DISSERTATION SUBMITTED FOR THE MASTER'S DEGREEIN MEDICAL BIOCHEMISTRY

TITLE

SERUM IRON AND TOTAL IRON BINDING CAPACITY IN HYPERTENSIVE PATIENTS AND CONTROL SUBJECTS

SUBMITTED

BY

SUDHAKAR SINGH

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DEPARTMENT OF BIOCHEMISTRY

INTEGRAL INSTITUTE OF MEDICAL SCIENCES AND RESEARCH

FACULTY OF HEALTH & MEDICAL SCIENCES

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INTEGRAL INSTITUTE OF MEDICAL SCIENCES AND RESEARCH INTEGRAL UNIVERSITY, LUCKNOW

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SUBMITTED

In partial fulfillment of the requirement for the award of degree of

Master of Science
In
Medical Biochemistry

By

SUDHAKAR SINGH

Enrollment No: 2000101980

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CERTIFICATE

This is to certify that **Mr. Sudhakar Singh** student of **M.Sc. Medical Biochemistry,** Integral University has completed his dissertation titled **"Serum Iron and Total Iron Binding Capacity in Hypertensive Patients and Control Subjects"** successfully. He has completed this work from the Department of Biochemistry, Integral Institute of Medical Sciences and Research, Integral University under my supervision. The dissertation was a compulsory part of his M.Sc. Degree.

I wish him good luck and a bright future.

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I wish him good luck and a bright future.

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Declaration by the Candidate

I hereby declare that Integral Institute of Medical Sciences & Research, Integral University, Lucknow shall have the right to preserve, use, and disseminate this dissertation in print/ electronic format for academic/ research purposes.

I will publish the research paper related to my dissertation only with the consent of my guide.

Date: **Sudhakar Singh**

Place:

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(Sudhakar Singh)

LIST OF ABBREVIATIONS

WHO	-	World health organization
WHF	-	World Health Federation
JNC	-	Joint National Organization
TIBC	-	Total Iron Binding Capacity
CVD	-	Cardiovascular disease
AHA	-	American Heart Association
BHS	-	British Hypertension Society
ACC	-	American College of Cardiology
OPD	-	Outpatient department
FNB	-	Food and Nutrition Board

CONTENTS

INTRODUCTION

A long-term medical condition called hypertension is characterized by persistently elevated arterial blood pressure readings compared to the range that is considered normal. According to the American Heart Association (AHA) and the American College of Cardiology (ACC), hypertension is defined as having a diastolic blood pressure of 80 mmHg or more and/or a systolic blood pressure of 130 mmHg or more (Whelton et al., 2022). These values indicate the threshold for diagnosing hypertension in adults. It's crucial to remember that the precise diagnostic standards and therapeutic goals may change depending on a number of factors, including age, presence of other medical conditions, and individual risk factors. Stroke, heart attack, and other problems are all caused by coronary artery disease, with hypertension being a major risk factor and commonly managed through lifestyle modifications and medication (Iqbal AM et al., 2022).

The condition of hypertension also referred to as higher or raised blood pressure, is characterized by persistently increased artery pressure (World Health Organization, 2013). Hypertension, often referred as "silent killer," is a condition that typically does not present noticeable warning signs or symptoms. Even when blood pressure levels are significantly elevated, many individuals may not experience any noticeable signs of the condition. However, in some cases, a few people may encounter certain symptoms such as dull headaches, vomiting, dizziness, or more frequent nosebleeds. It is crucial to understand that these signs are not unique to hypertension and can be brought on by a variety of different conditions. That is why hypertension is often undiagnosed until it is measured during routine medical check-ups (Joint National Commission 8, (2018)).

These symptoms often manifest when blood pressure levels have escalated to a severe or life-threatening stage. It is significant to emphasize that primary or essential hypertension affects around 90% of individuals with high blood pressure. Unknown causes of increased blood pressure are referred to as primary hypertension. And about 10% of those with high blood pressure also have secondary hypertension, which is brought on by an underlying illness or medication.

Determining the base cause of secondary hypertension is crucial for appropriate management. Regular blood pressure monitoring and early intervention are vital for both primary and secondary hypertensions to prevent complications and ensure optimal health (Saseen et al., 2014).

According to the World Heart Federation (WHF) report in 2015, hypertension is indeed considered the most significant cause of premature death globally. The report estimated that around 970 million individuals worldwide were living with high blood pressure at that time. Furthermore, it is projected that the prevalence of hypertension will continue to rise, with an increasing number of affected individuals by 2025 (Kearney PM et al., 2005).

Regarding the distribution of hypertension based on gender and age, the overall occurrence is generally similar between males and females. However, there are some variations observed with increasing age. Typically, around the age of 45 years, high blood pressure becomes more common in both men and women. However, compared to men in the same age group, women tend to have a greater risk of hypertension when they approach the age of 60 and the elderly (Saseen et al., 2014).

On a worldwide scale, hypertension is regarded as the main risk factor for fatalities and disability. In 2016, it was responsible for causing more than 10.5 million deaths worldwide (Lancet et al., 2017).

By 2025, hypertension is predicted to be present in 29.2% of people worldwide, up from 26.4% in 2000 (Kearney et al., 2005). Indeed, reduced worldwide disease burden and death from cardiovascular disease can be achieved by the detection and treatment of hypertension (Zhu Y et al., 2019).

According to (Lawes et al., 2008, Ong et al., 2007, Burt et al., 1995) reports, High blood pressure affects about 1 billion people globally, including 50 million Americans, indicating the need for some form of treatment. Even when it is within the ideal range, high blood pressure continues to be the greatest risk factor for death worldwide. Every year, uncontrolled hypertension

is thought to be the cause of 7.6 million fatalities. These statistics emphasize the urgent requirement for effective measures to diagnose, manage, and control hypertension to mitigate its significant impact on public health and reduce the associated mortality rate (Lawes et al., 2008).

As the demands and acceptance towards life continue to increase, hypertension is becoming a more prevalent health concern than other significant medical and public health issues. In many developed countries, individuals of higher age generally exhibit higher blood pressure levels (John et al., 2011). In populations over 60, hypertension is prevalent at high rates (60-80%).

Around the age of 50 to 55, both naturally hypertensive and untreated hypertension individuals frequently experience a decrease in diastolic blood pressure and rise in systolic blood pressure. Because of this, elderly hypertension patients have higher systolic and pulse pressures, which are important indicators of how they will fare (Azizi et al., 2003).

In a global analysis of hypertension burden, in 2005, it was identified that 20.6% of Indian men and 20.9% of Indian women had hypertension. These rates are expected to rise to 22.9% for Indian men and 23.6% for Indian women by 2025. It is important to note that hypertension is prevalent among patients with congestive heart failure, with up to 75% of hospitalized heart failure patients having hypertension as a contributing factor (Adams et al., 2005). Systolic blood pressure was reduced in the majority of effective heart failure trials to 110 to 130 mm Hg (Atkins et al., 2011).

In India, a significant proportion of deaths, with 57% attributed to stroke and 24% to coronary artery disease, are directly linked to hypertension. This highlights the strong association between hypertension and these cardiovascular conditions, emphasizing the critical role of hypertension as a risk factor in causing adverse health outcomes (Gupta R et al., 2004).

It is estimated that a large percentage, roughly 46%, of persons with hypertension are uninformed about their medical condition. The problem of hypertension is rapidly increasing due to drastic changes in diet and lifestyle, emphasizing the need for effective preventive measures.

There are two forms of hypertension, Primary (essential hypertension) that are responsible for 90% of instances, & hypertension accounts for 10% of cases due to other identified diseases (Porth C.M., Saladin K.S, 2017).

Based on evidence from various studies, including the research conducted by Packer et al. in (2002), it has been suggested that achieving a systolic blood pressure of <120mm Hg may be beneficial for certain patients. Consequently, the current recommendations for blood pressure targets in heart failure include aiming for a target of <120/80mmHg (Atkins et al.,2011).

Cardiovascular disease (CVD) and blood pressure are directly and clearly associated with each other in individuals of all genders, ages, races, ethnic groups, and countries, despite the existence of additional cardiovascular disease risk factors (Perkovic, V., et al., 2007).

Research-based on observations has demonstrated a progressive and linear increase in death from cardiovascular disease as soon as systolic and diastolic blood pressure exceed 115mmHg and 75mmHg, respectively (Mills et al., 2020). For every 20mm Hg systolic or 10mm Hg diastolic elevation of blood pressure in people aged 40 to 89, the mortality from ischemic heart disease and stroke doubles in every age group (Lenfant et al., 2003).

Iron is an essential component for nearly every living organism, playing a crucial part in multiple metabolic activities such as oxygen transfer, erythropoiesis (red blood cell creation), the synthesis of DNA, and electron flow (Abbaspour N et al., 2014). The body stores iron as the non-soluble protein ferritin, which is found inside cells. Transferrin facilitates the movement of ferritin, which is mostly found in the bone marrow, spleen, and liver, throughout the body. (Wood RJ et al., 2005).

Ferritin is present in all cells of the body, serving as a reserve of iron. While most ferritin is intracellular, small amounts are also secreted into the serum, where it contributes to the formation of essential proteins such as hemoglobin, myoglobin, and transferrin (Sahana et al., 2020).

According to the recommendations of the Food and Nutrition Board (FNB), for individuals

aged 19 to 50, an adequate daily intake of iron is 8 milligrams for males and 18 milligrams for women. The higher recommended intake for women and during pregnancy, which is 27 mg, is due to factors such as blood loss through menstruation and a woman's need for iron increases during pregnancy to sustain the fetus's rapid growth and the greater blood flow that is needed. Similarly, while breastfeeding, the recommended intake is 9 mg to support the nutritional needs of both the mother and the breastfeeding infant (Russell, R. et al 2001).

In the human body, iron is typically present in complex forms that are associated with proteins called hemoproteins. These haemoprotein include heme compounds such as hemoglobin and myoglobin, as well as nonheme compounds like transferrin and ferritin. Transferrin, a glycoprotein, is produced in the liver. In the plasma, the concentration of transferrin is approximately 300 mg/dL, which is adequate to transport around 300 micrograms of iron per deciliter of plasma (Rodwell et al., 2015).

Normal Reference Values of Serum Iron - Males = 60 - 160 µg/ dl, Females = 35 - 145µg/dl.

In a longitudinal study, it was observed that a high iron load, indicated by elevated ferritin levels, was accompanied by a decrease in Total Iron Binding Capacity (TIBC). Interestingly, the occurrence of hypertension was found to be favorably correlated with ferritin (iron) and TIBC levels despite their negative connection. It indicates that the pathophysiology of hypertension may be influenced by iron status, as indicated by ferritin and TIBC. To further understand the underlying mechanisms and the connection between iron levels, metabolism of iron, and the onset of hypertension, more research is nonetheless required. (Kim MK et al., 2012).

Normal Reference Values of TIBC = 250 – 400 µg/dl.

REVIEW OF LITERATURE

An arterial blood pressure value of >140/90 mmHg is considered hypertension according to the British Hypertension Society.

A medical disorder called hypertension sometimes referred to as high blood pressure or HTN is defined by unusually elevated arterial levels of blood pressure. The Joint National Committee 7 (JNC7) describes normal blood pressure as having a systolic pressure of less than 120 mmHg and a diastolic pressure of less than 80 mmHg. A systolic blood pressure of at least 140 mmHg and/or diastolic blood pressure of at least 90 mmHg indicate hypertension (Chobanian A. et al., 2003). This disorder can harm several organs over time and greatly raise the risk of morbidity and fatality. Cardiovascular disease, neurologic disease (which includes strokes), and kidney disorders are all directly related to hypertension. The long-term effects of hypertension can be detrimental to overall health and well-being. It is important to manage hypertension through appropriate interventions, including lifestyle modifications and medications, to mitigate the associated risks and prevent complications (Obeagu, Emmanuel, 2020).

The Joint National Commission 7 states that there is widespread consensus regarding hypertension as a qualitative rather than a quantitative disorder. In other words, it is characterized by elevated blood pressure levels rather than specific qualitative abnormalities. In the present scenario, one of the most prevalent diseases in primary care is hypertension. (Achala et al., 2014).

Nearly one-third of all fatalities worldwide, or 17 million per year, are caused by coronary artery disease. Worldwide, hypertension is responsible for 9.4 million fatalities per year. According to the World Health Organization (2013), hypertension is primarily accountable for 51% of mortality from a stroke and 45% of deaths from heart disease. The ninety-five percent confidence interval for the incidence of hypertension in 2017 was between 44.6% to 51.94%, with an average of 48.2%. 58.1% of men and 44.5% of women are affected (Joint National commission 8, (2018)). Population increase, aging, and behavioral risk factors like a poor diet, inactivity, being overweight, alcohol excessively, and stress are all associated with hypertension. (World health organization, 2013).

Many people who are impacted by hypertension and its harmful health effects also face additional risk factors. Complications are more likely to occur in people with high blood pressure if they have certain risk factors including cardiovascular disease, stroke, being obese, diabetes, elevated cholesterol levels, and using tobacco products. (World health organization, 2013).

As people get older, the prevalence of hypertension rises to a level where over fifty percent of those between the ages of 60 and 69 and around three-quarters of those over the age of 70 are affected. With advancing years, hypertension's incidence and prevalence both rise with age. Those who are 55 years of age and elderly with normal blood pressure have a 90% lifetime probability of getting hypertension (Lionakis et al., 2012).

According to multiple studies, 70% of those who experience a cardiac event for the first time and 80% of those who experience their first stroke both have high blood pressure. (Joint National commission 8, (2018)).

CRITERIA FOR HYPERTENSION

According to the 8th report of Joint National Committee (JNC), guidelines for the diagnosis of hypertension in individuals aged 18 years and above is defined as below-(Chobanian et al., 2021).

Table-1 Guidelines for diagnosis of hypertension as per JNC 8

DIAGNOSIS CATEGORIES	SYSTOLIC (mmHg)	DIASTOLIC (mmHg)
Normal	<120	and < 80
Pre- Hypertension	120-139	and/or 80-89
First stage hypertension	140-159	and/or 90-99
Second stage hypertension	≥160	and/or ≥100

CLASSIFICATION OF HYPERTENSION

Classification based on causes (Joint National commission 8,(2018))

1. Primary hypertension

- Also referred to as Essential Hypertension
- Unidentified causes
- It can't be cured, but with the right treatment, such as a healthy lifestyle and proper medication, the consequences can be managed.
- 90% of individual that have high blood pressure suffers from primary hypertension (Saseen and MacLaughin, 2014).

2. Secondary hypertension

- Kidney impairment is most important cause of secondary hypertension.
- Secondary hypertension can be controlled by managing underlying medical issues, such as kidney disease, tumors of the adrenal glands, and consumption of alcohol.
- Secondary hypertension, in contrast to primary hypertension, has a tendency to manifest abruptly and frequently leads to elevated blood pressure levels.
- 10% of people with high blood pressure also have secondary hypertension. (Saseen and MacLaughin, 2014).

CLASSIFICATION BASED ON AGE

Table-2 Classification of hypertension according to age (Iqbal et al., 2019)

AGE	BLOOD PRESSURE (SYSTOLIC/ DIASTOLIC)
<60 years old	<140/90 mmHg
>60 years old	<150/90mmHg

ADDITIONAL TYPES OF HYPERTENSION

Other classification of hypertension according to (Joint National commission 7, (2004))

- Masked hypertension

- It is a reflection of white-coat hypertension. (Pickering et al., 2011).
- Normal blood pressure of less than 140/90 mmHg combined with an increased daytime blood pressure of more than 135/85 mmHg is referred to be "masked hypertension." (Pickering et al., 2011).
- Lifestyle factors can contribute to this phenomenon, such as the consumption of alcohol, tobacco, caffeine, and the level of physical activity outside of the clinic or office (Pickering et al., 2011).

- White coat hypertension

- Blood pressure readings taken in a medical context might not always show an increased reading. Blood pressure readings taken in different settings, including the workplace, didn't indicate an increase. (Pickering et al., 2011).
- White coat hypertension or isolated office hypertension is the term used when this occurrence appears in subjects who do not use medication. (Pickering et al., 2011).
- It occurs more frequently in elderly men and women. (Pickering et al., 2011).

- Pseudo hypertension

- With growing age, the peripheral muscular arteries can undergo significant changes, including advanced arteriosclerosis and calcification. This can result in increased rigidity of the arteries, requiring the cuff pressure to be higher in order to effectively compress them during blood pressure measurement. Consequently, this can lead to falsely high blood pressure readings (Pickering et al., 2011).

- Clinical detection of this condition can be challenging, and as a result, patients with white coat hypertension or isolated office hypertension may be susceptible to receiving high antihypertensive medicine dosages (Nurdini et al., 2020).
- Approximately 2.5% of people aged 65 or older are thought to be at risk for pseudo-hypertension. (Anzal et al., 1996).

➢ Resistant hypertension

- True resistant hypertension is quite rare. (Atkins et al., 2011).

➢ Orthostatic hypertension

- This condition is defined as a decline in the diastolic and systolic blood pressure of a minimum of 10 and 20 mmHg, respectively, within three minutes of standing up. (Naschitz et al., 2007).
- Usually, symptoms are not seen in orthostatic hypertension, but some time few symptoms might be accompanied like cognitive impairment, faintness, feeling lightheaded, and vision blurring (Jordan et al., 2020).
- Among these patients, significant changes in blood pressure occur, leading to episodes of fainting or syncope due to profound hypotension upon standing, and they may experience severe hypertension when in a supine position (Ogedegbe et al., 2011).
- Supine hypertension in these individuals can lead to serious complications, including the development of left ventricular hypertrophy and an increased risk of stroke (Palma et al., 2020)

CAUSES OF HYPERTENSION

According to (Joint National commission 8, (2008)) the causes of hypertension is-

Table-3 Identifiable causes of hypertension.

