IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

A Review: Polypharmacy and Medication Adherence in Patients with COVID-19 Diseases

Ms. Dhrutika Patel[1], Mr. Vikesh Rathwa[2], Mr. Parshu Gavli[3], Mr. Avnish Paswan[4]
Mr. Rikin Patel[5], Mr. Vedish Patel[6], Mr. Talha Vahora[7], Dr. Richa Dayaramani[8]
B.Pharm Scholar[1,2,3,4]
Assistant Professor, Department of Pharmaceutics[5,6,7]
Principal, Shivam Pharmaceutical Studies & Research Centre,Valasan, Anand, Gujarat[8]
Shivam Pharmaceutical Studies & Research Centre, Valasan, Anand, Gujarat.
Corresponding Authors: patelrikin1211@gmail.com[5], vedishpatel1211@gmail.com[6], talha.vahora39@gmail.com[7], richadayaramani1976@gmail.com[8]

Abstract: *Surveys of community based elderly patients' shows that 2 to 9 prescription medications on average are taken per day. By survey 57% of US women aged >65 years took more than 4 prescription medication and 12% took more than 9 prescription medication. [1]On random day 8.3 % of the population were exposed to minor polypharmacy and 1.2% to major polypharmacy. The prevalence of polypharmacy increased with the age and from the age of 70 years, two third of all drug users were polypharmacy users. An elderly patient is at greater risk for adverse drug reactions and drug-drug interactions because the physiologic changes that occur with aging make the body more sensitive to the effects of medications. The burden of polypharmacy, may enhance the risk of morbidity and mortality, especially in cases of acute infections. The Middle East respiratory syndrome (MERS-CoV), severe acute respiratory syndrome (SARS-CoV), SARS- related coronavirus-2 (SARS-CoV-2), and corona virus disease (COVID-19) are members of the same family as coronavirus. Various studies reported that COVID-19 has a similar pathogenic potential to cause respiratory complications, disability, and death as SARS-CoV and MERS-CoV. Medication non-adherence includes delaying prescription fills, failing to fill prescriptions, cutting dosages, and reducing the frequency of administration. Non adherence with medication is a complex and multidimensional health care problem. The causes may be related to the patient, treatment, and/or health care provider.*

Keywords: Polypharmacy, Factors of Polypharmacy, Consequence of Polypharmacy, Prevention of Polypharmacy, Medication Adherence, Types of non-medication adherence, Role of Pharmacist, Covid-19 Disease.

I. INTRODUCTION

Surveys of community based elderly patients' shows that 2 to 9 prescription medications on average are taken per day. A survey by Kaufman et al found that 57% of US women aged >65 years took more than 4 prescription medication and 12% took more than 9 prescription medication. [1]On random day 8.3 % of the population were exposed to minor polypharmacy and 1.2% to major polypharmacy. The prevalence of polypharmacy increased with the age and from the age of 70 years, two third of all drug users were polypharmacy users.[2] In 2003, the World Health Organization (WHO) identified medication non-adherence as the leading cause of preventable morbidity, mortality, and health care costs. Meanwhile, research has set the price tag for the direct costs of medication non-adherence in the United States at a minimum of $100 billion. The New England Healthcare Institute estimates that nonadherence along with suboptimal prescribing, drug administration, and diagnosis costs the health care system as much as $290 billion per year and 13 percent of total health care expenditures.[3] Approximately 125,000 deaths per year in the United States are linked to medication non-adherence. Between 33 and 69 percent of medication-related hospital admissions in the U.S. are due to poor adherence, with total cost estimates for non-adherence ranging from $100-300 billion each year including costs for additional doctor visits, emergency room visits, hospital admissions, and the additional medicines.[4]

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

Pharmacotherapy is necessary for preventing, treating disease & for alleviating symptoms although non pharmacological treatments are available for the managing disease. Basic principles of pharmacotherapy is to provide maximal efficacy while minimizing the risk of adverse effects.[5]

An elderly patient is at greater risk for adverse drug reactions and drug-drug interactions because the physiologic changes that occur with aging make the body more sensitive to the effects of medications.[6] The use of several drugs concomitantly is justified in the treatment of multiple chronic disease may cause polypharmacy. When more than four drugs were taken, errors exceeded 35%. [7]

The unnecessary drug therapy problems frequently tend to be overlooked in polypharmacy prescribing.[8] Polypharmacy also makes compliance with medications more challenging. Noncompliance with prescribed medications can result in sub-optimal therapeutic effectiveness and can have major clinical consequences.[9]

Aging is typically accompanied by physiological changes, including a declined immune system, increased susceptibility to infections, deteriorated kidney function, and geriatric syndrome. These conditions, added to the burden of polypharmacy, may enhance the risk of morbidity and mortality, especially in cases of acute infections. The Middle East respiratory syndrome (MERS-CoV), severe acute respiratory syndrome (SARS-CoV), SARS- related coronavirus-2 (SARS-CoV-2), and coronavirus disease (COVID-19) are members of the same family as coronavirus.[10] These viruses may lead to fatal outcomes in humans, including acute respiratory distress syndrome, multiorgan failure, and death, particularly in geriatrics patients with multiple morbidities. [11] Various studies reported that COVID-19 has a similar pathogenic potential to cause respiratory complications, disability, and death as SARS-CoV and MERS-CoV.[12-13] A recent Chinese study showed that out of 138 hospitalized COVID-19 patients with pneumonia, 26.1% geriatric patients with multiple co-morbidities were transferred to the intensive care unit (ICU) compared with youngeradults with fewer co-morbidities.[14]

Studies have shown patient attitudes to be an important predictor for health related behaviours including medication adherence.[15]

Poor adherence undermines pharmacotherapy outcomes of individual patients and carries a significant human cost in terms of patient safety and quality of life. It also presents a serious problem for health systems, both in terms of inferior health outcomes, unnecessary treatments and hospitalizations, and in terms of resources wasted through the non-use of prescribed medicines funded by healthcare systems. Furthermore, low adherence is connected to the development of resistance, which is fast becoming an urgent global problem.[16]

