



IJPPR

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

ISSN 2349-7203




Human Journals

Research Article

May 2023 Vol.:27, Issue:2


© All rights are reserved by Vineeth Vidhyasagar. P et al.

Comparative Study on Dexamethasone and Methylprednisolone in Intensive Care Patients with COVID-19 and Management of Corticosteroid Induced Hyperglycemia in COVID-ICU Patients



IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

ISSN 2349-7203



HUMAN

Vineeth Vidhyasagar. P^{1*}, Hariharan. R. B¹, Bala Bharathi. V¹, C. K. Dhanapal¹, V. Manojkumar²

1 – Department of Pharmacy, Annamalai University, Annamalai Nagar-608002, Tamilnadu, India.

2 – Department of Medicine, Government Cuddalore Medical College & Hospital (RMMCH), Annamalai University. Tamilnadu, India.

Submitted: 27 April 2023
Accepted: 02 May 2023
Published: 30 May 2023

Keywords: COVID-19, Intensive Care Unit (ICU), corticosteroids, hyperglycaemia, dexamethasone, methyl prednisolone.

ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) originated in Wuhan, China in December 2019. Pathophysiology of COVID-19 is primarily attributed to excessive inflammatory reactions. Patient with severe COVID-19 quickly progressed to acute respiratory failure, pulmonary oedema and acute respiratory distress syndrome (ARDS). Corticosteroids therapy are the clinically preferred to improve clinical symptoms and oxygenation of patients with COVID-19. The treatment protocol recommends that use of steroids such as injectable methyl prednisolone, dexamethasone two dose daily usually for duration of 5 to 10 days for moderate and severe hospitalized COVID-19 patients. This study prospectively compares the effectiveness of Methylprednisolone to Dexamethasone in patients with SARS COV-2 requiring intensive care and the management of corticosteroid induces Hyperglycemia. Use of steroids increase the blood sugar by increasing the hepatic glycogenesis or production of glucose from the liver by enhancing the effects of regulatory hormones. This study takes place in a large tertiary teaching hospital were patient who tested positive and admitted to the ICU for COVID-19 from November 2021- April 2022 based on the inclusion & exclusion criteria compares the outcome of two groups of patients. This study will be helpful to know the drug of choice in treating COVID intensive care patients and also useful for management of corticosteroid induced hyperglycemia in COVID ICU patients.



www.ijppr.humanjournals.com

INTRODUCTION:

Coronavirus disease 2019 (COVID-19) caused by the novel coronavirus also known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) was declared as a global pandemic by the world health organization (WHO) on march 12, 2020. The severity and pathophysiology of the disease have been linked to hyper-inflammation. Therefore, a combination therapy of off-label drugs such as immunosuppressor/ immunomodulators, inflammatory cytokines antagonists, non-steroids anti-inflammatory drugs (NASIDS) may be importance in mitigating the potential effects of cytokine storm in the damaging phases of covid-19. Acute respiratory distress syndrome is a common complication of severe viral pneumonia such as influenza and COVID-19, that requires critical care including Ventilatory support, use of corticosteroids and other adjunctive therapies to reduce the massive airways inflammation^[1]. Supportive and adjuvant therapy have been recommended for the treatment of COVID-19 due to the absence of specific treatments such as antivirals. The histological pattern of pulmonary oedema, hyaline membrane formation and acute fibrinous and organizing pneumonia (AFOP) which characterize acute lung injury of the disease suggest that timely and appropriate use of corticosteroid may be beneficial in patients with severe COVID-19^[5]. Corticosteroid suppress inflammation induced lung injury by inhibiting lung inflammation in critically ill patients^[2]. Cytokine storm syndrome and systemic inflammatory response triggered by SARS-COV-2 play a crucial role in conferring pathogenicity during infection. Studies suggested that corticosteroids have potent anti-inflammatory effects that help reduce her immune response in severe COVID-19 infection. Low dose of systemic glucocorticoids and heparin may control inflammation mediated lung injury and mitigate the effects of cytokine storm syndrome, thereby preventing progression to respiratory failure and death. Various corticosteroids used in COVID-19 infection are Dexamethasone, Methyl prednisolone, Hydrocortisone, Prednisolone. Based on the positive results of the recovery trial, the National Institutes of Health (NIH) COVID-19 treatment guidelines and the World Health Organization (WHO) approved the findings on the beneficial use of dexamethasone and methyl prednisolone in treating critically ill patient with COVID-19^[3]. The updated treatment protocols for moderate cases advised considering methyl prednisolone 0.5 to 1 mg/kg or dexamethasone 0.1 to 0.2 mg/kg for three days, preferably within 48 hours of admission or if oxygen requirement is increasing and if inflammatory markers are increased^[4]. Thus the continuation of steroids for a prolonged time after discharge is not uncommon in the prevention of post-COVID pulmonary fibrosis. These

