DISCUSSION

Magnetic resonance imaging (MRI) is one the most rapidly advancing imaging techniques available today. It is normally used to produce detailed sectional images of the body in any imaging plane. Compared to the X-ray based medical diagnostic techniques e.g. general radiography, positron emission tomography (PET) and computed tomography (CT), MRI does not employ ionizing radiation but uses radiofrequency (RF) fields. Therefore, the modality is considered to have less health effects than the ionizing radiation-based imaging modalities.

The gradient magnetic field is the primary source of acoustic noise associated with MR procedures [2, 4, 37,117–122]. This noise occurs during the rapid alterations of currents within the gradient coils. These currents, in the presence of a strong static magnetic field of the MR system, produce significant (Lorentz)[36] forces that act upon the gradient coils. Acoustic noise, manifested as loud tapping, knocking, or chirping sounds, is produced when the forces cause motion or vibration of the gradient coils as they impact against their mountings which, in turn, also flex and vibrate.

Alteration of the gradient output (rise time or amplitude) caused by modifying the MR imaging parameters will cause the level of gradient-induced acoustic noise to vary. This noise is enhanced by decreases in section thickness, field of view, repetition time, and echo time. The physical features of the MR system, especially whether or not it has special sound insulation, and the material and construction of coils and support structures also affect the transmission of the acoustic noise and its subsequent perception by the patient and MR system operator.

Notably, measurements of sound pressure levels offer a limited amount of information with regard to the quality of the noise and its impact on health. In addition to measurements of noise level, several authors have recorded and analyzed the acoustic noise [2,117,120–122,123]. Similar noise levels and characteristics are found when comparing different clinical MR systems [124]. Frequency analysis of the noise shows that noise is pseudo-periodic, with variation in the degree of periodicity depending on the imaging parameters used.[124] Peak noise levels are found at the low-frequency region of the spectra.

According to WHO definition in 1946, health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity. In accordance with this definition, health assessment has gone beyond the presence or absence of disease. Thus, new “psycho-social” approaches are developed in terms of quality and survival for the patient. [124]

In general, stress effects have both psychological (annoyance, irritation, anger, strain) and physiological (endocrine, vegetative) components that can affect the cardiovascular systems and the metabolism. All these reactions can occur at noise levels much lower than 85 dB. Noise disturbances also cause impairment of work and communication, lower performance of mental processes, and can provoke stress reactions at low noise levels. [125]

The American Academy of Pediatrics and the National Campaign for Hearing Health also use 85 dB as a threshold for dangerous levels of noise. [125]

Noise affects human health as an important stress factor. People exposed to noise suffering from various health problems, one of which is noise-induced hearing loss. [126] It suggested that noise affects hearing system in two different ways: mechanical trauma directly to the organ of Corti due to high vibration level of noise and increased oxidative metabolism related to increased metabolic stress in the inner ear [127].Free oxygen radicals play an important role in tissue damage caused by metabolic stress. In different studies, it has been shown that free oxygen radicals in cochlea play a role in noise-induced hearing loss [126, 127]. If the free radicals produced by oxidative stress are not balanced by an antioxidant defense system, then they may lead to various damages in tissues. SOD and MDA are two of the endogenous antioxidants in the body. [128, 130]

The present work was aimed to study the potential MRI sound adverse effects on some biophysical (dielectric properties) and biochemical parameters (blood glucose level, malondialdehyde and superoxide dismutase) in the brain of experimental mice exposed to noise emitted from MRI system. This study was conducted on 40 mice exposed to different intensities of noise (90, 100 and 121 dB) arise from MRI system closed type 1.5T (Siemens AG 2005 Germany) during examination, and recorded on mp3.

In the present work dielectric measurements were performed on brain of all studied groups (control and exposed to different intensities of noise). Experimental evidence strongly suggests that the measurements of the changes in dielectric properties of the brain tissue after noise exposure can be used to quantify and predict the individual response of brain tissue to noise.

The relative permittivity of unexposed and exposed mice brain was measured at multiple frequencies. The unexposed brain tissue has highest permittivity than exposed mice brain with different exposure noise intensities, Fig. (31). Decrease in relative permittivity may be referred to change in the cell membrane potential, change in the concentration of sodium and potassium inside and outside the cell, release of excessive water due to cell membrane disturbance.

