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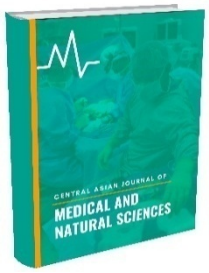

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# Features of the Course of Hypertension among Patients with Type 2 Diabetes Mellitus

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**ABSTRACT**: Type 2 diabetes mellitus (T2DM) is associated with a high risk of early mortality and hypertension. The prevalence of AH is higher in patients with diabetes than in patients without diabetes. The higher prevalence of hypertension among diabetic patients is due to hyperglycaemia, insulin resistance and dyslipidaemia. All these factors cause the development and progression of atherosclerosis by destroying the blood vessel wall, contributing to vascular inflammation and endothelial cell dysfunction, disturbance of various cell types, such as platelets, and promoting coagulation. Thus, age, place of residence, duration of DM2, BMI, cigarette smoking and glycaemic control are significantly associated with hypertension. Studies using a larger sample size are needed to investigate the causes of uncontrolled blood pressure among diabetic patients and to develop appropriate measures for the prevention of cardiovascular complications[2,4,12].

**Keywords**: Diabetes mellitus, arterial hypertension, hypertension, peripheral

**Introduction.** Type 2 diabetes mellitus (T2DM) is associated with a high risk of early mortality and morbidity from cardiovascular disease (CVD) such as hypertension (AH), stroke and end-stage renal failure. Arterial hypertension is the leading cause of morbidity and mortality in patients with T2DM associated with cardiovascular disease. The comorbidity of DM and arterial hypertension is increasing worldwide[1,5,7].

Hypertension contributes to the development and progression of microvascular (retinopathy, nephropathy and neuropathy) and macrovascular (atherosclerotic) complications of diabetes. It is a major risk factor for cardiovascular mortality and morbidity from its effects on target organs such as the brain, heart, eyes and kidneys, due to structural changes in the microcirculation secondary to oxidative stress, inflammation or endothelial dysfunction. Uncontrolled hypertension leads to heart attack, stroke, kidney disease or failure, vision loss, sexual dysfunction and peripheral artery disease (PAD) [6,8]. Hypertension induced organ damage is manifested by elevations in albumin excretion (proteinuria), and left ventricular hypertrophy and the presence of a left ventricular deformity pattern on the ECG. Moreover, the detection of solid exudate, cotton spots, optic disc oedema, retinal haemorrhages and microaneurysms on the fundus and the presence of ischaemic or haemorrhagic brain

damage on brain imaging by computed tomography (CT) are other manifestations of target organ damage caused by hypertension[9, 12]. Eighty per cent of diabetic patients die from CVD, especially from AH and stroke. Moreover, AH exacerbates diabetic cardiomyopathy and accelerates the progression of diabetic renal failure and cardiovascular disease. A study of diabetic patients showed that the coexistence of hypertension with diabetes mellitus was associated with a 44% and 41% risk of death and cardiovascular events, respectively, compared with a 7% and 9% risk in people with diabetes alone [2]. Hypertension is also the largest cause of high costs in patients with diabetes. The prevalence of AH is higher in patients with diabetes than in patients without diabetes [3,14,15]. The higher prevalence of hypertension among diabetic patients is explained by hyperglycaemia, insulin resistance and dyslipidaemia. All these factors cause the development and progression of atherosclerosis by destroying the blood vessel wall, contributing to vascular inflammation and endothelial cell dysfunction, disruption of various cell types, such as platelets, and promoting coagulation. All this leads to vasoconstriction and an increase in the total resistance of the peripheral arteries with the causes of hypertension. Hyperinsulinemia and insulin resistance contribute to high blood pressure, as insulin is known to promote sodium retention and increase sympathetic nervous system activity. In addition, insulin resistance is associated with inappropriate activation of the renin-angiotensin-aldosterone system (RAAS). After activation of the RAAS, several BP-raising mechanisms are activated. For example, angiotensin II, a product of RAAS activation, stimulates vasoconstriction and the production of aldosterone, the hormone responsible for salt and water retention in the kidneys, causing hypertension. In addition, the presence of renal insufficiency secondary to diabetes may impair the ability to excrete water and dissolved substances, thus perpetuating the increase in volume caused by various factors. In addition to DM2, constant salt intake in the diet is also attributed to the development of high blood pressure (BP). A diet high in salt increases the amount of sodium in the blood, which then reduces the kidneys' ability to eliminate water from the body due to its osmotic effect. This excess sodium in the blood causes excess water retention and hence high BP, which in turn puts extra strain on the arterial walls. To cope with this high BP, the arterial muscular layer thickens and increases BP by reducing the space in the vessel. Moreover, high salt intake causes microvascular endothelial inflammation, increased systemic peripheral resistance, changes in endothelial function and modification of sympathetic activity, ultimately leading to hypertension[17,18]. The incidence of arterial hypertension in patients with T2DM depends on the degree of obesity, advanced age and extensive atherosclerosis. A study in Iraq found an 89.6% prevalence of hypertension among diabetic patients, which was associated with age, BMI, insulin use and duration of diabetes. The prevalence of hypertension among patients with DM was 85.6%, 54.2% and 56.3% in Benghazi, Nigeria (54.2%) and Adama, Ethiopia respectively [4,19,20,21]. A study conducted on AD patients in Benghazi showed that hypertension was associated with older age, male gender, duration of AD and overweight. The prevalence of AH depends on type and duration of diabetes, age, gender, race/ethnicity, BMI and glycaemic control history [4,22]. Although hypertension is a significant and controllable risk factor for many diseases, its asymptomatic nature causes many people to develop life-threatening complications. Various studies have shown that 50% of all cases of AH were diagnosed in the study, indicating that AH is an under-diagnosed comorbid condition in patients with diabetes. Information on the prevalence of hypertension around the world is important for developing appropriate policies to counteract the impact of hypertension on DM [20,24,25]. In addition, recognition of the associated factors of hypertension among diabetic patients is important both for health professionals to successfully minimise its impact on patients and for policy-makers to develop appropriate strategies to avoid such factors. However, there is very, very little such data in our country.