supra-physiological doses may exacerbate hyperglycaemia individuals with diabetes, unmask diabetes in population at risk and precipitate acute complications. Insulin is the preferred drug for all hospitalized patient with COVID on steroids with [6].

This study was designed to compare the effectiveness of dexamethasone and methylprednisolone drug by monitoring the spo2 level, Duration of drug, recovery & mortality rate. The management of corticosteroid induced Hyperglycemia in COVID-ICU patients was performed by monitoring the CBG level, observing and reporting the treatment measures.

METHODS AND MATERIALS:

Ethical Clearance:

This prospective study was approved by Institutional Human Ethics Committee, Number: IHEC/872/2022 and permitted by Member Secretary, Institutional Human Ethics Committee, Government Cuddalore Medical College & Hospital (RMMCH), Annamalai University. The registration number of IEC is EC/NEW/INST/2020/1249.

Study Site:

The Study was conducted in Department of Medicine, Government Cuddalore Medical College & Hospital (RMMCH), Annamalai University, Annamalai Nagar, Chidambaram, Cuddalore, Tamil Nadu, which is a multi-speciality tertiary care teaching hospital located in rural south India.

Study Period:

The Study was carried out for a period of six months, starting from November 2021- April 2022.

Study Design:

Prospective Observational Comparative Cohort Study, where the medical records of the inpatient admitted in COVID-ICU during the period of November 2021- April 2022 were observed. One exposed group (Dexamethasone) is compared with another exposed group (Methyl prednisolone) to look for differences in their outcome.

Study Population:

All the Intensive Care COVID-19 patients admitted during the period (November 2021-April 2022). The selection criteria were based on the inclusion and exclusion criteria.

Inclusion Criteria:

- COVID positive patients admitted in the COVID Intensive Care Unit of the hospital COVID-19 patients with oxygen demand.
- COVID patients receiving Dexamethasone and Methylprednisolone drugs during the period of November 2021 to April 2022.

Exclusion Criteria:

- COVID negative cases & suspected cases.
- Patient with incomplete course of therapy.
- Cases with insufficient data.
- Mentally ill patients.
- Paediatric patients.
- Pregnancy & lactating women.



Sample Size Determination:

For infinite population,



$$S_i = \frac{Z^2 * P(1-P)}{M^2}$$

Z = z-score, P = Population Proportion (50% assumed = 0.5), M = Margin of error (5% = 0.05)

$$S_i = \frac{(1.96)^2 * 0.5(1-0.5)}{(0.05)^2}$$

$$S_i = 384.16$$

For required population,

$$S = \frac{S_i}{1 + (S-1/N)}$$
$$S = \frac{384.16}{1 + (384.16-1/180)}$$
$$S = 384.16$$
$$3.1$$
$$S = 124$$

The calculated sample size is 124. The obtained sample size during the study is 123.

