A Prospective Observational Study to Find out Prevalence of Polypharmacy, Co-Morbidities and Drug-Related Problems among Type 2 Diabetes Patients at a Tertiary Care Teaching Hospital

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Authors’ contributions
This work was carried out in collaboration among all authors. Authors RH, KG and JL designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors MT, SS and PP, author DJ and TR managed the analyses of the study. Authors RM and HSR managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Presently India, depicts 49% of the world’s diabetes burden, with an approximated 72 million cases in 2017. Comorbidities make type 2 Diabetes Mellitus (DM) management complicated for health care providers. Therefore, patients have been prescribed multiple drugs. As a result of polypharmacy, the chances of the occurrence of drug-related problems (DRPs) increase.

Objective: The present study aimed to find out the prevalence of comorbidities, polypharmacy, and drug-related problems among type 2 DM patients.

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Methodology: A prospective observational study was conducted for six months among 110 patients having type 2 DM. Based on inclusion and exclusion criteria data were collected. All collected cases were analysed for the number of medications prescribed and comorbidities present. Prescriptions were further assessed to find out the drug-related problem.

Results: Comparing the gender proportionality, male represents 59% (n=65) and female represents 41% (n=45) of the study population. The present study evaluated that 91% (n=100) of patients were having at least one comorbid condition or complication along with diabetes, the most common being cardiovascular disorders. The average number of drugs prescribed is 7.86±7.83 per patient. Polypharmacy was observed in 84.54% (n=93) of the patients. A total of 180 DRPs were found among 110 patients.

Conclusion: The present study concluded that the increase in the number of co-morbidities significantly increases the burden of polypharmacy which can further lead to DRPs. Reducing the number of pills and the presence of a clinical pharmacist in prescription monitoring can help to alleviate the problems of polypharmacy and its consequences.

Keywords: Diabetes mellitus; comorbidities; polypharmacy; drug-related problem.

1. INTRODUCTION

Diabetes is a chronic metabolic disease characterized by hyperglycaemia which results from flaws in insulin action or insulin secretion or both [1]. It can also be defined as metabolic circumstances in which the blood sugar levels are higher than usual [2]. Type 1 diabetes which is also known as childhood-onset diabetes or insulin-dependent mainly distinguished by a lack of insulin production. Type 2 diabetes which was earlier known as adult-onset diabetes or non-insulin-dependent is activated by the body’s insufficient utilization of insulin. It mostly results from the absence of physical activity and overweight. Gestational diabetes is an increase in the number of glucose levels which is first identified during pregnancy and it may cause serious health risks for both the mother and her child [3]. In 2017, about 425 million people with diabetes were recorded around the world; which will increase to around 629 million by the year 2045. The number of adults with type 2 diabetes is increasing in most countries worldwide. The maximum number of people with diabetes were found between the ages of 40-59 years [4]. A current Indian Council of Medical Research funded study suggests the wide-ranging seriousness of this condition with some regions showing prevalence as high as 13% across the urban and rural areas [5]. India at present portrays 49% of the world’s diabetes burden, with an approximated 72 million cases in the year 2017, a rate likely to nearly double to 134 million by the year 2025 [6]. Diabetes is usually associated with other comorbid conditions. Co-morbidity is denoted as the presence of one or more chronic disease outcomes in the same person with a primary-condition [7]. According to some of the previous studies conducted prevalence of no less than one co-morbid condition along with type 2 diabetes mellitus was found to be in the range of 83.3-84% [8,9]. The non-diabetic co-morbidities that are usually observed with type 2 diabetes are hypertension, obesity, chronic kidney disease, dyslipidaemia, cardiovascular disease, depression, sleep disorders, and cancer. The diabetic co-morbidities observed are diabetic neuropathy, diabetic retinopathy, and diabetic nephropathy [7,10]. Polypharmacy is defined as the concurrent use of multiple medications, whether over-the-counter or prescription, by an individual patient [11,12]. The problems of polypharmacy include unnecessary medications, inappropriate drug combinations, and unsuitable drugs for specific patients such as the geriatric. Moreover, polypharmacy may result in drug-drug interactions, potential duplication of drug therapy, decreased adherence, adverse drug events, increase in the costs to the drug therapy, hospitalizations, decreased quality of life, additional surgical or medical interventions [13]. A prior study was conducted to find the incidence of polypharmacy in type 2 diabetes patients in a tertiary care teaching hospital in south India which was found to be 82.9% (≥5 drugs) and 17.11% (<5 drugs) [14]. A Drug-Related Problem is an event or situation that comprises drug therapy that possibly or interferes with anticipated health outcomes [15]. Based on a study performed by Inamdar S Z et al., on “Drug-related problems in geriatric patients with type 2 Diabetes mellitus”, the average drug-related problems were found to be 2.96 ± 2.2 per patient [16]. Drug-related problems can be prevented by avoiding medication errors. By the usage of computerized physician order entry tools, the
interpretation, transcription, prescription errors can be reduced. Few other measures to prevent drug-related problems are the education of individuals concerned with the process of, prevention of look-a-like products, distribution of drugs, and creating systems for early identification of adverse drug events. Early identification is important for avoiding adverse drug reactions and therefore every hospital should have a system for the recognition of adverse drug reactions [17]. Need for the study: We have observed that very few studies were done on this in Gujarat and there is no combined study on the prevalence of comorbidities, polypharmacy, and drug-related problems in type 2 diabetes patients in India. Also, the majority of the studies on diabetes are done in the geriatric population and very few on adult populations so we planned to do this study.

