Original Article	**Alkaline Ionized Water Ameliorates the Structural and Ultrastructural Changes Induced by Hyperlipidemia on the Renal Cortex of the Adult Albino Rats**
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ABSTRACT

Background: Hyperlipidemia is considered a major medical and social problem leading to increasing morbidity and mortality. Disturbed lipid metabolism has been considered the possible cause of renal disease. Alkaline ionized water (AIW) was described to have impressive effects in prevention of lifestyle diseases.
Aim of the work: To study the ability of alkaline ionized water to diminish the destructive effects of hyperlipidemia on the renal cortex of the adult albino rats.
Material and Methods: Forty male albino rats were divided into four groups, ten rats each. Group (1) control rats, group (2) ten rats received AIW for twelve weeks, group (3) hyperlipidemic group: ten rats were received HFD daily for twelve weeks and group (4): ten rats received HFD daily for twelve weeks and AIW .
Results: Examination of the kidney of group (3) showed shrunken glomeruli with obliterated Bowman's space, dilated tubules with luminal hyaline casts and wide interstitial spaces with mononuclear cellular infiltrations. PAS-stained sections revealed strong positive reaction of the glomerular basement membrane, the tubular basement membrane and thickened Bowman's capsule. The brush border of the proximal tubules showed weak and disrupted reaction. Ultrastructurally, glomerular capillaries showed lipoprotein accumulation. Numerous lipid droplets were observed in the convoluted tubules especially the proximal tubules. The convoluted tubules showed also fragmented or swollen mitochondria. The lipid profile of this group showed the highest values of TC, TG and LDL and reduction of HDL. Examination of group (4) revealed that most of the glomerular capillaries retained their normal appearance together preserved lining epithelium of the convoluted tubules. The lipid profile of this group showed significant improvement as compared to group 3.
Conclusion: Consumption of AIW could protect the kidney from hyperlipidemia-induced deleterious effects by preventing renal cortical damage and disturbed serum lipids associated with dietary hyperlipidemia.

Key Words: Hyperlipidemia, Alkaline Ionized Water, Kidney, Rats.

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INTRODUCTION

Oxidative stress is produced by inability of radical scavenging system to eliminate the excessive dose of the free radicals *(Block et al., 2002)*. The condition of oxidative stress may be induced by some disorders such as diabetes, hypercholesterolemia, hyperlipidemia and obesity *(Marseglia et al., 2015)*.

Hyperlipidemia may be familial or associated with many conditions such as high-fat diet (HFD), liver failure and hypothyroidism. Hyperlipidemia induced by metabolic conditions leads to lipid accumulation mainly in the renal tissue with alterations in the cortex *(Vaziri, 2006)*.

Hyperlipidemia is considered a major medical and social problem. In many cases it is accompanied with diabetes mellitus leading to increasing morbidity and mortality. The major problem of hyperlipidemia is atherosclerosis, which leads to ischemic heart disease and cerebrovascular disease *(Moosa et al., 2006)*.

The world Health Organization announced that by the year 2020, the deaths caused by cardiovascular disease associated with hyperlipidemia will reach up to 40%. Each 1% increase in serum cholesterol concentration will result in 23%- increase in the risk of cardiovascular disease *(Hobbs, 2004)*.

Kidney dysfunction is associated with increased risk for cardiovascular disease that might progress over time to end-stage renal disease. The possible cause of these complications is abnormal lipid metabolism *(Ritz and Wanner, 2006)*.

The anti-hyperlipidemic drugs as, fibrates, anion–exchange resins, cholesterol absorption inhibitors, vitamin E and omega-3 marine triglycerides, have many adverse effects including, renal insufficiency, gastrointestinal upsetting effects, hyperuricemia, gout, impaired glucose tolerance and liver dysfunction. So, an alternative therapy for hyperlipidemia with minimal side effects was needed *(Kumar et al., 2008)*.

Alkaline ionized water (AIW) is safe to be drinkable and is recommended in the commercial and marketing literature as being useful for the management of gastro-intestinal problems, hypertension and cancer *(Henry and Chambron, 2013)*.

AIW refers to electrolyzed water produced from minerals such as magnesium and calcium and is characterized by high pH, micro-clustered water molecules, supersaturated hydrogen and a negative oxidation reduction potential. This alkaline water had been used as a feasible therapeutic strategy for health promotion and disease prevention *(Zong et al., 2012)*.

AIW acts as a scavenger of active oxygen species, protects DNA from oxidative damage and promotes metabolism. Furthermore, alkaline water was described to have impressive effects in prevention of lifestyle diseases such as type II diabetes and obesity *(Kajiyama et al., 2008)*.

Therefore, the aim of the present work was to study the ability of AIW to diminish the destructive effects of hyperlipidemia on the kidney of the adult albino rats.

MATERIAL AND METHODS

- **Animals:**

This study was carried on forty adult male albino (Sprague dawley strain) rats weighing 180 -220 grams each. The animals were housed in separate cages (five rats per cage) under standard laboratory and environmental conditions with free access to food and water. They were obtained from the animal house of Medical Research Centre, Faculty of Medicine, Ain Shams University. Male rats were used in this study to exclude the possible sex differences. All animal procedures were performed in accordance with the recommendations for the proper use and care of laboratory animals.

- **Diet protocol:**

The composition of diet was according to the formula of *Noeman et al., (2011)*. The normal diet for control rats included (Fat 5% [corn oil 5%], carbohydrates 65% [corn starch 15% and sucrose 50%], proteins 20.3% [casein 20% and DL-Methionine 0.3%], fiber 5%, salt mixture 3.7%, and vitamin mixture 1%). The HFD contained (fat 46% [corn oil 25.5%, and beef tallow 20.5%], carbohydrates 24% [corn starch 6% and sucrose 18%], proteins 20.3% [casein 20% and DL Methionine 0.3%], fiber 5%, salt mixture 3.7%, cholic acid (0.35%) and vitamin mixture 1%). Normal and HFD constituents were purchased from El-Gomhoria Company, Cairo, Egypt. HFD was preserved at 4°C until used *(Noeman et al., 2011)*.