Medication non-adherence includes delaying prescription fills, failing to fill prescriptions, cutting dosages, and reducing the frequency of administration. Non adherence with medication is a complex and multidimensional health care problem. The causes may be related to the patient, treatment, and/or health care provider. As a consequence, substantial numbers of patients do not benefit optimally from pharmacotherapy, resulting in increased morbidity and mortality as well as increased societal costs. The problem of non-adherence to medications is serious, but not insurmountable. With each passing day, tremendous progress is being made to understand the core reasons for non-adherence and design programs that will address these issues.[16]

II. POLYPHARMACY

One simple definition is based on the total number of different medications a patient takes concomitantly. A more clinically useful definition is "the prescription, administration, or use of more medications than are clinically indicated." Inappropriate drug combinations, unnecessary medications, and inappropriate drugs for specific patients (such as the elderly) constitute the problems of polypharmacy.[17] Thus, patients receiving only two medications could have polypharmacy. It also defined as the concurrent use of five or more medications and excessive polypharmacy defined as 10 or more medications.[18]

Use of multiple medications increases in a variety of ways the likelihood of an unintended therapeutic outcome. This is especially true in the case of elderly patients, who are particularly susceptible to adverse drug events. Although not specifically studied, it is likely that diabetic elderly patients are even more susceptible to problems related to polypharmacy because of significantly greater underlying physical disability. Thus, polypharmacy adds expense for multiple drugs, increases the chance of an adverse reaction to a single agent, increases the incidence of drug interactions, decreases patient compliance, and plays a part in unwanted geriatric syndromes. Finally, polypharmacy increases the likelihood of the prescribing and dispensing errors.[17]

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

The use of several drugs concomitantly is justified in the treatment of multiple chronic disease may cause Polypharmacy, but it also makes medication regimen more difficult.[19]

2.1 Who is at the Risk of Polypharmacy?[20]

If the patient is taking prescription drugs and answer yes to any of the questions below the patient could be at increased risk for polypharmacy:

- Does the patient take herbs, vitamins or OTC product?
- Does the patient have to take medicine more than once a day?
- Does the patient suffer from arthritis?
- Does the patient use different pharmacies to fill their prescription?
- Does the patient have poor eyesight or hearing?
- Does the patient sometimes forget to take their medication?

2.2 Factor that Influence the Development of Polypharmacy[21]

Polypharmacy may often develop due many reasons. Some of the factors that influence the development of polypharmacy includes:

- Increasing number of chronic illness with advancing age may increases the number of different physicians seen by the elderly, consequently physicians may prescribe different medications to achieve the same therapeutic end point. If the physician do not have the access to primary medical records therapy may initiate without the full scope patient's medication history.
- Using multiple pharmacies to fill prescription medication also can add risk of Polypharmacy. Elderly patients may go to various pharmacies to find the lowest cost for a medication; this can cause Polypharmacy in these patients.
- Patients lack of knowledge concerning medications and poor understanding of the medical condition, for which medications are prescribed, also lead to Polypharmacy. Patient education is vital to successful treatment of their medical condition.
- Increase in use of OTC or non-prescription drugs and additional herbal and nutritional supplements and other alternatives also lead to Polypharmacy. Many of these products have not proven to effective and also produces physiological response that with prescription medications.
- Also factors like susceptibility to product advertisement, tendency towards self treatment, hoarding of old medications, prohibitive cost of prescription products also will influence polypharmacy.

Many risk factors for polypharmacy have been identified and can be classified into 1 of 3 groups: demographic, health status and access to health care characteristic. Increased age, race & education are demographic characteristic associated with polypharmacy. Poor Health, depression, hypertension, anemia, asthma, angina, diverticulitis, osteoarthritis, gout, diabetes mellitus and use of > 9 medication are the health status characteristic associated with polypharmacy.[22]

2.3 Consequence of Polypharmacy[22]

There are many consequence associated with polypharmacy. Patients are at in increased risk of receiving inappropriate medication and having an adverse drug reaction, Non compliance, increased cost. polypharmacy has also been reported to increase risk of geriatric syndromes and morbidity / mortality.

A. Adverse Drug Reaction

The risk of ADRs may increase with increased number of drugs taken. ADRs have been reported to occur in 5% to 35% of outpatients and account for as many as 12% of hospital admission in older patients. The risk of ADRS is strongly associated with multiple comorbidities, use of specific types of drugs such as warfarin, and increasing number of drugs taken.**[X3] So**metimes patients may hospitalized with ADRs secondary to improper dosage of the medication rather than to the medication itself which may result from both sub therapeutic or super therapeutic drug level.[21]

- **Drug interaction:** Increasing the number of drugs consumed also predisposes patients to drug disease and drug-drug interaction, particularly in patients who have multiple pathologies and co-morbidities. Additional medication

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

may not only include prescription medication but also self treatment by the older patient with non-prescription products.[21]

- **Cost:** Higher the medication cost has been linked to an increase in noncompliance. Medications that are not essential may take priority over essential medication because the cost: benefits ratio of each drug has not been clarified with the adult.[21]
- **Noncompliance:** The main reason for most treatment failure of drug is noncompliance, which can cause serious medical complication. Rates of noncompliance have been estimated at 25% to 50% in elderly. Noncompliance with medication correlate more strongly with the number of medications given than with age of patient, the difficulty experienced by the elderly person in interpreting the importance of medication or the direction for use may lead to noncompliance.[21]

2.4 Geriatric Syndromes

Few studies showed that multiple medications with urologic activity increased the risk of urinary incontinence. The other study showed an increased risk of cognitive impairment with multiple medication.[22]

2.5 Prevention of polypharmacy[21]

Recognizing polypharmacy is the first step towards its prevention. A review of all aspects of the patients' daily life provides insight into physical, emotional or educational situation and helps to determine if polypharmacy has occurred. Medication history is valuable tool in determining the extent of polypharmacy and it should include any adverse reaction or allergies to medication.

Education regarding medication use is important in preventing polypharmacy in the elderly patients. Patient involvement in treatment options not only allows some control to the patients in treatments plans but also may help to prevent possible polypharmacy occurrences by their understanding possible ramification of noncompliance.

Simplification of drug regimen is another means by which health care provider can prevent polypharmacy. Prescribing medication without a found diagnosis intensifies the risk of polypharmacy. The benefit of an additional medication to therapeutic regimen must be weighed against the possible problems that may result from the addition.

