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EFFECTS OF DIATERY FIBER IN PATIENTS WITH TYPE 2 DIABETES MELLITUS A META ANALYSIS

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Biruni Üniversitesi Sağlık Bilimleri Enstitüsü Biyoistatistik Anabilim Dalında RAND MAAD SULTAN tarafından hazırlanan "Effects of Diatery Fiber in Patıents With Type 2 Diabetes Mellitus A Meta Analysis" adlı tez çalışması, jüri tarafından YÜKSEK LİSANS tezi olarak kabul edilmiştir.

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(Jüri Üyesinin Ünvanı, Adı, Soyadı ve Kurumu)	İmza

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I. DECLARATION

I hereby declare that the work in this thesis is my own except summaries, which have been duly acknowledged.

RAND MAAD SULTAN
Signature

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1. ÖZET

Bu meta-analizde dokuz tane yayınlanmış çalışma yer almıştır. Örneklem büyüklüğü 6 ile 35 kişi arasında değişmekte olup, çalışma grubu için 145 kişi, 6 ile 23 kişi bir araya gelerek kontrol grubu için toplam 129 kişiden oluşmaktadır. Fiber tüketimi günde 4 ile 40 gr arasında uzatıldı. Bu çalışmaya farklı lif türleri dahil edildi. Bu çalışmaya dahil edilen tüm çalışmalar, hem çalışma grubu hem de kontrol grupları için hemoglobin yüzdesi olarak mmol / l ve gliko hemoglobin içindeki açlık kan glikozunun ölçümünü kapsamıştır. Diyet yöntemleri farklıydı, farklı lif tipleri ile tedavi süreleri 4 haftadan 6 aya kadar değişiyordu. Genel ortalama fark, sabit etki modelinde plasebodan ve -1.17'den (% 95 CI: -1.97; -0.36) daha düşük olan 0.91 mmol / L (% 95 CI, 1.18-0.64) lif alımı ile FBG'nin azalmasıydı. Rastgele etki modelinde yüksek heterojenliğe şahit olunmuştur (p <0.01'den küçük, I ^ 2 =% 88.0). Genel ortalama fark, glikoz ile hemoglobinin, 1.03 mmol / L (% 95 CI, 1.31; -0.76) oranında, sabit etki modelinde plasebodan ve karışık etki modelinden daha fazla bir şekilde azaltılmasıydı; *-1.08 (95% CI: -1.94;-0.21)* rastgele etki modelinde bu şekildedir. Yüksek heterojenlik saptanmıştır (p:0.01'den az, I ^ 2 =% 89.0).

2. ABSTRACT

Nine published studies were involved in this meta- analysis, Sample size wide-ranging from 6 to 35 subjects, adding together 145 subjects for intervention group and from 6 to 23 subjects, totaling 129 for control group. Fiber consumption extended from 4 to 40g per day. Different types of fiber were involved in this study. All the studies included in this study involved measurement of fasting blood glucose in mmol/l and glycated hemoglobin as percentage of hemoglobin for both the intervention group and control groups. Methods of diet were different, the durations of treatment with different types of fiber were varied from 4-week period to 6-month period. The overall mean difference was a decrease of FBG by fiber intake of 0.91 mmol /L (95% CI, 1.18 –0.64) more than the decrease from placebo in fixed effect model and -1.17 (95% CI:-1.97 ; -0.36) in random effect model ,high heterogeneity was witnessed (p less than 0.01, I^2 = 88.0%). The overall mean difference was a reduction of glycosylated hemoglobin by fiber intake of 1.03 mmol/L (95% CI, 1.31; –0.76) more than the reduction from placebo in fixed effect model and -1.08 (95% CI: -1.94;-0.21) in random effect model. High heterogeneity was witnessed (p less than0.01, I^2 = 89.0%).

3. INTRODUCTION AND LITERATURES REVIEW

3.1. Introduction

The collection of abnormalities caused by deficiency of insulin is named diabetes mellitus. Roman physicians and Greek used the "diabetes" term to denote to condition in which the basic finding was a large urine volume. Two types of diabetes mellitus were distinguished, diabetes mellitus in which the urine exhibit sweet taste, and diabetes inspidus in which the patient urine was tasteless (Buse et al., 2003). Today the term diabetes inspidus is reserved for the condition produced by lesions of the supraoptic-posterior pituitary system, and the original word diabetes is generally used as a alternative word for diabetes mellitus (Atkinson et al., 2001). Polyuria, polydipsia, weight loss, polyphagia (increased appetite), hyperglycemia, glycosuria, ketosis, acidosis, and coma are the characteristics of diabetes mellitus. There are well-known biochemical abnormalities, to which most of them can be drawn are firstly a reduced glucose entry into different peripheral tissues and secondly an increased release of glucose from the liver into the circulation, meaning that increased glucogenesis (Poretsky, 2010).

For those reasons an extracellular excess and an intracellular deficiency of glucose, a situation which has been termed starvation in the midst of plenty. A decrease in the amino acids entry into muscles and an increased lipolysis were found (Shoback and David, 2011). Hyperglycemia itself is relatively harmless unless it is so marked that there are symptoms due to the hyperosmolality of the blood. Even with relatively mild hyperglycemia, however, as reabsorption of glucose is exceeded renal capacity glycosuria also present causing an excretion of the osmatically active molecules of glucose needs the loss of large amounts of water (Poretsky, 2009). The resulting dehydration will activates the regulating water intake mechanism, causing polydipsia. There is a considerable urinary loss of sodium ions and potassium ions also (Shoback & David, 2011). For every 1 gm of glucose excreted, there is 4.1 kcal are misplaced from the body. Growing oral caloric intake to cover this loss, only raises the blood glucose more and increases the glycosuria , as a result mobilization of endogenous fat and protein stores and weight loss cannot be prevented (Poretsky, 2009). In the absence of insulin, the glucose entry into skeletal muscle is increased

during exercise. This may attribute to relative oxygen deficiency which causes glucose entry into cell is increased under anaerobic conditions. Diabetics should take in extra calories or reduce their insulin dose when they exercise, as exercise can precipitate hypoglycemia in diabetics taking insulin (Dobson, 1976).

3.1.1. Intracellular glucose deficiency effects

The glucose excess outside the cells in diabetes contrasts with the intracellular insufficiency. Catabolism of glucose is normally a main source of energy for cellular activities, but in diabetes, the energy. Requirements can be encountered only by drawing on fat and protein reserves (Petit and Adamec, 2011). Activation of mechanisms that are significantly increases the catabolism of fat and protein, and ketosis is one of the outcomes of increased fat catabolism. Depletion of glycogen is a common outcome of intracellular glucose deficit, and the content of glycogen of liver and skeletal muscle in diabetics is usually decreased. Insulin regularly increases the glycogen content of skeletal muscle and liver unless it produces hypoglycemia to also activate glycogenolytic mechanisms (Bastak, 2005).

3.1.2. Diabetes management

The aim is to recover the life quality and output of diabetics. Two management approaches for diabetes mellitus

- Following healthy diet habits and physical activity.
- Using medicines or/and insulin for lowering blood sugar (Rambhade et al, 2010).

3.1.3. Education

Members in community including diabetic patients must learn about diabetes that is a chronic disease has no cure, and can be well-ordered only. Management involves:

- diabetics learning,
- eating of healthy foods, quantity and timing of meals,
- following programmed exercise,

- Proper administration of diabetes medications
- Regular medical examinations to detect the disease early.

Diabetics should be acquainted with detecting emergencies resulted from high or low blood sugar levels and when medical help is looked for. Pregnant women must be asked to check their blood sugars levels on a regular basis. Proper control of blood sugar is necessary to prevent diabetes and its related consequences. Diabetics have to take care of their feet to avoid wounds and ulcers and subsequent amputations.

3.1.4. Healthy diet

Taking a fiber-rich diet and following programmed physical activity could be useful in the managing of recently diagnosed diabetics, and must be continued.

3.1.5. Good dietary follows in the diabetes management

- Programmed physical activity and Proper diet is vital in retaining a perfect body weight.
- Decreased salt consumption, animal fat and refined foods is also necessary.
- Consuming useful food portion sizes and fiber-rich foods, such as root vegetable and fruits should be followed.
- At-least three meals per day must be eaten of a variety of foods.
- Avoiding alcohol and tobacco.
- Drinking of water is needed for normal body functioning. As a minimum two to three liters of water should be drank daily (Barnett, 2010).

3.1.6. Physical activity

Insulin sensitivity can be improved blood sugar control with regular physical activity (2-3 days/week), lasting about 20-30 min per session, with moderate intensity improving blood flow in the heart, thereby controlling blood pressure, maintenance of perfect body weight. Physical activities may include; housework, gardening, walking, climbing stair, rope jumping, swimming and indoor exercises,

etc. Diabetics need medical valuation prior doing any active physical activity. Appropriate foot wares must be worn by diabetics to avoid feet harms (Barnett, 2010).