- **Alkaline water:**

The alkaline water produced through KYK 33000 device purchased from KYK Co., Ltd Company.

- **Experimental design:**

The rats were divided into four groups, ten rats each (n=10).

Group1: **control group:** received only normal diet and tap water *ad libitum* for twelve weeks.

Group2: AIW group: received normal diet and alkaline water ad libitum for twelve weeks.

Group3: hyperlipidemic group: Rats received HFD and tap water daily for a period of eight weeks. The occurrence of hyperlipidemia was determined by measuring lipid profile (total cholesterol, triglycerides, low density lipoprotein (LDL) and high density lipoprotein (HDL). Animals with hyperlipidemia were the only used. Rats continued on HFD for extra four weeks.

Group4: hyperlipidiamic treated with AIW group: Rats received HFD for eight weeks as group 3 then rats with eight weeks were allowed to drink alkaline water for a period of four.

At the end of the experiment, blood samples were collected from rats, the serum levels of total cholesterol, total triglycerides, LDL and HDL were determined. The animals were sacrificed, their abdomens were dissected and the kidneys were collected. Kidney specimens were fixed for 48 h in 10% formalin processed and embedded in paraffin. Thick sections of the tissue were stained with Haematoxylin and Eosin (H& E) and periodic acid shief (PAS) for light microscopic study *(Bancroft and Gamble, 2002)*.

Transmission Electron Microscopic Study:

Kidneys were cut into small pieces of 1mm2 size and fixed in 2.5% glutaraldehyde for 24 hours. Specimens were washed in 0.1 M phosphate buffer at 4°c, then post- fixed in 1% osmium tetroxide at room temperature. Specimens were dehydrated in ascending grades of ethyl alcohol, and embedded in epoxy resin. Ultrathin sections (50 nm) were cut, mounted on copper grids and stained with uranyl acetate and lead citrate. Specimens were examined and photographed with (Jeol-Jem 1010 Japan) transmission electron microscope in Faculty of Science, Azhar University *(Woods et al., 2002)*.

Statistical analysis

One way Anova test was used to compare more than two groups. The Post-Hoc (Bonferoni) was used to compare every two groups. $P<0.05$ was considered significant.

RESULTS

A. Light microscopic results:

The H&E-stained sections of the kidney of the control group showed the normal architecture of the renal cortex, renal corpuscle, proximal and distal convoluted tubules. Renal corpuscles consisted of the glomeruli that appeared lobulated surrounded by Bowman's capsule and separated from it by renal space. Proximal convoluted tubules lined by eosinophilic pyramidal cells with narrow irregular lumina. Distal convoluted tubules lined by cubical cells with a wide lumen (Fig. 1). Bowman's capsule was formed of visceral and parietal layers separated by renal space. The parietal layer was lined by flat squamous cells. The visceral layer was composed of podocytes. Endothelial cell lining the capillaries and mesangial cells were also observed (Fig. 2). PAS-stained sections revealed a PAS-positive reaction of the basement membrane of glomerular capillaries, renal tubules and Bowman's capsule. The apical brush borders of the proximal convoluted tubules showed also positive reaction (Fig. 3).

Sections of AIW group showed a picture similar to the control group.

H&E-stained sections of the kidney of the hyperlipidemic group showed affected areas of renal cortex. Some areas showed glomeruli with obliterated Bowman's space. Many tubules were dilated with the luminal hyaline casts (Fig. 4). Other areas showed hypercellular glomeruli and wide interstitial spaces contained an acidophilic material, thick wall dilated blood vessel and focal areas of mononuclear cellular infiltrations (Fig. 4, 5). Some glomeruli were shrunken with few dense nuclei and surrounded by wide renal space. Some renal tubules showed marked cytoplasmic vacuolation of their lining epithelium with pyknotic or exfoliated nuclei (Fig. 6).

PAS-stained sections revealed a weak and disrupted PAS reaction of the disrubted brush border of the proximal tubules. The tubules contained positively stained hyaline casts. A

strong positive reaction of basement membrane of glomerular capillaries, the tubular basement membrane and thick walled Bowman's capsule was observed. The glomerular capillaries were congested with mesangial expansion (Fig. 7).

H&E-stained sections of the hyperlipidiamic rats treated with AIW group showed proximal convoluted tubules with preserved lining epithelium. Few tubules showed cytoplasmic vacuolation of their lining epithelium (Fig. 8). Most of the glomerular capillaries retained their normal appearance with restoration of the simple squamous epithelial lining of the parietal layer of Bowman's capsule, Podocytes and the mesangial cells (Fig. 9). PAS-stained sections revealed positive reaction in the basement membrane of glomerular capillaries, the renal tubules and Bowman's capsule. The brush border of the proximal convoluted tubules was preserved and showed positive reaction. A few tubules showed a weak reaction of their brush borders. Some glomeruli exposed mesangial expansion (Fig. 10).

B. Transmission electron microscopic examination:

TEM examination of the renal cortex of the control group showed a glomerular capillary network lined by the endothelial cell and surrounded by podocytes that had irregular nuclei and extensive cytoplasm. From the cell body of the podocytes, projections of several primary and secondary processes could be observed. The secondary processes anchored to the outer surface of the glomerular basal lamina. The glomerular basement membrane was uniformly thick and interposed between the secondary processes of the podocytes and the endothelial cells lining the glomerular capillaries. The intraglomerular mesangial cells with surrounding mesangial matrix material were also observed in between the glomerular capillaries (Fig. 11). The proximal convoluted tubules showed rounded basal euchromatic nucleus. The basal plasma membrane exhibited infoldings. The cytoplasm contained small electron-dense lysosomes. The mitochondria were elongated, radially arranged and basically located in the cells. The apical surface showed numerous microvilli projecting toward the lumen forming the brush border (Fig. 12). In the distal convoluted tubules, the lining cells had numerous elongated basal mitochondria within regular basal infoldings and a few blunt apical microvilli (Fig. 13).