2. METHODOLOGY

This was a prospective observational study conducted for six months in the Department of General Medicine at Dhiraj General Hospital, Sumandeep Vidyapeeth Deemed to be University, Vadodara, Gujarat (India). Patients who were diagnosed with Type 2 Diabetes Mellitus with or without co-morbidities as well as ≥35 years of age were enrolled in the study after explaining to the patients about the details of the study, the Informed consent form was taken. The cases who experienced adverse effects due to overdose, suicidal or accidental intake of drugs, substance abuse, and receiving another system of medicines (Ayurveda, Unani), patients who are pregnant and lactating/nursing a child; unconscious and severely disabled patients who cannot be interviewed, pediatric patients, critically ill patients were excluded. All the relevant data was obtained from the patients’ medical records and through counselling the patients who visited the Out-Patient Department (OPD) or In-Patient Department (IPD). The cases were analysed for the number of medications prescribed and co-morbid conditions present. Further prescriptions were categorized into monotherapy and polytherapy. Polypharmacy for this study was considered as concurrent use of 5 or more drugs. Co-morbidities present were classified into diabetic complications and non-diabetic co-morbidities. In this study, drug-related problems (DRPs) such as ADR(s), drug-drug interaction, and drug use problems were considered for analysis. The identified DRPs were assessed for their possible causes and were further intervened. After the data collection, all the data were exported to statistical software for statistical analysis. All the quantitative data were represented in percentage (%) and mean ± standard deviation. Comparative statistical differences were calculated using appropriate parametric tests. The categorical data were represented in the median and comparative statistical differences were calculated by using appropriate non-parametric statistical tests. (Chi-square test and independent t-test). The graphical representative was used for a better understanding of data. A p-value of ≤0.05 was considered significant.

3. RESULTS

A total of 110 patients were included in the study based on inclusion and exclusion criteria. Out of 110 patients interviewed, we noticed that the total inpatients were 91% (n=100) while the number of OPD patients was just 9% (n=10). Comparing the gender proportionality, male represents 59% (n=65) and female represents 41% (n=45). In our study, the age of patients varies from 35 years to 80 years with a mean age of 55.26 ± 11.87 years. The maximum number of patients were from the age group of 51-60 years [28.8% (n=31)] followed by age group 41-50 years [25.45% (n=28)], and least number of patients were found in age group of 71-80 years [10.91% (n=12)]. An attempt was made to understand the social habits of the study population. The study revealed that 10(26%) patients were alcoholics, 15(39%) patients were found to be smokers, 12(32%) patients were found to be tobacco user and 1(3%) patient was having another habit (opioid user) in the overall population. Out of a total of 110 study participants, 100 (91%) patients were having one or more comorbid conditions along with diabetes. The average number of co-morbid conditions found in the study population was 1.98±1.29. The maximum number of co-morbidities was found to be 6. Out of 110 patients, 9.09% (n=10) had no co-morbidities, 80% (n=88) had 1-3 co-morbidities and 10.91% (n=12) had 4 or more co-morbidities. The result shows that 1-3 co-morbidities are more prevalent among males than females with the prevalence of 81.54% and 77.78% respectively.