KNOWN CAUSES OF HYPERTENSION
Chronic kidney disease
An aortic coarctation
Cushing's syndrome
Obstruction of the urinary tract
Pheochromocytoma
Disorders of the thyroid and parathyroid

- Primary hypertension

Unknown causes

- Secondary hypertension

Table-4 Secondary causes of hypertension

SECONDARY CAUSES OF HYPERTENSION
Kidney disease
Congenital blood vessel disorders
Adrenal gland tumors
Alcohol
Thyroid disease
Non-steroidal, anti-inflammatory drugs (e.g. ibuprofen, naproxen)

ACTORS ASSOCIATED WITH THE DEVELOPMENT OF ELEVATED BLOOD PRESSURE AND ITS RISK FACTORS

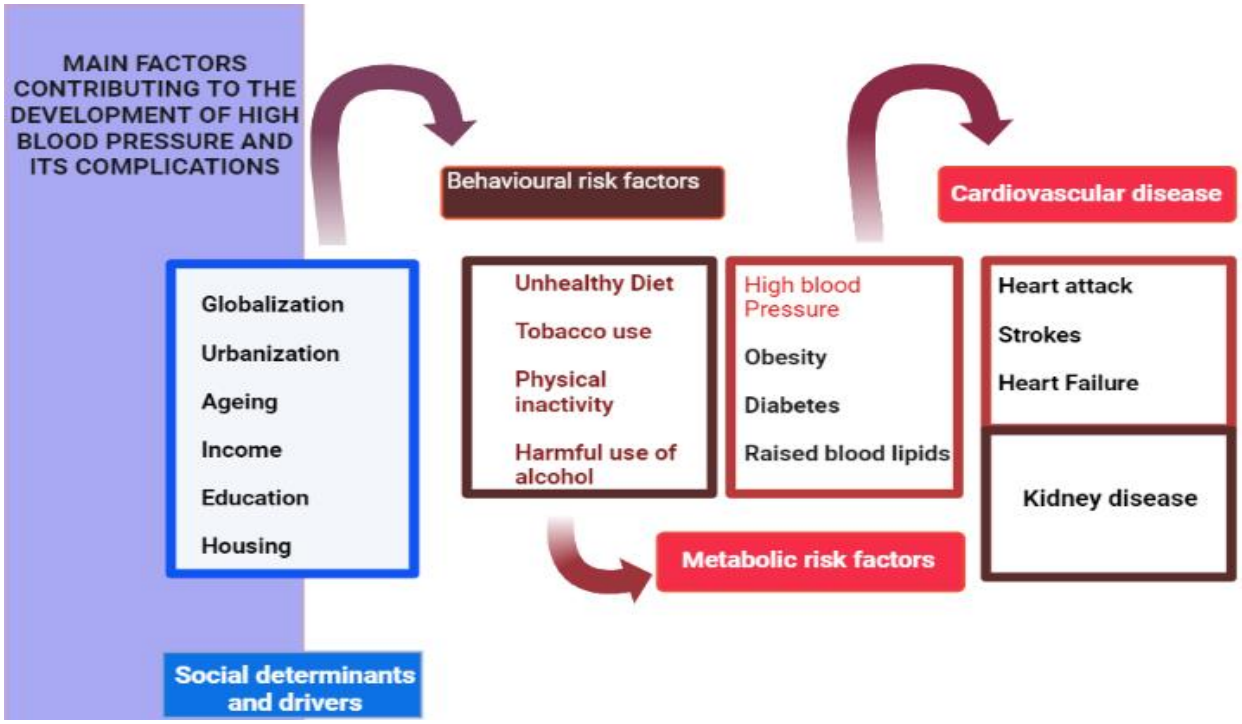


Figure-1 Factors associated with the development of increased blood pressure (World health organization, 2013).

COMPLICATIONS OF HYPERTENSION

- **<u>Cardiovascular Diseases</u>**

- Cardiovascular disorders that include, heart attacks, coronary artery disease, heart failure, and stroke all have hypertension as a vital risk factor. Elevated blood pressure can damage blood vessels, leading to the formation of plaque, restricted blood flow, and increased strain on the heart (Biswas, S., Dastidar, 2003).
- Coronary artery disease (CAD), according to the Centres for Disease Control and Prevention (CDC), is the most common form of cardiovascular disease and occurs when there is a build-up of coronary artery plaque in the vessels that carry blood to the heart muscle. Hypertension is a major risk factor for the development and progression of coronary artery disease. Over time, the plaque can narrow the arteries, reducing blood flow and increasing the risk of a heart attack (Shahjehan RD et al., 2023).

- A heart attack, medically referred to as a myocardial infarction, happens when there is a sudden interruption of blood supply to a specific part of the heart muscle. Hypertension increases the strain on the arteries and can contribute to the development of plaques and the risk of a heart attack. Hypertensive individuals are at a higher risk of experiencing heart attacks (Biswas, S., Dastidar, 2003)

➢ **Stroke**

- Hypertension is a leading cause of stroke. Across the body, high blood pressure affects blood vessels, including those in the brain. Weakened or narrowed blood vessels in the brain can rupture or become blocked, depriving the brain of oxygen and nutrients. This can result in an ischemic stroke (caused by a blockage) or a haemorrhagic stroke (caused by bleeding) (Xiao Z. et al., 2020)
- Similary to coronary events, there exists a logarithmic relationship between systolic as well as diastolic blood pressure and the occurrence of stroke (Wong et al., 2002).
- Approximately 60% of individuals who experience strokes have a previous history of hypertension, and among those who have hypertension, 78% of people have not been able to adequately regulate their blood pressure. (Droste et al., 2003).
- Blood pressure and various types of stroke interact in relatively different ways. (Pickering et al., 2011).
- The term "lacunar infarcts" refers to a large component of cerebral infarcts, which arise from lesions in small arteries that penetrate the deeper layers of the cerebral cortex, and approximately 70% of individuals who experience these types of infarcts have a history of hypertension (Fisher et al., 1979).
- Although only 50% of individuals with infarcts of the big cranial and extracranial arteries have hypertension, it is still the most significant risk factor. Infarcts of these arteries are more closely associated with atherosclerosis (Cole et al., 2017).

- After a stroke, blood pressure tends to increase quickly, and it is believed that this reaction helps to sustain brain perfusion in the infarct's penumbra zone (Droste et al., 2003).
- Younger patients having hypertension of systolic and diastolic and patients over 60 with isolated systolic hypertension have shown that treating hypertension reduces stroke risks by 35% to 44%. (Goldstein et al., 2006)
- In the treatment of hypertension, β-blockers are thought to be slightly less effective compared to other medication classes at preventing stroke. (Lindholm et al., 2005).
- There is some evidence suggesting that angiotensin-receptor blockers may be more effective in the treatment of hypertension (Abraham et al., 2015).

➢ **Heart failure**

- A significant factor of heart failure is blood pressure (Pickering et al., 2011).
- The risk of hypertension is twice as high in hypertensive males compared to normotensive males, and three times as high in hypertensive females. A history of past hypertension is also linked to 90% of new instances of cardiac failure (Mills et al., 2020).
- Systolic blood pressure is more strongly linked to this risk than diastolic blood pressure (Haider et al., 2003).
- In elderly people, treating hypertension reduces the risk of heart failure by about 50%. (Lionakis et al 2012).
- Up to 74% of heart failure cases in people with hypertension are thought to be caused by diastolic heart failure (Vasan et al., 1995).
- Patients diagnosed with diastolic heart failure exhibit increased arterial stiffness, particularly in the aorta, which can lead to amplified wave reflection from the periphery. This, in turn, contributes to elevated central aortic systolic pressure and decreased diastolic pressure (Hundley et al., 2001).

- **Chronic kidney disease**

- Uncontrolled hypertension can significantly increase the risk of renal (kidney) complications (Pugh et al., 2019).
- This is significant for two reasons: firstly, chronic kidney disease is a significant outcome of hypertension, and secondly, it is causally related to a substantially increased risk for heart disease (Ogedegbe & Pickering, 2011).
- In numerous research, it has been demonstrated that there is a significant association between blood pressure & the risk of getting end-stage renal disease (ESRD) (Hsu et al., 2005).

- **In obesity**

- It is thought that increased renal sympathetic nervous system activity plays a significant role in the process behind obesity-related hypertension (Lohmeier et al., 2013).
- With increasing weight, renal sodium resorption increases, leading to impaired pressure natriuresis and the development of excessive blood pressure, which is partially attributed to the activity of the renal sympathetic nervous system (John et al., 2011).
- Several studies have indicated that the combined blockade of alpha and beta-adrenergic receptors effectively reduces hypertension linked with obesity (Jiang et al., 2016).
- The sympathetic nervous system is more active in the kidneys and other tissues in obese people, as seen by higher tissue catecholamine overflow and other measurements (Hall et al., 2003).

- **In diabetes**

- Patients with hypertension are more likely to have diabetes, and having both ailments together greatly raises the risk of both diseases' consequences. (Atkins et al., 2011).
- Blood pressure readings of >140/90 mmHg are seen in more than half of diabetics (Khangura et al., 2000).

- More than 35% of people with hypertension also have diabetes, and 75% of people with diabetes are either taking medication or have a blood pressure that is above the ideal range of 130/80mmHg (Aronow et al., 2018).
- Diabetes is the main risk factor for end-stage renal disease (ESRD). An increased risk of getting ESRD is closely associated with raised blood pressure, and The onset of kidney disease is slowed by reducing blood pressure (Atkins et al., 2011).
- Thus, most antihypertensive agents are now recommended for use in individuals with diabetes who do not have neuropathy and albuminuria (Khangura et al., 2000).

➢ **<u>In eye problems</u>**

- Hypertension can affect the blood vessels in the eyes, leading to conditions such as hypertensive retinopathy, which can cause vision impairment or even vision loss.

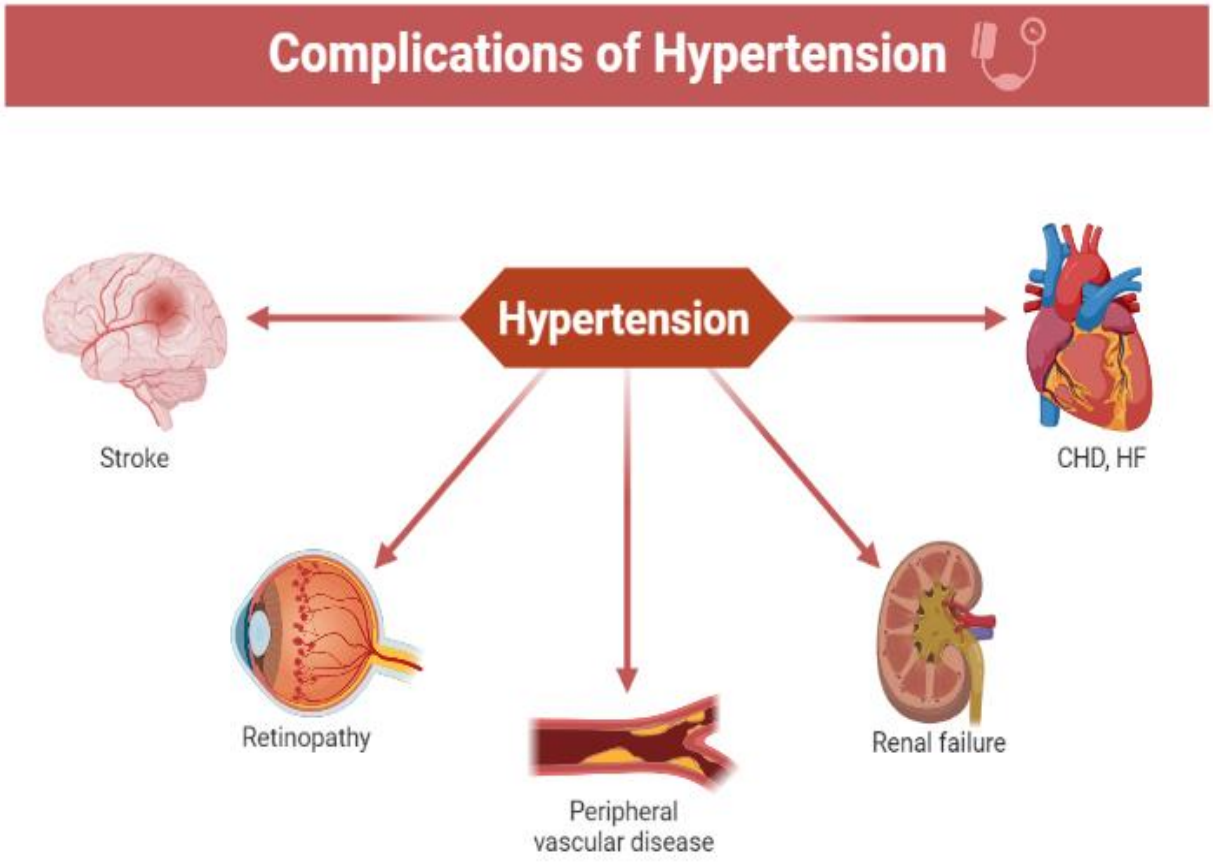


Figure-2 The main complications induced by hypertension (polygenic substrate): LVH—left ventricular hypertrophy; CHD—coronary heart disease; HF—heart failure. (Luca et al.,2021)

SYMPTOMS OF HYPERTENSION

Table-5 Symptoms of hypertension (Joint National commission 8, (2018))

SYMPTOMS OF HYPERTENSION
o Dull headache
o Chest Pain
o Shortness of breath
o Dizzy sleep
o Nosebleed
o Vomiting

PATHOPHYSIOLOGY OF HYPERTENSION

The body demands iron for a number of physiological functions, including the production of blood & the transportation of oxygen. Iron overload disorders, such as hereditary hemochromatosis, has been linked to a higher risk of hypertension. However, further research is needed to determine exactly how excess ferritin causes hypertension (Abbaspour et al., 2014)

One proposed mechanism is that iron overload can lead to dysfunction in endothelial cells, oxidative stress & inflammation, which can impair the normal functioning of blood vessels and contribute to the development of hypertension. Additionally, iron may affect the renin-angiotensin-aldosterone system (RAAS), a hormonal pathway involved in blood pressure regulation, although the specific interactions are not fully understood (Abbaspour et al., 2014).

The pathophysiology of hypertension involves two main factors: hormonal mechanisms like as the RASS (renin-angiotensin-aldosterone system) and disturbances in electrolyte balance (including sodium, potassium, and chloride). Natriuretic hormones can lead to elevated sodium concentrations in cells, resulting in increased blood pressure. In order to regulate arterial blood pressure, the RASS is essential (Fountain JH et al., 2023).

Angiotensin II & aldosterone are two hormones involved in the RAAS (renin-angiotensin-aldosterone system). Angiotensin II causes vasoconstriction, increases the release of vasoconstrictive chemicals, and stimulates aldosterone production. The vasoconstriction leads to increased peripheral resistance and elevated blood pressure. The hormone aldosterone, which is generated by the adrenal glands, makes it easier for the kidneys to reabsorb water and sodium, increasing the volume of blood and, as a result, high blood pressure (Oparil S. et al., 2018).

IRON AND TIBC

In living things, iron is essential for several metabolic activities including transport of oxygen, erythropoiesis, synthesis of DNA, and transportation of electrons. It is a protein found inside cells that are kept in the body as ferritin. They are typically found in the bone marrow, liver, and spleen and are stored in an insoluble form. Transferrin transports them throughout the body (MacCord J. Iron et al., 1998).

All body cells contain ferritin, which serves as a reservoir of iron in the body and is secreted in minute quantities into the serum for the production of hemoglobin, myoglobin, & transferrin (Sahana et al., 2020).

According to the FNB (Food and Nutrition Board) recommendations, daily recommended iron intake through food for adults aged 19-50 years is 18 milligrams for females, 8 milligrams for males, 27 milligrams for pregnant women, & 9 milligrams for breastfeeding females. The more advised dosages for women and during pregnancy are attributed to factors such as menstrual blood loss and the increased blood circulation required for the fetus's rapid development (Russell, R. et al 2001).

The majority of the iron in the human body is found in intricate forms that are attached to proteins (hemoproteins) as heme compounds (hemoglobin or myoglobin) or nonheme compounds (ferritin, transferring, & ferritin). Glycoprotein called transferrin is primarily synthesized in the hepatic system. By binding to iron and assisting its distribution throughout the entire body, it plays

a crucial role in iron transportation and homeostasis. The concentration of transferrin in the plasma is approximately 300 mg/dL (Ems T et al., 2023).

Iron is an essential mineral involved in various physiological processes, including the synthesis of red blood cells and oxygen transport. However, excessive iron can lead to oxidative stress and tissue damage. Iron metabolism is tightly regulated by the body to maintain a balance between iron absorption, storage, and utilization (Abbaspour et al., 2014).

Many people believe that iron's chemical characteristics account for its biological significance. The oxidative forms of iron are ferrous (Fe+2) and ferric (Fe+3). (Ana, et al., 2015). The oxidation of ferrous (Fe+2) to ferric (Fe+3) produces necessary insoluble ferric hydroxide $Fe(OH)_3$ and contributes to the production of harmful oxygen radicals, which in turn cause peroxidative damage to essential structures of cells (Halliwell B et al., 1990).

In epidemiological and clinical research to assess bodily iron storage, the levels of serum ferritin (SF), hemoglobin, soluble transferrin receptor (sTFR), & transferrin are the most frequently used biological indicators (Zhu Y et al., 2019).

The primary carriers of blood iron are transferrin (Tf) or ferritin. The monomeric glycoprotein known as transferring is synthesized in the hepatic system and is composed of a polypeptide chain of amino acids that is divided into two homologous domains, the N- and C-terminal, each of which has a Fe+3 linking region.

There are three main primary function of transferring - (Ana et al., 2015).

1. Solubilization of Fe+3.
2. By binding to the free ions, high-affinity iron binding helps in preventing the production of free radicals.
3. Iron is delivered to cells through its interaction with membrane receptors, facilitating its supply and utilization by the cells., i.e. transferring receptors (Tfrs).

Numerous Studies have shown that changes in TIBC & levels of iron in the blood have negative effects. The generation of reactive oxygen compounds, which leads to inflammation as well as oxidative stress and has negative effects on the functioning of mitochondria & results in hypertension, which may be influenced by iron overload (Ames BN et al., 2005).

The kidney's peritubular cells naturally produce the protein known as erythropoietin (EPO), a glycoprotein hormone that is essential for promoting the generation of erythrocytes. The absorption and utilization of iron or ferritin are directly correlated with erythropoietin, which may enhance the effects of oxidative stress and exacerbate hypertension (Rancourt ME et al., 2010).

There are a number of possible explanations for the connection between concentrations of ferritin and hypertension. One of them involves atherosclerotic formation (Kim MK. et al., 2012). The combination of LDL (low-density lipoprotein) and isoprostane oxidation, which act as indicators for oxidative stress, can cause endothelial damage from excessive amounts of iron, which can lead to the development and progression of atherosclerosis. Following is the atherosclerosis process, which could raise the possibility of hypertension (Luqman et al., 2022)

When infarction and reperfusion, superoxide radicals ($\cdot O_2^-$) & H_2O_2 (hydrogen peroxide) are produced (Horwitz LD et al., 1994). These types of compounds are weak oxidizers without iron that inbuilt scavenger enzymes inactivate (Floyd RA et al., 1983). Iron, through Fenton reaction, produce hydroxyl radical ($\cdot OH$) from (H_2O_2) and ($\cdot O_2^-$) and it is highly toxic to tissue. And No reliable endogenous protections exist to stop this incredibly reactive chemical. Iron chelation reduces the generation of $\cdot OH$ (hydroxyl radical) and protects cardiac cells from H_2O_2 damage. (Byler RM et al., 1994).

