CLINICAL PHARMACY ACTIVITIES IMPACTING CONTEMPORARY PRESCRIPTION PATTERN OF ORAL ANTI DIABETIC DRUGS AND ITS COMPLICATIONS IN TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT:
The main aim of the study is to observe the impact of clinical pharmacy activities on contemporary prescription pattern of oral anti diabetic drugs and its complications in tertiary care teaching hospital. Study was based only on those patients who have type 2 diabetes and admitted in a tertiary care hospital. The medication details of all these patients were collected and documented in a suitable data collection form. The patients’ socio demographic data such as age, sex, weight, height, Disease specific information like past medical history, reason for admission, allergies, Medication history including drug administered, route of administration, dosage, drugs involved type of drug related problems, reason for intervention, suggestion made by clinical pharmacist, Dietary habits, life style and medication adherence of patients, Acceptance and significances of pharmacist interventions were documented in a suitable designed patients data collection form. The analysis of our study has shown that patients with type-2 DM with complications, insulin therapy was preferred over OHAs. In majority cases, insulin therapy was used in combination with OHAs for the better control of diabetes in presence of alarming levels of glycemic levels. Insulin regular was the first choice of insulin therapy and metformin was the most prescribed OHAs. We also found that patient education regarding lifestyle modification and diabetes achieve maximum control of glycemic levels in patients. Implementation of clinical pharmacy services plays important role in educating and following up of suspected drug interactions that promotes improved quality of life. The present study suggested that management of diabetic patients including dietary changes, life style modifications can control high blood glucose levels. Effectiveness of therapy is...
influenced by selection of medication, as well as patient’s adherence with prescribed drug dosage regimens.

**Keywords:** Anti-diabetic drugs, Clinical pharmacy services , contemporary prescription pattern.

**INTRODUCTION:**
Diabetes is a reduced of metabolic sicknesses portrayed by hyperglycemia due to reduced insulin secretion, or activity or both. The ongoing hyperglycemia of diabetes is related with long term effects, complications on different organs, particularly the eyes, kidneys, nerves, heart and veins [1]. As per International Diabetes Federation (IDF), the quantity of individuals with in the world in 2013 was 382 million, which is said to nearly increment to very nearly 592 million by 2035. India has the questionable differentiation of being home to countless individuals experiencing diabetes. As indicated by IDF, 65.1 million of adults in India experienced diabetes in the year 2013 [2]. It has been anticipated that the pervasiveness of diabetes in the grown-up populace in India will be 6% continuously 2025 [3]. Present day standards of the board of diabetes center around infection counteraction, screening high risk people and forceful treatment of people in the pre-diabetic state. The current pharmacotherapy of diabetes mellitus incorporates treatment with medications like insulin and oral hypoglycemic specialists. Oral hypoglycemic specialists are heterogeneous in their methods of activity, security profiles and decency. The fundamental classes incorporate agents that mimic insulin discharge (sulfonylureas and fast acting secretagogues), diminish hepatic glucose creation (biguanides), defer assimilation and ingestion of gastrointestinal starch (α-glucosidase inhibitors), further develop insulin activity (thiazolidinediones) and incretin-based treatments like dipeptidyl peptidase-4 inhibitors [4-6]. As indicated by World Health Organization, drug usage is characterized as the promoting, appropriation, solution and utilization of medications in a general public with exceptional accentuation on the subsequent clinical, social and financial results [7]. A few medication usage studies on enemy of diabetic specialists are accessible across the world, including India [8-19]. The main aim of the study is clinical pharmacy activities impacting contemporary prescription pattern of oral anti diabetic drugs and its complications in tertiary care teaching hospital. The general objectives of study is to initiate the clinical pharmacy services for patients with Diabetes and its comorbidities

**STUDY METHODOLOGY:**
**Study design:** prospective, observational, study.
**Study location:** Study was carried out in a tertiary care hospital. From July 2018 to September 2019.
**Study setting:** Study was based only on those patients who have type 2 diabetes and admitted in a tertiary care hospital.
**Study criteria:**
**Inclusion criteria:** Patients who were diagnosed with Type 2 Diabetes admitted in hospital, and Patients with comorbid diseases were included in the study.
Exclusion criteria: Diabetes patients admitted in other departments except general medicine and surgery.