Study Recruitment Procedure:

- The recruitment of subjects was carried out with the help of physician who has good knowledge of patient's medical history.
- The study procedure was completely explained to the patients (or care takers) and a consent form has been collected from them.
- **Target Population:** Patients who were treated with Dexamethasone & Methylprednisolone in COVID-19 Intensive Care Unit.
- **Study Population:** Patient who fulfil both the inclusion and exclusion criteria.

Sources of Data:

- The data required for the study was collected from case sheets (inpatients) and personal interaction with the patient's care takers.
- Drug information obtained from physicians.
- Lab data collected from Department of Biochemistry.
- Case history and physical examination form.
- Treatment chart, Progress card, Discharge summary.

Designing of Patient Data Collection Form:

Data collection form was designed based on study. A data collection form was used to collect all the details of information like patient's name, age, gender, inpatient number, chief complaints, past medication history, laboratory finding, and therapeutic management. Data collection form includes the following sections:

- Patients Demographics.
- Hospital Admission
- Medical History
- Laboratory investigations (Sr. Ferritin, CRP, D-Dimer, Temperature, PR, RR)
- Confirmatory tests (swab test).
- Severity assessment (CT score, CO-RADS)
- Vitals Monitoring (Spo₂, CBG)
- Drug monitoring (Dose, Duration, Route & Frequency of Glucocorticoids)
- Duration of ICU stay.
- Discharge summary, Death summary.

Statistical Tools to Analysis Data:

- The data entry and data analysis were performed by using **Microsoft Excel 2016**.
- The frequency tables and descriptive statistics were used to describe the variables of interest.
- **Unpaired t test for testing statistical significance.**

Used to compare the means of two independent groups (Dexamethasone treated group & Methylprednisolone treated groups). To determine if there is a significance between the two.

- Normality of Length of hospital stay (Dexamethasone and Methylprednisolone group) was assessed with the **Shapiro-Wilk test**.

Alpha risk was set to 5% ($\alpha = 0.05$).

- "Statistical analysis was performed with the online software **EasyMedStat** (www.easymedstat.com; Neuilly-Sur-Seine; France)."

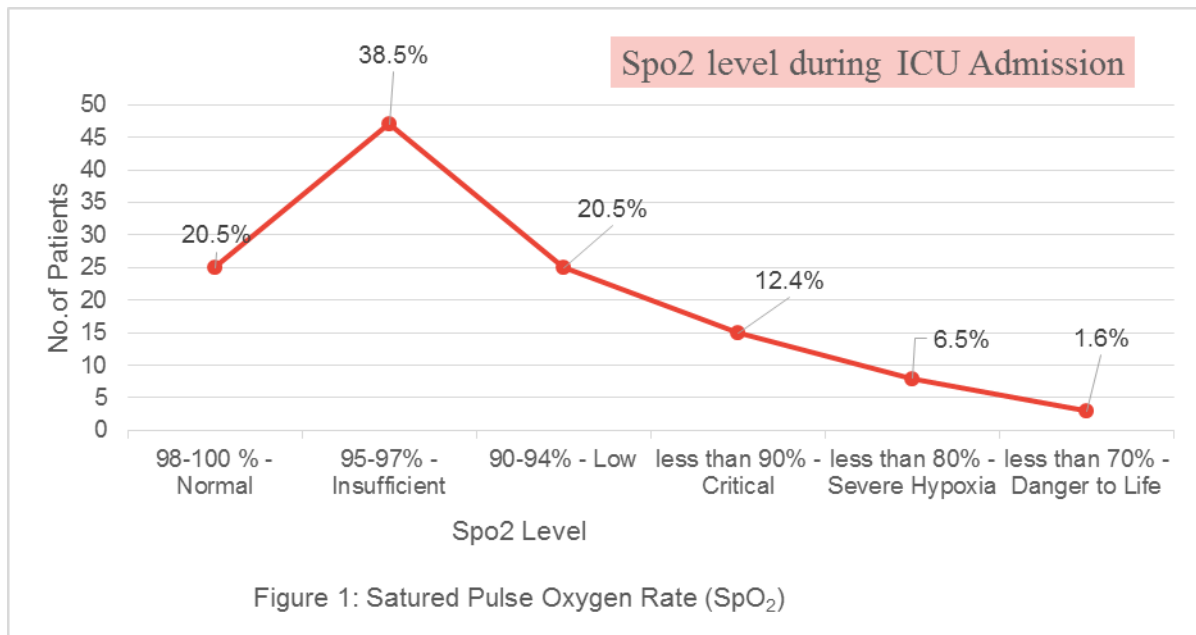
RESULTS AND DISCUSSION:

Patients with severe COVID-19 quickly progressed to acute renal failure, pulmonary edema and acute respiratory distress syndrome (ARDS). As a result, antiviral and anti-inflammatory treatments have become an increasing concern. As there is no standard treatment for this pandemic, steroidal treatments served its best in severe conditions. Although steroids do not directly interact with the viral replication, it reduces the complication made by virus in severe conditions like cytokine storm.

In our study, we compared steroidal drugs **Dexamethasone and Methylprednisolone**. Based on sample size calculation, we obtained a theoretical value of 124. But in our observational study, we observed **123** subjects. Out of that 123 patients, 72 patients received Methylprednisolone and 51 received Dexamethasone. We divided the subjects into two treatment groups receiving different steroidal drugs. We compared the various aspects of each treatment group.

In this study, the patients who were in Intensive Care Unit for COVID therapy were mostly from the age group of 60-69yrs which is 35.7%, of which males were affected more than females. Out of 123 patients Men (64.2%) and Women (35.8%) were affected.

The patients were admitted with various history of present illness, in which the most common causes were Fever (28.7%), Cold & Cough (24.5%), Shortness of breath (22%), Pain (9.5%), Headache (5.1%), Nausea & vomiting (3.5%).



Comorbidities have been considered as a higher concern in COVID 19 therapy. Patients with pre-existing condition face a higher mortality rate when compared to people affected without any comorbidities. From the data collected in our study, predominant comorbidities were Diabetes mellitus (41.7%), Systemic hypertension (29.8), Coronary artery disease (8.3%), Tuberculosis (5.2%), Bronchial Asthma (2.2%), COPD (2.2%). Some of the risk factors which boost the severity of infection were above 60yrs of age (40%), alcoholic (28.3%), smoker (24.1%), congenital heart disease (7.6%).

The admitted patients were primarily treated based upon the vitals measured. 69% of the patients had respiratory rate greater than 16. Since most of the patients suffer from fever, 67.6% had the temperature greater than 97.7⁰c. 20% of the patients had Blood pressure above normal level.

Figure 1 represent the normal percentage of oxygen in blood is usually 95% or higher. Lower oxygen levels can be early warning sign that medical care is needed. 20.5% of patients had low Spo2 (90-94%), 12.4% had critical Spo2(<90%), 6.5% had severe hypoxia (<80%).

Table 1 represent the laboratory biomarkers which shows the severity of the infection are **CRP, D-Dimer, ferritin level, and Interleukin-6**. The mean CRP of 112 patients was 8.05 mg/L, the mean serum Ferritin of 109 patients was 185.39 mcg/L, the mean IL-6 of 116 patients was 34.21 pg/ml, the mean D-Dimer of 118 patients was 2.81.

Table 1: Laboratory Biomarkers.

LABORATORY DATA	MEAN ± S.D	NO OF PATIENTS
CRP	8.05 ± 3.046	112
Ferritin	185.39 ± 41.56	109
IL-6	34.21 ± 22.91	116
Dimer	2.81 ± 2.29	118

PCR test was used to confirm the covid positive cases. Other diagnostic tests used were **CT Chest (score) and CORADS scale**. 21.5% patients had CT severity score 11-12/25, 34% patients had CT SS 37-40/40. 47.1% patients had very high level of CORADS scale (5). **Covid-19 vaccine** has shown an impact on the amount of infection by corona virus on lungs. Among 72 vaccinated patients **58** patients had their **first dose**, **14** had their **second dose** which shows that those who received two doses of covid vaccine has lesser probability of getting serious COVID-19 infection.

