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A Correlation Study of Diabetes Mellitus with Some of its Consequences Including Retinopathy

An Undergraduate Project Submitted in Partial Fulfillment of the Requirements for the Degree of Bachelor in Medicine at University of Diyala/College of Medicine

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Dedication

To those who were my secret, the reason for my success, and who came to me when life weighed me down...
To my beloved mother, the soul who gave me life twice: once when she gave birth to me, and once when she embraced my dreams and believed in me when I almost lost faith in myself. To those who stayed up all night praying for me, to those whose prayers were my lifeline, lifting me up whenever I needed to. Without you, I wouldn't be here today. Every success I have is a reflection of your sacrifices and your endless love.

To my dear father, the man who gave me his strength when I felt weak, and his determination when I was on the verge of surrendering. To the one who worked tirelessly to pave my path with hope, who saw my success as his own victory long before I did. I can never repay you, but I dedicate every achievement of mine as a token of my love and gratitude for your sacrifices.

To my dear brothers & sisters, to my comrades and dearest people,
To those who have supported and helped me at every moment, to those who have shared my joys and sorrows

To my dear friends, who were more than sisters, who shared the struggles, the late nights, and the pressure, who held my hand when I stumbled, and who became my lifeline when I felt I was on the verge of giving up. Your presence made everything easier, and the memories of this journey would be incomplete without you.

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With all my respect and gratitude, I sincerely thank you and pray that God rewards you abundantly, blesses your knowledge and efforts, and makes them a guiding light for your students always.

Doha Deaa

ABSTRACT

It might be challenging for many people with diabetes mellitus associated with hypertension and hyperlipidemia to control all three illnesses. Other associated conditions such as nephrology, anemia, and heart diseases are well known to have an impact on the life of diabetic mellitus patients. Being aware that the HbA1c test is the gold standard for assessing glycemic management as it is thought to represent a patient's average blood sugar level over a number of months, the primary goal of this research was to examine the possible changes in many associated variables accompanied with many different associated conditions in diabetic mellitus patients.

A total of 104 individuals were included in the sample, divided into two groups: those with and without diabetes mellitus (DM and Controls). Anemia, nephrology, hypertension, hyperlipidemia, HbA1c, and other cardiac conditions were among the variables included in the two sets of data. We also took into account the weight, gender, and age components of the data.

Our results showed that there had been a considerable shift in the HbA1c in DM patients compared to the controls. According to our findings, compared to controls, people with diabetes mellitus have higher rates of hyperlipidemia and hypertension. The findings also indicated that weight, gender, and age all had an effect on HbA1c. Using machine learning and the criteria we examined for this study, one of our objectives for the future is to develop an algorithm that can detect changes in those factors early.

Table of Contents

Chapter One 4

Introduction 4

1. Introduction 4

1.1 History and Epidemiology 5

1.2 Physiopathology 6

1.3 Clinical Manifestations 6

1.4 Diagnosis 7

1.5 Treatment and Follow up 8

1.6 Relationship of Diabetes Mellitus with Age and Gender 8

Chapter Two 11

Methods and Materials 11

2.1 Subjects and Data Collection 11

2.2 Statistical Analysis 12

Chapter Three 14

Results and Discussion 14

3.1 Data Distribution Based on the Gender, Gender, and Weight factors 14

3.2 HbA1c and Diabetes Mellitus 19

3.3 Hypertension, Hyperlipidemia, Anemia, Neuropathy and Heart Diseases in DM patients 20

3.4 Effect of Age Factor on HbA1c 21

3.5 Effect of Gender Factor on HbA1c 22

3.6 Effect of Weight Factor on HbA1c 23

Chapter Four 25

Conclusions and Future Directions 25

References 26

Chapter One

Introduction

Chapter One
Introduction

1. Introduction

One of the most common metabolic disorders, diabetes mellitus affects almost every community on the planet at variable rates, making it a global public health concern. It is typified by hyperglycemia, or elevated blood sugar levels, which are brought on by insufficient insulin secretion or resistance. In order to effectively manage diabetes, glycemic control is essential since inadequate control is linked to the emergence of complications [1], [2]. Every year, diabetes-related complications cause over 5 million deaths worldwide. An estimated 422 million adults worldwide already have diabetes, and by 2040, that number is expected to climb to 642 million. In the diagnosis and treatment of diabetes, glycosylated hemoglobin A1c (HbA1c) and fasting blood glucose levels are both essential diagnostic and treatment factors. Despite not being directly caused by the disease, diabetes is a leading cause of morbidity and mortality. Rather, they are associated with the illnesses that arise from long-term diabetes. These comprise disorders of the nerves as well as disorders of the large and small blood vessels, such as microvascular diseases like retinal and renal vascular diseases and macrovascular diseases like coronary heart disease and peripheral arterial disease.[1], [2], [3]. Diabetes mellitus can be classified into[3]:

- **Type 1 Diabetes Mellitus (T1DM)** in which, due to autoimmune attack by the immune system, pancreatic β-cells are destroyed, an absolute deficiency of insulin results. It is usually diagnosed in children and young adults and requires lifelong treatment with insulin [4].
- T**ype 2 Diabetes Mellitus (T2DM)** :The type 2 diabetes mellitus (T2DM) is a group of meta- bolic diseases characterized by hyperglycemia due to defects in insulin secretion, insulin action or both [4].

- **MODY diabetes** (mature onset diabetes of the young) is a monogenetic form of diabetes characterized by autosomal dominant transmission that presents early and is associated with β-cell defects that limit insulin secretion. MODY diabetes affects approximately 5% of the total number of patients with DM [4].

