight in the obese group'G2" as compared to the normal group"G1", and obesity as well as dyslipidemia are strongly linked to the high-fat diet (HFD). Obesity and obesity-related complications continue to be a global health concern, with a high-fat diet being one of the most common contributing factors to the onset

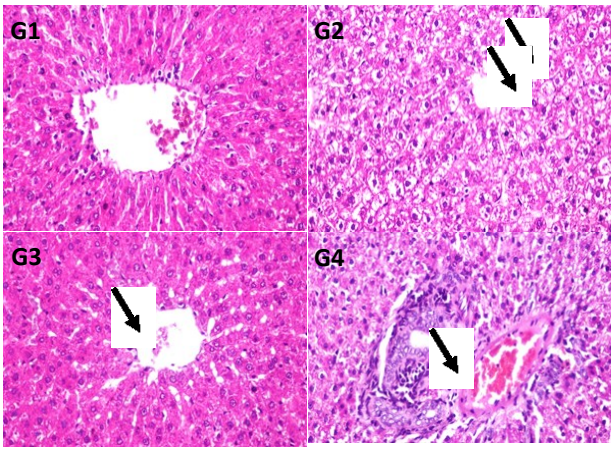


Figure 3. illustrates the harmful effects of a high-fat diet on the liver tissues in the obese group "G2" as compared to the normal group "G1". However, there are regenerative effects of the low dose irradiation in the obesity + irradiation group"G4" as compared with "G2". In the normal group"G1", the liver tissues showed normal hepatic parenchyma, normal hepatocytes, blood sinusoids, and central veins were observed. Meanwhile, in the obesity group "G2", the liver tissues showed glycogen infiltration and vacuolated hepatocytes with peripheral nucleus were noticed. On the contrary, in the irradiated group"G3", the liver showed slight portal tract changes. Meanwhile, in the obesity + irradiation group "G4", a fractionated low-dose radiation decreased the harmful effects of obesity (H&E X200).

of metabolic syndrome (MetS) [25]. In addition, obesity is a serious metabolic condition marked by increased energy intake and decreased energy production in relation to body weight and glucose metabolism [26]. Whereas, low doses of fractionated gamma irradiation "G4" have potential decreasing effects in both body and liver weight when compared with "G2". This may be related to low dose irradiation including radiotherapy which is known to reduce patients' dietary intakes caused by a loss of appetite.

Furthermore, there were significant increases in total lipid, total cholesterol and triglycerides in the liver of "G2" as compared to "G1". According to other researchers [27] obesity leads to steatosis and steatohepatitis in liver.

As a result of HFD, the amount of chylomicrons in the intestine increases. When the latter enters the blood, it produces free fatty acid (FFA), which is absorbed by the liver. These hepatic free fatty acids "FFAs" are either oxidized in mitochondria or esterified to produce triglycerides (TG).

Moreover, there was a significant decrease in glutathione (GSH), as well as a significant increase in malondialdehyde (MDA) in "G2" compared to "G1". Indeed, most HFD models resulted in increased mitochondrial hydrogen peroxide production, a greater incidence of oxidative damage markers (e.g., increased lipid oxidation and reduced aconitase activity), and decreased antioxidant defenses, implying that HFD animals suffer from oxidative

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imbalance [28]. This imbalance is induced by both GSH and MDA, GSH a non-enzymatic antioxidant, which acts as crucial factor for keeping the cellular redox balance in check. Due to the fact that redox active sulfhydryl group directly reacts with the oxidant, it works as a radical scavenger and changes itself into oxidized glutathione. According to recent data, patients with oxidative stress-related clinical illnesses had lower glutathione/antioxidant levels [29]. As a result, low glutathione levels are commonly believed to be an "index" of the increased reactive oxygen species "ROS" generation, and glutathione depletion leading to oxidative stress-induced cellular damage [30]. In addition, MDA is an end product derived from lipid peroxidation produced by different free radicals. During oxidative stress, there was an increase in MDA caused by ROS [31] that induced an alteration in the Na/P ATPase [32].