Conductivity of the material is a physical quantity that represents its free charge (the current density) induced in response to the applied electric field with unit amplitude. According to *Liewei (2002)* [131], "Every biological process is also an electric process" and "health and sickness are related to the bioelectric currents in our body". The electrical conductivity of a tissue depends on both the physico-chemical bulk properties, i.e., properties of tissue fluids and solids and the microstructural properties, i.e., the geometry of microscopic compartments.

In the present study, there is small increase in real conductivity (σ') as the applied frequency increased in the different modalities of noise exposure Fig.(30). The real conductivity is decreased as the intensity of noise increased. The Conductivity in the exposed tissues may be affected by variations in: temperature, oxygen levels, free radical activity, mineral concentrations in intracellular and extracellular fluid, the types of minerals present in intracellular and extracellular fluids, pH (both intracellular and extracellular), level of hydration (cell water content and extracellular water content), the

ratio of structural/ unstructural water inside of the cell, membrane lipid/sterol composition, the amount of negative charges present on the surface of cell membranes, and the presence of chemical electrophilic toxins within the cell. [132]

It is well documented that noise is a stress factor.[133,134] Because the noise exposure causes an excessive reactive oxygen species (ROS) generation as an unwanted by product of high metabolic activity [135], The reaction of free radicals and ROS on lipid molecules may lead to continuing cell damage after noise exposure [82]. this may explain the alteration in the measured dielectric properties of brain tissues of mice exposed to noise.

Noise exposure has long been used as a stressor to investigate its effect on biological and biochemical responses. [136] *Cheng ,et al (2011)* [137], determined the levels of oxidative stress in the critical region [e.g. inferior colliculus (IC)], auditory cortex (AC), and hippocampus, which are associated with the acoustic lemniscal ascending pathway. Noise-induced release of stress hormones, hypothesized to be caused by an increased activity in the sympathetic branch of the autonomic nervous system and hyper-activation of the hypothalamic-pituitary-adrenal(HPA) axis, is supported by a combination of observational *Babisch ,et al. (2001)* [138]**;** *Selander, et al. (2009a)* [139].

According to the World Health Organization data, 15% of workers are exposed to noise levels that create a health risk [140]. The exposure to noise leads to harmful behavioral and physiological roles by moderating central cholinergic system in the brain *Sembulingam K, et al (2003)*.[141] Noise can disrupt the physiological function of both auditory and non-auditory systems**.** Deleterious effects of noise on the central nervous system (CNS) may be produced by over-stimulation of audition-related structures and by increasing the activity of non-auditory structures. [142]

Effect of MRI acoustic noise on MDA level:

Nervous system is relatively more susceptible to free radical damage[143] . Ravindran, et al ***(2005)*** [23] reported that neurotransmitters in discrete brain regions were found to be increased during noise stress even after 15 days of exposure. In addition to generating free radical species, it also leads to increase in radical induced lipid peroxidation end products such as malondialdehyde (MDA) which is an indicator of lipid peroxidation processes. [90]

The present results show a significant increase in MDA levels after noise exposure Fig.(41). This is in accordance with what shown by *Manikandan ,et al (2005)* [144]**,** who found increased MDA levels in different areas of the brain after 30 days of 100 dB white noise exposure. *Srikumar and colleagues (2005)* [145], also found increased levels of MDA in the serum, thymus gland, and spleen tissue after a 15-day exposure to white noise. Similarly, high levels of lipid peroxidation have been indicated in other studies as an indirect sign of increased ROS production in the serum and different areas of the brain during acute, subacute, and chronic noise exposure [78,144,145]. Thus, ROS and free radicals can break down cell membranes through lipid peroxidation, leading to cell death [82]. Our study results are in accordance with these findings, as it found that noise increased MDA levels in the brain of all groups exposed. Another similarly, *Derekoy, et al (2001)* [90] found that MDA levels were increased in rabbits after exposed to 100 dB SPL (sound pressure level) broadband noise for 1 h.

