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## ORIGINAL ARTICLE

# Association of the Abdominal Visceral Fat in Complicating side effects of Extracorporeal Shock Wave Lithotripsy

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**ABSTRACT**
*Although extracorporeal shock wave lithotripsy (ESWL) is a non-invasive and effective treatment for renal calculi but it is not completely free side effects. The most common complications of ESWL, are kidney tissue injury and increased free radical formation. Regardless stone free status, this study considered renal oxidative stress and peroxide radical formation estimated from biomarker Malondialdehyde (MDA) after ESWL taking in account the abdominal visceral fat of patients as well as the physical properties of shocks .A total of 40 patients age 37.18 ± 10.64 (all older than18 years) harboring renal or ureteral stones, underwent extracorporeal shock wave lithotripsy. Abdominal visceral fat was measured by Omron Body Fat Monitor. Malondialdehyde (MDA) excretion was measured as an oxidative stress biomarker. The parameters such as MDA, occult blood (RBC), ketones, protein, and leukocytes (WBC) in the urine samples pre and post ESWL were measured using Bio Doctor Analyzer. The mean levels of urea MDA, occult blood (RBC) and ketones showed statistically significant elevation after SWL termination compared with pre-ESWL values. The elevation of MDA is likely to be more correlated with visceral fat of patients while, the hemorrhage elevation is likely to be more correlated with patient age.The high ESWL energies were, the more ketone bodies were released into the urine. Overweight/obese patients should be exposed to ESWL energy ranged (3-3.5J) and shock wave pulse rate (60-90 pulses/min)with 2300 as an optimal per session. The MDA urinary level after ESWL, should be considered as a routine test.*
***Keyword:*** *ESWL, Abdominal Visceral Fat, renal oxidative stress, Free Radicals, MDA*

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## INTRODUCTION

Extracorporeal shock wave lithotripsy (ESWL) is considered the first line treatment and has become the standard used for the majority of patients with renal and ureteric calculi, because of its advantages, which is convenient, noninvasive outpatient procedure, safe and with success rates of 60–99%[1–3].
In order to optimize the results of ESWL, several technical factors should be considered. These factors are related to the patient and the stone, such as its size, density, skin to stone distance, number of shock waves and location of stone, which help predict the chances of success [4–5].Also, different kinds of lithotripters may influence the success rate of ESWL since there are lots of differences in the way they work. However, the obesity metrics of body mass index (BMI) and skin-to-stone distance (SSD) have been evaluated as predictors of ESWL success. WhereSSD has demonstrated a strong correlation with success [6– 9].In contrast, some studies concluded that the outcomes of ESWL correlate with BMI. These studies revealed that higher quantities of abdominal fat, especially visceral fat, are associated with a lower calculus-free rate following ESWL treatment [10– 11].Therefore, the influence of body mass index on the complete clearance of renal stones remains an indistinct. This study preferred to use the abdominal visceral fat rather than BMI and body fat for two reasons. The first reason is that the AVF stored within the abdominal cavity and is therefore stored around a number of important internal organs such as the

liver, pancreas and kidney. The second reason is that both (BMI) and Body Fat (BF %) are significantly influenced by age and gender unlike the visceral fat [12] which can be measured easily without complex relationships with each of the age and gender.

Whether BMI influence the outcomes or not, it could be considered in the view point of the side effects of ESWL treatment. Despite the advantages of ESWL listed above, rare, but serious and potentially dire side effects have been discovered. The most common side effects that should be addressed are the tissue damage (bleeding and edema) [13]as well as cavitation. The hazardous potential of cavitation is not only of a physical nature but also of a chemical nature, because of the generation of free radicals,e.g. OH, .H and $'O_2$[14-15]. Whereas, ESWL is believed to induce free radical activity which gives rise to oxygen free radical compounds [16] which are most dangerous than bleeding and edema because of their hidden nature.

This study aimedto investigate the impact of abdominal visceral fat on SWL complications particularly oxidative free radicals which can be estimated from biomarker Malondialdehyde (MDA) taking in consideration the physical factors of SWL (Energy and No. of shock waves).In addition, other byproducts induced by SWL such as (ketones and protein) were studied.All these complications of ESWL were studied regardless of whether succeed or not.