TEM examination of the renal cortex of the hyperlipidemic group revealed excessive mesangial matrix deposition around the mesangial cells that showed heterochromatin nuclei with irregular nuclear envelope. Pyknotic nucleI of endothelial cells, thickening of the glomerular basement membrane and areas of effacement of foot process of the podocytes were also evident. Lipoprotein accumulation in glomerular capillaries was observed. The podocytes showed peripheral condensation of chromatin (Fig. 14). The proximal convoluted tubules showed shrunken nuclei with peripheral heterochromatin and vacuolated cytoplasm. The mitochondria were disintegrated and fragmented, while the electron-dense bodies were irregular. Focal destruction of apical microvilli were observed and the tubular lumina were filled by casts and large lipid droplets (Fig. 15). The distal convoluted tubules showed many small nuclei. Lipid droplets were observed in the upper part of their cell lining with fine granular appearance of the cytoplasm and destruction of the apical microvilli. Some mitochondria were swollen, others were small and irregularly arranged (Fig. 16).

TEM examination of the renal cortex of the hyperlipidemic treated with AIW group revealed a regular glomerular basement membrane with average thickness. The glomerular capillaries were lined by the endothelial cells and surrounded by podocytes with their regular foot processes. Increased deposition of the mesangial matrix was observed but with a lesser extent as compared with that of group 3 (Fig. 17). The proximal convoluted tubule showed preserved apical microvilli, euchromatic nuclei, rounded scanty mitochondria and few electron-dense lysosomes (Fig. 18). The distal convoluted tubule showed rounded, euchromatic nuclei and several mitochondria (Fig. 19).

C. Statistical results:

The lipid profile (Graph 1):

Analysis of variance revealed significant increase in serum levels of total triglycerides, total cholesterol, LDL with low level of HDL in hyperlipidemic rats as compared with the control

rats (*P*< 0. 01). Group 4 showed significant reduction in the levels of total triglycerides, total cholesterol, LDL and increased level of HDL as compared to the hyperlipidemic group (*P*< 0. 01).
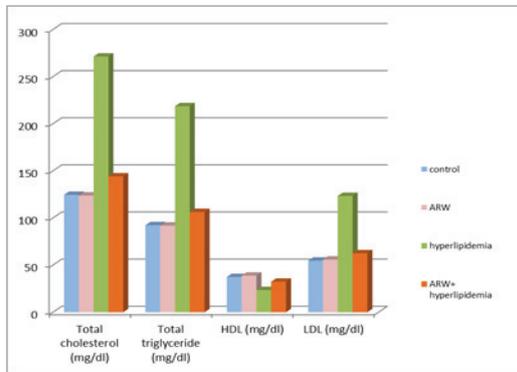
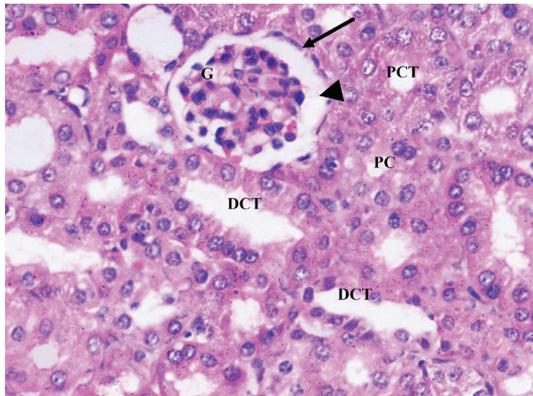**Graph 1:** lipid profile of all groups.

Fig. 1: A photomicrograph of the renal cortex of a control rat showing the normal architecture of the glomerulus (G) with its capillary tufts surrounded by the renal space (arrow head), proximal convoluted tubules (PCT) and distal convoluted tubules (DCT). The parietal layer of Bowman's capsule is lined by simple squamous epithelium (arrow).   H&E × 400
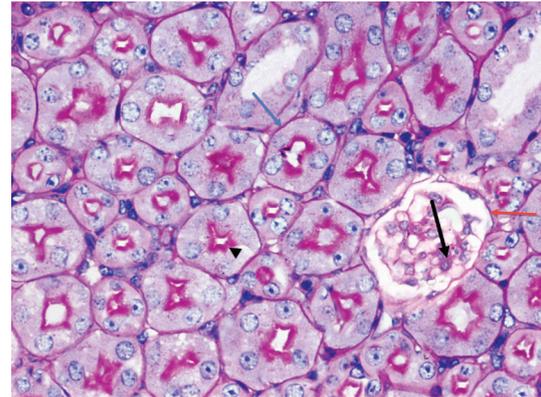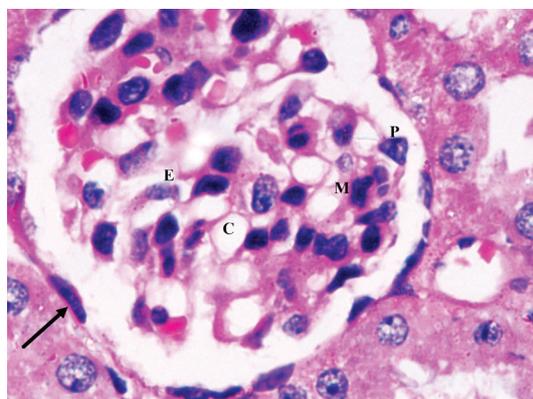
Fig. 3: A photomicrograph of the renal cortex of a control rat showing positive reaction in the basement membrane of glomerular capillaries (black arrow), the renal tubules (blue arrow) and Bowman's capsule (red arrow). The reaction can also be seen in the brush border of the proximal convoluted tubules (arrow head) .   PAS × 400
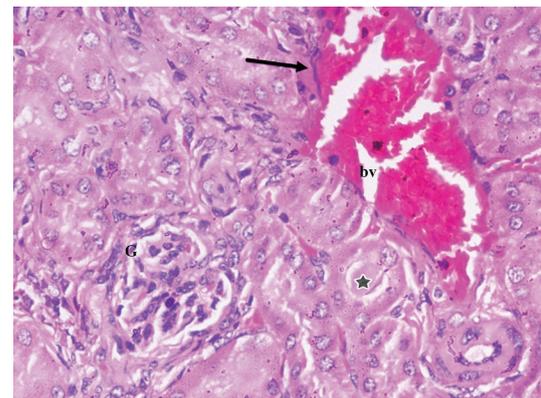

