*International Journal of Health Sciences and Research*
*Vol.14; Issue: 1; January 2024*
*Website: www.ijhsr.org*
*Review Article* *ISSN: 2249-9571*

# Type-II-Diabetes Mellitus- Etiology, Epidemiology, Risk Factors and Diagnosis and Insight into Demography (Urban Versus Rural)

**Umesh Kumar Sharma[a,b], Meenu Pujani[a], J. Anuradha[b]**

[a] Department of Laboratory Services, Metro Heart Institute with multispecialty Faridabad, India.
[b]NIMS Institute of Allied Medical Science and Technology, NIMS university, Rajasthan, Jaipur - 303121

Corresponding Author: Umesh Kumar Sharma

**DOI: https://doi.org/10.52403/ijhsr.20240136**

## ABSTRACT

Diabetes is a chronic metabolic disorder that affects the synthesis of insulin. Two major types of diabetes are Type I and type II. Type I Diabetes results from autoimmune disease due to destruction of insulin-producing beta cells in the pancreas' islets. While, type II insulin (T2DM) is caused by insulin resistance in muscle, fat and liver cells. Insulin resistance in T2DM leads higher triglyceride biosynthesis, decreased triglyceride and increased fatty acid flux. The various risk factors associated with T2DM includes dyslipidemia, hyperglycemia and cardio vascular diseases. T2DM, a chronic non-communicable disease, affects around 463 million people worldwide suffer from this disease and by 2040, that figure is predicted to increase to 640 million. The most common types of T2DM diagnostic tests are (i) FPG (fasting plasma glucose) ≥126 mg/dl assays (ii) The OGTT, or oral glucose tolerance test 2-h plasma glucose ≥200 mg/dl (iii) HBA1C (glycated hemoglobin) ≥6.5%. Due to their sedentary lifestyles and over nutrition, urban patients typically experience higher rates of T2DM than rural ones. A healthy lifestyle that includes eating low-fat, high-fiber meals, exercising moderately to vigorously, decreasing weight, and avoiding prolonged inactivity is key to preventing T2DM. In nations like India, with the use of epidemiological data diabetes prevention initiatives can more effectively target high-risk people.

***Keywords:*** Diabetes Mellitus, dyslipidemia, hyperglycemia, insulin, triglyceride, autoimmune disease

## INTRODUCTION

Diabetes is a metabolic disorder marked by defects in insulin secretion and function of insulin, which leads to long-term harm, organ failure, and dysfunction [1]. Diabetes arises from multiple pathological mechanisms, such as insulin resistance and autoimmune death of pancreatic β-cells, which impair the metabolism of proteins, fats, and carbohydrates due to insufficient insulin. Insufficient insulin secretion or reduced tissue responses can lead to deficient insulin action. These abnormalities frequently overlap in the same patient, making it difficult to identify which one causes hyperglycemia [2, 3]. Long-term consequences from diabetes include peripheral and autonomic neuropathy, nephropathy, eyesight loss, hypertension, increased risk of cardiovascular and cerebrovascular disorders, and changes in lipoprotein metabolism [4]

Increased fatty acid flow, increased hepatic triglyceride synthesis, decreased triglyceride clearance, and disruptions to processes such as apoprotein formation and cholesteryl ester action are all consequences of insulin

resistance in T2DM [2,5]. Intracellular hormone-sensitive lipase is activated by T2DM, which raises hepatic triglyceride synthesis and production. Triglyceride removal is determined by lipoprotein lipase, which is found on the vascular endothelium. It is downregulated in insulin resistance or insufficiency, which leads to postprandial lipemia (Figure 1). [2, 5].

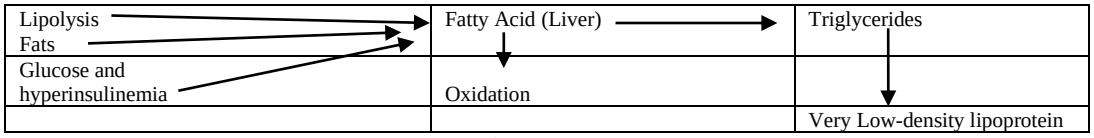


**Figure 1: Conversion of Fatty acids to triglycerides in liver**

## Etiology

Diabetes is categorized into two major types: type-I, type-II.