In contrast, low doses irradiation, showed a significant increase in GSH and a significant decrease in MDA, which may be related to low dose radiation inducing hormetic responses including synthesis of free radical scavenging [33] that can compensate, or even overcompensate, for the toxic effects of reactive oxygen species, which are by-products during normal metabolism [34]. Such responses are expected to aid in the prevention of a variety of negative health effects caused by the environment. According to a previous study [13], low-dosage irradiation suppresses lipid peroxidation in rats.

The current study also showed impaired liver functions in "G2" as compared to "G1", which may be due to fat accumulation in the liver tissues that can be very toxic [35]. Furthermore, non-alcoholic fatty liver disease (NAFLD) encompasses a variety of liver abnormalities involving fat buildup in hepatocytes, such as simple steatosis, a benign condition that can advance to catastrophic liver cirrhosis [36]. Moreover, HFD-induced fatty liver is linked to elevated levels of AST and ALT [37], a high level of ALP is often detected in animals with cholestatic liver disease [38], and HFD causes oxidative damage to hepatocellular proteins [39]. In addition, there are significant increases in lipase in "G2" as compared to "G1", and this elevation in pancreatic lipase could be interpreted as an attempt to boost pancreatic secretory lipolytic capacity following a high-fat diet [40].

Furthermore, CRP levels were much higher in "G2" than in "G1," and since CRP is one of the most inflammatory agents, the HFD-induced ROS-directed pro-inflammatory state could activate one of the primary transcription factors connected to inflammation. Furthermore, HFD promotes the production of inducible nitric oxide synthase (iNOS) through triggering ROS [41]. Because of the interaction between superoxide's and NO, activated iNOS produce too much nitric oxide (NO), resulting in an increase in the reactive nitrogen species (RNS) [42].

Overcoming all of these interconnected processes could indicate the emergence of many risk factors and chronic diseases associated with high-fat diet, systemic oxidative stress, and metabolic syndrome (MetS). Meanwhile, a low-dose gamma irradiation protects liver cells and decreases the levels of inflammatory agent(CRP) from this oxidative and damaged effects of HFD. this supposition is depend on data that a low dose irradiation may stimulate repairing of DNA as well as having antioxidant capacity, anti-inflammatory and apoptosis effects [43].

To confirm the aforementioned, biochemical analysis and histological studies for liver tissues were performed, which showed that HFD Glycogen infiltration. Vacuolated hepatocytes with peripheral nucleus as compared with normal liver were observed, which demonstrated the normal hepatic parenchyma. Additionally, normal hepatocytes, blood sinusoids, and central veins were noticed. According to several studies, a high-fat diet leads to dysfunctional mitochondria and mononuclear inflammation [44]. In NAFLD, lobular inflammation, per-cellular fibrosis, portal fibrosis, and hepatocellular ballooning are demonstrated to occur as a result of oxidative stress and mitochondrial dysfunction [45]. Moreover, HFD leads to mononuclear cell infiltration, portal fibrosis, micro- vesicular fat globules and decreased glycogen content [46].

Meanwhile, low-dose gamma irradiation decreases these adverse effects on liver tissues by decreasing the oxidative stress of obesity via stimulating DNA repair by balancing the rate of DNA damage (which increases linearly with dosage) and the rate of DNA repair. Therefore, at low doses of irradiation, DNA repair processes are effective [47].

CONCLUSIONS

There is a growing body of evidences that low-dose irradiation, actually promotes health rather than posing risks. One of these health effects is the potential and effective role of low-dose gamma irradiation against the harmful effects of high fat diet as demonstrated in the current study. Despite the fact that several studies have investigated the biological consequences of low-dose irradiation, as well as the data from the current study, there are a number of crucial concerns that must be further investigated in order to determine the safety as well as health effects of low-dose gamma irradiation.

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Conflict of interest: All authors declare that they have no conflict of Interest.

Ethical approval: All applicable international, national, and/or institutional guidelines for the care

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and use of animals were followed. All procedures performed in the study were in accordance with the ethical standards of the institutional and national research committee.

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***Author contribution*:** All authors contributed equally to the design of the study, data collection and analysis, and the writing of the manuscript. All authors read and approved the final manuscript.

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