Original Article

Assessment of Medication Complexity and Adherence in Geriatric Patients

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ABSTRACT

Objectives: The main objective of the study was to assess the medication complexity and adherence in geriatric patients. **Materials and Methods:** On the geriatrics department of a tertiary care hospital, prospective observational research was done. A total of 280 patients were analyzed with the data collection form by interviewing the patients about the demographic questionnaire. The complexity of the regimen was assessed using the Medication Regimen complexity Index (MRCI) tool. The data were collected from the inpatient and out-patient department for a period of six months. The data are subjected to statistical tests like the Chi-square test using SPSS software. **Results:** There were 280 geriatric patients in all, with male patients outnumbering female patients 176. The majority of geriatric patients (79.27%) were in the 60–75 year age range. Cardiovascular illnesses were reported to be the most prevalent ailment in 94 (33.57%) patients. Level of complexity was higher for majority of prescriptions 196 (70%) with Tablets/ Capsules 280 (100%) and 'Once in a day' dosing frequency 276 (98.57%), additional/ administration instruction was prescribed for only few prescriptions 206 (73.57%) and if the patient was prescribed with more than 5 drugsfor about 218 patients (77.86%). The bulk of the population, or 156 people, exhibit moderate adherence (55.71%), followed by good adherence (76 people, 27.14%), and lastly low adherence (48 people, 17.15%). The complexity of the regimen was identified as the primary cause in 56 (27.45%) patients, and a comparison of the MRCI and MMAS revealed that patients on less complex regimens demonstrated moderate (40.148% patients) or good (34.124% patients) adherence. **Conclusion:** Geriatrics, which affects predominantly senior men (60 to 75 years old). The current study revealed a correlation between high MRCI scores for dosage form, dosing frequency, and additional/administration instructions and the current medical condition, the number of co-morbidities present, and the number of drugs prescribed; as a result, the MRCI serves as a better tool to assess the complexity of regimens. MMAS helps to assess the adherence level in geriatrics, which can be improved by removing barriers. With this, we can raise the geriatrics' quality of life in terms of their health.

Keywords: Geriatrics, Medication regimen complexity index (MRCI), Dosage form, Dosing frequency, Additional/administration instructions, Moriskys medication adherence scale (MMAS).

INTRODUCTION

Geriatrics is one of the internal medicine branch which deals with the health needs of the aged people.[1] Based on the age, geriatrics is of 3 categories- Elderly-60-75 years, Old-76-90 years, Very Old- above 91 years.[2]

Due to greater awareness about healthy life-style and enhanced health care facilities, the number and the proportion of people aged above 60 years[3] is expected to be increased in the world from 900 million to two billion between 2015 and 2050 and while those aged 80 years will be increased to around 400 million in the world.[1] In relation to global trends, Men are living shorter life when compared to women.

The older people present a wide range of

Received: 09-09-2022;
Revised: 15-10-2022;
Accepted: 17-10-2022.

DOI: 10.5530/097483261391

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challenges like physical, psychological, emotional, social, economic[4] and also physiological ageing changes leads to pharmacokinetic and dynamic changes in the geriatric patients.[5-7] As we all know, geriatrics usually have chronic and multiple conditions, so they need a very complex pharmacotherapy to manage their clinical conditions, so it leads to polypharmacy and increased risk for adverse drug reactions.[8,9] Hence, we need to monitor patient's medication regimen for complexity and adherence by taking various patient and clinical related factors for better therapeutic results.[10]

In general, medication complexity is commonly measured by simply counting the number of medications, which is usually considered as an inadequate method to deal with the complexity of the regimen.[11] Later, in order to quantify medication regimen complexity, Medication Regimen Complexity Index (MRCI) was developed and validated by George *et al.*, in 2004. The study was conducted on chronic obstructive pulmonary disorder (COPD) patients to measure disease specific prescription drugs and ignored over the counter drugs. For each category in the medication regimen; weighted scores were assigned in relation to the complexity in the administration instructions.[11]

