ISSN- 0975-1491 Vol 3, Suppl 4, 2011

Review Article

A BRIEF OVERVIEW OF DIABETES

MURUGESH SHIVASHANKAR.*DHANDAYUTHAPANI MANI

Pharmaceutical Chemistry division, VIT University, Vellore-14, Tamilnadu India, *Assistant Professor (senior), Pharmaceutical Chemistry division, VIT University, Vellore-14 Tamil nadu.India. Email: mshivashankar@vit.ac.in

Received: 11 May 2011, Revised and Accepted: 13 June 2011

ABSTRACT

In this modern world science improved a lot, but still now most of the people lack awareness about diabetes. Due to life style and food habit changes are the major cause for the diabetes diabetes is the term roughly translate as excessive sweet urine. There are three types of diabetes type 1 type 2 and gestational diabetes. Main causes include lack of physical work, obesity, and life style modification. Symptoms of diabetes are polydipsia and polyuria etc.prevalence of diabetes shows that India will be in first rank in the diabetic population in 2030. many medications are used for controlling diabetes like allopathy, ayurveda etc.In allopathic medicines,the drugs like metformin, glibenclamide etc. are plays a major role meanwhile, In ayurveda, the plants like neem, bitter guard, bael fruit, etc. are also helps to control. One of the best way is to control the diabetes is to increase physical work, avoid of consuming junk foods. Moreover people should consume ragi and other low carbohydrate content foods will help to maintain the diet and prevent from diabetes.

Keywords: Diabetes, WHO, Mortality, Morbidity, Prevalence, Allopathy, Ayurveda.

INTRODUCTION

Diabetes is a life long disorder, which is markedly affected by day to day variations in diet, exercise, infection and stress. These factors have to be addressed on daily basis while managing diabetes and the patient is the person best equipped to deal with the situation. Hence, a thorough knowledge of the disease and how it alters normal body functions and the awareness of its acute and chronic complications is necessary .it enables the diabetic patient to take better care of him or herself. Awareness of diabetes, its complications and better health care has proved to improve the long term outlook of this disease. The management of diabetes is intimately linked to food therefore; knowledge about food and nutrition and the scientific base of biochemistry, physiology, and pathogenesis go a long way towards the understanding and dealing with the disorder ¹.

Diabetes is major cause of morbidity ^{2.} And mortality world wide ^{3.} The word diabetes is from the Greek *diabanein* which means to pass through, in reference to the excessive urine produced as a symptom of these diseases. And the term *diabetes*, without qualification, usually refers to diabetes mellitus, which roughly translates to excessive sweet urine (known as "glycosuria").

Several rare conditions are also named diabetes. The most common of these is diabetes insipidus in which large amounts of urine are produced (polyuria), which is not sweet (insipidus meaning "without taste" in Latin) Diabetes mellitus appears to have been a death sentence in the ancient era. Hippocrates makes no mention of it, which may indicate that he felt the disease was incurable. Aretaeus did attempt to treat it but could not give a good prognosis; he commented that "life (with diabetes) is short, disgusting and painful"⁴.

Sushruta (6th century BCE) identified diabetes and classified it as *Medhumeha* ^{5.} He further identified it with obesity and sedentary lifestyle, advising exercises to help "cure" it. The ancient Indians tested for diabetes by observing whether ants were attracted to a person's urine, and called the ailment "sweet urine disease" (Madhumeha).

Types of Diabetes

Majorly diabetes can be classified into three broad classification, they are type 1, type 2, and 3, gestational diabetes.

Type1 diabetes mellitus is characterized by loss of the insulinproducing beta cells of the islets of Langerhans in the pancreas leading to insulin deficiency. This type of diabetes can be further classified as immune-mediated or idiopathic. The majority of type 1 diabetes is of the immune-mediated nature, where beta cell loss is a T-cell mediated autoimmune attack 6 .

There is no known preventive measure against type 1 diabetes. Most affected people are otherwise healthy and of a healthy weight when onset occurs. Sensitivity and responsiveness to insulin are usually normal, especially in the early stages. It was traditionally termed "juvenile diabetes" because it represents a majority of the diabetes cases in children

It is formerly non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes .it is a metabolic disorder that is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency ⁷. Diabetes is often initially managed by increasing exercise and dietary modification. As the condition progresses, medications may be needed. Unlike type 1 diabetes, there is very little tendency toward ketoacidosis⁸ though it is not unheard of One effect that can occur is nonketonic hyperglycemia. Long-term complications from high blood sugar can include increased risk of heart attacks, strokes, amputation, and kidney failure.