While in previous study shown significant elevation of serum MDA level following MRI examination, indicating that, it associated with significant free radical activity resulting in considerable degree of lipid peroxidation [146], and result seems to be of clinical importance in several diseases with proven oxidative assault and consequently an increment in free radical activity such as diabetes mellitus[147], cancer [148]. Haemoglobinopathies [149], hypertension with renovascular disease [150],osteoarthritis [151], and chronic hepatitis.[152]

Regarding the effect of type of MRI examination, those underwent brain MRI showed marked rise in MDA levels following MRI examination. [146]

Effect of MRI acoustic noise on SOD activity level:

There are some defense mechanisms to prevent the formation of free radicals and their harmful effects. Several antioxidant enzymes within the framework of the antioxidant defense system enable these mechanisms. Several findings, which show both increase and decrease in SOD levels in case of oxidative stress, are available in the literature. [141,142, 144] In this study, the brain SOD activity level of the mice exposed to noise were significantly lower compared to those of the control group Fig.(42). Our results are similar to those obtained by *Srikumar, et al (2006)* [153] *and Ilhan ,et al (2004)* [154].The decrease in SOD activity accompanied by increased lipid peroxidation, might be explained by the consumption of antioxidant enzymes developed by the increase in lipid peroxidation, a decrease in SOD levels in the brain may indicate that it is more sensitive to noise.[95]

Fetoni,et al (2013)[155], addressed the relationship between cochlear oxidative damage and auditory cortical injury in a rat model of repeated noise exposure. They reported that hearing loss and damage in hair cells and spiral ganglion was determined by noise-induced oxidative stress.[156] Oxidative stress is defined as an imbalance between reactive oxygen species (ROS), e.g., superoxide and hydroxyl radicals and cellular antioxidant defense. Generation of ROS is ubiquitous since ROS are generated during aerobic metabolism, i.e., mitochondrial oxidation and phagocytosis.[157] Each brain cell is estimated to produce more than 10^{11} free radicals per day, and oxidative stress leads to brain ageing as well as in several neurodegenerative disorders. In the nervous system, ROS are produced mainly by microglia and by astrocytes.[158] The Ca^{2+} rise stimulates the release of superoxide radical via activation of NADPH oxidase. In the presence of superoxide dismutase, superoxide radical is dismutase to H_2O_2 as a diffusible messenger and might affect neighboring GAB Aergic terminals either directly or via dismutation into the highly reactive hydroxyl radical.[159]

While in another studies, showed a significant early (on 1st day after noise exposure) increase in SOD activity and late (on 7th day after noise exposure) increase in catalase CAT activity [160], because the noise exposure firstly increases levels of ROS such as superoxide radicals, hydroxyl radicals and hydrogen peroxide. Secondly activity of antioxidants and related enzymes increases in order to eliminate the overproduced ROS due to noise [161]. The results indicate that adaptation to noise stress does not occur immediately in all the brain regions.

Effect of MRI acoustic noise on blood glucose:

The present study, we study the effect of acute noise exposure on blood glucose in all groups, we found a significant elevation in blood glucose of acute noise exposure groups as compared to control group Fig.(32).This is in agreement with *Sørensen, et al (2013)* [159] **,** investigated the link between environmental noise exposure and the metabolic system, he found that, animal exposed to noise of 80 dB, showed significant increase in blood glucose as compared to control**.** Sufficient exposure to noise can also cause physical damage to structures within the HPA axis, which may have both short- and long-term effects on maintenance of homeostasis. [162-164] The elevation in blood glucose may be due to elevation of plasma corticosterone levels and this could increase responsiveness of pancreatic β cells to glucose, while low insulin levels of the stressed animals as found by *Zardooz et al. (2005***).** [165]

Acute immobilization stress that has a psychological component (*van de Kar and Blair, 1999*) [166], increased plasma glucose and corticosterone levels during the stress session, whereas plasma insulin concentration was increased at the beginning of the stress session and returned to its normal value at the end *(Yamada, et al., 1993*) [167] .

Since stress can increase plasma catecholamine beside corticosterone levels and the secretion of the catecholamines is a part of the "fight or flight" response that stimulates glycogenolysis and increases the basal metabolic rates and productions of glucose and insulin as well *(Teague, et al., 2007)* . [168]

Effect of MRI acoustic noise on complete blood picture:

The effect of acute noise stress on certain hematological parameters such as disturbance in serum lipid, triglycerides, platelet count, plasma viscosity and glucose was studied,[136, 169,170] and they found that stress could affect the blood cell parameters. This finding was in accordance with our results which showed change in most of hematological parameters as a result of acute noise exposure.

All these are established biological risk factors for hypertension, arteriosclerosis or myocardial infarction *(Grunberg,1995)*[171],when considering the cause effect chain, i.e.: sound - annoyance (noise) - physiological arousal (stress indicators) - changes in biological risk factors - morbidity - mortality *(Babisch ,et al., 2001)* [138]. On arrival, hematological parameters of red blood cell count and hematocrit values were within the limits of reference range.

