International Journal of Community Medicine and Public Health
Limaye D et al. Int J Community Med Public Health. 2017 Sep;4(9):3180-3185
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: http://dx.doi.org/10.18203/2394-6040.ijcmph20173653

Original Research Article

Cost-effectiveness study of antidiabetic drugs in type 2 diabetes mellitus patients from Mumbai, India

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Received: 14 July 2017
Revised: 29 July 2017
Accepted: 31 July 2017

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ABSTRACT

Background: Diabetes is fast gaining the status of a potential epidemic in India, with >62 million individuals currently diagnosed with the disease. India currently faces an uncertain future in relation to the potential burden that diabetes may impose on the country. An estimated US$ 2.2 billion would be needed to sufficiently treat all cases of type 2 diabetes mellitus (T2DM) in India. Many interventions can reduce the burden of this disease. However, health care resources are limited; thus, interventions for diabetes treatment should be prioritized. The present study assesses the cost-effectiveness of antidiabetic drugs in patients with T2DM from Mumbai, India.
Methods: A prospective cross-sectional study was performed to assess the cost-effectiveness of antidiabetic drugs in patients with T2DM. Face-to-face interviews were conducted by using a validated questionnaire in a total of 152 (76 males, 76 females) patients with T2DM from F-North Ward, Mumbai, India. Cost-effectiveness was determined on the basis of cost of antidiabetic drug/s, efficacy, adverse drug reactions, safety of administration, frequency of administration, and bioavailability.
Results: For treatment of T2DM in non-obese participants, Glimepiride+Pioglitazone costed least (₹ 3.7) per unit of effectiveness followed by Glimepiride (₹ 6.6), Gliclazide (₹ 8.1), Repaglinide (₹ 24.5), and Vildagliptin (₹ 45.2). For treatment of T2DM in obese participants, Metformin cost least (₹ 6.7) per unit of effectiveness followed by Glimepiride + Metformin (₹ 5.9) and Repaglinide (₹ 24.5).
Conclusions: In case of non-obese participants, cost effectiveness and prescribed treatments did not show a match, while for obese participants prescribed treatments were in line with cost effectiveness.

Keywords: Antidiabetic, Cost-effectiveness, Diabetes mellitus, India

INTRODUCTION

Diabetes Mellitus is a chronic metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in the insulin secretion, insulin action, or both.[1,2]

The status of diabetes has changed from being considered as a mild disorder of the elderly to one of the major causes of morbidity and mortality affecting the youth and middle aged people over the past 30 years. Six percent of the world population is affected by diabetes mellitus (DM).[1] It is important to note that the rise in prevalence is seen in all six inhabited continents of the globe.[3]

Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease.[4,5] In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively. According to Wild et al the prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India.[3] It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India, while China (42.3 million) and the United States (30.3 million) will also see significant increases in those affected by the disease.[3,7]

Rationale

Worldwide, diabetes mellitus has been recognized as the greatest challenge for all health care systems.[8] Care of diabetes presents a high burden for individuals and society. People with diabetes are at increased risk of macrovascular and microvascular complications and are more likely than people without diabetes to have other cardiovascular problems.[9] Diabetes prevalence and incidence rates in India are increasing rapidly, along with the high economic burden of its complications.[3] An estimated US$ 2.2 billion would be needed to sufficiently treat all cases of type 2 diabetes mellitus (T2DM) in India.[10] India currently faces an uncertain future in relation to the potential burden that diabetes may impose on the country. It is very important to conduct studies focusing on economic evaluations to make evidence based health decisions and, consequently, to offer the best risk and cost-effective treatment choices along with better quality of life for patients with diabetes. Present study was designed to assess the cost-effectiveness of antidiabetic drugs in patients with T2DM from Mumbai, India.

METHODS

Study design and participants

A prospective, randomized, cross sectional study was designed based on validated survey questionnaire. It was conducted in F-North ward of Mumbai, Maharashtra, India. Ethical approval was obtained from V.V. Hospital Independent Ethics Committee, Thane, India. Study was conducted from 1st February 2016 to 30th April 2016. Information about apartments and family members was acquired from the office of F-North ward, Mumbai Municipal Corporation. From their database, 1000 apartments having subjects with age of 30 – 75 were randomly selected. These apartments were visited by trained pharmacy students and a total of 200 subjects satisfying the inclusion criteria were identified from which 166 agreed to participate.