## PATIENTS AND METHODS

A hospital based cross-sectional study was conducted on 40 stone-formers patients aged (37.18 ± 10.64) and (7 up to 15 mm in size) taken from outpatient at lithotripsy unit in Vajeen Private Hospital from January to April 2016. The patients were 20 males (50%) and 20 females (50%). The stone localization (pelvic, calyceal, or ureteral stones) and stone size were not specified. The physical measurements were, weight (kg), and visceral fat which was measured by Omron Body Composition and Body Fat Monitor (BF508). In accordance to the recommendations of the WHO, patients were categorized into two groups concerning their AVF,normal weight (AVF <12) and overweight and obese (AVF>12). The patients were subjected to Siemens electromagnetic Modular is Lithotripter (Cplus) which was installed at the private hospital since (2012). The energy levels were between (2.5–5 joules, 38 steps to adjust) and penetration depth up to140 mm on the focus center. All necessary procedures for patient were done before the start of the ESWL.Treatment session consist of shock waves ranged 1700 up to 3000 pulses (average pulse 120 per minute) depending on technical protocol and patient parameters. Treatment time ranged from 25 to 45 minutes. All procedures were completed without any need for anesthesia. Prior to the shock wave therapy and post treatment, urine was collected for test using Bio Doctor (BS502). The predicted time between the 1st and 2nd samples depended on the treatment time. The urine test involved measuring of MDA, occult blood (RBC), ketones, protein, and leukocytes (WBC) as well. The patients consent were obtained before we begin research and were informed that data would be used for a research exclusively. In this study, data were analyzed using the Statistical Package for Social Science (SPSS). Data were represented as mean values and standard deviations of the different exposure conditions in the Pre and Post ESWL. Fold change were calculated as the ratio between post and pre values of ESWL treatment. Differences were tested for significance with the two-sided t test. Level of statistical signification was set as ≤ 0.05. While <0.0001 was considered to be highly statistic significant.

## RESULTS

Demographic data of the patients are shown in table 1. The mean of abdominal visceral fat was low which reflects the fact that the percentages of overweight and obesity were quite low.

**Table 1: patient demographic data and body fat characteristics**

| Parameters | Mean ± SD |
|---|---|
| Age (year) | 37.18 ± 10.64 |
| Height (cm) | 165.03 ± 8.24 |
| Weight (Kg) | 77.52 ± 14.39 |
| BMI (Kg) | 28.06 ± 4.37 |
| Visceral Fat (Kg) | 10.04 ± 3.93 |

Table2 shows results of urine analysis of pre and post ESWL treatment. Values of each parameter of urine test before and after ESWL were compared by a paired t-test. When comparing values of urine test parameters there was no statistical difference in protein and WBC. In contrast,results also showhighly significant ($P < 0.0001$) difference in MDA, RBC, and Ketones before and after ESWL treatment.

**Table 2: Statistical analysis of the urinary measurement data pre and post ESWL**

| Parameter | Pre ESWL Mean ± SD | Post ESWL Mean ± SD | P-value |
|---|---|---|---|
| **MDA** (fp) | 5414.1 ± 1896.82 | 9096.7 ± 2587.18 | 0.0001 |
| **RBC** / µl | 29.26 ± 38.13 | 112.18 ± 54.96 | 0.0001 |
| **Ketones** mg/dl | 10.73 ± 23.58 | 28.1 ± 32.74 | 0.0001 |
| **Protein** mg/dl | 37.45 ± 17.51 | 45.78 ± 41.83 | 0.185 |
| **WBC** /µl | 10.9 ± 7.47 | 27.65 ± 48.24 | 0.029 |

Although the urine analysis reveals statistically significant changes in most parameters level, but more information is needed to determine their biophysical interpretations and mechanisms. The challenge is to bring these parameters individually and together with other physical factors such as abdominal visceral fat, total number of shock waves and shock wave energy to determine their impact and interpret theses correlations.

In this context, the correlation and analysis of the combine experimental data for MDA, ketone bodies, blood hidden (RBC) and protein in the urine were explored under the influence of each of the visceral fat, number of shock waves (pulse per minute) and shock wave energy.