1.1 History and Epidemiology

There are more than 500 million people with diabetes globally, and its prevalence is rising due to factors like obesity, urbanization, and physical inactivity. The United States, South Asia, and the Middle East have the highest rates. T2DM accounts for the majority of reported cases, although 5–10% of patients with diabetes have T1DM, formerly known as juvenile diabetes. [2],[5]. Every nation has a significant and growing diabetic disease burden, which is driven by a worldwide rise in obesity and poor lifestyles. According to the most recent projections, 382 million individuals worldwide had diabetes in 2013, and by 2035, that number is predicted to increase to 592 million. Diabetes' etiological classification is now generally acknowledged. The two primary forms of diabetes are type 1 and type 2, with type 2 diabetes making up the majority (>85%) of all cases [5], [6], [7].

An estimated 1.5 million people were diagnosed with diabetes in 2005. While prevalence (current instances of diabetes) represents the disease's overall impact on the population, the incidence on the other hand (or new cases of diabetes) describes increases in the number of individuals afflicted by the condition. Data on the prevalence of diabetes in the US are derived from two population-based sources: the Behavioral Risk Factor Surveillance System (BRFSS) and the National Health Interview Survey (NHIS). Since these sources determine whether a person has been informed by a doctor or other health care provider that they have diabetes, they have only been able to provide the prevalence of diagnosed diabetes, even if they offer reliable self-reported statistics on the disease across the US [5], [8].

1.2 Physiopathology

Five to ten percent of all instances of diabetes are type 1 diabetes. Environmental, genetic, and autoimmune factors are among its risk factors. As of right present, type 1 diabetes cannot be prevented. Ninety to 95 percent of all instances of diabetes that are diagnosed are type 2. This type of diabetes usually starts as insulin resistance, and the pancreas may produce less insulin or none at all because the body cannot generate enough of it to treat the resistance. Insulin resistance is primarily caused by obesity. When oral medications are unable to adequately stimulate insulin release, patients typically need to take insulin over time [8], [9], [10], [11]. Women who are obese, belong to a minority group, have a family history of diabetes, or have experienced gestational diabetes during a prior pregnancy are more likely to develop gestational diabetes than other women. To avoid delivery difficulties for the growing baby, women with gestational diabetes must have strict glycemic control and maintenance. The risk of type 2 diabetes in later life is 20% to 50% higher for women who have had gestational diabetes[8], [9], [10], [11].

1.3 Clinical Manifestations

The severity of the blood sugar level determines the symptoms of diabetes. Some people may not exhibit symptoms, particularly if they have type 2 diabetes, gestational diabetes, or prediabetes [4], [6], [12], [13], [14].

Symptoms of type 1 diabetes are typically more severe and appear more soon. Type 1 and type 2 diabetes symptoms include the following[8]:

- Feeling thirstier than normal.
- Frequent urination.
- Losing weight without making an effort.
- Ketones are present in the urine.
- Feeling weak and exhausted.

- Mood variability.
- Hazy vision.
- Sores that usually don't heal quickly.
- Infections.

1.4 Diagnosis

1.5 Medical professionals can identify prediabetes and diabetes using three tests [5], [8], [13], [14], [15], [16]:

- **HbA1C (A1C or glycosylated hemoglobin test):** Diabetes and prediabetes can be diagnosed using the A1C test. It calculates the blood glucose control average over the last two to three months. The amount of glycosylated hemoglobin (A1C) in the blood is used to measure blood sugar. Since there is no need for fasting, this test is more convenient. Individuals are prediabetes and at high risk of getting diabetes if their A1C is between 5.7% and 6.4%. When the A1C is 6.5% or more, diabetes is diagnosed.
- **Fasting Plasma Glucose Test (FPG):** A blood glucose test quantifies the blood's glucose (sugar) content. Eating or drinking anything other than water for eight hours prior to a fasting plasma glucose test is required. This test will require a blood sample. Milligrams per deciliter (mg/dL)unit is used to measure blood glucose.
- **Oral Glucose Tolerance Test:** This test evaluates the body's ability to process a typical quantity of glucose. Subject should go at least eight hours without eating or drinking anything but water in order to complete this test. After the blood is drawn, subject will be given a glucose-containing beverage by the healthcare provider. After 30 and 60 minutes, blood is taken once again. Three hours may be needed for the test. Then the healthcare provider will compare the levels of glucose in the plasma before and after. The unit of measurement for these amounts is mg/dL.

1.5 Treatment and Follow up

The three main components of diabetes management are glycemic control, lifestyle changes, and preventing complications. In T1DM, insulin therapy is required for life, whereas in T2DM, oral hypoglycemics, diet, and exercise are utilized first, with insulin therapy added in later stages of the illness. To avoid major consequences, blood pressure (<130/80 mmHg), cholesterol levels, and yearly screenings for neuropathy, nephropathy, and retinopathy must be controlled. To preserve eyesight in patients with advanced diabetic retinopathy, anti-VEGF injections, corticosteroids, or this laser therapy may be required.[6], [7], [13], [15], [16].

