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AN OBSERVATIONAL STUDY ON COST BURDEN AND COST EFFECTIVENESS OF ANTI-DIABETIC MEDICATIONS

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Abstract:

Objective: To evaluate the economic burden and to study the cost effectiveness of antidiabetic medications in patients with Type II DM and their comorbidities.

Methodology: A prospective observational study was conducted in outpatient department of diabetic clinic for a period of 6 months.

Results: Expenditure incurred by diabetic patients included annual cost of medications, physician visit and laboratory expenses. Among 320 patients, we found that, expenses of patients on metformin therapy included an average annual cost of Rs. 5857/-, direct annual drug cost of Rs.1375.2/-, laboratory cost of Rs. 2010/- and physician visit cost Rs.1800/-. Patients on metformin with Glimepiride therapy included an average annual cost of Rs. 19,952/-, Patients on metformin with voglibose therapy included an average annual cost of Rs.10,200 Rs/-, direct annual drug cost Rs. 8978.4/-. Patients on metformin with teneligliptin therapy included an average annual cost of Rs.13,200/- and direct annual drug cost of Rs. 7757.2/-. Patients on metformin with sitagliptin therapy included an average annual cost of Rs. 15,400/-, with a direct annual drug cost Rs.9096/-. Patients on metformin with mixtard therapy included an average annual cost of Rs.18,500/-, and direct annual drug cost of Rs.11,215.2/-. Patients on mixtard only therapy included an average annual cost of Rs. 23,560/- and direct annual drug cost of Rs.12,720/-.

Conclusion: For the initial treatment of Type II DM, Metformin may be considered as cost effective monotherapy. Glimepiride may be suggestive in terms of cost effective therapy as an add on to Metformin who are inadequately controlled with monotherapy. Clinical pharmacist plays an important role in educating the patients about proper use of medication, screening for drug interactions, explaining monitoring devices and proper management of complications associated with diabetes

Key words: Type II Diabetes Mellitus, Cost effectiveness, Cost burden

INTRODUCTION:

Diabetes Mellitus (DM) is a metabolic disorder characterized by the presence of chronic hyperglycemia accompanied by greater or lesser impairment in the metabolism of carbohydrates, lipids and proteins. The origin and etiology of DM can vary greatly that include defects in either insulin secretion or resistance or both at some point in the course of disease. Mostly patients with diabetes mellitus have either type I DM (which is immune-mediated or IDDM) or type II DM (NIDDM). Type II DM is the most common form characterized by hyperglycemia, insulin resistance and relative insulin deficiency [1]. The global prevalence of diabetes is estimated at 415 million in 2019. Moreover, worldwide approximately 193 million diabetics remain undiagnosed predisposing them to the development of several long-term complications of untreated chronic hyperglycemia. The major pathologic hallmark of DM involves the vasculature leading to both microvascular and macrovascular complications. Abnormal glycemic index which is leading to hyperglycemia is associated with long-term damage and failure of various organ systems mainly affecting the eyes, nerves, kidneys, and heart [2]. Diabetes and its complications not only affect the quality of patient, but also cause large economic loss. The diabetes economic burden is significant and is expected to increase over time.

Diabetes is one of the leading in terms of economic burden on society. This burden is related to health system costs gained by society in managing the disease, which includes direct costs such as physician visit, laboratory cost and drug therapy cost. Indirect costs resulted from productivity losses due to patient disability and premature mortality, time spent by family members accompanying patients when seeking care, and intangible costs [3]

MATERIALS AND METHODS:

Data has been collected from outpatient department of a diabetic Clinic Hanumakonda. This was a prospective observational study conducted for a period of 6 months

Inclusion criteria: All diabetic patients including co-morbidities were included in study except,

1. Patients with Type-I DM

2. Patients with Gestational diabetes and age >75 years old

Necessary information was collected from case sheets and collecting detailed history from patients. Information about the cost of laboratory services and medications was obtained from laboratory and pharmacy department of the hospital. Parameters to be considered are age (young onset <20 years, middle age onset (21-64), elderly >65) gender, educational level (basic, medium, higher), comorbidities (CVD, renal disorders, stroke, epilepsy, thyroid disorders, pulmonary- disorders) complications (DM + ONE complication, DM + TWO complications, DM+ THREE complications) duration of diabetes, diabetes treatment (OHA, insulin and OHA, only insulin, dual insulin) FBS, PLBS, HbA1C, lipid profile, albumin to creatinine ratio (ACR), social habits, direct medical cost (physician visit cost, laboratory cost, treatment cost)