**MDA**

The results shows that the amount of MDA fold generated during shock-wave treatment was significantly ($p<0.05$)increased with the applied energy of ESWL began at 3.4 J.This was found in both normal weight and overweight patients with obvious increases in the last group.

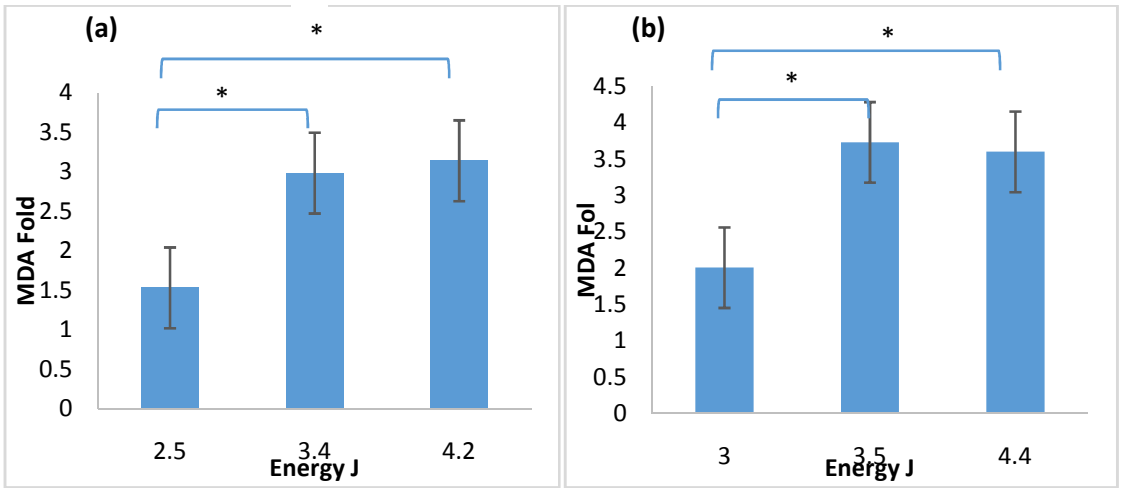


**Figure (1) MDA fold as a function of applied energy for both groups: (a) normal weight, (b) overweight patients**

The relationships between MDA fold versus visceral fat at two different energies (3.5 J and 4.6 J) were plotted as shown in figure (2). These relations reveal the significant ($p<0.05$) impact for visceral fat on MDA produced by ESWL especially for those who were treated with high energy.

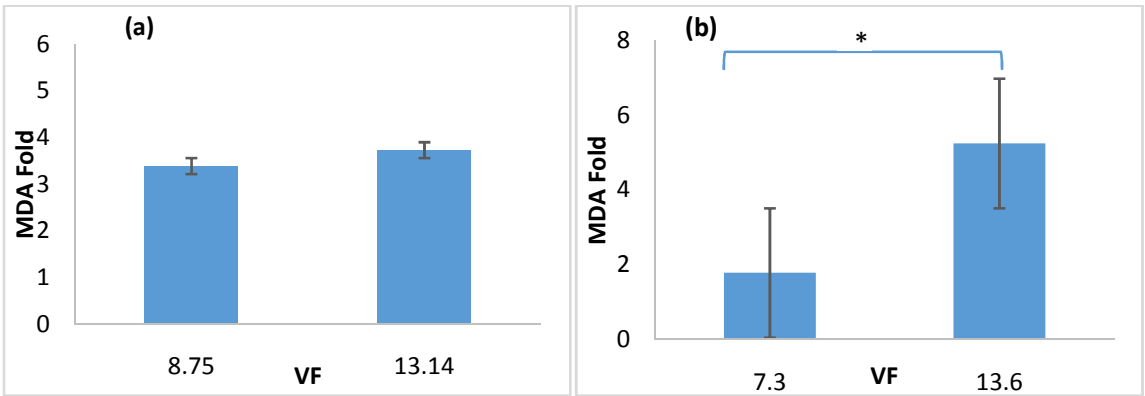


**Figure (2)** MDA fold as a function of visceral fat for both groups: (a) at energy of 3.5 J, (b) at energy of 4.6 J

In order to test the visceral fat levels for a quantifiable effect on MDA formation in terms of number of pulses, MDA levels were plotted vs pulses before and after ESWL as illustrated in figure (3). It seemed that the proportionality of MDA fold with number of shock depends on the visceral fat of the patients. This no significant proportionality a little tend to become an inverse proportion for normal weight patients while it was significantly ($p<0.05$) direct proportional for overweight patients.