Study Duration: The study was carried out for a period of (from July 2018 to September 2019)

Sources of data: The data for the study was taken from case sheets of patients who had type 2 diabetes, Treatment charts, Investigation reports, ADR notification form, Drug intervention and interaction forms. Personal interviews with patient/patient’s attendant Personal interviews with reporting persons/clinicians Past history of medication use, which are generally obtained from-Past prescriptions, Reports of Medical and surgical interventions, Referral letters, discharge cards/Advice on discharge.

Study procedure: Ethical committee clearance and formal permission from medical superintendent (MS) of tertiary hospital were obtained prior to initiation of the study. The clinical pharmacist impact of clinical pharmacy services can improve the patient quality of life. All the clinical pharmacy services will be subjected for verification by consultation with the clinical pharmacist in department of pharmacy practice.

Data Collection and Pharmacist intervention: All these inpatients admitted to wards will be reviewed on daily basis. The medication details of all these patients were collected and documented in a data collection form. The patients’ socio demographic data such as age, sex, weight, height, Disease specific information like past medical history, reason for admission, allergies, Medication history including drug administered, route of administration, dosage, drugs involved type of drug related problems, reason for intervention, suggestion made by clinical pharmacist, Dietary habits, life style and medication adherence of patients, Acceptance and significances of pharmacist interventions will be documented in a suitable-designed patients data collection form. During the study period patient was reviewed on daily basis, if any change in medication orders or laboratory details were obtained and updated in the patient data collection form. All the collected patient data and medical data will be subjected for independently review by clinical pharmacists to identify the drug related problems.

Drug related problems suggestions: All identified drug related problems were provided at the earliest possible time to concerned health care professional for suitable actions. The suggestions of drug related problems will be categorized as any one of the following: Change in dosage form, change in drug dose, Addition of drug, Cessation of drug, Substitution of drug, change in route of administration, change in frequency of administration, Change in duration of therapy, Others.

Evidenced of Intervention consulted: The drug information resource consulted for each student pharmacist intervention were classified as follows

Primary sources: Scientific journals, literatures, abstracts.
Secondary sources: Databases: Micromedex,
Tertiary sources: Textbooks such as Martindale, Stockley's drug interactions, AHFS guidelines, Goodman and Gillman of pharmacology and therapeutics, Pathophysiological approach by Dipiro.
American association of Diabetes guidelines, National kidney foundation-Sydney, JNC 8 guidelines

**Patient counselling & medication adherence:** Patient counselling was done by providing patient information leaflets which includes information about the Disease, Diet, Exercise and lifestyle modification. Medication adherence was measured by asking relevant questionnaires.

**Analysis of the results**
All the data collected were analysed by descriptive analysis and represented as charts and tables.

**RESULTS:**

**Age group and gender wise categorization of hypertensive patients**
In present study patients were grouped gender wise into male and female and their respective percentage proportion was calculated. A total of 205 patients were found during the study. Among 205 patients, 123 (60%) were male and 82 (40%) were female patients. Majority 27 (32.68%) were 40-49 years followed by 20 (26.34%) were 50-59 years, followed by 17 (23.90%) were 60-69 years, followed by 12 (9.75%) 70-79 years, followed by 5 (3.90%) were above 80 years age group patients. Results were summarized in figure 1 and 2.

**Age group and gender wise categorization of hypertensive patients**
In present study patients were grouped gender wise into male and female and their respective percentage proportion is calculated. A total of 450 patients were found during the study. Among 450 patients, 265 (58.88%) were male and 185 (41.11%) were female patients. Majority 123 (27.33%) were 70 years & above age group, followed by 119 (26.44%) were 60-69 years, followed by 102 (22.66%) 50-59 years, followed by 80 (17.77%) were 40-49 years, followed by 24 (5.33%) 30-39 years, followed by 2 (0.44%) were 20-29 years age group patients.

**Alcoholic and smoker patients:**
This study reveals the social habits of the patients admitted in a hospital. Out of 205 patients’ majority are nonalcoholic and nonsmokers 136 (66.34%) were found, 45 (21.95%) were alcoholic, 24 (11.70%) were found. Results were summarized in figure 3.

**Complications of diabetes mellitus:**
In the study out of 205 patients 91 (44.39%) were found majority with both macrovascular and microvascular complications, 26 (12.68%) was found microvascular complications, and 88 (42.92%) were macrovascular complications. Results were summarized in figure 4. Majority of microvascular complications nephropathy 12 (5.85%) and very less neuro and retinopathy 01 (0.48%) were found. Majority of macrovascular found with hypertension 38 (18.53%) and very less PVD, ANGINA, IHD + LEFT VENTRICULAR DYSFUNCTION each 1 prescription (0.48%) were found. Results were summarized in figure 5 and 6.