III. Medication Adherence

Medication adherence is defined as the extent to which a patients medication taking behaviour coincides with the intention of health advice given to them. Poor adherence imposes a significant financial burden on individual patients and the health care system as whole.[23]

Adherence to treatment is a key link between process and outcome in medical care. Rationally prescribed medications are a principle intervention in primary care and a major element when considering the economics of health care. Low compliance to prescribed medical interventions is an ever present and complex problem, especially for patients with a chronic illness. With increasing numbers of medications shown to do more good than harm when taken as prescribed, low compliance is a major problem in health care.**[13]** 40-45% non – adherence was likely shown to the elderly patients. This may results from forgetfulness, avoidance of troublesome adverse effect, cognitive decline, physical inability to self administer medicine, economic limitations and intentional under dosage.[17,24]

Medication adherence is generally referred specifically to administration of prescribed drugs. Successful medication adherence requires a collaborative relationship between patient (or caregiver) and his/her healthcare provider. Compliance implies one way relationship in which the healthcare provider gives directions with little or no input from the patients. The term adherence is intended to be non judgemental, a statement of fact rather than of blame of the patient, prescriber or treatment. Compliance & concordance are synonyms of adherence. Medication adherence is most likely to be achieved when an equal partnership exists between the patients and Healthcare teams.[24]

3.1 Categorizing Medication Adherence[23]

- Adherent
- Partially adherent
- Non-adherent

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

Partially adherent is defined as adherence to more than 70 % of the medication regimen, while complying with more than 80 % of the prescribed regimen is termed as adherent. If the adherence is less than 70% it is non-adherence. Patient medication adherence may vary on a day-to-day basis, and may vary for different medications depending on the patient beliefs about the need for and efficacy of a particular medication.

3.2 Types of Non-Adherence[23]

There are different situation in which patients demonstrated medication nonadherence. They have been categorised based on whether the prescription was honoured, underuse or overuse of the prescription medication or use of nonprescription medicines. Medication non-adherence can be categorized as primary and secondary

- **Primary:** Patient not having a prescription dispensed. This may be due to unavailability of medication or financial problems
- **Secondary:** Intentional: The patient does not adhere to the prescription on his own volition. The patient may take less than the prescribed dose with an assumption that the prescribed dose is high or may take more than prescribed dose expecting a quicker recovery from the disease. Sometimes the patient benefit from his action and that is termed as 'intelligent nonadherence'.
- **Unintentional:** This occurs when the patient has misunderstood or forgotten the doctor's direction, or fails to adhere to the prescribed dosage regimen due to cognitive problems such as memory loss or confusion.

3.3 Method to Determine Medication Non-Adherence[23]

There are various methods to determine non-adherence. But there is no gold standard for measuring adherence. Method to determine medication non-adherence are as follows.

A. Direct Methods

Measure the concentration of drug in blood or in the urine. This gives indication of short-term adherence. It is limited by drug half-life and by individual absorption and metabolism pattern. It can also be measured by adding marker to the medicine.

B. Indirect Methods- Objective

- **Pill count method:** These method have continued to be frequently used measures of compliance, particularly in research and clinical settings. This is done by counting the tables remaining in container.
- **Prescription refill**: Data on prescription filled at pharmacies were used to calculate patients actual medication use pattern. Here compliance is determined by comparing the number the number of days elapsing between refills with number of days which should have elapsed. Pharmacy refill may be as reasonable as self reported in measuring compliance.

C. Medication Event Monitoring System

It is the one of the best method for assessing adherence. It consists of a microprocessor placed in the cap of a medication bottle. When a pill being pushed from the pack the bottle cap being opened and the microprocessor record the date and time but disadvantage with this device is, opening of vials does not assure that the medication was taken.

D. Indirect Methods- Subjective

- **Patient Interview:** This method is based on asking the patients if they have taken adhere to the prescribed regimens. Its advantages are, it is very simple and easy to perform and may provide additional information about the patients attitude towards the illness and medication use. Its disadvantages are it may not be very accurate and difficulty to accurately assess medication adherence for longer periods of time due to recall bias.
- **Diary Keeping:** It is one of the commonly used method. It involves the patient maintaining a standard diary where the occurrence and severity of various symptoms and medication use is recoded. The diary is reviewed during every consultation. It is very easy to use and practical. Disadvantages are that some patients may find it too time

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

consuming, that patients need to be literate and that there is no objective measure that the patients has taken the drug.

3.4 Utilization of Health Care Services

Hospital / clinic Attendance: In this method patient is asked to visit the clinic at regular interval for assuring adherence for a particular therapy. e.g. DOTS (Directly Observed Treatment Strategy) therapy.

- **Appointment making:** This refers to promise made by patients to meet the health care professional on a date that is set, but this is not a reliable method.
- **Appointment Keeping:** This is effort on the participation of the patient to keep the promise that had to meet the health care professional. It is a better method, patients who make appointment may not keep them but patients who keep appointment are genuinely interested in their medication.
- **Preventive visits:** This method is based on increasing medication adherence among dually diagnosed patients, requires attention to their social and day to day lives in order to engage them in treatment.

3.5 Therapeutic Outcome Measures

It involves therapeutic efficacy.
E.g. Blood pressure control, survival.

3.6 Factor Affecting on Medication Adherence

Healthcare providers (as part of a healthcare team within the health system) are an integral part of the five interacting dimensions of medication adherence identified by the World Health Organization (WHO), which include social/ economic factors, medical condition related factors, therapy related factors and patient behaviors.

A. Health Care System Related Factors

- Provider patient relationship.
- Patient information materials written at too high literacy level.
- Poor access or missed appointments.
- Lack of positive reinforcement from the healthcare provider.
- Lack of continuity care.

B. Social and Economic Factors

- Limited English language proficiency.
- Low health literacy.
- Lack of family or social support network.
- Unstable living condition; homelessness.
- Limited access to health care facilities.
- Medication cost.
- Elder abuse.
- Inability or difficulty accessing pharmacy.

C. Patients' Condition Related Factors

- Chronic conditions.
- Lack of symptoms.
- Depression.
- Psychotic disorder.
- Mental retardation / developmental disability.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

D. Therapy Related Factors

- Complexity of medication regimen.
- Treatment requires mastery of certain techniques (injections, inhalers).
- Duration of therapy.
- Frequent changes of medication regimen.
- Lack of immediate benefit of therapy.
- Actual or unpleasant side effect.
- Treatment interferes with lifestyle or requires significant behavioural changes.