- **T1DM (Type I Diabetics):** It is a form of the disease known as autoimmune destruction of beta cells in the pancreas that produce insulin, leading to a complete lack of insulin. This condition is typically observed in children and teenagers. Ninety percent of cases of T1DM occur in adults and are a kind of autoimmune diabetes that results from the death of pancreatic beta cells. There is a strong genetic susceptibility to the major histocompatibility complex (MHC) and human leukocyte antigens (HLA). Because type I diabetes is caused by a complete lack of insulin secretion, it can be recognized by genetic markers and autoimmune pathologic processes. [2]
- **T2DM:** Ninety percent of cases of diabetes are caused by T2DM, a disease that results in insulin resistance. Usually, it is observed in those over the age of 45. Obesity, physical inactivity, and diets high in calories are making it more common in kids, teens, and young adults. Insulin resistance in liver, muscle, and fat cells as well as insufficient pancreatic insulin synthesis is the main causes of T2DM. Due to a combination of insufficient insulin secretory response and resistance to insulin action, T2DM can result in hyperglycemia that is asymptomatic and does not cause any clinical signs. There are two forms of Type II diabetes:

(a) Predominantly insulin resistance with relative insulin deficiency, and predominantly an insulin secretory defect with insulin resistance.

(b) Non-insulin-dependent diabetes: Ninety to ninety-five percent of people with diabetes have this type of diabetes. Commonly it is referred to as type II diabetes or adult-onset diabetes. It typically involves insulin resistance and relative deficiency, without insulin treatment. Without insulin therapy, it usually entails relative deficit and insulin resistance.

**Function of insulin in T2DM:** Insulin, a pancreatic hormone that regulates how the body uses sugar by releasing insulin when blood sugar levels fall and allowing sugar to enter cells, and releasing less insulin when blood sugar levels rise (Figure 1).

## Function of Glucose in T2DM

The main source of energy for muscle and tissue cells is glucose, a type of sugar. It enters the bloodstream through insulin after being absorbed from meals and the liver. When blood sugar levels rise in T2DM, the pancreas releases more insulin, which damages insulin-producing cells (Figure 1).

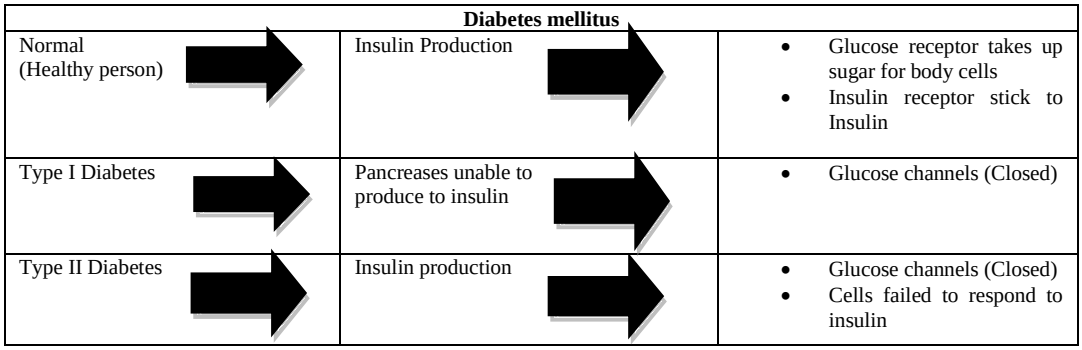


**Figure 2: Role of glucose and Insulin in Type I and Type II Diabetes.**

## Dyslipidemia-associated with T2DM

Dyslipidemia, or an aberrant lipid profile, is a significant public health concern, particularly in low-income countries like India, where patterns of hypercholesterolemia and hypertriglyceridemia have almost doubled since 2000 [6]. Research indicates that a number of variables, including age, inadequate physical activity, blood pressure, fasting glucose, BMI, dietary habits, smoking, and changes in lifestyle, are linked to the rising incidence of dyslipidemia in people with T2DM.non-communicable diseases such as cardiovascular diseases are common in developing nations, and dyslipidemia plays a major role in the development of CVD, T2DM, and atherosclerosis. It would be beneficial to assess the prevalence and pattern of dyslipidemia as well as the risk factors associated with it among patients with type II diabetes in order to help achieve the desired control of lipid parameters and to lessen the incidence, prevalence, and complications of diabetic dyslipidemia.

