Study of the effect of low-dose aspirin on physiological and biochemical parameters of patients with diabetes and hypertension in Thi-Qar governorate

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Abstract---Background: Aspirin has been widely used around the world for more than 100 years. Aspirin has a wide range of biological activities and clinical applications that interact with cellular signaling and metabolism, especially in diabetics and hypertensive. It acts as an antiplatelets drug. Objectives: To compare the effects of aspirin on patients with diabetes and high blood pressure who use aspirin with those who do not use aspirin by studying the effects of aspirin on a group of chemical, immunological, and hormonal tests and knowing the extent of the effect of aspirin on those parameters to determine the usefulness of aspirin for those who use it. Methodology: In the current study, only male patients with diabetes and hypertension were selected, meaning the same patient with type 2 diabetes and hypertension was divided into three groups. The first group had diabetes-hypertension and used aspirin, the second group had diabetes-hypertension and did not use aspirin, and the third group was the control group. Samples were taken and tests were conducted at the specialized center for endocrinology and diabetes after obtaining the patient’s consent on a special form. Results: It was found that the use of low-dose aspirin (100 mg) can be beneficial for patients with diabetes-high blood pressure. Through the experiment, it was found that there are statistically significant differences between aspirin abusers and non-aspirin users, especially with the presence of
multiple risk factors for patients, such as age, obesity, and smoking, and the differences were positive for aspirin users.

**Keywords**—Aspirin, diabetes mellitus, hypertension, platelets, dyslipidemia.

**Introduction**

Aspirin has a clear role in reducing cardiovascular disease and mortality in high-risk patients with myocardial infarction or stroke, and secondary prevention (Collins *et al.*, 2009). According to the American Diabetes Association (ADA) and the American Heart Association (AHA), aspirin therapy (75 to 162 mg/day) is indicated as a primary prevention strategy in patients with diabetes who are at increased cardiovascular risk, including those over 40 years of age or who have additional risk factors such as a family history of diabetes and hypertension, smoking, CVD, dyslipidemia, and albuminuria (Buse *et al.*, 2007). Aspirin widely prescribe low-dose aspirin to patients for secondary prevention of cardiovascular disease (CVD) because the benefit is well known compared to the potential for major bleeding (Rodriguez *et al.*, 2020). One of the important medical benefits of aspirin is the suppression of platelet aggregation by inhibiting the cyclooxygenase enzymes (Hinz, *et al.*, 2007). Low-dose aspirin therapy is critical because discontinuing it carries significant clinical and risks, including an increase in the consequences of ischemic and CVD in secondary prevention users (Soriano *et al.*, 2013). Diabetes mellitus (DM) is a major public health problem worldwide, it is considered a major obstacle to health care in the twenty-first century. However, the World Health Organization has defined diabetes as an endocrine metabolic problem recognized by chronic hyperglycemia with a significant problem with carbohydrate, protein and fat metabolism as a result of a lack of insulin production or a defect in insulin action (Chowdhury, 2014; WHO, 2016). In addition, diabetes mellitus is associated with long-term macrovascular and microvascular complications, morbidity, mortality, and economic and social impact, and health care costs include cardiovascular disease (CVD), peripheral arterial disease, and Cerebrovascular disease. Microvascular complications include retinopathy, nephropathy, and polyneuropathy (Chawla, Chawla and Jaggi, 2016; Aung, 2017). Diabetes is the fifth leading cause of death worldwide, with approximately 3 million deaths per year, and the main causes of increased mortality in diabetes are atherosclerosis, cardiovascular disease, and kidney failure. Atherosclerosis is a cardiovascular disease that affects the arteries of the heart and many peripheral vascular diseases and strokes occur in patients with diabetes at a higher rate compared to non-diabetics (Thabah and Sharma, 2018). High blood pressure is one of the most common non-communicable diseases among adults around the world and is a significant risk factor for early cardiovascular disease. In addition, because of its increasing health burden around the world, high blood pressure is a major global health issue, According to the World Health Organization (Hypertension, 2020; Azegami *et al.*, 2021). An estimated 1.28 billion people worldwide suffer from high blood pressure, a rise in the number of people with hypertensive infections has been observed globally in the past 30 years (Risk and Collaboration, 2021). They also lead to 10.4 million deaths per year (Stanaway *et al.*, 2018). In addition, hypertension is known to be
the most important factor, that increases the risk of premature cardiovascular diseases (Yusuf et al., 2019). Every 20-mmHg increase in systolic blood pressure (BP) is related to a more than 2-fold rise in death rates from stroke and ischemic heart disease in middle-aged people, because stroke and heart disease contribute to the impairment of people in daily living (Dunlay et al., 2015; Id et al., 2019). Despite this, it is important to control high blood pressure to avoid complications and life-threatening risks, as well as to reduce the cost of health care for individuals with this disease (Gaziano et al., 2009). Hypertension and diabetes mellitus (DM) are the most common conditions that almost always coexist. In addition, both are risk factors for cardiovascular disease and microvascular complications, so it is essential that both conditions are treated (Grossman and Grossman, 2017). It was found that 80% of diabetics have high blood pressure and it is more common in T2DM compared to non-diabetics (Whelton et al., 2018). Also, diabetes is associated with many heart diseases and strokes (Emerging and Factors, 2010).