In other words, it is a non-autoimmune, complex, heterogeneous and polygenic metabolic disease condition in which the body fails to produce enough insulin, characterized by abnormal glucose homeostasis. Its pathogenesis appears to involve complex interactions between genetic and environmental factors^{9.} It occurs when impaired insulin effectiveness is accompanied by the failure to produce sufficient ß-cell insulin ^{10.}

Gestational diabetes is one of the diabetes mellitus conditions which occur in a non-diabetic pregnancy woman. This condition usually develops near the end of the 3rd trimester or the beginning of the 4th trimester. This condition usually returns to normal soon after delivery. It affects the way the body uses glucose. Glucose is used by the cells in the body for fuel for growth and energy. Abnormal glucose levels while pregnant can be extremely harmful to both the mother and the baby ¹¹.

A 2008 study completed in the U.S. found that the number of American women entering pregnancy with preexisting diabetes is increasing. In fact the rate of diabetes in expectant mothers has more than doubled in the past 6 years 12 .

Latent autoimmune diabetes of adults (LADA) is a condition in which Type 1 diabetes develops in adults. Adults with LADA are frequently initially misdiagnosed as having Type 2 diabetes, based on age rather than etiology.

Pre-diabetes indicates a condition that occurs when a person's blood glucose levels are higher than normal but not high enough for a diagnosis of type 2 diabetes. Many people destined to develop type 2 diabetes spend many years in a state of pre-diabetes which has been termed "America's largest healthcare epidemic" 13.

Causes of Diabetes

Diabetes having so many causes they are, In type 1 diabetes is also partly inherited and then triggered by certain infections, with some evidence pointing at Coxsackie B4 virus. There is a genetic element in individual susceptibility to some of these triggers which has been traced to particular HLA genotypes these are the genetic "self" identifiers relied upon by the immune system.

In case of type 2 diabetes, it is due to a combination of lifestyle 14 . And genetic factors 15 .the other causes include age, obesity, food habit modification, etc.

Several Numbers of changes in life and food habit modifications¹⁶ is happened among the people in the name of modern trend and fashion. In one study, those who had high levels of physical activity, a healthy diet, did not smoke, and consumed alcohol in moderation had an 82% lower rate of diabetes. When a normal weight was included the rate was 89% lower. In this study a healthy diet was defined as one high in

fiber, with a high polyunsaturated to saturated fat ratio, and a lower mean glycemic index. ¹⁷.

The other major risk factor is obesity .it has been found to contribute to approximately 55% of cases of type 2 diabetes, ^{18.}

The association between increasing body mass index (BMI) and greater weight gain and risk of diabetes is most pronounced among Asians, suggesting that lower cut off BMI values are needed to identify Asians at a higher risk of diabetes¹⁹. BMI cut point for Indians for any cardio-metabolic risk factors is 23 kg/min both sexes, whereas that of waist circumference (WC) is. 87cm for men and 82cm for women ²⁰ in case of abdominal adiposity, there is also a probable indication that there is a preferential abdominal adiposity in Indians irrespective of the degree of general adiposity ²¹.

Now a days the working pattern of people are also changed ,the work patterns from labour to sedentary, the increase in computerization and mechanization, and improved transport are just a few of the changes that have had an impact on human metabolism in recent days the increased rate of childhood obesity in between the 1960s and 2000s is believed to have led to the increase in type 2 diabetes in children and adolescents ²² some other causes like Genes significantly associated with developing type 2 diabetes, include TCF7L2, PPARG, FTO, KCNJ11, NOTCH2, WFS1, CDKAL1, IGF2BP2, SLC30A8²³, JAZF1, and HHEX²⁴ Monogenic forms, e.g., MODY, constitute 1–5 % of all cases ²⁵.