E. Patient Related Factors

Physical Factors

- Visual impairment.
- Hearing impairment.
- Cognitive impairment.
- Impaired mobility or dexterity.
- Swallowing problems.

Psychological / Behavioral Factors

- Knowledge about disease.
- Perceived risk/ susceptibility to disease.
- Expectation or attitudes towards treatment.
- Motivation.
- Fear of possible adverse effects.
- Fear of dependence.
- Feeling stigmatized by disease.
- Frustration with healthcare providers.
- Psychosocial stress, anxiety, anger.
- Alcohol or substance abuse.

IV. ROLE OF PHARMACIST[23]

Pharmacists are in a unique position to improve medication adherence because they can actually show the medication to patient and relate any information to the medication itself. There are few studies that provide evidence of improved patient medication adherence as result of patient education provided by pharmacist. The information that patients need to know, which pharmacist can provide include name and purpose of drug, when and how to take the medication, possible side effect, precaution, interaction with food or other drugs, duration of therapy action to take if a dose is missed etc. Pharmacists can improve the adherence by other means like advising the physician on the simplification of drug regimen, providing patients with medication cards or medication aids such as dose test and identifying predisposing, enabling and reinforcing factors which can lead to medication non adherence. Though patient interview pharmacist can identify patients' knowledge and belief about their disease and drugs and adopt appropriate strategies to overcome the patients' medication non adherence.[23]

V. COVID-19

5.1 History [25,26,27]

Corona viruses are enveloped positive sense RNA viruses ranging from 60 nm to 140 nm in diameter with spike like projections on its surface giving it a crown like appearance under the electron microscope; hence the name corona virus [25]. Four corona viruses namely HKU1, NL63, 229E and OC43 have been in circulation in humans, and generally cause mild respiratory disease. There have been two events in the past two decades wherein crossover of animal beta-corona viruses to humans has resulted in severe disease. The first such instance was in 2002–2003 when a new coronavirus of the β genera and with origin in bats crossed over to humans via the intermediary host of palm civet cats in the Guangdong province of China. This virus, designated as severe acute respiratory syndrome coronavirus affected 8422 people mostly in China and

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

Hong Kong and caused 916 deaths (mortality rate 11%) before being contained [26]. Almost a decade later in 2012, the Middle East respiratory syndrome corona virus (MERS-CoV), also of bat origin, emerged in Saudi Arabia with dromedary camels as the intermediate host and affected 2494 people and caused 858 deaths (fatality rate 34%) [27].

5.2 Origin and Spread of COVID-19 [28,29]

In December 2019, adults in Wuhan, capital city of Hubei province and a major transportation hub of China started presenting to local hospitals with severe pneumonia of unknown cause. Many of the initial cases had a common exposure to the Huanan wholesale seafood market that also traded live animals. The surveillance system (put into place after the SARS outbreak) was activated and respiratory samples of patients were sent to reference labs for etiologic investigations. On December 31st 2019, China notified the outbreak to the World Health Organization and on 1st January the Huanan sea food market was closed. On 7th January the virus was identified as a corona virus that had >95% homology with the bat corona virus and > 70% similarity with the SARSCoV. Environmental samples from the Huanan sea food market also tested positive, signifying that the virus originated from there [28]. The number of cases started increasing exponentially, some of which did not have exposure to the live animal market, suggestive of the fact that human-to-human transmission was occurring [29].

5.3 Clinical Features [30-33]

The clinical features of COVID-19 are varied, ranging from asymptomatic state to acute respiratory distress syndrome and multi organ dysfunction. The common clinical features include fever (not in all), cough, sore throat, headache, fatigue, headache, myalgia and breathlessness. Conjunctivitis has also been described. Thus, they are indistinguishable from other respiratory infections. In a subset of patients, by the end of the first week the disease can progress to pneumonia, respiratory failure and death. This progression is associated with extreme rise in inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNFα [31]. The median time from onset of symptoms to dyspnea was 5 d, hospitalization 7 d and acute respiratory distress syndrome (ARDS) 8 d. The need for intensive care admission was in 25–30% of affected patients in published series. Complications witnessed included acute lung injury, ARDS, shock and acute kidney injury. Recovery started in the 2nd or 3rd wk. The median duration of hospital stay in those who recovered was 10 d. Adverse outcomes and death are more common in the elderly and those with underlying co-morbidities (50–75% of fatal cases). Fatality rate in hospitalized adult patients ranged from 4 to 11%. The overall case fatality rate is estimated to range between 2 and 3% [30].

Disease in neonates, infants and children has been also reported to be significantly milder than their adult counterparts. In a series of 34 children admitted to a hospital in Shenzhen, China between January 19th and February 7th, there were 14 males and 20 females. The median age was 8 y 11 mo and in 28 children the infection was linked to a family member and 26 children had history of travel/residence to Hubei province in China. All the patients were either asymptomatic (9%) or had mild disease. No severe or critical cases were seen. The most common symptoms were fever (50%) and cough (38%). All patients recovered with symptomatic therapy and there were no deaths. One case of severe pneumonia and multi-organ dysfunction in a child has also been reported [32]. Similarly the neonatal cases that have been reported have been mild [33].

5.4 Diagnosis [34]

A suspect case is defined as one with fever, sore throat and cough who has history of travel to China or other areas of persistent local transmission or contact with patients with similar travel history or those with confirmed COVID-19 infection. However cases may be asymptomatic or even without fever. A confirmed case is a suspect case with a positive molecular test. Specific diagnosis is by specific molecular tests on respiratory samples (throat swab/ nasopharyngeal swab/ sputum/ endotracheal aspirates and bronchoalveolar lavage). Virus may also be detected in the stool and in severe cases, the blood. It must be remembered that the multiplex PCR panels currently available do not include the COVID-19. Commercial tests are also not available at present. In a suspect case in India, the appropriate sample has to be sent to designated reference labs in India or the National Institute of Virology in Pune. As the epidemic progresses, commercial tests will become available.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

5.5 Treatment [35-37]

Treatment is essentially supportive and symptomatic. The first step is to ensure adequate isolation (discussed later) to prevent transmission to other contacts, patients and healthcare workers. Mild illness should be managed at home with counseling about danger signs. The usual principles are maintaining hydration and nutrition and controlling fever and cough. Routine use of antibiotics and anti-virals such as oseltamivir should be avoided in confirmed cases. In hypoxic patients, provision of oxygen through nasal prongs, face mask, high flow nasal cannula (HFNC) or non-invasive ventilation is indicated. Mechanical ventilation and even extra corporeal membrane oxygen support may be needed. Renal replacement therapy may be needed in some. Antibiotics and antifungal are required if co-infections are suspected or proven. The role of corticosteroids is unproven; while current international consensus and WHO advocate against their use, Chinese guidelines do recommend short term therapy with low-to-moderate dose corticosteroids in COVID-19 ARDS [35,36]. Detailed guidelines for critical care management for COVID-19 have been published by the WHO [37]. There is, as of now, no approved treatment for COVID-19. Antiviral drugs such as ribavirin, lopinavirritonavir have been used based on the experience with SARS and MERS. In a historical control study in patients with SARS, patients treated with lopinavir-ritonavir with ribavirin had better outcomes as compared to those given ribavirin alone [29].