3.1.7. Diabetes management using drugs

Medicines of Diabetes can be:

- Oral tablets to lower blood sugar
- Injections of insulin (Anderson, 2008).

Tablets-lowering sugar can be administered orally to control of blood glucose which is not attained by following healthy diet and physical activity. However, diabetics presently taking these tablets may in future need insulin injection to regulate their blood glucose, as these tablets may not useful alone (Laurence and Bennett, 1992). In some cases, Insulin injection or oral tablets may be given for purpose of diagnosis of diabetes when blood glucose is very high. That is a FBG levels are more than 11 mmol/L or random blood glucose levels are more than 15 mmol/L. Type 1 diabetic should be remained on insulin continuously.

3.1.8. Insulin administration principles

Abdomen, thigh, and the outer upper arm are the injection sites used for insulin administration commonly Abdomen site give fastest rate of absorption. Thigh site should be avoided when effort is to be done, because this enhances absorption rate of insulin. At a particular time of day, one area should be used for an injection and the injection site must be rotated, to prevent hard scar formation (Clark and Lee, 1997). The injection should be done perpendicularly on the skin using specialized syringe for insulin administration. After injection, the needle should be fixed in injected site for 10 sec before removal (Hardman and Limbird, 1996).

3.2. Literature Review

3.2.1. The definition and classification of diabetes

Diabetes mellitus abbreviated as DM is a disease produced by relative or complete absence of insulin which shows elevating in blood sugar levels. Under the

ancient system diabetics were classified as either Insulin Dependent Diabetes Mellitus (IDDM) or Non-Insulin Dependent Diabetes Mellitus (NIDDM). In 1998, a new system of classification relayed on what we called etiological causes of diabetes was proposed by the WHO, this became the known system for diabetes mellitus classifying (Guyton and Hall, 2010).

A) **Type 1 diabetes**: absolute insulin deficiency caused by immune mediated and idiopathic forms of cell disorder. This autoimmune mediated disease process produces total insulin deficiency and thereby total dependency on insulin for surviving (Hardman and Limbird, 1996).

B) **Type 2 diabetes**: adult commencement disease, which originates from secretory defect of insulin, its resistance and relative insulin deficiency. This disease, look likes to exhibit a strong genetic predisposition and it result from a mixture of insulin insufficiency secretion and its insensitivity by tissues of the body, so diabetics of this type show relative insulin insufficiency (Guyton and Hall, 2010).

C) **Type 3 diabetes**: It represents an extensive-ranging of particular types diabetes comprising of different genetic defects in insulin action, and pancreas disorders (Nussey and Whitehead, 2001).

D) **Type 4 diabetes:** which is gestational diabetes, the disease discovered during pregnancy for the first time, as the pregnant cannot produce sufficient insulin to encounter the extra pregnancy needs. It vanishes after delivery and may point toward an increased possibility of type 2 diabetes (Guyton and Hall, 2010).

3.2.2. Diabetes mellitus history

Ancient Egyptians have described group of clinical countenances similar to diabetes mellitus 3000 years ago. Indian physicians also identified this disease and classified it as honey urine causes attract ants. Type 1 and 2 diabetes were known as separate conditions for the first time by the Indian physicians Sushruta Charka in 400-500 CE with type 1 associated with youth and type 2 with obesity, and the term "diabetes" was first used in 250 BC by the Greek Apollonius of Memphis. The term "mellitus" or "from honey" was added by Thomas Willis in the late 1600s (Medvei and Victor Cornelius, 1993).

Diabetes mellitus looks to be a causative factor of death in the old. The first whole medical explanation of diabetes was given by the Ancient Greek physician Aretaeus of Cappadocia (1st century CE). He noted that, the diabetics produce excessive amount of urine. And Avicenna (980–1037) delivered a detailed explanation on diabetes mellitus in The Canon of Medicine, describing the unusual appetite of the diabetic patients and sexual dysfunctions. He also reported the sweet taste of diabetic urine. Before Aretaeus, Avicenna recognized primary and secondary diabetes and described diabetic gangrene, diabetes treatment by using a mixture of lupine, trigonella (fenugreek), and zedoary seed, which gives a significant decrease in sugar excretion. This treatment is still followed nowadays. Avicenna also defined diabetes insipidus accurately, though it was much later that Thomas Willis differentiated it from diabetes mellitus in his book Pharmaceutics rationales in 1674 (Rosenthal and Glewm, 2009).

3.2.3. Incidence

Incidence of Diabetes mellitus as a lifetime disorder which is growing worldwide and can be an epidemic. Thirty millions of people had diabetes mellitus global in 1985 according to World Health Organization estimation. This number has raised to 135 million on 1995 and so statistic indicates that there are nearly 217 million people with diabetes around the world in 2005. 1.5 million People have died by diabetes in 2012. On year 2030 WHO expects the number of diabetics will increase to about 365 million. This growing in diabetes prevalence is mainly due to prevalence of type 2 diabetes occurring in developing and developed countries. Type1 diabetes incidence is also growing in parallel to that of type 2 global. In Turkey, diabetics women are more common than diabetic men (Satman and Yilmaz, 1999). Because of Lack of work outside the home and the exercise is confined to work outside home, most women have no interesting in sports. All these factors can give rise higher incidence of obesity and glucose intolerance among Turkish women. This survey has showed 30% of Turkish women are obese and 28% are overweight (Marrero, 1998). In Turkey, nearly 2.7 million adults have diabetes, 30% of whom unacquainted of their disease. An additional 2.4 million persons have undiagnosed diabetes (Satman and Yilmaz, 1999).

3.2.4. Prevalence of diabetes and associated risk factors

World Health Organization guesses that, worldwide, 423 million persons over 18 years in age were having diabetes in 2014. The largest numbers of people with diabetes were estimated for the WHO South-East Asia and Western Pacific Regions (Table 2), accounting for about 50% of the diabetics globally (Geiss et al., 2006). The number of diabetics having a FBG ≥ 7.0 mmol/L or on diabetes- lowering drug or raised blood sugar) has progressively risen over the past decades, due to population growing, the increased average age of the population, and the increased diabetes prevalence at each age. Globally, diabetics number has considerably increased between 1980 and 2014, rising from 108 millions to recent numbers that are four folds higher (Table 2). 40% of this growth

Is expected to produce from population growth and aging, 28% from a rise in age-specific prevalence, and 32% from the interaction of the two. In the past three periods the prevalence (age-standardized) of diabetes has risen significantly in countries at all levels of income, reflecting the global increase in the number of obese people. The global prevalence of diabetes has grown from 4.8% in 1980 to 8.6% in 2014. Over the last decade, diabetes prevalence has risen faster in low- and mid-income countries than in high in income countries. The WHO Eastern Mediterranean Region has experienced the greatest rise in diabetes prevalence 13.7% (Ackermann et al, 2008)

Table 1: Estimated prevalence & number of people with diabetes (adults18+)

	Prevalence (%)		**number (millions)**	
	1980	**2014**	**1980**	**2014**
African region	3.134	7.112	4.213	25.11
Region of the Americas	5.002	8.303	18.12	62.20
Eastern mediterranean region	5.905	13.71	6.004	43.00
European region	5.341	7.331	33.11	64.01
South east Asia region	4.402	8.403	29.00	131.0
Western pacific region	4.400	8.423	29.05	131.1
Total	4.734	8.529	108.0	422.1

3.2.5. Risk factors of diabetes

These can be summarized into two groups:

1. Non-modifiable factors include aging and family of diabetes history.

2. Modifiable factors include obesity and overweight, alcohol and Smoking habit, Physical inactivity, stressful lifestyle and Unhealthy diet (Medvei and Cornelius, 1993).

3.3. Morbidity

Diabetes comprises a massive load of illness on subjects and society. Diabetics aged between 44-65 years are 24 times more likely to be recorded blind than non-diabetic population of the identical age. Diabetic retinopathy is the principal cause of blindness in this group of age. Kidneys are often affected by diabetes and up to 40% of type 1 diabetics aged below 30 years can expect to develop diabetes nephropathy. A substantial number of these will develop to renal failure requiring long term treatment with renal dialysis. 30% of diabetics develop diabetic neuropathy leading to problems such as foot ulceration, sexual difficulties, cardiac arrhythmias and sudden death (Ackermann et al, 2008).

3.4. Mortality

Approximately more than 20,000 person yearly die early because of diabetes related disease, basically due to macrovascular complications of diabetes including myocardial infarctions and cerebrovascular disorders. The number of people dying early in the diabetic population is double that of the non-diabetic population (Knowler et al., 2002).