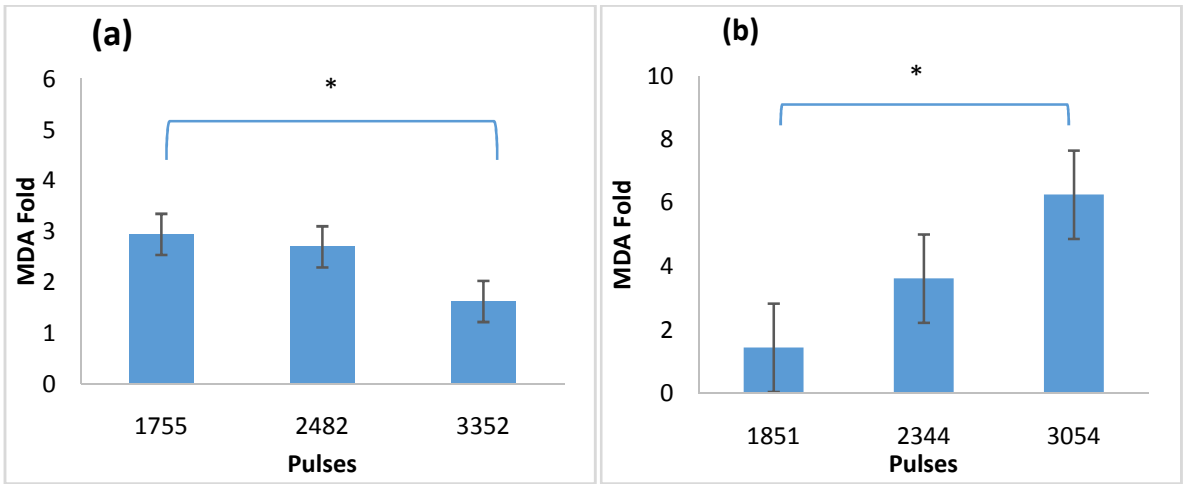


**Figure (3)** MDA fold as a function of number of shock waves: (a) for normal patients, (b) for overweight patients

**Occult Blood (RBC)**

Occult Blood (RBC) mostly inverse related to applied energy for both groups as demonstrated in figure (4). The same relation was confirmed in young patients. However, this is in contrast to old patients treated with same energy levels, which demonstrate a significant ($p<0.05$) increase in the occult blood (RBC) as shown in figure (5- b). Figure (6) illustrates significant increases of occult blood with respect to patient age. Occult blood in old patients increased almost twice over that in the younger patients.