The 65 item MRCI is a valid and reliable tool for quantifying prescribed medication regimen complexity[12] as it includes weighted scores for, Sub-score of A - Dosage forms accounts for 32 items, Sub-score of B - Dosing frequency accounts for 23 items and Sub-score of C - Additional administration instructions accounts weighted score of 10 in total 65 MRCI score. The higher the medication regimen complexity index score, the more complex is the medication regimen. Therefore, it serves as a tool to address polypharmacy, adverse effects, adherence in patients and also it helps to determine medication regimen complexity. As there is increased no. of medications and complicated schedules /special instructions, it can contribute to the greater difficulty/interest by geriatrics to take medications. So we can state that there is a link connecting medication regimen complexity and non-adherence.[13] There are many factors which affect the medication adherence like social, economic, health care system, condition related, therapy related and patient related.[14] Hence, medication adherence is considered as a major responsibility for the health care professional in order to decrease morbidity and mortality.[15] Adherence can be measured either directly or indirectly.[16] Direct method detects the presence of drugs in patient's body using urine, blood and other body fluids. This method is high cost and do not provide feedback on patient care. Indirect methods include electronic drug monitoring, pill counts, pharmacy refills (no. of times the prescription is refilled at the pharmacy), medical record review, directly observed therapy, clinical assessment, self reports and patient questionnaire[17] But, each method has its own pros and cons, patient questionnaire is most frequently used method as it is the most simple and low cost method, even though they are susceptible to biased response, as the participants generally overstate the actual adherence levels.[18] The 8-item Morisky's medication adherence scale (MMAS) consists of eight questions.[19,17] Adherence in patients is interpreted on a scale from 0-8 and then classified its score into 3 groups based on the obtained results.[20] Score of 8 is considered as good adherence, 6-8 points is considered as the moderate adherence 0-5 points is considered as the low adherence.[21] It is the most simple and widely used method to determine the adherence level, as it highlights mainly on medication taking behaviour such as underuse, forgetfulness etc. So, the barriers can be recognized. Researchers also reveal that majority of patients usually do not communicate their concerns regarding their medication and few were uncertain about whether the medications are necessary, safe, effective or whether the disease is dangerous and also stated that educated and responsible patients are more concerned about their health and are able to manage their therapies.[22,23] So, the patients active involvement in medication taking decision helps to improve their adherence.[24]

- The main objective of the study is to estimate the entire medication regimen complexity to ascertain potential targets to simplify the regimen and also to assess the medication adherence in geriatric patients in order to reduce further progression of diseases and also to improve the quality of life of the geriatric patients.

MATERIALS AND METHODS

A prospective observational study was conducted on geriatric patients in Kamineni Hospital for duration of 6 months.

The data was collected from the out-patient and in-patient department by interviewing the patients and their prescriptions. The data collection format was verified and authenticated by the hospital preceptors for the study. Study involved 280 subjects who were Subjects with age greater than 60 years with polypharmacy prescriptions and also with co-morbid conditions were included. Incomplete patient case sheet, Patients who are not willing to consent, death of the patients before being discharged and Patient left against medical advice were excluded from the study.

Written informed consent was taken from the patient or care provider. The data collection form includes– Socio-demographic information included age, sex, height, weight, past medication history, family history, social history, personal history, diagnosis, and relevant lab data. Medication complexity was calculated using MRCI scale which contains sub scores for dosage form, dosing frequency and additional information. Medication adherence was assessed using Morisky's medication adherence scale, it includes-8 questions regarding the adherence of the patient.

Descriptive statistics was done by using SPSS software to determine mean and standard deviation of collected data. The statistical tool Chi square test was performed to determine *p*-value between the different collected data (Age v/s Gender, Present illness v/s No. of Drugs, No. of Drugs v/s Medication Complexity, No of Drugs v/s Medication Adherence, Medication Complexity v/s Medication Adherence, Age v/s Medication Complexity, Age v/s Medication Adherence). The *p*-value is used to determine the statistical significance with in statistical hypothesis significance for the drug related problems in Geriatric patients to the base line visit. The *p*-value was set at < 0.05 and confidence interval was 95%.

RESULTS

In present study around 280 cases were included as per our criteria. Table 1 indicates mean, standard deviation and *p*-value of various parameters considered in our study. There were male patients 176 (62.85%) predominated over female patients of 104 (37.15%). Majority of the geriatric patients were under age group of 60-75 years (79.27%), 3 comorbidities were seen in 78 (27.85%) patients and Figure 1 indicates the most frequently repeated type of comorbidity present in geriatrics, Hypertension is most common co-morbidity seen in geriatrics i.e. 192(68.57%) patients and lipid disorders are less commonly seen, which is only in 6 (2.14%) patients. Figure 2 indicates the present illness of the geriatric population, Cardiovascular disorders are higher (33.57%) in our study population whereas, carcinomas and gynecological patients are lower (0.71%) in range. Figure 3 indicates the level of medication complexity in geriatric patients, percentage of medication complexity is high (70%) in majority of study population. Figure 4 indicates the dosage forms used in geriatric population, 100% of population are prescribed with tablets which is higher in range, whereas, suppositories are least commonly prescribed (0.71%). Figure 5 indicates the dosing frequency used in geriatric population, once in a day is the most commonly used dosing frequency (98.57%) and once in a week is least commonly used dosing frequency (1.42%). Figure 6 indicates the additional/administration instruction is given while dosage form administration, Related to time administration instruction is higher in range (72.85%) and multiple units at one time is the least in range (3.57%). Figure 7 indicates No. of drugs used in geriatric study population and it is compared with the MRCI score, Patients taking less than 5 drugs are of 62(22.14%), in this majority of patients revealed low complexity in the regimen, Patients taking 6-10 drugs are more in range i.e. 148(52.85%) patients and majority of them shown high complexity i.e. 112(40%) patients and with this it revealed that, medication complexity is higher when the no. of drugs increased and lower when no. of drugs is less. Figure 8 indicates level of medication adherence in geriatric study population; it states that no. of patients showing moderate adherence (55.14%) is higher in range than good (27.14%) and low adherence (17.15%). Figure 9 indicates the comparison between no. of drugs and no. of patients with changes in MMAS Score, 1-5 drugs prescribed patients majorly shown good adherence

Table 1: Mean, Standard deviation and p-value table.