Method:

Cost effective analysis: Cost effective analysis was done by obtaining incremental cost effective ratio (ICER)**.** ICER was obtained using the formula:

Incremental Cost-Effective Ratio (ICER) =[Cost of drug A- Cost of drug B] **/**[Effect A- Effect B]

RESULTS:

A total of 320 patients were selected and their prescription data was analysed. Among them 182 (56.8 %) patients were controlled and 138 (43.1 %) were uncontrolled

Table 1: Gender wise classification of patients

Gender	No. of cases	Controlled	Uncontrolled
Male	146 (45.6 %)	81(55.4 %)	65 (44.5 %)
Female	174 (54.3 %)	101(58 %)	73 (41.9 %)

Of total study population, female (174, 54.3 %) were predominant over male (146, 45.6 %) and diabetes was better controlled in female than male.

Table: 2 Type II DM patients with comorbidities

Type II DM with Co-morbidities	No of patients
Type II DM with HTN	123 (43.1 %)
Type II DM with HTN, Stroke	6 (2.1 %)
Type II DM with hypothyroidism	6 (2.1 %)
Type II DM with Dyslipidemia	15 (5.2 %)
Type II DM with CKD, HTN	21 (7.3 %)
Type II DM with HTN, Dyslipidemia	7 (2.4 %)
Type II DM with HTN, hypothyroidism	9 (3.1 %)
Total	217

In our study HTN (123, 43.1 %) was most common comorbid illness seen followed by CKD with HTN, (21, 7.3 %); Dyslipidemia (15, 5.2 %); hypothyroidism (6, 2.1 %), HTN+ Stroke (6, 2.1 %), HTN+ hypothyroidism (9, 3.1 %) and HTN+ Dyslipidemia (7, 2.4 %);

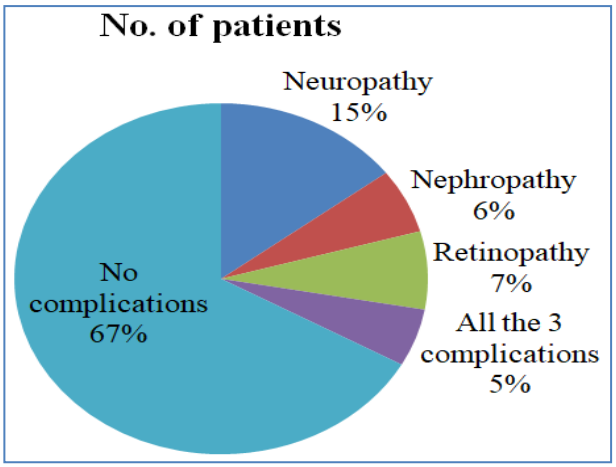

Fig 1: Type II DM patients with complications

In our study, among 320 patients diabetes associated micro vascular complications included neuropathy (47, 14.6 %); retinopathy (23, 7.1 %); nephropathy (19, 5.9 %); all complications (17, 5.3 %) and patients with no complications are (214, 66.8 %).

Table: 3 Distribution of patients based on different treatment patterns

Treatment Pattern	No. of patients	male	female	Controlled	Uncontrolled
Metformin	82	27	55	58	24
Metformin & Glimepiride	129	66	63	57	72
Metformin & Voglibose	5	3	2	3	2
Metformin & Teneligliptin	49	28	21	22	27
Metformin & Sitagliptin	8	5	3	8	0
Metformin & Mixtard	19	6	13	15	4
Mixtard	13	5	7	7	6

39 patients (12.1 %) of our study population had diagnosed with newly onset of DM. 82 (26.5 %) patients are under monotherapy and 191 (59.6 %) patients are under dual therapy. Patients under insulin therapy were 13 (4 %) and Insulin with OHA was 19 (5.9 %).