Fig. 4: A photomicrograph of the renal cortex of hyperlipidemic rat showing a hypercellular glomerulus (G) with obliterated Bowman's space. Notice the congested dilated peritubular blood vessel (bv), the interstitial acidophilic material (arrow) and the tubular luminal hyaline casts (star).   H&E ×400

Fig. 2: A photomicrograph of the renal cortex of a control rat showing the simple squamous epithelium lining the parietal layer of Bowman's capsule (black arrow). Notice Podocytes (P), the glomerular capillaries (C), endothelial cell (E) and the mesangial cells (M).   H&E × 1000
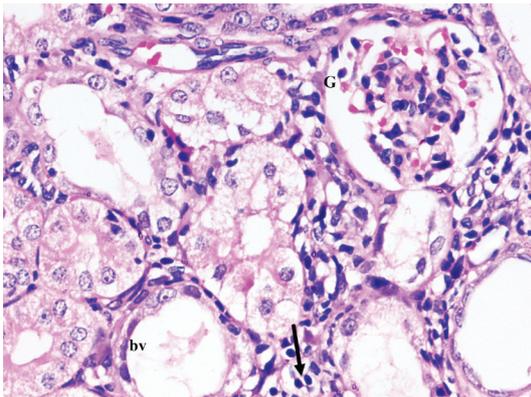
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Fig. 5: A photomicrograph of the renal cortex of hyperlipidemic rat showing wide interstitium with mononuclear cellular infiltration (arrow). Notice the thick wall dilated blood vessel (bv) and hypercellular glomeruli with dilated Bowman's space (G). H&E ×400

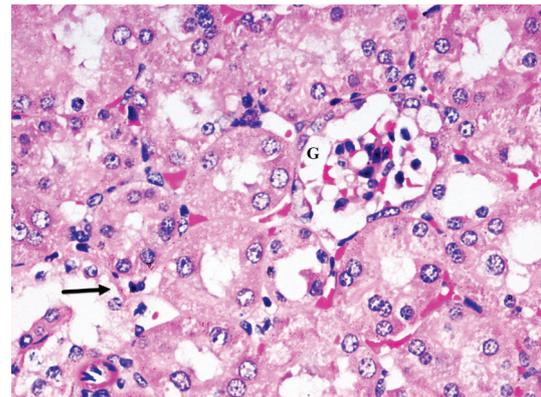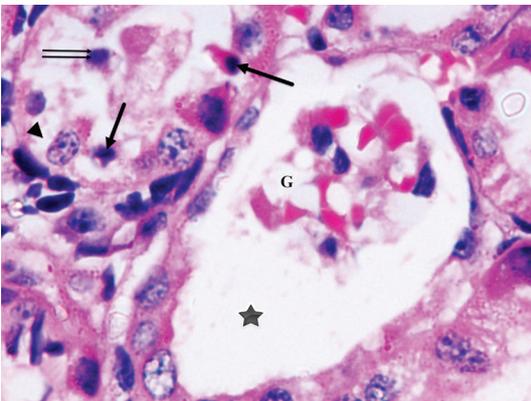**Fig. 6:** A photomicrograph of the renal cortex of hyperlipidemic rat showing a shrunken glomerulus (G) with few dense nuclei and apparent widening of the Bowman space (star). The epithelial lining of some renal tubules shows cytoplasmic vacuolation (arrow heads) and pyknotic (arrow) or exfoliated nuclei (double arrow). H&E ×1000

Fig. 8: A photomicrograph of the renal cortex of hyperlipidemic rat treated with AIW showing preservation of the glomerular structure (G) and restoration of their tubular lining epithelium. Notice cytoplasmic vacuolation in the lining epithelium of a few tubules (arrow). H&E ×400
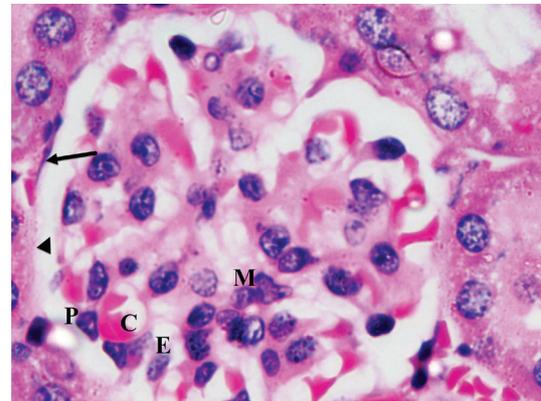