3.5. Etiology and clinical features

Type 1 diabetes characteristically is found in the juveniles with a short history of weight loss, unbelievable thirst and polyuria. Such patients are often thin, there are often no family history of diabetes and although the illness underline is unknown. Type 2 diabetes characteristically presents later in lifetime. Such newly diagnosed patients are often overweight and there is a strong family history of the diabetes. It is thought to be that the disease is related to over consumption of foods. Comparing to

type 1 diabetes, type 2 diabetics are often asymptomatic when during diagnosis whilst a physician is examining some other complaint (Wareham and Rahilly, 1998).

3.6. The Diagnosis of Diabetes Mellitus

3.6.1. Diagnosis and diagnostic tests

Usually the body is able to maintain glucose concentrations stable. The normal fasting blood sugar is between 3.5-6.7mmol/L. Occasionally, it exceeds 8mmol/L after a meal. There is no glucose in urine in healthy human since the normal threshold above which glucose would be excreted in the urine is 10mmol/L. Below 10mmol/l the kidneys reabsorbs glucose back into the circulation and for this reason glucose will not appear in the urine unless the glucose concentration exceeds the threshold of its absorption (Guyton, 1996).

Dipsticking urine is used for the presence of glucose as a screening test for diabetes mellitus. The diagnosis of diabetes mellitus is done by finding fasting blood glucose of more than 6.7mmol/L or a random glucose of 10mmol/L. If a patient presents with symptoms of diabetes and is found to have a single very high glucose measurement 15mmol/L then this can be considered as diabetic patient. Further test can be performed to clear any doubt about the diagnosis. Oral glucose tolerance test (OGTT), it reflects the body respond to a glucose load. The fasting overnight patient is given a drink contains 75 g of glucose in 300ml water, after taking fasting blood glucose. The next two hours another blood sample is collected and analyzed. From the results of the glucose tolerance test the patient can be either diagnosed as diabetic, impaired glucose tolerance or no anomaly of glucose handling (Knowler et al., 2002).

3.7. Diabetes Complications

These can be classified as:

3.7.1. The acute complications (diabetic medical emergencies)

These include diabetic ketoacidosis and hypoglycemia.

3.7.2. Diabetes chronic complications

These include microvascular and macrovascular complications, they occur due to prolonged exposure of the body's tissues to hyperglycemia, hypoinsulinemia or their related metabolic disorders. Most diabetics fear of these potential chronic complications; however about 40% of patients with type 1 diabetes can live for over 40 years after the diagnosed disease, 50% of them without developing significant complications (Zimmet and Alberti, 1997). Classification of chronic complications of diabetes:

1. Microvascular (microangiopathic): These include diabetic retinopathy, diabetic neuropath, and diabetic nephropathy and diabetic skin (foot) problems.

2. Macrovascular: They speed up tendency to atherosclerosis/atheroma development Peripheral vascular disease coronary heart disease, myocardial infarction, hypertension and cerebrovascular disease.

3. Hypercholesterolemia is a disorder related to metabolic anomalies (Alvin, 2006).

4. Increased susceptibility to infection.

For unidentified causes, diabetics have an increased susceptibility to bacterial infection .This is an vital factor in the ulceration development of diabetic foot leading to higher risk of limb amputation (Knowler et al., 2002).

3.7.3. Microvascular (microangiopathic) disease

This is specific to and characteristic of diabetes. It leads to the damage of capillary wall and its main clinical signs are diabetic retinopathy, diabetic neuropathy, diabetic nephropathy and the development of diabetic foot ulcers (Zimmet and Alberti, 1997).

3.7.4. Normal capillary wall.

It comprises the basement membrane sandwiched between the endothelial cells inside and pericytes or mesangial cells as supporting cells outside. The capillary wall acts as a highly specialized filter, regulates the transfer of various compounds between the blood and the tissues. The principle components of this filter are the specialized supporting cells and the basement membrane. The supporting cells

surrounding the capillary basement membrane have tiny pores that form a mechanical filter. The basement acts both as a mechanical filter augmenting that of the supporting cells, it has also an intrinsic electric potential which acts as an electrical barrier to particles of the same electrical polarity. The capillary wall in diabetics is structurally altered in 3 ways with passage of the time:

1. Pericyte/ mesangial cells die and are lost effectively opening up holes in the previously tight physical filter.

2. The basement membrane becomes thickened and ceases to act as an effective physical or as an electrical barrier.

3. The endothelial cells lining the capillary inside start to express receptors, boosting the bodies clotting system to stick to them.

The blood of diabetic becomes more sticky and as a result the capillaries get clogged with small blood clots and are effectively destroyed (Zimmet and Alberti, 1997).

3.8. Diabetic Retinopathy

Retinopathy is a readily visible sign of extensive microvascular disease. After 20 years of diabetic life, nearly all patients will have evidence of background retinopathy, but proliferative changes only develop in about 30% of diabetics and this represent a subgroup with a specific inherited susceptibility to the disease. Diabetes may impend sight by one of two mechanisms:

A) Macular oedema: As stated above, microvascular disease has increased vascular permeability sign. Susceptible people to developing capillary leakage at the macular, leading to tissue edema, structural interruption of the photoreceptors resulting in visual disturbance at the end . Fluorescein angiography and photocoagulated with focal laser are used to identify these leaking capillaries. When the leaking areas have effectively cured, the edema resolves with some vision improvement (Gaede et al, 2003).

B) Ischemia of retina: Ischemic retinal can influence vision in two ways:

- The retina’s response to ischemia is to produce antigenic factors that stimulate new vessel formation to reperfuse the ischemic areas. Newly

formed vessels are unsupported and have a propensity to bleed. Visual loss due to preretinal or vitreous hemorrhage is the immediate outcome of this; the long term squeals includes the proliferation of fibroblasts, the formation of fibrotic membranes, retinal traction and finally retinal detachment. Ischemic changes are responsible for one of the late serious outcomes that are rubeosis iridis.

- Retinal ischaemia at the center of macula leads to loss of neural elements at the fovea. Clinically is the loss of central vision; ischaemic diabetic maculopathy. Unlike macular oedema, ischaemic maculopathy cannot be treated (Perneger, et al,1994).

3.9. Diabetic Neuropathy

Diabetes mellitus can affect the somatosensory system causing variable sensory and motor deficits and affects the autonomic nervous system as well. Thirty percent of diabetics have sign of asymptomatic neuropathy on formal testing. Diabetic neuropathy may manifest clinically in one of two ways.

A) Focal or multifocal acute neuropathy in which individual nerves are picked off by discrete, presumably, vascular insults.

B) Diffuse, often symmetrical pattern of sensory loss in which the longest nerves are often the most susceptible.

This type of neuropathy is insidious in its onset, gradually progressive and with time leads to the loss of cutaneous and proprioceptive sensation. Causing factors of diabetic neuropathy are referred to hyperglycemia and vascular damage. Hyperglycemia aggravate neuropathy mechanism is not fully implicated but glycosylation of proteins, a structural change which has clear functional outcomes, has been implicated (Perneger et al., 1994).

3.10. Diabetic Nephropathy

It is a specific microvascular disease affecting the renal glomerulus and it is almost associated with retinopathy. It is the public reason of early death of 25% of diabetics type1. Renal glomerulus is the principle site of this filtration of entire blood many times daily and is a highly specialized capillary structure. In diabetes this filter

becomes extremely disrupted with two outcomes; it starts to leak proteins in the urine (proteinuria), and fails to excrete waste products effectively. This disruption of the renal glomeruli of kidneys is called diabetic nephropathy, and the most reliable clinical sign of diabetic kidney damage (Bishop et al., 2000) end stage diabetic nephropathy can have a reflective effect on vision. Diabetics who are in renal failure, tend to progress rapidly to proliferative retinopathy, macular edema and once this is recognized, it is often difficult in treatment. Diabetic patients with end stage renal failure have to be kept on renal dialysis

Treatment; every 2 or 3 days, to remove the waste products. Renal transplant surgery can be useful in selected patients, but typically early death is ten times higher in diabetic than non-diabetic patients in receipt of renal transplant therapy (Bishop et al., 2000).

3.11. Skin and the Diabetic Foot

Foot care is a vital portion of the cure of the diabetics as a small ulcer may rapidly growth and threaten the foot viability. Peripheral neuropathy means patients are frequently unaware of skin trauma making foot ulceration more communal. Pain sensation losing may be accompanied by poor eye sight. Because of diabetics have an increased tendency to bacterial infection, any untreated skin wound can promptly get infected and because of reduced circulation, infection spreads very quickly and responds slowly to treatment. So such diabetic foot ulcer needing antibiotic for months waiting for a small ulcer to heal and often amputation is the only way of overcoming the infected tissue. For this reason, the limb amputation rate in diabetic population is greater than in general population. Even though microvascular disease is only seen in diabetics, they are also disposed to developing atherosclerosis and arteriosclerosis, large blood vessels disorders of that affect the general population (Bishop et al, 2000). But diabetics get both these diseases at an earlier age and they are at least two times as likely to progress complications related with heart attacks, than non-diabetics (Onat et al, 1991).

