MATURITY ONSET DIABETES OF THE YOUNG (MODY) GUIDE

MATURITY ONSET DIABETES OF THE YOUNG (MODY)

Maturity Onset Diabetes of the Young (MODY) is the monogenic form of heterogeneity autosomal dominant disorder caused due to mutations in gene variations which results in beta cell dysfunction occurs below 35 years of age.

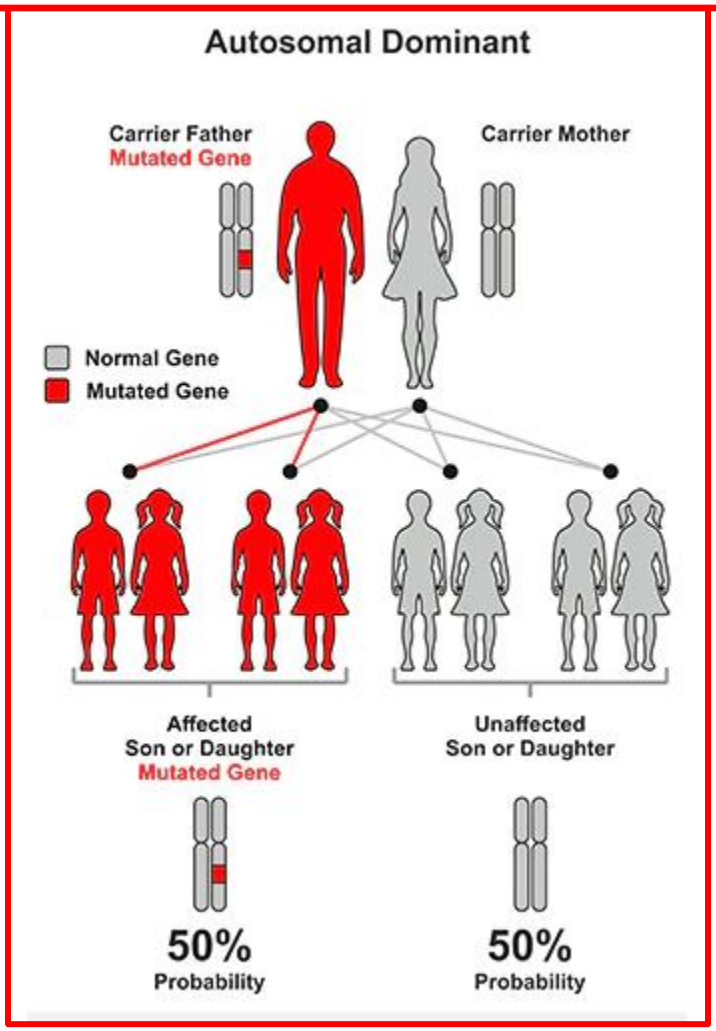
Found by Fajans and Conn in the year 1950 at the University of Michigan.

In 1973 Fajan and Tattersall differentiated this diabetes from type 1 diabetes and finally 1974 they named it as 'fasting hyperglycaemia diagnosed under age 25 which could be treated without insulin for more than two years.

Maturity Onset Diabetes of the Young (MODY) is rarely prevalent as 1%–2% of all diabetes.

