

## REVIEW ON CO-MORBIDITIES IN DIABETES MELLITUS

A.Srikanth<sup>1</sup>, A.Maithri<sup>1</sup>, J. Karthik<sup>1</sup>, K. Tharun<sup>1</sup>, K. Mahesh<sup>1</sup>, T.Praveen<sup>1</sup>, P. Narayana Swamy<sup>2</sup>

<sup>1</sup>B.Pharmacy final year student, Jagan's Institute of Pharmaceutical Sciences, Nellore

<sup>2</sup>Associate Professor, Dept.of Pharmacy Practice, Jagan's Institute of Pharmaceutical Science, Nellore

**\*Corresponding Author**

**P. Narayana Swamy**

DOI: <https://doi.org/10.47957/ijciar.v6i1.144>

Received: 11 Jan 2023 Revised: 17 Feb 2023 Accepted: 14 March 2023

### Abstract

**Aim and objectives:** The aim of this study was to determine cost of illness and cost of utility in the study population and making recommendations to decrease the economic burden of the treatment by following the life style modifications.

**Methodology:** It is a cross sectional pharmacoepidemiological study. Totally 132 diabetic patients both in-patients and out patients of medical and surgical departments in a secondary level referral hospital were included in this study which was conducted for a period of 6 months. All patients with diabetes type-II, continuing anti diabetic drugs (Metformin, Glibenclamide and Insulin,) for their diabetes management are included and patients who are diagnosed as Diabetic type-I and pregnancy and pediatric patients were excluded. Data was analyzed by Carlson comorbidities Index.

**Results:** A total of 132 diabetic patients were included, in which male and females were nearly equal in number. Based upon the comorbid conditions, it was found that the most of the subjects (69%) were suffering with diabetes along with hypertension and 9.9% are having comorbidity of hypertension & acute renal failure along with DM and treatment costs more economic burden to the patients. The average utility of drugs is more for the combination of Metformin+Glibenclamide+Insulin than metformin+glibenclamide.

**Conclusion:** Finally we concluded that study place is a rural area and most of people are with poor knowledge and having lack of awareness on both disease and treatment. By applying Charlson Co morbidities index we found the patient's economic status by which we found that many of the diabetic patients facing economic burden, especially daily wagger are feeling much difficulty to face even therapy cost also. In co morbidities side, we noticed 55% of the study population are having diabetes with hypertension. Although all the patients were provided with education regarding their disease and drugs for improving their quality of life, but it has an influence on very few people.

**Keywords:** Diabetes, Epidemiology, Antidiabetics, Pharmacoeconomics.

©2023 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



### Introduction

#### Diabetes

Diabetes is a chronic disease. The term "diabetes mellitus" describes a metabolic disorder of multiple aetiologies most common reason considered is when pancreas does not produce insulin and it is characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs (WHO 1999) [1]. There are two main types of diabetes Type 1 diabetes (T1B) usually patients require lifelong insulin injections for survival [2]. Type 2 diabetes (T2B): This is the most common type of diabetes (representing 90% of diabetic cases worldwide).

### **Type 2 diabetes (Non-insulin-dependent diabetes mellitus (NIDDM)).**

- It majorly occurs due to insulin resistance which is characterised by hyperglycemia and it develops in adulthood who are at risk of obesity, decreased physical activity and unhealthy diets and can be managed with the help of oral hypoglycemic agents and lifestyle modifications such as diet, exercise etc.
- Patients are at lower risk of micro vascular and macro vascular complications unlike Type 1 diabetes.

#### **Symptoms [2]**

- Patients may have no symptoms at all or minimal symptoms such as polyuria, polydipsia, polyphagia, and unexplained weight loss before diagnosing.
- May also experience numbness in extremities, pain in feet (disesthesias), and blurred vision and may have recurrent and severe infections.
- Patients may present with loss of consciousness or coma but this is less common than in Type-1 diabetes.