Effect of MRI acoustic noise on Hemoglobin (Hb %):

The effect of noise on hemoglobin was studied, it is clear that, the hemoglobin percentages were reduced in all groups exposed to acute noise as compared to control(33). This results in accordance with that studied by others.[102,172,173]

Effect of MRI acoustic noise on white blood cell (WBC) counts:

The present study revealed increased in WBC counts of mice exposed to acute noise as compared to control Fig.(39). Acute noise stress increases the peripheral total leucocytes cells (TLC) counts.[136] The mechanisms underlying noise induced reduction of the immune function may be related not only to neuro-endocrine change, but also to the imbalance of

oxidative stress. White blood cell count is a routine haematological parameter for the assessment of tissue damage, infection and many inflammatory conditions.[136]

Many researchers have studied the immunosuppressive effect of noise stress in animal models.[174,175] *Hioshi and Kanehisa (1996)* [176] reported that during arithmetic mental stress the absolute number of leukocytes lymphocytes, CD8+ cells, and CD16+ cells increased significantly, [136] another study revealed that, total WBC count was significant increased by13% between 8th day and 24th day after noise exposure**.** [177] Previous theories stated that, noise may be considered as a causative agent which influences body's immune system where it reduces both total white blood cell and lymphatic cell count[178] .Previous studies have been reported that the total number of white blood cells in animals increase when they are subjected to stress**.** [179]

Effect of MRI acoustic noise on platelet counts:

Blood indices also remained within the physiological range following acute noise stress. Platelets are no true cells; they are cytoplasmic fragments of megakaryocytes in bone marrow, released from the bone marrow into the blood stream. [136] Brain derived neurotrophic factor (BDNF) is stored in human platelets and circulates in plasma. BDNF levels in serum, platelets, and plasma were significantly increased in participants with asthma. Enhanced platelet BDNF is associated with airflow limitation and airway hyperresponsiveness in asthma. [180]

The present study revealed elevation in platelet counts as a result of acute noise exposure as compared to control Fig.(40). *Oureshi FJ, et al (2002)* [169]*, Sabahi AR, et al (2002)* [177] *and Laderbogen F ,et al (2009)* [101] are reported that, stress produces changes in blood cell parameters and increased platelet count. Another study similar by *Jern ,et al* (1989)[181] found that there was a significant increase of platelet during psychological arousal. Because in these situations of sympathetic and endocrine arousal, concentrations of stress hormones in the blood are increased.[83] This platelet activation may be a mechanism linking psychosocial stress with increased coronary risk, and may also play a role in the emotional triggering of acute coronary syndromes in patients with advanced coronary disease. [182]

Effect of MRI acoustic noise on mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC):

Our results revealed significant reduction in mean corpuscular volume (MCV), mean cell hemoglobin (MCH), and mean cell hemoglobin concentration (MCHC) shown Figures (35,36, 37). Similarly, results obtained by *Sabahi (2002)* [177] who showed reduction in (MCV), (MCH), and (MCHC) when rats exposed to noise. On the other hand, *Marita GK .et al (2012*) [136] showed no significant change in hemoglobin concentration between 8th day and 24th day after acute noise stress. *Patterson ,et al*. (1993) [183] according to which psychological stress can cause acute intravascular hemoconcentration through a decrease in plasma volume, which leads to an increase in the concentration of blood cell, plasma proteins and circulating lipoproteins.

Effect of MRI acoustic noise on Red blood cell (RBC) and Hematocrit:

A decreased RBC number in blood of exposed mice was observed in our study as a result of acute noise exposure for all exposed groups Fig.(38). A decreased hematocrit value was observed in our study as a result of noise exposur Fig.(34)**.** Hematocrit (HCT) is the red blood cell (RBC) volume concentration compared to the whole blood volume, the reduction of HCT result of pathological (anemia), the result is a decrease in the viscosity of blood. However, the blood's oxygen carrying capabilities are reduced. [184]

The changes in biochemical parameters that primarily contribute to alterations in red blood cells (RBCs) during oxidative stress.Exposure to high concentrations of oxygen radicals, the lack of nucleus and mitochrondria, inability to synthesize new protein and degradation of detoxifying enzymes makes red blood cells (RBCs) uniquely vulnerable to oxidative stress. As one of the first cells to be affected by changes in the red ox status of the body, alterations in red blood cells are widely used in first step-diagnoses of a number of pathological conditions. Several parameters of red cells get negatively affected as evidenced by decreased/increased level of markers of oxidative stress.[185]