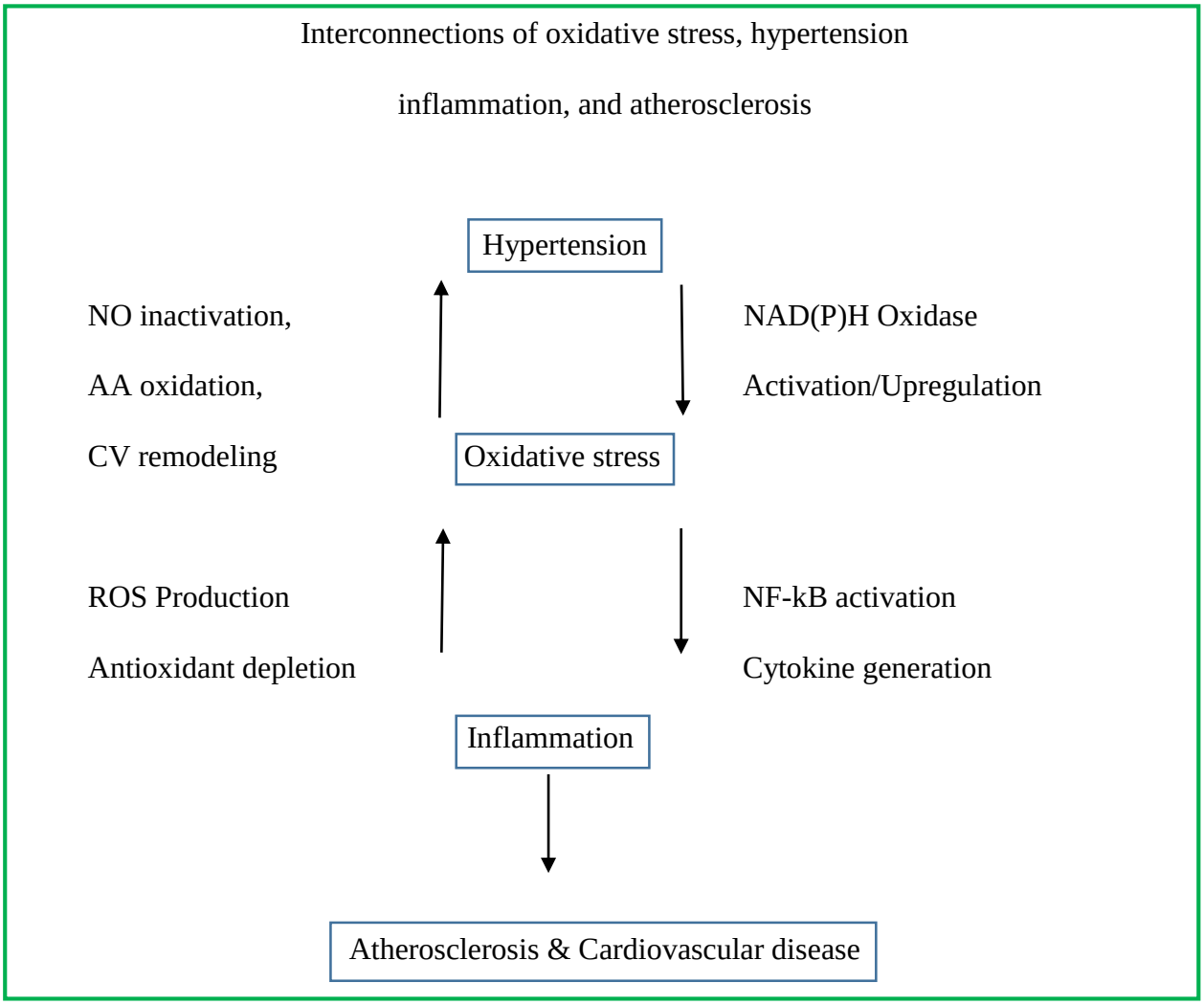


Figure- 3 (CVD- cardiovascular disease, AA- arachidonic acid; CV- cardiovascular; NF-κB- Nuclear factor-κB; NAD(P)H- Reduced nicotinamide adenine dinucleotide phosphate; ROS- Reactive oxygen species, NO-Nitric oxide) (Vaziri, N. (2008).

Iron binding capacity (IBC) is of two types, one is Total iron-binding capacity (TIBC) & second one is UIBC (unsaturated iron-binding capacity). Transferrin, a type of protein responsible for iron transport, is produced in greater quantities in the blood when iron reserves are reduced. Since transferrin is normally only saturable with iron to one-third of its volume, the remaining transferrin in serum has an additional 67% binding capacity. As more iron is required, this enables its binding & transport. This is the ability to bind iron unsaturatedly. TIBC contain serum iron and UIBC (Faruqi et al., 2022). Most patients with iron shortage are likely to have higher total iron binding capacity (TIBC) readings. Consequently, it is reasonable to infer that a shortage of iron may be intimately linked to the onset of hypertension (Ruiter G. et al., 2011).

TIBC is an indirect measure of transferrin levels, which are inversely related to serum iron levels. When iron levels are low, transferrin production increases, leading to higher TIBC levels. Conversely, when iron levels are high, transferrin production decreases, resulting in lower TIBC levels (Faruqi A et al., 2022).

Iron deficiency anemia, which can be associated with low serum iron levels, may also affect TIBC. In iron deficiency, TIBC levels tend to increase as the body tries to compensate for the low iron levels by producing more transferrin (Faruqi A et al., 2022). Similarly, in conditions of iron overload, such as hereditary hemochromatosis or chronic transfusion therapy, TIBC levels may be lower due to decreased transferrin production (Kotze et al., 2009).

The occurrence of hypertension had a positive association with both ferritin and TIBC (total iron binding capacity), both of which are indicators of excessive iron overload (Kim MK et al., 2012). The ability of transferrin, a protein made in the liver, to bind and transport iron throughout the body, is referred to as iron binding capacity.

Total Iron-Binding Capacity (TIBC) of serum is a measurement of how much iron can be transported in the bloodstream by transferrin. TIBC reflects the body's ability to transport and bind iron. In hypertension, there may be some associations between TIBC levels and blood pressure, although the relationship is not fully understood.

IRON AND TIBC IN HYPERTENSION

In hypertension, there can be associations between serum iron levels and blood pressure, but the relationship is complex and not fully understood. Here are a few key points regarding serum iron in hypertension: -

Iron overload can lead to increased oxidative stress, endothelial dysfunction, and inflammation, which may contribute to the development of hypertension and cardiovascular diseases (Yan et al., 2022).

The occurrence of hypertension is influenced by a rise in oxidative stress caused due to too much iron (Kim MK et al., 2012). Reactive oxygen species (ROS), which are made up of free radicals of oxygen and other chemical components, are what cause oxidative stress in the body (Maiese et al., 2008). which may turn less reactive free radicals such as superoxide radicals, H_2O_2, hydroxyl, singlet oxygen ($\cdot O_2^-$), NO, & peroxynitrite into more reactive free radicals. Also Iron, through Fenton reaction, produce hydroxyl radical ($\cdot OH$) from H_2O_2 and ($\cdot O_2^-$) and it is highly toxic to tissue (Luqman et al., 2022).

Inflammation plays a role in both hypertension and iron metabolism. Chronic low-grade inflammation can affect iron homeostasis and contribute to endothelial dysfunction and vascular remodeling, leading to increased blood pressure. CRP (C-reactive protein) & interleukin-6 (IL-6) are examples of inflammatory indicators that have been linked with alterations in iron metabolism and hypertension (Ansar et al., 2016).

Iron deficiency, is characterized by decreased oxygen-carrying capacity, which can result in increased cardiac output and peripheral vascular resistance, potentially contributing to elevated blood pressure (Hegde et al., 2006). Because the body produces more transferrin to make up for the low iron levels when there is an iron deficit, TIBC levels frequently rise (Faruqi A et al., 2022).

After studying different articles, several studies have found significant association and few studies have found no significant association with Iron and (TIBC) Total iron binding capacity in hypertensive patients in different populations. As a result, it is still unclear what mechanism underlies the link between iron and TIBC in hypertension. Thus, the current study is conducted to assess their relationship with hypertension.

AIM
&
OBJECTIVES

AIM

The aim of the present study was to evaluate and analyze levels of serum iron and total iron binding capacity (TIBC) in diagnosed cases of hypertensive patients and apparently healthy controls.

OBJECTIVES

1. To estimate serum iron level in patients of hypertensive and apparently healthy controls.
2. To estimate total iron binding capacity level in patients of hypertensive and apparently healthy controls.
3. To correlate serum iron level and TIBC (total iron binding capacity) level between hypertensive patients and apparently healthy controls.

MATERIALS AND METHODS

RESEARCH QUESTION

Is there any change in the levels of serum Iron and Total Iron Binding Capacity (TIBC) in diagnosed cases of hypertension as compared to apparently healthy controls?

STATISTICAL HYPOTHESIS

Null hypothesis (Ho): There is no significant change in the levels of serum Iron and Total Iron Binding Capacity (TIBC) in diagnosed patients of hypertension and compared to apparently healthy controls.

Alternate hypothesis (H_1): There is a significant change in the levels of serum Iron and Total Iron Binding Capacity (TIBC) in diagnosed patients of hypertension and compared to apparently healthy controls.

METHODOLOGY

Study Design: - Prospective

Type of study: - Case-control study

SUBJECTS SELECTION

Selection of Controls

1. Apparently healthy individuals.
2. Subjects within the age of 30 to 60 years.
3. Subjects who have agreed to sign the consent form.

Selection of Cases

Inclusion criteria

1. Diagnosed cases of hypertensive patients.
2. Subjects within the age of 30 to 60 years.
3. Patients who have agreed to sign the consent form.

Exclusion criteria

1. Pregnant and lactating females.
2. History of Malabsorption of iron.
3. History of any chronic illness.
4. History of Iron deficiency anemia.

SAMPLE SIZE

The formula for determining the sample -

$$\mathbf{N} = \left(\frac{r+1}{r}\right)\frac{\sigma^2(Z_\beta + Z_{\alpha/2})^2}{(d\text{ifference})^2}$$

Reference: Charan J Biswas, 2013

N = sample size

(r+1)/r = ratio of case to control

σ = standard deviation (taken from previous studies)

Zβ = represent the desired power

Zα/2 = represent the desired level of statistical significance (Zα/2=1.96)

d (Difference) = effect size (the difference in means of study group and comparison group taken from the previous studies)

Then,

For 80% power, Zβ = (0.84)

For 0.05 significance level, Zα/2=1.96

r = 1 (equal to number of case and control)

σ = 14.95

d = 7.7 (Muhammed, Z. H., & Al-Hakeim, 2011).

$$\mathbf{N} = \frac{2\,(14.95)^2\,(.84+1.96)^2}{(7.7)^2}$$

Therefore, N = 59.10 ≈ 60

The study will include **30** cases and **30** controls.

PLACE OF STUDY

Department of Biochemistry, Integral Institute of Medical Science and Research, Lucknow.

COLLABORATING DEPARTMENT

Department of General Medicine, OPD at IIMS&R, Lucknow.

ENROLLMENT OF PARTICIPANTS

Cases were enrolled from the hypertensive attending the Integral Hospital.

SELECTION OF CASES

Subjects in the age group of 30 to 60 years with diagnosed hypertension attending general medicine OPD at IIMS&R, Lucknow were selected based on the exclusion / inclusion criteria.

SELECTION OF CONTROLS

Apparently healthy subjects in the age group of 30 to 60 years were selected.

SAMPLING METHOD

Non-probability, Purposive sampling.

COLLECTION OF SAMPLES

3 ml of venous blood was collected from the subjects under aseptic conditions in a plain vial. The blood sample was allowed to clot at room temperature for 15 minutes. The sample was then centrifuged at 1000 rpm for 10 minutes to separate the serum (Henry J. B., 1979). 1 ml serum was used for the determination of Iron and Total Iron Binding Capacity (TIBC).

STORAGE OF SAMPLES

The serum samples for the determination of iron and total iron binding capacity (TIBC) were stored at -20°C until testing in Central Clinical Laboratory, Department of Biochemistry, IIMS&R, Lucknow (U.P.)

LABORATORY INVESTIGATIONS

1. Estimation of serum Iron and TIBC by Ferrozine method using Erba chem 7 semi auto analyzer

Principle

Iron, bound to transferrin is released in an acidic medium and the ferric ions are reduced to ferrous ions. The Fe (II) ions react with the Ferrozine to form a violet-colored complex. The intensity of the complex formed is directly proportional to the amount of iron present in the sample.

For TIBC, the serum is treated with an excess of Fe (II) to saturate the iron binding sitesof transferrin. The excess iron (II) is absorbed and precipitated and the iron content in the supernatant is measured to give the TIBC.

Fe (III) $\xrightarrow{\text{Acidic medium}}$ Fe (II)

Fe (II) + Ferrozine $\longrightarrow$ Violet Colored Complex.

Normal Reference Values

Serum Iron

Males = 60 - 160 µg/dl

Females = 35 - 145µg/dl

TIBC = 250 – 400 µg/dl

Procedure

Wavelength/filter: 570nm (Hg578nm)/Yellow

Temperature: Room temperature (RT)

Light path: 1cm

Iron Assay:

Pipette into clean dry test tubes labelled as Blank (B), Standard (S), Sample Blank(SB) and Test (T);

Addition Sequence	B (ml)	S (ml)	SB (ml)	T (ml)
Iron Buffer Reagent(L1)	1	1	1.05	1
Distilled water	0.2	-	-	-
Iron Standard (S)	-	0.2	-	-
Sample	-	-	0.2	0.2
Iron color Reagents(L2)	0.05	0.05	-	0.05

Mix well and incubate at R.T. for 5min, measure the absorbance of the blank (abs B), Standard(abs S), Sample blank (abs SB) and test sample (abs T) against Distilled water.

TIBC Assay:

Pipette into a clean dry test tube.

Serum	0.5 ml
TIBC Saturating Reagent (L1)	1.0 ml

Mix well and allow standing R.T for 10 minutes and adding.

TIBC Precipitating Reagent (L2)	≈ 50 mg

Mix well and allow to stand at room temperature for 10 min. centrifuge at 2500 – 3000 rpmfor 10 min. to obtain a clear supernatant. As per the iron assay, ascertain the supernatant's iron content. (Siedel, J., et. al. 1984).

ETHICS REVIEW

Permission from the Institutional Ethics Committee was taken (IEC/IIMS&R/2023/66).

DATA COLLECTION

Details from the subjects were obtained using data collection proforma after taking written consent.

STATISTICAL ANALYSIS PLAN

Statistical analysis was performed using SPSS software (version 16), Graph Pad (Prism 6.0) and Microsoft – Excel (version 2016). All the data were expressed as mean ± standard deviation. An unpaired t-test was performed to compare the study parameters between cases and controls. Karl Pearson's correlation analysis was employed to determine the relationship between variables. p-value <0.05 was considered statistically significant.

OBSERVATIONS
&
RESULTS

IRON

The difference in the level of iron between cases and controls was statistically significant (p-value= 0.023) (Table-6 & figure-4).

Table-6 Mean and standard deviation of the study groups.

SERUM IRON (µg/dl)					
Groups	N	Mean	Standard Deviation (SD)	p-value	Significance
Controls	30	140.46	± 49.98	0.023	Statistically Significant
Cases	30	173.44	± 59.00		

N= Number of controls or cases, p-value <0.05 is considered statistically significant.

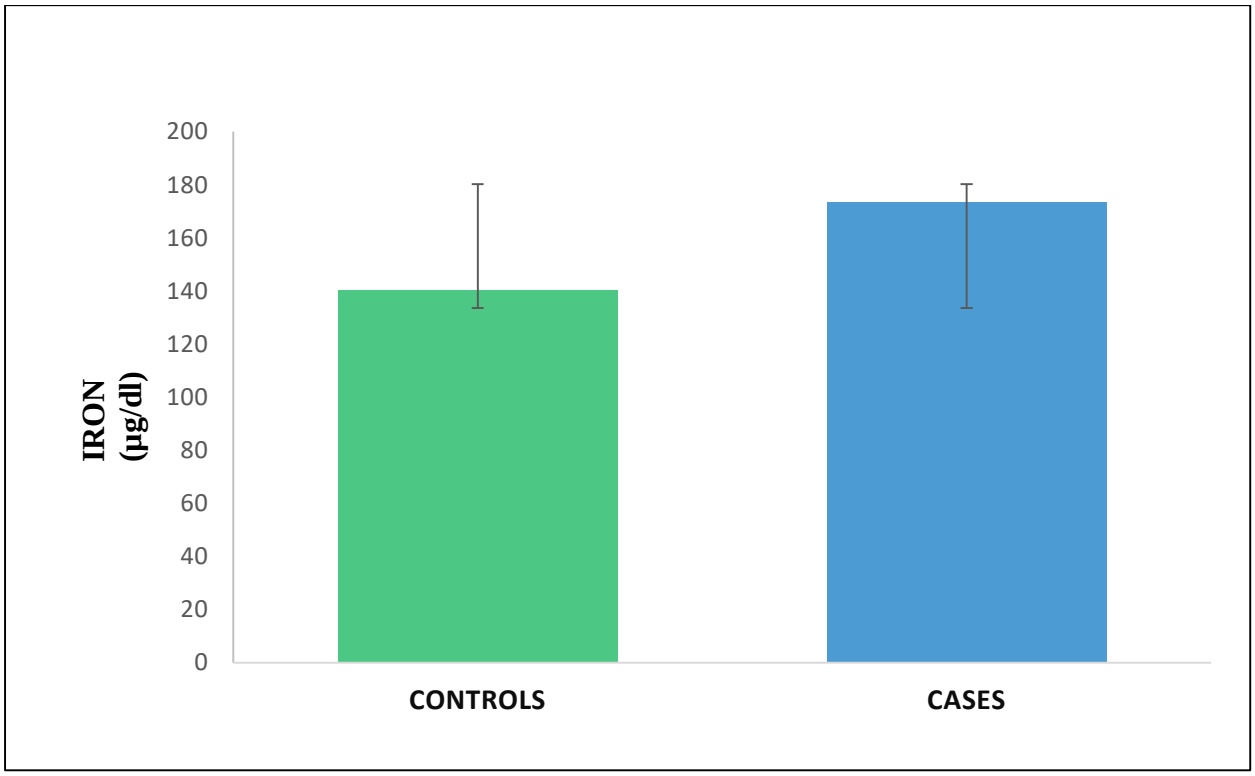


Figure-4 Comparison of Serum Iron in controls and cases.

TOTAL IRON BINDING CAPACITY

The difference in the level of iron binding capacity between cases and controls was statistically significant (p-value= 0.0422) (Table-7 & figure-5).

Table-7 Mean and standard deviation of the study groups.

TOTAL IRON BINDING CAPACITY (TIBC) (µg/dl)					
Groups	N	Mean	Standard Deviation (SD)	p-value	Significance
Controls	30	295.39	± 41.96	0.0422	Statistically Significant
Cases	30	225.31	± 179.94		

N= Number of controls or cases, p-value <0.05 is considered statistically significant.

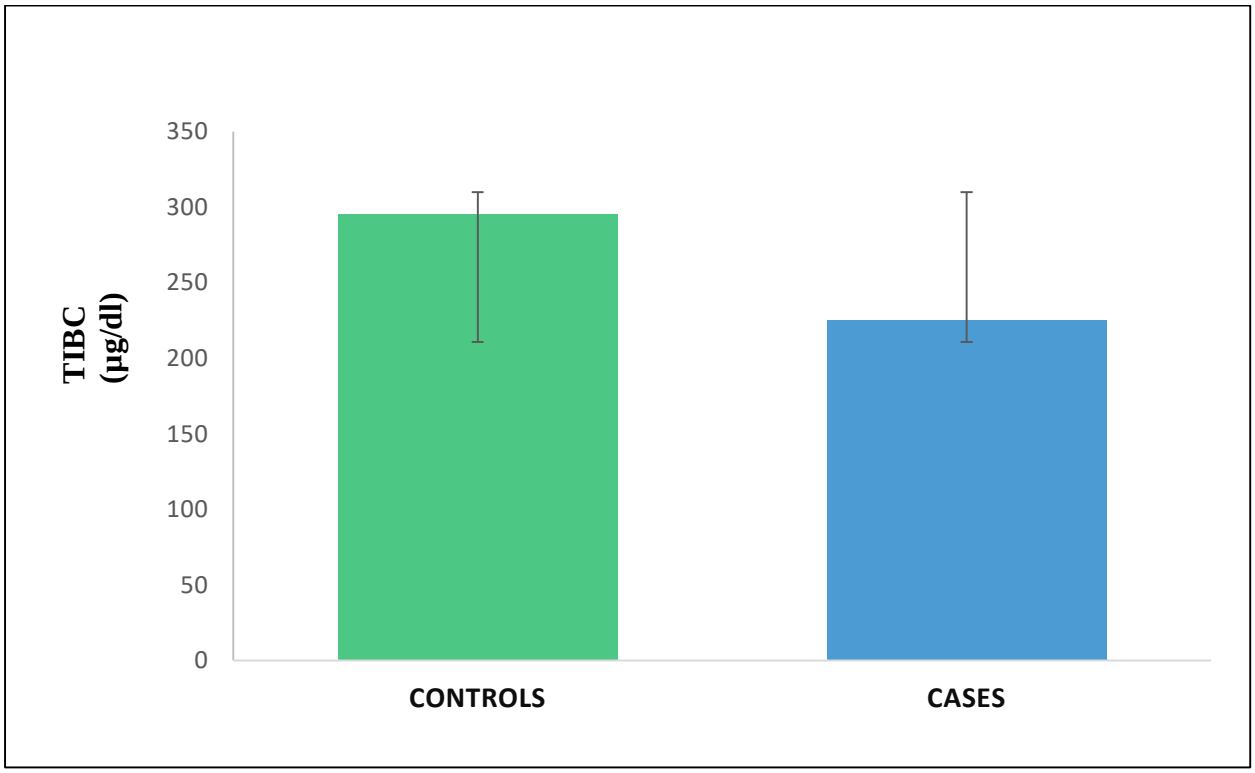


Figure-5 Comparison of TIBC in controls and cases.