#### **Diagnosis [2]**

- Diagnosis is made by the presence of classic symptoms of hyperglycemia and an abnormal blood test.
- A plasma glucose concentration  $\geq 7$  mmol/L (or 126 mg/dL) or  $\geq 11.1$  mmol/L (or 200 mg/dL) 2
- In a patient without classic symptoms, diagnosis can also be made by HbA1C test which is done to approximate metabolic control over previous 2-3 months and to guide treatment decisions. This test can also be used to diagnose type 2 diabetes.
- Some patients are diagnosed through "opportunistic screening" of high risk groups who are asymptomatic.
- For example, age  $>45$  years of age, a BMI  $>25$  kg/m<sup>2</sup> may, being of certain ethnic group or being hypertensive may prompt a screening test or the patient him/herself requests screening.

#### **Treatment [2]**

The main aim of the treatment is to prevent or delay the complication of diabetes. It is also necessary to provide the education regarding the importance of diet, exercise, and foot care.

#### **Diabetic Treatments**

- 1) Oral hypoglycemic therapy.
- 2) Insulin treatment.
- 3) Diet (combined with exercise)

#### **Pharmacoeconomics [9]**

The field of study that evaluates the behaviour of individuals, firms, and markets relevant to the use of pharmaceutical products, services and programs, and which frequently focuses on the costs (inputs) and consequences (outcomes) of that use.

Thus, pharmacoeconomics (PE) is a subfield of health economics. Operationally, the field of Pharmacoeconomics consists of comparing outcomes (clinical, economic, and humanistic) and costs (resource consumption) of pharmaceutical products, programs and/or services to the next best alternatives from selected perspectives. The aim of this approach is to identify, measure, value, and establish a link between both resource consumption and outcomes so that relative worth of selected pharmaceutical products, programs and/or services can be established.

The basic task of economic evaluation is to identify, measure, value, and compare the costs and consequences of the alternatives being considered [2].

The two distinguishing characteristics [2] of economic evaluation are as follows:

- (1) Is there a comparison of two or more alternatives?
- (2) Are both costs and consequences of the alternatives examined?

A full economic evaluation encompasses both characteristics, whereas a partial economic evaluation addresses only one.

#### **Cost –Utility Analysis**

Cost-utility analysis (CUA) is a method for comparing treatment alternatives and also can compare cost, quality and quantity of patient years that integrates patient preferences and HRQOL.

Cost is measured in dollars, and therapeutic outcome is measured in a quality-adjusted life year (QALY) gained.

#### **Advantages of cost–utility analysis**

Cost–utility analysis was developed to address the problem of conventional cost effectiveness analysis, which did not allow decision-makers to compare the value of interventions for different health problems.

Cost–utility analysis can capture the value of improvements in morbidity and mortality.

Cost–utility analysis thus increasingly facilitates the transparency of resource allocation processes.

#### **Disadvantages of cost–utility analysis**

- With many healthcare interventions, there are significant concerns about the ability of cost–utility analysis to capture all the valued characteristics.
- It is undoubtedly true that QALYs do not capture differences in the process characteristics of interventions, and there is substantial evidence that patients do attach value to these.
- There is also concern that the descriptive instruments and the utilities they generate are insufficiently sensitive to differences in treatments for milder conditions.
- For chronic conditions, the assumption that the utility of a health state is independent of the time spent in that health state is considered problematic.
- Similarly, that the preceding and subsequent health states do not affect the utility of a specific health state is a strong assumption in the context of chronic conditions, especially conditions where disability accumulates over time.

#### **Cost-of-Illness**

Cost-of-illness studies measure the economic burden of a disease or diseases and estimate the maximum amount that could potentially be saved or gained if a disease needs to be eradicated. Numerous cost-of-illness studies have been conducted over the past 30 years. Many of these studies have been instrumental in public health policy debates because they highlight the magnitude of the impact of an illness on society or a part of society and it can help policy makers to decide which diseases need to be addressed first by health care and prevention policy. Additionally, these studies can indicate the diseases for which curing would be valuable in reducing the burden of disease. For specific stakeholders, such as the federal government, cost-of-illness studies can show the financial impact of a disease that has on public programs, such as Medicare and Medicaid.