Diabetic Mellitus (DM) patients usually suffer from various diabetic complications. In present study out of 110 patients, 19.09% (n=21) patients have diabetic complications. The number of patients with a single diabetic complication was found to be 18 which
Among 865 prescribe study population with an average of 7.86±7.83 total of 865 drugs were prescribed among 110 diabetes mellitus patients with co-morbidities. Out of all the patients with non-diabetic co-morbidities, the most common respiratory disorder was bronchial asthma (13.97%). The most common cardiovascular disorders were hypertension, IHD (Ischaemic heart disease), and heart failure. The second most prevalent non-diabetic co-morbidity was respiratory disorder (13.97%). The most common respiratory disorder was bronchial asthma and URTI (Upper respiratory tract infection). Rheumatoid Arthritis (0.52%) was the least prevalent non-diabetic co-morbidity that occurred in the patients. Out of all the patients with non-diabetic co-morbidities, metabolic syndrome was developed in only one patient (Fig. 1).

On foresight for prescribing pattern for type-2 diabetes mellitus patients with co-morbidities, a total of 865 drugs were prescribed among 110 study population with an average of 7.86±7.83 drugs per patient. Among 865 prescribed drugs the total number of anti-diabetic drugs observed was 181, while the remaining 684 were drugs other than anti-diabetic. The minimum number of drugs prescribed was found to be 3 and the maximum number of drugs was 17 among inpatients throughout their hospital stay. Human insulin was the most commonly prescribed anti-diabetic drug observed in the study comprising 54% followed by biguanides which comprise 13% of the total anti-diabetic drugs. Among the diabetics, 44.55% were prescribed with a single antidiabetic drug, 43.64% with two antidiabetics, 9.09% with three antidiabetics while 0.91% (n=1) with 4 antidiabetic drugs during their hospital stay. The most prescribed class of drugs other than anti-diabetic were found to be antihypertensive agents constituting 21% followed by antacids and antibiotics where both constituted 12% respectively.

Polypharmacy, for this study, is defined as the concurrent use of 5 or more drugs after excluding all the vitamin and dietary supplements. Polypharmacy was seen in 93(84.54%) patients out of 110 patients. A total number of 51 male patients out of 65 were found to be prescribed with polypharmacy which constituted 78.46%. On the other hand, 42 female patients out of 45 were prescribed polypharmacy which constituted 93.33%. Results reveal the prevalence of polypharmacy is greater among females when compared to male patients. Considering the age of patients, 38 out of 93 patients experiencing polypharmacy were ≥60 years of age. Polypharmacy was highest seen in the age group of 51-60 with 30.11% (n=28). Analytical results of polypharmacy show that majority of the patients took 5-8 drugs which constitute 68.81% followed by 9-12 drugs which were taken by 23.65% of patients. Prevalence of co-morbidities among patients with polypharmacy: Out of 93 patients experiencing polypharmacy, 92.47% (n=86) patients had co-morbid diseases. Amongst which 79.06% (n=68) patients had only non-diabetic co-morbidities, 3.48% (n=3) patients had only diabetic complications while 17.44% (n=15) patients had both diabetic complications as well as non-diabetic co-morbidities.