Table: 4 Distribution of Annual cost in different treatment groups only in DM patients

Treatment group	Total no. of patients	only DM	AVG annual cost
Metformin	82	12	Rs 5857/-
Metformin & Glimepiride	129	40	Rs 12,230 /-
Metformin & Voglibose	5	4	Rs 10,200/-
Metformin & Teneligliptin	49	21	Rs 13,200/-
Metformin & Sitagliptin	8	2	Rs 15,400/-
Metformin & Mixtard	19	5	Rs 18,500/-
Mixtard	13	7	Rs 23,560/-

The total annual cost in patients with DM alone were high in mixtard group (n=7) of about Rs 23,560/- followed by metformin with mixtard (n=5), metformin with sitagliptin (n=2), metformin with teneligliptin (n=21), metformin with glimepiride (n=40), metformin with voglibose (n=4), metformin (n=12) respectively.

Distribution of Annual cost in different treatment groups with comorbidities

Table: 5 Distribution of annual cost in different treatment groups in HTN patients

Treatment group	Total no. of patients	DM+HTN	AVG annual cost
Metformin	82	39	Rs 12,350 /-
Metformin & Glimepiride	129	47	Rs 13,450/-
Metformin & Voglibose	5	1	Rs 16,450/-
Metformin & Teneligliptin	49	16	Rs 14,630/-
Metformin & Sitagliptin	8	4	Rs 18,430/-
Metformin & Mixtard	19	11	Rs 21,250/-
Mixtard	13	5	Rs 23,560 /-

The total annual cost in patients with DM and HTN were high in mixtard group (n=5) of about Rs 23,560/- followed by metformin with mixtard (n=11), metformin with sitagliptin (n=4), metformin with voglibose (n=1), metformin with teneligliptin (n=16), metformin with glimepiride (n=47), metformin (n=39) respectively.

Table: 6 Distribution of annual cost in different treatment groups in HTN with stroke

Treatment group	Total no. of patients	DM, HTN with stroke	AVG annual cost
Metformin	82	2	Rs 5853 /-
Metformin & Glimepiride	129	3	Rs 8156 /-
Mixtard	13	1	Rs 19,800/-

The total annual cost in patients with DM, HTN and stroke were high in mixtard group (n=1) of about Rs 19,800/- followed by metformin with glimepiride (n=3), metformin (n=2) respectively.

Table: 7 Distribution of annual cost in different treatment groups in DM with complications

Treatment group	Total no. of patients	DM with complications	AVG annual cost
Metformin	82	4	Rs 9480 /-
Metformin & Glimepiride	129	10	Rs 10,150/-
Metformin & Voglibose	5	1	Rs 14,300/-
Metformin & Teneligliptin	49	5	Rs 16,450/-
Metformin & mixtard	19	1	Rs 19,890/-

The total annual cost in patients with DM and complications were high in metformin and mixtard group (n=1) of about Rs 19,890/- followed by metformin with teneligliptin (n=5), metformin with voglibose (n=1), metformin with glimepiride (n=10), metformin (n=4) respectively.

Table: 8 Distribution of annual cost in different treatment groups in DM with Chronic kidney disease

Treatment group	Total no. of patients	DM + HTN+CKD	AVG annual cost
Metformin	82	10	Rs 11,154.7/-
Metformin & Glimepiride	129	12	Rs 10,628.5/-
Metformin & Teneligliptin	49	2	Rs 9061/-

The total annual cost in patients with DM, HTN and CKD were high in metformin with glimepiride group (n=12) of about Rs 10,628.5/- followed by metformin alone (n=10), metformin with teneligliptin (n=2) respectively.

Table: 9 Distribution of annual cost in different treatment groups in DM with Dyslipidemia

Treatment group	**Total no. of patients**	**Dyslipidemia**	**AVG annual cost**
Metformin	82	5	Rs 7488.2 /-
Metformin& Glimepiride	129	6	Rs 10,890.6/-
Metformin & Teneligliptin	49	2	Rs 8547.2/-
Metformin & Sitagliptin	8	2	Rs 10,598/-

The total annual cost in patients with DM and dyslipidemia were high in metformin with glimepiride group (n=6) of about Rs 10,890.6/- followed by metformin with sitagliptin (n=2), metformin with teneligliptin (n=2), metformin (n=5) respectively.