Characteristics	N	Mean	Standard deviation	*p*-value
Age	280	1.2214	4.4910	0.0043
Gender	280	1.3714	4.8910	0.0048
Type of comorbidities	280	5.8929	3.32407	0.0210
No. of comorbidities	280	3.5214	1.39876	0.0125
Presentillness	280	3.1643	2.30197	0.01130
Level of medication Complexity	280	1.3000	4.5908	0.00464
Dosage form prescribed	280	3.3214	2.60759	0.0118
Dosing frequency prescribed	280	4.8000	2.28506	0.0171
Additional/administration instructions prescribed	280	2.4357	1.38714	0.0086
No. of drugs prescribed	280	2.0643	7.5927	0.00737
Level of medication adherence	280	2.2857	8.6580	0.0081
Reason for non-adherence	280	4.7286	2.95932	0.0168

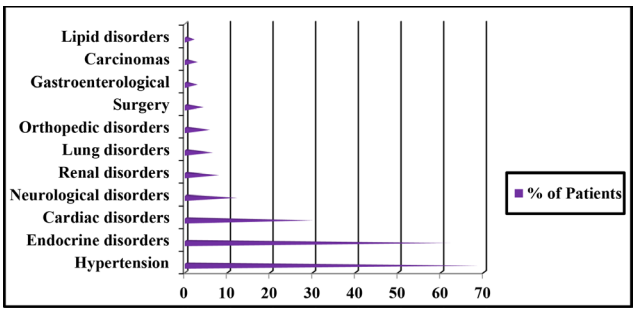

Figure 1: Type of comorbidity present in geriatric study population.

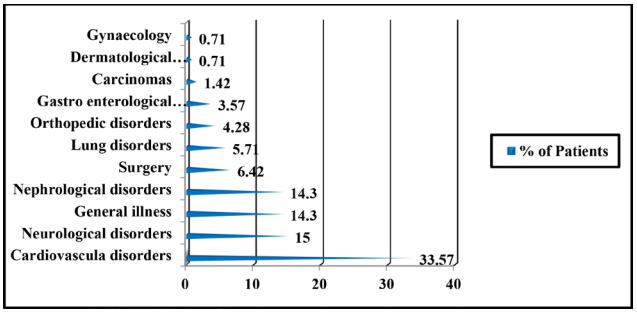

Figure 2: Present Illness of the Patients.

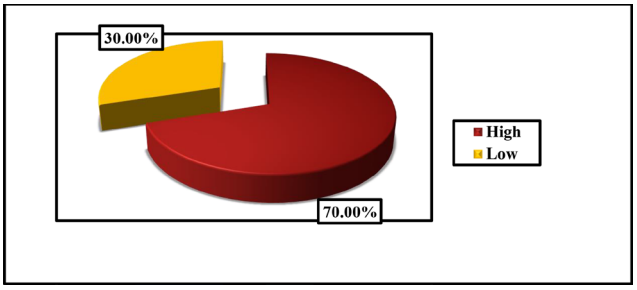

Figure 3: Level of medication complexity.

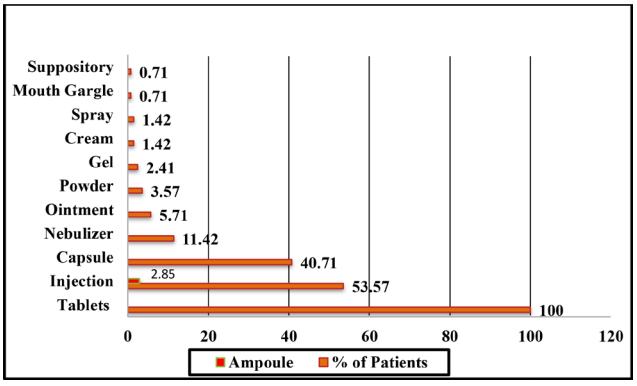

Figure 4: Type of dosage forms prescribed.