A total of 110 patient cases were reviewed were 82.72% (n=91) patients experienced 180 DRPs with an average of 1.63 DRPs per patient. Out of these 91 patients, the number of male patients was 54.94% (n=50) while the number of female patients were 44.56% (n=41). Drug-
Fig. 1. Prevalence rate of non-diabetic co-morbid condition

Table 1. Overall polypharmacy prevalence

| Polypharmacy                                                                 | Frequency (%) |
|------------------------------------------------------------------------------|---------------|
| Gender                                                                       |               |
| Male                                                                          | 51 (78.46)    |
| Female                                                                        | 42 (93.33)    |
| Number of Drugs Prescribed                                                   |               |
| <4                                                                           | 9.09          |
| 5-8                                                                           | 54.55         |
| 9-12                                                                          | 26.36         |
| ≥13                                                                           | 10            |
| Drugs Prescribed other than Antidiabetics                                     |               |
| Antihypertensive                                                             | 21            |
| Antacids                                                                     | 12            |
| Antibiotics                                                                  | 12            |
| Others                                                                        | 55            |

Table 2. Prevalence rate of diabetic complications

| Name of diabetic co-morbidities | Cases of Diabetic Complications | Percentage |
|---------------------------------|---------------------------------|------------|
| Diabetic cystopathy             | 1                               | 4.17%      |
| Diabetic foot                   | 2                               | 8.33%      |
| Diabetic ketoacidosis           | 1                               | 4.17%      |
| Diabetic ketoacidosis           | 9                               | 37.50%     |
| Diabetic neuropathy             | 4                               | 16.67%     |
| Diabetic retinopathy            | 7                               | 29.17%     |
| Total                           | 24                              | 100.00%    |
Table 3. Categories of DRPs

| Categories of DRPs                        | Frequency | Percentage (%) | Patients with DRP (n=110) |
|-----------------------------------------|-----------|----------------|---------------------------|
| Drug Use Problem                        |           |                |                           |
| Prescribed drug not available           | 6         | 3%             | 6                         |
| Drug not taken at all                   | 4         | 2%             | 4                         |
| Drug Duplication                        | 4         | 2%             | 4                         |
| Patient forgot to take drug             | 2         | 1%             | 2                         |
| Patient unable to use drug form as directed | 1         | 1%             | 1                         |
| Drug-drug interaction                   | 158       | 88%            | 69                        |
| Adverse drug reaction                   | 5         | 3%             | 5                         |
| Total                                   | 180       | 100%           | 91                        |

related problems in this study were mainly classified into drug-drug interactions (DDI), adverse drug reactions (ADR), and drug use problems (DUP). Drug-drug interactions: A total number of 158 drug-drug interactions were theoretically identified throughout the study. Out of these 158 drug-drug interactions; 34 (21.52%) were recorded as mild interactions, 101 (63.92%) were recorded as moderate drug interactions while the remaining 23 (14.56%) were recorded as major drug interactions. Drug-drug interactions were checked using Micromedex and Medscape. Adverse drug reaction: During the study period, 5 ADRs were identified and reported among the study participants. The identified ADRs were, (i) Metformin-induced abdominal pain, (ii) drug-induced thrombocytopenia, (iii) insulin-induced hypoglycaemia, (iv) anticoagulant-induced bruising, and (v) increased serum creatinine due to angiotensin receptor blocker (ARB). All the ADRs were assessed for causality and severity. As per the WHO causality assessment scale, out of 5 ADRs, 4 ADRs belong to the 'Possible' category while 1 ADR belongs to the 'Probable' category. According to Naranjo's causality assessment 4, ADRs were classified as 'Probable' while 1 ADR was classified as 'Possible'. Severity assessment was performed using Hartwig & Seigel severity assessment scale and it was found that all ADRs belong to the 'Mild (level 1 and 2)' category. Drug use problems: Drug use problems in this study include drug duplication, the drug not taken at all, a prescribed drug not available, patient forgot to take the drug, and patient unable to use drug form as directed. A total of 11 drug use problems were identified throughout the study. The most common cause of drug use problem was prescribed drug not available (n=6) in the hospital pharmacy due to certain circumstances. The second most common cause was drug not taken at all (n=4) by the patient. Another reason was drug duplication (n=4) where the same drug was given for more than one time either individually or in combination which exceeds its daily dosing limits.