Dyslipidemia, which is defined as aberrant lipid profiles brought on by insulin resistance, is one the risk factor for T2DM. Atherogenic lipoprotein phenotype, another name for dyslipidaemia, is a major metabolic risk factor. it is characterized by increased triglycerides, low high density lipoprotein, and normal to slightly raised in low density lipoprotein [7,8]. T2DM is characterized by hypertriglyceridemia, decreased HDL cholesterol, and elevated LDL particles, with dyslipidemia playing a major role. Though its specific etiology is uncertain, insulin resistance is the main cause of diabetes dyslipidemia, which leads to increased free fatty acid flow. When combined with dyslipidemia, elevated HBA1C increases the risk of cardiovascular disease (CVD) in diabetics by 18% for every one percentage increase in absolute HBA1C [6].

Gender and age-specific patterns of dyslipidemia differ, and obesity and hypertension are independent risk factors. There may be a reciprocal relationship between dyslipidemia and T2DM, as glycated hemoglobin and lipid profile parameters are substantially associated in T2DM patients. In order to lessen the risk of CVD, clinicians should strive to treat hyperglycemia, hyperlipidemia, and hyperglycemia by medication and lifestyle changes. For diabetic patients, this means lowering blood pressure and cholesterol objectives. The following are risk factors for T2DM: age, gender, diabetes, hypertension, tobacco use, excessive alcohol intake, sedentary lifestyle, and poor diet. Patients with T2DM have higher cardiovascular disease risk factors due to metabolic syndromes such as dyslipidemia, hyperglycemia, and hypertension, which result in elevated blood pressure, aberrant cholesterol levels, and elevated glucose levels[6]. The frequency of dyslipidemia is rising worldwide, especially in developing

nations like Bangladesh, India, Ethiopia, Kenya, and Sri Lanka. It also considerably raises cardiovascular risk for diabetic patients, with 70–80% of them dying from cardiovascular disease [9–12].

Hyperglycemia, a metabolic disease brought on by abnormalities in either insulin secretion, insulin action, or both is characterized T2DM. The risk of T2DM is further increased by other lifestyle choices such as using tobacco, abusing alcohol, living a sedentary lifestyle, and eating an unhealthy diet that results in obesity. Chronic hyperglycemia can harm organ systems and result in potentially fatal consequences including macro- and microvascular disorders [2,13]. Obesity, hypertension and T2DM have been recognized as risk factors for dyslipidemia. There can be a mutual link between T2DM and dyslipidemia. Certain studies have demonstrated a substantial correlation between glycated hemoglobin (HBA1C) and lipid profile measures in patients with T2DM [2,13].

Many high-risk populations, such as those with T2DM, still lack a dyslipidemia diagnosis and treatment plan. The main factor causing the lipid changes associated with diabetes acid reflux due to insulin resistance is an increase in free fatty acids. The primary objective of the clinician ought to be the management of lifestyle-related dyslipidemia and hyperglycemia, as well as the mitigation of cardiovascular disease risk. Dyslipidemia is a key risk factor for cardiovascular disease, and T2DM is a metabolic illness characterized by hyperglycemia due to insulin abnormalities, commonly accompanied by aberrant lipoprotein metabolism [1,3].

## Epidemiology

T2DM, a chronic non-communicable disease, about 463 million people worldwide suffer from T2DM. By 2030, that figure is predicted to increase to 578 million, and by 2040, it will reach 640 million [14]. Obesity and changes in lifestyle have led to an increase in diabetes prevalence worldwide. Roughly half of patients with T2DM patients are unaware of possible side effects, which might increase morbidity and mortality [14]. Heart disease, stroke, and life expectancy are all increased two to four times by T2DM, which also increases cardiovascular mortality and morbidity worldwide. Another issue that is becoming more and more of a worry is impaired glucose tolerance, which raises the risk of illness, poor quality of life, and early death. Diabetes is the 14$^{th}$ leading cause of disability and causes 10% of all deaths worldwide. Because of its south Asian heritage, India, the largest and most populous country in South Asia, is experiencing a serious public health crisis with T2DM [14,15].