Cost-of-illness studies are often cited in disease studies that attempt to highlight the importance of studying a particular disease, as well as in cost-effectiveness and cost-benefit studies. Cost-of-illness studies can demonstrate which diseases may require increased allocation of prevention or treatment resources, but they are limited in determining how resources are to be allocated because they do not measure benefits.

### **Methodology**

#### **Study design**

It is a Pharmacoepidemiological study involving cohort study design. Stratified convenience sampling with matching for factors such as gender, age is used. All diabetic type 2 patients under medication of Metformin, Glibelcamide and insulin were included. Medial records and patients reports were assessed for data collection.

#### **Data collection and processing**

In-patients and out patients of medical and surgical departments in a secondary level referral hospital were included and study was done for a period of 6 months.

Data was collected from patients diagnosed as Diabetic type-II and continuing anti diabetic drugs (Metformin, Glibelcamide, and Insulin and others<sup>20</sup>) for their diabetes management.

We have collected the data from patients in regular intervals regarding medical history, medication history, and comorbid conditions, drugs used along with the contact details. Data was processed using Microsoft excel.

#### **Inclusion Criteria**

1. All in patients and out patients who are diagnosed as Diabetic type-II.
2. Continuing anti diabetic drugs (Metformin, Glibelcamide and Insulin,) for their diabetes management.
3. All patients of above 40 years old.
4. Who visit hospital for their regular check-up of disease.
5. Diabetics with Co-morbidities were also involved in this study.

#### **Exclusion Criteria**

1. Patient who are diagnosed as Diabetic type-I.
2. Those who are non-compliant.
3. Those who have communication problems.
4. Patients with pregnancy.
5. Paediatric patients.

6. Patients who are not willing to participate in the study.

**Results**

**Patient’s demographic details**

A total of 132 diabetic patients are considered, in which males are 63 and females are 69 which are almost equal in number. Patients with Co morbidity by involving co morbidity scale we included all the diabetic patients who are suffering with co morbidities.

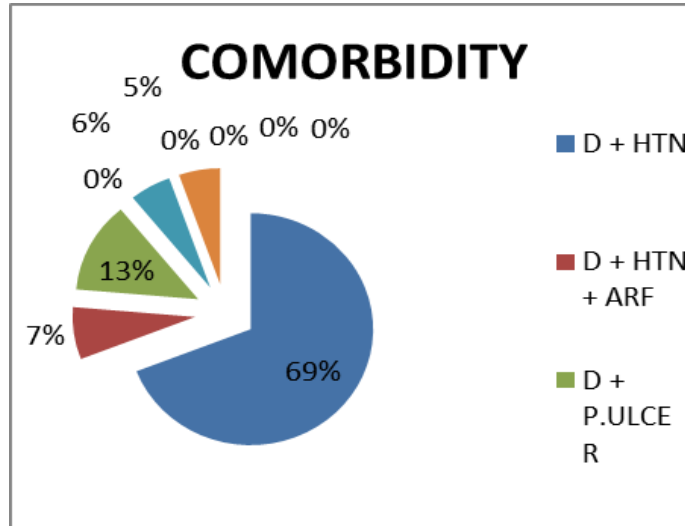


Figure-1: Percentage of co-morbidities in study population.

**Cost Analysis for Calendar Year**

We calculated cost of therapy according to co-morbidity.No of patients: patients who are suffering from particular disease. Avg cost of therapy: average cost of entire therapy through one year. Cost of drugs: total expenditure of amount on medicines from all patients. Other hospital cost: laboratory and hospital charges.