4. DISCUSSION

Diabetes is often associated with various diabetic and non-diabetic complications leading to an increased number of prescribed drugs. Polypharmacy not only increases pill burden to the patients but also increases the risk of associated DRPs. The present study evaluates the prevalence of co-morbidities, polypharmacy, and drug-related problems among type 2 diabetes mellitus patients. We studied 110 patients out of which 10 were OP patients while 100 were IP. Comparing gender proportionality, male patients (n=65) encountered were more than female patients (n=45). It was observed that the highest number of patients were of 51-60 years age group (28.8%) which was similar to the study carried out in Bhubaneswar (34.4%) [8]. An attempt to study the social history of the patients revealed that the majority of the patients were smokers (39%) followed by tobacco users (32%) and alcoholics (26%) which was in concordance with the study carried out in Kolkata among type 2 diabetes mellitus patients where smokers were 18% while alcoholics were 6% [9] The total number of co-morbidities occurring among the patients along with diabetes was analyzed and the results showed that the average number of co-morbid conditions among the study population had 1-3 co-morbidities per patient. Among 110 patients, the majority (91%) of the patients were diagnosed with at least one co-morbid condition. Out of these patients with co-morbidities, most of them had 1-3 co-morbidities (80%). Similar results were obtained in the previous study carried out in Bhubaneswar where the
prevalence of overall co-morbidities among the study population was 80% while a total of 70% of patients had 1-3 co-morbidities [8]. A higher prevalence of co-morbidities was observed in female patients where 90.76% and male patients had co-morbidities while 91.11% of these co-morbid conditions were further divided into diabetic complications and non-diabetic complications. The prevalence of patients with only diabetic complications was found to be 19.09% which was higher than the study conducted in Karnataka (18.02%) and was lower than the study conducted in Bijapur (21.95%). The prevalence of patients with only non-diabetic complications was found to be 87.27% which was relatively higher than the study conducted in Karnataka (66.67%) and was lower than the study conducted in Bijapur (74.80%) [16,18].

The most commonly occurring diabetic complication among the study population was diabetic nephropathy (37.5%) followed by diabetic retinopathy (29.17%) and diabetic neuropathy (16.67%) which was in contrast with the study carried out in eastern Ethiopia on DRPs among type 2 diabetes mellitus patients with hypertension where diabetic nephropathy (31.2%) was the most commonly occurring complication followed by diabetic retinopathy (17.4%) and diabetic nephropathy (16%) [19]. Similarly, most commonly occurring non-diabetic co-morbidity among the study population was found to be related to cardiovascular disorder (44.85%) followed by respiratory disorder (13.92%) which was relatable to the study conducted in vijaypur where the prevalence of cardiovascular disorder and respiratory disorder was 71.21% and 14.65% respectively [18]. We also analyzed the prescribing pattern among the study population and observed that the average number of drugs prescribed was 9.68±1.94 per patient which resembled the study done in Kolkata where the average number of drugs prescribed was 4.72±0.11. The total number of drugs prescribed in inpatients (IP) throughout their hospital stay ranged from 3 to 17 [15]. Insulin (54%) was the most commonly prescribed class of antidiabetic drug followed by biguanides (13%). These results were supported by a study done in Karnataka where insulin was prescribed in 34.46% and biguanides in 31.68% [16]. In contrast to our results, a study conducted in Kolkata reported biguanides (96%) as the most prescribed drugs [9]. The maximum prescribed class of drugs other than antidiabetics was antihypertensive drugs (21%) followed by antacids (12%) and antibiotics (12%).