Methodology

The study design

In this study collected 120 blood samples from diabetic-hypertension patients at the Specialized Center for Endocrinology and Diabetes and Nasiriyah Teaching Hospital in Nasiriyah City/Thi Qar Governorate. Those patients were divided into three groups: the first group suffers from diabetes and high blood pressure and takes aspirin; the second group from diabetes and high blood pressure and does not take aspirin; and the third group is a control healthy group. Samples were collected during the months of December 2021 - February 2022 after agreement from the patients. Some personal data and daily habits of the patients were also taken according to a special forma prepared for this purpose, also determining the men patients for this study.

Sample collection

5 ml of blood were collected from patient for each pre-selected group, for a total of 120 blood samples, which were divided into 40 hypertensive and diabetic patients taking aspirin and another 40 hypertensive and diabetic patients not taking aspirin, in addition to 40 healthy people.

Serum preparation

After the blood is pulled, we take 3 ml of the total sample and put it in a gel tube to start the coagulation process, which isolates the serum from the blood. First, we put the gel tube in the centrifuge at 4000 round per minute (rpm) for five minutes to obtain the serum, then we transfer the serum to the Eppendorf tube and store it at minus -20 degrees, and then began the test.

Whole Blood

After the blood is pulled from the patient, 2 ml of blood is drawn and put into an EDTA tube, which is an anticoagulant tube, and then we perform the in vitro
analyses: complete blood count (CBC), Erythrocyte Sedimentation Rate (ESR), Hemoglobin A1C (HbA1c).

**Result**

**Lipid Profile Estimation in Diabetic-Hypertensive Patients and the Control Group**

The current results indicated there were significant differences in all lipid profile parameters, the results also noted the low levels of cholesterol, TG, HDL, LDL, and VLDL in patients using aspirin, while showing the high levels of cholesterol, TG, LDL, HDL, and VLDL in patients who did not use aspirin at a p value < 0.05 as in Table 3-1.

**Table 3-1**
Lipid Profile Estimation

<table>
<thead>
<tr>
<th>Lipid Profile Groups</th>
<th>CHOL Mean ± SD</th>
<th>TG Mean ± SD</th>
<th>HDL Mean ± SD</th>
<th>LDL Mean ± SD</th>
<th>VLDL Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use Aspirin</td>
<td>152.7 ± 33.3</td>
<td>202.5 ± 30.4</td>
<td>24.1 ± 6.7</td>
<td>60.6 ± 17.7</td>
<td>45.4 ± 11.3</td>
</tr>
<tr>
<td>Not Use</td>
<td>187.4 ± 33.1</td>
<td>249.0 ± 65.2</td>
<td>28.8 ± 8.3</td>
<td>82.8 ± 22.4</td>
<td>49.1 ± 15.2</td>
</tr>
<tr>
<td>Control</td>
<td>198.0 ± 24.8</td>
<td>124.2 ± 20.9</td>
<td>41.9 ± 5.5</td>
<td>129.3 ± 24.6</td>
<td>25.2 ± 25.2</td>
</tr>
<tr>
<td>p. value</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>LSD</td>
<td>13.5</td>
<td>19.1</td>
<td>3.0</td>
<td>9.6</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Note the cases in each group are 40 cases