**Table 1: Cost of illness in different co morbidities.**

Disease	No of Pt's	Total Drugs cost	Avg drug cost	Total other hosp cost	Other Avg Hosp Cost	Total cost	COI %	COI
DM	19	22,800	1,200	2888	152	25688	1352	1
DM+HTN	41	63,960	1,560	23370	570	87330	2130	1.57
DM+HTN+P.ULCER	11	52,800	4,800	12540	1140	65340	5940	2.78
DM+ HTN+LEU	3	16,200	5,400	4560	1520	20760	6920	1.16
DM+HTN+CHF	5	30,000	6,000	4650	930	34650	6930	1.0
DM+ HTN+LYM	5	31,000	6,200	7325	1465	38325	7665	1.10
DM+ HTN+CRF	9	1,03,644	11,516	15480	1760	119124	13236	1.72
DM+ HTN+ARF	13	1,69,000	10,090	20475	1575	189475	14575	1.10
DM+ HTN+NEURO	3	49,500	16,500	5265	1755	54765	18255	1.25
DM+HTN+ALF	6	1,03,500	17,250	11880	1980	115380	19230	1.05
DM+ HTN+TUMOR	5	93,000	18,600	12850	2570	105850	21170	1.10
DM+HTN+MLD	4	79,040	19,760	7436	1859	86476	21619	1.02

**Average Utility of Drugs**

**Table 2: Comparison of utility and cost of drugs per number of patients.**

Drugs	Number of pts	Avg utility	Avg cost
M + Gli	93	0.7	7036
Met+Glib+Ins	39	0.8	10665

**Comparison of Co morbidity with Age Group****Table 3: CCI in Co morbidity.**

S.NO	Disease	No: of Pts	Avg age	Avg CCI
1.	DM	19	41-55	3
2.	DM+HTN	41	46-59	4
3.	DM+HTN+P,ULCER	11	45-65	5
4.	DM+HTN+CHF	7	56-70	5
5.	DM+HTN+ALF	13	52-79	6
6.	DM+HTN+MLD	4	60-82	9
7.	DM+HTN+ARF	13	50-70	5
8.	DM+HTN+CRF	9	56-80	7
9.	DM+HTN+LEU	3	58-70	6
10.	DM+HTN+LYM	5	62-80	6
11.	DM+HTN+TUMOR	5	59-77	11
12.	DM+HTN+NEU	9	63-89	7

**Table 4: All Patient Data Showing With Charlson Co morbidity Index.**

Age group	Number	Avg utility	CCI
41-50	36	0.8	5.0
51-60	40	0.7	6.3
61-70	46	0.6	7.0
71-80	7	0.5	6.7
>80	3	0.5	6.0

**Comparison of utility with Charlson Co-morbidity index**

Through this average utility of drugs with scoring of Charlson co-morbidity index of every individual for years of disease was explained.

**Table 4: CCI for years of disease.**

Suffering from years	Numbers	Avg utility	CCI
1-2	23	5	6
2-5	33	5.2	6.01
5-10	38	6.7	7.06
10-20	24	7.9	8.0
Above 20	14	8.8	9.01

**Discussion**

In this study, a total of 132 diabetic patients were included out of which male and females are nearly equal in number and adults are higher than the geriatric patients. In our study, higher number of patients are having the comorbidity of hypertension and other comorbidities include peptic ulcer, congestive cardiac failure, acute renal failure, chronic renal failure, leukemia, lymphoma, other tumors, nephropathy, acute liver disease, moderate liver disease.

Diabetes mellitus is lifelong threatening condition which causes the economic burden in subjects with low socio- economic status. However, some government hospitals are helping the patients from poor economic background by providing health care to all of them without charging money for consultation and providing all the useful medicine.

By this study, we had analyzed cost per individual patients according to their disease status with cost of therapy per year. Finally we concluded that diabetic with co morbidities are facing more economic burden per year wise when compared with subjects having only diabetes. Average utility of therapy: comparison of utility and cost for number of patients was analyzed and its seems like combination therapy of Metformin + Glibenclamide was most popularly consumed when compared with other combinations. Insulin is advised to very few patients and other oral antidiabetics were given in combinations based on patient disease condition. Cost of hospitalization with co morbidities: In total 132 study subjects, 60% of patients are hospitalized with comorbidities and facing economic burden for hospitalization, travelling and other

costs like cost of diagnosis. In our study many of the participants are daily wagers, they will loosen their economic source if they get struck with hospitalization.

Basically study place is rural area with most of the subjects are with poor knowledge about disease and its complications. In our study it was identified that, many of the patients are facing economic burden, even sometimes they are not able to consume sufficient quantity of medications due to the high costs.