The other major causes for diabetes are represented in the following table $^{\rm 26}$

Table 1: Other causes of diabetes

Genet	ic defects of β-cell Function	•	Endocrinopathies
0	Maturity onset diabetes of the young (MODY)	Growth hormone excess (acromegaly)	
0	Mitochondrial DNA mutations	0	Cushing syndrome
•	Genetic defects in insulin processing or insulin action	0	Hyperthyroidism
0	Defects in proinsulin conversion	0	Pheochromocytoma
0	Insulin gene mutations	0	Glucagonoma
0	Insulin receptor mutations	•	Infections
•	Exocrine Pancreatic Defects	0	Cytomegalovirus infection
0	Chronic pancreatitis	0	Coxsackievirus B
0	Pancreatectomy	•	Drugs
0	Pancreatic neoplasia	0	Glucocorticoids
0	Cystic fibrosis	0	Thyroid hormone
0	Hemochromatosis	0	β-adrenergic agonists
0	Fibrocalculous pancreatonathy		

Signs and Symptoms

The classical symptoms of diabetes are polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger) 27 . Symptoms may develop rapidly (weeks or months) in type 1 diabetes while in type 2 diabetes they usually develop much more slowly and may be subtle or absent.

Prolonged high blood glucose causes glucose absorption, which leads to changes in the shape of the lenses of the eyes, resulting in vision changes; sustained sensible glucose control usually returns the lens to its original shape. Blurred vision is a common complaint leading to a diabetes diagnosis; type 1 should always be suspected in cases of rapid vision change, whereas with type 2 changes are generally more gradual, but should still be suspected.

In type 1 diabetes the people usually may also present with diabetic ketoacidosis, a state of metabolic dysregulation characterized by the smell of acetone; a rapid, deep breathing known as Kussmaul breathing, nausea, vomiting and abdominal pain; and an altered states

of consciousness. A rarer but equally severe possibility is hyperosmolar nonketotic state, which is more common in type 2 diabetes and is mainly the result of dehydration.

Often, the patient has been drinking extreme amounts of sugarcontaining drinks, leading to a vicious circle in regard to the water loss. A number of skin rashes can occur in diabetes that is collectively known as diabetic dermadromes.

Diagnosi

The World Health Organization definition of diabetes is for a single raised glucose reading with symptoms otherwise raised values on two occasions, of either: ^{28.}

- Fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl) Or
- With a glucose tolerance test, two hours after the oral dose a plasma glucose ≥ 11.1 mmol/l (200 mg/dl)

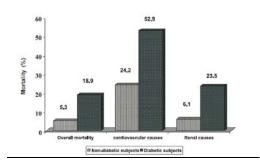
Table 2: WHO diabetes criteria

2006 WHO Diabetes criteria ^{29.}				
Condition	2 hour glucose	Fasting glucose		
	mmol/l(mg/dl)	mmol/l(mg/dl)		
Normal	<7.8 (<140)	<6.1 (<110)		
Impaired fasting glycaemia	<7.8 (<140)	≥ 6.1(≥110) & <7.0(<126)		
Impaired glucose tolerance	≥7.8 (≥140)	<7.0 (<126)		
Diabetes mellitus	≥11.1 (≥200)	≥7.0 (≥126)		

Morbidity and Mortality of Diabetes

Global Morbidity and Mortality associated with Diabetes

It is close to four million deaths in the age group of 20-79 years in 2010. Accounting for 6.8% of global all-cause mortality in this age group in 2010 ,IDF 2006 reported >50 million diabetes people in South East Asia 30 . Approximately 7.97 million DALYs were lost because of diabetes 31 .



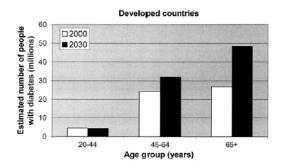
Graph 1: mortality of diabetes

Diabetes Morbidity and Mortality in India

A report says that diabetes is responsible for 109 thousand deaths in 2004.approximately 1.157 million years of life lost in 2004^{32} .nearly 2.263million disability adjusted life years (DALYs) in India during 2004^{33} .

Prevalence

The number of cases of diabetes worldwide in the year 2000 among adults was estimated to be 171 million and will rise to 366 million by $2030^{\,34}$.

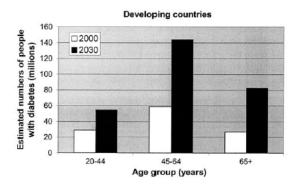


Graph 2: prevalence of diabetes in developed countries

The National Diabetes Information Clearinghouse estimates that diabetes costs \$132 billion in the United States alone every year. About 5%-10% of diabetes cases in North America are type 1 35 . The fraction of type 1 in other parts of the world differs. Most of this difference is not currently understood.