Table: 10 Distribution based on cost of illness of DM with duration of disease

Duration	No. of patients(N=320)	%	Cost of illness
<1 year	39	12.1 %	Rs 4362.5 /-
1-5 years	209	65.3 %	Rs 7019.22 /-
6-10 years	54	16.8 %	Rs 6786/-
>10 years	18	5.6 %	Rs 5616 /-

Cost of illness with duration of disease were more predominant in 1-5 years (n=209) with average annual cost of Rs 7019.22/- followed by 6-10 years (n=54), >10 years (n=18), <1 year (n=39)

Table: 11 Cost effective comparison in different treatment regimens

Treatment pattern	No of patients	Avg. fasting blood sample
Metformin	82	116.5 mg/dL
Metformin & Glimepiride	129	129 mg/dL
Metformin & Voglibose	5	123 mg/dL
Metformin & Teneligliptin	49	139.8 mg/dL
Metformin & Sitagliptin	8	126 mg/dL
Metformin & mixtard	19	113 mg/dL
Mixtard	13	133 mg/dL

Analysis of cost effective ratio:

Cost effective analysis was done by obtaining Incremental Cost Effective Ratio (ICER) for a period of 6 months, by using Wilcoxon signed rank test.

Incremental Cost Effective Ratio (ICER) = [cost of drug A- cost of drug B]/ [FBG A- FBG B]

In this different treatment pattern metformin group was compared with other treatment groups to obtain incremental cost effective value.

1. Comparison between Metformin & Glimepiride and Metformin

Incremental cost effective ratio (ICER) = [cost of drug A- cost of drug B]/ [FBG A- FBG B]

A= Glimepiride& Metformin B= Metformin

ICER= [182.5 – 16.3]/ [129- 116.5] = 13.28 mg/dL

Cost of Metformin and Glimepiride for 1 strip (10 tablets) = Rs 182.50/- and cost of metformin for 1 strip (10 tablets) = Rs 16.30/-

Cost effective ratio of 13.28 mg/dL was achieved comparing Metformin and Glimepiride. It shows that metformin alone intervention is more cost effective with Rs.16.3/- per cost effectiveness compared to combination of metformin and Glimepiride of Rs.182.5/- per cost effectiveness.

2. Comparison between Metformin & Voglibose with Metformin

Incremental cost effective ratio (ICER) = [cost of drug A- cost of drug B]/ [FBG A- FBG B]

A= Metformin & voglibose B= Metformin

ICER= [89 – 16.3] / [123- 116.5] = 11.18 mg/dL

Cost of Metformin and Voglibose for 1 strip (10 tablets) = Rs 89 /- and cost of Metformin for 1 strip (10 tablets) = Rs 16.30/-

Cost effective ratio of 11.18 mg/dL was achieved comparing Metformin and voglibose and shows that metformin alone intervention is more cost effective with Rs.16.3/- per cost effectiveness compared to combination of metformin and voglibose of Rs.89/- per cost effectiveness.

3. Comparison between Metformin & Teneligliptin with Metformin

Incremental cost effective ratio (ICER) = [cost of drug A- cost of drug B]/ [FBG A- FBG B]

A= Metformin& teneligliptin B= Metformin

ICER= [128.60 – 16.3]/ [139.8- 116.5] = 4.8 mg/dL

Cost of Metformin and Teneligliptin for 1 strip (10 tablets) = Rs 128.60/- and cost of Metformin for 1 strip (10 tablets) = Rs 16.30/-

Cost effective ratio of 4.8 mg/dL was achieved comparing Metformin and teneligliptin and shows that metformin alone intervention is more cost effective with Rs.16.3/- per cost effectiveness compared to combination of metformin and teneligliptin of Rs.128.60 /- per cost effectiveness.

4. Comparison between Metformin & Sitagliptin with Metformin

Incremental cost effective ratio (ICER) = [cost of drug A- cost of drug B]/ [FBG A- FBG B]

A= Metformin& sitagliptin B= Metformin

ICER= [379.50 – 16.3]/ [126- 116.5] = 38.23 mg/dL

Cost of Metformin and Sitagliptin for 1 strip (10 tablets) = Rs 379.50/- and cost of Metformin for 1 strip (10 tablets) = Rs 16.30/-

Cost effective ratio of 38.23 mg/dL was achieved comparing Metformin and Sitagliptin and shows that metformin alone intervention is more cost effective with Rs.16.3/- per cost effectiveness compared to combination of metformin and Sitagliptin of Rs.379.50/- per cost effectiveness.