3.12. Atherosclerosis in Diabetics

Atherosclerosis is the plaques deposition of a mixture of lipid, and fibrovascular tissue (atheroma) inside of the large blood vessel wall. These plaques usually slowly increase in size with two clinical concerns (Selvin et al., 2005).

A) Chronic ischemia: This includes coronary heart disease and peripheral vascular disease. Because the atheromatous plaques get larger the blood lumen vessel gets narrower and the total blood flow along the affected vessel is gradually decreased leading to ischemia of the tissue. This is the pathological progression

Behind the progress of coronary heart disease and peripheral vascular disease. At rest the narrowed blood vessel may be able to deliver enough blood to meet the needs of the heart muscles, but while the exercise the narrowed blood vessel can no longer supply the heart muscles with blood they need and they becomes ischemic. This appears as chest pain or what it is called angina pectoris.

B) Acute vessel ischemia: Atheromatous plaques may break and activates the intrinsic clotting system that forms a blood clot over the breaking site, blocking the affected vessel and cause acute ischemia and tissues death supplied by the affected vessel. If the plaque rupture occurred in the coronary vessels, it can lead to acute myocardial infarction (heart attack).

3.13. Arteriosclerosis in Diabetes

It is a histological word implicating the loss of elastic tissue from the medium and large arteries walls (arterio-), which then become stiff (-sclerosis) and become increasingly less able to absorb the pressure wave pumped into the circulation during heartbeat, the blood pressure within the system therefore rises and the blood pressure rises also. Untreated hypertension and diabetes are a principally bad combination for diabetics. High blood pressure speeds up the event to kidney failure; atherosclerosis, and increased mortality from strokes and heart attacks (Herman et al., 2015).

3.14. Other Metabolic Disorders Associated With Diabetes

Even though hyperglycemia the most intense metabolic disorder in diabetes, other metabolic troubles also occur namely hyperlipidemia or hypercholesterolemia that contribute in a substantial risk factor for heart disease because it most likely

speed up the formation of atheroma, therefore diabetics must check their blood cholesterol level continually (Klein et al., 2004).

Table 2: High blood glucose age standardized mortality rates /100000 by WHO region age 20+

	Both sexes	Female	Male
African region	111.3	110.9	111.1
Region of the Americas	72.62	63.90	82.90
Eastern mediterranean region	139.6	140.2	138.3
European region	55.72	46.51	64.51
South-east Asia region	115.3	101.8	129.1
Western pacific region	67.01	65.81	67.80

3.15. Diabetes Management

This can be grouped into four parts:

a. Pyschologic support by the community for diabetics with different disabilities.

b. Primary fluctuation of blood sugar treatment.

c. Correction of blood pressure and cholesterol levels.

d. Management of complications of diabetes (Eledrisi et al., 2006).

3.16. Diabetes Treatment

The diabetes treatment with drug is composite and it needs to follow strict regimen of what is called diabetic diet. A diabetic should eat a healthy and balanced diet. The goal and way of treating type 1 diabetics is essentially different to the treatment of type 2 diabetics (Alberti and Zimmet, 1998).

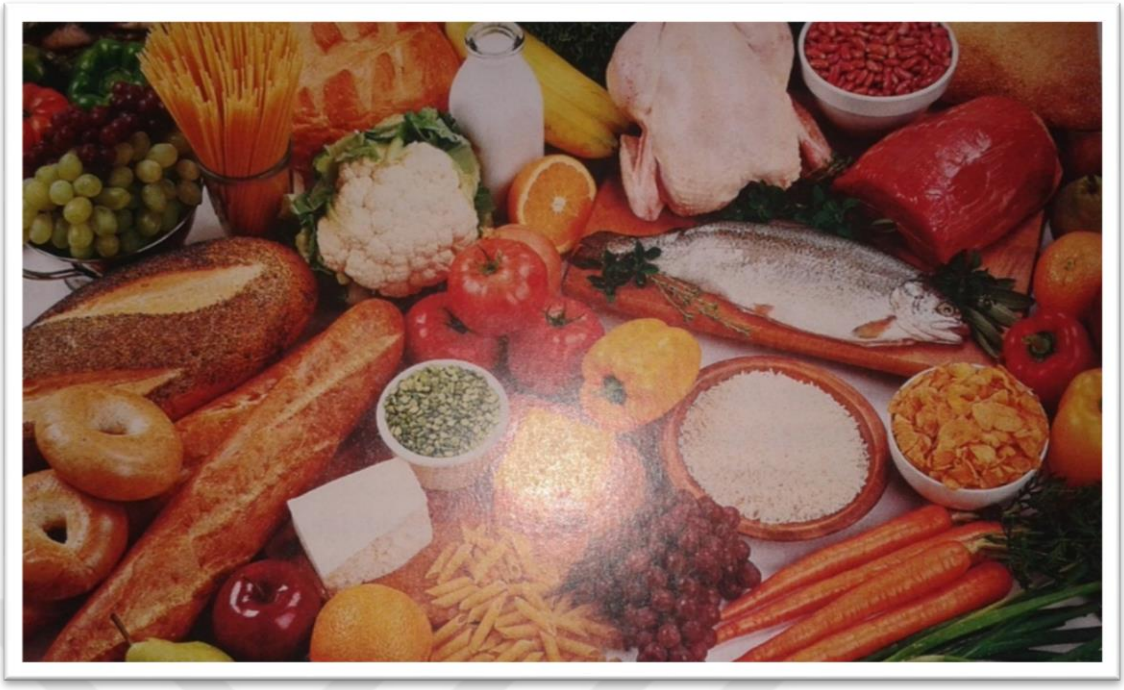

Figure 1: Carbohydrates from a variety of foods are essential component of the diet

3.16.1. Treatment of type 1 diabetes

Type1 diabetics have inability to produce insulin from their pancreas and they are dependent upon administered insulin to be sustained. So type 1 diabetes treatment Is therefore relatively straight forward insulin (Eledrisi et al., 2006). Daily insulin needs for each individual are variable and depend upon age, sex, build and physical activity, but an average daily need of insulin is about 1unit/Kg body wt/day. There are different types of insulin; long acting, medium acting, short acting, or a mixture of them but the selection of insulin is governed by a patient's needs and life style (Alberti and Zimmet, 1998). A youth with irregular eating habits and meal require some elasticity to take a variable dose of short acting insulin before every meal enabling them to assess the dose of insulin to the meal size. They also have to increase their evening dose with longer acting insulin to meet their overnight requirements of insulin (Eledrisi et al., 2006).

3.16.2. Type 2 diabetes treatment

Type 2 diabetics have small remaining inadequate insulin production in their pancreas. The type 2 diabetics are in a situation of relative insulin deficiency. This can be managed by two ways, tablets or insulin. The beginning with one type of

tablet, if this fails to control the blood sugar satisfactorily then the other type of tablet is added. If the blood sugar is still not regulated one has to go for insulin therapy (Alberti and Zimmet, 1998).

3.17. Oral Hypoglycemic Agents

The presently available oral hypoglycemic agents can be classified as follows:

A) Guanidine derivatives which was found to lower the blood glucose levels, but toxic effect related with their use have limited their use. They include phenformin which is more safe and non-toxic than the parent compound. It is then followed by metformin. Biguanide acts by enhancing liver sensitivity, fat, muscle, and other tissues to the uptake and effects of insulin, thereby lowers the blood glucose level. It does not increase the insulin concentration in the circulation and therefore don't cause undue decreasing in blood sugar level when used alone.

B) Sulphonyl ureas: these include first generation sulphonyl ureas such as tolbutamid, chlorpropamide, tolazamide and acetohexamide and second

Generation sulphonyl ureas such as glyburide and glipizide, they are more lipid soluble and are considered to be more potent than the first generation sulphonyl ureas. All sulphonyl ureas lower the blood sugar levels by stimulating the production and release of insulin from beta cells of pancreas. The initiation of the use of sulphonyl ureas is that they should be given to the patients who have retained considerable amount of pancreatic beta cell that is sulphonylureas can only be used in treatment of type 2 diabetics.