5.6 Prevention [38,39]

Since at this time there are no approved treatments for this infection, prevention is crucial. Several properties of this virus make prevention difficult namely, non-specific features of the disease, the infectivity even before onset of symptoms in the incubation period, transmission from asymptomatic people, long incubation period, tropism for mucosal surfaces such as the conjunctiva, prolonged duration of the illness and transmission even after clinical recovery. Isolation of confirmed or suspected cases with mild illness at home is recommended. The ventilation at home should be good with sunlight to allow for destruction of virus. Patients should be asked to wear a simple surgical mask and practice cough hygiene. Caregivers should be asked to wear a surgical mask when in the same room as patient and use hand hygiene every 15–20 min. The greatest risk in COVID-19 is transmission to healthcare workers. In the SARS outbreak of 2002, 21% of those affected were healthcare workers [38]. Till date, almost 1500 healthcare workers in China have been infected with 6 deaths. The doctor who first warned about the virus has died too. It is important to protect healthcare workers to ensure continuity of care and to prevent transmission of infection to other patients. While COVID-19 transmits as a droplet pathogen and is placed in Category B of infectious agents (highly pathogenic H5N1 and SARS), by the China National Health Commission, infection control measures recommended are those for category A agents (cholera, plague). Patients should be placed in separate rooms or cohorted together. Negative pressure rooms are not generally needed. The rooms and surfaces and equipment should undergo regular decontamination preferably with sodium hypochlorite. Healthcare workers should be provided with fit tested N95 respirators and protective suits and goggles. Airborne transmission precautions should be taken during aerosol generating procedures such as intubation, suction and tracheostomies. All contacts including healthcare workers should be monitored for development of symptoms of COVID-19. Patients can be discharged from isolation once they are a febrile for atleast 3 d and have two consecutive negative molecular tests at 1 d sampling interval[39].

5.7 Aim

To study polypharmacy and medication adherence in patients with covid-19 diseases.

5.8 Objectives

A. Primary Objective

To determine the incidence of a polypharmacy & its impact on medication adherence in patients with covid-19 diseases.

B. Secondary Objectives

- To establish the extent of non-adherence to prescribed medication.
- To determine the factors of medication non-adherence.
- To investigate the adverse event outcome in study population.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

5.9 Methodology

A. Study Design

It is single centre prospective study at tertiary care hospital in Anand region. This study was carried out on patients suffering from covid-19 diseases.

B. Study Setting and Duration

This study was carried on outdoor patients suffering from covid-19 diseases at faith Hospital, Anand for period of 3 months from December 2021 to February 2022.

C. Study Selection Criteria

The indoor patients at Faith Hospital were enrolled in to the study after taking their consent and by considering following inclusion and exclusion criteria.

D. Inclusion Criteria

- Identification of disease.
- Patients must had covid-19 diseases.
- Patients were receiving two or more than two drugs.
- Patients willing to participate in the study.

E. Study Procedure

Pre Study

- Protocol, Patient information sheet, Informed consent form and patient data collection form were prepared.
- Medication adherence assessment questionnaire was developed by using general medication questionnaire, more risky scale and tool for adherence behavior (TABS) questionnaire.
- Pilot study was conducted for reliability assessment and to check internal consistency of medication adherence assessment questionnaire (MAAQ).
- Protocol & other required documents submitted to ethics committee & approval of study was taken from the ethics committee.

During study

- Patients were identified from all visited patients.
- Patients were screened and informed about the study. informed consent form was obtained from patients.
- All patients were checked for Inclusion criteria and enrolled them into study.
- Demographic details, vital signs & medication details were collected and entered into patients data collection from.
- Obtained the completed MAAQ from patients.
- All the required data was collected at follow up visit.

Post study

- All the necessary data were collected and compiled.
- Statistical analysis applied to respective data.
- Final report was prepared and reviewed.

Source data

- Patient's case records.
- Prescriptions.
- Treatment charts.
- Medication adherence assessment questionnaire.
- Patient's personal or telephonic interview.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

Patients' data were derived from patient's case records and prescription. If the patient previously admitted to hospital then medical history was collected from treatment charts and discharge summary. The all necessary data like demographic details, vital signs, medication details were collected and entered into data collection form. Other data were collected from the interview of the patients. Medication adherence assessment questionnaire were completed by patients with the help of investigator at each visit. This data were collected and added at each visit.

5.10 Development of Medication Adherence Assessment Questionnaire

At first gathered the all the questionnaire on medication adherence like general medication questionnaire, more risky scale, tool for adherence behavior (TABS). Then all the questionnaire & there related published literature were reviewed for the assessment of medication adherence in patients with multiple disorders. A final questionnaire on medication adherence assessment questionnaire (MAAQ) was developed as to measure the assessment of medication adherence. The questionnaire contains total 12 question based on memory, cost, side effect etc. Which are the probable cause for the medication non-adherence. Each question had answer like always, frequently, occasionally, rarely, never which was ranged from 1 to 5 respectively. The medication adherence increased with the higher score of medication adherence assessment questionnaire.

A. Pilot study

The designed questionnaire was tested though pilot study with small sample size of 20 patients. These 20 patients were enrolled in pilot study with same criteria as this protocol. This questionnaire was administered twice to all patients in one week interval.