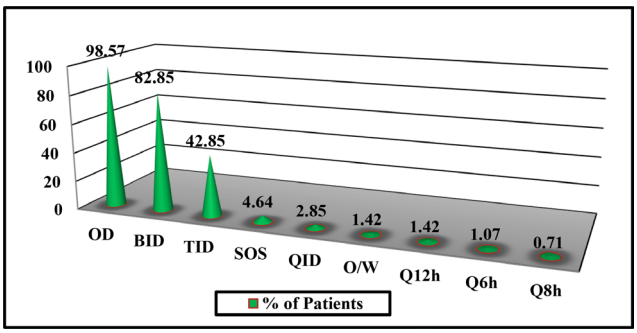

Figure 5: Type of dosing frequency used in geriatric study population.

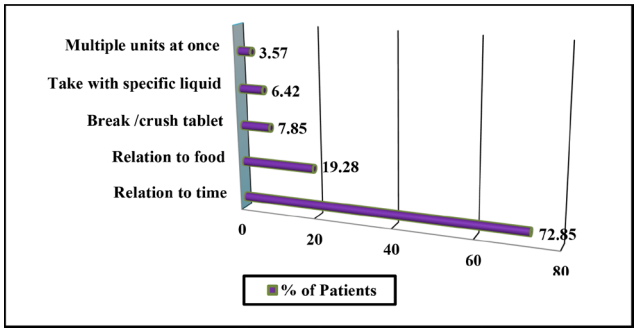

Figure 6: Additional/Administration instructions prescribed.

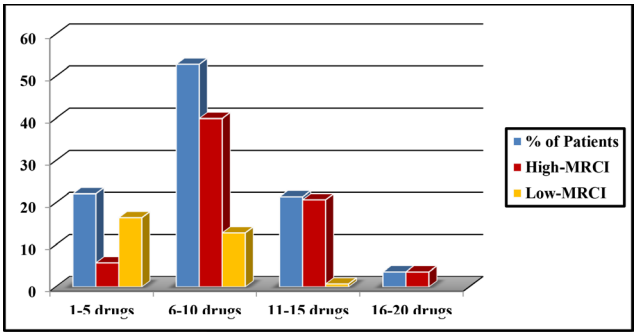

Figure 7: Comparision between no. of drugs prescribed and MRCI score.

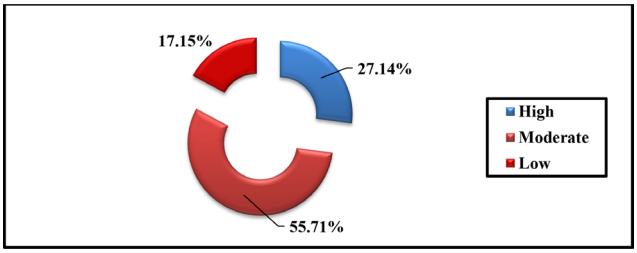

Figure 8: Level of Medication Adherence.

i.e.30(10.71%) patients and 16-20 drugs are least prescribed (3.58%) and these patients did not show good adherence. With this, it indicates that as the no. of drugs prescribed increasing, the adherence is either moderate or low and the majority of geriatric population is showing moderate adherence (55.72%). Figure 10 indicates the reasons for non-adherence in geriatric study population, complexity of regimen is main reason for non-adherence in 56(27.45%) geriatrics, and lack of time and negligence are least reasons for non-adherence in 6(2.94%) geriatric study population. Figure 11 indicates the comparison

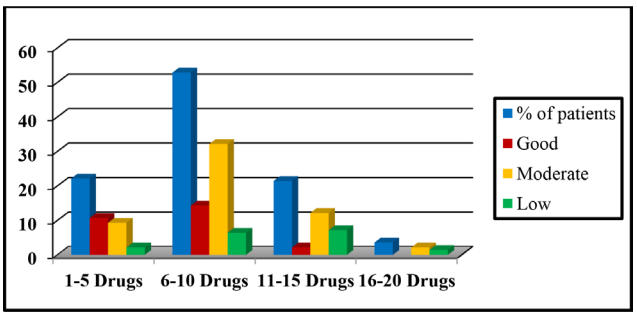

Figure 9: Comparison between no. of drugs prescribed and MMAS score.

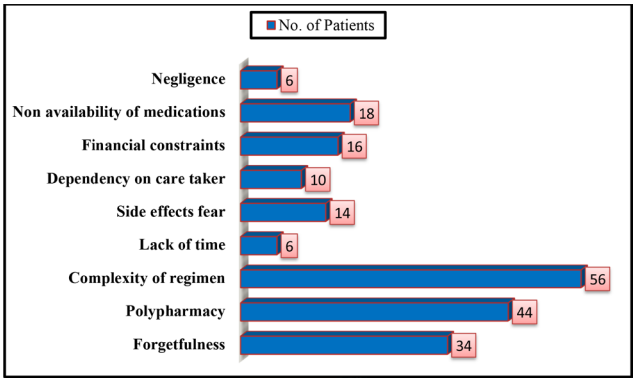

Figure 10: Reasons for Non Adherence.