Diabetes mellitus is a major public health concern in India which is characterized by increased morbidity, mortality, and life quality. It imposes a heavy financial burden on affected patients [14,15]. In 2019, it was anticipated that 77 million Indians had diabetes, representing an 8.9% adult prevalence. With 1 in 6 person's worldwide suffering from diabetes, India has the second-highest diabetes population in the world. With 1.37 billion people living with the disease and a sizable diaspora, diabetes has a major influence on society, the economy, and global health.

Diabetes mellitus is a leading cause of death worldwide; however its prevalence is lower in emerging nations like India. Healthcare disparities and elevated risk may be encountered by rural a community, which includes older adults and members of ethnic minorities. Several nations are creating national policies to curb the disease, with India poised to bear the brunt of it. Effective diabetes prevention and control efforts in underprivileged communities are hampered by a lack of data.

**Key point for diagnosis of T2DM**

- **Fasting Plasma Glucose (FPG)**
  Fasting is known as lack of intake of calories for at least eight hours.
  After eight hours of fasting overnight, a blood sample is taken.
  Exceeding 126 mg/dL (7.0 mm/L) in FPG is in agreement with the diagnosis.

- **Oral glucose tolerance test (OGTT)**
  This test determines the plasma glucose level prior to and two hours following the ingestion of 75 grams of glucose. Diabetes is identified if the plasma glucose level from the 2-hour sample is more than 200 mg/dL (11.1 mmol/L). Despite being a standard test as well, it is more costly and inconvenient than FPG and has serious variability issues

- **Glycated Hemoglobin HBA1C**
  This test gives an average of blood glucose for the previous two to three months. T2DM is diagnosed in patients whose HBA1C is more than 6.5% (48 mmol/mol). The HBA1C test is quick, easy to use, standardized, and less susceptible to fluctuation from pre-analytical factors. HBA1C is expensive, has a lot of problems, and has decreased sensitivity. Many situations, including hemodialysis, pregnant women, sickle cell disease, blood loss or transfusions, and erythropoietin therapy, might alter it [16, 17].

**Risk Factors**

Diabetes mellitus is connected with risk factors such as dyslipidemia and hypertension. Diabetes can lead to both microscopic and macroscopic consequences, such as peripheral artery disease, stroke, neuropathy, retinopathy, and nephropathy. Low immunity and dental disease are additional consequences; high body mass index is a major contributor to insulin resistance and T2DM. Risk factors for type II diabetes include race/ethnicity, weight, fat distribution, inactivity, and family history. There is an elevated risk due to factors such as aging, obesity, living conditions, physical inactivity, hypertension, and socioeconomic level.

- **Obesity:** This is the primary risk factor. Individuals who meet the criteria for obesity or overweight and whose BMI is 25 kg or above.
- **Inactivity:** Inactivity (absence of exercise) itself raises the chance of T2DM, while a family history raises the risk.
- **Races:** The disease is more common in some races and ethnic groups.
- **Age:** Low HDL cholesterol and elevated triglycerides are associated with an increased risk of T2DM, especially in elderly [19].
- **Polycystic ovary syndrome** also increases diabetes risk.
- **Family history:** First-degree relative suffering from diabetes
- **Diseases:** Cardiovascular disease or hypertension history, reduced HDL cholesterol or elevated triglycerides are linked to T2DM.

Prediabetes-a condition characterized by elevated blood sugar levels but not diabetes—often develops into that full blown diabetes if left untreated. Women with diabetes mellitus should get lifelong testing every three years or more [18].

**Prevention**

A healthy lifestyle that includes eating low-fat, high-fiber meals, exercising moderately to vigorously, decreasing weight, and avoiding prolonged inactivity is key to preventing type II diabetes. Losing 7% to 10% of body weight can help people with pre-diabetes avoid becoming diabetes. Preventing extended periods of inactivity can also raise your risk of type II diabetes. If lifestyle modifications

are not effective in lowering blood sugar levels, older persons may be prescribed the diabetes drug metformin [20].