We included various aspects and statistical tools to compare the efficacy of two drugs. E.g., Days on steroidal therapy, dose, Spo2 level etc., Table 2 compares the two drugs. The mean and S.D of age in Dexamethasone treated group was 50.47±15.02 & Methylprednisolone treated group was 59.9±11.3. Dexamethasone treated group involves 66.6% of patients below 60 years of age and 33.4% of patients above 60 years of age. In Methylprednisolone treated group 42.3% of patients were below 60 years and 57.7% of patients were above 60 years. The gender wise distribution in each treatment group were as follows: In Dexamethasone treatment group 60.8% of patients were male and 39.2% were female. In Methylprednisolone treated group 62% were male and 38% were female. Comorbidities had a vital effect in COVID-19 severity. Major comorbidities included Diabetes mellitus, Hypertension, Bronchial asthma, COPD and CAD. Comorbidities in Dexamethasone treatment group include: Diabetes mellitus (39.2%), Hypertension (27.4%), Bronchial asthma (1.9%), COPD (3.9%), CAD (1.9%). Comorbidities in Methylprednisolone treatment included: Diabetes mellitus (48.6%), Hypertension (38.8%), Bronchial asthma (2.7%), COPD (1.4%), CAD (16.6%). The patients in Dexamethasone treated group also received: Remdesivir (68.6%), Tocilizumab (27.4%), Antibiotics (100%), Anthelmintics (23.5%). The patients in Methylprednisolone treated group also received: Remdesivir (62.5%), Tocilizumab (20.8%), Antibiotics (95.8%), Anthelmintics (18%). The mean days on steroidal treatment in

Dexamethasone treated group is **7.1±3.4** and Methylprednisolone treated group is **6.8±3.6**. on comparing the mean (days on steroid) in both treatment groups, we concluded that **Methylprednisolone group received treatment for a shorter period** when compared to Dexamethasone group.

Table 2: Demographic Table Comparing Dexamethasone and Methylprednisolone Treated Groups.

CRITERIA		DEXAMETHASONE (N=51)	METHYL PREDNISOLONE (N=72)
AGE	Mean	50.47	59.9
	S.D	15.02	11.3
	Mean ± S.D	50.47 ± 15.02	59.9 ± 11.3
	% < 60 years	66.6	42.3
	% ≥ great	33.4	57.7
SEX (%)	Male	60.8	62
	Female	39.2	38
CO-MORBIDITIES (%)	DM	39.2	48.6
	SHTN	27.4	38.8
	Bronchial Asthma	1.9	2.7
	COPD	3.9	1.4
	CAD	1.9	16.6
OTHER TREATMENT RECIEVED(%)	Remdesivir	68.6	62.5
	Tocilizumab	27.4	20.8
	Antibiotics (Ceftriaxone/ Piperacillin/Azithro)	100	95.8
	Anti-coagulant (Heparin/LMWH)	58.8	55.5
	Anthelmintic (Ivermectin)	23.5	18
DAYS ON STEROID		7.1 ± 3.4	6.8 ± 3.6

Route of administration of drugs in each group were as follows: 96% of Dexamethasone drug was administered in parenteral route and 4% of Dexamethasone drug was administered in oral route. 99% of Methylprednisolone drug was administered in parenteral route and 1% of Methylprednisolone drug was administered in oral route.

Figure 2 & 3 represent the dose distribution of both the drugs. The generally administered **Dexamethasone** dose in oral route included: 2mg,4mg ,6mg ,8mg. in parenteral administration 4mg/ml, 8mg/ml, 10mg/ml as Intravenous route.72% of patients were given **8mg/ml IV**. The generally administered **Methylprednisolone** dose in oral route included: 2mg,4mg 8mg ,16mg. In parenteral administration 40mg/ml, 60mg/ml as Intravenous route.72.2% of patients were given **40mg/ml IV**.