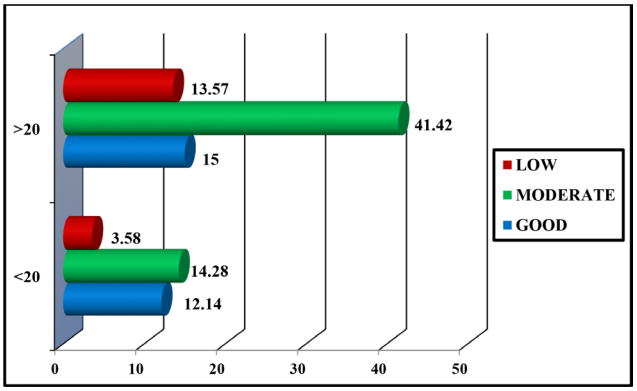

Figure 11: Comparison between MRCI and MMAS scores.

between MRCI and MMAS scores; it states that if MRCI score is <20, patient are showing majorly either moderate (14.28%) or good adherence (12.14%) but if the MRCI score>20, then the patient are showing higher moderate adherence (41.42%).

Chi square test was performed between variables like Age vs gender (0.001), Present illness vs no. of drugs (0.001), Age vs medication complexity (0.001), no. of drugs vs medication complexity (0.001), Age vs medication adherence (0.001), no. of drugs vs medication adherence (0.001), Medication complexity vs medication adherence (0.001) and the *p*-value was clinically significant (<0.005).

DISCUSSION

A prospective observational study, "ASSESSMENT OF MEDICATION COMPLEXITY AND ADHERENCE IN GERIATRIC PATIENTS" was conducted in a tertiary care hospital on geriatrics. The data was collected from the inpatient and outpatient departments using data collection forms.

In our study we assessed medication regimen complexity using medication regimen complexity index (MRCI) which is similar to Anne M. Libby, Douglas N. Fish *et al.*[11] and Sunny A.Linnebur, Joseph P. Vande *et al.*[25] and our study revealed that 70% geriatrics shown high complexity and low complexity is shown by 30% geriatric population.

We also correlated no. of drugs with MRCI scores and it revealed that patients taking more than 5 drugs are about 218(77.85%) which is similar to the study done by Ana Margarisa Advinha, Sofia Oliveria *et al.*[26] and multiple co-morbidities patients have more complexity in the regimen and also stated that no. of drugs and no. of daily doses taken was strongly correlated to MRCI score which resembled the study done by Narmain Mansur *et al.*[27] and another study done by Juliana M. Ferreira, Dayani Galato and Angelita C.Melo.[28]

All of the 280(100%) patients in our study are prescribed with tablet dosage form, enlightening the supremacy of this dosage form in clinical practice, and the dosing frequency plays a major role in patients medication regimen, 'once in a day 'dosing frequency is most commonly prescribed for 276(98.57%) patients, which resembled the study done by Juliana M. Ferreira, Dayani Galato and Angelita C. Melo[28] and Relation to time administration instruction is highly prescribed i.e. for 102(72.85%) patients, which resembled the study done by Margaret V Mc Donald *et al.*[13] and also to the another study done by Sunny A. Linneur, Joseph P. Vande Griendet *et al.*[25]

In our study, Medication adherence in geriatrics is assessed using Morisky's Medication Adherence Scale (MMAS), which is similar to the work done by R. Shruthi, R. Jyothi *et al.*[29] Medication adherence in geriatrics revealed that majority of patients shown moderate adherence i.e. 156(55.71%) which is similar to the study done by Voratima Silavanich *et al.*[30] and is contrast to the study done by R. Shruthi, R. Jyothi *et al.*[29] as their study revealed that majority of population shown good adherence 114(45.41%) patients and low adherence was shown by 48(17.15%), which is least in range in our study population and this is similar to the work done by R. Shruthi, R. Jyothi *et al.*[29]

Medication adherence in geriatrics shown strong correlation with the polypharmacy and complexity of the regimen because in our study, majority of patients i.e. 218(77.85%) are prescribed with more than 5 drugs and it resulted in moderate adherence i.e. 130(59.63%) patients or low adherence. i.e. 42(19.26%) patients, which is similar to the study done by Ashley Smaje, Marsye Weston-clark *et al.*[24]

Complexity of medication regimen shown by 56(27.45%) patients was the main reason for non adherence in our geriatric study population, which resembled the study done by Margaret V Mc Donald *et al.*[13] and another study done by Lais Lessa Pantuzza *et al.*[31] revealed that there is a strong correlation between medication regimen complexity and adherence rates.

Chi-square test was performed for our study using SPSS software. It showed that the p-value was clinically significant for all demographic details no. of drugs, Medication Complexity and Medication Adherence.

