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The Role of Insulin Resistance in the Development of Hypertension: A Case-Control Study

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Annotation: Hypertension represents a significant global health challenge, impacting approximately 1.28 billion adults globally. It is a major risk factor for cardiovascular illnesses, stroke, and renal failure, leading to considerable morbidity and mortality. Despite extensive knowledge and advancements in therapy, the exact mechanisms behind hypertension remain incompletely elucidated, especially concerning the roles of metabolic and inflammatory processes. This study comprises a case-control design involving 150 participants: 100 patients and 50 healthy controls. The research was conducted from October 2023 to July 2024. Patients with hypertension were selected from AL Nasiriyah Teaching Hospital. The age, gender, family history, smoking status, social activity, and food habits of each individual were documented. The history of diseases, certain social activities, HbA1c levels, random blood sugar measurements, and other sociodemographic variables of the patients were collected using a reported technique (questionnaire). Individuals afflicted with hypertension and chronic illnesses. The mean red blood cell count in the patient group was (87.9980±17.83), compared to (68.3716±13.71) in the control group, with a P value <0.05. Conversely, the mean cumulative sugar test did not differ between the groups, with the patient

group at (5.0148±0.43) and the control group at (5.0498±0.22), yielding a P value >0.05. In contrast, insulin and HOMA-IR tests demonstrated elevated levels (7.5478±4.41 and 1.1380±0.73, respectively) as compared to the control group (5.9392±3.81 and 0.6351±0.46, respectively), with a P value of <0.05. Elevated insulin resistance and glucose levels may be regarded as potential factors contributing to hypertension. The initiation of insulin treatment resulted in a considerable increase in both systolic and diastolic blood pressure among the patient group.

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Introduction (*Heading 1*)

1. Introduction

Hypertension, or high blood pressure, is a chronic medical disorder characterised by the sustained elevation of blood pressure against arterial walls. Blood pressure is quantified by two values: Systolic pressure (the arterial pressure during cardiac contraction, represented by the top number) and Diastolic pressure (the arterial pressure during cardiac relaxation, represented by the bottom number). [1]. Normal blood pressure is generally below 120/80 mmHg, however hypertension is identified when measurements routinely exceed 140/90 mmHg or as specified by clinical standards [2]. Hypertension is frequently referred to as the "silent killer" due to its lack of discernible signs until considerable harm has been inflicted on essential organs such as the heart, brain, kidneys, or eyes. It is a significant risk factor for severe health issues such as heart disease, stroke, and kidney failure.

Hypertension is a significant global health issue impacting around 1.28 billion persons globally. It is a major risk factor for cardiovascular illnesses, stroke, and renal failure, leading to considerable morbidity and mortality [4]. Despite extensive awareness and advancements in treatment, the exact mechanisms underlying hypertension remain incompletely elucidated, especially concerning the roles of metabolic and inflammatory processes [5].

Oxidative stress is associated with the onset and advancement of numerous diseases, principally through its role in chronic inflammation, cellular damage, and disrupted physiological functions.

Oxidative stress denotes the disparity between the generation of reactive oxygen species (ROS) and the organism's capacity to mitigate these detrimental chemicals using antioxidants. This imbalance may result in vascular injury and inflammation, both of which are pivotal in the onset of hypertension [7]. Research indicates that hypertension people display elevated levels of oxidative stress indicators relative to normotensive individuals, implying that oxidative stress significantly influences blood pressure regulation [8].

Reactive oxygen species (ROS) contribute to endothelial dysfunction, a critical component in the pathogenesis of hypertension and atherosclerosis. Oxidative stress induces inflammation and diminishes the bioavailability of nitric oxide (NO), a vital vasodilator for sustaining vascular health, by harming endothelial cells [9]. Oxidative stress contributes to the advancement of insulin resistance by disrupting insulin signalling pathways.

Reactive oxygen species (ROS) can obstruct insulin receptor substrate (IRS) functionality, leading to diminished glucose absorption in cells [10].

Insulin resistance is a pathological state wherein the body's cells exhibit diminished responsiveness to the hormone insulin, hindering glucose's entry into the cells and its subsequent utilisation for energy. This dysfunction is pivotal in the onset of type 2 diabetes, metabolic syndrome, and is associated with obesity, cardiovascular disease, and non-alcoholic fatty liver disease (NAFLD) [11].

Insulin resistance may manifest in multiple tissues, such as the liver, skeletal muscle, and adipose tissue. The pathogenesis entails a complex interaction of genetic, environmental, and behavioural variables, with oxidative stress, inflammation, and changes in lipid metabolism serving critical roles [12].