The commonly followed frequency of administration in both Dexamethasone and Methylprednisolone drug was **BD** (twice a day).

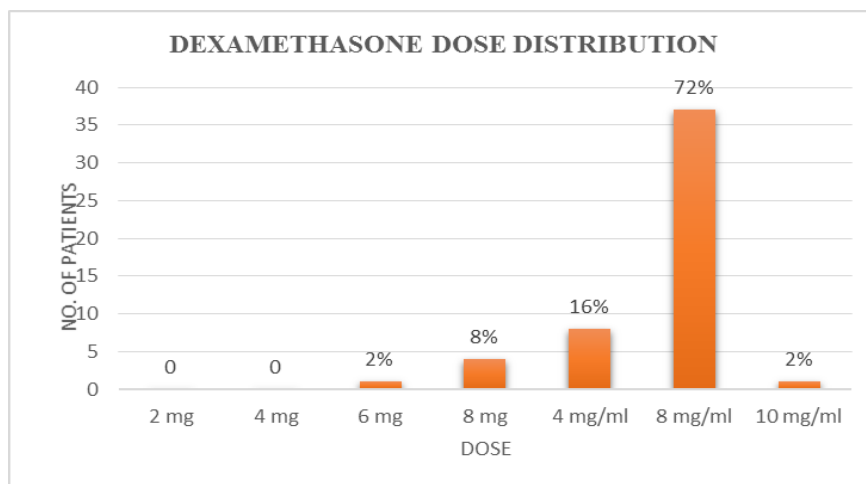


Figure 2: Dose Distribution of Dexamethasone

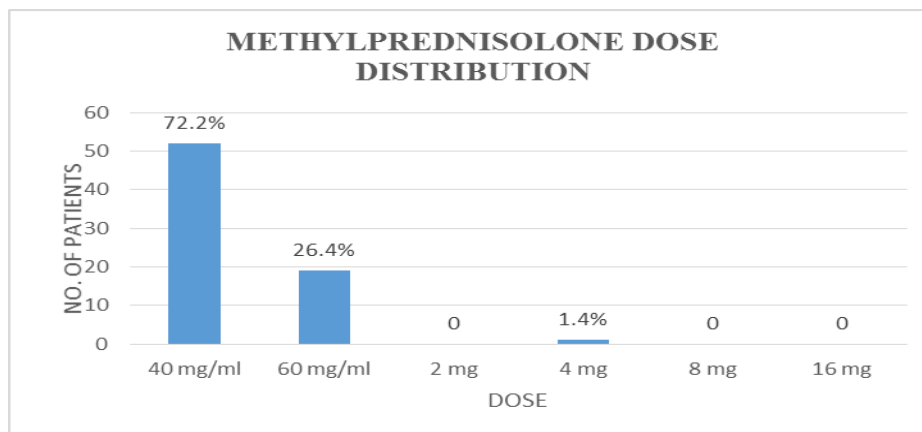


Figure 3: Dose Distribution of Methylprednisolone.