1.6 Relationship of Diabetes Mellitus with Age and Gender

The onset, progression, and consequences of diabetes mellitus (DM) are significantly influenced by gender and age. Age-related metabolic changes, decreased insulin sensitivity, and pancreatic β-cell dysfunction may all contribute to the increased risk of Type 2 Diabetes Mellitus (T2DM), particularly beyond the age of 40. Additionally, diabetes-related comorbidities such cardiovascular disease, nephropathy, and neuropathy are more common in older persons. Conversely, type 1 diabetes mellitus (T1DM) is more common in children and young adults, although latent autoimmune diabetes in adults (LADA) might appear later and is frequently misdiagnosed as type 2 diabetes [3], [4], [16], [17]. Additionally, gender affects the risk of developing diabetes and its complications. Because visceral fat is directly linked to insulin resistance and men collect more visceral fat than women, type 2 diabetes develops at a lower body mass index (BMI) in men than in women. However, compared to men, women with diabetes have a higher relative risk of cardiovascular disease, which is probably caused by hormonal and metabolic variations. Furthermore, almost 50% of women with gestational diabetes mellitus (GDM) develop type 2 diabetes within ten years, increasing their lifelong risk of developing the disease. Hormonal variables may also provide some protection against difficulties associated to diabetes; premenopausal women appear to

be less vulnerable to these issues. However, it is evident that this protective effect diminishes after menopause, increasing the risk of various problems associated with diabetes in middle-aged and older women [3], [11].

1.7 Diabetic retinopathy

Diabetic retinopathy (DR) is one of the major microvascular complications of diabetes characterized by progressive damage to the retinal blood vessels, resulting in visual impairment and possibly blindness. It is seen in both Type 1 and Type 2 DM, and risk intensifies with the prolonged duration of DM and poor glycemic control. DR can be divided into non-proliferative diabetic retinopathy (NPDR), which is characterized by retinal microaneurysms, hemorrhages, and capillary occlusion, and proliferative diabetic retinopathy (PDR), the pathology in which neovascularization develops with an elevated risk of developing vitreous hemorrhage and retinal detachment [7], [10], [12], [18], [19]. Both eyes are typically affected by diabetic retinopathy. A person's risk of developing diabetic retinopathy increases with the length of their diabetes. Diabetic retinopathy might result in blindness if treatment is not received. Long-term elevated blood sugar levels in diabetics can cause fluid to build up in the lens, which regulates focus in the eye. This modifies the lens's curvature, which alters vision. However, the lens will typically regain its original shape and eyesight will recover once blood sugar levels are under control. Diabetic retinopathy will develop and proceed more slowly in patients with diabetes who are able to better regulate their blood sugar levels. [14], [19].

Chapter Two

Methods and Materials

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Methods and Materials

2.1 Subjects and Data Collection

To get a better understanding of the prevalence of hypertension, hyperlipidemia, anemia, and nephrology as well as the mechanism of diabetic mellitus and its influencing factors among diabetes mellitus patients in the community in Baquba city at Diyala province in Iraq, and to be able to make recommendations about the disease and its consequences including retinopathy, there should be a comprehensive study involving all these factors among diabetic mellites patients. To achieve this goal, an investigation of the possible changes in those parameters is necessary. As a first step toward achieving this goal, I started my project by gathering my data from September 2024 to January 2025 at the Baquaba Teaching Hospital / Department of Ophthalmology in Diyala following the rules of ethics established by the University of Diyala College of Medicine. One hundred and four individuals made up our data sample, and they were divided into two groups: normal participants (those without diabetes mellitus) and patients with DM. Each category had different data points. The study included details about the types of diabetes mellitus, its duration, HbA1c, hypertension, hyperlipidemia, anemia, and nephropathy. The study additionally investigated at how age, weight, and gender affected some of those variables. The data was collected using a specially built and filled-out form, and once the parameters were entered into an Excel sheet, the Mat.file was extracted using MATLAB 2020. All statistical analysis and coding were done using MATLAB software.

2.2 Statistical Analysis

Hypertension, hyperlipidemia, nephropathy, and total HbA1c variations were statistically evaluated using the Wilcoxon signed-rank test. A statistical analysis of the effects of age, weight, and gender on those variables was conducted using the Wilcoxon rank-sum test, also referred to as the Mann-Whitney test. The means of two continuous distributions are compared using this test. We chose it for our analysis since it is more effective than the two-sample t-test when used in the case of non-normal distributions. The Kolmogorov-Smirnov test was used to statistically evaluate the difference between some sets of our data to see if data comes from a normal distribution. The p-value was deemed statistically significant if it was less than 0.05.

Chapter Three

Results and Discussion

Chapter Three
Results and Discussion

3.1 Data Distribution Based on the Gender, Gender, and Weight factors

The total data points in our study were 104, which were divided into 47 females (representing 45% of the sample) and 57 males (representing 55%), as shown in figure (3.1). The two percentages are sufficiently similar to allow for reliable comparison and deduction. Of the 104 people in this study, 52% males were identified as having diabetic mellitus, while 48 females were having the condition. There was a small less percentage in the second group that included data from individuals who did not have diabetic mellitus. Out of that sample, 75% were females, see figure (3.1).

Regarding age gender, the 104 data points were first classified into six subgroups with age range of 50-60 years old to have the highest percentage (38%), followed by age range 40-50 years old (33%), and then age range of 60-70 years old with a percentage of 18. While the lowest percentage (2%) belonged to age subgroups (1-30) and (70-80) years old, age subgroup with age range (70-80) years old had 7%, figure (3.2). Among the subjects who did have diabetic mellitus, there were six age groups (1–30, 30–40, 40–50,50-60, 60-70, and 70–80 years old. Of the total data points, 41% of the participants were between the ages of 50 and 60, 32% were between the ages of 40 and 50, and 20% were between ages of 60-70 years old. As seen in figure (3.2), the age ranges of 30-40, 1-30, and 70-80 years old accounted for 7%, 2%, and 1% of total data in that group, respectively. In the normal group without diabetic mellitus disease, 42% were between the ages of 30 and 40; 25% were between the ages of 1 and 30;17% were between the ages of 40 and 50; and 8% between the ages of 50 -60 and 60-70 years old respectively. According to this distribution, we can see that there is a variation in the age range and its corresponding number of patients or

individuals which makes it difficult to apply t-test as the data of such groups will not follow the normal distribution required for application of the t-test.