It was observed from our study that, As the geriatric age increases, No. of co morbidities increases, with this the no. of drugs prescribed increases so, we assessed the Medication Complexity using MRCI tool, which helped us to correlate the complexity of the regimen using various sub scores of dosage forms, dosing frequency and additional information. The Medication Adherence showed that decrease in adherence levels occurs, as there is a increase in medication level complexity it was assessed using MMAS. Therefore, MRCI and MMAS serves as valid tools to assess complexity and adherence levels.

CONCLUSION

Due to various age related physiological changes in geriatrics, they suffer from more than 2 comorbidities. As there is an increase in co-morbidity level in geriatrics, no. of drugs prescribed also increases. So, Medication regimen complexity index (MRCI) helps to identify the complexity of the regimens and revealed that majority of prescriptions had complex regimens with 'Tablets/ capsules' dosage form and 'Once in a day' dosing frequency are prescribed in almost all of the prescriptions revealing their supremacy in prescribing of medications in clinical practice, but additional administration instructions was given to only few prescriptions and if there are more than 5 drugs in a prescription with other than oral dosage form and with increased dosing frequency and if the patients needs to remember any other additional administration instructions before taking the medication contributed to the higher complexity in the regimens. So, with this MRCI serves as a better tool to identify the factors that contributes to the complex therapies.

As we all know, majority of geriatrics generally face various social, emotional and economic challenges, so if more than 5 drugs are prescribed, these people doesn't feel to take medications properly and it lead to non-adherence, The level of medication adherence in geriatrics was assessed using 8- questionnaire Morisky's Medication Adherence Scale (MMAS), it revealed that majority of population shown moderate adherence.

Comparison between MRCI and MMAS score revealed that patients with low medication complexity shown, higher moderate and good adherence and higher complexity medication regimens revealed that moderate adherence is higher in range in these patients. With this it helps to correlate medication complexity with adherence rates.

So, we can state that as the no. of co-morbidities increases, no. of drugs prescribed increases, then the medication complexity increases and finally adherence level decreases.

Therefore, the study recommends that proper involvement of clinical pharmacist service is to identify patients with more complex medication regimens and non adherent patients. If the patient feels complexity in regimen, we as a clinical pharmacists must simplify the dose or dosing schedules and prefer combinations of drugs and must also evaluate the need for vitamin supplements and OTC drugs use in geriatrics, and medication adherence can be improved by creating a faith in health care provider and removing/minimizing the barriers for adherence in geriatrics. If the patient frequently forgets to take the medication, we must prepare dosing cards, remainder calls, texts to the patients and we must also prescribe according to the financial status of the geriatrics and also recommend the use of generic and online pharmacies.

A detailed explanation about the nature of the disease and the drugs prescribed would increase the participation of patients in treatment. So the awareness on health care providers, prescribers and pharmacists will be valuable.

By doing so, morbidity and mortality in geriatrics can be decreased and we can improve the health related quality of life.

ACKNOWLEDGEMENT

It is a moment of gratification and pride to look back with a sense of contentment at the long travelled path

to be able to recapture some of the fine moments, to be able to thank infinite number of people, some who were with me from the beginning some who joined us at some stage during the journey, whose kindness, love and blessing has brought this day. I wish to thank each one of them from the core of my heart. First of all, lam very much grateful to the Almighty and my beloved Parents for their blessings upon me at each and every stage of my life. I wish to sincerely thank our Chairman Sri. A.V. Ramana Reddy Garu, and Secretary Sri M. Rajendra Krishna Garu, for providing fully equipped and sophisticated labs. Principal. Dr. D. Venkataramana, M.Pharm., Ph.D. Samskruti College of Pharmacy, for providing adequate facilities for the successful completion of our work successfully It gives me a great pleasure to thank my esteemed supervisor and teacher Dr. Nikhilesh Andhi. For the enthusiasm with which he guided us to carry out this work. He has shown tremendous patience and understanding without which this project would not have been succeeded. I wish to express my sincere thanks to our Faculty members and non-teaching staff of our college for their well cooperation, and timely help. I am thankful to my Classmates for their constant help. suggestions and encouragement in fulfilling my project work. As a final word, I would like to thank each and every individual whose name I may have forgotten to mention and who have been a source of support and encouragement and helped me to achieve my goal and complete my project work successfully. – J.Pravalika

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVATIONS

CGA: Comprehensive Geriatric Assessment; **MRCI:** Medication Regimen Complexity Index; **COPD:** Chronic Obstructive Pulmonary Disorder; **PMRCI:** Patient Level Medication Regimen Complexity Index; **MARS:** Medication Adherence Rating Scale; **MMAS:** Morisky's Medication Adherence Scale; **SEAMS:** Self Efficacy for Appropriate Medication use Scale; **BMQ:** Brief Medication Questionnaire; **EMR:** Electronic Medical Records; **WHO:** World Health Organization.