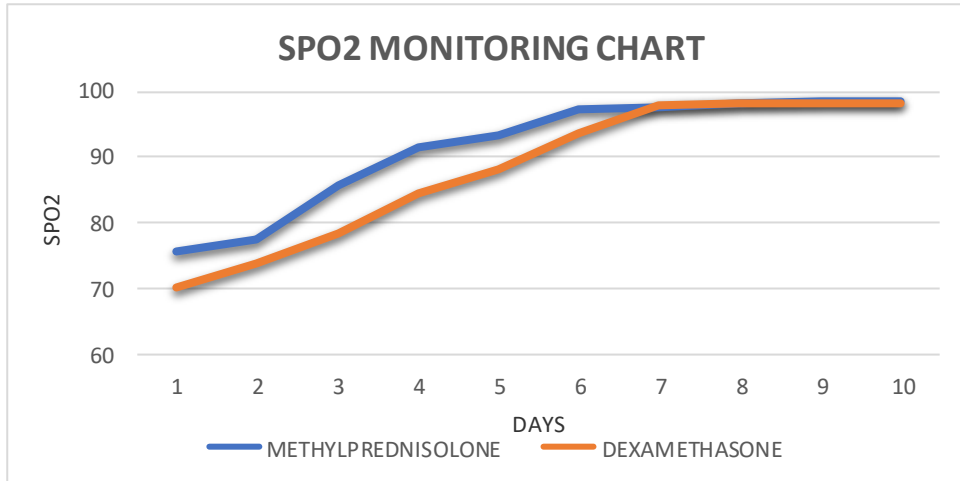


Figure 4: Duration of Therapy Given in Dexamethasone & Methylprednisolone Treatment Groups.

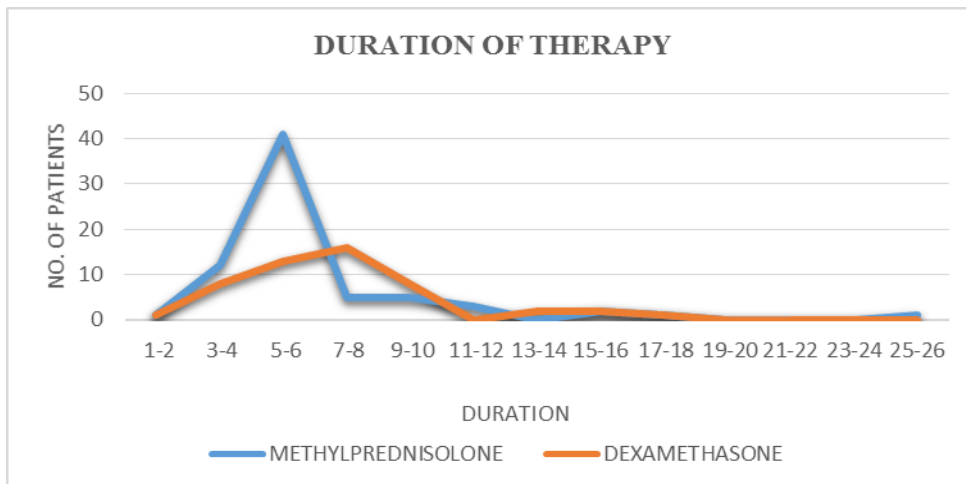


Figure 5: SpO² Monitoring in Each Treatment Group.

Since all the COVID admitted ICU patients had insufficient blood oxygen level. Our main objective of the therapy is to attain the normal Spo2 level. The anti-inflammatory property of corticosteroid helps to increase the Spo2 level. By this way, Dexamethasone and Methylprednisolone was used to treat the Covid ICU patients. Figure 5: From the data observed from our study, we concluded that the patients treated with Methylprednisolone has attained the **normal Spo2 level** in range from **4-6 days** while the Dexamethasone group has attained the normal Spo2 level in range from **7-9 days**.

Steroids increase the blood sugar by increasing the hepatic glucogenesis or production of glucose from the liver by enhancing the effect of counter regulatory hormones. Elevations in

the level of inflammatory cytokines further worsen the insulin resistance. Hyperglycaemia increases the incidence and severity of COVID-19 infection, prolonged hospital and intensive care unit (ICU) stay; contributes to poor disease outcomes; and is associated with higher mortality.

In our study, CBG levels were monitored thrice a day. Based on the CBG level, dose of the steroidal drug was adjusted and control measures were taken to maintain the normal glucose range. Diabetic patients were closely monitored while using steroidal therapy, because blood glucose level rise upto high levels.