 Results of a study conducted in vijaypur shared similar results reporting antihypertensive drugs in 14.14% followed by antacids (10.17%) and antibiotics (11.95%) [18]. In contrast to our results, a study conducted in Kolkata reported antihyperlipidemic (72%) as the maximum prescribed class of drugs followed by antihypertensive drugs (68%) while antibiotics were prescribed in 1.95% [9]. Polypharmacy, for this study, is defined as the concurrent use of 5 or more drugs after excluding all the vitamin and dietary supplements. Polypharmacy (≥5 drugs) was experienced by 84.54% (n=93) of the total study population while 15.45% of patients were prescribed with <5 drugs. This was in concordance with the study done in south India on the incidence of polypharmacy in type 2 diabetes mellitus patients where 82.89% patients received ≥5 drugs while 17.11% patients received <5 drugs [14]. Out of 93 patients experiencing polypharmacy, the number of male patients was 51 while the number of female patients was 42. While comparing the age group, maximum polypharmacy was seen in the 51-60 age group (30.11%) followed by 41-50 age group (26.8%) and 61-70 age group (18.28%) which was similar to the study results conducted in Bhubaneswar in which maximum cases of polypharmacy were from 50-59 age group (34.4%) thereafter 60-69 age group (27.5%) and 40-49 age group (21.7%) [8]. Analytical data shows a positive association between the prevalence of polypharmacy and elderly patients. Out of 93 patients experiencing polypharmacy 40.86% (n=38) were of 60 or more years of age. We also studied drug-related problems occurring among the study population due to polypharmacy. A total of 180 DRPs were experienced by 91 patients with an average of 1.64 DRPs per patient. Out of these 91 patients, the number of male patients was 50 (54.94%) while the number of female patients was 41 (44.56%). In our study, drug-related problems were mainly classified into DDI, ADR, and DUP. 158 drug-drug interactions were theoretically identified which contributes 88% of the total DRPs. These results were in contrast to the study carried out in Indonesia where the DDI identified was 18% [20]. These identified DDI were further classified into mild interaction (21.52%), moderate interactions (63.92%), and major interaction (14.56%) During the study period, 5 ADRs were identified and reported among the study participants. These were further assessed for causality and severity. According to the WHO causality assessment, 1...
ADR belonged to the ‘Probable’ category and 4 ADRs belonged to the ‘Possible’ category. According to Naranjo’s causality assessment 80% (n=4) ADRs were identified as ‘Probable’ while 20% (n=1) ADR was identified as ‘Possible’ which was in contrast to the study conducted in New Delhi where 30.8% (n=8) were identified as ‘Probable’ while 69.2% (n=18) were identified as ‘Possible’ [21]. Severity assessment was performed using Hartwig and Seigel severity assessment scale and it was found that all ADRs belong to the ‘Mild (level 1 and 2)’ category. Drug use problem according to this study includes; prescribed drug not available (3%), the drug not taken at all (2%), drug duplication (2%) and patient forget to take the drug (1%). The study done in Indonesia shows similar results where prescribed drug not available contributed 0.7%, a drug not taken at all contributed 3.5%, drug duplication contributed 7.7% while patient forgot to take drug contributed 4.1% [20].

5. CONCLUSION
To conclude, that the increase in the number of comorbidities can significantly increase the burden of polypharmacy which can further lead to DRPs. Reducing the number of pills and the presence of a clinical pharmacist in prescription monitoring can help to alleviate the problems of polypharmacy and its consequences.

CONSENT
As per international standard or university standard, patients’ written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL
The study was initiated after getting the approval from Sumandeep Vidyapeeth Institutional Ethics Committee. (SVIEC/ON/Phar/BNPG18/D19002).

COMPETING INTERESTS
Authors have declared that no competing interests exist.