C) Miscellaneous Agents: one of them is acarbose, it is an oral hypoglycemic agent which is used to control blood glucose levels in type 2 diabetic patients. Acarbose which is synthetic oligosaccharide slows down the action of alpha-amylase released by pancreas to digest larger carbohydrates into smaller carbohydrates units resulting in the lowering of blood glucose levels after meals (Zimmet and Lefebvre, 1996).

3.18. Monitoring Treatment

In order to reduce microvascular and macrovascular diabetic complications rate, active glycemic control should be accomplished by monitoring the treatment

effectively. Glycemic monitoring can be accomplished by measuring capillary blood sugar to showing an immediate reading of the blood sugar and help to decide how much insulin to take before a meal (Sato et al., 2009).

Blood sugar monitoring for long time can be accomplished by a formal blood test seeing at what percentage of HbA1c has been glycosylated. This acts as a very accurate indicator of what the ambient blood sugar level has been over the month prior to the test and it serves as a useful sign to whether the blood sugar has been successfully controlled over the past period (Zhang et al., 2010).

3.18.1. Normal homeostasis of glucose

It is convenient to divide the regulation of carbohydrate metabolism into two parts as the two are functionally related:

A) Factors affecting the blood glucose

B) The regulation of carbohydrate metabolism at the cellular and enzymatic level. The maintenance of stable of blood glucose levels is one of the most finely regulated of all homeostatic mechanisms in which the liver, the extra-hepatic tissues, and several hormones play a part. Liver cells appear to be freely permeable to glucose whereas extra-hepatic tissues cells are relatively impermeable. This result in the passage through the cell membrane being the rate –limiting step in the uptake of glucose in extra-hepatic tissues, where it is probable that the activity of certain enzyms and the concentration of key intermediates exert a much more direct effect in the uptake or output of glucose from liver. Nevertheless, the concentration of glucose in the blood is an important parameter in determining the rate of uptake of glucose in both liver and extra-hepatic tissues. The body has very complex elegant systems that regulate the use, production and storage of glucose by the hormone of insulin. Mechanisms that control the synthesis, use and storage of glucose and its accompanying energy substrate the ketone bodies (Granner, 2000).

3.18.2. Glucose and ketone bodies sources

Glucose can be obtained from carbohydrates in the diet upon digestion, it can be synthesized by the body from various glucogenic compounds which undergo gluconeogenesis such as amino acids, propioinate, and lactate. There is a complex

relation between glucose and its energy stores, instantly after a meal there is an excess glucose in blood and the body therefore the body stores the excess glucose, some hours later when the blood glucose level drops, the balance swings back; the body starts to synthesize glucose from its own energy stores and the level of glucose in the blood is return to normal level (Murry et al., 2000).

Glucose can be stored as glycogen or protein. When these stores are filled the body converts the excess glucose into fat. Indeed, although in times of glucose excess the body can turn glucose into fat, it cannot do this in reverse during hypoglycemia condition and the only way to utilize the energy stored in the fat is to turn it into ketone bodies which are used as source of energy by most of body tissues (King, 2004).

3.19. The Acute Diabetic Emergences

3.19.1. Diabetic ketoacidosis (DKA).

It is produced by sudden and total lack of insulin in the body. Because entry of glucose into cells is completely dependent on insulin, so when insulin is absent the cells cannot utilize glucose present in the circulation and become starved and consequently die. So the starving cells start to mobilize their energy stores like fats, carbohydrates and proteins in attempt to survive converting them into glucose and ketone bodies to feed on. For this purpose that diabetic ketoacidosis known as "starvation in the midst of plenty" (Guyton and Hall, 2002). Furthermore, the very high generated glucose and ketone bodies levels in the blood can lead to catastrophic problems (Ganong, 2003). During the time of hyperglycemia, kidneys cannot deal such a high level of glucose and start to leak considerable amounts of it into the urine. Kidneys cannot doing so without water excretion in large volumes so polyuria is produced causing patients to get dehydrated and start to drink lots of water in to substitute the water losing (polydypsia). Lastly, the high levels of ketone bodies produced by hypoglycemia are acids, the patient becomes acidotic with serious concerns for the brain (Satman et al., 1997). Diabetic ketoacidosis is a dangerous disease which whose treatment requires urgent hospitalization. It only affects patients with type 1 diabetes and it is characterized by unwell of patient over a few minutes, however this can be occurred during hypoglycemia. Diabetic ketoacidosis is treated

with insulin and rehydration, otherwise the patient can no longer survive (Ganong , 2005).

3.19.2. Hypoglycemia

Hypoglycemia is the most common of the acute diabetic emergencies. Diabetics who experience of hypoglycemia can be somewhat well one minute and distressingly unwell the next as they become sweaty, pale and confused, or sometime unconscious in case of severe episode. The essential problem is a sudden drop of circulating glucose leading to the starvation of the cells of energy and stop working appropriately and as the brain cells are the most metabolically active they are the ones that affected first, and therefore subjects become confused, aggressive and sometimes comatose. In normal subject because the body balance its insulin production with the blood glucose accurately, if there is no eating at all, the feel of hunger may be produced but the glucose concentration in circulation won't change greatly as the body lowers its insulin production and the cells don't starve. Diabetics have very reduced control of this balance between blood glucose concentration and production of insulin. Once they take their insulin dose, or a tablet that augment the insulin effects, they have to eat a certain amount of food in their meals to sense of balance (Edwards et al., 1996). The hypoglycemic patient can be given anything that may contain glucose, such as sweets. In case of unconscious patients, they must be given an injection of glucagon hormone, to raise the level of blood glucose for rapid recovery (Marcus et al., 2007).

3.20. Insulin structure, biosynthesis & secretion

Insulin is a polypeptide comprising two chains of amino acids connected by disulfide bridges, with a molecular weight approximates 5734 Daltons (Fig 1). There are minor differences in the amino acid composition of the molecule from species to species making the insulin as antigenic without affecting its biological activity. It is synthesized in the endoplasmic reticulum of the beta cells of pancreas as a single chain and folded in the beta cell, and the disulfide links are formed and then transported to Golgi complex to be packed in the membrane-bound beta granules which move to the cell wall, and fused their membranes with the membrane of the cell, expelling the insulin to the exterior by exocytosis process. The insulin must then

cross the basement membranes of the beta cell and a neighboring capillary and endothelium of the capillary to reach the circulation (Roith and Zick, 2001).

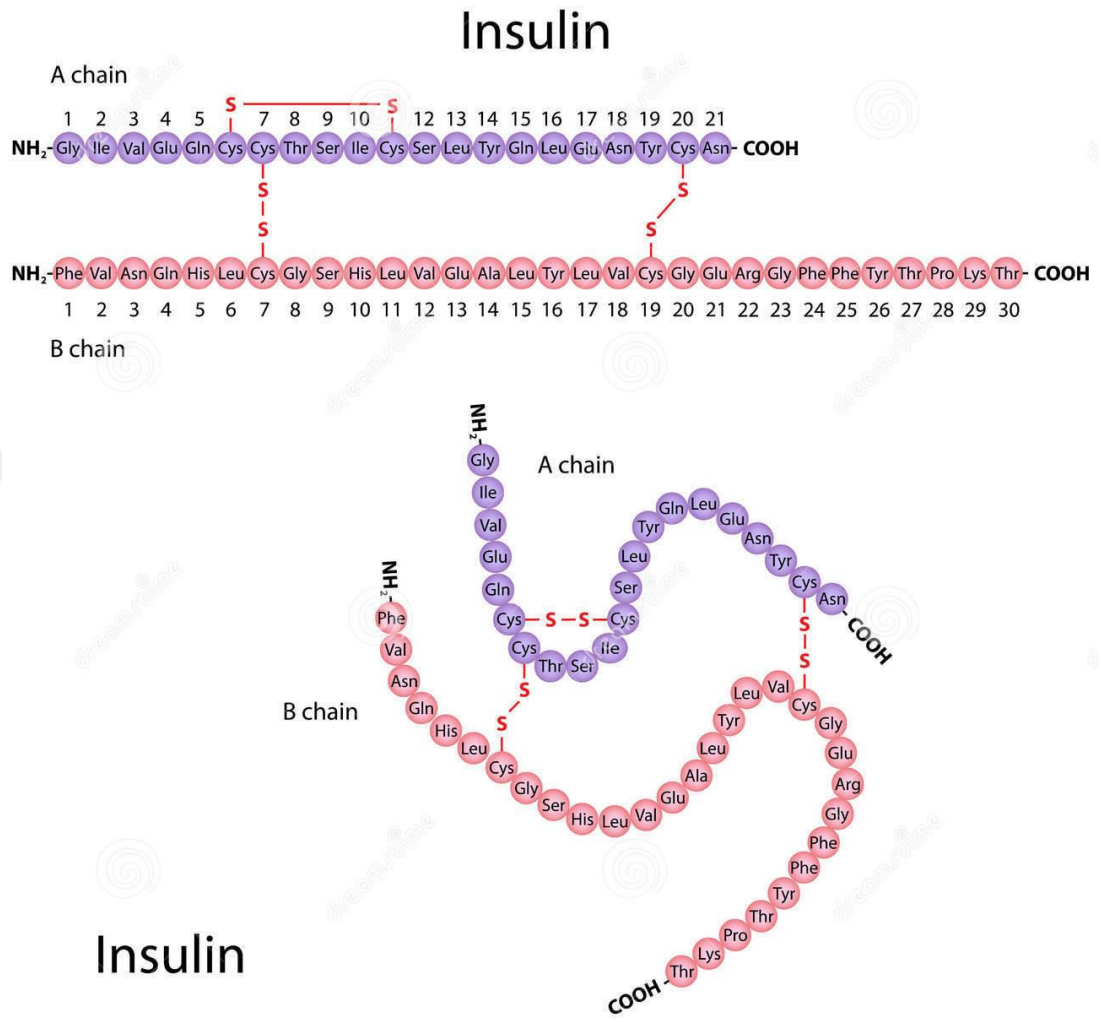

Figure 2: Structure of human insulin

3.20.1. Functions of insulin

A) It enhances uptake and storage of glucose into the tissues as glycogen, protein or fat.