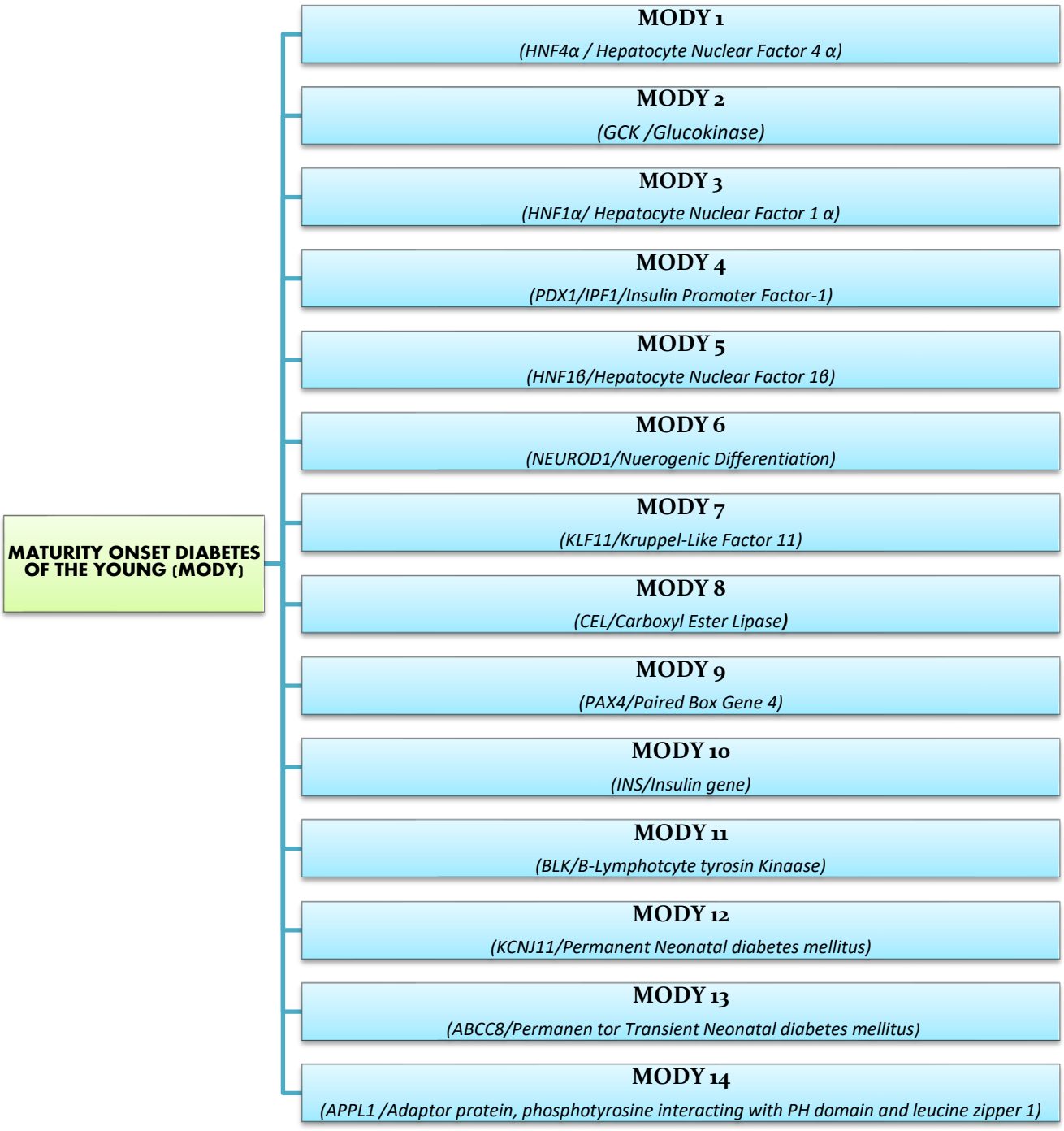
It is often misdiagnosed or undiagnosed.

Travel of Maturity Onset Diabetes of the Young (MODY) in the family



(National Institute of Diabetes and Digestive and Kidney Diseases Health Information Center (NIDDK), 2017)

TYPES OF MATURITY ONSET DIABETES OF THE YOUNG (MODY)



PREVALENCE RATE, PATHOPHYSIOLOGY, CLINICAL CHARACTERISTICS AND TREATMENT OF MATURITY ONSET DIABETES OF THE YOUNG (MODY)

THESE TABLES SHOULD BE POPPED IN THE PREVIOUS TYPES OF MODY SCREEN

MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 1	HNF4α *(Hepatocyte Nuclear Factor 4 α)*	5%-10% Adolescent/ early adult	β-Cell dysfunction	Birth weight less than 800g above normal, Neonatal diabetes, hyperinsulinemic hypoglycemia during infancy, low triglycerides	Sensitive to sulfonylurea

TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 2	GCK *(Glucokinase)*	30%-50% Since birth	Glucose sensing defect	Stable mild fasting glucose	No medication, Diet

MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 3	HNF1α *(Hepatocyte Nuclear Factor 1 α)*	30-65% Adolescent/ early adult	β-Cell dysfunction	Glycosuria	Sensitive to sulfonylurea

MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 4	*PDX1/IPF1 (Insulin Promoter Factor-1)*	1% Early adult	β-Cell dysfunction	Homozygote: permanent neonatal diabetes, pancreas agenesis	Diet or Oral Anti Diabetic Diet or insulin

MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 5	*HNF1β (Hepatocyte Nuclear Factor 1β)*	<5% Adolescent	β-Cell dysfunction	Renal malformations, genito-urinary tract anomalies, pancreatic hypoplasia, low birth weight	Insulin

MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 6	*NEUROD1 (Neurogenic Differentiation)*	<1% Early adult	β-Cell dysfunction	Neonatal diabetes, child or adult-onset diabetes neurological abnormalities.	Oral Anti Diabetic Diet or insulin

MODY TYPES	MODY gene	Prevalence of MODY	Pathophysiology	Other Characteristics/Symptoms	Possible treatment

		(in percent)			
MODY 7	*KLF11 (Kruppel-Like Factor 11)*	<1% Early adult	β-Cell dysfunction	Similar to type 2 diabetes	Oral Anti Diabetic Diet or insulin

MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 8	*CEL (Bile salt dependent lipase-Carboxyl Ester Lipase)*	<1% Early adult	Pancreas endocrine and exocrine dysfunction	Exocrine dysfunction, lipomatosis	Oral Anti Diabetic Diet or insulin

MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 9	*PAX4 (Paired Box Gene 4)*	<1% Early adult	β-Cell dysfunction	Ketoacidosis-prone	Diet or Oral Anti Diabetic Diet or insulin

MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 10	*INS (Insulin gene)*	<1% Early adult	Insulin gene mutation	Neonatal diabetes, child or adult-onset diabetes	Oral Anti Diabetic Diet or insulin

MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 11	BLK *(B-Lymphocyte Kinase)*	<1% Early adult	Insulin secretion defect	Overweight, relative insulin secretion failure	Diet or Oral Anti Diabetic Diet or insulin