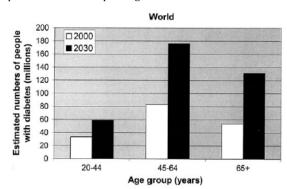
The American Diabetes Association cite the 2003 assessment of the National Center for Chronic Disease Prevention and Health Promotion (Centers for Disease Control and Prevention) that 1 in 3 Americans born after 2000 will develop diabetes in their lifetime ³⁶ · This graph shows that, a drastic change in the prevalence of diabetes in 2000 and 2030 in developed countries.

In case of developing countries, the people belongs to the age 45-64 shows a wide variation in the prevalence of diabetes at the year of 2030



Graph 3: prevalence of diabetes in developing countries

According to the American Diabetes Association, approximately 18.3% (8.6 million) of Americans age 60 and older have diabetes ^{37.} Diabetes mellitus prevalence increases with age, and the numbers of older persons with diabetes are expected to grow as the elderly population increases in number. The National Health and Nutrition Examination Survey (NHANES III) demonstrated that, in the population over 65 years old, 18% to 20% have diabetes, with 40% having either diabetes or its precursor form of impaired glucose tolerance ^{38.}



Graph 4: prevalence of diabetes in world:

India stands first in the diabetic population this table will give a clear information about the top ten countries having high diabetic population.

Table 3: top 10 countries having diabetes population

	2000		2030	
Ranking	Country	People with diabetes (millions)	Country	People with diabetes (millions)
1	India	31.7	India	79.4
2	China	20.8	China	42.3
3	U.S.	17.7	U.S.	30.3
4	Indonesia	8.4	Indonesia	21.3
5	Japan	6.8	Pakistan	13.9
6	Pakistan	5.2	Brazil	11.3
7	Russian Federation	4.6	Bangladesh	11.1
8	Brazil	4.6	Japan	8.9
9	Italy	4.3	Philippines	7.8
10	Bangladesh	3.2	Egypt	6.7

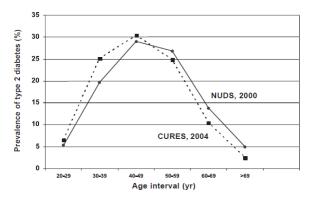
Regarding with the prevalence of type 2 diabetes, CURES has demonstrated that the awareness about diabetes in urban areas is extremely low ³⁹, nearly 25% of the residents, moreover even among the diabetic subjects, the knowledge and awareness about complications was poor and less than 505 knew that diabetes in preventable. This graph shows that the prevalence of diabetes is high in between the age group of 40-49.

Table 4: Indian diabetes risk score

Table. Indian Diabetes Risk Score (IDRS	5)	
Particulars		
Age (yr):		
< 35 (reference) 35-49	0 20	
>50	30	
Abdominal obesity:		
Waist <80 cm (female), <90 (male) (reference)	0	
Waist \geq 80-89 cm (female), \geq 90-99 cm (male)	10	
Waist ≥90 cm (female), ≥100 cm (male)	20	
Physical activity:		
Vigorous exercise or strenuous (manual)		
labour at home/work	0	
Mild to moderate exercise or mild to		
moderate physical activity at home/work	20	
No exercise and sedentary activities		
at home/work	30	
Family history:		
No family history (reference)	0	
Either parent		
Both parents		
Minimum score	0	
Maximum score	100	

Interpretation: Score < 30 low risk, score 30-50 medium risk and score > 60 high risk for type 2 diabetes and cardiovascular diseases

This score card provides the score and the diabetic parameters, which clearly helps to know about the risk factor of diabetes regarding with the scores. it also helps to predict the cardio vascular diseases among the persons by the scores.



Graph 5: prevalence of type 2 diabetes

Treatment

Type 1 treatments usually include combinations of regular or NPH insulin, and/or synthetic insulin analogs. And for the treatment of type2 diabetes mainly people are preferred oral medications the oral drugs⁴⁰, classes include sulfonylureas, biguanides, Alpha-glycosidase inhibitors, Thiazolidinediones, Meglitinides

Sulfonylureas 41

Drugs

Tolbutamide, chlorpropamide these are the drugs in the first generation. In second generation drugs like glibenclimide, glipizide, gliclazide, glimepiride etc

Side Effects

- low blood sugar,
- an upset stomach ,
- skin rash or itching,
- Weight gain.