As it is well-known that diabetic mellitus and weight are strongly correlated, we first looked our data distribution based on weight factor. Figure (3.3) shows that for all data points of the sample, there were eight weight groups with the highest percentage of 34% for participants with 70-80 kg, followed by 22% for participants with weight of 90-100 kg, then 19% and 14% for 80-90 kg and 60-70 kg respectively. Weight groups of 100-110, 110-120, and 120-130 kg had the following percentages: 4%, 2%, and 1%. Finally, there was 4% who had weight of 50-60 kg in that classification. Again, the difference in range of weight is wide which make the comparison difficult the classical tests such as t-test. For diabetic mellitus patients, the highest percentages of the weight were: 36, 21, 21, and 11% for participants with weight of : 70-80 kg, 80-90 kg, 90-100 kg, and 60-70 kg, respectively. Other weight subgroups which occupied the smallest percentages were for participants with weight of: 100-110, 110-120, 120-130 kg, and 50-60 kg with the following percentages: 4%, 2%, 1%, and 4%. Finally, normal participants who did not have diabetes mellitus had the following weight ranges: 50-60 kg, 60-70 kg, 70-80, and 80-90 kg with the following percentages in sequence: 42%, 17%, 8%, and 33%. In all three groups (total, diabetic mellitus, and normal), it is very obvious that weight is a factor that is really affect and plats a role in developing diabetic mellitus disease. This confirm the fact that has been documented in may studies that the most important and substantial risk factor for the onset and progression of diabetes mellitus (DM), type 2 in particular, across all age groups is obesity or excessive weight gain.

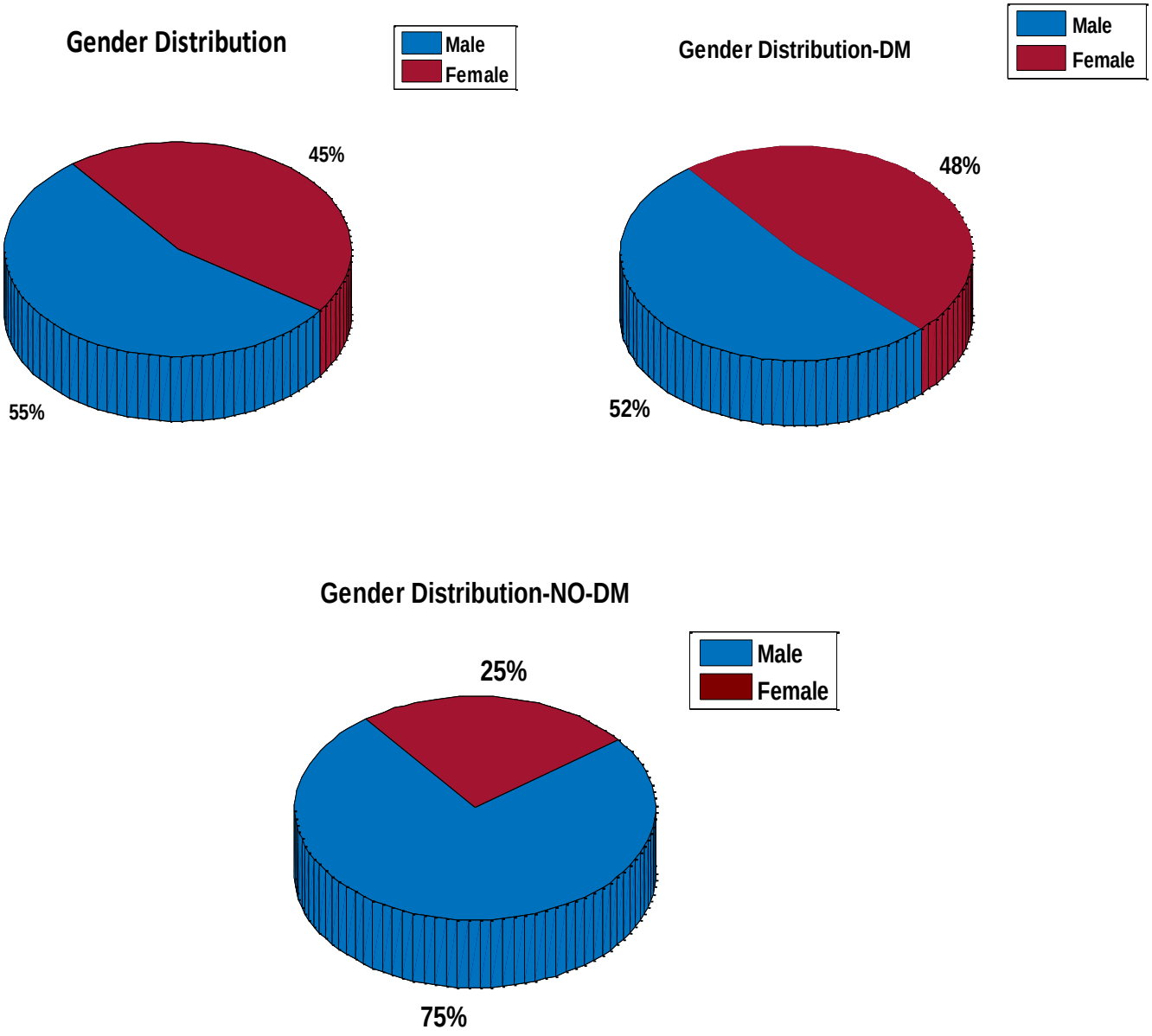


Figure 3.1: Data distribution based on gender factor.