KARL PEARSON'S CORRELATION OF COEFFICIENT BETWEEN IRON AND TIBC IN CASES OF HYPERTENSION

There was significant association between Serum Iron and TIBC in cases of hypertension (p-value = 0.041).

Table-8 Karl Pearson's correlation coefficient between Serum Iron and TIBC.

Correlations			
		IRON (µg/dl)	**TIBC (µg/dl)**
IRON (µg/dl)	Pearson Correlation	1	-.566**
	Sig. (2-tailed)		0.041
	N	30	30
TIBC (µg/dl)	Pearson Correlation	-.566**	1
	Sig. (2-tailed)	0.041	
	N	30	30

N= Number of cases, **. Correlation is significant at the 0.05 level (2-tailed)

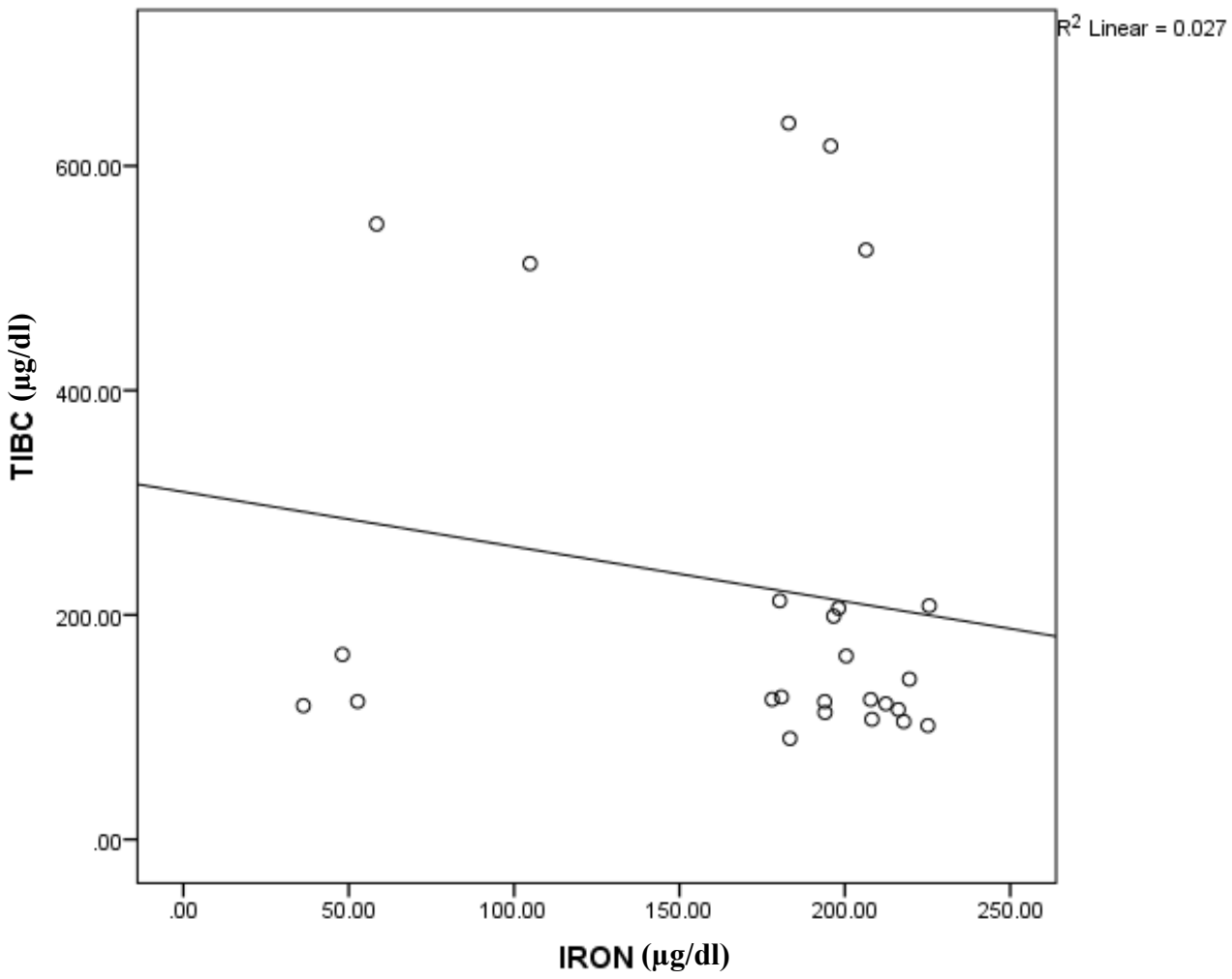


Figure-6 Serum iron and TIBC are correlated, as shown in the scatter diagram.

RESULTS

- As compared to controls the activity of Serum iron was statistically significant in cases (p = 0.023) (Table-6 and Figure-4).
- As compared to controls the concentration of TIBC (Total iron binding capacity) was statistically significant in cases (p = 0.0422) (Table-7 and Figure-5).
- There was an association between TIBC and serum iron (p = 0.041) among cases.

DISCUSSION

A chronic medical condition called hypertension, sometimes known as high blood pressure, is characterized by consistently excessive levels of arterial blood pressure (Chobanian A. et al., 2003). High blood pressure is a significant, independent risk factor for the development of heart disease.

In this investigation, we found that hypertension people' serum iron activity was considerably higher when compared to normotensive individuals (p-value = 0.023). Our investigation showed, there was increased iron and decreased TIBC levels compared with patients suffering from hypertension and normal individuals without any chronic illness.

This result is consistent with Kim MK et al.'s (2012) study that the emergence of hypertension was positively correlated with increased iron & decreased TIBC.

Also Lee DH et al., (2010) revealed that ferritin levels were positively correlated with the prevalence of high blood pressure in their cross-sectional investigation conducted in Korea.

Also, Kiechl S, Willeit Tuomainen, (2007) according to their research, cardiovascular disease (CAD) and body iron levels are positively associated.

In my present study, some cases show that there are increased TIBC levels and decreased iron levels are also found in patients with hypertension.

Ruiter G et al., (2011) found in some cases that there is increased TIBC value and decreased iron levels in patients with hypertension may also show a positive correlation.

Elevated body iron levels can lead to stress from oxidation that may transform less reactive free radicals into more reactive forms such as hydroxyl radicals (·OH), hydroxide radicals (OH), & ($O_2^{\bullet-}$) superoxide anions, which may contribute to the development of hypertension and cardiovascular diseases (Galan P et al., 2010). The formation of reactive oxygen species, which enhances oxidative stress and inflammation and may lead to an increase in arterial blood pressure, may be influenced by both excess iron and inadequate iron levels (Yan et al., 2022).

Sempos CT et al., (2004) observed no evidence of a link between stored iron & high blood pressure.

Additionally, no significant correlation between iron reserves and heart disease was observed by Rauramaa R et al., (2010).

Our investigation showed that it was a statistically significant inverse association between iron & TIBC.

Hence, I found in my study that there was elevated iron levels and decreased TIBC levels but in some cases, there was also increased TIBC and decreased iron status have been found. So it is not clearly understood the mechanism of iron and TIBC in cases of hypertension. Though, this study will require more investigations using a bigger sample size to correlate the iron and TIBC in cases of hypertensive patients.

SUMMARY
AND
CONCLUSION

SUMMARY

The current study's objective was to compare the total iron binding capacity (TIBC) and serum iron levels in patients with hypertension & apparently healthy controls.

The estimated parameters were:

- Serum Iron
- Serum TIBC

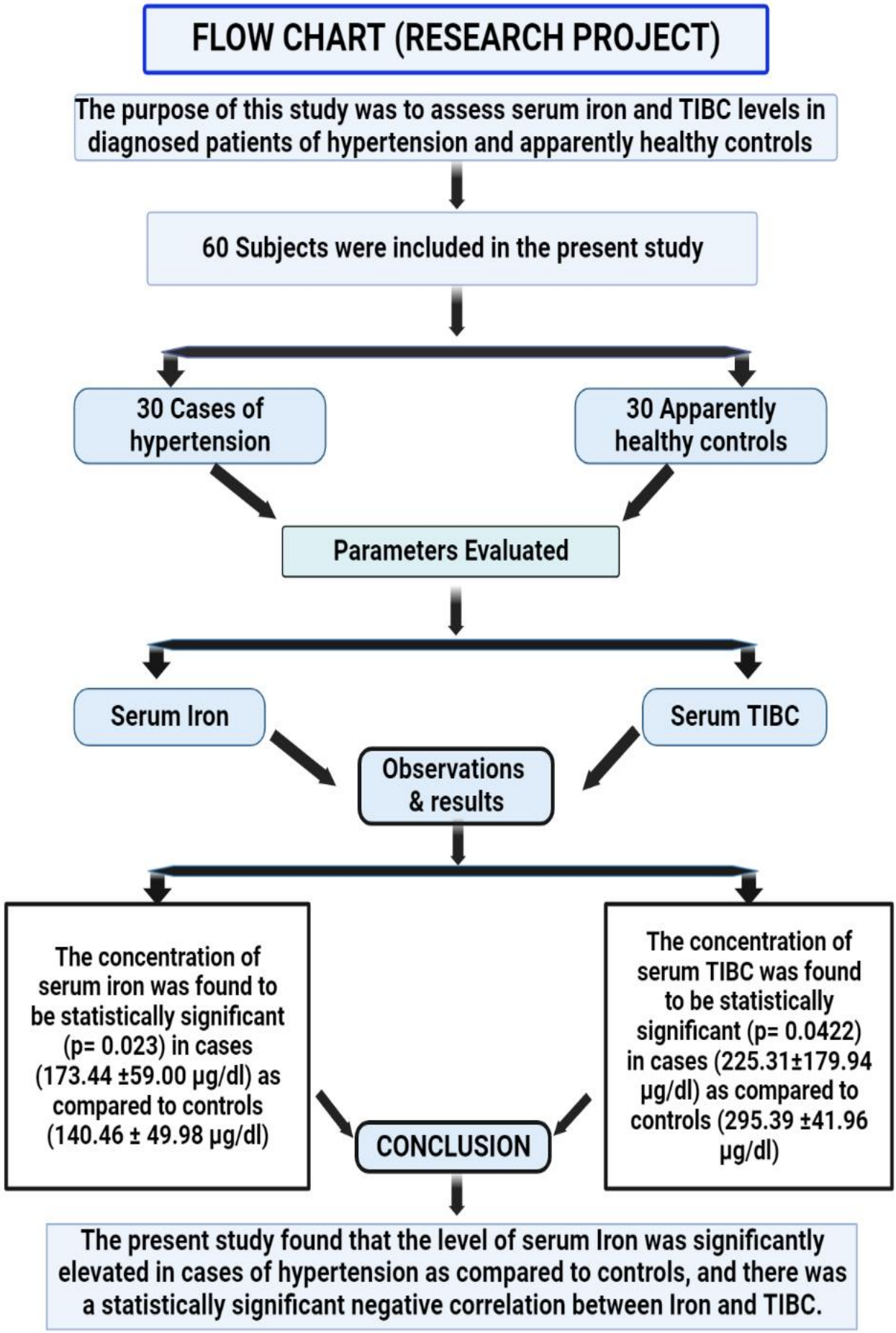
The following observations were obtained during the study:

- In comparison to controls, the level of serum iron was considerably increased in cases ($p = 0.023$) (Table-6 and Figure-4).
- In comparison to controls, the level of TIBC was considerably increased in cases ($p = 0.0422$) (Table-7 and Figure-5).
- There was an association between TIBC and serum iron ($p = 0.041$) among cases.

CONCLUSION

The current investigation found that serum iron level was significantly higher in hypertension cases compared to controls, whereas serum Total iron binding capacity was shown to be significantly lower in cases compared to controls. According to several research, serum iron level and Total iron binding capacity are linked to an increased risk of hypertension.

Thus, elevated blood pressure is indicated by increased serum Iron and decreased Total Iron Binding Capacity, Therefore, it is crucial to investigate the unique roles of serum iron and total iron binding capacity in the pathophysiology of hypertension. The relationship between serum iron and TIBC in hypertension condition requires further investigation and analysis with larger sample size.


FLOW CHART (RESEARCH PROJECT)
The purpose of this study was to assess serum iron and TIBC levels in diagnosed patients of hypertension and apparently healthy controls
60 Subjects were included in the present study
30 Cases of hypertension
30 Apparently healthy controls
Parameters Evaluated
Serum Iron
Serum TIBC
Observations & results
The concentration of serum iron was found to be statistically significant (p= 0.023) in cases (173.44 ±59.00 µg/dl) as compared to controls (140.46 ± 49.98 µg/dl)
The concentration of serum TIBC was found to be statistically significant (p= 0.0422) in cases (225.31±179.94 µg/dl) as compared to controls (295.39 ±41.96 µg/dl)
CONCLUSION
The present study found that the level of serum Iron was significantly elevated in cases of hypertension as compared to controls, and there was a statistically significant negative correlation between Iron and TIBC.

REFERENCES

Abbaspour, N., Hurrell, R., & Kelishadi, R. (2014). Review on iron and its importance for human health. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences, 19(2), 164.

Abbaspour, N., Hurrell, R., & Kelishadi, R. (2014). Review on iron and its importance for human health. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences, 19(2), 164.

Abraham, H. M. A., White, C. M., & White, W. B. (2015). The comparative efficacy and safety of the angiotensin receptor blockers in the management of hypertension and other cardiovascular diseases. Drug safety, 38, 33-54.

Adams, KF, Fonarrow, GC, Emerman, CL, et. al., (2005). Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). Am Heart J, 149(2), 209-216.

Ames BN, Atamna H, Killilea DW. Mineral and vitamin deficiencies can accelerate the mitochondrial decay of aging. Mol Aspects Med. 2005 Aug-Oct;26(4-5):363-78. doi: 10.1016/j.mam.2005.07.007. PMID: 16102804.

Ana, M., (2015). Iron metabolism. Reviewing Basic Sciences.3(2):123-126.Anzal, M, Palmer, AJ, Starr, J, et. al., (1996). The prevelance of pseudohypertension in the elderly. J Hum Hypertension, 10(6), 409-411.

Anchala, R., Kannuri, N. K., Pant, H., Khan, H., Franco, O. H., Di Angelantonio, E., & Prabhakaran, D. (2014). Hypertension in India: a systematic review and meta-analysis of prevalence, awareness, and control of hypertension. Journal of hypertension, 32(6), 1170–1177.

Ansar, W., & Ghosh, S. (2016). Inflammation and Inflammatory Diseases, Markers, and Mediators: Role of CRP in Some Inflammatory Diseases. Biology of C Reactive Protein in Health and Disease, 67–107.

Anzal, M, Palmer, AJ, Starr, J, et. al., (1996). The prevelance of pseudohypertension in the elderly. J Hum Hypertension, 10(6), 409-411.

Aronow, W. S., & Shamliyan, T. A. (2018). Blood pressure targets for hypertension in patients with type 2 diabetes. Annals of translational medicine, 6(11).

Azizi, F, Rashidi, A, Ghanbarian, A, et. al., (2003). Is systolic blood pressure sufficient for classification of blood pressure and determination of hypertension based on JNC-VI in an Iranian adult population? Tehran Lipid and Glucose Study (TLGS). J Hum Hypertens, 17(4), 287-291.

Biswas, S., Dastidar, D. G., Roy, K. S., Pal, S. K., Biswas, T. K., & Ganguly, S. B. (2003). Complications of hypertension as encountered by primary care physician. Journal of the Indian Medical Association, 101(4), 257–259.

Burt, VL, Whelton, P, Roccella, EJ, et. al., (1995). Prevelance of hypertension in the U.S adult population. Results from the Third National Health and Nutrition Examination Survey, 1998-1991. Hypertension, 25, 305-313.

Byler RM, Sherman NA, Wallner JS, Horwitz LD. Hydrogen peroxide cytotoxicity in cultured cardiac myocytes is iron dependent. Am J Physiol 1994; 266: H121-27.

Charan, J., & Biswas, T. (2013). How to calculate sample size for different study designs in medical research? Indian journal of psychological medicine, 35(2), 121–126.

Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jones DW, Materson BJ, Oparil S, Wright JT, Roccella EJ., National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA. 2003 May 21;289(19):2560-72.

Cole, J. W. (2017). Large artery atherosclerotic occlusive disease. CONTINUUM: Lifelong Learning in Neurology, 23(1), 133.

Dr. Sahana, KR., & Dr. kruthi, BN. (2020). Correlation of serum ferritin and thyroid hormone status among hypothyroidism. International journal of biochemistry, 16(1), pp.51- 57.

Droste, DW, Ritter, MA, Dittrich, R, et. al., (2003). Arterial hypertension and ischaemic stroke. Acta Neurol Scand, 107(4), 241-250.

Ems T, St Lucia K, Huecker MR. Biochemistry, Iron Absorption. [Updated 2023 Apr 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-.

Faruqi A, Mukkamalla SKR. Iron Binding Capacity. [Updated 2022 Jan 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.

Faruqi A, Mukkamalla SKR. Iron Binding Capacity. [Updated 2023 Jan 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-.

Fisher, CM, (1979). Capsular infarcts: the underlying vascular lesions. Arch Neurol, 36(2), 65-73.

Floyd RA, Lewis CA. Hydroxyl free radical formation from hydrogen peroxide by ferrous iron-nucleotide complexes. Biochemistry. 1983 May 24;22(11):2645-9. doi: 10.1021/bi00280a008. PMID: 6307343.

Fountain JH, Kaur J, Lappin SL. Physiology, Renin Angiotensin System. [Updated 2023 Mar 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-

Galan P, Vergnaud AC, Tzoulaki I, Buyck JF, Blacher J, Czernichow S, Hercberg S. Low total and nonheme iron intakes are associated with a greater risk of hypertension. J Nutr 2010; 140:75–80.

Goldstein, LB, Adams, R, Alberts, MJ, et. al., (2006). Primary prevention of ischemic stroke: a guideline from the American Heart Association / American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the quality of care and outcomes Research

Interdisciplinary Working Group. Circulation, 113(24), 873-923.

Gupta, R. Trends in hypertension epidemiology in India. J Hum Hypertens 18, 73–78 (2004).

Gupta, S., McLaughlin, E., & Gomez, M. (2019). Guest Satisfaction and Restaurant Performance. The Next Frontier of Restaurant Management: Harnessing Data to Improve Guest Service and Enhance the Employee Experience, 33-53.