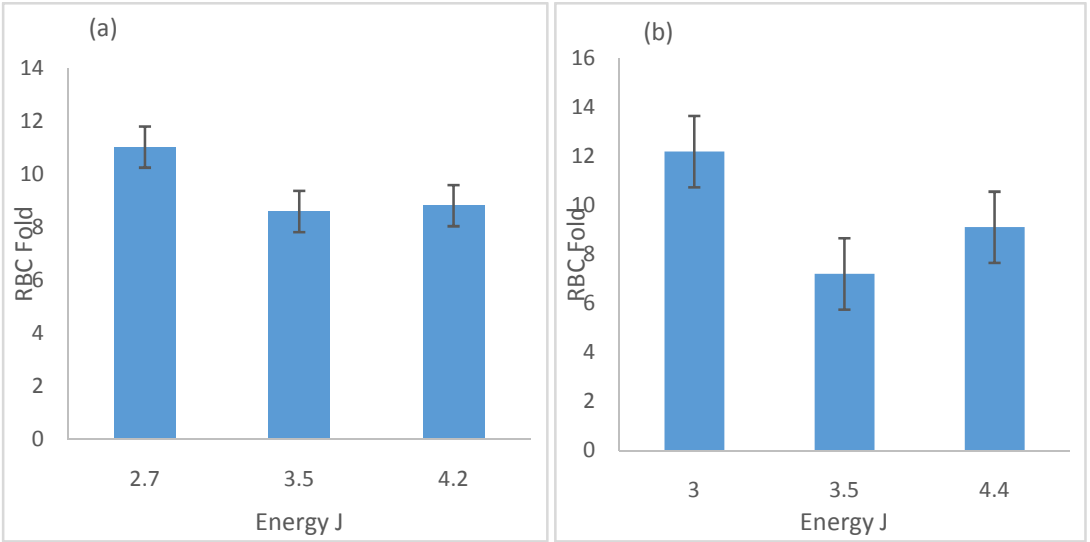


**Figure (4)** Occult Blood (RBC) with respect to applied energy: (a) for normal patients, (b) for overweight patients

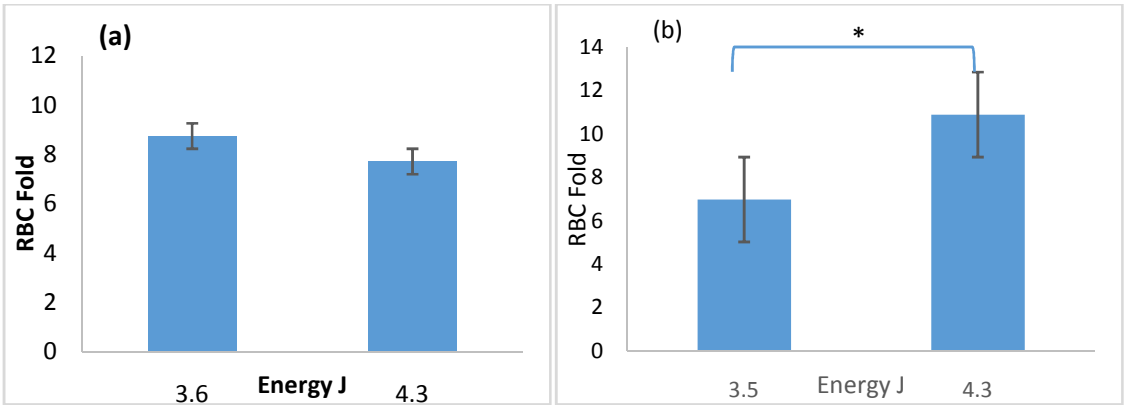


**Figure (5)** Occult Blood (RBC)with respect to applied energy: (a) for young patients, (b) old patients

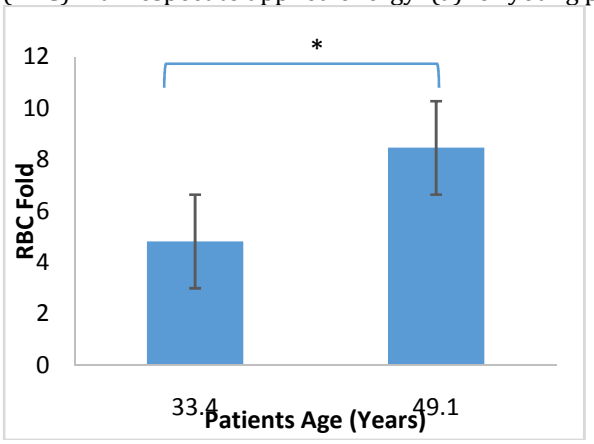


**Figure (6)** Occult Blood (RBC) with respect to patients age.

**Ketones**

Concerning ketones, there was a considerable amount of ketones in urine which indicated an increase in fatty acid metabolism by the liver after shock wave treatment. This was found for both groups of patients ($p<0.05$) as illustrated in figure (7)