Insulin resistance, a characteristic of type 2 diabetes and metabolic syndrome, is also associated with the onset of hypertension. It is marked by the reduced capacity of cells to respond to insulin, resulting in hyperglycemia and compensatory hyperinsulinemia [13]. The hyperinsulinemic condition can lead to heightened salt retention, vascular rigidity, and compromised vasodilation, all of which raise blood pressure. Evidence indicates a robust link between insulin resistance and hypertension, as persons with insulin resistance are more predisposed to developing high blood pressure than those who are insulin-sensitive [14].

This study sought to examine the influence of insulin resistance on the onset of hypertension.

Materials and Methods

Study Design

The present study has a case-control design including 150 subjects: 100 patients and 50 healthy controls. The research was conducted from October 2023 to July 2024. Patients with hypertension were selected from AL Nasiriyah Teaching Hospital. The age, gender, family history, smoking status, social activity, and food habits of each individual were documented. The history of diseases, certain social activities, HbA1c levels, random blood sugar measurements, and other sociodemographic variables of the patients were collected using a reported technique (questionnaire). Individuals afflicted with hypertension and chronic illnesses.

inclusion Criteria

Participants were chosen based on the following criteria: individuals (male and female) aged between 25 and 60 years with a BMI under 25, all diagnosed with hypertension and devoid of any comorbidities, as well as no history of myocardial infarction or angina. A comprehensive clinical history, clinical examination, and relevant laboratory investigations were conducted on all patients. The physician diagnosed hypertension according to the latest clinical practice recommendations from the WHO. The kind of hypertension was identified through the analysis of laboratory measures during the clinical evaluation of hypertension.

Exclusion criteria

Exclusion criteria for diabetic patients include individuals undergoing immunosuppressive medicine, such as corticosteroids, those with autoimmune diseases, and patients with myocardial infarction (MI) or angina. Surgery, antioxidant supplementation, pregnancy, persistent infections, and chronic diseases.

Study variables

Independent Variable: Age, gender and some social activities. Clinical Chemistry : Fasting insulin , Random Blood Sugar (RBS) ,Hemoglobin A1c (HbA1c) .

Approval of the Ethical Committee

The protocol for the study was approved by the Ethical Committee in Basrah pharmacy College .

Ethical Committee and the cardiologist consultant unit committee at L_Hussein Teaching hospital , Serum samples were obtained with the agreement of patients.

Specimen Collection

1. Blood sample Collection

Blood samples were collected from all participants by the staff in the outpatient section of Al Hussein Teaching Hospital. Five millilitres of blood were extracted via venipuncture using 5 millilitre disposable syringes and subsequently allowed to stand at room temperature for fifteen minutes in a plain tube.

2. Serum Separation

Serums were isolated by centrifugation for 10 minutes at 4000 xg. To reduce several freeze-thaw cycles, serum samples were preserved at -20°C for further analysis. Disposable, non-pyrogenic, and endotoxin-free blood collection tubes were utilised.

Assay Procedure for Random Blood Sugar (RBS) measurement

Reagents and Materials

- ✓ Glucose reagent (GOD-POD method) (Ready-to-use, single-reagent system)
- ✓ Calibrators and controls (Traceable to reference standards)
- ✓ Distilled water for reagent preparation and washing
- ✓ Serum or plasma samples (Collected in fluoride-oxalate, EDTA, or heparin tubes).

Results

Demographics distribution of study groups

Our collected samples included ,100 patients suffer from hypertension consist of 47 male and 53 female with mean age (56.491±11.57) and mean BMI (27.11±4.98) as patients group ,with 50 individuals consist of 31 males and 19 females with mean age (55.68±8.96) and mean BMI(26.1575±2.214) collected as a control group.As shown in table(1).

Table 1. Demographics, Clinical Parameters, and Blood Pressure Measurements of Patients and Controls

Parameters	Control N (50) mean±SD		Patients N (100) mean±S D	P value
Mean age	55.68±8.96		56.491±11.57365	0.495
Gender ratio (Male: female)	31:19		47:53	0.083
Mean BMI	26.1575±2.214		27.11±4.98063	0.204
Systolic BP	132.3±9.68904		143.2±13.69804	0.001
Diastolic BP	73.2±9.78128		84.35±8.95147	0.001
Marital status	married	80%	86%	0.003
	unmarried	20%	14%	
Smoking history	No	68. 0%	72.0%	0.612
	Yes	32.0%	28.0%	
Drug allergy	negative		negative	0.216

According to the findings, the oldest age group had the highest prevalence of hypertension. Hypertension, often known as high blood pressure, is a serious health issue that many older persons face. because the vascular system, the body's network of blood vessels, varies with age. Blood pressure rises when arteries become more rigid. Even those who lead heart-healthy lives

and are in good health may experience this. Despite the fact that almost half of adults have high blood pressure, many may not even be aware that they have it [15]. These findings are consistent with a study by Ramezankhani et al. (2019), which found that the great majority of the participants were elderly persons with a mean age of 51± 7.49 [16].