Fig. 9: A photomicrograph of the renal cortex of hyperlipidemic rat treated with AIW showing a glomerulus surrounded by a Bowman's space (arrow head). The arrow points to the simple squamous epithelial lining of the parietal layer of Bowman's capsule. Notice Podocytes (P), the glomerular capillaries (C), endothelial cell (E) and the mesangial cells (M). H&E × 1000
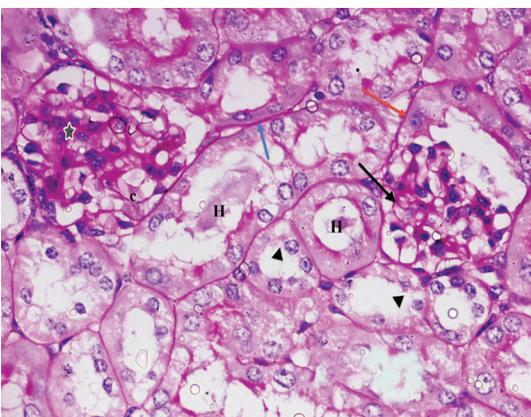
Fig. 7: A photomicrograph of the renal cortex of hyperlipidemic rat showing a weak and disrupted reaction of the brush border (arrow head) of the proximal convoluted tubules. A strong positive reaction of basement membrane of glomerular capillaries (black arrow), the tubular basement membrane (blue arrow) and thick wall Bowman's capsule (red arrow) can also be observed. Notice the positively stained hyaline casts (H). Notice also a glomerulus with mesangial expansion (star), congested capillaries (c). PAS × 400
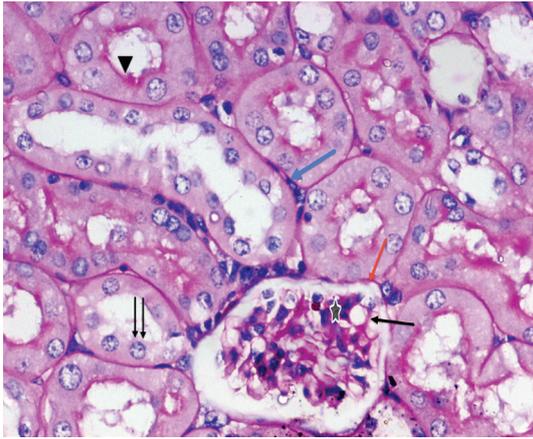
Fig. 10: A photomicrograph of the renal cortex of hyperlipidemic rat treated with AIW showing a positive reaction in the basement membrane of glomerular capillaries (black arrow), the renal tubules (blue arrow) and Bowman's capsule (red arrow). Notice the positive reaction of the preserved brush border (arrow head) of proximal convoluted tubules. Notice also the mesangial expansion of a glomerulus (star).   PAS × 400

Fig. 11: An electron micrograph of the renal cortex in control rats showing glomerular capillaries (C) lined by the endothelial cell (E) and surrounded by podocytes (P) with their primary (white arrow) and secondary (black arrow) foot processes. Mesangial cells (M) surrounded by mesangial matrix (star) are also seen. Notice the uniform thickness of the glomerular basement membrane (arrow head).   × 5000
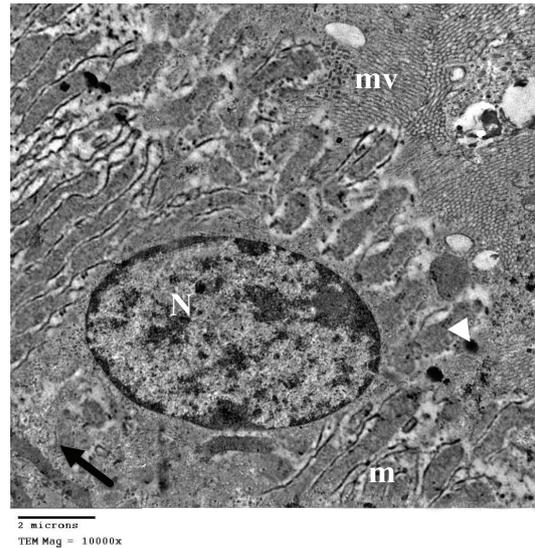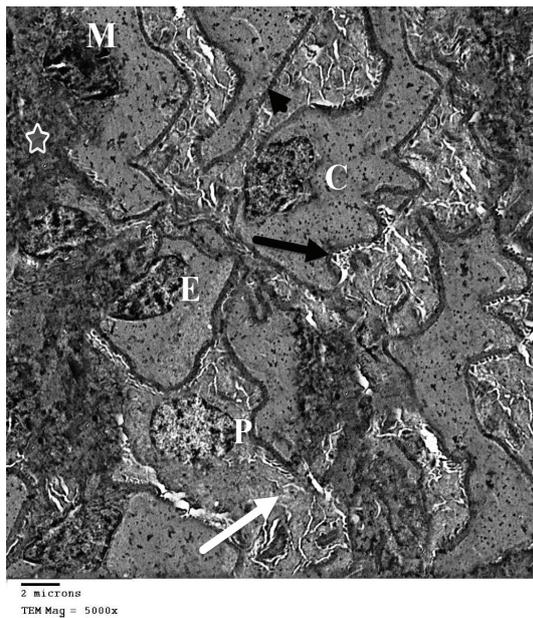

Fig. 12: An electron micrograph of a cell lining of a proximal convoluted tubule in control rats showing basolateral plasma membrane invaginations (arrow), rounded euchromatic nucleus (N), elongated basal radially arranged mitochondria (m), electron-dense bodies (arrow head) and numerous apical microvilli (mv).   × 10000
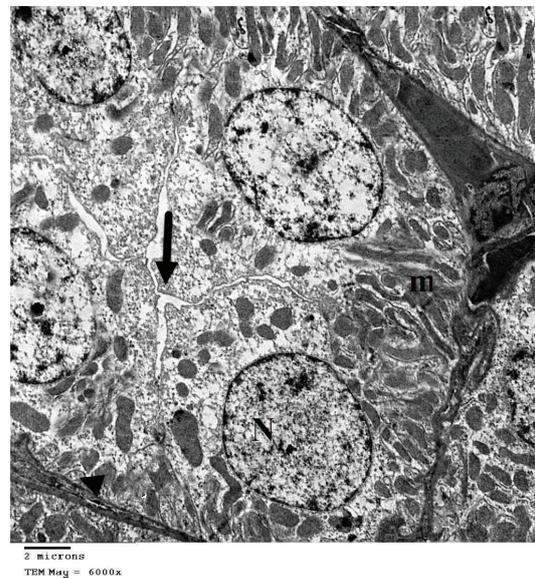