**Pattern of drug regimen prescribed for diabetic patients:**
Out of 205 patients insulin were prescribed more 167 (41.03%) in diabetic patients followed by OHAs combination drug regimen 145 (35.62%) and mono drug regimen were 95 (23.34%) prescriptions. Results were summarized in figure 7.

Out of 95 mono drug regimen metformin were prescribed more 48 (23.41%) followed by glimiperide 26 (12.68%) and very less dapagliflozin, canagliflozin each 1 (0.48%) were found. Results were summarized in figure 8.

145 two drug regimens were prescribed. Majority are metformin + glimiperide 112 (77.24%) were found and very less are glyburide + metformin 06 (2.9%). Results were summarized in figure 9.

167 prescriptions were prescribed with insulin. Majority are insulin regular 86 (41.95%) were found. Results were summarized in figure 10.

Assessment of DDI in anti-hypertensive prescriptions

During the study total 125 DDI’s were found. Out of the 56 (27.31%) were major, 69 (33.65%) were moderate drug interactions. Out of these 56 major DDI’s 24 (11.70%) DDI’s were of Glimiperide + Aspirin and 69 moderate interactions majority interactions 12 (5.85%) DDI’s were of Metformin + Metoprolol. Results were summarized in figure 11 and 12.

Study of efficacy of hypoglycemic agents on diabetic patients

During the hospital stay the various types of hypoglycemic drugs were prescribed to patients to reduce RBS & FBS. Out of these Metformin significantly reduced FBS ($p=0.216$), Glimiperide reduced SBP significantly ($p=0.0034$) and there was significant reduction were found in RBS ($P=0.0034$) on discharge when compared with respective Random blood sugar on admission.

In combination therapy metformin + glyliperide showed significant reduction in RBS ($p=0.034$) and FBS ($p=0.144$) on discharge day when compared with RBS on admission respectively and other combinations like Metformin + sitagliptin show reduced RBS ($p=0.6253$) significantly as compared with RBS on admission. Remaining results were summarized in Table 1.

Comparison of efficacy between mono and combination therapy

Here we had chosen 1 drug and their combinations to compare the efficacy of drugs. Mean reduction in RBS increased significantly ($p=0.018$) in patients prescribed. Metformin and Glimiperide combination when compared with mean reduction in RBS of only Metformin treated patients. Likewise Table 4 reveals mean reduction in RBS increased significantly ($p=0.451$) in Metformin And Sitagliptin received patients as compared with Metformin alone treated and there is significant increase in mean reduction in FBS in patients treated with combination of Metformin And Sitagliptin as compared with alone Metformin remaining combinations doesn’t show any significant difference. Results were summarized in table 2.

Clinical Pharmacy Services in Diabetic Patients at A Tertiary Care Hospital:

Clinical pharmacy services provided in Diabetic Patients patients admitted in a tertiary care hospital. Out of 205 patients 125 (60.97%) drug drug interactions (major + moderate), 156 (76%) patient counseling were provided, 03 (1.46%) adverse drug reactions were found, 12 (5.85%) medication errors were found, and 53 (25.85%). Accompanying major age groups...
having Type 2 diabetes mellitus is 40-49 years i.e. 32.68% and 50-59 years i.e., 26.34%. Results were summarized in figure 13.

Figure 1: Male and female patients

Figure 2: Age wise distribution of patients.
Figure 3: Alcoholic and smoker patients

Figure 4: Graphical representation of frequency of complications in diabetes mellitus

Figure 5: Graphical representation of frequency of microvascular complications
Figure 6: Graphical representation of frequency of macro vascular complications.
Figure 7: Drug therapy given to the patients

Figure 8: Monotherapy of OHA’S
Figure 9: combination therapy of oral hypoglycemic agents

Figure 10: Insulin therapy
Figure 11: Graphical representation of major drug interactions found in 205 prescriptions

Figure 12: Graphical representation of moderate drug interactions were found in 205 prescriptions
Table 1: Efficacy of Monotherapy Oral hypoglycaemic Drugs in Patients in A Tertiary Care Hospital:

<table>
<thead>
<tr>
<th>Random blood sugar</th>
<th>ON ADMISSION</th>
<th>ON DISCHARGE</th>
<th>p-Value</th>
<th>t-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEAN±SEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin</td>
<td></td>
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<tr>
<td>RBS</td>
<td>250±6.268</td>
<td>130±2.981</td>
<td>0.116</td>
<td>2.561</td>
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<tr>
<td>FBS</td>
<td>86.75±5.126</td>
<td>80.26±2.45</td>
<td>0.0138</td>
<td>2.135</td>
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<tr>
<td>Glimiperide</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>RBS</td>
<td>234±6.761</td>
<td>130.5±2.589</td>
<td>0.0286</td>
<td>2.506</td>
</tr>
<tr>
<td>FBS</td>
<td>82.75±5.126</td>
<td>76.25±1.830</td>
<td>0.2522</td>
<td>1.194</td>
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<tr>
<td>Sitagliptin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBS</td>
<td>215.1±13.22</td>
<td>128.4±1.601</td>
<td>0.5253</td>
<td>0.6543</td>
</tr>
<tr>
<td>FBS</td>
<td>85.36±12.22</td>
<td>82.29±2.012</td>
<td>0.8561</td>
<td>0.4561</td>
</tr>
<tr>
<td>Teneligliptin</td>
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</tbody>
</table>

Figure 13: Clinical pharmacy services
<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Mono Metformin</th>
<th>Combination 1 Metformin + Glimperide</th>
<th>Combination 2 Metformin + Sitagliptin</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=48</td>
<td>N=112</td>
<td>N=12</td>
<td></td>
</tr>
<tr>
<td>Mean reduction in RBS</td>
<td>45.15±8.255</td>
<td>12.0±18.0</td>
<td>43.50±17.95</td>
</tr>
<tr>
<td>Mean Reduction in FBS</td>
<td>12.50±5.369</td>
<td>4.5±1.0</td>
<td>12.0±12.29</td>
</tr>
</tbody>
</table>

Table 2: Comparison of efficacy between mono and combination therapy of Metformin

DISCUSSION:
Diabetes mellitus (DM) is a chronic illness along with disturbance of carbohydrate, protein, and fat metabolism due to defects in insulin secretion and/or insulin response that requires life-long medical care and ongoing patient self-management and support to prevent acute complications and to reduce the risk of morbidity and mortality. It is a major public health service challenge worldwide with global prevalence estimated to increase from 2.8% in 2000 to 4.4% in 2030, an increase from 171 million people to 366 million people in 30 years. The most recent Global Burden of Disease study estimates the diabetes is the seventh leading cause of mortality with disability worldwide. Diabetes is associated with reduced quality of life and life expectancy.

In this study, an attempt has been made to evaluate the prescribing attitude of a physician along with the implementation of clinical pharmacy services on patients with type-2 DM with complications in the hospital. The present study was based on ADA guidelines. The study procedure used here includes prospective and cross-sectional studies using the data collection forms and hospital information system. The analysis of the prescribing pattern of a physician promotes the rational use of drugs, also increases the efficacy of treatment. This also increases the safety of patients by promoting the decrease in morbidity and mortality rates in patients.
A total of 205 subjects were included in this study, our study suggests that out of 205 patients who were treated with the anti-diabetic drugs all of the subjects were having type-2 DM with complications in which male patients (60%) has more prevalence rate than female patients (40%). Our results provide a direct evidence of an increasing burden of type-2 DM with complications especially among the middle aged population. Prevalence of type-2 DM with complications is mostly seen with in the age groups of 40-49 yrs (32.68%) and 50-59 yrs (26.34%).

Our study shows that 4% of the patients were obese who are leading an unhealthy lifestyle who have a major chance to be prone to diabetes at an young age along with the 11.70% of patients who were smokers and 21.95% were alcoholic, these results indicates the risk factors of type-2 DM with complications. Out of 205 subjects, only 12.68% were suffering from microvascular complications which are only seen in patients with type-2 DM, a majority of 42.92% were having macrovascular complications which are also seen in patients with cardiac disorders and 44.39% of patients had both micro and macrovascular complications. In microvascular complications nephropathy (5.85%) was most commonly seen and in macrovascular complications (18.53%) of hypertension cases were seen.

During our study period we have assisted with the clinical pharmacy services provided to the patient. The services provided were: Identifying the Drug interactions and reporting them, Adverse drug reactions, Medication errors, Counselling the patients. Some drug interactions found in the prescriptions were: Glimepride+Aspirin(11.70%), Metformin+Aspirin(8.78%), Metformin+Metoprolol (5.85%), Insulin Aspart+Metformin (3.41%). Adverse Reactions Found Were 1.46%, Medication errors found and rectified were 5.85%. Total patient counsellings done were to 156 Patients.