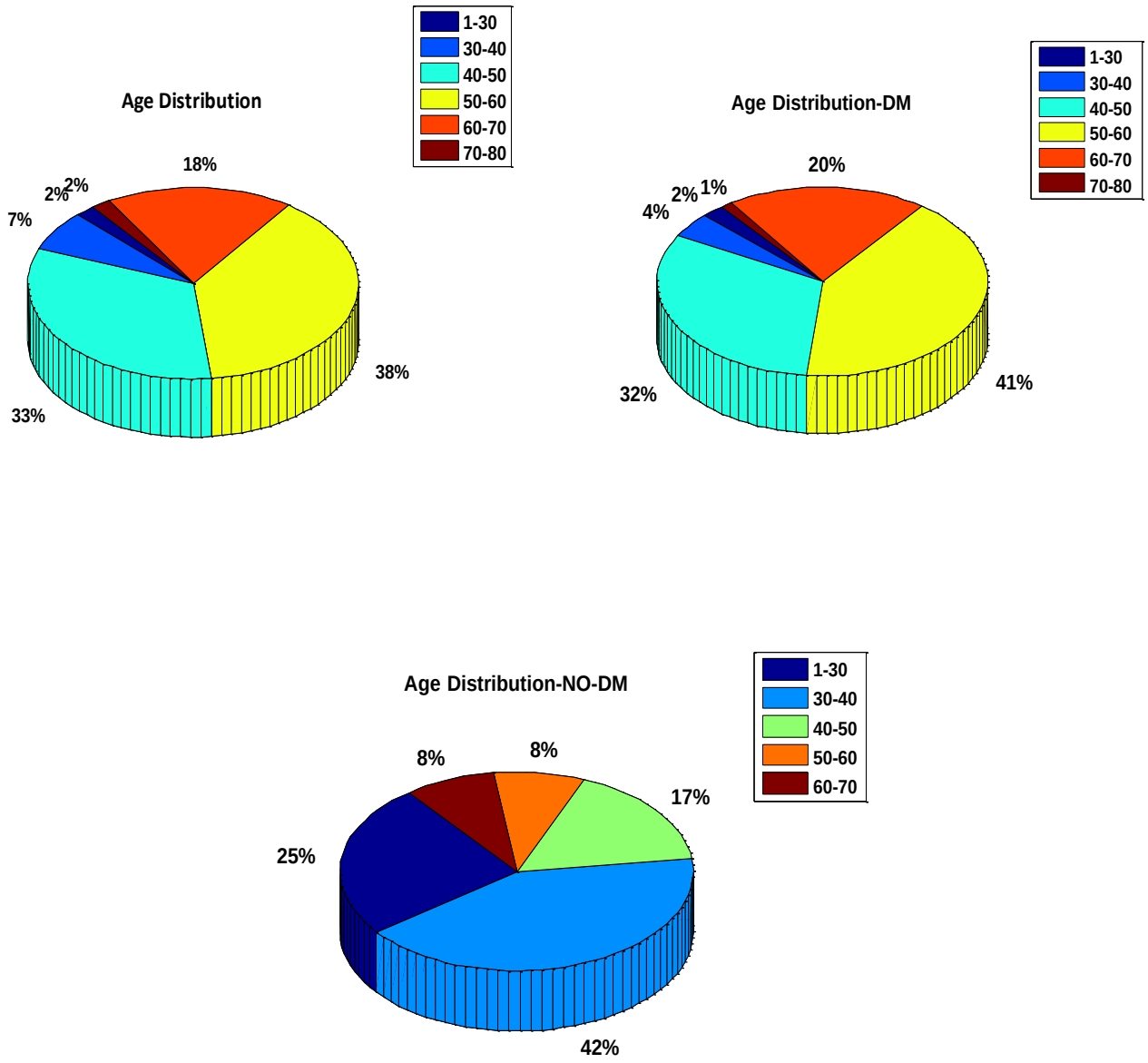


Figure 3.2: Data distribution based on Age factor.