B) It prevents the synthesis of glucose and ketone bodies from these energy stores.

C) It plays a vital role in glucose transport system in all cells. If insulin is absent, cells are unable to take glucose from the blood and they will effectually be hungry. With the exclusion of type1 diabetics, insulin creation is not ever allowed to be zero (Reaven, 2004). In brief through times of glucose excess, insulin enhances

the body to store the excess. Therefore, the glucose concentration in blood decline and insulin production is decline also. If the blood glucose continues to fall such that a state of glucose deficiency is created, insulin production is reduced still further allowing the reverse of the process is initiated by other hormones (Simonson and Kendall, 2005). The stored glucose is now stimulated to synthesize and released back into the circulation returning the blood glucose level to normal.

Other hormones involved in glucose homeostasis (cortisol, adrenaline and glucagon) compete against the insulin actions, and are released when the glucose level falls. Glucagon is one of these hormones which can be injected into diabetic who become hypoglycemic to blood sugar (Zhao et al., 2010).

3.20.2. Insulin resistance

Is a situation characterized by impaired biological and physiological reactions to insulin in tissues However, there is a substituted increase in insulin concentrations (hyperinsulinemia) in its early stages. It results in overexpression of actions in tissues that preserve normal or minimally impaired sensitivity to insulin. This metabolic disorders leads to a group of abnormalities with severe clinical outcomes like cardiovascular disease, chronic kidney disease and diabetes type 2. Insulin resistance can be caused by abnormalities in prereceptor, receptor, or postreceptor. Pre-receptor causes is development of antibody to insulin and

Formation of abnormal insulin (mutation).The receptor causes include reduced in the number of receptors, structural modification of the insulin receptor itself, and formation of insulin receptor blocking antibody. Causes of pre- and receptor of insulin resistance occur rarely; the most common cause is post-receptor in nature and involves the post-receptor signaling Pathway (Reaven, 1995). Insulin has acute and chronic physiological actions: the acute ones include those that control intermediary metabolism, and chronic ones include the growth and proliferative actions of insulin (Kruijshoop et al., 2004).

3.21. Meta-analysis

Meta-analysis is a arithmetical system for uniting the results from different types of studies to evaluate the medical efficiency of new interventions, by merging statistics from two or larger than two randomized control trials in order to giving a

accurate estimation of treatment effect, giving owing weight to the size of the diverse studies involved (Antman et al, 1992). Systematic review quality on which it meta analyses based includes total coverage of all related studies, looking for the heterogeneity value obtained, and discover the strength of the main results by means of sensitivity analysis (Mulrow, 1994).

Figure 3: The pyramid of work that provides the best evidence

3.21.1. Sstematic reviews

Approach of systematic review is the meta analysis core. It needs to give efforts to find maximum number of the relevant studies and to evaluate the mechanical quality of the design and presentation of each study involved (Moher et al., 1999). The goal of systematic review is to reach a balanced and fair summary of the obtainable research, permitting decisions on efficiency to be established on all studies included of acceptable value. Commonly, systematic reviews gives a quantifiable statistical estimation of clear benefit combined over all the included studies. This is called a meta-analysis (Higgins and Green, 2006).

3.21.2. Precision

The precise effect size of an effect depends on the number of subjects participant in the study largely. Meta analyses, have good ability to detect even small but clinically significant effects and give more precise estimation of the disclosed

effects size. This is vital when a researcher is looking for valuable effects in definite subgroups of patients. Singular studies occasionally enclosed very little contributors in the interested subgroup but with valuable information (Chalmers et al., 1981).

3.21.3. Conducting meta-analyses

Meta-analysis needs a wide-ranging approach of searching which cross-inspects several electronic databases (Medline, Embase, Cochrane Central Register of Controlled Trials). Searching by hand of journals and checking of the reference lists of papers obtained is also required (Egger et al., 1997). The approach should write as an order of needs: involve studies with specified terms, following certain research designs, exclude papers that do not meet certain criteria (Peters et al., 2006).

3.21.4. Calculating effect sizes

Medical trials normally show their outcomes as the rate of recurrence of some outcome in both intervention groups and control Group (Sterne et al., 2001). In meta-analysis these are usually grouped as a ratio of the frequency of the happenings in the intervention to that in the control group. Formerly, the summary measure of effect size was the odds ratio, but now the risk ratio (relative risk) can be assumed. Although they are technically different, the odds ratios and relative risks are usually interpreted in the same way (Lau et al., 2006). The results of singular studies can be united with suitable statistical technique and others are used for combining odds ratios, relative risks and further outcome measures (Terrin et al., 2005).

3.21.5. Presenting the findings

Forest plot is a pictorial representation and the typical method of showing data from a meta-analysis is used to display the findings from each individual study as a spot or square, with squares towards the left side indicating the new treatment to be better, whereas those on the right refer the new treatment to be less effective. The size of the spot or square is related to the study precision of the (the sample size). A horizontal line (the 95% confidence interval) is drawn around each of the studies' squares to represent the uncertainty of the estimate of the treatment effect. The total effect size obtained by combining all the studies is displayed as a diamond (Schmid et al., 2004).

3.21.6. Heterogeneity

It is the extent to which we can mix different kind of studies. Meta-analysis is a statistical that combines several independent but combinable clinical trials results. To get an exact answer to a particular question, only studies that closely match the question should be involved. Unluckily, studies can differ on the types of patient studied which can affect the amount of treatment use (the effect size), leading to what is named heterogeneity between studies (Biondi et al., 2006). Existence of heterogeneity is done by Cochrane's Q, a statistic based on the chi^2 test however it sometimes fails to detect heterogeneity while it is existent. To solve this, another test, the I^2 statistic was proposed where it scores heterogeneity from 0% to 100%. Furthermore, a rule of thumb was suggested, with 25% equivalent to low heterogeneity, 50% to moderate and 75% to high. Presence or absence of heterogeneity affects the consequent method of analysis. When heterogeneity is absent, then the analysis uses what is named fixed-effects modeling. This presumes the size of treatment effect is the same or fixed across all studies and the variant seen between studies is due to the play of chance only. Random effects models presume that the treatment effect really does vary between studies. This tends to increase the variance of the summary measure, Making it more difficult to obtain significant results. When heterogeneity value is large, it is unsuitable to calculate an overall summary of effect size. To overcome the heterogeneity problem, meta regression technique is introduced (Moja et al., 2005).

3.21.7. Meta-regression

Meta-regression is a technique uses summary data from each trial to discover which types of factors related to patient or to study design can contribute to the heterogeneity. In actual, it is struggling to recognize which patient factors are related to the size of treatment effect (LeLorier et al., 1997). Luckily, another method, using individual patient data, to give solutions to the imperative question: which patients are most expected to use this treatment?. This permits a greater elasticity in analysis, and matters can be explored that were not involved in the original trials (Villar et al., 1995).

4. MATERIALS AND METHODS

A hand searching of required published studies was performed randomly on internet network on April 2018, using “dietary fiber” and “type2 diabetes mellitus” as keywords. The studies references that met our criteria were examined for more probable related studies.

4.1. Selection of the Studies

Inclusion measures of our meta-analysis comprised randomized trials that included a rise in intake of dietary fiber as an intervention. Evaluated of HbA1c and FBG as a result, used human contributors with known diabetes mellitus type 2. Exclusion criteria included are those on diets different other than fiber, lack of specific effect data, patients other than diabetics type 2 included or comparison of two types of fiber (absence of control group). Table 2.1 shows the details of the intervention of the nine studies.