Biguanides 42

Drugs

Metformin

Side Effects

- Abdominal pain
- Nausea
- Metallic taste
- Mild diarrhea
- Anorexia

Alpha- glycosidase inhibitors43

Drugs

Acarbose and miglitol

SideEffects

may cause stomach problems such as gas, bloating and diarrhea

Thiazolidinediones 44.

Drugs

Pioglitazone and troglitazone

Side Effects

- Plasma volume expansion
- Edema
- · Weight gain
- Headache

- Myalgia
- · Mild anemia

Meglitinides 45.

Drugs

Repaglinide and nateglinide

Side Effects

- Weight gain
- · Low blood sugar

Plants Used in the Treatment of Diabetes

Plants playa a major role in controlling diabetes from early times compare to allopathic medications it is not showing any side effects so recent days the people are returning to natural medications .some of the plants used in the treatment are:

Aegle marmelos Corr (baelfruit) 46, Azardirachta indica Ajuss (neem tree)47, Emblica officinalis S Gaertn (gooseberry)48, Mimosa pudica Linn(touch me not plant)⁴⁹, Momordica charanti Linn(bitter guard)⁵⁰, Jatropha curcas Linn(bio diesel plant) 51, Acacia catechu W&A(Leguminosae)⁵², ,Aerva lanata Juss (Amarantaceae)⁵³,Alpinia Rosc(zingiberaceae)54,Benincasa calcarata hispida Thunb(Cucurbitaceae)55, Capsicum annum Linn (Solanaceae)56,Cedrus Roxb(Coniferae)57, deodara Coccinia indica W&A(Cucurbitaceae)⁵⁸,Eugenia jambolana Lam(Myrtaceae)59,Ficus gibosa BI (Moraceae)60, Ficus glomerata Roxb (Moraceae)61, Helicteres Linn (Sterculiaceae)62, Holostemma annulare K.Schum(Asclepiadaceae)63,Plumbago rosea Linn(Plumbaginaceae)^{64,}Rubia cordifolia Linn(Rubiaceae)^{65,} Salacia oblonga Wall (Hippocrateaceae)66, Saraca indica Linn(Leguminosae)67, Stroblanthus hyneanus Nees (Acanthaceae)68, Tinospora cordifolia Miers (Menispermaceae)^{69,} Tragia involucrate Linn (Euphorbiaceae)^{70,} Tribulus terrestris Linn (Zygophyllaceae)71, etc.these are the plants having the activity of controlling the diabetes.

Management of Diabetes

It is a chronic disease which is difficult to cure. Management concentrates on keeping blood sugar levels as close to normal ("euglycemia") as possible without presenting undue patient danger. This can usually be with close dietary management, exercise, and use of appropriate medications (insulin only in the case of type 1 diabetes mellitus. Oral medications may be used in the case of type 2 diabetes, as well as insulin). Patient education, understanding, and participation is vital since the complications of diabetes are far less common and less severe in people who have well-managed blood sugar level 72. Wider health problems may accelerate the deleterious effects of diabetes. These include smoking, elevated cholesterol levels, obesity, high blood pressure, and lack of regular exercise 73.

CONCLUSION

India is considering as a diabetes capital of the world. In recent days most of the youths are affected by diabetes because lack of physical work. In the name of modernization all the daily activities are carried by the machines to make the work easy, but it makes the life difficult to managing the diabetes. Low calorie food items like ragi etc., are eradicated by the pizza and burger it paves a way to obesity. Atlast due to the life style modification, it gives diabetes as a gift to the people so, increasing the physical work and maintaining the proper diet will help to control the diabetes and also a best way to prevent.

REFERENCE

- Rita Malik and T.K.Malik winning over diabetes, Ane books India, third edition, pg 6
- G. Roglic, N. Unwin, P.H. Bennett, C. Mathers, J. Tuomilehto S. Nag, et al., The burden of mortality attributable to diabetes: realistic estimates for the year 2000, Diabetes Care 28 (2005) 2130–2135.