B. Validation of Questionnaire

Validation of questionnaire was done by using Pearson correlation and Cronbach alpha coefficient. Pearson correlation coefficient was used for assessment of reliability. It was calculated from score of MAAQ of 20 patients in one week interval. Cronbach alpha coefficient was used for assessment of internal consistency of all question of questionnaire

C. Medication adherence assessment

Medication adherence of the study patients would be calculated by medication adherence assessment questionnaire. The questionnaire would be used at the enrollment visit, 15 days (first follow- up visit), 30 days (second follow- up visit).

$$\% \text{ Adherence} = \frac{\text{Patient's MAAQ score} * 100}{\text{Maximum score of MAAQ}}$$

Maximum score that a patient with complete medication adherence was 60. The 75 % of medication adherence and above was considered as adherent patients.

D. Statistical Method

Normal statistic like mean, average, percentage were used for calculation of medication adherence by Microsoft excel. Pearson correlation and Cronbach alpha coefficient test were used for validation of the medication adherence assessment questionnaire.

VI. RESULT

Till now, total of 60 patients were reviewed and enrolled into the study from December 2021 to February 2022. From total of 60 patients, 39 patients were suffering from covid-19 disease.

6.1 Incidence of Polypharmacy in Study Patients

The overall incidence of polypharmacy in study completed patients was 43.3 %. The table for the incidence of polypharmacy is shown below.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

Number of patient with (%) Disease Patient Patient with poly pharmacy		
Covid-19 29 11 37.9		

Table: Incidence of polypharmacy with study completed patient

6.2 Demographic Details of Study Patients

From total patients, 54.2% of patients were male. Patients with diabetes mostly received 2-4 drugs (51.7%), 5-7 drugs (48.3%). Same as patients with covid-19 mostly received 2-4 drugs (54.5%), 5-7 drugs (42.4%). Mostly patients (48.5%) have 1-2 co-morbidities. Demographic details of study patients is shown below.

Number of patient (%) Demographic covid-19 Parameter (n=29)	
Age	
18-30 3(10.3%)	
31-40 4(13.8%)	
41-50 6(20.7%)	
51-60 9(31.0%)	
≥60	7(24.1%)
Sex	
Male 17(58.6%)	
Female 12(41.4%)	
Co-morbidities	
Nil 5(17.2%)	
1-2 14(51.7%)	
3-4	9(31.0%)
No.of drugs	
2-4	15(51.7%)
5-7 14(48.3%)	
8-10	0(0.0%)

Table: Demographic details of study patient

6.3 Average Number of Drug Distribution in Patients

The average number of the drugs used for patients in covid-19 group were respectively 4.7. Range of drugs and average number of drugs group wise shown below.

Disease Average number of drugs Range		
Covid-19	4.7	2-7

Table: Average number of drug distribution in patients

6.4 Medication Adherence Assessment by Medication Adherence Assessment Questionnaire (MAAQ)

Medication adherence of the completed patients was assessed by using MAAQ, which consist of 12 questions. It consist the question regarding cost, memory, side effect, carelessness, inconvenience. Each question had answer like always, frequently, occasionally, rarely, never which was ranged from 1 to 5 respectively. Total Maximum score of MAAQ was 45. Medication adherence was calculated by using the formula of mentioned in methodology. The medication adherence rate of 75% and above was considered to be adherent, others are considered as non-adherent.

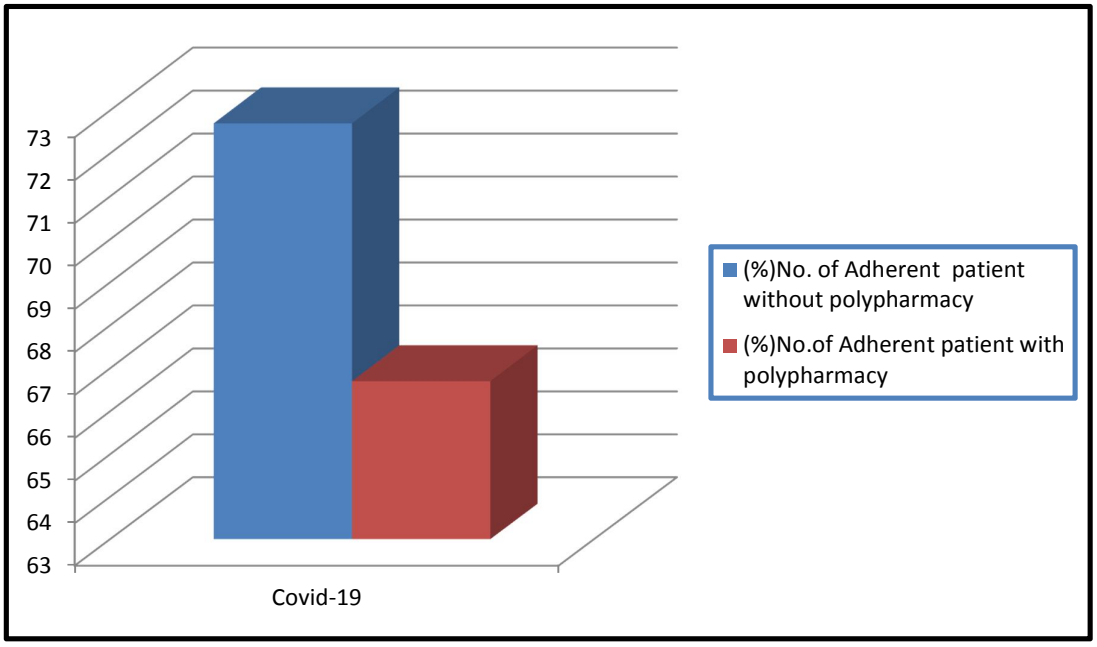
IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

6.5 Impact of Polypharmacy on Medication Adherence

From patients without polypharmacy 65.5% of patients were found adherent while patients with polypharmacy only 35.7% of patients were adherent.