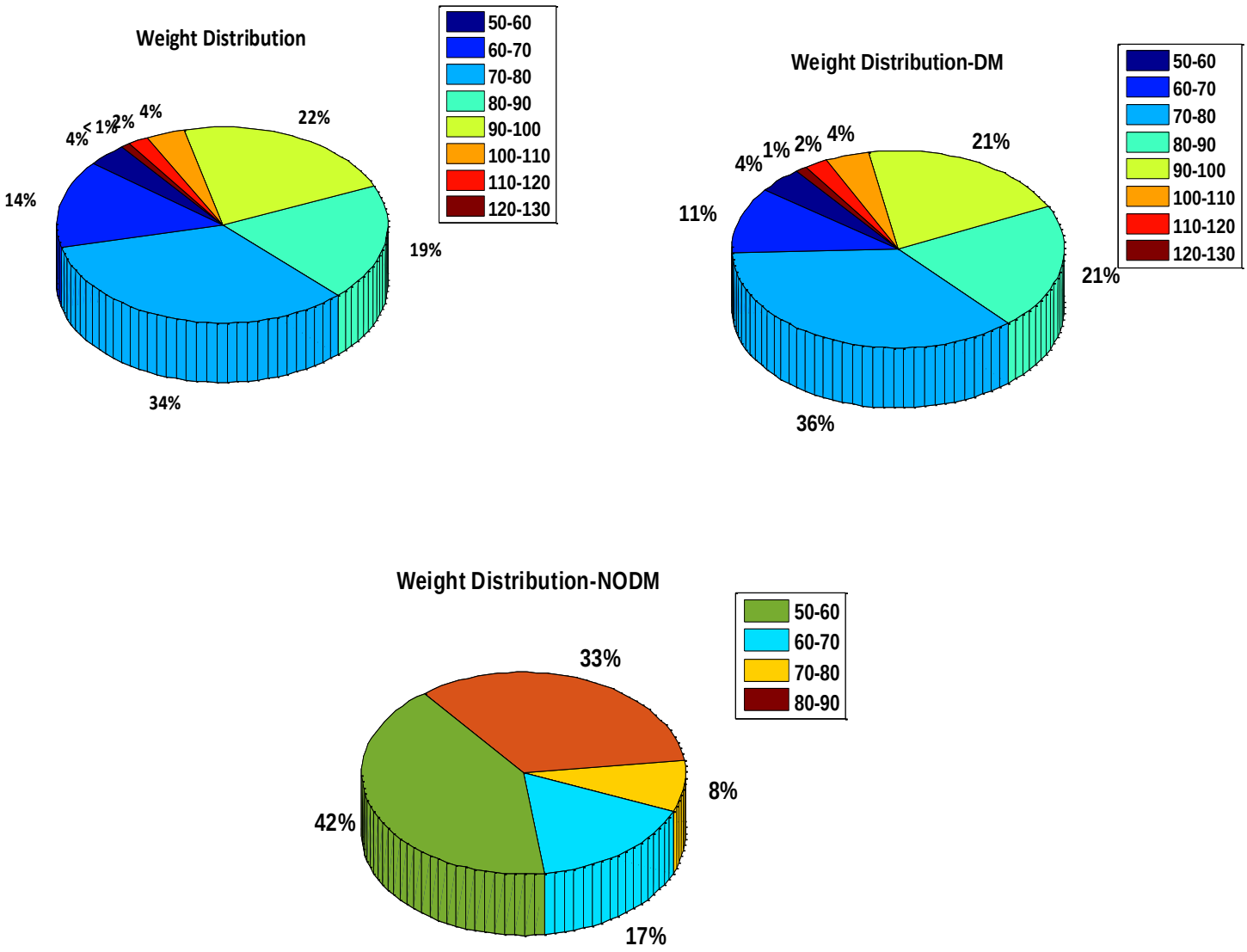


Figure 3.3: Data distribution based on weight factor.

3.2 HbA1c and Diabetes Mellitus

Glycated hemoglobin (HbA1c) which was first recognized many years ago as abnormal hemoglobin in diabetic patients. It is a measure of the average plasma glucose levels for the preceding eight to twelve weeks. In contrast to the controls, who had a HbA1c of 4.7, our results indicated that the HbA1c was about 9, as we know that a point of impact of 6.5% is advised for the diagnosis of diabetes. The shift of the red trace of the empirical cumulative distribution function plot (ecdf) in figure 3.4 shows the data points of our data from lowest to highest versus their percentiles. Here, we are focused on 50 percentiles to obtain the HbA1c measurement. We employed the Kolmogorov Smirnov test for statistical analysis in order to compare the two distributions (Controls and DM), and the results showed that the HbA1c values differed significantly ($p\text{-}value < 0.05$).

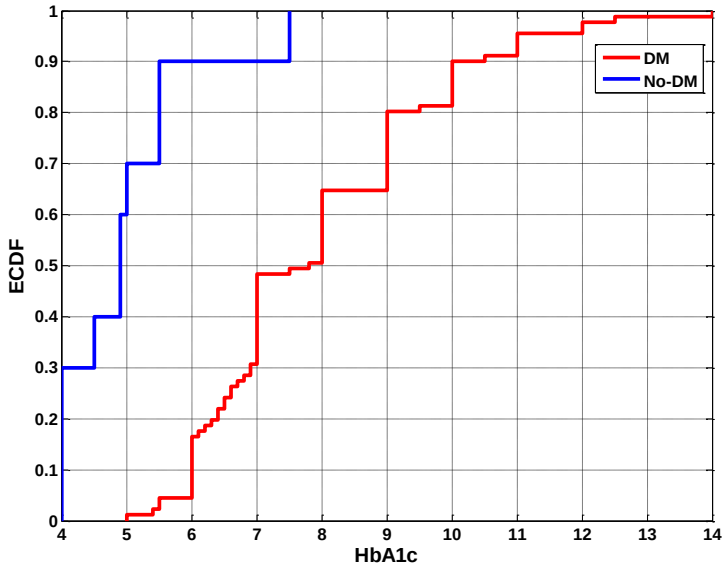


Figure 3.4: ECDF of the HbA1c for both DM patients and Controls. It is clear that there is a significant difference between the two distributions as one can notice by the shift of the red trace to have value of 8 on x-axis which represents the HbA1c. The significant difference was confirmed by applying (KS-test), with p-value less than 0.05.

3.3 Hypertension, Hyperlipidemia, Anemia, Neuropathy and Heart Diseases in DM patients

Since individuals who have diabetes are twice as likely to have hypertension than those without the disease, and as those with hypertension are more likely to develop insulin resistance and diabetes than individuals without the disease, we examined the related hypertension in both groups and compared them. Our data revealed that out of 93 patient with DM, there were 61 with hypertension and 23 with other associated heart diseases such as angina, cardiac arrhythmia, and chest pain which was not unexpected. Since hyperlipidemia is well known to be associated with DM patients, our data examined this point and we found that 50 patients with DM had hyperlipidemia as well, see table (3.1). Regarding anemia and nephropathy, our data showed that there were only 17 and 7 patients who had anemia and nephropathy respectively and as shown in the table 3.1.