4.2. Extraction of Data

Data were taken out from all studies are pass in Excel spreadsheet (Microsoft, Corp., Redmond, WA). Population factors such as number of subjects, fasting blood glucose and glycated hemoglobin. Final means of HbA1c and FBG of the intervention groups and control groups were measured as outcomes. Mean standard deviation of studies were used. If studies described FBG in mg/dl, this is multiplied by 0.0555 in order to convert it to the standardized international unit of mmol/L. Table 3 and table 4 summarize means and SD of FBG and HbA1c for the selected studies.

Table 3: Means & SD of FBG for the nine studies

FBG in mmol/l						
studies	Intervention group			Control group		
	N	Mean	SD	N	Mean	SD
Fuessl	18	8.290	0.470	18	8.700	0.510
James	8	12.00	1.400	8	12.22	1.330
Ikem	35	5.901	1.300	17	8.000	2.300
Tommy	7	7.001	1.400	6	7.501	1.400
Chandalia	6	7.101	2.100	7	7.550	2.000
David	23	7.500	0.310	23	7.900	0.410
Dall Alba	23	7.101	2.800	21	7.100	1.800
Ziai	27	9.410	0.391	22	12.09	0.585
Simpson	7	6.501	0.400	7	7.400	0.500

Table 4: Means & SD of HbA1c% for the nine studies

HbA1c %						
Studies	Intervention group			Control group		
	N	Mean	SD	N	Mean	SD
Fuessl	18	8.700	0.330	18	9.010	0.310
James	8	8.100	0.500	8	7.130	0.610
Ikem	35	7.230	0.500	17	8.230	0.211
Tommy	7	5.501	0.700	6	5.900	0.590
Chandlia	6	6.900	1.200	7	7.201	1.300
David	23	7.201	0.220	23	7.400	0.310
Dall Alba	23	6.600	0.800	21	6.901	0.900
Ziai	27	8.901	0.200	22	10.50	0.600
Simpson	7	8.500	0.300	7	9.500	0.400

4.3. Analysis and Data Synthesis

Meta-analysis of the mean differences was officiated with Review Manager (version 5.0.23, The Nordic Cochrane Center, Copenhagen, Denmark). Distinct analysis was done for FBG and glycated hemoglobin. By using inverse variance method, final means in control and intervention groups were matched by calculating a mean difference. Studies possessing less variance in their effect assessment are given more weight. Together fixed effect model and random effects model were

introduced in this analyses. Comparison of final means is deemed a proper analysis method in randomized trial since, baseline data of both intervention and control groups in a randomized effect model are statistically same, so final values for each trial should represent a change from common baseline. A heterogeneity test was done to decide if a fixed-effect model results can be considered lawful. When heterogeneity showed P equal or less than 0.05, the results of a random effect model would be deemed valid only. Forest plots for HbA1c and FBG were generated.

Table 5: Intervention details of included studies

Study	Type Of fiber	Intervention
Fuessl (1987)	Guar Granules	Eighteen patients with T2DM were given 5g granules sprinkled on each meal for 4 weeks, and 4 weeks placebo period (separated by 14 days),5g wheat bran was given. Mean FBG and HbA1c on completion of study were reduced than after period of placebo.
James (1991)	Insoluble oat fiber	8 type2 diabetics were given 30g of insoluble hull oat fibers for 2 weeks in hosoital and further 10 weeks on discharge.The hospital oat fibers decreased FBG by 13% but the values returned to pretreatment values after discharge period.
Ikem (2007)	Not specified	35 type2 diabetics were given 40g/day for 8 weeks ,on the completion of the study, mean FBG was reduced by 4.9±2.7 mmol/L.
Tommy (2009)	Not specified	13 type2 diabetics were given Paleolithic diet including fruits, root vegetable, lean meat, fish, , , and nuts in 2 successive 90-days periods. Results included decrease of means of FBG and HbA1c values.
Chandalia (2000)	Not specified	13 patients with T2DM were given 50g of dietary fibers for 6 weeks compared with 24g of dietary fibers for same period the two diets were isoenergetic.On completion the study, the mean FBG was lower by 8.9% with 50g fiber diet ,HbA1c also was reduced from 7.2 to 6.9 .
David (2002)	Wheat bran	23 patients with T2DM were given 19g/d cereal fibers for two 3-month phases .On the finish of the study ,there were no significant differences in the means of FBG and HbA1c levels.
Dall Alba (2013)	soluble fibre	23 subjects with T2DM were compared with 21 controls were given 10g /d,the duration of treatment was 10 weeks. The means of HbA1c was decreased but FBG didn't change.
Ziai (2005)	Psyllium husk fiber	49 subjects with T2DM were given 5.1g twice a day for 8 weeks.On the end of the study ,psyllium showed decrease in FBG &HbA1c.
Simpson (1979)	Cereal food & Tubers vegetabl	14 diabetic patients were treated with high CHO modified fat diet for 6 weeks.This diet resulted in a fall in FBG & HbA1c%.

5. RESULTS AND DISCUSSION

5.1. Study Characteristics

Nine studies were involved in this meta-analysis table 2.1 shows intervention details of included studies, Sample size wide-ranging from 6 to 35, adding together 145 subjects for intervention group and from 6 to 23, totaling 129 for control group. Fiber involvements extended from 4 to 40g/day of addition fiber. Three studies did not postulate the dietary fiber type (Chandalia, 2000), (Tommy, 2009) and (Ikem, 2007). (Fuessl, 1987) reported on guar granules, (James, 1991) reported on insoluble oat fiber, (David, 2002) reported on Wheat bran fiber, (Dall Alba, 2013) reported on soluble fibers, (Seyed Ali, 2005) reported on Psyllium husk fiber and (Simpson, 1979) reported on cereal food & tuber vegetable dietary fiber. All the studies included measurement of fasting blood glucose in mmol/L and glycated hemoglobin as percentage of hemoglobin for both the intervention group and controls. Methods of diet were different, the durations of treatment with different types of fiber were varied from 4-week period (Fuessl, 1987) to 6-month period (Tommy (2009), David (2002)).

5.2. Meta-Analysis on Fasting Blood Glucose

Meta-analysis results of FBG are shown in fig 3.1 which shows the odd ratios for individual studies and combined studies for the intervention fiber against placebo intake. The overall mean difference was a decrease of FBG by fiber intake of 0.91 mmol /L (95% CI, 1.18 –0.64) more than the decrease from placebo in fixed effect model and -1.17 (95% CI:-1.97; -0.36) in random effect model ,high heterogeneity was witnessed (p less than 0.01, I^2 = 88.0%). This result is line with high heterogeneity.

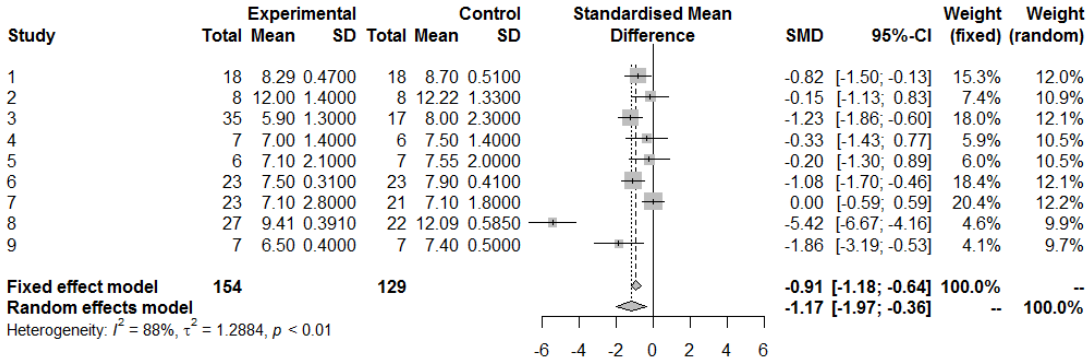

Figure 4: Forest plot for FBG.
Mean, SD, and mean difference are in mmol/l units

5.3. Meta-Analysis on Glycated Hemoglobin

HbA1c meta-analysis results are shown in Fig 3.2 .The overall mean difference was a reduction of glycosylated hemoglobin by fiber intake of 1.03 mmol/L (95% CI, 1.31 –0.76) more than the reduction from placebo in fixed effect model and -1.08 (95% CI: -1.94;-0.21) in random effect model. High heterogeneity was witnessed (p less than0.01, I^2 = 89.0%). This result is line with high heterogeneity.