Disease Patient with Polypharmacy	Adherence patient with Polypharmacy(%)	Patient without Polypharmacy	Adherent patient without Polypharmacy(%)
Covid-19 11	8(72.7%)	21	12(66.7%)

Table: Impact of polypharmacy on medication adherence



Graph: Impact of polypharmacy on medication adherence

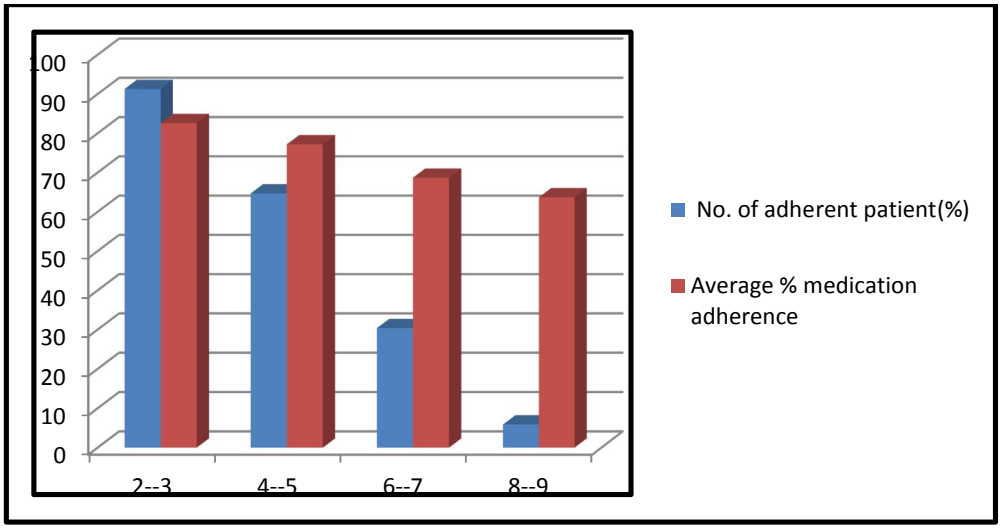
6.6 Medication Adherence of Patients with No. of Drugs

As shown below medication adherence of patient decreased with the increased number of drugs. From patients who received 2 – 3 drugs, majority of patients (91.3%) were found to be adherent compare to (64.7%) patients who received 4 – 5 drugs. Average medication adherence was high in patients treated with 2 – 3 drugs. Average percentage medication adherence was also decreasing as the number of drugs increase.

Table: Average percentage of medication adherence with No. of drug

No. of drugs	No. of Patient	No. of patient Adherent	Average% medication adherence
2-3	23	21(91.3%)	82.6
4-5	34	22(64.7%)	77.2
6-7	23	7(30.4%)	68.7
8-9	17	1(5.9%)	63.7

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252



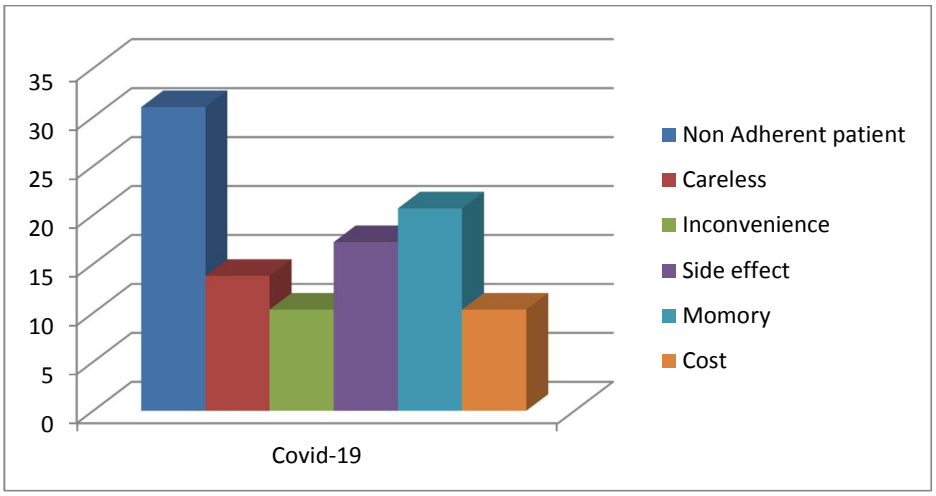
Graph: Average percentage of medication adherence with No. of drugs.

6.7 Predictors of Medication Non-Adherence

Questionnaire contain question regarding careless, Inconvenience, side effect, memory, cost. Careless attitude was containing factor like medication carelessness and poor provider patient relationship. Inconvenience was containing factors like long term medication and multiple medications at same time. Careless (34.8%) and Inconvenience (32.6%) were low predictors for medication non-adherence. Of the all non-adherent patient, side- effect (52.2%) and memory (58.7%) were considered the major predictors of medication non-adherence. The (43.5%) cost of medication and healthcare also showed some effect on medication non-adherence. The predictors of medication non-adherence presented in below table and graph.

No. of patient(29) Covid-19	
Non Adherent patient 9(31.0%)	
Careless	4(13.7%)
Inconveniance 3(10.3%)	
Side effect 5(17.2%)	
Memory 6(20.6%)	
Cost 3(10.3%)	

Table: Predictors of medication non-adherence



Graph: Average percentage of medication adherence with No. of drug.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

VII. CONCLUSION

Our study revealed that polypharmacy showed major impact on medication non adherence. Average percentage medication adherence of study population was also decreased with increased polypharmacy. Major predictors identified as a reason for medication non-adherence were memory and side effect. Incidences of adverse event were also affected by polypharmacy. Percentages of medication adherent were also affected by age and co-morbidities of patients. To improve the medication adherence this study may be extended to by using medication monitoring system or medication compliance equipment. Simplify the prescribed medication regimen can also improve medication adherence to greater extent.

ACKNOWLEDGEMENT

We have taken efforts in this project. However, it would not have been possible without the kind support and help of many individuals. We would like to extend our sincere thanks to all of them.

We are highly indebted to **Mr. Rikin Patel, Assistant Professor, Shivam Pharmaceutical Studies & Research Centre** for their guidance and constant supervision as well as for providing necessary information regarding the project and also for their support in completing the project. Her constant guidance and willingness to share her vast knowledge made us understand this project and its manifestations in great depths ad helped us to complete the assigned tasks on time.

We would also like to thanks **Dr. Hetal Solanki**, **H.O.D, S.P.S.R.C** and all the teaching staff who helped us anytime whenever we need any help.

We acknowledge our deep sense of gratitude to our loving parents for being a constant source of inspiration and motivation. We also thank our friends who have played a significant role throughout the project and life.

REFERENCES

[1]. Hajjar E., "Polypharmacy in Elderly." The American journal of Geriatric Pharmacotherapy, 2007, 5(4), 345-351.