Table 3.1: Hypertension, Hyperlipidemia, Anemia, Neuropathy and Heart Diseases in DM patients

Variable	DM		No-DM	
	YES	NO	YES	NO
Hypertension	61	32	5	7
Hyperlipidemia	50	42	3	9
Anemia	17	75	0	0
Nephropathy	7	85	0	0
Heart Diseases	23	69	2	10

3.4 Effect of Age Factor on HbA1c

Figure 3.5 shows that there are variations in the value of HbA1c within the age. The age groups that were considered here to investigate the age effect were: '30-40', '40-50','50-60' ,'60-70','70-80','80-90' respectively which were displayed as: 1, 2, 3, 4, 5, and 5 groups on x-axis and their corresponding values of HbA1c were displayed on the series "1" row. Obviously, there is a general reduction trend as patients go from age range of '30-60' to older ranges with some ups and downs that could be the effect of some other factors including gender, obesity, and some other associated diseases.

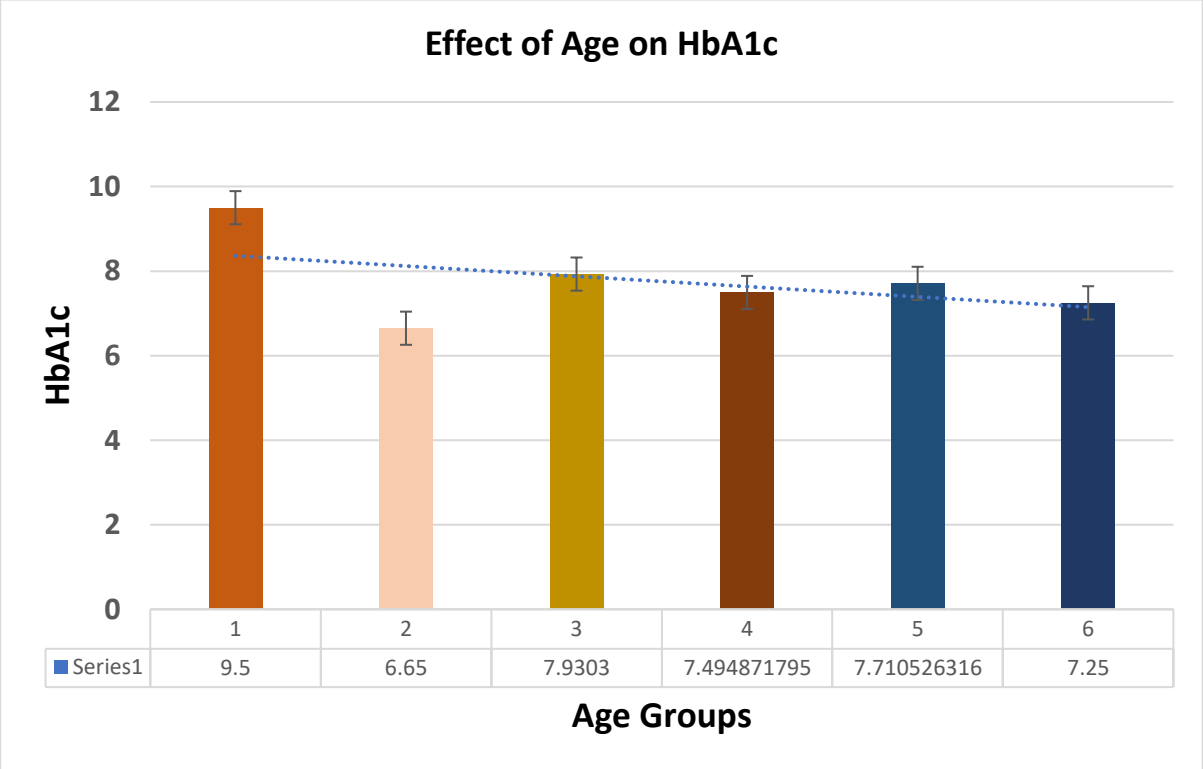


Figure 3.5: Effect of Age on HbA1c. A general reduction trace is evident with some variations after age of 40 years.

3.5 Effect of Gender Factor on HbA1c

While there are some conflicts about the effect of gender on HbA1c values as some studies have documented that there is no effect and others reported that HbA1c is higher in males compared than females, our data showed that it is higher in males than females, the data revealed that while HbA1c value was 7.57 in females, it was 7.73 in males. Though, it didn't reach the level of significance (p-value >0.05, Mann-Whitney test) but there is a clear difference between the two groups as shown in figure (3. 6).