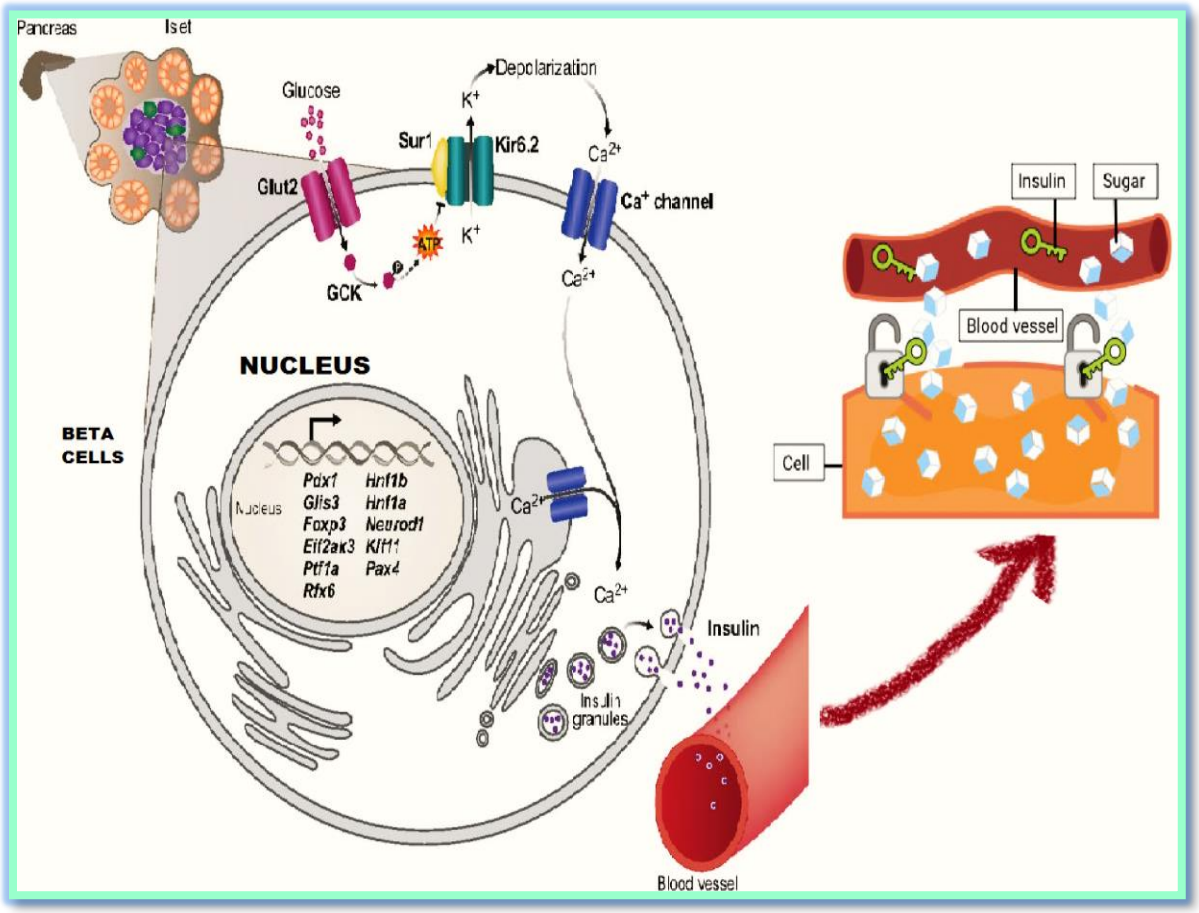
MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 12	KCNJ11 *(Potassium inwardly rectifying Channel subfamily J member 11)*	<1% Early adult	ATP-sensitive potassium channel dysfunction	Homozygote: neonatal diabetes	Oral Anti Diabetic Diet or insulin

MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 13	*ABCC8 (ATP-Binding Cassette transporter sub-family C member 8)*	<1% Early adult	ATP-sensitive potassium channel dysfunction	Homozygote: permanent neonatal diabetes, Heterozygote: transient neonatal diabetes	Oral Anti Diabetic Diet (sulfonylurea)

MODY TYPES	MODY gene	Prevalence of MODY (in percent)	Pathophysiology	Other Characteristics/Symptoms	Possible treatment
MODY 14	*APPL1 (Adaptor protein, phosphotyrosine interacting with PH domain and leucine zipper 1)*	<1% Early adult	Insulin secretion defect	Child or adult-onset diabetes	Diet or Oral Anti Diabetic Diet or insulin

CAUSES OF INCREASE IN BLOOD GLUCOSE LEVEL IN MATURITY ONSET DIABETES OF THE YOUNG (YOUNG)

Normal insulin production and glucose absorption



The genes [HNF4α (Hepatocyte Nuclear Factor 4 α), GCK (Glucokinase), HNF1α (Hepatocyte Nuclear Factor 1 α), PDX1/IPF1 (Insulin Promoter Factor-1), HNF1β (Hepatocyte Nuclear Factor 1β), NEUROD1 (Neurogenic Differentiation), KLF11 (Kruppel-Like Factor 11), CEL (Bile salt dependent lipase-Carboxyl Ester Lipase), PAX4 (Paired Box Gene 4), INS (Insulin gene), BLK (B-Lymphocyte Kinase), KCNJ11 (Potssium inwardly rectifying Channel subfamily J member 11), ABCC8 (ATP-Binding Cassette transporter sub-family C member 8), APPL1 (Adaptor protein, phosphotyrosine interacting with PH domain and leucine zipper 1)] involved in the production of insulin got mutated and it causes Maturity Onset Diabetes of the Young (MODY).