The inclusion criteria were age of 18–65 years, type 2 diabetes diagnosed within the 2 years prior to initiation of the present study, a consultation and a diabetes report from a physician within the period of 30 days prior to the interview date and written informed consent to participation in the study. Exclusion criteria were subjects with serious illness or pregnancy.

Study instrument

A survey questionnaire was designed in English after discussion with experts and a literature review of similar studies. The questionnaire was translated into Marathi and Hindi (local language) by experienced translator and back translated to English to ensure the content uniformity by another experienced translator. The validity of the questionnaire was evaluated in pilot studies, in a sub sample of 30 subjects to ensure that the questionnaire would be appropriate, and understandable among the prospective respondents. The pilot testing allowed wording modifications in questions and also gave estimate of the average time required for interview and filling of the questionnaire. This population was not part of the final study.

Collection of data

Each selected apartment was visited by trained pharmacy student to collect the data. The purpose of the research was explained to the participant. Anonymity and confidentiality were guaranteed and maintained. The researchers complied with the international ethical guidelines for research. The information collected from each participant included the gender, age, occupation, marital status, education, monthly family income per family member, waist/hip ratio, date since type 2 diabetic, fasting and post prandial glucose, glycosylated hemoglobin HbA1c report from physician (in last 30 days), name, formulation, strength, price of antidiabetic/s medication, and side effects if any. Data was recorded into predesigned case report form (CRF) by interviewers.

Data entry and analysis

Collected data from individual CRF was entered into Microsoft excel and was verified by the authors other than interviewers. The data were analyzed by Microsoft excel for finding out relevant statistics. Qualitative variables were analyzed statistically, presented as frequencies and percentages.

Cost- effectiveness calculations

Cost effectiveness calculations were done by following method.

- *Bioavailability*: It was identified from the standard pharmacology text book.[6]
- *Tolerability*: Percentage adverse drug reactions (ADR) were determined by following formula= (Number of adverse drug reactions/Number of patients on the treatment)×100.

- Tolerability was calculated as= 100-%ADR
- *Efficacy*: Efficacy calculations were done by following formulas.
  - Fasting blood glucose (FBG) efficacy. (Participants' FBG–130)/1.3
  - Post prandial glucose (PPG) efficacy. (Participants' PPG–180)/1.8
  - Drug efficacy for single patient = (FBG efficacy + PPG efficacy)/2
  - Average efficacy for a treatment = total efficacy for treatment/number of patients on that treatment.
- *Safety of administration*: For oral drugs was 100%.
- *Frequency of administration*: ratings were as follows OD=100, BD=50, TID=33.3, QD=25.
- Effectiveness of a treatment option = Sum of all criterion rating,
  - Where (Criterion Rating=Criterion value ×Assigned weight).
  - Assigned weights were based on the earlier study done by Abdulganiyu.[11]
- Cost effectiveness Analysis (CEA) was done by following method:
  - Anti-diabetic therapy is a lifelong management but follow up visit to physician is every 2-3 months. So for all treatments, the duration of therapy was considered as 3 months for calculations of cost effectiveness.
  - CEA= (Total cost for a treatment option for 3 months/ Effectiveness of the treatment option).
- This was done and compared for each antidiabetic treatment option presently prescribed for the respondents in this study.
- Sensitivity analysis was performed to test whether the decisions change when specific variable (e.g. cost, effectiveness) were altered within reasonable range (10-25%) in favor of less cost-effective option in the management of type 2 diabetes.

RESULTS

Table 1 shows the socio-demographic parameters of participants from Mumbai under study. A total of 152 participants with 76 (50%) males, 76 (50%) females were studied. The mean age was 54±11 years. Marital status, occupation, income and education of the participants is as shown in Table 1.

Table 1: Socio-demographic parameters of study participants from Mumbai.