The prevalence of hypertension among type 2 DM patients has been studied by many scientists, where they found, 59.5% hypertension among type 2 DM patients, which is consistent with studies in Hosanna (55%), Adama, Ethiopia (56.3%), Botswana (63.1%), and Israel (60.2%) [21,30]. However,

the current data are higher than the prevalence reported in Jimma, Ethiopia (46.5%). A possible reason for this may be due to the presence of an age difference between the two study populations. The age of participants in the Jimma study was <45 years among 48.9% of patients, resulting in a lower prevalence of arterial hypertension, whereas only 22.5% of the population in our study was younger than 50 years with a high proportion of the population over 50 years. This may be a possible reason for the higher prevalence of hypertension, due to the fact that increased age is associated with a higher prevalence of hypertension. The prevalence of hypertension in this study is also higher than in Nigeria (54.2%). This difference could be due to the higher mean duration of DM2 (11.8 years) in the Jonas A. study than in the Nigeria study (6.6 years). Various studies have shown that increased duration of type 2 DM is associated with increased prevalence of arterial hypertension [5, 19,25]. In contrast, the prevalence of AH in this study is lower than the results from Jordan (72.4%) and Iraq (89.6%) [20,28]. The prevalence of hypertension among type 2 DM patients has been studied by many scientists, where they found, 59.5% hypertension among type 2 DM patients, which is consistent with studies in Hosanna (55%), Adama, Ethiopia (56.3%), Botswana (63.1%), and Israel (60.2%) [9,14]. However, the current data are higher than the prevalence reported in Jimma, Ethiopia (46.5%). A possible reason for this may be due to the presence of an age difference between the two study populations. The age of participants in the Jimma study was <45 years among 48.9% of patients, resulting in a lower prevalence of arterial hypertension, whereas only 22.5% of the population in our study was younger than 50 years with a high proportion of the population over 50 years. This may be a possible reason for the higher prevalence of hypertension, due to the fact that increased age is associated with a higher prevalence of hypertension. The prevalence of hypertension in this study is also higher than in Nigeria (54.2%). This difference could be due to the higher mean duration of DM2 (11.8 years) in the Jonas A. study than in the Nigeria study (6.6 years). Various studies have shown that increased duration of type 2 DM is associated with increased prevalence of arterial hypertension [19,25]. In contrast, the prevalence of AH in this study is lower than the results from Jordan (72.4%) and Iraq (89.6%) [5,8]. The chances of getting AH among patients with T2DM are higher in the 50-59 age group than in the <50 age group. This is supported by studies in Israel, Iraq, Botswana and Jordan which report that the prevalence of AH increases with age. This may be due to vascular changes during aging. As we age, arterial stiffness and thickening will be caused by a complex change in each layer of blood vessels. Intimal thickening caused by ageing compromises endothelial integrity and reduces the availability of vasodilators such as nitric oxide. The hardening of the arterial walls disrupts normal blood flow, creating favourable conditions for the accumulation of calcium and fatty deposits within the arteries, leading to further arterial narrowing and the occurrence of hypertension. Patients from urban areas were more prone to hypertension than patients from rural areas. This is consistent with the findings of other studies[13,16,19]. Sedentary lifestyles and changes in eating habits following increasing urbanisation are the main causes of increased hypertension in urban areas. Increased duration of DM2 has been associated with an increased likelihood of developing AH. Consistent with other studies, duration of T2DM is directly related to the prevalence of arterial hypertension. This may be because the effects of hyperglycaemia, dyslipidaemia and insulin resistance will be more pronounced as the duration of T2DM increases[20,28,30]. As duration increases, diabetes-induced changes such as microvascular damage, sympathetic nervous system damage, increased renin-angiotensin system and decreased insulin sensitivity will worsen and exacerbate hypertension. Similarly, age also increases, so blood vessels become stiffer, which in turn is significantly associated with the development of hypertension. Patients with a high BMI are many times more likely to develop hypertension than patients with a normal BMI. This finding is consistent with data from various studies in different countries. A possible rationale for the association between BMI and hypertension is that obesity increases reabsorption of salt and water in the kidneys through direct activation of mineralocorticoid receptors, which leads to increased blood volume and finally to hypertension. In addition, obesity usually decreases parasympathetic tone and increases sympathetic activity, leading to increased cardiac output and vasoconstriction with a consequent increase in blood pressure. Sympathetic