Haider, AW, Larson, MG, Franklin, SS, et. al., (2003). Systolic blood pressure, diastolic blood pressure, and pulse pressure as predictors of risk for congestive heart failure in the Framingham Heart Study. Ann Intern Med, 138(1), 10-16.

Hall, JE, (2003). The kidney, hypertension, and obesity. Hypertension, 41, 625-633.

Hall, JE, Hildebrandt, DA, Kuo, JJ, (2001). Obesity hypertension:role of leptin and sympathetic nervous system. Am J Hypertens, 14, 103S-105S.

Halliwell B, Gutteridge JM. Role of free radicals and catalytic metal ions in human disease: an overview. Methods Enzymol. 1990; 186:1-85.

Hegde, N., Rich, M. W., & Gayomali, C. (2006). The cardiomyopathy of iron deficiency. Texas Heart Institute journal, 33(3), 340–344.

Henry, JB (1979) Clinical Diagnosis and Management by Laboratory Methods, W.B Saunders Company, Philadelphia, PA, Volume 1, p 60.

Horwitz LD, Fennessey PV, Shikes RH, Kong Y. Marked reduction in myocardial infarct size due to prolonged infusion of an antioxidant during reperfusion. Circulation. 1994 Apr;89(4):1792-801.

Hsu, C. Y., McCulloch, C. E., Darbinian, J., Go, A. S., & Iribarren, C. (2005). Elevated blood pressure and risk of end-stage renal disease in subjects without baseline kidney disease. Archives of internal medicine, 165(8), 923-928.

Hundley, WG, Kitzman, DW, Morgan, TM, et. al., (2001). Cardiac cycle dependent

changes in aortic area and distensibility are reduced in older patients with isolated diastolic heart failure and correlate with exercise intolerance. J Am Coll Cardiol. 38(3), 796-802.

Iqbal AM, Jamal SF. Essential Hypertension. [Updated 2022 Jul 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-.

Jiang, S. Z. (2016). Lu w, Zong XF, Ruan HY, Liu Y. Obesity and hypertension. Exp Ther Med, 12(4), 2395-9.

John M., Flack, Yadao, A. M., Purkayastha, D., Samuel, R., & White, W. B. (2012). Comparison of the effects of aliskiren/valsartan in combination versus valsartan alone in patients with Stage 2 hypertension. Journal of the American Society of Hypertension, 6(2), 142-151.

Joint National Commission 7, 2004 August

Joint National Commission 8. 2018 March 1

Jordan, J, Biaggioni, I, (2002). Diagnosis and treatment of supine hypertension in autonomic failure patients with orthostatic hypotension. J Clin Hypertens (Greenwich), 4(2), 139-145.

Jordan, J., Ricci, F., Hoffmann, F., Hamrefors, V., & Fedorowski, A. (2020). Orthostatic Hypertension. Hypertension, 75(5), 1151–1158.

Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet. 2005 Jan 15-21;365(9455):217-23.

Khangura, D. S., Salam, M. W., Brietzke, S. A., & Sowers, J. R. (2000). Hypertension in diabetes. Endotext. South Dartmouth: MDText. com, Inc.

Kiechl S, Willeit J, Egger G, Poewe W, Oberhollenzer F. Body iron stores and the risk of carotid atherosclerosis: prospective results from the Bruneck study. Circulation 2007; 96:3300-3307

Kim MK, Baek KH, Song KH, Kang MI, Choi JH, Bae JC, Park CY, Lee WY, Oh KW. Increased serum ferritin predicts the development of hypertension among middle-aged men. Am J

Hypertens. 2012 Apr;25(4):492-7. doi: 10.1038/ajh.2011.241. Epub 2012 Jan 26. PMID: 22278211.

Kotze, M. J., van Velden, D. P., van Rensburg, S. J., & Erasmus, R. (2009). Pathogenic Mechanisms Underlying Iron Deficiency and Iron Overload: New Insights for Clinical Application. EJIFCC, 20(2), 108–123.

Kuriakose, D., & Xiao, Z. (2020). Pathophysiology and treatment of stroke: present status and future perspectives. International journal of molecular sciences, 21(20), 7609.

Lawes, CM, Vander Hoorn, S, Rodgers, A, (2008). International Society of Hypertension.Global burden of blood-pressure-related- disease. Lancet, 371, 1513-1518.

Lee DH, Kang SK, Choi WJ, Kwak KM, Kang D, Lee SH. Association between serum ferritin and hypertension according to the working type in Korean men: the fifth Korean National Health and nutrition examination survey. Ann Occup Environ Med. 2010; 30:40.

Lee DH, Kang SK, Choi WJ, Kwak KM, Kang D, Lee SH. Association between serum ferritin and hypertension according to the working type in Korean men: the fifth Korean National Health and nutrition examination survey. Ann Occup Environ Med. 2010; 30:40.

Lenfant, C., Chobanian, A. V., Jones, D. W., & Roccella, E. J. (2003). Seventh report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) resetting the hypertension sails. Hypertension, 41(6), 1178-1179.

Lindholm, LH, Carlberg, B, Samuelsson, O, (2005). Should beta blockers remain first choice in the treatment of primary hypertension? A meta-analysis.Lancet, 366(9496), 1545-1553.

Lionakis, N., Mendrinos, D., Sanidas, E., Favatas, G., & Georgopoulou, M. (2012). Hypertension in the elderly. World journal of cardiology, 4(5), 135–147.

Lionakis, N., Mendrinos, D., Sanidas, E., Favatas, G., & Georgopoulou, M. (2012). Hypertension in the elderly. World journal of cardiology, 4(5), 135–147.

Lohmeier, T. E., & Iliescu, R. (2013). The sympathetic nervous system in obesity

hypertension. Current hypertension reports, 15, 409-416.

Luca, C. T., Crisan, S., Cozma, D., Negru, A., Lazar, M. A., Vacarescu, C., ... & Iurciuc, S. (2021). Arterial Hypertension: Individual Therapeutic Approaches—From DNA Sequencing to Gender Differentiation and New Therapeutic Targets. Pharmaceutics, 13(6), 856.

Luqman Hafeez, Sevy Puri, Sahil Chhabra, Nehal Patel, Kiran Kumar Singal, Nitish Thakur. "Association between serum ferritin levels and elevated blood pressures: A case control study". European Journal of Molecular & Clinical Medicine, 9, 2, 2022, 78-81.

Maiese K, Chong ZZ, Li F, Shang YC. Erythropoietin: Elucidating new cellular targets that broaden therapeutic strategies. Prog Neurobiol. 2008a doi: 10.1016/j.pneurobio.2008.02.002

McCord J. Iron, free radicals and oxidative injury. Semin Hematol 1998; 35: 5−12.

measurement in humans and experimental animals: part 1: blood pressure measurement in humans: a statement for professionals from the subcommittee of professional and public Education of the American Heart Asssociation Council on High Blood Pressure Research. Circulation, 111(5), 697-716.

Mills, K. T., Stefanescu, A., & He, J. (2020). The global epidemiology of hypertension. Nature Reviews Nephrology, 16(4), 223-237.

Muhammed, Z. H., & Al-Hakeim, H. K. (2011). Iron Status in Patients with Primary Hypertension. Al-Kufa University Journal for Biology, 3(1).

Naschitz, J. E., & Rosner, I. (2007). Orthostatic hypotension: framework of the syndrome. Postgraduate medical journal, 83(983), 568–574.

Naschitz, J. E., & Rosner, I. (2007). Orthostatic hypotension: framework of the syndrome. Postgraduate medical journal, 83(983), 568-574.

NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants. Lancet. 2017 Jan 7;389(10064):37-55. doi: 10.1016/S0140-6736(16)31919-5. Epub

2016 Nov 16. Erratum in: Lancet. 2020 Sep 26;396(10255):886. PMID: 27863813; PMCID: PMC5220163

Nuredini, G., Saunders, A., Rajkumar, C., & Okorie, M. (2020). Current status of white coat hypertension: where are we? Therapeutic advances in cardiovascular disease, 14, 1753944720931637.

Obeagu, Emmanuel. (2020). Changes in Iron Status of Hypertensive Patients. International Journal of Research Studies in Medical and Health Sciences. 5. 2456-6373. 10.22259/ijrsmhs.0502002. of interpretation and uses of dietary reference intakes, and the standing committee on the scientific evaluation of dietary reference intakes food and nutrition board Institute of medicine, 797.

Ong, KL, Cheung, BM, Man, YB, et. al., (2007). Prevelance, awareness, treatment and control of hypertension among United States Adults 1999-2004. Hypertenion, 49, 69-75.

Oparil, S., Acelajado, M. C., Bakris, G. L., Berlowitz, D. R., Cífková, R., Dominiczak, A. F., ... & Whelton, P. K. (2018). Hypertension. Nature reviews Disease primers, 4(1), 1-21.

Packer, M, Fowler, MB, Roecker, EB, et. al., (2002). Effect of carvedilol on the morbility of patients with severe chronic heart failure results of the Carvedilol Prospective Randomized Cumulative Survival (COPERNICUS) study. Circulation, 106(17), 2194-2199.

Palma, J. A., Redel-Traub, G., Porciuncula, A., Samaniego-Toro, D., Vernetti, P. M., Lui, Y. W., ... & Kaufmann, H. (2020). The impact of supine hypertension on target organ damage and survival in patients with synucleinopathies and neurogenic orthostatic hypotension. Parkinsonism & related disorders, 75, 97-104.

Palma, J. A., Redel-Traub, G., Porciuncula, A., Samaniego-Toro, D., Vernetti, P. M., Lui, Y. W., ... & Kaufmann, H. (2020). The impact of supine hypertension on target organ damage and survival in patients with synucleinopathies and neurogenic orthostatic hypotension. Parkinsonism & related disorders, 75, 97-104.

Perkovic, V, Huxley, R, Wu, Y, et. al., (2007). The burden of blood pressure-related disease: a neglected priority for global health.Hypertension. 50, 991-997.

Pickering, T. G., Eguchi, K., & Kario, K. (2011). Masked hypertension: a review. Hypertension research: official journal of the Japanese Society of Hypertension, 30(6), 479–488.

Pickering, TG, Davidson, K, Gerin, W, et. al., (2002). Masked hypertension. Hypertension, 40(6), 795-796.

Pickering, TG, Hall, JE, Appel, LJ, et. al., (2005). Recommendations for blood pressure.

Pugh, D., Gallacher, P. J., & Dhaun, N. (2019). Management of hypertension in chronic kidney disease. Drugs, 79, 365-379.

Rancourt ME, Rodrigue ME, Agharazii M, Larivière R, Lebel M. Role of oxidative stress in erythropoietin-induced hypertension in uremic rats. Am J Hypertens. 2010 Mar;23(3):314-20. doi: 10.1038/ajh.2009.242. Epub 2009 Dec 17. PMID: 20019674.

Rodwell, V.W., Bender, D.A., Botham, K.M., Kennelly, P.J. & Weil, P.A. (2015). Harper's Illustrated Biochemistry (30th. Ed.). United states, The McGraw-Hill Education.

Rauramaa R, Vaisanen S, Mercuri M, Rankinen T, Penttila I, Bond MG. Association of risk factors and body iron status to carotid atherosclerosis in middleaged eastern Finnish men. EurHeartJ1994; 15:1020-1027.

Ruiter G, Lankhorst S, Boonstra A, Postmus PE, Zweegman S, Westerhof N, van der Laarse WJ, Vonk-Noordegraaf A. Iron deficiency is common in idiopathic pulmonary arterial hypertension. Eur Respir J 2011; 37:1386–1391

Ruiter G, Lankhorst S, Boonstra A, Postmus PE, Zweegman S, Westerhof N, van der Laarse WJ, Vonk-Noordegraaf A. Iron deficiency is common in idiopathic pulmonary arterial hypertension. Eur Respir J 2011; 37:1386–1391

Russell, R., Beard, J. L., Cousins, R. J., Dunn, J. T., Ferland, G., Hambidge, K., ... & Yates,

A. A. (2001). Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. A report of the panel on micronutrients, subcommittees on upper reference levels of nutrients and

Saladin K.S., Porth C.M. (2017): Anatomy & Physiology: The Unity of Form & Function. 8th Edition. McGrawHill.p:709.

Saladin K.S., Porth C.M. (2017): Anatomy & Physiology: The Unity of Form & Function. 8th Edition. McGrawHill.p:709.

Saseen, J, maclaughlin.hypertension.in: Dipiro, JT, Talbert, RL, Yee, GC, Matzke, Wells, BG, Posey, LM, (2014). Pharmacotherapy: A pathophysiologic approach.9th ed. New York: McGraw-Hill Medical, chapter 3

Saseen, JJ. (2013). Essential hypertension. In: All dredge BK, Corelli RL, Ernst ME, Guglielmo BJ, Jacobson PA, Kradjan WA, Williams BR, editors. Koda-Kimble and Young's.

Sempos CT, Looker AC, Gillum RF, Makuc DM. Body iron stores and the risk of coronary heart disease. N Engl J Med 2004; 330:1119-1124.

Shahjehan, R. D., & Bhutta, B. S. (2022). Coronary artery disease. In StatPearls [Internet]. StatPearls Publishing.

Siedel III, G. J., Hildebrandt, H. W., & Miller, E. L. (1984). An executive appraisal of the importance of business law. Am. Bus. LJ, 22, 249.

Vasan, RS, Benjamin, EJ, levy, D (1995). Prevelance, clinical features and prognosis of diastolic heart failure, an epidemiologic perspective. J Am Coll Cardiol, 26(7), 1565-1574.

VAZIRI, N. (2008). Causal link between oxidative stress, inflammation, and hypertension.

Whelton, P. K., Carey, R. M., Mancia, G., Kreutz, R., Bundy, J. D., & Williams, B. (2022). Harmonization of the American College of Cardiology/American Heart Association and European Society of Cardiology/European Society of Hypertension Blood Pressure/Hypertension Guidelines: Comparisons, Reflections, and Recommendations. Circulation, 146(11), 868–877.

Wong, C. K., & White, H. D. (2002). Relation between blood pressure after an acute coronary event and subsequent cardiovascular risk. Heart, 88(6), 555-558.

Wood RJ, Ronnenberg A. Iron. In: Shils ME, Shike M, Ross AC, Caballero B, Cousins RJ, editors. Modern Nutrition in Health and Disease. 10th ed. Baltimore: Lippincott Williams & Wilkins; 2005. pp. 248–70.

World health organization; 2013 April 7.

World Heart Federation; 2015 Jan 26.

Xie, X., Atkins, E., Lv, J., Bennett, A., Neal, B., Ninomiya, T., ... & Rodgers, A. (2016). Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. The Lancet, 387(10017), 435-443.

Yan, F., Li, K., Xing, W., Dong, M., Yi, M., & Zhang, H. (2022). Role of Iron-Related Oxidative Stress and Mitochondrial Dysfunction in Cardiovascular Diseases. Oxidative medicine and cellular longevity, 2022, 5124553.

Zhu Y, Chen G, Bo Y, Liu Y. Markers of iron status, blood pressure and incident hypertension among Chinese adults. Nutr Metab Cardiovasc Dis. 2019 Aug;29(8):830-836. doi: 10.1016/j.numecd.2019.04.012. Epub 2019 May 8. PMID: 31255378.

ANNEXURES

Unique Identification No:

INTEGRAL INSTITUTE OF MEDICAL SCIENCES AND RESEARCH

LUCKNOW -226026

INCLUSION AND EXCLUSION CRITERIA – FOR CASES

Inclusion Criteria

S.N.	Criteria	YES	NO
1.	Diagnosed cases of hypertension		
2.	Subjects within the age of 30 to 60 years		

Exclusion Criteria

S.N.	Criteria	YES	NO
1.	Pregnant females and lactating females		
2.	History of Malabsorption of iron.		
3.	History of any chronic illness.		
4.	History of Iron deficiency anemia.		

Subject is eligible for the study, if all **INCLUSION** criteria are **YES** and all **EXCLUSION** criteria are **NO**.

INVESTIGATOR STATEMENT

I have verified the data entered in the case report form and have determined that it is complete, accurate and compatible with the source documents

Investigator's name Investigator's signature Date

Unique Identification No:

IDENTIFIERS- FOR CASES

Registration No:

Contact No:

Name:

Father's Name /Husband's Name:

Address:

DEMOGRAPHICS- CASES

Age:

Sex: Male ☐ Female ☐

Place of Residence: Urban ☐ Rural ☐

Social / Economical Status: a) Upper b) Upper Middle c) Lower Middle
d) Upper Lower e) Lower

Education: a) Illiterate b) Primary c) Middle d) High School e) Intermediate
f) Graduation g) Post-graduation & above

ANTHROPOMETRIC PARAMETERS- CASES

Height (mts) ☐

Weight (kgs) ☐

Body Mass Index (kg/ m^2) ☐

Unique Identification No:

INTEGRAL INSTITUTE OF MEDICAL SCIENCES AND RESEARCH

LUCKNOW -226026

SELECTION CRITERIA-- FOR CONTROLS

S.N.	Criteria	YES	NO
1.	Apparently healthy individuals		
2.	Subjects within the age of 30 to 60 years		

Subject is eligible for the study, if all **INCLUSION** criteria are **YES** and all **EXCLUSION** criteria are **NO**.

INVESTIGATOR STATEMENT

I have verified the data entered in the control report form and have determined that it is complete, accurate and compatible with the source documents

Investigator's name Investigator's signature Date

Unique Identification No:

IDENTIFIERS- FOR CONTROL

Registration No:

Contact No:

Name:

Father's Name /Husband's Name:

Address:

DEMOGRAPHICS- CONTROL

Age:

Sex: Male ☐ Female ☐

Place of Residence: Urban ☐ Rural ☐

Social / Economical Status: a) Upper b) Upper Middle c) Lower Middle
d) Upper Lower e) Lower

Education: a) Illiterate b) Primary c) Middle d) High School e) Intermediate
f) Graduation g) Post-graduation & above

ANTHROPOMETRIC PARAMETERS- CONTROL

Height (mts) ☐

Weight (kgs) ☐

Body Mass Index (kg/ m^2) ☐

Unique Identification No:

INFORMED CONSENT FORM (FOR CASE)

Study title: Serum Iron and Total Iron Binding Capacity in Hypertensive Patients and Control Subjects

Subject's name…….....…. Age…… Sex…….

I confirm that I have read and understood/have been explained the information given by the researcher/moderator and I had an opportunity to ask questions. I understand that the participation in the study is voluntary and I am free to withdraw at any time without giving any reason and without being my medical care and legal rights being affected. I understand that my identity will not be revealed to any third party or in publication. I understand that the researchers/ regulatory authorities'/ ethics committee will not need my permission to access my health records if necessary for the current study. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). I agree to take part in the above study.

Signature of the subject……..… **Date…….**

Name of the Investigator (printed)…….

Signature of the investigator…… **Date…….**

Name and signature of the impartial witness with date if required

……

Unique Identification No:

INFORMED CONSENT FORM (FOR CONTROL)

Study title: Serum Iron and Total Iron Binding Capacity in Hypertensive Patients and Control Subjects

Subject's name……. Age…… Sex……...

I confirm that I have read and understood/have been explained the information given by the researcher/moderator and I had an opportunity to ask questions. I understand that the participation in the study is voluntary and I am free to withdraw at any time without giving any reason and without being my medical care and legal rights being affected. I understand that my identity will not be revealed to any third party or in publication. I understand that the researchers/ regulatory authorities' / ethics committee will not need my permission to access my health records if necessary for the current study. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). I agree to take part in the above study.

Signature of the subject…….……. Date…….

Name of the Investigator (printed)……

Signature of the investigator…… Date…….