Parameters (N=152)	Frequency	Percentage (%)
Gender		
Male	76	50
Female	76	50
Religion		
Hindu	152	100
Marital status		
With partner	145	95.4
Single	7	4.6
Occupation		
Employed	51	33.6
Business	40	26.3
Housewife	44	28.9
Retired	17	11.2
Monthly income / person		
Upper high class (≥10,000 INR)	38	25
High class (5000 to 9999 INR)	114	75
Education		
Graduate	93	61.2
Non graduate	59	38.8

Based on waist to hip ratio measurements, central obesity was seen in 33 (43.4%) male and 37 (48.7%) female participants.

Out of total 82 non obese participants, maximum were treated with glimepiride 33 (40.2%) followed by Vildagliptin 15 (18.3%), Gliclazide 14 (17.1%), Glimepiride+Pioglitazone 12 (14.6%), and Repaglinide 8 (9.8%). While out of 70 obese participants, maximum were treated with metformin 35 (50%) followed by Glimepiride+metformin 31 (44.3%), and Repaglinide 4 (5.7%).

As shown in Table 2, when effectiveness alone was considered as the criteria rating for Glimepiride+Pioglitazone (96.4) was higher than Glimepiride (95.6), Gliclazide (88.4), Vildagliptin (87.6) and Repaglinide (73.4) in non-obese participants. While in obese participants the criteria rating for Glimepiride+Metformin (90.8) was higher than Metformin (80.9) and Repaglinide (73.4).

Table 2: Effectiveness of a treatment options used in the study.

		Glimepiride N=33		Vildagliptin N=15		Gliclazide N=14		Glimepiride and pioglitazone N=12		Repaglinide* N=12		Metformin N=35		Glimepiride and metformin N=31	
		Non-obese participants										Obese participants			
Criteria	Assigned weight	Value	Criteria rating	Value	Criteria rating	Value	Criteria rating	Value	Criteria rating	Value	Criteria rating	Value	Criteria rating	Value	Criteria rating
Efficacy	0.4	94	37.6	89	35.6	85	34	96	38.4	68	27.2	94	37.6	93	37.2
Tolerability	0.2	90	18	100	20	100	20	100	20	100	20	86.6	17.3	93	18.6
Safety	0.1	100	10	100	10	100	10	100	10	100	10	100	10	100	10
Frequency	0.1	100	10	50	5	50	5	100	10	50	5	50	5	100	10
Bioavailability	0.2	100	20	85	17	97	19.4	90	18	56	11.2	55	11	75	15
Sum	1		95.6		87.6		88.4		96.4		73.4		80.9		90.8

Table 3: Cost effectiveness analysis (CEA) and sensitivity analysis of treatment options used in the study.

Treatment option	frequency per day	Cost of one tablet (₹)	daily cost (₹)	cost for 3 months (₹)	criteria value	CEA	increase 25 %cost	decrease 25% cost	criteria value	CEA with 25% more	CEA with 25% less
Non-obese participants											
Glimepiride and pioglitazone	1	4	4	360	96.4	3.7	450	270	96.4	4.7	2.8
Glimepiride	1	7	7	630	95.6	6.6	787.5	472.5	95.6	8.2	4.9
Gliclazide	2	4	8	720	88.4	8.1	900	540	88.4	10.2	6.1
Repaglinide	2	10	20	1800	73.4	24.5	2250	1350	73.4	30.6	18.4
Vildagliptin	2	22	44	3960	87.6	45.2	4950	2970	87.6	56.5	33.9
Obese participants											
Metformin (HCL)	2	3	6	540	80.9	6.7	675	405	80.9	8.3	5
Glimepiride and metformin	1	6	6	540	90.8	5.9	675	405	90.8	7.4	4.5

As shown in Table 3, for treatment of T2DM in non-obese participants, Glimepiride+Pioglitazone costed least (₹ 3.7) per unit of effectiveness followed by Glimepiride (₹ 6.6), Gliclazide (₹ 8.1), Repaglinide (₹ 24.5), and Vildagliptin (₹ 45.2). For treatment of T2DM in obese participants, Metformin cost least (₹ 6.7) per unit of effectiveness followed by Glimepiride+Metformin (₹ 5.9) and Repaglinide (₹ 24.5).

Sensitivity analysis done by assuming 25% increase in the cost and 25% decrease in the cost, indicated that the decision remains valid, confirming Glimepiride +Pioglitazone was most cost effective treatment for non – obese T2DM participants while for obese T2DM participants it was Metformin.