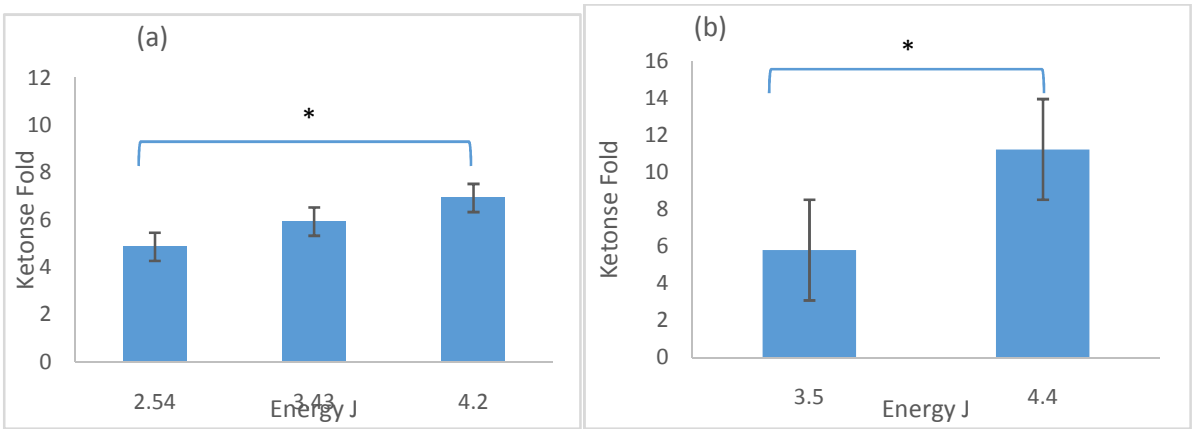


**Figure (7)** Ketones fold vibration with respect to applied energy: (a) for normal patients, (b) for overweight patients

However, ketones fold demonstrated significant ($p<0.05$) reverse relationship with visceral fat level at low and mid energy. While,a significant ($p<0.05$)positive correlation at high energy was shown as in figure (8)

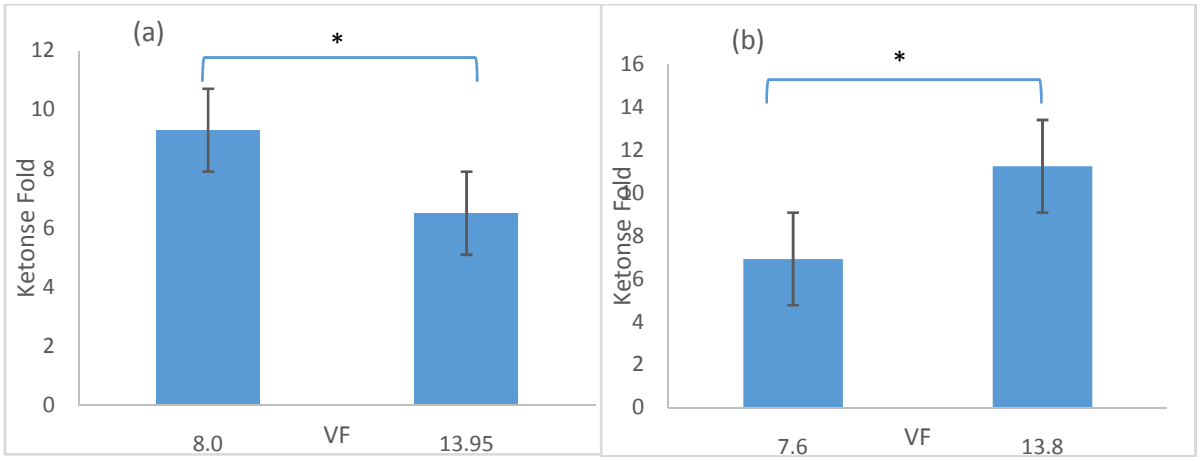


**Figure (8)Ketones fold as a function of visceral fat for both groups: (a) at energy of 3.4 J, (b) at energy of 4.3 J**

**Protein**

Protein levels were determined in urine samples before and after ESWL. There was slightly increases in protein levels of urine among the treatment groups in terms of applied energy and visceral fat as well. This could be seen in figures (9) and (10) respectively.