SUMMARY

Geriatric is the branch of general medicine concerned with clinical and social aspects of illness in the elderly patients. The term Geriatric generally refers to patient aged 60 years and above. WHO classified geriatric as Elderly-60-75years, Old -76-90 years, Very old –above 90years. Medication Complexity; The complexity of medication regimen can be defined by the number of medications (Polypharmacy) and the number of times per day or doses that the patient takes the medication (multiple doses schedule) Challenges of Medication Complexity:Polypharmacy, Challenges around adherence, Failure to accomplish treatment goals resulting from inadequate or inappropriate drug regimens and Avoidable complications or harm caused by medication (Adverse drugs events). Thus our study deals with Identification and measurement of medication complexity; involving, Direct Methods (Confirmatory/Suspected) i.e; Multiple drugs, Different dosage forms, Many Frequencies, Multiple conditions, Frequent readmission and Complex administration instruction. As noted above Medication Regimen Complexity Index (MRCI) is a reliable and valid tool for quantifying drug regimen complexity with potential applications in both practice and Research beyond the number of medications to include weighted scores for types of Prescribed dosage forms, Dosing frequency, and Additional administration directions.

Medication adherence in our study helps determines the therapeutic outcomes, especially in patients suffering from chronic illness or disease, Adherence to treatment is the key between treatment and outcome in medical care, Pharmacists are in unique position to improve medication adherence because they can actually show the medication to patient. Usage of Morisky's Medication Adherence Scale (MMAS) in our study helped to differentiate poorly adherent patients, from medium to high adherence patients with respect to their regimen.

In the end, through our study, we want to assess the Geriatric patients condition, using Medication regimen complexity index (MRCI) and Morisky's Medication Adherence Scale (MMAS), as it allows the clinicians to acknowledge more efficient and structured way to identify prescriptions with complex regimen and non-adherent patients experiencing sub-optimal emergent care needs. It also helps to simplify patients drug regimen and also to identify patients who may be benefited from the management during hospital stay and also after discharge from the hospital. Thus it helps to improve the health related quality of life of the geriatric patients by reducing morbidity and mortality.

REFERENCES

1. Ronald C. merrell MD. Richmond: Virginia Commonwealth University, Background and evidence for telemedicine as a way to address the challenges