**Liver Function (LF) Estimation in Diabetic-Hypertensive Patients and the Control Group**

The current results showing there were significant differences in all liver function enzymes between the patients and the control group. The results noted the high levels of ALP, AST, and ALT in the patients, and the low level of ALP and increased in ALT level in patients taking aspirin at a p value < 0.05 as in table 3-2.
Table 3-2
Liver function estimation

<table>
<thead>
<tr>
<th>L. Function Groups</th>
<th>ALP Mean ± SD</th>
<th>AST Mean ± SD</th>
<th>ALT Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use Aspirin</td>
<td>184.9 ± 54.6</td>
<td>28.3 ± 5.9</td>
<td>34.0 ± 9.6</td>
</tr>
<tr>
<td>Not Use</td>
<td>220.6 ± 40.7</td>
<td>28.5 ± 6.0</td>
<td>28.3 ± 6.6</td>
</tr>
<tr>
<td>Control</td>
<td>79.45 ± 8.66</td>
<td>11.0 ± 2.0</td>
<td>11.5 ± 2.8</td>
</tr>
</tbody>
</table>

p. value
< 0.05 < 0.05 < 0.05
LSD
17.3 2.2 3.1

Diabetic Parameters and Insulin Estimate in Diabetic-Hypertensive Patients and the Control Group

The current results explain that there were significant differences in all diabetic parameters between the patient groups and the control group. The results noted a high level of HbA1c, insulin, homo-insulin resistance, and fasting blood sugar in the patients at a p value of 0.05, as shown in table 3-3.

Table 3-3
Diabetic Parameter Estimation

<table>
<thead>
<tr>
<th>Diabetic test Groups</th>
<th>HbA1c Mean ± SD</th>
<th>Insulin Mean ± SD</th>
<th>FBS Mean ± SD</th>
<th>Homa-IR Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use Aspirin</td>
<td>8.17 ± 1.71</td>
<td>26.5 ± 7.3</td>
<td>244.1 ± 47.0</td>
<td>16.7 ± 3.91</td>
</tr>
<tr>
<td>Not Use</td>
<td>8.01 ± 1.84</td>
<td>32.1 ± 7.8</td>
<td>231.3 ± 49.0</td>
<td>18.3 ± 4.09</td>
</tr>
<tr>
<td>Control</td>
<td>5.15± 0.35</td>
<td>4.26 ± 0.9</td>
<td>90.82 ± 11.3</td>
<td>0.95 ± 0.23</td>
</tr>
</tbody>
</table>

p. value
< 0.05 < 0.05 < 0.05 < 0.05
LSD
0.65 2.7 17.6 2.16

Estimation of Erythrocyte Sedimentation Rate (ESR) in Diabetic-Hypertensive Patients and Control Group

The current results explain that there were significant differences in immunological parameters ESR between the patient groups and the control
group, with an observed increase in levels of ESR in the patients who did not use aspirin at a p value of 0.05, as shown in table 3-4.

### Table 3-4
Estimation of ESR

<table>
<thead>
<tr>
<th>Immune</th>
<th>ESR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td></td>
</tr>
<tr>
<td>Use Aspirin</td>
<td>19.4 ± 5.4</td>
</tr>
<tr>
<td>Not Use</td>
<td>22.1 ± 6.7</td>
</tr>
<tr>
<td>Control</td>
<td>10.8 ± 1.6</td>
</tr>
<tr>
<td>p. value</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>LSD</td>
<td>2.2</td>
</tr>
</tbody>
</table>