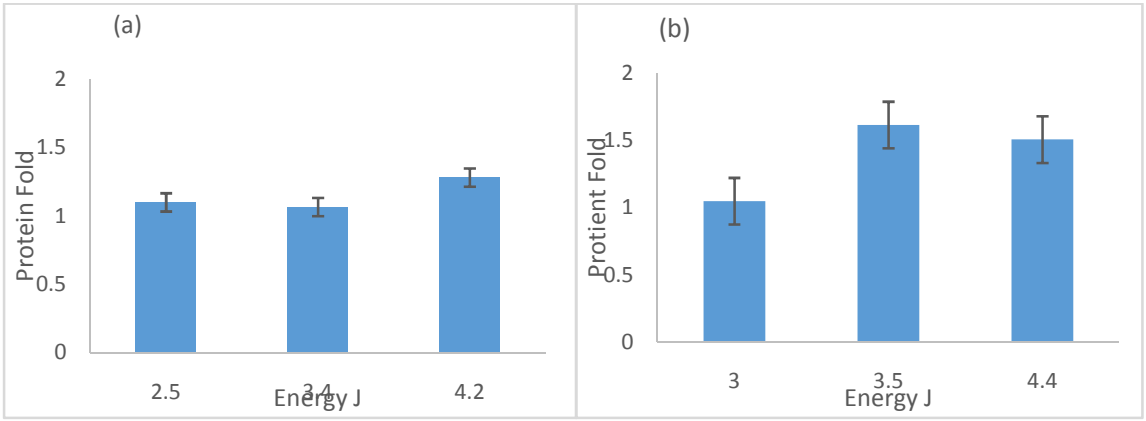


**Figure (9) protein fold as a function of applied energy: (a) for normal patients, (b) for overweight patients**

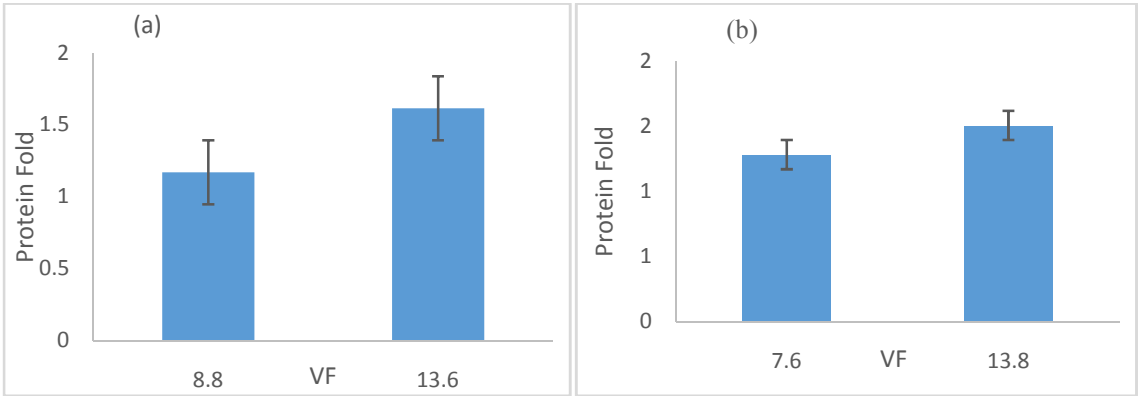


**Figure (10)protein fold as a function of visceral fat for both groups: (a) at energy of 3.5 J, (b) at energy of 4.4 J**

- *All asterisk means statistically significant differences* ***p<0.05***

## DISCUSSION

The present study addressed directly the impact of abdominal visceral fat on the complications of SWL particularly oxidative free radicals. According to the results, the mean levels of urea MDA proteins and ketones have statistical significant elevation after SWL termination compared with pre-ESWL values with respect to both, shock energy and patient's visceral fat. While, Occult Blood (RBC) was significantly dependent on patient age. However, despite the fact that the success rate of SWL is directly proportional to number of pulses, the results showed that this proportionality is almost null, especially for patients who had normal visceral fat.