5. Comparison between Metformin& Mixtard with Metformin

Incremental cost effective ratio (ICER) = [cost of drug A- cost of drug B]/ [FBG A- FBG B]

A= Metformin& Mixtard B= Metformin

ICER= [265 – 16.3]/ [113- 116.5] = 71 mg/dL

Cost of Metformin and Mixtard for penfil injection = Rs 265/- and cost of Metformin for 1 strip (10 tablets) = Rs 16.30/-

Cost effective ratio of 71 mg/dL was achieved comparing Metformin and Mixtard and shows that metformin alone intervention is more cost effective with Rs.16.3/- per cost effectiveness compared to combination of metformin and Mixtard of Rs.265/- per cost effectiveness

6. Comparison between Mixtard with Metformin

Incremental cost effective ratio (ICER) = [cost of drug A- cost of drug B]/ [FBG A- FBG B]

A= Mixtard B= Metformin

ICER= [265 – 16.3]/ [133- 116.5] = 15 mg/dL

Cost of Mixtard for penfil injection = Rs 265/- and cost of Metformin for 1 strip (10 tablets) = Rs 16.30/-

Cost effective ratio of 15 mg/dL was achieved comparing Metformin and Mixtard and shows that metformin alone intervention is more cost effective with Rs.16.3/- per cost effectiveness compared to Mixtard of Rs.265/- per cost effectiveness

From the study combination therapy of metformin and mixtard was a more effective pharmacological treatment regimen with 78.9 % achieving glycemic control compared to metformin only therapy with 70.7 % .

DISCUSSION:

Of total study population, female (174, 54.3 %) were predominant over male (146, 45.6 %) and diabetes was better controlled in female than male.

Gender: Our results are similar to the study conducted by Peter gramblage *et.al,*[4]. Of 3810 patients in their study, 67.2 % were female and male 64.7 %. This could be due to lack of physical activity and unhealthy life style changes leading to obesity resulting in changes in BMI or waist circumference. Our results are contrast to another study done by T. Tamilselvan *et.al,*[5] where in among 141 patients, male were 77 (54.6 %) predominant than females patients (64, 45.4 %). This could be due to their social habits and life style resulting in metabolic changes leading to complications and comorbidities associated with DM.

Comorbidities: In our study HTN (123, 43.1 %) was most common comorbid illness seen followed by CKD with HTN, (21, 7.3 %); dyslipidemia (15, 5.2 %); hypothyroidism (6, 2.1 %), HTN+ Stroke (6, 2.1 %), HTN+ hypothyroidism (9, 3.1 %) and HTN+ dyslipidemia (7, 2.4 %); Hypertension and dyslipidemia was the most common comorbid associated with diabetes mellitus. Our results are similar to the study conducted by shuichi suzuiki *et.al*,[6] where in HTN (1092, 40.7 %); dyslipidemia (1274, 47.5 %); severe hypoglycemic events (55, 2.0 %) and CAD (385, 14.3 %) were observed. Our results are similar to study conducted by T. Tamilselvan *et.al,*[5] HTN (67, 47.5 %); chronic kidney disease (17, 12.1 %); followed by hypothyroidism (13, 9.21 %). In the study conducted by Peter bramlage *et.al,*[4] comorbidities was found to be CAD (23, 11.7 %), MI (38, 24.1 %). The prevalence of HTN is high in diabetes mellitus and it may be because of metabolic action of insulin, which indirectly affects the metabolism of body. Hypertension & DM are interrelated disorders & independent causative factors associated with CV and renal disorders. Association of comorbidities along with abnormal glycemic control can lead to serious micro & macro vascular complications which increased mortality, morbidity significantly and decrease the quality of life of the patient leading to psychological stress.

Complications: In our study, diabetes associated micro vascular complications included neuropathy (47, 14.6 %); retinopathy (23, 7.1 %); nephropathy (19, 5.9 %); all complications (17, 5.3 %) and none complications (214, 66.8 %)

Our results are in contrast with study conducted by Shuichi Suziki *et.al,* [6]. They found that nephropathy (158, 5.9 %) is more prevalent than retinopathy (17, 0.6 %), neuropathy (8, 0.3 %). Our results are similar to study conducted by Annie Y. Chou *et.al,* [7] where neuropathy (8124, 59.4 %) is more predominant compared to nephropathy (4240, 31 %); retinopathy (1311, 9.5 %)

The prevalence of neuropathy is more when compared with retinopathy and nephropathy. These might be due to abnormal glycemic index for a prolonged period of time resulting in abnormality in biochemical pathways, as these tissues (ex; nerves, blood vessels, kidneys, brain) doesn't require insulin for transport of glucose into cells. It depends on concentration of glucose uptake in to cells. These might be the reason for early prevalence of micro vascular complications which is affecting patient disease status as well as quality of life, which resulting in psychological distress.