**Prevalence of diabetics in rural versus urban population**

Diabetes and pre-diabetes are very common in India's rural and urban areas, with the gap between the two becoming less noticeable. Therefore, it is essential to develop immediate primary and secondary preventive programs in order to restrict future expansion in areas with high incidence. Diabetes is not widely known or understood in India, particularly in rural regions. This highlights the need for widespread diabetes education and awareness initiatives [21].

Research examined health disparities between elderly populations in India's rural and urban areas, with a particular emphasis on the variations between the two in terms of pre-diabetes, diabetes prevalence, and factors as a result of unequal living conditions and economic development [21]. Approximately 80 percent of the 537 million people with diabetes globally live in low- and middle-income nations. The increased frequency is associated with changing dietary, occupational, and physical activity trends as well as urbanization. With higher expansion in low- and middle-income countries, rural areas are also at risk. Increased basic healthcare services are required in low- and middle-income nations due to the growing prevalence of diabetes in rural areas. Like the majority of the Indian subcontinent, India has rapidly urbanized, which has increased the prevalence of non-communicable diseases like diabetes in rural communities Difficulties include decreasing spending, lack of health workers, and remote locations. The lack of data on disparities in rural health makes it difficult for policy makers to allocate funds. In the upcoming ten years, there will likely be a major increase in the number of diabetics, with Asian nations predicted to bear the brunt of this burden [22].

Urbanization promotes obesogenic and diabetic lifestyle patterns, and changes in diet raise the risk of overnutrition and associated diseases including diabetes and overweight/obesity. For elderly people living in both urban and rural locations, it is essential to comprehend the factors that contribute to diabetes and the variations between these two settings. Comprehending the disparities in diabetes prevalence between urban and rural areas is crucial for formulating evidence-based approaches and public health regulations. [22, 23].

**Gender differences**

Gender differences are important when it comes to diabetes outcomes, treatment, pathogenesis, and epidemiology. Obesity is more common in women, while males are more likely to be diagnosed at lower body mass indices and ages. According to studies, the prevalence of diabetes varies throughout India, with less developed states seeing the most growth [24].

## CONCLUSIONS

In nations like India, which has the largest population, epidemiological research can assist in identifying high-risk groups for diabetes prevention initiatives. Its necessary to accurately determine the true burden and create appropriate national diabetes treatment policies that take into account a variety of ethnicity, caste, religious beliefs, and lifestyle factors, a comprehensive, countrywide survey of diabetes prevalence is nevertheless required. Notably, the majority of research on the prevalence of diabetes in India is limited to the urban areas. Studies on rural predominance are only conducted in small towns close to large metropolis.

***Declaration by Authors***
**Ethical Approval:** Not Required
**Acknowledgement:** None
**Source of Funding:** None
**Conflict of Interest:** The authors declare no conflict of interest.