Name and signature of the impartial witness with date if required

……

विशिष्ट पहचान संख्या :

सूचित सहमति प्रपत्र (मामले के लिए)

अध्ययन का शीर्षक: उच्च रक्तचाप रोगियों और नियंत्रण सदस्यों में रक्त सीरम आयरन और कुल आयरन बाइंडिंग क्षमता

विषय का नाम..... आयु ..... लिंग .....

मैं पुष्टि करता हूं कि मैंने शोधकर्ता/मॉडरेटर द्वारा दी गई जानकारी को पढ़ और समझ लिया है/समझाया गया है और मुझे प्रश्न पूछने का अवसर मिला था। मैं समझता हूं कि अध्ययन में भाग लेना स्वैच्छिक है और मैं किसी भी समय बिना कोई कारण बताए और मेरी चिकित्सा देखभाल और कानूनी अधिकारों को प्रभावित किए बिना वापस लेने के लिए स्वतंत्र हूं। मैं समझता हूं कि मेरी पहचान किसी तीसरे पक्ष या प्रकाशन में प्रकट नहीं की जाएगी। मैं समझता हूं कि वर्तमान अध्ययन के लिए आवश्यक होने पर शोधकर्ताओं/नियामक प्राधिकरणों/नैतिकता समिति को मेरे स्वास्थ्य रिकॉर्ड तक पहुंचने के लिए मेरी अनुमति की आवश्यकता नहीं होगी। मैं इस अध्ययन से उत्पन्न होने वाले किसी भी डेटा या परिणाम के उपयोग को प्रतिबंधित नहीं करने के लिए सहमत हूं, बशर्ते ऐसा उपयोग केवल वैज्ञानिक उद्देश्यों के लिए हो। मैं उपरोक्त अध्ययन में भाग लेने के लिए सहमत हूं।

विषय के हस्ताक्षर .....दिनांक .....

अन्वेषक का नाम (मुद्रित) .....

अन्वेषक के हस्ताक्षर ..... दिनांक .....

यदि आवश्यक हो तो तारीख के साथ निष्पक्ष गवाह का नाम और हस्ताक्षर

.....

विशिष्ट पहचान संख्या :

सूचित सहमति प्रपत्र (नियंत्रण के लिए)

अध्ययन का शीर्षक: उच्च रक्तचाप रोगियों और नियंत्रण सदस्यों में रक्त सीरम आयरन और कुल आयरन बाइंडिंग क्षमता

विषय का नाम..... आयु ..... लिंग .....

मैं पुष्टि करता हूं कि मैंने शोधकर्ता/मॉडरेटर द्वारा दी गई जानकारी को पढ़ और समझ लिया है/समझाया गया है और मुझे प्रश्न पूछने का अवसर मिला था। मैं समझता हूं कि अध्ययन में भाग लेना स्वैच्छिक है और मैं किसी भी समय बिना कोई कारण बताए और मेरी चिकित्सा देखभाल और कानूनी अधिकारों को प्रभावित किए बिना वापस लेने के लिए स्वतंत्र हूं। मैं समझता हूं कि मेरी पहचान किसी तीसरे पक्ष या प्रकाशन में प्रकट नहीं की जाएगी। मैं समझता हूं कि वर्तमान अध्ययन के लिए आवश्यक होने पर शोधकर्ताओं/नियामक प्राधिकरणों/नैतिकता समिति को मेरे स्वास्थ्य रिकॉर्ड तक पहुंचने के लिए मेरी अनुमति की आवश्यकता नहीं होगी। मैं इस अध्ययन से उत्पन्न होने वाले किसी भी डेटा या परिणाम के उपयोग को प्रतिबंधित नहीं करने के लिए सहमत हूं, बशर्ते ऐसा उपयोग केवल वैज्ञानिक उद्देश्यों के लिए हो। मैं उपरोक्त अध्ययन में भाग लेने के लिए सहमत हूं।

विषय के हस्ताक्षर .....दिनांक .....

अन्वेषक का नाम (मुद्रित) .....

अन्वेषक के हस्ताक्षर ..... दिनांक .....

यदि आवश्यक हो तो तारीख के साथ निष्पक्ष गवाह का नाम और हस्ताक्षर

.....

INSTITUTIONAL ETHICS COMMITTEE (IEC)

IIMS&R INTEGRAL UNIVERSITY, LUCKNOW

IEC/IIMS&R/2023/66

CERTIFICATE

This is to certify that research work entitled **"Serum Iron and Total Iron Binding Capacity in Hypertensive Patients and Control Subjects"** submitted by **Sudhakar Singh, Dr. Priyanka Thapa** for ethical approval before the Institutional Ethics Committee IIMS&R. The above mentioned research work has been approved by Institutional Ethics Committee, IIMS&R with consensus in the meeting held on **30th December 2022.**

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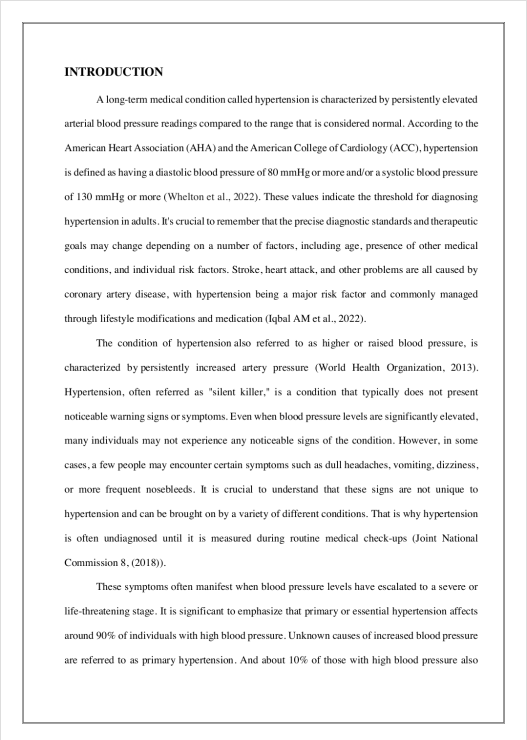

INTRODUCTION

A long-term medical condition called hypertension is characterized by persistently elevated arterial blood pressure readings compared to the range that is considered normal. According to the American Heart Association (AHA) and the American College of Cardiology (ACC), hypertension is defined as having a diastolic blood pressure of 80 mmHg or more and/or a systolic blood pressure of 130 mmHg or more (Whelton et al., 2022). These values indicate the threshold for diagnosing hypertension in adults. It's crucial to remember that the precise diagnostic standards and therapeutic goals may change depending on a number of factors, including age, presence of other medical conditions, and individual risk factors. Stroke, heart attack, and other problems are all caused by coronary artery disease, with hypertension being a major risk factor and commonly managed through lifestyle modifications and medication (Iqbal AM et al., 2022).

The condition of hypertension also referred to as higher or raised blood pressure, is characterized by persistently increased artery pressure (World Health Organization, 2013). Hypertension, often referred as "silent killer," is a condition that typically does not present noticeable warning signs or symptoms. Even when blood pressure levels are significantly elevated, many individuals may not experience any noticeable signs of the condition. However, in some cases, a few people may encounter certain symptoms such as dull headaches, vomiting, dizziness, or more frequent nosebleeds. It is crucial to understand that these signs are not unique to hypertension and can be brought on by a variety of different conditions. That is why hypertension is often undiagnosed until it is measured during routine medical check-ups (Joint National Commission 8, (2018)).

These symptoms often manifest when blood pressure levels have escalated to a severe or life-threatening stage. It is significant to emphasize that primary or essential hypertension affects around 90% of individuals with high blood pressure. Unknown causes of increased blood pressure are referred to as primary hypertension. And about 10% of those with high blood pressure also

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have secondary hypertension, which is brought on by an underlying illness or medication. Determining the base cause of secondary hypertension is crucial for appropriate management. Regular blood pressure monitoring and early intervention are vital for both primary and secondary hypertensions to prevent complications and ensure optimal health (Saseen et al., 2014).

According to the World Heart Federation (WHF) report in 2015, hypertension is indeed considered the most significant cause of premature death globally. The report estimated that around 970 million individuals worldwide were living with high blood pressure at that time. Furthermore, it is projected that the prevalence of hypertension will continue to rise, with an increasing number of affected individuals by 2025 (Kearney PM et al., 2005).

Regarding the distribution of hypertension based on gender and age, the overall occurrence is generally similar between males and females. However, there are some variations observed with increasing age. Typically, around the age of 45 years, high blood pressure becomes more common in both men and women. However, compared to men in the same age group, women tend to have a greater risk of hypertension when they approach the age of 60 and the elderly (Saseen et al., 2014).

On a worldwide scale, hypertension is regarded as the main risk factor for fatalities and disability. In 2016, it was responsible for causing more than 10.5 million deaths worldwide (Lancet et al., 2017).

By 2025, hypertension is predicted to be present in 29.2% of people worldwide, up from 26.4% in 2000 (Kearney et al., 2005). Indeed, reduced worldwide disease burden and death from cardiovascular disease can be achieved by the detection and treatment of hypertension (Zhu Y et al., 2019).

According to (Lawes et al., 2008, Ong et al., 2007, Burt et al., 1995) reports, High blood pressure affects about 1 billion people globally, including 50 million Americans, indicating the need for some form of treatment. Even when it is within the ideal range, high blood pressure

continues to be the greatest risk factor for death worldwide. Every year, uncontrolled hypertension is thought to be the cause of 7.6 million fatalities. These statistics emphasize the urgent requirement for effective measures to diagnose, manage, and control hypertension to mitigate its significant impact on public health and reduce the associated mortality rate (Lawes et al., 2008).

As the demands and acceptance towards life continue to increase, hypertension is becoming a more prevalent health concern than other significant medical and public health issues. In many developed countries, individuals of higher age generally exhibit higher blood pressure levels (John et al., 2011). In populations over 60, hypertension is prevalent at high rates (60-80%).

Around the age of 50 to 55, both naturally hypertensive and untreated hypertension individuals frequently experience a decrease in diastolic blood pressure and rise in systolic blood pressure. Because of this, elderly hypertension patients have higher systolic and pulse pressures, which are important indicators of how they will fare (Azizi et al., 2003).

In a global analysis of hypertension burden, in 2005, it was identified that 20.6% of Indian men and 20.9% of Indian women had hypertension. These rates are expected to rise to 22.9% for Indian men and 23.6% for Indian women by 2025. It is important to note that hypertension is prevalent among patients with congestive heart failure, with up to 75% of hospitalized heart failure patients having hypertension as a contributing factor (Adams et al., 2005). Systolic blood pressure was reduced in the majority of effective heart failure trials to 110 to 130 mm Hg (Atkins et al., 2011).

In India, a significant proportion of deaths, with 57% attributed to stroke and 24% to coronary artery disease, are directly linked to hypertension. This highlights the strong association between hypertension and these cardiovascular conditions, emphasizing the critical role of hypertension as a risk factor in causing adverse health outcomes (Gupta R et al., 2004).

It is estimated that a large percentage, roughly 46%, of persons with hypertension are uninformed about their medical condition. The problem of hypertension is rapidly increasing due

to drastic changes in diet and lifestyle, emphasizing the need for effective preventive measures. There are two forms of hypertension, Primary (essential hypertension) that are responsible for 90% of instances, & hypertension accounts for 10% of cases due to other identified diseases (Porth C.M., Saladin K.S, 2017).

Based on evidence from various studies, including the research conducted by Packer et al. in 2002, it has been suggested that achieving a systolic blood pressure of <120mm Hg may be beneficial for certain patients. Consequently, the current recommendations for blood pressure targets in heart failure include aiming for a target of <120/80mmHg (Atkins et al.,2011).

Cardiovascular disease (CVD) and blood pressure are directly and clearly associated with each other in individuals of all genders, ages, races, ethnic groups, and countries, despite the existence of additional cardiovascular disease risk factors (Perkovic, V., et al., 2007).

Research-based on observations has demonstrated a progressive and linear increase in death from cardiovascular disease as soon as systolic and diastolic blood pressure exceed 115mmHg and 75mmHg, respectively (Mills et al., 2020). For every 20mm Hg systolic or 10mm Hg diastolic elevation of blood pressure in people aged 40 to 89, the mortality from ischemic heart disease and stroke doubles in every age group (Lenfant et al., 2003).

Iron is an essential component for nearly every living organism, playing a crucial part in multiple metabolic activities such as oxygen transfer, erythropoiesis (red blood cell creation), the synthesis of DNA, and electron flow (Abbaspour N et al., 2014). The body stores iron as the non-soluble protein ferritin, which is found inside cells. Transferrin facilitates the movement of ferritin, which is mostly found in the bone marrow, spleen, and liver, throughout the body. (Wood RJ et al., 2005).

Ferritin is present in all cells of the body, serving as a reserve of iron. While most ferritin is intracellular, small amounts are also secreted into the serum, where it contributes to the formation of essential proteins such as hemoglobin, myoglobin, and transferrin (Sahana et al., 2020).

According to the recommendations of the Food and Nutrition Board (FNB), for individuals aged 19 to 50, an adequate daily intake of iron is 8 milligrams for males and 18 milligrams for women. The higher recommended intake for women and during pregnancy, which is 27 mg, is due to factors such as blood loss through menstruation and a woman's need for iron increases during pregnancy to sustain the fetus's rapid growth and the greater blood flow that is needed. Similarly, while breastfeeding, the recommended intake is 9 mg to support the nutritional needs of both the mother and the breastfeeding infant (Russell, R. et al 2001).

In the human body, iron is typically present in complex forms that are associated with proteins called hemoproteins. These haemoprotein include heme compounds such as hemoglobin and myoglobin, as well as nonheme compounds like transferrin and ferritin. Transferrin, a glycoprotein, is produced in the liver. In the plasma, the concentration of transferrin is approximately 300 mg/dL, which is adequate to transport around 300 micrograms of iron per deciliter of plasma (Rodwell et al., 2015).

Normal Reference Values of Serum Iron - Males = 60 - 160 μg/ dl, Females = 35 - 145μg/dl.

In a longitudinal study, it was observed that a high iron load, indicated by elevated ferritin levels, was accompanied by a decrease in Total Iron Binding Capacity (TIBC). Interestingly, The occurrence of hypertension was found to be favorably correlated with ferritin (iron) and TIBC levels despite their negative connection. It indicates that the pathophysiology of hypertension may be influenced by iron status, as indicated by ferritin and TIBC. To further understand the underlying mechanisms and the connection between iron levels, metabolism of iron, and the onset of hypertension, more research is nonetheless required. (Kim MK et al., 2012).

Normal Reference Values of TIBC = 250 – 400 μg/dl.

REVIEW OF LITERATURE

An arterial blood pressure value of >140/90 mmHg is considered hypertension according to the British Hypertension Society.

A medical disorder called hypertension sometimes referred to as high blood pressure or HTN is defined by unusually elevated arterial levels of blood pressure. The Joint National Committee 7 (JNC7) describes normal blood pressure as having a systolic pressure of less than 120 mmHg and a diastolic pressure of less than 80 mmHg. A systolic blood pressure of at least 140 mmHg and/or diastolic blood pressure of at least 90 mmHg indicate hypertension (Chobanian A. et al., 2003). This disorder can harm several organs over time and greatly raise the risk of morbidity and fatality. Cardiovascular disease, neurologic disease (which includes strokes), and kidney disorders are all directly related to hypertension. The long-term effects of hypertension can be detrimental to overall health and well-being. It is important to manage hypertension through appropriate interventions, including lifestyle modifications and medications, to mitigate the associated risks and prevent complications (Obeagu, Emmanuel, 2020).

The Joint National Commission 7 states that there is widespread consensus regarding hypertension as a qualitative rather than a quantitative disorder. In other words, it is characterized by elevated blood pressure levels rather than specific qualitative abnormalities. In the present scenario, one of the most prevalent diseases in primary care is hypertension. (Achala et al., 2014).

Nearly one-third of all fatalities worldwide, or 17 million per year, are caused by coronary artery disease. Worldwide, hypertension is responsible for 9.4 million fatalities per year. According to the World Health Organization (2013), hypertension is primarily accountable for 51% of mortality from a stroke and 45% of deaths from heart disease. The ninety-five percent confidence interval for the incidence of hypertension in 2017 was between 44.6% to 51.94%, with an average of 48.2%. 58.1% of men and 44.5% of women are affected (Joint National commission 8, (2018)).

Population increase, aging, and behavioral risk factors like a poor diet, inactivity, being

overweight, alcohol excessively, and stress are all associated with hypertension. (World health organization, 2013).

Many people who are impacted by hypertension and its harmful health effects also face additional risk factors. Complications are more likely to occur in people with high blood pressure if they have certain risk factors including cardiovascular disease, stroke, being obese, diabetes, elevated cholesterol levels, and using tobacco products. (World health organization, 2013).

As people get older, the prevalence of hypertension rises to a level where over fifty percent of those between the ages of 60 and 69 and around three-quarters of those over the age of 70 are affected. With advancing years, hypertension's incidence and prevalence both rise with age. Those who are 55 years of age and elderly with normal blood pressure have a 90% lifetime probability of getting hypertension (Lionakis et al., 2012).

According to multiple studies, 70% of those who experience a cardiac event for the first time and 80% of those who experience their first stroke both have high blood pressure. (Joint National commission 8, (2018)).

CRITERIA FOR HYPERTENSION

According to the 8th report of Joint National Committee (JNC), guidelines for the diagnosis of hypertension in individuals aged 18 years and above is defined as below-(Chobanian et al., 2021).

Table-1 Guidelines for diagnosis of hypertension as per JNC 8

DIAGNOSIS CATEGORIES	SYSTOLIC (mmHg)	DIASTOLIC (mmHg)
Normal	<120	and < 80
Pre- Hypertension	120-139	and/or 80-89
First stage hypertension	140-159	and/or 90-99
Second stage hypertension	≥160	and/or ≥100

CLASSIFICATION OF HYPERTENSION

Classification based on causes (Joint National commission 8,(2018))

1. Primary hypertension

- Also referred to as Essential Hypertension
- Unidentified causes
- It can't be cured, but with the right treatment, such as a healthy lifestyle and proper medication, the consequences can be managed.
- 90% of individual that have high blood pressure suffers from primary hypertension (Saseen and MacLaughin, 2014).

2. Secondary hypertension

- Kidney impairment is most important cause of secondary hypertension.
- Secondary hypertension can be controlled by managing underlying medical issues, such as kidney disease, tumors of the adrenal glands, and consumption of alcohol.
- Secondary hypertension, in contrast to primary hypertension, has a tendency to manifest abruptly and frequently leads to elevated blood pressure levels.
- 10% of people with high blood pressure also have secondary hypertension. (Saseen and MacLaughin, 2014).

CLASSIFICATION BASED ON AGE

Table-2 Classification of hypertension according to age (Iqbal et al., 2019)

AGE	BLOOD PRESSURE (SYSTOLIC/ DIASTOLIC)
<60 years old	<140/90 mmHg
>60 years old	<150/90mmHg

ADDITIONAL TYPES OF HYPERTENSION

Other classification of hypertension according to (Joint National commission 7, (2004))

- Masked hypertension

- It is a reflection of white-coat hypertension. (Pickering et al., 2011).
- Normal blood pressure of less than 140/90 mmHg combined with an increased daytime blood pressure of more than 135/85 mmHg is referred to be "masked hypertension." (Pickering et al., 2011).
- Lifestyle factors can contribute to this phenomenon, such as the consumption of alcohol, tobacco, caffeine, and the level of physical activity outside of the clinic or office (Pickering et al., 2011).