stimulation and compression of the kidney due to visceral obesity leads to activation of the RAAS, resulting in increased levels of angiotensinogen II and aldosterone in the blood, which increase blood volume through different mechanisms [14,25]. At the same time, angiotensinogen II is a potent vasoconstrictor. These effects together lead to hypertension. Patients with poor glycaemic control had a higher chance of hypertension than patients with good glycaemic control. This finding is consistent with that of many other studies. This association is explained by persistent hyperglycaemia. Excess glucose chemically attaches to free amino groups of proteins, collagen and other long-lived proteins in the blood vessel walls, which in turn can trap circulating low-density lipoprotein (LDL), which promotes cholesterol deposition in the intima, thereby accelerating atherogenesis and subsequent hypertension. In addition, hyperglycaemia increases the osmolality of extracellular fluid, causing water to move from intracellular to extracellular space and causing increased volume and high BP. Patients with diabetes who currently smoked cigarettes were more likely to develop AH than those who did not. This finding is consistent with other studies. This could be the result of the ill effects of nicotine and other ingredients in cigarettes on blood vessels. Nicotine inhibits vasodilation by disrupting nitric oxide production. It also stimulates the release of catecholamine, which increases platelet aggregation, thrombosis and vasoconstriction. In addition, nicotine causes insulin resistance, dyslipidaemia, vascular inflammation and abnormal vascular growth. Activation of endogenous free radicals by nicotine or free radicals directly from cigarette smoke leads to oxidative stress, which is a major factor in the development of atherosclerosis. All these effects constrict blood vessels and predispose to hypertension[20,23] .Age, cigarette smoking and high BMI (≥25 kg/m2), which were significantly associated with arterial hypertension in patients with T2DM in the current study, were also significantly associated with arterial hypertension in patients without diabetes in other studies. But the extent to which the above factors are associated with hypertension is different in the two populations. In diabetics, they are more strongly associated with hypertension. Current diabetic smokers in the current study had a higher probability of hypertension (3.9%) than current non-diabetic smokers in Nepal (2.0%), Jordan (1.8%), Jilin Province, China (1.2%), and Kenya (1.1%). The likelihood of hypertension (3.7%) in diabetics with high BMI was higher than in nondiabetics with the same high BMI in Nepal (1.2%), Ethiopia (2%), Kenya (2.4%), and Greece(2.6%). Similarly, older patients with diabetes are more likely to have hypertension than older people without diabetes in various studies. These results suggest that these factors of hypertension are worse in people with DM2 than in patients without DM [22,27,29].

**Conclusions:** Thus, age, place of residence, duration of DM2, BMI, cigarette smoking and glycaemic control are significantly associated with hypertension. Studies using a larger sample size are needed to investigate the causes of uncontrolled blood pressure among diabetic patients and to develop appropriate measures for the prevention of cardiovascular complications.

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