Because health conditions like pregnancy, birth control, and hormonal changes before and after menopause can raise the risk of developing high blood pressure, the patient group demonstrates a high participation rate among females compared to males. This indicates a gender-related risk of hypertension. Where Nearly 52% of high blood pressure deaths occur in women [17]. This finding is in line with studies by Segawa et al. (2021) and Manfredini et al. (2017), which discovered that a significant portion of women had excessive blood pressure [18,19].

Because the average systolic and diastolic blood pressure rose noticeably and linearly with BMI levels, the data also show that the majority of patients had high BMIs [20]. In summary, we discovered a gradient of rising blood pressure as BMI increased. These findings are consistent with a study by Shin et al. (2021) that found a strong participant with a mean BMI of 29 ±5.81 [21].

The current study indicated that married participants had a higher percentage of hypertension disease than unmarried ones, indicating that material status also has an impact on hypertension. Previous research findings demonstrated that married participants, or those living with a spouse [22], regardless of age or race, had poorer control over their hypertension. People who live alone have well-controlled hypertension, according to Shah and Cook [23].

Because the percentage of smokers is higher than that of non-smokers, the data indicate that smoking may be a risk factor for hypertension. This could be because smoking destroys arteries and increases the risk of heart disease. The compounds in tobacco products also raise blood pressure while you're smoking [24].

Well-known risk factors for hypertension include demographics (e.g., age or sex), socioeconomics (e.g., income, marital status, education, etc.), and health behaviours (e.g., drinking, smoking, body mass index [BMI], etc.) [25]. The results of studies on the relationship between marital status and hypertension were inconsistent because some of them showed that married people had a higher risk of hypertension, while other studies showed that unmarried people had the highest number of participants in hypertension [26–29]. Marital status was also a significant risk factor for hypertension in earlier research. Marital status was not linked to the control of hypertension, according to a prior study [30]. Socioeconomic factors and sex variations in marital status have been found to influence the risk of hypertension in studies like the one conducted by Defianna et al. [31].

B. Relationship Between Insulin Resistance And Hypertension

Table (2) demonstrated the mean of red blood cells count in patients‘group was (87.9980±17.83) and in control group (68.3716±13.71) with (P value <0.05), while mean cumulative sugar test didn‘t differ between both groups where in patients group was(5.0148±0.43) and in control group was (5.0498±0.22) with (P value >0.05). Conversely, about insulin and HOMA-IR tests which exhibited increased levels (7.5478±4.41 , 1.1380±0.73 respectively comparing with control group(5.9392±3.81 , 0.6351±0.46 respectively) with (P value<0.05)

Table 2. Comparison of Glucose Metabolism & Insulin Resistance between control and hypertension patients

parameters	Control N (50) mean±SD	Patients N (100) mean±SD	P value
RBS	68.3716±13.71881	87.9980±17.83905	0.001
HbA1c	5.0498±0.22805	5.0148±0.43404	0.594
insulin	5.9392±3.81995	7.5478±4.41387	0.019
HOMA-IR	0.6351±0.46921	1.1380±0.73304	0.001

According to the results, the patient group had higher levels of insulin, insulin resistance (HOMA-IR), and red blood cell count than the control group. This could be because insulin resistance is linked to increased activity of the sympathetic and renin-angiotensin systems, which can lead to fluid retention, hypertension, and increased renal sodium reabsorption [32].

The primary hypothesis is that compensatory hyperinsulinemia may occur in certain prediabetic patients who become resistant to the effects of insulin [33]. Therefore, knowledge of insulin resistance seems to be essential to comprehending the pathogenesis of diabetes mellitus that is not insulin-dependent [34]. A group of cardiovascular disease risk factors known as the "insulin resistance syndrome" have been linked to the emergence of atherosclerosis, dyslipidemia, hypertension, and obesity [35].

Our study's findings are consistent with other research that found a high prevalence of metabolic abnormalities in diabetic patients raises the risk of hypertension, microvascular disease, and macrovascular disease development and progression [36]. According to another study, renal salt retention is elevated in patients with hyperinsulinemia and glucose intolerance [37]. Numerous investigations have shown that the development of insulin resistance and hyperinsulinemia, which resulted in high blood pressure, may also be induced by underlying abnormalities in the Na+/K+ pump activity or intracellular electrolyte management (calcium, magnesium) [38–40].

When insulin treatment began, the systolic and diastolic blood pressure rose sharply, but it later fell; four months into the insulin regimen, the blood pressure values dropped until they were below their pretreatment levels [41].

C. Correlation between demographic parameters and systolic and Di systolic blood pressure

As shown in table (3) to investigate the correlation between some demographic parameters with systolic and Di systolic blood pressure in patients group, appositive correlation between age, BMI, material status and smoking with systolic and Di systolic blood pressure, while there was a negative correlation between gender and systolic and Di systolic blood pressure with P value <0.05.