Treatment patterns: 39 patients (12.1 %) of our study population were diagnosed with newly onset of DM. 82 (26.5 %) patients were under monotherapy and 191 (59.6 %) patients are under dual therapy. Patients under insulin therapy were 13 (4 %) and Insulin with OHA were 19 (5.9 %). In the study done by Prashant *et al,* [8], among 520 patients, under oral hypoglycemic therapy are 225 (43.2 %) patients, insulin therapy are 18 (3.46 %) patients, OHA with

insulin combination therapy are 95 (37.5 %) patients, and 82 patients (15.76 %) were not under any of the treatments. In our study, we had observed that treatment with oral hypoglycemic agents was most common pattern followed by combinational therapy with insulin and OHA and insulin only therapy. Patient education is most important strategy for the administration of insulin dosage forms. Patient centered approach is also a key aspect which benefits the patient from misuse of product and also helps the patient in maintaining tight glycemic status.

COST BURDEN:-

Cost burden in DM alone with different treatment regimens:

Metformin therapy:

Of the study population, 25.6 % (n=82) patients were on metformin, 14.6 % (n=12) patients are diagnosed only with DM and without comorbidities. Metformin only therapy is initiated in 14.6 % (n=12) patients with an average annual cost of Rs. 5857/-, direct annual drug cost of Rs.1375.2/-, laboratory cost of Rs. 2010/- and physician visit cost Rs.1800/-.

Our results are similar to study conducted by Chirstina S. kwon *et al,* [9] who found that direct annual cost of metformin drug was Rs.1650 /- Our results are consistent to the study conducted by T. Tamilselvan *et al,*[5] who stated that average direct annual cost of metformin drug was Rs.1300.32/- with 1.1 % reduction of HbA_1c.

Metformin with Glimepiride therapy:

In our study, 40.3 % (n=129) patients were under metformin with glimepiride therapy among them, patients diagnosed with DM and without comorbidities were 31 % (n=40) with an average annual cost of Rs. 12,230/-, direct annual drug cost of Rs.3912/-, laboratory cost of Rs.2010/- and Physician visit cost Rs.1800/-. In contrast to our study results A Marcellusi *et al,* [10] had stated that average annual cost of Rs.33,649/- was noticed in patients under metformin with glimepiride therapy. Our results are almost similar to study conducted by T. Tamilselvan *et al,*[5] who stated that direct annual cost of metformin with glimepiride therapy was Rs.2556.72/-

Metformin with Voglibose therapy:

In our study 1.5 % (n=5) were under Metformin with Voglibose therapy, among them patients diagnosed with DM and without comorbidities were 80 % (n=4) with an average annual cost of Rs.10,200 /-, direct annual drug cost Rs. 8978.4/-

Metformin with Teneligliptin therapy:

15.3 % (n=49) of the study population were under Metformin with Teneligliptin therapy, among them patients diagnosed with DM and without comorbidities were 42.8 % (n=21) with an average annual cost of Rs.13,200/- and direct annual drug cost of Rs. 7757.2/-

Metformin with Sitagliptin therapy:

In our study 2.5 % (n=8) were under Metformin with Sitagliptin therapy among them patients diagnosed with DM and without comorbidities were 25 %) (n=2) with an average annual cost of Rs. 15,400/-, with a direct annual drug cost Rs.9096/-. Our results are consistent with the study conducted by T. Tamilselvan *et al,* [5] with a direct annual drug cost Rs.9382/-. Our results are contrast to the study conducted by Chirstina S. kwon *et al,* [9] with the direct annual drug cost of Rs. 246,680/-

Metformin with Mixtard therapy:

In our study 5.9 % (n=19) patients were under Metformin with Mixtard therapy, among them patients diagnosed with DM and without comorbidities were 55 % (n=5) with an average annual cost of Rs.18,500/-, and direct annual drug cost of Rs.11,215.2/-

Mixtard therapy:

In our study 13, 4 % of the patients were only under insulin (Mixtard) therapy, among them patients diagnosed with DM and without comorbidities were 53.8 % (n=7) with an average annual cost of Rs. 23,560/- and direct annual drug cost of Rs.12,720/-

Cost variations are due to inadequate control of disease along with duration of disease process. Individuals under metformin therapy who had inadequately controlled due to the following reasons such as abnormal glycemic index, improper follow up, non-adherence to medication, irregular screening for laboratory tests, unhealthy life style changes or lack of physical activity which will resulted in switching from monotherapy to dual therapy, further towards triple and injectable therapies.