- N.J. Morrish, S.L. Wang, L.K. Stevens, J.H. Fuller, H. Keen Mortality and causes of death in the WHO Multinational study of vascular disease in diabetes, Diabetologia 44 (2001) S14–S21.
- Medvei, Victor Cornelius (1993). The history of clinical endocrinology. Cornforth, Lancs. U.K: Parthenon Pub. Group. pp. 23–34.
- Dwivedi, Girish & Dwivedi, Shridhar (2007). History of Medicine: Sushruta – the Clinician – Teacher par Excellence. National Informatics Centre (Government of India).
- Rother KI (April 2007). "Diabetes treatment—bridging the divide". The New England Journal of Medicine 356 (15): 1499– 501.
- Kumar, Vinay; Fausto, Nelson; Abbas, Abul K.; Cotran, Ramzi S.; Robbins, Stanley L. (2005). Robbins and Cotran Pathologic Basis of Disease (7th Ed.). Philadelphia, Pa.: Saunders. pp. 1194–1195.
- 8. Fasanmade, OA; Odeniyi, IA, Ogbera, AO. "Diabetic ketoacidosis: diagnosis and management." African journal of medicine and medical sciences 37 (2): 99-105.
- Gupta V, Khadgawat R, Saraswathy KN, Sachdeva MP and Kalla AK. Emergence of TCF7L2 as a Most Promising Gene in Predisposition of Diabetes Type II. Int J Hum Genet, 2008, 8(1-2): 199-215.
- 10. Permutt MA, Wasson J, Cox N. Genetic Epidemiology of Diabetes. Journal of clinical Investigation 2005, 115:1431–1439.
- 11. http://diabetes.co.in/gestational-diabetes.
- 12. Lawrence JM, Contreras R, Chen W, Sacks DA. "Trends in the prevalence of preexisting diabetes and gestational diabetes mellitus among a racially/ethnically diverse population of pregnant women, 1999–2005". Diabetes Care 31 (5): 899–904.
- Handelsman Yehuda, MD. "A Doctor's Diagnosis: Prediabetes". Power of Prevention 1 (2): 2009.
- 14. Risérus U, Willett WC, Hu FB. "Dietary fats and prevention of type 2 diabetes". Progress in Lipid Research 48 (1): 44–51.
- 15. Ripsin CM, Kang H, Urban RJ. "Management of blood glucose in type 2 diabetes mellitus". Am Fam Physician 79 (1): 29–36.
- Tri Murti et.al. The association of diabetes- related factor and quality of life in type 2 diabetes, IJPPS, vol 2 issue1, 2010.
- Mozaffarian D, Kamineni A, Carnethon M, Djoussé L, Mukamal KJ, Siscovic, D. "Lifestyle risk factors and new-onset diabetes mellitus in older adults: the cardiovascular health study". Archives of Internal Medicine 169 (8): 798–807.
- Centers for Disease Control and Prevention (CDC). "Prevalence of overweight and obesity among adults with diagnosed diabetes— United States, 1988–1994 and 1999–2002". MMWR. Morbidity and Mortality Weekly Report 53 (45): 1066–1108.
- Shai I, Jiang R, Manson JE, Stampfer MJ, Willett WC, Colditz GA, Hu FB. Ethnicity, Obesity, and Risk of Type 2 Diabetes in Women. Diabetes Care, 2006, 29:1585–1590.
- 20. Mohan V, Deepa M, Farooq S, Narayan KM, Datta M, Deepa R. Anthropometric cut points for identification of cardiometabolic risk factors in an urban Asian Indian population. Metabolism C and Experimental, 2007, 56:961–968.
- Ramachandran A, Sneha latha C, Viswanathan V. Burden of type 2 diabetes and its complications – The Indian scenario. Current Science, 2002, 83:1471–1476.
- 22. Arlan Rosenbloom, Janet H Silverstein (2003). Type 2 Diabetes in Children and Adolescents: A Clinician's Guide to Diagnosis, Epidemiology, Pathogenesis, Prevention, and Treatment. American Diabetes Association, U.S. pp. 1
- Lyssenko V, Jonsson A, Almgren P, et al. "Clinical risk factors, DNA variants, and the development of type 2 diabetes". The New England Journal of Medicine 359 (21): 2220–32.
- McCarthy, M. I. Feero, W. G.; Guttmacher, A. E. eds. "Genomics, Type 2 Diabetes, and Obesity". The New England Journal of Medicine 363 (24): 2339–50.
- Monogenic Forms of Diabetes: Neonatal Diabetes Mellitus and Maturity-onset Diabetes of the Young". National Diabetes Information Clearinghouse (NDIC) (National Institute of Diabetes and Digestive and Kidney Diseases, NIH).