REFERENCES
1. World Health Organization. Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1, Diagnosis and classification of diabetes mellitus. World Health Organization; 1999.
2. Diabetes.co.uk: the global diabetes community. What is diabetes. [online]; 2019. Available:https://www.diabetes.co.uk/what-is-diabetes.html. [Accessed06 April 2019].
3. World health organisation, India; 2019. [online]. Available:www.searo.who.int/india/about/en/. [Accessed 06 April 2019].
4. Idf.org. 2019. International diabetes federation - facts & figures. [online] Available:https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html. Accessed 07 April 2019
5. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, Adhikari P, Rao PV, Saboo B, Kumar A, Bhansali A. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR–INDIAB population-based cross-sectional study. The lancet Diabetes & endocrinology. 2017;5(8):585-96.
6. Firstpost. National Family Health Survey (NFHS). 2015-16. Diabetes is India’s fastest growing disease:72 million cases recorded in 2017, figure expected to nearly double by 2025. Weblog. [Online]. Available:https://www.firstpost.com/india/diabetes-is-indias-fastest-growing-disease-72-million-cases-recorded-in-2017-figure-expected-to-nearly-double-by-2025-4435203.html.[Accessed 07 April 2019].
7. KM Mohammed Rashid, Anandhasayanam A, Kannan S, Noon MS. Prevalence of Co-morbidities in Type 2 Diabetes Mellitus Patients, the Awareness Level and the Impact of Pharmacist’s Patient Education Program. International Journal of Pharma Research and Review. 2015;4(5):11-20.
8. Pati S, Schellevis FG. Prevalence and pattern of co morbidity among type2 diabetics attending urban primary healthcare centers at Bhubaneswar (India). PloS One. 2017;12(8):e0181661.
9. Indu R, Adhikari A, Maisnam I, Basak P, Sur TK, Das AK. Polypharmacy and comorbidity status in the treatment of type 2 diabetic patients attending a tertiary care hospital: An observational and questionnaire-based study. Perspectives in clinical research. 2018;9(3):139.
10. American Association of Clinical Endocrinologists. Management of common
comorbidities of diabetes. United states of America 2004. [Online]. Available:http://care.diabetesjournals.org/content/32/6/1119. [Accessed 11 April 2019]

11. Stawicki SP, Gerlach AT. Polypharmacy and medication errors: Stop, listen, look, and analyze. Opus. 2009;12:6-10.

12. Austin RP. Polypharmacy as a risk factor in the treatment of type 2 diabetes. Diabetes Spectrum. 2006;19(1):13-6.

13. Priyanka T, Lekhanth A, Revanth A, Gopinath C, Babu SC. Effect of polypharmacy on medication adherence in patients with type 2 diabetes mellitus. Indian J Pharm Prac. 2015;8(3):126-32.

14. Chitti R, Kumaraswamy M, Acharya A, Vijay CH, Dhakal K, Rayamajhi M, Islam AM, Kibria FA. Incidence of Polypharmacy in Type 2 Diabetic Patients in a Rural Tertiary Care Teaching Hospital in South India. International Journal of Pharmaceutical Sciences and Nanotechnology. 2017;10(6):3906-8.

15. Foundation PCNE. PCNE Classification for Drug related problems Europe 2006. [Online]. Available from: https://www.pcne.org/upload/files/16_PCNE_classification_V5.01.pdf,[Accessed 09 April 2019]

16. Inamdar S, Kulkarni R. Drug related problems in elderly patients with type 2 diabetes mellitus. Journal of Diabetology. 2016;7(1):1-12.

17. Shashikala CW, Ganachari MS, Praveen T, Prakash RB, Tarang S, Geetanjali SS. Obstacles and Preventions of Drug Related Problems-A Review. Indian Journal of Pharmacy Practice. 2013;6(2).

18. Mable Babu, Nataraj G R, SR Vagesh Kumar, Bharathi DR, Joice Joseph. Evaluation of Prescription Pattern and Associated drug interactions in Type 2 diabetes mellitus patients with comorbidities and complications in a teaching care hospital. International Research Journal of Pharmacy. 2016;7:48-52.

19. Ayele Y, Melaku K, Dechasa M, Ayalew MB, Horsa BA. Assessment of drug related problems among type 2 diabetes mellitus patients with hypertension in Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia. BMC research notes. 2018;11(1):1-5.

20. Zazuli Z, Rohaya A, Adnyana IK. Drug-related problems in type 2 diabetic patients with hypertension: a prospective study. Journal of Basic and Clinical Pharmacy. 2017;8(4).

21. Singh A, Dwivedi S. Study of adverse drug reactions in patients with diabetes attending a tertiary care hospital in New Delhi, India. The Indian journal of medical research. 2017;145(2):247.