Our study suggests that most of the patients needed insulin therapy (81.03%) to control their blood glucose levels. This suggests that insulin therapy was more commonly used than that of the OHAs. This suggests that subcutaneous route were the most desired routes of administration of drugs than oral route. This study on prescribing pattern suggests that insulin therapy along with OHAs is the choice of most physicians in the treatment of type-2 DM. Insulin Regular And Human Mixtard Were The Most Commonly Prescribed Insulins, Whereas In Ohas Biguanides(Metformin) Were The First Choice Followed By Sulfonylureas (Glimepride). The Use Of Combination Therapy Is To Achieve Better Glycemic Control.

In Monotherapy Of Insulin, Insulin Regular(41.95%), Human Mixtard(25.36%), Insulin Glargine(3.90%), Insulin Aspart(3.41%), Insulin Glulisine(0.97%), Insulin Detemir(0.48%) Were The Major Choice. In Combination Therapy, Insulin Aspart+Insulin Aspart Protamine(4.39%), Insulin Lispro+Insulin Lispro Protamine (0.97%) were the most common choice.

In Monotherapy Of Ohas, Metformin (23.41%), Glimepiride (12.68%), Sitagliptin (2.92%), Voglibose (0.97%), Acarbose (0.48%), Saxagliptin (1.95%), Teneligliptin (2.43%), Canagliflozin (0.48%) Dapagliflozin (0.48%), Gliclazide (0.48%) Were Prescribed. In Fixed Combination Therapy Of Ohas, Metformin + Glimepiride (54.63%) Were Most Commonly Prescribed, Sitagliptin + Metformin (5.85%), Vidagliptin + Metformin (3.90%), Glyburide +
Metformin (2.92%) Were Commonly Prescribed. In Triple Therapy Glimepiride + Metformin + Voglibose (3.41%) was mostly used.

In the analysis of the prescribing pattern, we found out that the drugs were prescribed based on the brand name instead of the generic name. This suggests the influence of pharmaceutical companies and the popularity of brands in the market. This study also suggests that in some hospitals still insulin based therapy is still dominant over the OHAs.

This study also suggests that monotherapy of insulin or OHAs was the most successful therapy and also shows success levels in the control of glycemic levels in the subjects. This also makes a strong point that insulin therapy is most commonly used rather than OHAs.

The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014. The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014. The prevalence of diabetes has been seen increased in low-income countries. Diabetes has been seen increased in middle aged people. Diabetes is more prevalent in people who smokes and consume alcohol. Diabetes is the major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation. An estimated 3.4 million deaths were reported in 2015 due to diabetes. Almost half the deaths were seen in patients before 70 years. In an article, WHO mentioned that diabetes will be the 7th leading cause of death in 2030. Healthy diet, regular physical activity, etc are some of the ways to prevent the onset of type-2 DM. Diabetes and its complications can be prevented with diet, regular physical activity, medication, regular screening of blood glucose levels.

The analysis of our study has shown that a few guidelines in prescribing pattern had been deviated by preferring insulin therapy over OHAs as per AMERICAN DIABETES ASSOCIATION. In majority of cases, insulin therapy was used in combination with OHAs for the better control of diabetes in presence of alarming levels of glycemic levels. INSULIN REGULAR was the first choice of insulin therapy and METFORMIN was the most prescribed OHA’s. We also believe that patient education regarding lifestyle modification and diabetes is strongly advised to achieve the maximum control of glycemic levels in patients. We also believe that implementation of clinical pharmacy services by proper involvement of a clinical pharmacist is very important and also a slight change in the prescribing pattern will enhance better results in patient safety.

**CONCLUSION:**
The analysis of our study has shown that in patients with type-2 DM with complications, insulin therapy was preferred over OHAs. In majority cases, insulin therapy was used in combination with OHAs for the better control of diabetes in presence of alarming levels of glycemic levels. Insulin Regular Was The First Choice Of Insulin Therapy And Metformin Was The Most Prescribed OHA’S. We also believe that patient education regarding lifestyle modification and diabetes is strongly advised to achieve the maximum control of glycemic levels in patients. We also believe that implementation of clinical pharmacy services plays important role in educating and following up of suspected drug interactions that promotes improved quality of life. The result of our study suggests management of diabetic patients including dietary changes, life style modifications can control high blood sugar levels.
Effectiveness of therapy is influenced by selection of medication, as well as patient’s adherence with prescribed drug dosage regimens.

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