DISCUSSION

In case of non-obese participants, effectiveness for Glimepiride+Pioglitazone (96.4) was higher than Glimepiride (95.6), Gliclazide (88.4), Vildagliptin (87.6) and Repaglinide (73.4). This is in agreement with UKPDS report which established that, although relatively effective in the short term, oral agent monotherapy with sulfonylureas or metformin is insufficient to maintain glycemic control against the relentless background of progressive beta cell failure.[12] The addition of metformin to a sulfonylurea generally provides only temporary respite and many patients require further additional therapies.[13,14] The advent of thiazolidinediones has provided clinicians with further options for oral agent combination therapy. Combining a thiazolidinedione and a sulfonylurea would appear to be a rational therapeutic approach in type 2 diabetes as their distinct complementary glucose-lowering mechanisms of action provides potential for synergy.[12] Derosa has shown the potential benefits of combining pioglitazone plus glimepiride on patient compliance, targeting the dual effects of insulin resistance and beta-cell dysfunction and affecting a number of metabolic and cardiovascular parameters.[12] However it was seen that in clinical practice maximum non obese participants were treated with glimepiride 33 (40.2%) followed by Vidagliptin 15 (18.3%), Gliclazide 14 (17.1%), Glimepiride+ Pioglitazone 12 (14.6%), and Repaglinide 8 (9.8%). This shows the gaps between the available scientific information and it's use in clinical practice.

While a look at the results in case of obese participants effectiveness for Glimepiride+Metformin (90.8) was higher than Metformin (80.9) and Repaglinide (73.4). Quite similar number of participants were treated with metformin 35 (50%) followed by Glimepiride+ metformin 31 (44.3%), and least were treated with Repaglinide 4 (5.7%).

This is in line with the study done by Kim which showed combination therapy with metformin and glimepiride had superior efficacy than metformin alone.[15] Glimepiride and metformin are the most common and widely used oral hypoglycemic agents in the world. Metformin improves insulin resistance, and is recommended as the first choice medication for newly diagnosed type 2 diabetes patients by most guidelines. Glimepiride is a third generation sulfonylurea that stimulates insulin secretion. Unlike conventional sulfonylurea, glimepiride has high selectivity toward the pancreatic ATP-sensitive potassium channel, increases glucose transport, and shows various extrapancreatic effects in muscle and fat cells.[16,17] For these benefits, glimepiride is prescribed as a primary monotherapy or in combination with metformin.[18]

Cost effectiveness analysis results were line with the effectiveness of treatments used in the present study, Glimepiride+Pioglitazone cost least (₹ 3.7) per unit of effectiveness in case of non-obese participants. Metformin (₹ 6.7) and Glimepiride+Metformin (₹ 5.9) were similar in terms of cost per unit of effectiveness in case of obese participants.

The results of this study support the reported fact that cost effectiveness analysis could help to make decisions about whether new drugs should be included in a drug formulary list where decisions are made. These decisions are made based on the principle that if a drug is not better than a comparable product, it should not cost more, if it is superior to existing therapies but more expensive (a common situation) and funds are available, any extra expenditure should represent "value for money".[19]

The present finding is significant because it has given a guide to institutional treatment and formulary system development for anti-diabetic therapy based on cost effectiveness. Institutional Treatment Guideline for anti-diabetic therapy and Hospital Drug Formulary based on cost-effectiveness could therefore be developed using this and/or similar research methodology. This pharmaco-economic approach is presently lacking in Indian public and private Hospitals. The work provides evidence based information that could be used to change prescription practice- irrational prescription of less cost-effective anti-diabetics over more cost-effective ones, by using the information for educational intervention at prescribers' and managerial levels. The resultant effect will be cost savings in drug therapy. The use of valid economic evaluation methods to measure the value and impact of new services can increase acceptance of such programs by the medical profession, third party payers and consumers

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Limaye D, Todi K, Shroff J, Ramaswamy A, Kulkarni P, Limaye V, et al. Cost-effectiveness study of antidiabetic drugs in type 2 diabetes mellitus patients from Mumbai, India. Int J Community Med Public Health 2017;4:3180-5.