- Mitchell, Richard Sheppard; Kumar, Vinay; Abbas, Abul K.; Fausto, Nelson". Table number 20.5" Robbins Basic Pathology. Philadelphia: Saunders. . 8th edition.
- Cooke DW, Plotnick L. "Type 1 diabetes mellitus in pediatrics". Pediatr Rev 29 (11): 374–84;
- World Health Organization. "Definition, diagnosis and classification of diabetes mellitus and its complications: Report of a WHO Consultation. Part 1. Diagnosis and classification of diabetes mellitus". http://www.who.int/diabetes/publications/en
- "Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia" (PDF). World Health Organization www.who.int.2006. http://www.who.int/diabetes/publications/Definition%20and% 20diagnosis%20of%20diabetes_new.pdf.
- International Diabetes Federation. Diabetes Atlas. 3rd ed. 2006. Brussels, Belgium:
- 31. Interna tional Diabetes Federation Jönsson B. The economic impact of diabetes. Diabetes Care. 1998 Dec; 21 Suppl 3:C7-10.
- Venkataraman K, Kannan AT, Mohan V. Challenges in diabetes management with particular reference to India. International Journal of Diabetes in developing Countries, 2009, 29:103–109
- ICMR. Assessment of Burden of NCDs. Indian Council of Medical Research, 2006.
- Wild S, Roiglic G, Grren A, Sicree R, King H. Global Prevalence of Diabetes. Diabetes Care, 2009 27:1047–1053.
- Narayan KM, Boyle JP, Thompson TJ, Sorensen SW, Williamson DF (October 2003). "Lifetime risk for diabetes mellitus in the United States". JAMA 290 (14): 1884–90.
- 36. American Diabetes Association (2005). "Total Prevalence of Diabetes & Pre-diabetes". http://web.archive.org/web/20060208032127/http://www.diabetes.org/diabetes-statistics/prevalence.jsp...
- "Seniors and Diabetes". Elderly and Diabetes-Diabetes and seniors. LifeMed Media. 2006. http://www.dlife.com/dLife/do/ShowContent/daily_living/seniors/.
- 38. Australian Institute for Health and Welfare. "Diabetes, an overview".

 http://web.archive.org/web/20080617222036/http://www.aih w.gov.au/indigenous/health/diabetes.cfm.
- 39. Mohan D,Raj D ,Shanthirani CS ,Datta M, Unwin NC,Kapur A , et.al.Awareness and knowledge of diabetes in Chennai- the (CURES-9). J Assoc Physicians India 2005; **53:283**-87
- Rana Ibrahim, Diabetes mellitus type 2: review of oral treatment options, IJPPS Vol 2, supp, 2010
- 41. UK prospective diabetes study group: intensive blood glucose control with sulfonylurea or insulin compared with conventional regimen and risk of complications in patients with type 2 diabetes (UKPDS 33) lancet 352:837-853, 1998.
- diabetes prevention program (DPP) research group: reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin.N Engl J med 346:393-403, 2002.
- Chaisson JL et al. acarbose treatment and risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance: the stop-NIDDM trial, JAMA 290:486, 2003.
- KD Tripathi, essential of medical pharmacology, jaypee brother's medical publishers (p) ltd sixth edition, 269.
- 45. www.ndep.nih.gov.
- 46. Leticia VCL,Muhmud THK,Arjumand A,Diego VW,Paula CJ,Claudia P,Maria EAM and Manoel OM,studies on the anticancer potential of plants used in Bangladeshi folk medicine, J Ethanopharmacol,19(2005)21.
- Devakumar C and mukerjee SK, chemistry of neem bitter principles, IARI res bull, 40(1983)1.
- Ishaq GM, Zia ul Arifeen S, Ahmed BD, Mainuddin G,Ahmad AK and Devi K, hypotensive potential of aqueous extract of *Emblica* officinalis on anaesthetized dogs, JK pract, 12(4)(2005)213.