### **Conclusion**

The costs for patients with comorbidities were substantially higher when compared to the patients without comorbidities and the cost was found to increase progressively with increase in number of complications. Therefore, the burden of this disease was significant for patients as well as their families, so the health policy makers should emphasize on the initiatives to prevent the disease prevalence. Proper care and counselling should be provided continuously to the patients with diabetes to manage the disease effectively and to prevent the devastating complications. Lastly we recommend that more economic studies should be done which play an important role in applying the frame work for resources allocation in diabetes prevention and control.

### **Conflict of Interest**

Authors are declared No Conflict of Interest

### **Acknowledgement**

Not Applicable

### **Author Contribution**

All Authors Contributed equally

### **Ethical Considerations**

Not Applicable

### **Funding**

No Funding

### **References**

1. Vijaya Sundararajana, Toni Hendersona et al. New ICD-10 version of the Charlson comorbidity Index predicted in-hospital mortality. *Journal of Clinical Epidemiology*, 2004; 57: 1288–1294.
2. Hyun-Ju Seo, Seok-Jun Yoon, was published an article regarding —A comparison of the Charlson comorbidity index derived from medical records and claims data from patients undergoing lung cancer surgery in Korea: a population-based investigation|| 30 March 2010 Accepted: 13 August 2010 *BMC Health Services Research*, 2010; 10: 236.
3. New ICD-10 version of the Charlson Comorbidity Index predicted in-hospital mortality *Journal of Clinical Epidemiology*, 2004; 57: 1288–1294.
4. West KM. *Epidemiology of diabetes and its vascular complications*. Elsevier, New York, 1978.
5. *Clinical pharmacology* by P.N.BENNET &M.J.BROWN / 9th edition / Section 8 Endocrine System, *Metabolic/ 679*.
6. Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Res Clin Pract*, 2011; 94: 311–321.
7. Struijs JN, Baan CA, Schellevis FG, Westert GP, van den Bos GA. Comorbidity in patients with diabetes mellitus: impact on medical health care utilization. *BMC Health Serv Res.*, 2006; 6: 84.
8. Mo F, Pogany LM, Li FC, Morrison H. Prevalence of diabetes and cardiovascular comorbidity in the Canadian Community Health Survey 2002–2003. *Scientific World Journal*, 2006; 6: 96–105.
9. Roglic G, Unwin N, Bennett PH, Mathers C, Tuomilehto J, Nag S, Connolly V, King H. The burden of mortality attributable to diabetes: realistic estimates for the year 2000. *Diabetes Care*, 2005; 28: 2130–2135.