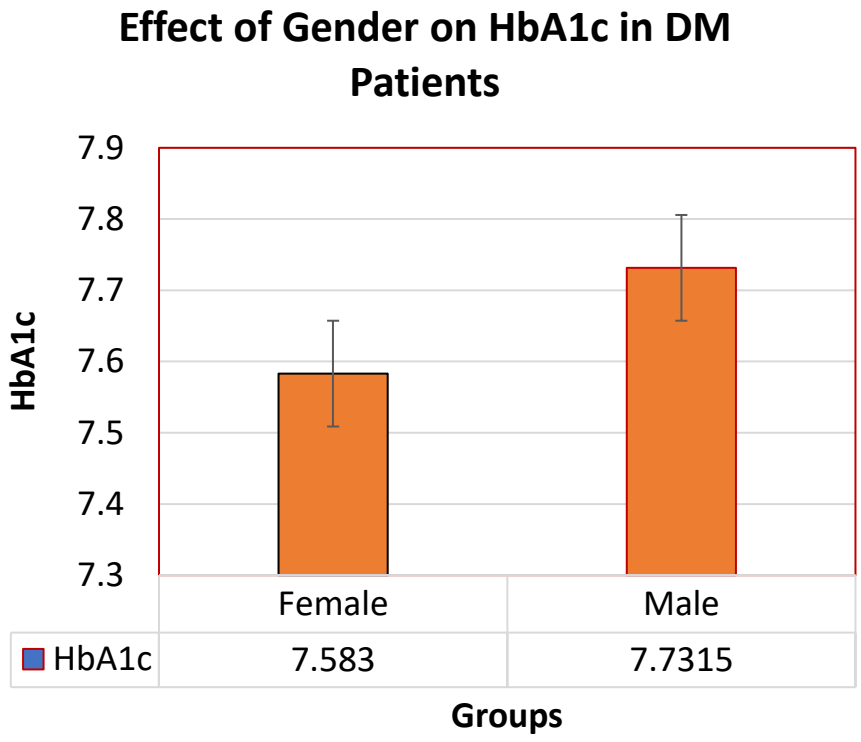


Figure 3.6: Effect of Age on HbA1c.

3.6 Effect of Weight Factor on HbA1c

According to figure 3.6, there are variances in the HbA1c value within the weight. In this study, the weight groups that were taken into consideration to examine the weight effect were: 60-70', 70-80', 80-90', 90-100', 100-110', and 110-120' kg respectively. These groups were shown as 1, 2, 3, 4, 5, and 6 on the x-axis, and the series "1" row showed the corresponding values of HbA1c. It is evident that there is a general upward tendency as patient weights rise, which makes sense, with occasional fluctuations that might be caused by other variables. We may observe that the increase becomes considerably more noticeable when the weight exceeds 100 kg. The t-test has shown a significant difference with a p-value of less than 0.05.

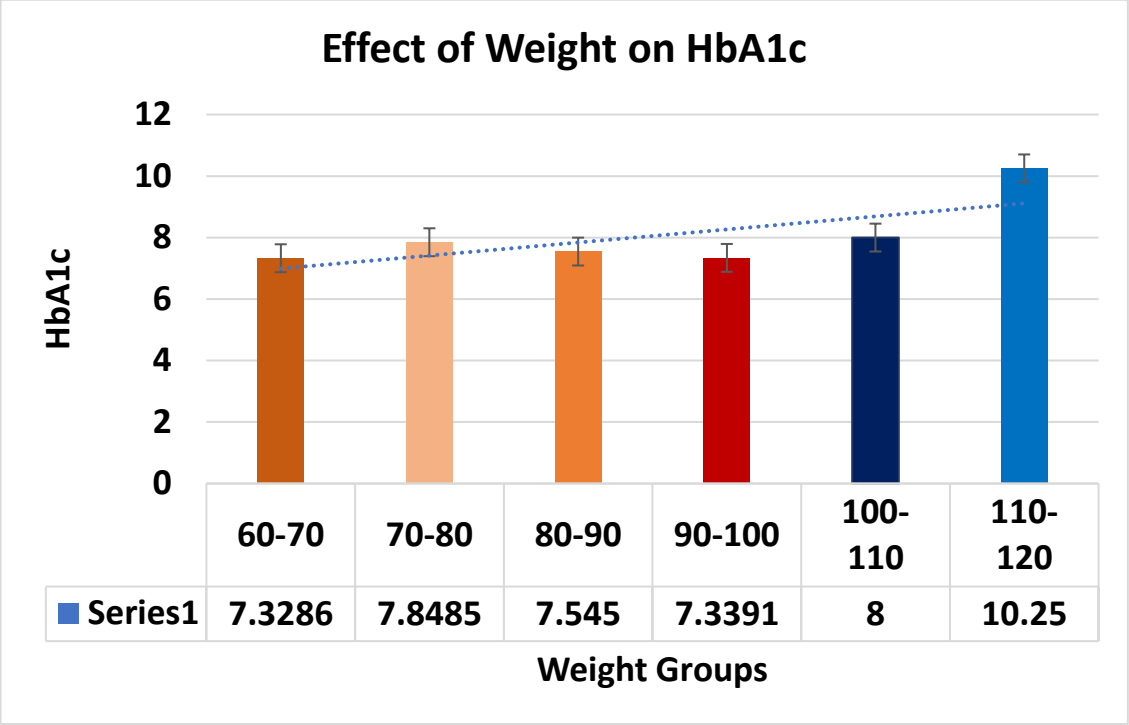


Figure 3.7: Effect of weight on HbA1c. More weight is associated with higher HbA1c value.

Chapter Four

Conclusions and Future Directions

Chapter Four
Conclusions and Future Directions

Vascular risk factors can affect different organ systems differently, even if they frequently occur together and have similar effects, like atherosclerosis. For instance, through pathophysiological pathways that are at least partially unique to type 2 diabetes and hypertension, these diseases are significantly linked to damage to endogenous organs in the kidney and retina. The link between obesity and dyslipidemia and injury to the kidneys and retina is there as well. Our data concluded that patients with diabetic mellitus are associated with more hyperlipidemia, hypertension compared to controls. The results also showed that there is an impact of the age, gender, and weight on the HbA1c. According to our research, HbA1c values rise with advancing age and are impacted by gender variations. Healthcare workers that possess this expertise will be able to provide their patients with more effective and individualized care. Furthermore, this research can improve our knowledge of diabetes mellitus and age-related physiological changes. As a result, the conclusions of this study can help progress medical knowledge overall and have implications for the clinical environment.

The following crucial future steps can be suggested in light of the study's scope and certain shortcomings, such as the lack of sufficient information regarding retinopathy and nephrology: A larger sample size would increase certainty about changes in the related disorders; further information about the management can be obtained by analyzing age and gender variables using 2-ways ANOVA.

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