- Mukherjee J and Biswas S, Purification and characterization of a nucleoside triphosphatase from *Mimosa pudica*, Indian J biochem&biophy 17 (1980)452.
- 50. Leatherdale BA,PanesarPK,Singh G,Atkins TW,Bailey CJ,and Biqnell AH, improvement in glucose tolerance due to *momordica charantia*, Br Med J,**282**,(6279)(1981)1823.
- 51. Majumdar AM, Upadhye AS, and Misar AV, studies on antidiarrhoel activity of *Jatropha curcas* root extract in albino mice, J Ethnopharmocol, **70**(2)(2000)183.
- 52. Deshpande VH& Patil AD, Flavonoids of *Acacia catechu* heart wood, Indian J chem., **20** B (1981)628.
- Vetrichelvan T& Jegadeesan M ant diabetic activity of alcoholic extract of *Aerva lanata* (L) in rats, J.Ethanopharmacol, 80(2-3) (2002)103.
- Kong LY, Qin MJ and Niwa M, New catatoxic bis-labdanic diterpenoids from Alpinia calcarata, Plant Med, 68(9) (2002)813.
- Grover JK, Adiqa G, Vats V & Rathi SS, Extracts of Benincasa hispida prevent development of experimental ulcers, J Ethanopharmacol, 78(2-3)(2001)159.
- Duke J, CRC Handbook of Medicinal Herbs, (Boca Raton, CRC Press, USA), (1985)
- 57. Gilman EF & Watson DG, Cedrus deodara, Fact sheet ST-134, 1993.
- 58. Mukerje DE, Effects of Coccinia indica on alloxan diabetes in rabbits, Indian J Med Sci, **7**(1953)1665.
- Schossler DRC, Mazzanti CM, da Luz SCA, Filappi A, Prestes D, da silveira AF & Cecim M, Syzygium cumini and the regeneration of insulin positive cells from the pancreatic duct. Braz J Vet Res Anim Sc, 41(4) (2004)1413.
- Musabayane CT,Bwititi PT&Ojewole JA,Effects of oral administration of some herbal extracts on food consumption and blood glucose levels in normal and streptozotocin treated diabetic rats, Exp Clin Pharmacol, 28(4)(2004)223.
- 61. Rahman NN, Khan M & Hasan R, Bioactive components from *Ficus glomerata*, Pure Appl Chem, **66**(1994)2287.
- Qu WH, Li JG&Wang MS, Chemical studies on the *Helicteres isora*, Zhongguo Yaoke Daxue Xuebao, 22(4) (1991)203.
- Gamble JS, Flora of the presidency of madras, Vol 1(Adlard&sons, London) (1935)834.
- Panichayupakaranant P & Tewtrakul S, Plumbagin production by root cultures of *Plumbago rosea*, Electronic J Biotechnol, 5 (2001)717.
- Della A Hadjichambi PD & Hadjichambis AC, An ethanobotanical survey of wild edible plants of paphos and Larnaca countryside of Cyprus, J Ethnobiol Ethnomed,2(2006)34.
- 66. Huang TH,Peng G,Li GQ,Yamahara J,Roufogatis BD &Li V, Salacia oblonga root improves postprandial hyperlipidemia & hepatic steatosis in zucker diabetic fatty rats: Activation of PPAR-α,Toxicol Appl Pharmacol,210(3)(2006)225.
- 67. Ray S &Chatterjee BP, Saracin: a lectin from *Saraca indica* seed integument recognizes complex carbohydrates, Phytochemistry, 40(3) (1995)325.
- Singh SS,Pandey SC,Srivastava S, Gupta VS,Patro B& Ghosh AC, Chemistry and medicinal properties of *Tinospora cordifolia*, Indian | Pharmacol,35(2003)83.
- 69. Dhara AK,Pal S &Nag chaudri AK, Psychopharmacological studies on *Tragia involucrate* root extract, Phytother Res .16(4)(2002)326.
- Amin A ,Lotfy M, Shafiullah M & Adeghate E, The protective effect of *Tribulus terrestris* in diabetes, Ann Acad Sci, 1084(2006)391.
- 71. Gamble JS, Flora of the presidency of madras, **Vol 2**(Adlard&sons, London) (1935)1033.
- Nathan DM, Cleary PA, Backlund JY, et al. "Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes". The New England Journal of Medicine 353 (25): 2643–53
- 73. "The effect of intensive diabetes therapy on the development and progression of neuropathy. The Diabetes Control and Complications Trial Research Group". Annals of Internal Medicine 122 (8): 561–8. April 1995.