## REFERENCES

1. Tomic D, Shaw, JE and Magliano, DJ The burden and risks of emerging complications of diabetes mellitus. Nat Rev Endocrinol 18:525–539. 2022. https://doiorg/101038/s41574-022-00690-7
2. Chen L, Chen R, Wang H, Liang F. Mechanisms linking inflammation to insulin resistance. Int J Endocrinol. 2015. 1–9
3. Bakker W, Eringa EC, Sipkema P, van Hinsbergh VW. Endothelial dysfunction and diabetes: Roles of hyperglycemia, impaired insulin signaling and obesity Cell Tissue Res 2009;335:165–189 doi: 101007/s00441-008-0685-6
4. Alam, S, Hasan, MK, Neaz S; Hussain N, Hossain, MF, Rahman, T Diabetes Mellitus: Insights from Epidemiology, Biochemistry, Risk Factors, Diagnosis, Complications and Comprehensive Management Diabetology 2021, 2, 36-50 https://doiorg/103390/ diabetology2020004
5. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C Pathophysiology of Type 2 Diabetes Mellitus Int J Mol Sci 2020 Aug 30;21(17):6275 doi: 103390/ijms21176275
6. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk Eur Heart J 2020;41(1):111–88
7. Schofield JD, Liu Y, Rao-Balakrishna P, Malik RA, Soran H Diabetes dyslipidemia Diabetes Ther 2016 7(2):203–19 https://doiorg/101007/s13300-016-0167-x
8. Artha I, Bhargah A, Dharmawan NK, et al High level of individual lipid profile and lipid ratio as a predictive marker of poor glycemic control in type-2 diabetes mellitus Vasc Health Risk Manag 2019. 15:149–157 doi:102147/VHRMS209830
9. Ozder A Lipid profile abnormalities seen in T2DM patients in primary healthcare in Turkey: a cross-sectional study Lipids Health Dis 2014. 13:183
10. Haile K, & Timerga A Dyslipidemia and its associated risk factors among adult type-II diabetic patients at Jimma University Medical Center, Jimma, Southwest Ethiopia Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2020. 13, 4589
11. Kiplagat SV, Lydia K, Jemimah K, & Drusilla M Prevalence of dyslipidemia and the associated factors among Type 2 diabetes patients in Turbo Sub-County, Kenya J Endocrinol Diabetes, 2017. 4(5), 1–9
12. Katulanda P, Dissanayake H A, De Silva S Netal Constantine G Ret al Prevalence, patterns, and associations of dyslipidemia among Sri Lankan adults - Sri Lanka Diabetes and Cardiovascular Study in 2005–2006 Journal of clinical lipidology. 2018 12(2), 447–454
13. Fowler, M J Microvascular and macrovascular complications of diabetes Clin Diabetes.2008. 26, 77–82.
14. Guariguata L, Whiting DR, Hambleton I et al Global estimates of diabetes prevalence for 2013 and projections for 2035," Diabetes Research and Clinical Practice. 2014. 103: 137–149
15. Ke C, Narayan, KMV, Chan, JCN et al Pathophysiology, phenotypes and management of type 2 diabetes mellitus in Indian and Chinese populations Nat Rev Endocrinol 18, 413–432. 2022. https://doiorg/101038/s41574-022-00669-4
16. Robertson, R, Zhou, H, Zhang, T & Harmon, J S Chronic oxidative stress as a mechanism for glucose toxicity of the beta cell in type 2 diabetes Cell Biochem Biophys. 2007. 48, 139–146.
17. Genuth S, Alberti KG, Bennett Petal Expert Committee on the Diagnosis and Classification of Diabetes Mellitus Follow-up report on the diagnosis of diabetes mellitus Diabetes Care. 2003.26: 3160–3167
18. Miyata, M Intensive lipid-lowering therapy in high-risk diabetic patients Hypertens Res 44,

1676–1677. 2021. https://doiorg/101038/s41440-021-00773-4
19. Zagrebin EA, Shevchenko EA, Ivanchenko EY, et al Correlation of lipid profile and glycated hemoglobin as a new prognostic criterion for Type 2 diabetes mellitus development and progression Sovrem Tekhnologii Med 2020;1 2(2):87–91 doi:1017691/stm20201221111
20. Rajlic S, Treede H, Münzel T, Daiber A, Duerr GD Early Detection Is the Best Prevention - Characterization of Oxidative Stress in Diabetes Mellitus and Its Consequences on the Cardiovascular System. Cells 2023. 12(4):583 https://doiorg/103390/cells12040583
21. Krishnamoorthy, Y, Rajaa, S, Verma, M *et al* Spatial Patterns and Determinants of Diabetes Mellitus in Indian Adult Population: a Secondary Data Analysis from Nationally Representative Surveys. Diabetes Ther. 14; 63–75. 2023. https://doiorg/101007/s13300-022-01329-6
22. Ghosh K, Dhillon P, Agrawal G Prevalence and detecting spatial clustering of diabetes at the district level in India J Public Health 2020. 28(5):535–45
23. Barua S, Saikia N, Sk R Spatial pattern and determinants of diagnosed diabetes in southern India: evidence from a 2012–13 population-based survey J Biosoc Sci 2021;53(4):623–38 https://doiorg/101017/S002193202000044 9
24. Kautzky-Willer, A, Leutner, M & Harreiter, J Sex differences in type 2 diabetes Diabetologia. 2023. 66, 986–1002. https://doiorg/101007/s00125-023-05891-x

How to cite this article: Umesh Kumar Sharma, Meenu Pujani, J. Anuradha. Type-II-diabetes mellitus- etiology, epidemiology, risk factors and diagnosis and insight into demography (urban versus rural). *Int J Health Sci Res.* 2024; 14(1):283-290. DOI: *10.52403/ijhsr.20240136*

******