- White coat hypertension

- Blood pressure readings taken in a medical context might not always show an increased reading. Blood pressure readings taken in different settings, including the workplace, didn't indicate an increase. (Pickering et al., 2011).
- White coat hypertension or isolated office hypertension is the term used when this occurrence appears in subjects who do not use medication. (Pickering et al., 2011).
- It occurs more frequently in elderly men and women. (Pickering et al., 2011).

- Pseudo hypertension

- With growing age, the peripheral muscular arteries can undergo significant changes, including advanced arteriosclerosis and calcification. This can result in increased rigidity of the arteries, requiring the cuff pressure to be higher in order to effectively compress them during blood pressure measurement. Consequently, this can lead to falsely high blood pressure readings (Pickering et al., 2011).

- Clinical detection of this condition can be challenging, and as a result, patients with white coat hypertension or isolated office hypertension may be susceptible to receiving high antihypertensive medicine dosages (Ogedegbe et al., 2011).
- Approximately 2.5% of people aged 65 or older are thought to be at risk for pseudo-hypertension. (Anzal et al., 1996).

➢ Resistant hypertension

- True resistant hypertension is quite rare. (Atkins et al., 2011).

➢ Orthostatic hypertension

- This condition is defined as a decline in the diastolic and systolic blood pressure of a minimum of 10 and 20 mmHg, respectively, within three minutes of standing up. (Naschitz et al., 2007).
- Usually, symptoms are not seen in orthostatic hypertension, but some time few symptoms might be accompanied like cognitive impairment, faintness, feeling lightheaded, and vision blurring (Jordan et al., 2002).
- Among these patients, significant changes in blood pressure occur, leading to episodes of fainting or syncope due to profound hypotension upon standing, and they may experience severe hypertension when in a supine position (Ogedegbe et al., 2011).
- Supine hypertension in these individuals can lead to serious complications, including the development of left ventricular hypertrophy and an increased risk of stroke (Palma et al., 2020)

CAUSES OF HYPERTENSION

According to (Joint National commission 8, (2008)) the causes of hypertension is-

Table-3 Identifiable causes of hypertension.

KNOWN CAUSES OF HYPERTENSION
Chronic kidney disease
An aortic coarctation
Cushing's syndrome
Obstruction of the urinary tract
Pheochromocytoma
Disorders of the thyroid and parathyroid

- Primary hypertension

Unknown causes

- Secondary hypertension

Table-4 Secondary causes of hypertension

SECONDARY CAUSES OF HYPERTENSION
Kidney disease
Congenital blood vessel disorders
Adrenal gland tumors
Alcohol
Thyroid disease

FACTORS ASSOCIATED WITH THE DEVELOPMENT OF ELEVATED BLOOD PRESSURE AND ITS RISK FACTORS

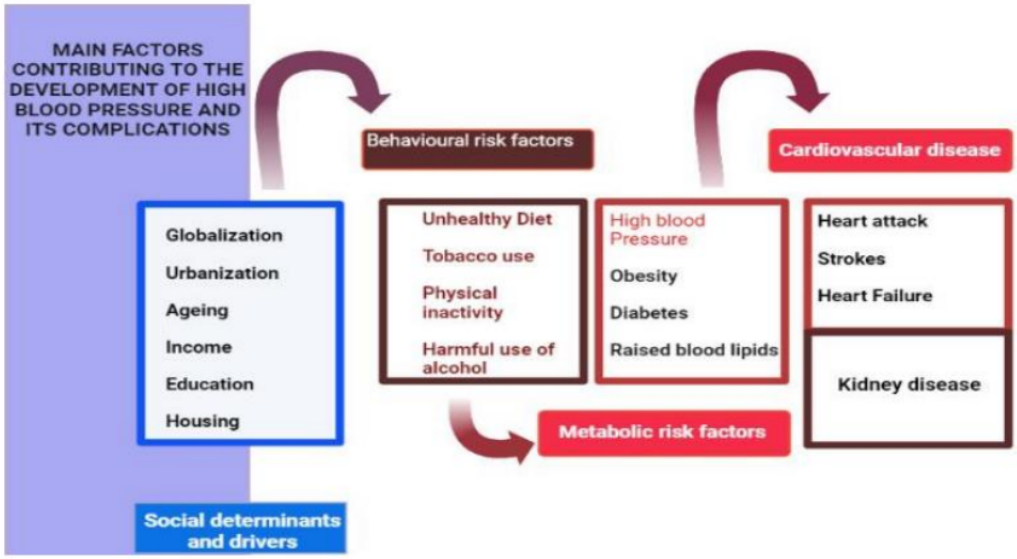

Figure-1 Factors associated with the development of increased blood pressure (World health organization, 2013).

COMPLICATIONS OF HYPERTENSION

➢ **Cardiovascular Diseases**

- Cardiovascular disorders that include, heart attacks, coronary artery disease, heart failure, and stroke all have hypertension as a vital risk factor. Elevated blood pressure can damage blood vessels, leading to the formation of plaque, restricted blood flow, and increased strain on the heart (Biswas, S., Dastidar, 2003).
- Coronary artery disease (CAD), according to the Centres for Disease Control and Prevention (CDC), is the most common form of cardiovascular disease and occurs when there is a build-up of coronary artery plaque in the vessels that carry blood to the heart muscle. Hypertension is a major risk factor for the development and progression of coronary artery disease. Over time, the plaque can narrow the arteries, reducing blood flow and increasing the risk of a heart attack (Shahjehan RD et al., 2023).

- A heart attack, medically referred to as a myocardial infarction, happens when there is a sudden interruption of blood supply to a specific part of the heart muscle. Hypertension increases the strain on the arteries and can contribute to the development of plaques and the risk of a heart attack. Hypertensive individuals are at a higher risk of experiencing heart attacks (Biswas, S., Dastidar, 2003)

➢ **Stroke**

- Hypertension is a leading cause of stroke. Across the body, high blood pressure affects blood vessels, including those in the brain. Weakened or narrowed blood vessels in the brain can rupture or become blocked, depriving the brain of oxygen and nutrients. This can result in an ischemic stroke (caused by a blockage) or a haemorrhagic stroke (caused by bleeding) (Xiao Z. et al., 2020)
- Similary to coronary events, there exists a logarithmic relationship between systolic as well as diastolic blood pressure and the occurrence of stroke (Wong et al., 2002).
- Approximately 60% of individuals who experience strokes have a previous history of hypertension, and among those who have hypertension, 78% of people have not been able to adequately regulate their blood pressure. (Droste et al., 2003).
- Blood pressure and various types of stroke interact in relatively different ways. (Pickering et al., 2011).
- The term "lacunar infarcts" refers to a large component of cerebral infarcts, which arise from lesions in small arteries that penetrate the deeper layers of the cerebral cortex, and approximately 70% of individuals who experience these types of infarcts have a history of hypertension (Fisher et al., 1979).
- Although only 50% of individuals with infarcts of the big cranial and extracranial arteries have hypertension, it is still the most significant risk factor. Infarcts of these arteries are more closely associated with atherosclerosis (Cole et al., 2017).

- After a stroke, blood pressure tends to increase quickly, and it is believed that this reaction helps to sustain brain perfusion in the infarct's penumbra zone (Droste et al., 2003).
- Younger patients having hypertension of systolic and diastolic and patients over 60 with isolated systolic hypertension have shown that treating hypertension reduces stroke risks by 35% to 44%. (Goldstein et al., 2006)
- In the treatment of hypertension, β-blockers are thought to be slightly less effective compared to other medication classes at preventing stroke. (Lindholm et al., 2005).
- There is some evidence suggesting that angiotensin-receptor blockers may be more effective in the treatment of hypertension (Abraham et al., 2015).

➢ **Heart failure**

- A significant factor of heart failure is blood pressure (Pickering et al., 2011).
- The risk of hypertension is twice as high in hypertensive males compared to normotensive males, and three times as high in hypertensive females. A history of past hypertension is also linked to 90% of new instances of cardiac failure (Mills et al., 2020).
- Systolic blood pressure is more strongly linked to this risk than diastolic blood pressure (Haider et al., 2003).
- In elderly people, treating hypertension reduces the risk of heart failure by about 50%. (Lionakis et al 2012).
- Up to 74% of heart failure cases in people with hypertension are thought to be caused by diastolic heart failure (Vasan et al., 1995).
- Patients diagnosed with diastolic heart failure exhibit increased arterial stiffness, particularly in the aorta, which can lead to amplified wave reflection from the periphery. This, in turn, contributes to elevated central aortic systolic pressure and decreased diastolic pressure (Hundley et al., 2001).

- **Chronic kidney disease**

- Uncontrolled hypertension can significantly increase the risk of renal (kidney) complications (Pugh et al., 2019).
- This is significant for two reasons: firstly, chronic kidney disease is a significant outcome of hypertension, and secondly, it is causally related to a substantially increased risk for heart disease (Ogedegbe & Pickering, 2011).
- In numerous research, it has been demonstrated that there is a significant association between blood pressure & the risk of getting end-stage renal disease (ESRD) (Hsu et al., 2005).

- **In obesity**

- It is thought that increased renal sympathetic nervous system activity plays a significant role in the process behind obesity-related hypertension (Lohmeier et al., 2013).
- With increasing weight, renal sodium resorption increases, leading to impaired pressure natriuresis and the development of excessive blood pressure, which is partially attributed to the activity of the renal sympathetic nervous system (John et al., 2011).
- Several studies have indicated that the combined blockade of alpha and beta-adrenergic receptors effectively reduces hypertension linked with obesity (Jiang et al., 2016).
- The sympathetic nervous system is more active in the kidneys and other tissues in obese people, as seen by higher tissue catecholamine overflow and other measurements (Hall et al., 2003).

- **In diabetes**

- Patients with hypertension are more likely to have diabetes, and having both ailments together greatly raises the risk of both diseases' consequences. (Atkins et al., 2011).
- Blood pressure readings of >140/90 mmHg are seen in more than half of diabetics (Khangura et al., 2000).

- More than 35% of people with hypertension also have diabetes, and 75% of people with diabetes are either taking medication or have a blood pressure that is above the ideal range of 130/80mmHg (Aronow et al., 2018).
- Diabetes is the main risk factor for end-stage renal disease (ESRD). An increased risk of getting ESRD is closely associated with raised blood pressure, and The onset of kidney disease is slowed by reducing blood pressure (Atkins et al., 2011).
- Thus, most antihypertensive agents are now recommended for use in individuals with diabetes who do not have neuropathy and albuminuria (Khangura et al., 2000).

➢ **In eye problems**

- Hypertension can affect the blood vessels in the eyes, leading to conditions such as hypertensive retinopathy, which can cause vision impairment or even vision loss.

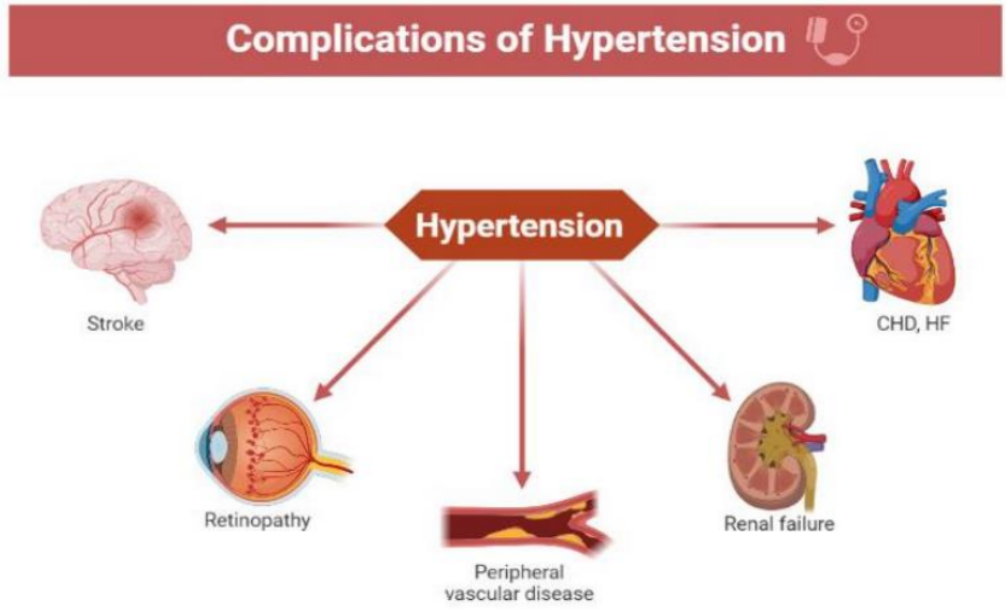

Figure-2 The main complications induced by hypertension (polygenic substrate): LVH—left ventricular hypertrophy; CHD—coronary heart disease; HF—heart failure. (Luca et al.,2021)

SYMPTOMS OF HYPERTENSION

Table-5 Symptoms of hypertension (Joint National commission 8, (2018))

SYMPTOMS OF HYPERTENSION
○ Dull headache
○ Chest Pain
○ Shortness of breath
○ Dizzy sleep
○ Nosebleed
○ Vomiting

PATHOPHYSIOLOGY OF HYPERTENSION

The body demands iron for a number of physiological functions, including the production of blood & the transportation of oxygen. Iron overload disorders, such as hereditary hemochromatosis, has been linked to a higher risk of hypertension. However, further research is needed to determine exactly how excess ferritin causes hypertension (Abbaspour et al., 2014)

One proposed mechanism is that iron overload can lead to dysfunction in endothelial cells, oxidative stress & inflammation, which can impair the normal functioning of blood vessels and contribute to the development of hypertension. Additionally, iron may affect the renin-angiotensin-aldosterone system (RAAS), a hormonal pathway involved in blood pressure regulation, although the specific interactions are not fully understood (Abbaspour et al., 2014).

The pathophysiology of hypertension involves two main factors: hormonal mechanisms like as the RASS (renin-angiotensin-aldosterone system) and disturbances in electrolyte balance (including sodium, potassium, and chloride). Natriuretic hormones can lead to elevated sodium concentrations in cells, resulting in increased blood pressure. In order to regulate arterial blood pressure, the RASS is essential (Fountain JH et al., 2023).

Angiotensin II & aldosterone are two hormones involved in the RAAS (renin-angiotensin-aldosterone system). Angiotensin II causes vasoconstriction, increases the release of vasoconstrictive chemicals, and stimulates aldosterone production. The vasoconstriction leads to increased peripheral resistance and elevated blood pressure. The hormone aldosterone, which is generated by the adrenal glands, makes it easier for the kidneys to reabsorb water and sodium, increasing the volume of blood and, as a result, high blood pressure (Oparil S. et al., 2018).

IRON AND TIBC

In living things, iron is essential for several metabolic activities including transport of oxygen, erythropoiesis, synthesis of DNA, and transportation of electrons. It is a protein found inside cells that are kept in the body as ferritin. They are typically found in the bone marrow, liver, and spleen and are stored in an insoluble form. Transferrin transports them throughout the body (MacCord J. Iron et al., 1998).

All body cells contain ferritin, which serves as a reservoir of iron in the body and is secreted in minute quantities into the serum for the production of hemoglobin, myoglobin, & transferrin (Sahana et al., 2020).

According to the FNB (Food and Nutrition Board) recommendations, daily recommended iron intake through food for adults aged 19-50 years is 18 milligrams for females, 8 milligrams for males, 27 milligrams for pregnant women, & 9 milligrams for breastfeeding females. The more advised dosages for women and during pregnancy are attributed to factors such as menstrual blood loss and the increased blood circulation required for the fetus's rapid development (Russell, R. et al 2001).

The majority of the iron in the human body is found in intricate forms that are attached to proteins (hemoproteins) as heme compounds (hemoglobin or myoglobin) or nonheme compounds (ferritin, transferring, & ferritin). Glycoprotein called transferrin is primarily synthesized in the hepatic system. By binding to iron and assisting its distribution throughout the entire body, it plays

a crucial role in iron transportation and homeostasis. The concentration of transferrin in the plasma is approximately 300 mg/dL (Ems T et al., 2023).

Iron is an essential mineral involved in various physiological processes, including the synthesis of red blood cells and oxygen transport. However, excessive iron can lead to oxidative stress and tissue damage. Iron metabolism is tightly regulated by the body to maintain a balance between iron absorption, storage, and utilization (Abbaspour et al., 2014).

Many people believe that iron's chemical characteristics account for its biological significance. The oxidative forms of iron are ferrous (Fe+2) and ferric (Fe+3). (Ana, et al., 2015). The oxidation of ferrous (Fe+2) to ferric (Fe+3) produces necessary insoluble ferric hydroxide Fe(OH)3 and contributes to the production of harmful oxygen radicals, which in turn cause peroxidative damage to essential structures of cells (Halliwell B et al., 1990).

In epidemiological and clinical research to assess bodily iron storage, the levels of serum ferritin (SF), hemoglobin, soluble transferrin receptor (sTFR), & transferrin are the most frequently used biological indicators (Zhu Y et al., 2019).

The primary carriers of blood iron are transferrin (Tf) or ferritin. The monomeric glycoprotein known as transferring is synthesized in the hepatic system and is composed of a polypeptide chain of amino acids that is divided into two homologous domains, the N- and C-terminal, each of which has a Fe+3 linking region.

There are three main primary function of transferring - (Ana et al., 2015).

1. Solubilization of Fe+3.
2. By binding to the free ions, high-affinity iron binding helps in preventing the production of free radicals.
3. Iron is delivered to cells through its interaction with membrane receptors, facilitating its supply and utilization by the cells., i.e. transferring receptors (Tfrs).

Numerous Studies have shown that changes in TIBC & levels of iron in the blood have negative effects. The generation of reactive oxygen compounds, which leads to inflammation as well as oxidative stress and has negative effects on the functioning of mitochondria & results in hypertension, which may be influenced by iron overload (Ames BN et al., 2005).

The kidney's peritubular cells naturally produce the protein known as erythropoietin (EPO), a glycoprotein hormone that is essential for promoting the generation of erythrocytes. The absorption and utilization of iron or ferritin are directly correlated with erythropoietin, which may enhance the effects of oxidative stress and exacerbate hypertension (Rancourt ME et al., 2010).

There are a number of possible explanations for the connection between concentrations of ferritin and hypertension. One of them involves atherosclerotic formation (Kim MK. et al., 2012). The combination of LDL (low-density lipoprotein) and isoprostane oxidation, which act as indicators for oxidative stress, can cause endothelial damage from excessive amounts of iron, which can lead to the development and progression of atherosclerosis. Following is the atherosclerosis process, which could raise the possibility of hypertension (Luqman et al., 2022)

When infarction and reperfusion, superoxide radicals ($\cdot O_2^-$) & H_2O_2 (hydrogen peroxide) are produced (Horwitz LD et al., 1994). These types of compounds are weak oxidizers without iron that inbuilt scavenger enzymes inactivate (Floyd RA et al., 1983). Iron, through Fenton reaction, produce hydroxyl radical ($\cdot OH$) from (H_2O_2) and ($\cdot O_2^-$) and it is highly toxic to tissue. And No reliable endogenous protections exist to stop this incredibly reactive chemical. Iron chelation reduces the generation of ·OH (hydroxyl radical) and protects cardiac cells from H_2O_2 damage. (Byler RM et al., 1994).