10. Köster I, Huppertz E, Hauner H, Schubert I. Direct costs of diabetes mellitus in Germany - CoDiM 2000–2007. *Exp Clin Endocrinol Diabetes*, 2011; 119: 377–385.
11. Shiv Chandra Singh, A., Yu, A., Chang, B., Li, H., Rosenzweig, A. and Roh, J.D., 2021. Exercise Training Attenuates Activin Type II Receptor Signaling in the Aged Heart. *Circulation*, 144(Suppl\_1), pp.A14259-A14259.
12. Kaiser A, Vollenweider P, Waeber G, Marques-Vidal P. Prevalence, awareness and treatment of type 2 diabetes mellitus in Switzerland: the CoLaus study. *Diabet Med.*, 2012; 29: 190–197.
13. Haffner SM, Stern MP, Hazuda HP, Mitchell BD, Patterson JK: Cardiovascular risk factors in confirmed prediabetic individuals. Does the clock for coronary heart disease start ticking before the onset of clinical diabetes?. *JAMA*, 1990; 263: 2893- 2898. 10.1001/jama.1990.03440210043030.
14. World Health Organization. Diabetes Factsheet. Geneva: World Health Organization; 2013.
15. Gillies CL, Lambert PC, Abrams KR, et al. Different strategies for screening and prevention of type 2 diabetes in adults: cost effectiveness analysis. *BMJ*. 2008; 336(7654): 1180–1185.
16. Currie CJ, Gale EA, Poole CD. Estimation of primary care treatment costs and treatment efficacy for people with Type 1 and Type 2 diabetes in the United Kingdom from 1997 to 2007\*. *Diabet Med.*, 2010; 27(8): 938–948.
17. Massi-Benedetti M. The cost of diabetes Type II in Europe: the CODE-2 Study. *Diabetologia*, 2002; 45(7): S1–S4.
18. Liebl A, Neiss A, Spannheimer A, et al. Complications, co-morbidity, and blood glucose control in type 2 diabetes mellitus patients in Germany—results from the CODE-2 study. *Exp Clin Endocrinol Diabetes*, 2002; 110(1): 10–16.
19. Bottomley JM, T2ARDIS Steering Committee Managing care of type 2 diabetes. Learnings from T2ARDIS. *Br J Diabetes Vasc Dis.*, 2001; 1: 68–72.
20. Singh, A., Srinivasan, A.K., Chakrapani, L.N. and Kalaiselvi, P., 2019. LOX-1, the common therapeutic target in hypercholesterolemia: a new perspective of antiatherosclerotic action of aegeline. *Oxidative medicine and cellular longevity*, 2019.
21. Williams R, Van Gaal L, Lucioni C. Assessing the impact of complications on the costs of Type II diabetes. *Diabetologia*, 2002; 45(7): S13–S17.
22. Liebl A, Spannheimer A, Reitberger U, Gortz A. Costs of long-term complications in type 2 diabetes patients in Germany. Results of the CODE-2 Study. *Med Klin (Munich)*, 2002; 97(12): 713–719.
23. Mata M, Antonanzas F, Tafalla M, Sanz P. The cost of type 2 diabetes in Spain: the CODE-2 study. *Gac Sanit*, 2002; 16(6): 511–520.
24. Xie X, Vondeling H. Cost-utility analysis of intensive blood glucose control with metformin versus usual care in overweight type 2 diabetes mellitus patients in Beijing, P.R. China. *Value Health*, 2008; 11(1): S23–S32. [PubMed]
25. Clarke PM, Gray AM, Briggs A, Stevens RJ, Matthews DR, Holman RR. Cost-utility analyses of intensive blood glucose and tight blood pressure control in type 2 diabetes (UKPDS 72) *Diabetologia*, 2005; 48(5): 868–877.
26. Singh, A., Gowtham, S., Chakrapani, L.N., Ashokkumar, S., Kumar, S.K., Prema, V., Bhavani, R.D., Mohan, T. and Sathyamoorthy, Y.K., 2018. Aegeline vs Statin in the treatment of Hypercholesterolemia: A comprehensive study in rat model of liver steatosis. *Functional Foods in Health and Disease*, 8(1), pp.1-16.
27. Gray A, Clarke P, Farmer A, Holman R. Implementing intensive control of blood glucose concentration and blood pressure in type 2 diabetes in England: cost analysis (UKPDS 63) *BMJ*, 2002; 325(7369): 860.
28. Gray A, Raikou M, McGuire A, et al. Cost effectiveness of an intensive blood glucose control policy in patients with type 2 diabetes: economic analysis alongside randomised controlled trial (UKPDS 41). United Kingdom Prospective Diabetes Study Group. *BMJ*, 2000; 320(7246): 1373–1378.
29. Singh, A., Kumar, A. and Kalaiselvi, P., 2018. Aegeline, targets LOX1, the receptor for oxidized LDL to mitigate hypercholesterolemia: a new perspective in its anti-atherosclerotic action. *Free Radical Biology and Medicine*, 128, p.S41.
30. Centers for Disease Control and Prevention. National diabetes fact sheet: general information and national estimates on diabetes in the United States, 2007. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2008.
31. Singh, A., 2022. Hyperlipidemia in cardiovascular health and digestion. In *Nutrition and Functional Foods in Boosting Digestion, Metabolism and Immune Health* (pp. 141-150). Academic Press.
32. Rappange DR, Job N, van Exel A, Feenstra TL, Rutten FFH, Brouwer WBF: Unrelated medical costs in Life-Years gained. *Pharmacoeconomics*, 2008; 26: 815-830.