CREATE VIDEO FOR THIS PAGE

WAYS TO FIND MATURITY ONSET DIABETES OF THE YOUNG (MODY)

AGE

(below 35 years)

Family History

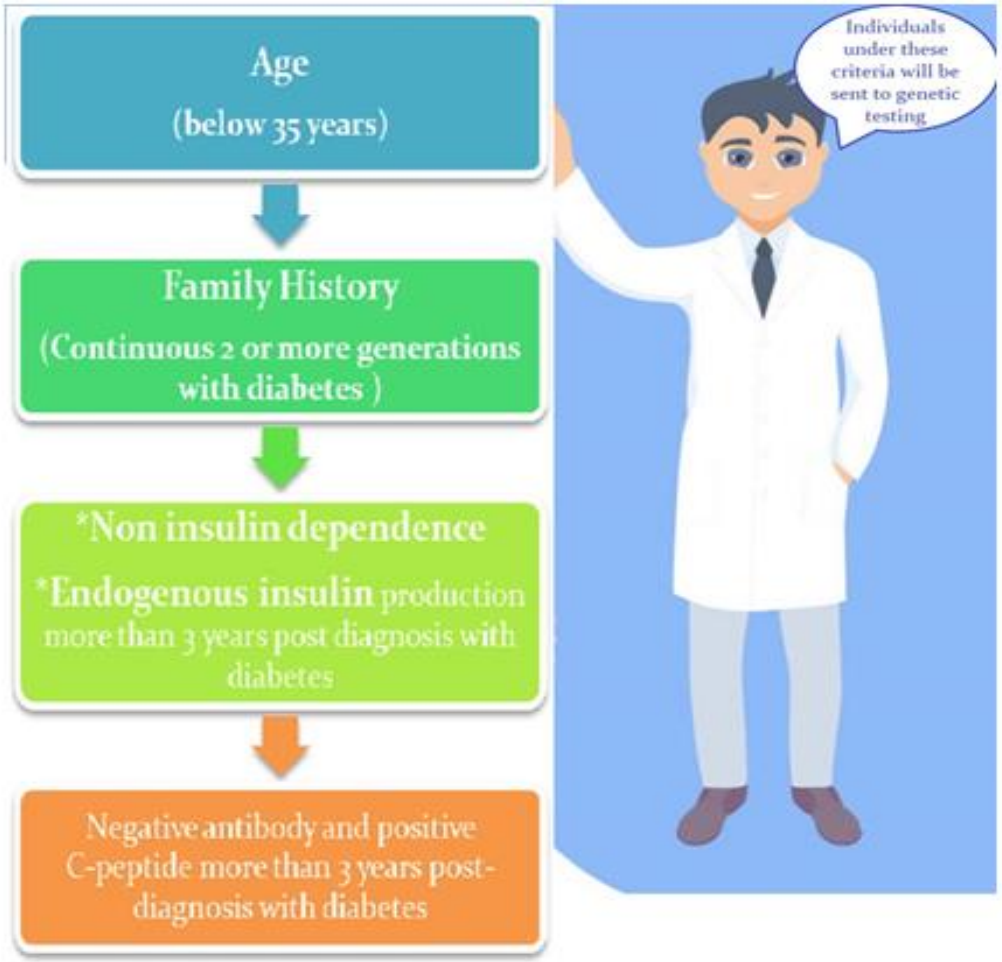
(3 Generations with diabetes)

Clinical examination and Physical examination

(Mild, stable fasting hyperglycemia,non-obese, absence of autoantibodies,normal lipid level)

Genetic Testing

GENETIC TESTING CRITERIA FOR MATURITY ONSET DIABETES OF THE YOUNG (MODY)



REASONS FOR DIAGNOSING MATURITY ONSET DIABETES OF THE YOUNG (MODY)