Fig. 13: An electron micrograph of the cells lining the distal convoluted tubule in control rats apical euchromatic nuclei (N), basolateral plasma invaginations (arrow head), elongated basal mitochondria (m) and a few blunt apical microvilli (arrow).   × 6000

Fig. 14: An electron micrograph of the renal cortex in hyperlipidemic rats showing the glomerular capillaries (C) with thickened basement membrane (arrow head) and lipoprotein accumulation (LP). Some podocytes showed peripheral condensation of heterochromatin (P) with effacement of their foot process (arrow). Notice the mesangial cell with irregular nuclear envelope and partial margination of heterochromatin of nuclei (M), excessive mesangial matrix deposition (star) and pyknotic nucleus of endothelial cell (E).   × 5000

Fig. 16: An electron micrograph of the distal convoluted tubule in hyperlipidemic rats showing large, lipid droplets (ld) in the upper part of its lining cells with fine granular appearance of the cytoplasm, and swollen mitochondria (m), while other mitochondria are small and irregularly arranged (arrow head). N = nucleus.
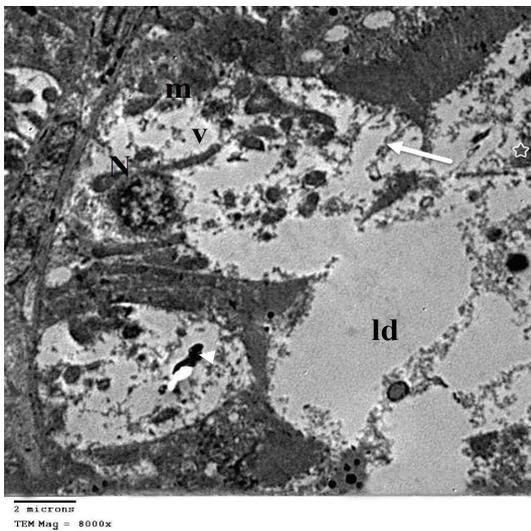
× 6000

Fig. 15: An electron micrograph of a cell lining of a proximal convoluted tubule in hyperlipidemic rats showing pyknotic nuclei (N) with peripheral heterochromatin. Notice the vacuolated cytoplasm (v), disintegration and fragmentation of mitochondria (m), focal destruction of apical microvilli (white arrow) large lipid droplets (ld), electrone dense bodies (arrow head) and a luminal cast (star).   × 8000
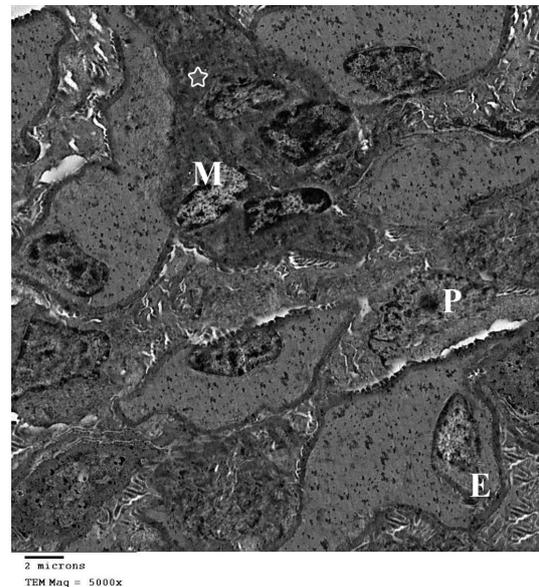

Fig. 17: An electron micrograph of the renal cortex in hyperlipidiamic treated with AIW rats showing the relatively preserved structure of the glomerular capillaries lined by the endothelial cell (E) and surrounded by podocytes (P) and their processes. Notice mesangial cells (M) surrounded by mesangial matrix (star).   × 5000
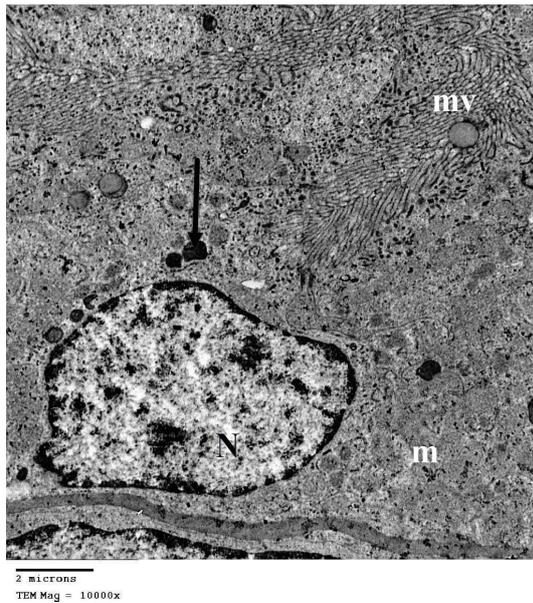
Fig. 18: An electron micrograph of a cell lining of a proximal convoluted tubule in hyperlipidiamic treated with AIW rats showing reappearance of their apical microvilli (mv), euchromatic nuclei (N), mitochondria (m), electron-dense lysosomes (arrow).   × 10000
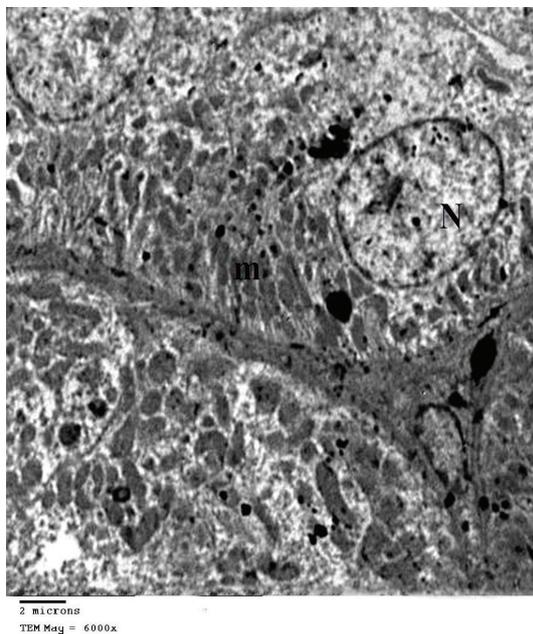