of geriatrics. The Korean Medication Informatics; Oct 31, 2015. doi: 10.4258/hir.2015.21.4.223.
2. Facts on ageing and the life course. WHO; 2012.
3. Mishra N. Ageing in India: Concerns and challenges. 2014;24(4).
4. Miren Taberna FGM, Jane-Saias E, Rebollo Maite A. Use of geriatric assessment in oncology and the multidisciplinary team approach and quality of care. Front Oncol. Mar 2020,doi;00085. doi: 10.3389/fonc.2020.
5. Graf C, Mick DJ. Ackeman MH. NursClin N Am, Watters JM. Functional decline in hospitalized older adults, Criticare nursing for older adults, Surgery in the elderly. J Can Chir. 2006;106(1):58-67. quiz 67-8. doi: 10.1097/00000446-200601000-00032.
6. Roger walker and Cate whittlesea, Clinical pharmacy and therapeutics. 5th ed, 5th sep 2011.
7. Katzung BG, Masters SB, Trevor AJ. Basic and clinical pharmacology. 12th ed. A LANGE Medical Book; 1982.
8. Nyborg G, Straand J, Brekke M. Inappropriate prescribing for the elderly–a modern epidemic? Eur J Clin Pharmacol. 2012;68(7):1085-94. doi: 10.1007/s00228-012-1223-8, PMID 22349159.
9. Hubbard RE, O'Mahony MS, Woodhouse KW. Medication prescribing in frail older people. Eur J Clin Pharmacol. 2013;69(3):319-26. doi: 10.1007/s00228-012-1387-2, PMID 22965651.
10. Nashwa Masnoon S. And Gillian E. Caughey, What is poly pharmacy? A systemic review of definitions. BMC Geriatr. 2017;17:230. doi: 10.1186/s12877-017-0621-2.
11. Libby AM, Fish DN, Hosokawa PW, Linnebur SA, Metz KR, Nair KV, *et al*. Patient level medication regimen complexity across populations with chronic disease. Clin Ther. 2013;35(4):385-398.e1. doi: 10.1016/j.clinthera.2013.02.019, PMID 23541707.
12. Hirsch JD, Metz Kr, *et al*. Validation of a patient –lev Corrine I. Voils, Rick H. Hoyle, and William S. Yancy, Jr. Improving the measurement of self reported medication non-adherence. J Clin Epidemiol. 2011;64(3):250-4. doi: 10.1016/j.jclinepi.2010.07.014.
13. McDonald MV, Peng TR, Sridharan S, Foust JB, Kogan P, Pezzin LE, *et al*. Automating the medication regimen complexity index. J Am Med Inform Assoc. 2013;20(3):499-505. doi: 10.1136/amiajnl-2012-001272, PMID 23268486.
14. Voils CI, Hoyle RH, Thorpe CT, Maciejewski ML, Yancy WS, William S. Yancy, Jr. Improving the measurement of self reported medication non-adherence. J Clin Epidemiol. 2011;64(3):250-4. doi: 10.1016/j.JCLINEPI.2010.07.014, PMID 21194887.
15. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med. 2005;353(5):487-97. doi: 10.1056/NEJMra050100, PMID 16079372.
16. Yap AF, Thirumoorthy T, Kwan YH. Medication adherence in the elderly. Journal of Clinical Gerontology and Geriatrics. 2016;7(2):64-7. doi: 10.1016/j.jcgg.2015.05.001.
17. Feldman MD, Christensen JF, Satterefield JM, editors. Behavioural Medicine: A Guide for clinical practice. 4th ed. New York: McGraw-hill; 2014.
18. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self reported measure of medication adherence. Med Care. 1986;24(1):67-74. doi: 10.1097/00005650-198601000-00007, PMID 3945130.
19. George J, Phun YT, Bailey MJ, Kong DC, Stewart K. Development and validation of the medication regimen complexity index. Ann Pharmacother. 2004;38(9):1369-76. doi: 10.1345/aph.1D479, PMID 15266038.
20. Janežič A, Locatelli I, Kos M. Criterion validity of 8 item Morisky Medication Adherence scale in patients with asthma. PLOS ONE. 2017;12(11):e0187835. doi: 10.1371/journal.pone.0187835, PMID 29190693.
21. World health organization adherence to long term therapies: Evidence for action. Switzerlan. WHO, 2003.
22. Jankowska-Polańska B, Uchmanowicz I, Dudek K, Mazur G. Relationship between patients knowledge and medication adherence among patients with hypertension. Patient Prefer Adherence. 2016;10:2437-47. doi: 10.2147/PPA.S117269, PMID 27994443.
23. Chen Y, Yang L, Hu H, Chen J, Shen B. How to Become a smart patient in the era of precision Medicine? Adv Exp Med Biol. 2017;1028:1-16. doi: 10.1007/978-981-10-6041-0_1, PMID 29058213.
24. Smaje A, Weston-Clark M, Raj R, Orlu M, Davis D, Rawle M. Factors associated with medication adherence in older patients: A Systematic review. Aging Med(Milton). 2018;1(3):254-66. doi: 10.1002/agm2.12045, PMID 31410389.
25. Linnebur SA, Vande Griend JP, Metz KR, Hosokawa PW, Hirsch JD, Libby AM. Patient level medication regimen complexity in older adults with depression. Clin Ther. Nov 1 2014;36(11):1538-1546.e1. doi: 10.1016/j.clinthera.2014.10.004, PMID 25456562.
26. Advinha AM, De Oliveira-Martins S, Mateus V, Pajote SG, Lopes MJ. Sofia de oliveira-Martins, *et al*. Medication Regimen Complexity in Institutionalized Elderly People in an ageing Society. Int J Clin Pharm. 2014;36(4):750-6. doi: 10.1007/s11096-014-9963-4.
27. Mansur N, Weiss A, Beloosesky Y. Looking beyond polypharmacy: Quantification of medication regimen complexity in the elderly. Am J Geriatr Pharmacother. 2012;10(4):223-9. doi: 10.1016/j.amjopharm.2012.06.002, PMID 22749668.
28. Ferreira JM, Galato Dayani, Melo AC. Medication regimen complexity in adults and the elderly in A primary healthcare setting: Determination of high and low complexities. Pharm Pract. 2015;13(4):659. doi: 10.18549/PharmPract.2015.04.659, PMID 26759621.
29. Shruthi R, Jyothi R, *et al*. A study of Mdication compliance in geriatric patients with chronic illnesses at A tertiary Care Hospital. J Clin Diagn Reasearch. 2016. doi: 10.7860/JCDR/2016/21908.9088.
30. Silavanich V, Nathisuwan S, Phrommintikul A, Permsuwan U. Relationship of medication adherence and quality of life among heart failure patients. Heart Lung. 2019;48(2):105-10. doi: 10.1016/j.hrtlng.2018.09.009, PMID 30384984.
31. Pantuzza LL, Ceccato MDGB, Silveira MR, Junqueira LMR, Reis AMM. Association between medication regimen complexity and pharmacotherapy adherence: A systematic review. Eur J Clin Pharmacol. 2017;73(11):1475-89. doi: 10.1007/s00228-017-2315-2, PMID 28779460.