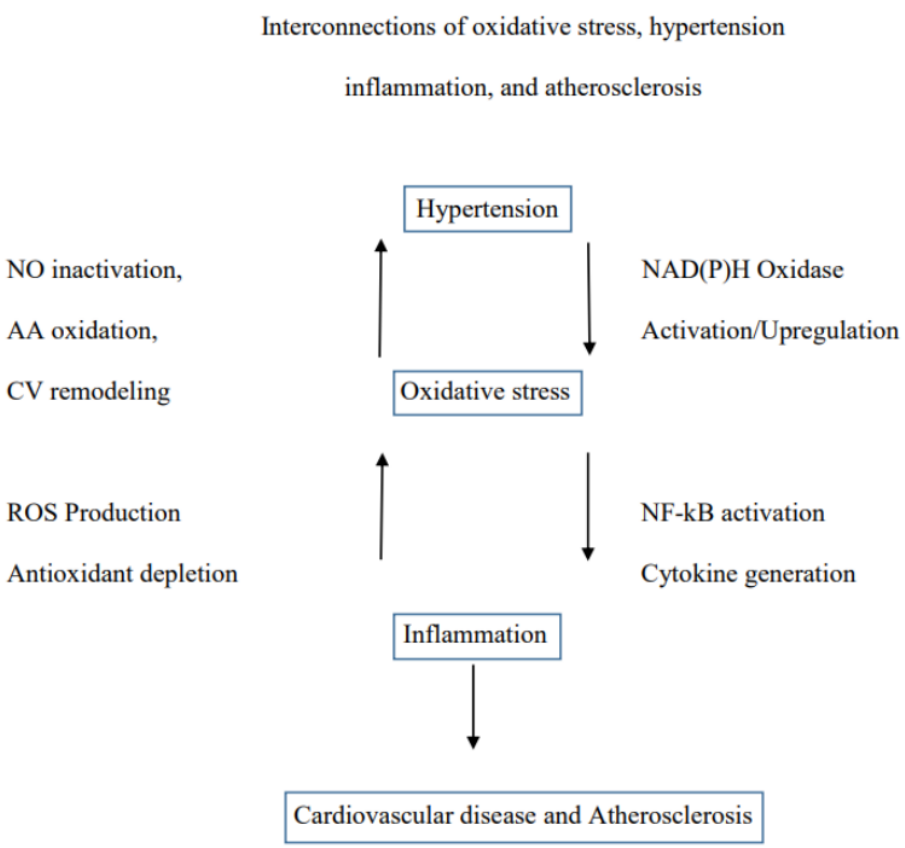

Figure- 3 (CVD- cardiovascular disease, AA- arachidonic acid; CV- cardiovascular; NF-κB- Nuclear factor-κB; NAD(P)H- Reduced nicotinamide adenine dinucleotide phosphate; ROS- Reactive oxygen species, NO-Nitric oxide) (Vaziri, N. (2008).

Iron binding capacity (IBC) is of two types, one is Total iron-binding capacity (TIBC) & second one is UIBC (unsaturated iron-binding capacity). Transferrin, a type of protein responsible for iron transport, is produced in greater quantities in the blood when iron reserves are reduced. Since transferrin is normally only saturable with iron to one-third of its volume, the remaining transferrin in serum has an additional 67% binding capacity. As more iron is required, this enables its binding & transport. This is the ability to bind iron unsaturatedly. TIBC contain serum iron and UIBC (Faruqi et al., 2022). Most patients with iron shortage are likely to have higher total iron binding capacity (TIBC) readings. Consequently, it is reasonable to infer that a

shortage of iron may be intimately linked to the onset of hypertension (Ruiter G. et al., 2011).

TIBC is an indirect measure of transferrin levels, which are inversely related to serum iron levels. When iron levels are low, transferrin production increases, leading to higher TIBC levels. Conversely, when iron levels are high, transferrin production decreases, resulting in lower TIBC levels (Faruqi A et al., 2022).

Iron deficiency anemia, which can be associated with low serum iron levels, may also affect TIBC. In iron deficiency, TIBC levels tend to increase as the body tries to compensate for the low iron levels by producing more transferrin (Faruqi A et al., 2022). Similarly, in conditions of iron overload, such as hereditary hemochromatosis or chronic transfusion therapy, TIBC levels may be lower due to decreased transferrin production (Kotze et al., 2009).

The occurrence of hypertension had a positive association with both ferritin and TIBC (total iron binding capacity), both of which are indicators of excessive iron overload (Kim MK et al., 2012). The ability of transferrin, a protein made in the liver, to bind and transport iron throughout the body, is referred to as iron binding capacity.

Total Iron-Binding Capacity (TIBC) of serum is a measurement of how much iron can be transported in the bloodstream by transferrin. TIBC reflects the body's ability to transport and bind iron. In hypertension, there may be some associations between TIBC levels and blood pressure, although the relationship is not fully understood.

IRON AND TIBC IN HYPERTENSION

In hypertension, there can be associations between serum iron levels and blood pressure, but the relationship is complex and not fully understood. Here are a few key points regarding serum iron in hypertension: -

Iron overload can lead to increased oxidative stress, endothelial dysfunction, and inflammation, which may contribute to the development of hypertension and cardiovascular diseases (Yan et al., 2022).

The occurrence of hypertension is influenced by a rise in oxidative stress caused due to too much iron (Kim MK et al., 2012). Reactive oxygen species (ROS), which are made up of free radicals of oxygen and other chemical components, are what cause oxidative stress in the body (Maiese et al., 2008). which may turn less reactive free radicals such as superoxide radicals, H_2O_2, hydroxyl, singlet oxygen ($\cdot O_2^-$), NO, & peroxynitrite into more reactive free radicals. Also Iron, through Fenton reaction, produce hydroxyl radical ($\cdot OH$) from H_2O_2 and ($\cdot O_2^-$) and it is highly toxic to tissue (Luqman et al., 2022).

Inflammation plays a role in both hypertension and iron metabolism. Chronic low-grade inflammation can affect iron homeostasis and contribute to endothelial dysfunction and vascular remodeling, leading to increased blood pressure. CRP (C-reactive protein) & interleukin-6 (IL-6) are examples of inflammatory indicators that have been linked with alterations in iron metabolism and hypertension (Ansar et al., 2016).

Iron deficiency, is characterized by decreased oxygen-carrying capacity, which can result in increased cardiac output and peripheral vascular resistance, potentially contributing to elevated blood pressure (Hegde et al., 2006). Because the body produces more transferrin to make up for the low iron levels when there is an iron deficit, TIBC levels frequently rise (Faruqi A et al., 2022).

After studying different articles, several studies have found significant association and few studies have found no significant association with Iron and (TIBC) Total iron binding capacity in hypertensive patients in different populations. As a result, it is still unclear what mechanism underlies the link between iron and TIBC in hypertension. Thus, the current study is conducted to assess their relationship with hypertension.

AIM

The aim of the present study was to evaluate and analyze levels of serum iron and total iron binding capacity (TIBC) in diagnosed cases of hypertensive patients and apparently healthy controls.

OBJECTIVES

1. To estimate serum iron level in patients of hypertensive & apparently healthy controls.
2. To estimate total iron binding capacity level in patients of hypertensive & apparently healthy controls.
3. To correlate serum iron & TIBC (total iron binding capacity) levels between hypertensive patients & apparently healthy controls.

IRON

Statistics showed that there was a statistically significant difference in iron levels between patients and controls (p-value = 0.023). (Table-6 & figure-4).

Table-6 Mean and standard deviation of the study groups.

SERUM IRON (µg/dl)					
Groups	**n**	**Mean**	**Standard Deviation (SD)**	**p-value**	**Significance**
Controls	30	140.46	± 49.98	0.023	Statistically Significant
Cases	30	173.44	± 59.00		

n= controls or cases in numbers, p-value <0.05 is regarded as statistically significant

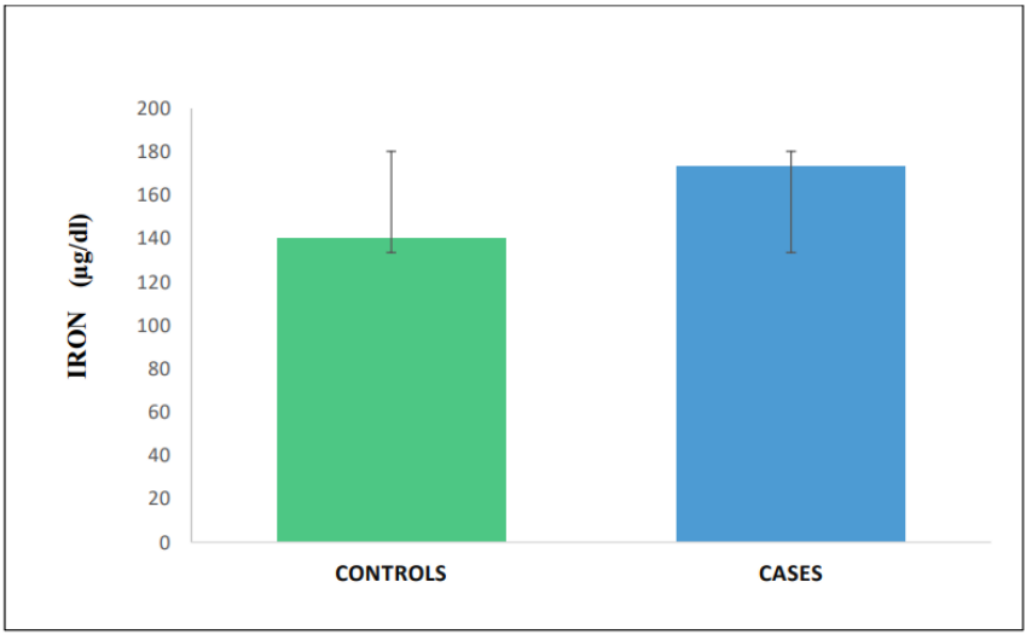

Figure-4 Comparison of Serum Iron (µg/dl) in controls and cases.

TOTAL IRON BINDING CAPACITY

Statistics showed that there was a statistically significant difference in TIBC levels between patients and controls (p-value= 0.0422) (Table-7 & figure-5).

Table-7 Mean and standard deviation of the study groups.

TIBC (TOTAL IRON BINDING CAPACITY) (µg/dl)					
Groups	**n**	**Mean**	**Standard Deviation (SD)**	**p-value**	**Significance**
Controls	30	295.39	± 41.96	0.0422	Statistically Significant
Cases	30	225.31	± 179.94		

n= controls or cases in numbers, p-value <0.05 is regarded as statistically significant

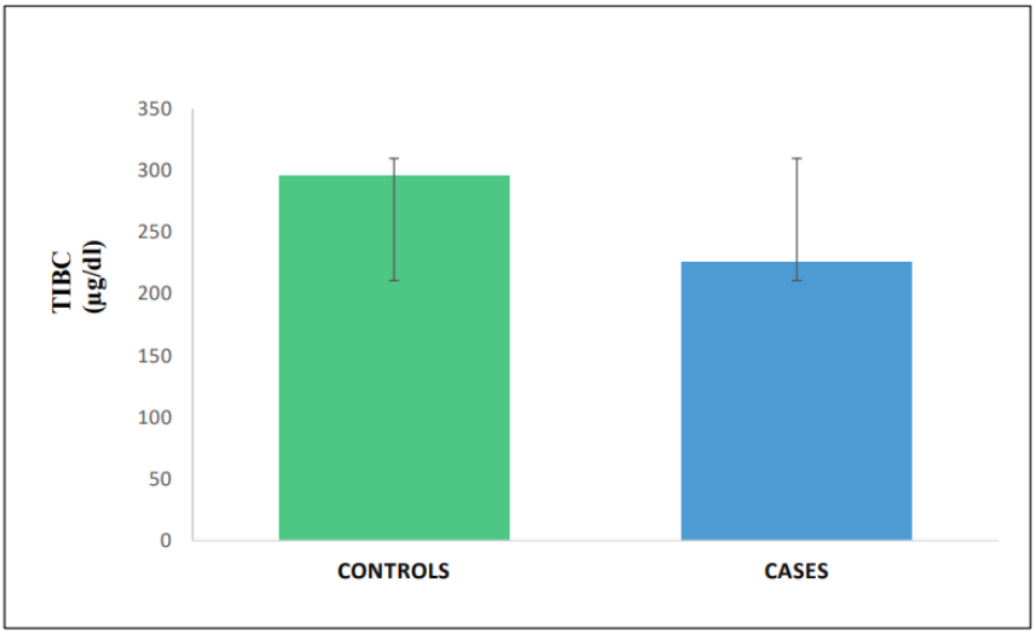

Figure-5 Comparison of TIBC (µg/dl) in controls and cases.

KARL PEARSON'S CORRELATION OF COEFFICIENT BETWEEN IRON AND TIBC IN CASES OF HYPERTENSION

There was significant association between Serum Iron and TIBC in cases of hypertension (p-value = 0.041).

Table-8 Karl Pearson's correlation coefficient between Serum Iron and TIBC.

Correlations			
		IRON (µg/dl)	**TIBC (µg/dl)**
IRON (µg/dl)	Pearson Correlation	1	-.566**
	Sig. (2-tailed)		0.041
	n	30	30
TIBC (µg/dl)	Pearson Correlation	-.566**	1
	Sig. (2-tailed)	0.041	
	n	30	30

n= Number of cases, **. Correlation is significant at the 0.05 level (2-tailed).

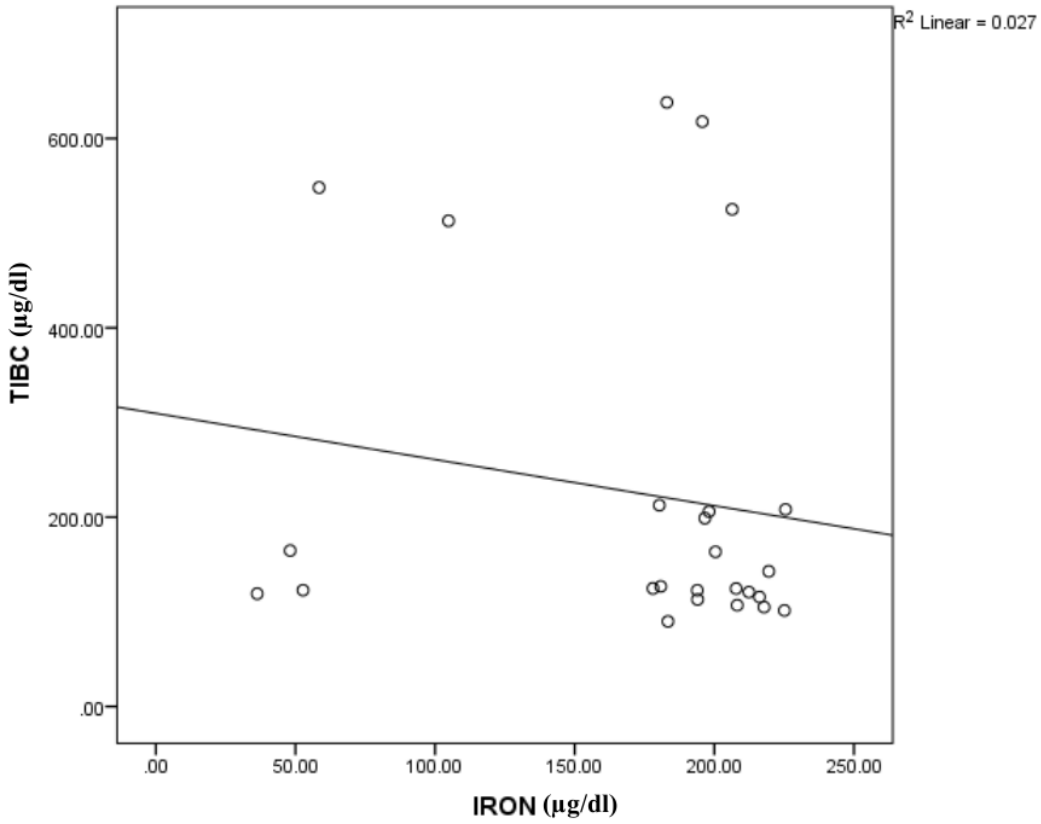

Figure-6 Serum iron and TIBC are correlated, as shown in the scatter diagram.

RESULT

- As compared to controls the activity of Serum iron was statistically significant in cases (p = 0.023) (Table-6 and Figure-4).
- As compared to controls the concentration of TIBC (Total iron binding capacity) was statistically significant in cases (p = 0.0422) (Table-7 and Figure-5).
- There was an association between TIBC and serum iron (p = 0.041) among cases.

DISCUSSION

A chronic medical condition called hypertension, sometimes known as high blood pressure, is characterized by consistently excessive levels of arterial blood pressure (Chobanian A. et al., 2003). High blood pressure is a significant, independent risk factor for the development of heart disease.

In this investigation, we found that hypertension people' serum iron activity was considerably higher when compared to normotensive individuals (p-value = 0.023). Our investigation showed, there was increased iron and decreased TIBC levels compared with patients suffering from hypertension and normal individuals without any chronic illness.

This result is consistent with Kim MK et al.'s (2012) study that the emergence of hypertension was positively correlated with increased iron & decreased TIBC.

Also Lee DH et al., (2010) revealed that ferritin levels were positively correlated with the prevalence of high blood pressure in their cross-sectional investigation conducted in Korea.

Also, Kiechl S, Willeit Tuomainen, (2007) according to their research, cardiovascular disease (CAD) and body iron levels are positively associated.

In my present study, some cases show that there are increased TIBC levels and decreased iron levels are also found in patients with hypertension.

Ruiter G et al., (2011) found in some cases that there is increased TIBC value and decreased iron levels in patients with hypertension may also show a positive correlation.

Elevated body iron levels can lead to stress from oxidation that may transform less reactive free radicals into more reactive forms such as hydroxyl radicals (·OH), hydroxide radicals (OH), & ($O_2^{\bullet-}$) superoxide anions, which may contribute to the development of hypertension and cardiovascular diseases (Galan P et al., 2010). The formation of reactive oxygen species, which enhances oxidative stress and inflammation and may lead to an increase in arterial blood pressure, may be influenced by both excess iron and inadequate iron levels (Yan et al., 2022).

Sempos CT et al., (2004) observed no evidence of a link between stored iron & high blood pressure.

Additionally, no significant correlation between iron reserves and heart disease was observed by Rauramaa R et al., (2010).

Our investigation showed that it was a statistically significant inverse association between iron & TIBC.

Hence, I found in my study that there was elevated iron levels and decreased TIBC levels but in some cases, there was also increased TIBC and decreased iron status have been found. So it is not clearly understood the mechanism of iron and TIBC in cases of hypertension. Though, this study will require more investigations using a bigger sample size to correlate the iron and TIBC in cases of hypertensive patients.

SUMMARY

The current study's objective was to compare the total iron binding capacity (TIBC) and serum iron levels in patients with hypertension & apparently healthy controls.

The estimated parameters were:

- Serum Iron
- Serum TIBC

The following observations were obtained during the study:

- When compared to controls, the level of activity of serum iron was considerably increased in cases ($p = 0.023$). (Table-6 and Figure-4).
- In comparison to controls, the level of TIBC was considerably increased in cases ($p = 0.0422$) (Table-7 and Figure-5).
- There was an association between TIBC and serum iron ($p = 0.041$) among cases.

CONCLUSION

The current investigation found that serum iron level was significantly higher in hypertension cases compared to controls, whereas serum Total iron binding capacity was shown to be significantly lower in cases compared to controls. According to several research, serum iron level and Total iron binding capacity are linked to an increased risk of hypertension.

Thus, elevated blood pressure is indicated by increased serum Iron and decreased Total Iron Binding Capacity, Therefore, it is crucial to investigate the unique roles of serum iron and total iron binding capacity in the pathophysiology of hypertension. The relationship between serum iron and TIBC in hypertension condition requires further investigation and analysis with larger sample size.

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