**Discussion**

**Lipid Profile in Diabetic-Hypertensive Patients**

It was found that there were significant differences between patients using aspirin and non-users of aspirin in the lipid profile, lipids are an essential part of the cell components in mammals and are considered an essential partner in biological processes in the human body. Dyslipidemia is described as a change in level or abnormality in one or more of the lipid profiles in the body, such as increased total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), decreased high density lipoprotein (HDL) and very low density lipoprotein (VLDL) (Ni et al., 2015). The results showed that there were significant differences in the lipid profile between aspirin users and non-aspirin users. It was found that cholesterol, triglycerides, low-density lipoprotein and VLDL were higher in those who did not use aspirin. While the control group showed a high level of cholesterol and low-density lipoprotein due to the fact that this group was not fasting when performing the lipid profile test as the patient groups. Although the results were shown to be close to the results of the patient groups. The results of this study showed that they agreed with the results of Alsop et al. (2015) It was found through experiments that aspirin has the property of being attracted to phospholipid membranes, and this leads to a change in the physical and structural properties of the membrane. The current findings agree with those of Paseban et al. (2019), who investigated the effects of aspirin, atorvastatin, captopril, and metformin in diabetes mellitus and found that diabetics who used aspirin had lower cholesterol levels than diabetics who did not use aspirin. The study by Su et al. (2019) recorded the elevated glucose levels, triglycerides, and LDL in diabetics during fasting that accelerate the risk of CV events and found that it offered an additional prognostic benefit in predicting CV events in patients with type 2 diabetes. The TG index includes both triglycerides and fasting
glucose, and it has been demonstrated to be a good marker of insulin resistance and a predictor of T2DM. The higher level of FBS was associated with an increased risk of CV events in the patients with diabetes mellitus and offered an additional prognostic benefit. Abnormal level of glucose metabolism can accelerate the formation of atherosclerosis and plaque, contribute to plaque rupture and thrombosis, and impair normal endothelial function (Mawson et al., 2017).

**Liver Function in Diabetic-Hypertensive Patients.**

The current study found there were significant differences among patient groups and control groups, as well as between patients using aspirin and non-users of aspirin, in the liver function test. The results showed an increase in the levels of ALP in the patients who did not use aspirin. AST did not show any difference between those who used aspirin and non-users of aspirin. However, they show levels higher than the control groups. As well as an increased level of ALT in aspirin users. Our results match those of the National Institute of Diabetes and Digestive and Kidney Diseases (NLM, 2017). Between 2004-2013, an 899-case prospective study in the United States found no incidences of drug-induced liver damage linked to aspirin. According to the age groups and BMI, the results did not show a significant difference in the levels of liver function between those who used and those who did not use aspirin. However, based on smoking, there was a significant difference in the level of AST for non-users of aspirin. Duration and use of aspirin may be associated with hepatotoxicity in medium and high doses, and patients often have elevated ALT enzyme. Hepatotoxicity is usually mild with aspirin and may be accompanied by an increase in bilirubin, and hepatotoxicity may occur due to abnormalities in lipids and mitochondria. There have been no significant reports of aspirin-induced acute liver failure, chronic liver damage, or chronic bile duct syndrome. However, there is a special type of aspirin toxicity called Reye’s syndrome. These results differed from the results of Rafeeq et al, which indicated the opposite of these results (Rafeeq et al., 2016). Salicylate poisoning occurs when the level of salicylate in the blood is greater than the therapeutic dose and may be life-threatening at high doses (Biff F et al., 2020). Also in this study, the results of the ALP enzyme were different from the rest of the studies; the value of ALP for aspirin users was higher than the value of ALP for non-users of aspirin in this study, and thus this study was different from the other studies as stated in the study by Zhang et al., (2017).