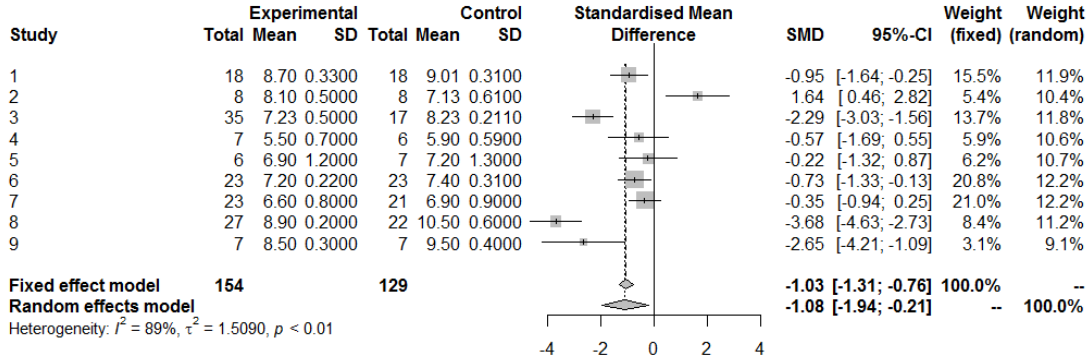

Figure 5: Forest plot for glycosylated hemoglobin.

6. DISCUSSION

The term dietary fibers, was well-defined by American Association of Cereal Chemists International, are the eatable but indigestible and non-absorbable portions of vegetation or related carbohydrates (DeVries, 2001). Growing in total dietary fiber consumption has showed a decrease in body fat (Tucker and Thomas, 2009), improve glycemic response and reduce blood pressure (Chandalia et al., 2000), triglycerides and low-density lipoprotein (Jenkins et al., 2002), (Brown et al., 1999). Dietary fiber intake was proposed to encourage weight loss in obese people and avoid weight recover (Solah et al., 2017), (Abete et al., 2010), (Parnell and Reimer, 2009), (Trigueros et al., 2013). Confirmation of consumption of dietary fiber and its weight regulating effect has been studied (Brownlee et al., 2017), (Slavin, 2005), (Pereira and Ludwig, 2001), (Howarth and Saltzman, 2001). The mechanisms by which dietary fiber affect diabetes are proposed to be associated to energy dilution),(Howarth and Saltzman, 2001), lessening in nutrients absorption rate (Eastwood and Morris, 1992), appetite clampdown (Lee et al., 2016), (Ye et al., 2015), (Lafond et al., 2015), regulation of energy homeostasis (Byrne et al2015), (Chambers et al., 2015), (Sanchez et al., 2012), and change of gut microbial (Benitez et al., 2016). Dietary fiber eating has showed decline the risk of type 2 in observation studies (Cho et al., 2013) and meta-analyses (Ye et al., 2012). Insulin resistance and glucose tolerance in diabetics and subjects those having weakened glucose tolerance was improved and observed in intervention studies (Garcia et al., 2007), (Pereira et al., 2002). The worthwhile dietary fiber effects on insulin resistance may attribute to increasing glycemic index of food (Consortium, 2015), reducing the obesity (Sanchez et al., 2012), (Consortium, 2015), improving homeostasis of glucose (Benitez et al., 2016), (Galisteo et al., 2008), regulating hormonal responses (Weickert Pfeiffer, 2008), modulating inflammatory cytokines (Dandona et al., 2005), and changing gut microbiota (Benitez et al., 2016). The dietary fiber effect on GIT is via its physical and chemical properties through their size of particle, type and amount of fiber, viscosity, content of amylose and amylopectin, delaying time of emptying, reducing sugar concentration (Leslere et al., 1994), (Jenkins et al., 1978), (Torsdottir et al., 1980).

6.1. Discussion on the Meta-Analysis

Meta-analysis technique was officiated to epitomize observational studies on the relation between dietary fibers consuming and its effects on diabetics type 2. Our meta-analysis grouped together FBG and HbA1c studies, and presented a converse relationship between consuming of dietary fiber and FBG and the same with HbA1c% mean values. On interpreting the meta-analysis results, many factors are worthy to be Taken in consideration such as duration of treatment and the amount of fiber that is given to the subjects per day, subjects adherence with the diet etc. The criteria for management of T2DM can affect the results and must be considered fussily. A random and fixed effect models were applied to combine the effect of fiber intake on the FBG and HbA1c in diabetic patients type 2. Test of heterogeneity was officiated using the I^2 and Q statistic. The I^2 statistic prescribes variation % crossways studies due to heterogeneity instead of chance (Higgins and Thompson, 2002). I^2 less than 25% was deemed as few or no heterogeneity, 25 to 50% was deemed as moderate heterogeneity, and more than50% proposed as high heterogeneity, correspondingly. For the Q statistic, p less than 0.1 were deemed significant statistically (Higgins et al., 2003). Fixed effect model, by referring to fig 3.1, the dietary fiber effect on FBG is proposed to be more apparent in study (8) and weakened in study (7). Although the amount of fiber intake in the two studies were 10.2 g/day versus 10 g/day respectively, the mean of FBG reduced by 28% in the former study while it remained unchanged in the latter, this may attribute to the difference in duration of treatment between the two studies. This does not affect the common effect as the study (8) has small wt%, the same effect also affect the common effect by study (9). Studies (2, 4 and 5) showed small effect of fiber intake on FBG , their weights and their confidence intervals were convergent, there is no significant variances between the three studies. Studies (1, 3 and 6) exhibit convergent confidence intervals and close wt% overlap each other in their CI , so the studies shift the common effect toward its value -0.91 with CI(-1.18; -0.64) reflecting the inverse relationship between fiber intake and FBG of diabetics . Two studies (8 and 9) have close confidence intervals but high variances between the study (not overlap each other) causing the mean effect to shift toward the left as the sum of their weights in random effect is 19.6%. Studies (1, 3 and 6) showed significant negative effect of fiber intake on FBG with close wt% and CI overlap each other and with

studies (2, 4, 5 and 7) with smaller effect and smaller wt% . All these above studies give rise the mean effect of -1.17 with CI (-1.97;-0.36). Overall P- values was 0.0001 in fixed effect model and 0.0044 in random effect model making the two models are valid as the two values are less 0.1 High heterogeneity value expressed by I^2 was 88.1% and therefore reflects the

Presence of variances within the studies as well as variances between the studies. Various types of fiber act in the treatment of T2DM in different mechanisms (Robert E, 2012), the study proposes a decreased FBG with increasing intake of dietary fiber. This is in line with our results about the effect of fiber intake on FBG of diabetic patients type 2. Fixed effect model in fig 3.2 shows higher wt% for studies (1,6 and 7) with variable confidence intervals overlap each other with (4,5) of smaller wt% around common effect and balance the remaining studies with smaller wt% that is (2, 3, 8 and 9) with variable confidence intervals not overlap each other except for (8,9) which are overlapping. The common effect is -1.03 with CI (-1.31;0.76) which means inverse relationship between fiber intake and HbA1c% Study (2) showed positive relationship between fiber intake and HbA1c%, and this does not affect the final result greatly unless other studies have same relationship are present. In random effect model fig 3.2, study (9) exhibit 9.1% by wt however its wt% is 3.1% in fixed effect model, but here its effect is more profound as it has largest CI among the studies and this affect the mean effect of the final result especially when it overlaps with two studies (8 and 3) and to some extent with (1 and 4). All these factors make the mean effect to shift toward study (9). In addition, the overlapping of the studies (1,4,5,6 and 7) potentiate the mean effect value around its magnitude ,that is -1.08 with CI (-1.94;-0.21). Again study (2) didn't affect the mean effect, although it exhibit good wt% and CI because there is no such studies potentiate its effect. Heterogeneity of 89.2% in term of I^2 can be considered high enough because the presence of sufficient variances between the nine studies as well as within the studies themselves. This result is consistent with the result of (Robert E, 2012) who stated that presence of inverse relationship between fiber intake and HbA1c%. Overall P- values was 0.0001 in fixed effect model and 0.0144 in random effect model making the two models are valid as the two values are less 0.1.

7. CONCLUSION

Evidence that based on nutrition principles and recommendations to treat diabetes mellitus and its problems has been established in many countries. It is obvious that there is a vital role of particular food products with a desirable chemical structure used for diabetes mellitus treatment and its related consequences. The specialized nutritional foods should encounter the physiological body nutrition and energy, and exhibit preventive and therapeutic bioactivities to return to normal and reduce abnormalities of body metabolism. In general, an intervention with supplementation of dietary fiber for type 2 diabetes can reduce FBG by 0.91 mmol/L according to the fixed effect model and by 1.17 mmol/L according to the random effect model and HbA1c by 1.03% according to the fixed effect model and 1.08% according to the random effect model.

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9. CURRICULUM VITAE

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Puplications (if avialable)

Awards (if avialable)