Cost burden in comorbidities:

DM with HTN:

Metformin therapy:

Of the study population, 25.6 % (n=82) were under metformin therapy, among them 47.5 % (n=39) are diagnosed with DM and HTN who were under metformin only therapy with an average annual cost of Rs.12,350/-, direct annual drug cost Rs.1375.2/-, laboratory cost of Rs.2010/-, physician visit of Rs.1800/- respectively.

Metformin with Glimepiride therapy:

In our study 40.3 % (n=129) were under metformin with glimepiride therapy, among them 36.4 % (n=47) are diagnosed with DM and HTN who were under metformin with glimepiride therapy with an average annual cost of Rs.13,450/-, direct annual drug cost Rs.3912/-, laboratory cost of Rs.2010/- and Physician visit Rs.1800/- respectively. Results of our study are in distinction to the study conducted by Ian F. Walker *et al,* [11] where the direct annual cost was found to be Rs.27,020/-.

DM with HTN and Stroke:

Metformin therapy:

In our study 25.6 % (n=82) were under metformin only therapy and among them 2.4 % (n=2) were diagnosed with DM, HTN and Stroke who were on metformin only therapy. The average annual cost, direct annual drug cost, laboratory cost and physician visit cost were found to be Rs.5853/-, Rs.1375.2/-, Rs.2010/-, and Rs.1800/- respectively.

Metformin with Glimepiride therapy:

Of total study population 40.3 % (n=129) of the patients were under metformin with glimepiride therapy, among them 2.3 % (n=3) were diagnosed with DM, HTN and Stroke who were under metformin with glimepiride therapy. The average annual cost, direct annual drug cost, laboratory cost and physician visit cost were found to be Rs.8156 /-, Rs.3192/-, Rs.2010/- and Rs.1800/- respectively. In contrast to our results, Christian S kwon *et al,* [9] had stated that direct annual cost is about Rs.555, 730/-

DM with microvascular complications:

Metformin therapy:

Of the study population, 25.6 % (n=82 of the patients were under metformin only therapy, among them 4.8 % (n=4) were diagnosed with DM and microvascular complications who were under metformin only therapy. The average annual cost, direct annual drug cost, laboratory cost and physician visit cost was found to be Rs. 9480/-, Rs.1375.2/-, Rs.2010/- and Rs.1800/- respectively.

Metformin with Glimepiride therapy:

In our study 40.3 % (n=129) of the patients were under metformin with glimepiride therapy. Of these, 2.3 % (n=10) of the patients were diagnosed with DM and microvascular complications who were under Metformin with Glimepiride therapy. The average annual cost, direct annual drug, laboratory cost and physician visit cost was found to be Rs.10150/-, Rs.3912/-, Rs.2010 /- and Rs.1800 /- respectively.

Metformin with Teneligliptin therapy:

Of 15.3 % (n=49) patients who were under metformin with teneligliptin therapy, 10.2 % (n=5) patients were diagnosed with DM and microvascular complications who were under metformin and teneligliptin therapy. The average annual cost, direct annual drug cost, laboratory cost and physician visit cost were found to be Rs.16,450/-, Rs.7757.2/-. Rs.2010/- and Rs.1800/- respectively.