Fig. 19: An electron micrograph of the distal convoluted tubule in hyperlipidiamic treated with AIW rats showing its cell lining with rounded, euchromatic nuclei (N) and several mitochondria (m).   × 6000

DISCUSSION

Disturbed lipid metabolism has been considered a possible cause of renal disease. Hyperlipidemia is contributed to the progression of primary kidney diseases. Proteinuria associated with elevation in serum cholesterol and triglycerides twice increased the possibility to cause renal dysfunction as compared to proteinuria with normal lipid profile. Treatment with antihyperlipidemic agents had been demonstrated to decrease lipid parameters and to improve renal function *(Dalrymple and Kaysen, 2008).*

The current study revealed that high fat diet resulted in hyperlipidemic changes. There were increased serum levels of triglycerides, total cholesterol, LDL and low level of HDL as compared to control. This finding is in accordance with that of *Noeman et al., (2011).*

Hyperlipidemia is characterized by increased serum levels of triglycerides, cholesterol or both. It causes lipid accumulation in various organs such as liver, kidney and pancreas *(Sano et al., 2004).*

In the present study, hyperlipidemia caused several glomerular changes as thickened glomerular basement membrane, shrunken glomeruli and obliterated Bowman's space. TEM examination revealed lipoprotein accumulation in glomerular capillaries, degenerated endothelial cell, areas of disruption of foot process of the podocytes, excessive mesangial matrix deposition around the degenerated mesangial cells.

The thickening of the glomerular basement membrane was in agreement with the finding of *(Selim et al., 2013).* The glomerular basement membrane matrix structure altered by reactive oxygen species and became more permeable and passed more proteins than normal basement membrane *(Shah, 1995).*

Greiber et al. (1998) explained podocyte injury on the basis of hyperlipidemia-induced oxidative stress. In contrast, *Bruneval et al. (2002)* suggested that the podocyte is not affected in cholesterol-induced glomerular injury. Foot process effacement observed in this

study was in line with the finding of *Abdel-Hafez et al., (2011)* who explained that this effacement represented alteration in cell to cell connections, which ranged from shortening of the processes to a complete loss of the inter-digitating foot process.

Foot process effacement leads to focal epithelial defects so that albumin selectively leaks leading to proteinuria. The definitive podocytes lesion was the detachment from the glomerular basement membrane, attachment of glomerular tufts to the Bowman's capsule obliterating the renal space, and the denuded capillary came into contact with parietal cells of Bowman's capsule *(Kriz et al., 1998)*.

In the present study, mesangial expansion, congestion and dilatation of the glomerular capillaries were observed. These are in agreement with the findings of *(Bruneval et al., 2002)*. In contrast, *(Balarini et al., 2011)* reported that hypercholesterolemia didn't affect the glomerular tuft and Bowman's capsule in ApoE mice. Moreover they explained the mesangial expansion by the accumulation of lipids in the macrophages to form foam cells *(Balarini et al., 2011)*.

In hyperlipidemia, the circulating lipids bind to and become trapped by extracellular matrix molecules and oxidation occur forming reactive oxygen species, such as hydrogen peroxide and superoxide anion. Lipoprotein oxidation plays a key role in increased matrix deposition *(Abrass, 2004)*.

With regard to the renal tubules, the current study revealed variable degrees of damage in the renal cortex of the affected group. These included loss of basal infoldings, intracellular vacuoles, pyknotic or exfoliated nuclei, variable degrees of mitochondrial degeneration, numerous lipid droplets, partial loss of apical microvilli in proximal convoluted tubules and tubular luminal casts.

Dyslipidemia induces affection of renal lipid metabolism by disturbance of lipogenesis and lipolysis in the kidney; systemic metabolic alterations and subsequent Pyknotic configuration of mitochondria indicating impaired oxidative phosphorylation *(Selim et al., 2013)*.

Excess fatty acids delivered to the kidney were esterified and deposited as triglycerides in intracellular lipid droplets. Lipid accumulation in cells, that couldn't handle large lipid loads, has been associated with cellular injury. This process has been known as lipotoxicity which causes mitochondrial potential loss with ATP depletion and activation of apoptosis *(Unger et al., 2010)*.

Glomeruli and renal tubules (particularly proximal tubules) were considered as being most vulnerable to lipid accumulation due to the absence of a basement membrane that separates the mesangium from the capillary stream and the fenestrated epithelium lining the glomerular and peritubular capillaries *(Bobulescu, 2010)*.

Hyperlipidemia might affect the kidney directly by causing injurious renal lipid effects (renal lipotoxicity), and indirectly through oxidative stress, systemic inflammation, vascular damage and hormonal changes *(Ruan et al., 2009)*.

It was suggested that renal tubular damage might also be caused by low urinary pH and weak ammonium urinary excretion with mitochondrial dysfunction in proximal tubular cells *(Bobulescu, 2010)*.