Most of the previous studies have conducted MDA concentration as a function of time post operation and treatment EWSL. As far as we know, none of them conducting the impact of patient visceral fat level on the MDA combining with alteration in energy and number of shock waves. Therefore, this study was conducted to show the impact of visceral fat level on MDA in urine after ESWL as a potential side effect of treatment. MDA level was significantly ($p<0.05$) higher after ESWL than before in the patients who have high visceral fat level (overweight group) comparing with those who have less fat. So, the more level of visceral fat of the patients, the high MDA fold after ESWL. This could be explained by mechanism of oxidation products. Free radical formation has been reported during ESWL treatment, hence, subsequently reactions generate lipid peroxides and oxidation products, among which is MDA [17, 18]. Where, MDA is an excellent index of lipid peroxidation. Our interesting results of MDA could explained through a biophysics mechanism for interaction of ultrasound waves with fat. Independently of the gender, the higher values of the velocity correspond to lean individuals, while the lower values—to the overweight ones. In turn, this mean a high attenuation of ultrasound in fat. The attenuation measured represents the sum of the ultrasonic energy elastically scattered by in homogeneities in the fat and the energy absorbed by the fat via energy conversion. This imparted energy of shock wave induced cavitation which is the major mechanism responsible for ultrasound shock waves side effects. The cavitation generated free radicals through two main ways either by means of mechanical effects (microstreaming, microjets and shear stresses) or by chemical effects (heating and diffusion) as reported by [13].Consequently, the high levels of free radical induced the great assessed measuring MDA levels which consistent with the previous studies[19].This finding is particularly important, because patients with high visceral fat level are more likely to have oxidative stress.

The other potential side effect was conducted in this study is occult Blood (RBC). The significant evolution in RBC of urine manifested as hemorrhage in patients which is the more common complication of ESWL. Number of pulses waves and energy delivered were influenced hemorrhage only in elderly patients. Where low energy waves delivered at a slower rate, decrease the risk of hematoma formation in aged patients. This fully in line with the previous study [20]. Hemorrhage is almost always temporary without apparent long-term adverse effect and does not require medical or surgical treatment [12]. However, the probability of hematoma increased significantly as patient age at treatment increased. For 15-year increase in treatment age the probability of hematoma increased 1.75 times as shown in figure (6). Increased age is associated with increased risk of post-SWL hemorrhage.

Despite the lack of genuine connection between the ketones and ESWL, significant alteration can be seen in the level of ketones after treatment. The high level of ketones pretreatment (higher than normal values ≤ 1 mg/dl) could be attributed to the long fasting period of the patients (about 24 hours) in order to fulfill the pretreatment conditions where all the ESWL sessions were at evening at the private hospital. In normal states these ketones will be completely metabolized so that very few will appear in the urine. If for any reason the body cannot get enough glucose for energy it will switch to using body fats, resulting in an increase in ketone production making them detectable in the blood and urine. On contrast, ESWL may be responsible for high level of ketones post treatment possibly caused by alteration in intrarenal metabolism [21] in order to repair the damaged tissues due to the high ESWL energies. Whereas, the ultrasound wave serve as non-thermal effects that increase the local metabolism. Another possible explanation is the activation of abnormal lipid metabolism and production of high ketones resemble to that occur in Diabetes Mellitus, which must be considered in future studies.

Although no statistical significant difference was observed in proteinuria, even with respect to patient group and shock energy, an increasing has been shown. This could be due to free radicals which cause severe tissue damage leading to a release of cytoplasmic proteins, e.g. the Tamm-Horsfall protein which was also measured in the urine of patients as a parameter for kidney damage after shock-wave lithotripsy [13].This proteinuria return to near-normal levels within a few days [22]. Finally, the WBC levels indicate that not one of the patients had urinary tract infection or sepsis right away after treatment in the current study.

## CONCLUSION

Although the shockwaves has the same success rate in fragmenting stones whether they pass through the fatty or non-fatty tissues, it is often accompanied by some side effects and complications such as increasing urinary levels of oxidative stress biomarker (MDA), hemorrhage and proteins. This was more evident for patients with high abdominal visceral fat. Accordingly, this may require evaluation of patient's visceral fat to adjust suitable energy and pulse rate of the shock waves. This study recommends exposing the overweight/obese patients who treated with ESWL to energy and shock pulse rate 3-3.5J and 60-90 pulses/min respectively. This mean that the optimum pulses per session is about 2300.

## CONFLICTS OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this paper.

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