Table 3. Correlation of Demographic Factors with Systolic and Diastolic BP"

		Age	Gender	BMI	Marital status	Smoking History
Systolic BP	**Pearson Correlation**	0.382	-0.055	0.164	0.013	0.110
	P value	0.001	0.507	0.045	0.874	0.180
Diastolic BP	**Pearson Correlation**	0.365	-0.030	0.181	0.152	0.105
	P value	0.001	0.720	0.027	0.064	0.199

As age increases, systolic and diastolic BP tends to increase. This is a common finding, as blood pressure often rises with age due to various factors like changes in vascular health and elasticity.

As BMI (Body Mass Index) increases, systolic and diastolic BP also tends to increase. This is consistent with the known association between overweight/obesity and higher blood pressure, due to factors like increased cardiac workload and higher levels of body fat.

the correlation (r) is negative (Male: 1 Female: 0), this suggests that males

tend to have lower systolic and diastolic BP than females.

Positive Correlation (r > 0)(Smoker: 1 Non-Smoker: 0): Indicates that smokers tend to have higher systolic and diastolic BP on average compared to non-smokers.

Positive Correlation (r > 0): Suggests that married individuals tend to have

higher systolic and diastolic BP compared to unmarried individuals.

Correlation between insulin resistance and systolic and Di systolic blood pressure

Our results found a positive correlation between (red blood cells count ,insulin level and insulin resistance) with blood pressure in patients group , while there was a negative correlation between cumulative sugar level and blood pressure. As shown in table (4)

Table (4): Correlation of Glucose Metabolism, and Insulin Resistance with Blood Pressure Parameters

		RBS	HbA1c	insulin	HOMA-IR
Systolic BP	**Pearson Correlation**	.039	-.039	.104	.124
	P value	.699	.702	.305	.219
Diastolic BP	**Pearson Correlation**	.172	-.019	.060	.152
	P value	.088	.849	.553	.130

1. As RBS increases, both systolic and diastolic BP tend to rise.
2. Higher insulin resistance (indicated by higher HOMA-IR) is associated with higher systolic and diastolic BP.
3. As insulin levels rise, systolic and diastolic BP are also rise higher.
4. Predicting and potential markers for Hypertension disease

At this part we try to found which parameter of mentioned parameters in our study that‘s acts as a potential marker or a predictor for Hypertension disease. So, we calculate the Logistic Regression Analysis for each parameter and found there were a significant positive statistical relation with (TNF,IL-6,MDA and H2O2) with (P value <0.05). As shown in table (5).

Table 5: Predictors of Hypertension: Logistic Regression Analysis of Insulin Resistance Parameter.

Predictor	Regression coefficient (B)	P value
HOMA-IR	.282	.457

6. A positive relationship for each of these predictors in binary logistic regression suggests they are risk factors for the outcome (e.g., hypertension or cardiovascular disease). As the levels of these variables increase, the likelihood of developing or worsening hypertension also increases. This highlights the interconnected role of inflammation, oxidative stress, kidney function, and insulin resistance in conditions like hypertension and metabolic diseases.

Conclusion

Significant statistical P value <0.05 indicates that demographic characteristics (age, gender, BMI, systolic and di systolic pressure, smoking history, and material status) can impact hypertension illness severity.

Demographic and health behaviour factors (smoking, BMI, etc.) are well-known hypertension risk factors. Hypertension may be caused by insulin resistance and excessive glucose levels. Patients' systolic and diastolic blood pressure increased considerably after insulin treatment.

REFERENCES

NOTE: The style used in UTJsci is IEEE style

References in Text:

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NOTE: Use et al. when three or more names are given for a reference cited in the text. or as nouns: as demonstrated in [3]; according to [4] and [6–9].

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- In all references, the given name of the author or editor is abbreviated to the initial only and precedes the last name. Use commas around Jr., Sr., and III in names.
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Article

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Examples:

1. H. Cui, Z. Feng, W. Wang, X. Peng, and J. Hu, "Adsorption Behavior of Pd-Doped PtS_2 Monolayer Upon SF_6 Decomposed Species and the Effect of Applied Electric Field," *IEEE Sensors Journal*, vol. 22, pp. 6764-6771, 2022.
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4. J. K. Author, "Title of chapter in the book," *in Title of His Published Book*, xth ed. City of Publisher, (only U.S. State), Country: Abbrev. of Publisher, year, ch. x, sec. x, pp. xxx–xxx.

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7. Theses (B.S., M.S.) and Dissertations (Ph.D.)
8. J. K. Author, "Title of thesis," M.S. thesis, Abbrev. Dept., Abbrev. Univ., City of Univ., Abbrev. State, year.
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