Renal tubular damage was also suggested to be secondary to hyperlipidemia-induced glomerular injury and proteinuria leading to obstruction of tubular lumina by protein casts *(Rasch et al., 2002)*.

In this study, AIW supplementation revealed a noticeable improvement of hyperlipidemia-induced renal structural changes in renal corpuscles and tubules by light and electron microscopic examination. These protective effects of alkaline water on renal cortical structure were associated with a marked correction of serum lipid profile.

Salemi et al., (2015) concluded that daily intake of AIW can improve the antioxidant activity and the serum lipid parameters and could lower the risk of oxidative stress diseases.

It was demonstrated that AIW had a protective effect against the accumulation

of lipid and cholesterol in the body *(Jin et al., 2006)*. AIW had been reported to reduce oxidative stress in patients with chronic renal disease *(Huang et al., 2003)*.

It is suggested that the moderately alkaline nature of the water might affect cholesterol, dietary lipids absorption and also might increase bile acid excretion. It is stated that the absorption rate of fatty acid and cholesterol from the small intestine favors a lower pH *(Linscheer et al., 1994)* and that the pancreatic enzymes and bile action were improved by the addition of pH. Therefore, the high luminal pH induced by the alkaline water might decrease the uptake of both cholesterol and fat. AIW could increase bile excretion with and without a meal *(Albertini et al., 2007)*.

AIW exhibits high pH that affects its water molecules hence decreasing water cluster size. This little cluster molecules efficiently enter the cells and increase intracellular hydration so removing waste from accumulating in the cell *(Ignacio et al., 2013)*.

Fat plays significant roles in immune functions by releasing inflammatory cytokines like TNF-α, IL-1β, and IL-6 *(Aggarwal, 2010)*. As such, obesity caused disturbed cytokine balance. AIW administration regained pro- and anti-inflammatory cytokine balance that was disturbed by high fat diet *(Chang et al., 2011)*.

CONCLUSION

alkaline water protected the kidney from hyperlipidemia-induced deleterious effects. It can play important role in preventing renal cortical damage and disturbed serum lipids associated with dietary hyperlipidemia. Therefore, consumption of alkaline water is advised particularly for those who consume a high-fat diet.

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الماءالقلوى المؤين يقلل من التغييرات التركيبية والتركيبيةالدقيقة فى القشرة الكلوية الناجمه عن ارتفاع الدهون فى الدم فى الجرذان البيضاء البالغة

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ملخص البحث

الخلفية: يعتبر ارتفاع الدهون فى الدم بوصفه مشكلة طبية واجتماعية كبيرة ويؤدي إلى زيادة معدلات الاعتلال والوفيات. وقد اعتبراختلال التمثيل الغذائي للدهون كسبب محتمل لأمراض الكلى. وقد وصف الماء القلوي المؤين بتأثيره الفعال في الوقاية من الأمراض المؤثرة سلبا على نمط الحياة.

الهدف من الدراسة: لدراسة قدرة الماء القلوي المؤين للحد من الآثار المدمرة ارتفاع الدهون فى الدم على القشرة الكلوية فى الجرذان البيضاء البالغة.

المواد والطرق: تم تقسيم أربعين من ذكور الجرذان البيضاء إلى أربع مجموعات، عشرة فئران لكل منهم. المجموعة (1) وشملت الجرذان الضابطة، المجموعة (2) وشملت الجرذان التي تلقت الماء القلوي المؤين ، المجموعة (3) ارتفاع الدهون فى الدم: الجرذان التي تغذت على غذاء مذود بنسبة عالية من الدهون يوميا لمدة اثنى عشر أسبوعا والمجموعة (4) وشملت الجرذان المعرضة لارتفاع الدهون فى الدم كما هو الحال في مجموعة وتم علاجها بالماء القلوي المؤين.

النتائج: وأظهر فحص الكلى من المجموعة (3) العديد من الكبيبات المنكمشة مع طمس فراغ بومان، كما لوحظ العديد من الأنابيب المنتفخه الممتلئه بالقوالب الزجاجيه ، مع وجود اتساع بالنسيج بين الأنابيب الكلوية والذى يحتوى على خلايا المناعية وحيدة النواة.واوضحت المقاطع المصبوغه بكاشف شيف الحامضى تفاعل ايجابى قوى فى الغشاء القاعدي الكبيبي، والغشاء الأنبوبي ،وغشاء حوصلة بومان السميك. بينما خميلات الأنابيب الملتوية الدانيه اظهرت تفاعل ضعيف ومضطرب. كما أظهر الفحص الدقيق تراكم البروتين الدهني في الشعيرات الدموية الكبيبية. وقد لوحظت قطرات دهون عديدة في الأنابيب الملتوية وخاصة الأنابيب الملتوية الدانيه. وأظهرت الأنابيب الملتوية وجود ميتوكوندريا ممزقة ومتورمه. وقد سجل مستوى الدهون لهذه المجموعة اعلى مستوى فى الكولسترول، والدهون الثلاثية، والبروتين الدهنى منخفض الكثافة. في حين لوحظ انخفاض فى مستوى البروتين الدهني عالي الكثافة. كشفت دراسة المجموعة (4) أن معظم الشعيرات الدموية الكبيبية احتفظت بمظهرها الطبيعي مع الحفاظ على الخلايا الطلائيه المبطنه لجدار الأنابيب الملتوية. كما أظهرمستوى الدهون من هذه المجموعة تحسنا كبيرا بالمقارنة مع مجموعة 3.

الخلاصة: استهلاك الماء القلوي المؤين يمكن أن تحمي الكلى من الآثار الضارة الناجمة عن ارتفاع الدهون فى الدم. ويمكن أن تلعب دورا هاما في منع الضرر عن القشرية الكلوي ومنع الاختلال فى مستوى الدهون في الدم المرتبط بتناول غذاء مذود بنسبة عالية من الدهون.