[2]. Bjerrum L., Sogaard J., Hallas J., and Kragstrup J., "Polypharmacy: correlations with sex, age and drug regimen." Eur J Clin Pharmacol, 1998, 54, 197-202.

[3]. World Health Organization. Adherence to Long-term Therapies: Evidence for Action.January2003.Available http://www.who.int/chp/knowledge/publications/adherence_report/en/index.html

[4]. Osterberg L., and Blaschke T. "Adherence to medication." N Engl J Med. 2005, 353(5), 487-97.

[5]. Parker KL., Brunton LL. and Lazo JS., Goodman & Gilman's the Pharmacological basis of Therapeutics, edited by John A. Oates, 11th Edn, McGraw-Hill Medical publishing division, 2006.

[6]. Galavis R., and Wooten J., " Polypharmacy: Keeping elderly safe", August 2005,http://www.modernmed icine.com/modern-edicine/news/ polypharmacykeeping-elderly-safe.

[7]. Koh Y., Kutty F., Li S., "Therapy related hospital admission in patients on Polypharmacy in Singapur." Pharma word Sci, 2003, 25(4), 135-137

[8]. Richardson K., Moore P., "Polypharmacy in adults over 50 in Ireland: Opportunity for cost saving and improved healthcare." The irish study on aging, 2012, 1-29.

[9]. Richardson K., Moore P., "Polypharmacy in adults over 50 in Ireland: Opportunity for cost saving and improved healthcare." The irish study on aging, 2012, 1-29.

[10]. Alsuwaidan A, Almedlej N, Alsabti S, et al. A comprehensive overview of polypharmacy in elderly patients in Saudi Arabia. Geriatrics. 2019;4(2):36. doi:10.3390/geriatrics4020036

[11]. Zelko E, Klemenc-Ketis Z, Tusek-Bunc K. Medication adherence in elderly with polypharmacy living at home: a systematic review of existing studies. Mater Sociomed. 2016;28(2):129–132. doi: doi.10.5455/msm.2016.28.129-132.

[12]. Mahase E. China coronavirus: what do we know so far? BMJ. 2020;368:m308. doi:10.1136/bmj.m308

[13]. Thompson WW, Shay DK, Weintraub E, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. JAMA. 2003;289(2):179–186. doi:10.1001/jama.289.2.179

[14]. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020:e201585. doi:10.1001/jama.2020.1585.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, April 2022
Impact Factor: 6.252

[15]. Richardson M., McCabe R., and Priebe S., "Are attitudes towards medication adherence associated with medication adherence behaviours among patients with psychosis? A systematic review and meta analysis" Soc PsychiatryPsychiatr Epidemiol, 2012, 1-9.
[16]. Horne R., "Compliance, adherence and concordance: implications for asthma treatment." Chest, 2006,130, 65-72.
[17]. Good C., "Polypharmacy in Elderly Patients with Diabetes." Diabetes Spectrum, 2002, 15(4), 240-248.
[18]. Richardson K., Moore P., "Polypharmacy in adults over 50 in Ireland: Opportunity for cost saving and improved healthcare." The irish study on aging, 2012, 1-29.
[19]. Richardson K., Moore P., "Polypharmacy in adults over 50 in Ireland: Opportunity for cost saving and improved healthcare." The irish study on aging, 2012, 1-29.
[20]. Polypharmacy in older adults. http://www. md.edu.
[21]. Corcoran M., "Polypharmacy in older Patient with Cancer" Cancer Control,4(5), 1-15.
[22]. Hajjar E., "Polypharmacy in Elderly." The American journal of Geriatric Pharmacotherapy, 2007, 5(4), 345-351.
[23]. Mahesh PA., and Parthasarthi G., "A Textbook of Clinical Pharmacy Practice". 8th Edn, Oriented Longman Pvt Ltd.,2003, pp 53-71.
[24]. MacLaughlin E., Raehl C., Treadway A., Sterling T., Zolle D., Bond C., "Assessing Medication Adherence in the Elderly." Drugs Aging, 2005, 22(3), 231-255.
[25]. Richman DD, Whitley RJ, Hayden FG. Clinical Virology, 4th ed. Washington: ASM Press; 2016.
[26]. Chan-Yeung M, Xu RH. SARS: epidemiology. Respirology. 2003;8:S9–14.
[27]. Middle East Respiratory Syndrome Coronavirus. Available at:https://www.who.int/emergencies/mers-cov/en/. Accessed 16 Feb 2020
[28]. Xinhua. China's CDC detects a large number of new coronaviruses in the South China seafood market in Wuhan. Available at:
[29]. https://www.xinhuanet.com/2020-01/27/c_1125504355.htm. Accessed 20Feb 2020.
[30]. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395: 497–506.
[31]. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395:507–13
[32]. Coronavirus Outbreak. Available at: https://www.worldometers. info/coronavirus/. Accessed 23 Feb 2020.
[33]. Chen F, Liu ZS, Zhang FR, et al. First case of severe childhood novel coronavirus pneumonia in China. Zhonghua Er Ke Za Zhi.2020;58:E005.3
[34]. Zeng LK, Tao XW, YuanWH,Wang J, Liu X, Liu ZS. First case of neonate infected with novel coronavirus pneumonia in China. Zhonghua Er Ke Za Zhi. 2020;58:E009
[35]. Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus [2019-nCoV] infected pneumonia [standard version]. Mil Med Res. 2020;7:4.
[36]. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet. 2020;395:473–5.
[37]. Zhao JP, Hu Y, Du RH, et al. Expert consensus on the use of corticosteroid in patients with 2019-nCoV pneumonia. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43:E007.
[38]. WHO. Clinical management of severe acute respiratory infection when novel coronavirus [nCoV] infection is suspected. Available at: https://www.who.int/publications-detail/clinical-managementof- severe-acute-respiratory-infection-when-novelcoronavirus- [ncov]-infection-is-suspected. Accessed 9 Feb 2020.
[39]. Chang D, Xu H, Rebaza A, Sharma L, Dela Cruz CS. Protecting health-care workers from subclinical coronavirus infection. Lancet Respir Med. 2020.
[40]. https://doi.org/10.1016/S2213-2600(20)30066-7.
[41]. Li J, Li J, Xie X, et al. Game consumption and the 2019 novel coronavirus. Lancet Infect Dis. 2020.https://doi.org/10.1016/ S1473-3099(20)30063-3.