Stop misdiagnosing between type 1 and type 2 diabetes/Undiagnosed

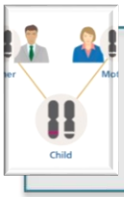
Proper treatment

(Mostly, it is treated with the cost effective sulfonyl urea tablet as a good choice)

Digging out the family members with Maturtiy Onset Diabetes of the Young(MODY)

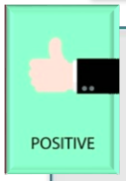
(Predictive testing)

A GUIDE TO MODY TESTING AND LIVING WELL

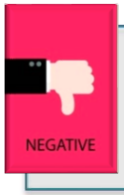


Dominant inheritance of MODY* illustrated using pictorial family tree.

Affect an individual at any stage of life with 99.3 % life risk of developing diabetes.



Presymptomic positive predictive analysis result may cause stress among individual and family , and, it also paves way to monitor blood glucose level.



Presymptomic negative predictive result may reduce the stress and diabetes screening is not necessary.

Planning future aspects like planning for insurance and suitable jobs.

Motivate the family members for predictive genetic testing.

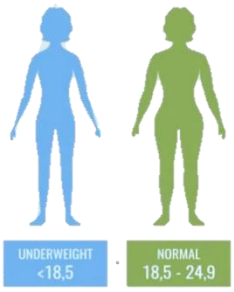
Doubts will be cleared and they will also know their status of the diabetes.

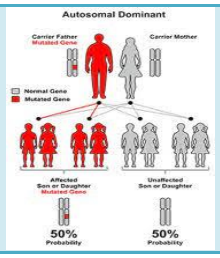
Predictive testing can be postponed but screening for diabetes will be arranged yearly.

Testing options are discussed (blood or salaiva test)

**MODY-Maturity Onset Diabetes of the Young*

DIFFERENCE OF MATURITY ONSET OF THE DIABETES OF THE YOUNG (MODY) FROM OTHER DIABETES

		Type 1	Type 2	MODY
Background Information	**Type of diabetes**	Polygenic	Polygenic	Monogenic
	Causes	Polygenic and external lifestyle factors	Polygenic and external lifestyle factors	Single genetic mutation in autosomal dominant gene
	Life stage and Age of diagnosis	Children ≤ 15 years 	Adult <40 years 	Young Adult <25 years 
Physical examination	**Body Mass Index (BMI)**	Underweight or Normal 	Overweight or Obese 	Normal and mildly overweight 
Clinical Profile 	**Symptoms & Complications**	Polyuria, polyphagia, polydipsia, tiredness, Diabetic neuropathy, diabetic nephropathy, diabetic foot, cardiac problems, ketoacidosis	Polyuria, polyphagia, polydipsia, tiredness, Diabetic neuropathy, diabetic nephropathy, diabetic foot, cardiac problems, ketoacidosis(less common),obesity	Has common diabetic symptoms and in some cases along with renal cysts, deafness, partial lipodystrophy, severe insulin resistance in absence of obesity, severe obesity with other syndromic features, lack of ketoacidosis when insulin treatment is stopped
	Glycemic conditions	Hyperglycemia	Hyperglycemia	Mild fasting hyperglycemia
	HbA1C	>6.5 percent	>6.5 percent	<7.5 percent

	Serum Insulin level (Normal value- 0.7-9µIU/mL)	Low	High	Normal
	Glutamic Acid Decarboxylase Antibodies (GADA)	Present	Absent	Absent
	Insulin Autoantibodies (IAA)	Present	Absent	Absent
	C peptide (Normal value - 0.9 to 1.8 nanograms per milliliter)	*Low levels of C-peptide*	High levels of C-peptide happens in type 2 diabetes secretes more insulin where insulin resistance condition made the insulin not to be used by the body	≥0.2 nmol/mmol
Treatment	**Tablet or insulin or Diet**	Insulin, Diet, and Exercise 	Tablet, Insulin, Diet and Exercise 	Tablet in most of the cases (especially sufonyl urea)/Insulin prescription is rare, Diet and Exercise 
Family Inheritance		<15 percent	>50 percent	50 percent

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