**Diabetic Parameters and Insulin in Diabetic-Hypertensive Patients**

The current study reflects significant differences in diabetic parameters among aspirin users and non-aspirin users compared to the control group in HbA1c, Insulin, FBS, and Homa-IR. An extensive review summarizing a group of studies in 2007 that compared HbA1c and FPG with an OGTT as an ideal standard for measuring diabetes found that HbA1c results were similar to those of FPG upon screening. The current results of this study indicated that HbA1c and FBS tests had similar results for diabetic patients. Also recorded were the statistically significant differences between the patient groups and the control group. In a study published by the American Diabetes Association, it was confirmed that early control of high blood sugar has lasting effects in controlling diseases such as cardiovascular conditions and mortality, and this was noted after the end of
the study period and the experience that lasted for 10 years with a low level of HbA1c (Laiteerapong et al., 2019). Furthermore, exposure to HbA1c of 8.0% was associated with an increased risk of developing microvascular events in diabetic patients, whereas exposure to HbA1c of 9.0% in less than 4 years was associated with an increased risk of developing macrovascular events. A Chinese study was conducted to determine the relationship between atherosclerosis in type 2 diabetes patients based on the measurement of HbA1c and a study of the effect of high blood pressure on atherosclerosis. This Chinese study found that patients with HbA1c values as high as 7.0% had a higher level of atherosclerosis, indicating that HbA1c was the key point in the development of complications and is essential to preventing atherosclerosis (Xu et al., 2009). A study by Xu et al. (2009) also showed an increase in arterial stiffness in people with diabetes and high blood pressure, as arteriosclerosis worsens with no control over the high blood sugar level (Levin et al., 2010). In a study conducted by the Kidney Research Institute and Division of Nephrology at the University of Washington, a high concentration of FBS and insulin was shown to be associated with an increased risk of hypertension in a wide group of patients. In addition, these elevated levels were independent of obesity and other factors causing hypertension, so these results support the hypothesis that the damage that occurs to the walls of the arteries and kidneys as a result of high levels of glucose in the blood (Levin et al., 2010). A Japanese study was conducted on a number of patients for the benefit of a group of medical colleges that lasted for 5 years to determine the relationship between high indicators of diabetes and the risk of high blood pressure for the study sample, and concluded that approximately 50% of the participants were exposed to the risks of high blood pressure, and some of them started taking blood pressure medications, and high levels of FBG, HbA1c, and HOMA-IR were also found to be a 2.21-fold risk factor for hypertension (Tatsumi et al., 2019). A Michigan State University study suggests that low-dose aspirin therapy can reduce blood sugar levels in diabetic patients to prevent diabetes complications (Loss et al., 2011). A study by Senarathne et al., measuring FBS and MetS levels in hypertensive and non-hypertensive groups, found that FBS and MetS levels were higher in hypertensive patients than in non-hypertensive patients (Senarathne et al., 2021). A Chinese study also supported these results (Sun et al., 2009). The current study did not record significant differences for FBS depending on age between groups, but it did find significant differences based on body mass in the group of aspirin users in the obesity category, and no significant differences were seen depending on smoking between groups. Also found in this study was a significant difference in the levels insulin and insulin resistance between the patient groups and the healthy group, as the proportion of insulin and insulin resistance was higher among non-users of aspirin than among aspirin users. As a result of insulin resistance, the pancreas secretes more insulin to compensate, resulting in hyperinsulinemia (Reaven, 2012). Research and studies have shown the role of insulin resistance and the complications of insulin resistance on the heart and blood vessels, and their main role in atherosclerosis in both diabetic and non-diabetic patients (Lambie et al., 2022). Gast et al., (2012). Demonstrate that insulin signaling leads to regulation of metabolism through fat storage in adipocytes by inhibiting lipolysis and stimulating triglyceride synthesis. However, the action of the hormone insulin is complex, especially on the blood vessels, sometimes having beneficial and sometimes harmful effects, the positive effect is by activation of endothelial nitric
oxide synthase (eNOS), while the negative effects include stimulating an increase in the number of vascular smooth muscle cells (VSMC), vasoconstriction, and pro-inflammatory activity (Fu et al., 2021).

**Erythrocyte Sedimentation Rate (ESR) in Diabetic-Hypertensive Patients and Control Group**

The current study showed a significant difference in ESR levels among the patient group and the control group, and the ESR was higher among non-users of aspirin, which is evidence of inflammation in patients with diabetes and hypertension, these results were identical with some studies like Undas et al., (2007) that concluded that there is a role for aspirin in increasing the permeability of the fibrinogen network in diabetic patients, as it was found that aspirin has a role in changing some properties of fibrin-fibrinogen and its effect on the properties the fibrin network. Individuals at high risk of cardiovascular diseases, such as patients with diabetes and nephrotic syndrome, as well as patients with manifest Cardio vascular diseases, have a tighter and less permeable fibrin network structure, which appears to be significant in the development of atherothrombotic events(Collet et al., 2006).

**Conclusion**

Aspirin may be useful in the primary prevention of cardiovascular complications in diabetics and hypertension patients, this experience and the experiences of previous researchers demonstrated the benefit of aspirin in reducing risks and complications resulting from diabetes and high blood pressure. As the percentage of harmful fats was lower among aspirin users. In addition to the role of aspirin in reducing the damage of inflammation through its effect on the permeability of the fibrin network and the damage this network causes in the aggregation of red blood cells, platelets, and the rest of the coagulation factors and its participation in thrombus formation, studies have also shown its role in suppressing Akt and mTOR, which may contribute to insulin sensitization through aspirin (Gao et al., 2003).

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