Metformin with Mixtard therapy:

In our study 5.9 % (n=19) patients were under metformin with mixtard therapy and among them 5.2 % (n=1) of the patients were diagnosed with DM and microvascular complications who were under metformin with mixtard therapy. The average annual cost, direct annual drug cost, laboratory cost and physician visit cost were found to be Rs.19,890/-, Rs.11215.2/-, Rs.2010/- and Rs.1800/- respectively. Results of our study are consonance to the results of Leelavathi D. Acharya *et al,* [12] who stated that the average annual cost of the patients who were diagnosed with DM and complications (n=116) were noticed to be about Rs. 17,382.12/-. The direct annual drug cost, laboratory cost and physician visit cost were noticed to be Rs. 17370/-, Rs. 1080/- and Rs.1200/- respectively. These results might be due to dominance of poverty in the urban and rural areas. These patients are vulnerable to delay in diagnosis of the condition and incomplete follow-up

DM+HTN+CKD:

Metformin therapy:

In our study 25.6 % (n=82) of the patients were under metformin only therapy. 12.1 % (n=10) were diagnosed with DM, HTN and CKD who were prescribed metformin only therapy. The average annual cost, direct annual drug cost, laboratory cost and physician visit was found to be Rs.11154.7/-, Rs.1375.2/-, Rs.2010/- and Rs.1800/- respectively.

Metformin with Glimepiride:

In our study 40.3 % (n=129) were under on metformin with glimepiride therapy. 9.3 % (n=12) were diagnosed with DM, HTN and CKD who were under metformin with glimepiride therapy. The average annual cost, direct annual drug cost, laboratory cost and physician visit cost was found to be Rs. 10628.5/-, Rs. 3912/-, Rs.2010/- and Rs.1800/- respectively. Our results are in contrast with the study conducted by Kerry A. Mc Brien *et al,*[13] where in the average annual cost in outpatient department of about Rs. 429,660/-.

Cost of illness with duration of disease:

In our study 12.1 % (n=39) of the patients with <1 year of duration of illness had tackled an average annual cost of illness of about Rs.4362./-. 65.3 % (n=209) of the patients with the 1-5 years of duration of illness had faced an average annual cost of illness of about Rs.7019.22/-. 16.8 % (n=54) of the patients with the 6-10 years of duration of illness had a burden of average annual cost of illness of about Rs.6786/-. 5.6 % (n=18) of the patients with >10 years of duration of illness of disease had met an average annual cost of illness of about Rs.5616/- in our study.

In consistent to our results, Behaylu assefa *et al,* [3] had stated that among the total study population (n=130), 70.78 % (n=92) of the patients with the duration of illness for 1-5 years had faced an average annual cost of illness of about Rs.6,230/-. 20 % (n=26) of the patients with duration of illness for 6-10 years faced an average annual cost of illness of about Rs. 6090/-. 53.8 % (n=7) of the patients with the duration of illness >10 years had faced an average annual cost of illness Rs. 5040/-

CONCLUSION:

Of total study population (n= 320) patients incidence of Type II DM was more in middle aged. Female were more predominant over male. Oral hypoglycemic agents were the most commonly prescribed followed by a combination of insulin in addition to oral hypoglycemic agents. Metformin was the most commonly preferred anti diabetic medication than TZD's, sulphonyl ureas and insulin. Metformin is more effective when compared to other monotherapy. Combination of metformin and DPP4 inhibitors is found to be more effective than any other combinations (Metformin& Teneligliptin, Metformin & Glimepiride, Metformin & Voglibose). Economic evaluation of therapy should be encouraged to ensure cost effective therapy for diabetic patients. For the initial treatment of Type II DM, Metformin may be considered as cost effective monotherapy. If blood glucose levels are inadequately controlled with monotherapy, Glimepiride may be suggestive in terms of cost effective therapy as an add on to Metformin. Patients who do not obtain optimal glycemic control with a fixed dose combination of oral hypoglycemic agents can be considered with fixed dose triple combinations, out of which combination of Glimepiride, Metformin, and Pioglitazone was found to be best options. Cost burden of DM is more in insulin therapy in comparison with other treatment patterns. Clinical pharmacist plays an important role in educating the patients about proper use of medication, screening for drug interactions, explaining monitoring devices and proper management of complications associated with diabetes. It is important to create awareness among health care professionals as well as every individual in early recognition of symptoms will be effective in prevention of disease process.

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ABBREVIATIONS:

BMI: Body Mass Index

CKD: Chronic Kidney Disease

CVD: Cardio Vascular Disease

FBS: Fasting Blood Sugar

HbA1c: Glycated Hemoglobin

HTN: Hypertension

IDDM: Insulin Dependent Diabetes Mellitus

NIDDM: Non-Insulin Dependent Diabetes Mellitus

OHA: Oral Hypoglycemic Agents

PLBS: Post Lunch Blood Sugar

TZD's: Thiazolidinediones

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