In our study, the patients in each treatment group were categorized into diabetic and non-diabetic patients. In Dexamethasone treatment group, out of 51 patients 39.2% were diabetic and 60.8% were non diabetic. In Methylprednisolone treatment group 50% were diabetic and 50% were non diabetic.

From the data observed in our study, CBG level of **diabetes patients** were increased initially with Methylprednisolone & Dexamethasone and later decreased with therapeutic management. Methylprednisolone treated patients with diabetic have increase blood sugar on 6th day which then gradually decreased with certain management. Where in case of Dexamethasone treated patients with diabetic, have the blood sugar levels increased on the 5th day which then gradually decreased with certain management?

Patients who were treated with Methylprednisolone in **non-diabetic group** had the CBG value between 120-170mg/dl, in case of Dexamethasone CBG level between 120-260mg/dl which caused spike in blood sugar levels among non-diabetic patients.

The corticosteroid induced hyperglycaemic condition in non-diabetic patients was not severe. The elevation in blood glucose level was temporary, which would normalize soon after the withdrawal of the drug. No measures would be taken to reduce blood glucose level until serious adverse effects appear. But CBG levels were monitored regularly in non-diabetic patients to avoid severe hyperglycaemic effects. Anti-hyperglycaemic drugs were not preferred in case of non-diabetic patients as it may cause hypoglycaemia.

The hyperglycaemic effect due to corticosteroids in diabetic patients was severe. As diabetic patients have already elevated blood glucose level, corticosteroid administration further worsens the condition. Hence regular monitoring of blood glucose level in diabetic patients is mandatory. The severe hyperglycaemic effect in diabetic patients was controlled by anti-

hyperglycaemic drugs and Insulin administration. Human Actrapid and Human Monotard are generally preferred insulin to treat the uncontrolled blood glucose level.

From our observational study, the **mean CBG level** observed in Dexamethasone treated group (51 patients) was 291 ± 100 in diabetic (20 patients) and 196 ± 49.5 in non-diabetic (31 patients). The mean CBG level observed in Methylprednisolone treated group (72 patients) was 287 ± 71.3 in diabetic (36 patients) and 147 ± 17.6 in non-diabetic (36 patients).

The CBG monitoring showed that **Dexamethasone produces greater hyperglycaemic effect than Methylprednisolone**. As per pharmacology, the effect of Dexamethasone (Long acting) is five times more potent than Methylprednisolone (Intermediate acting) in equivalent dose.

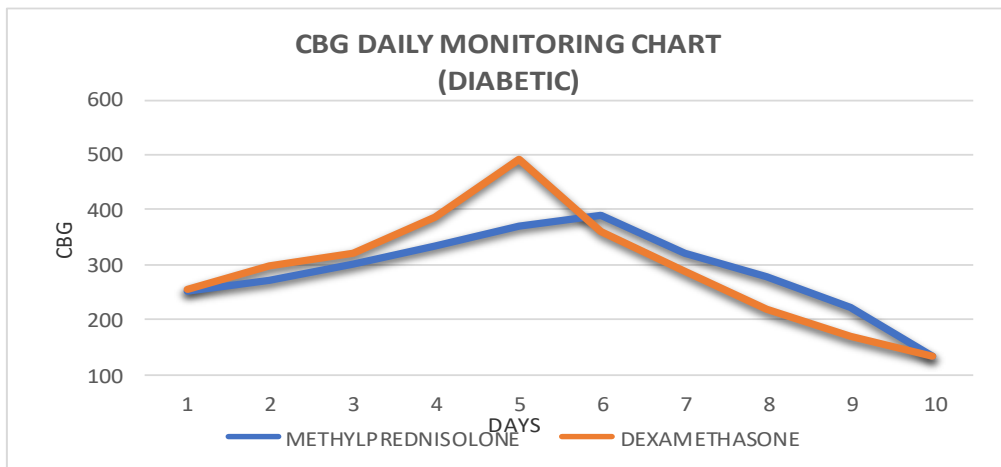


Figure 6: CBG Monitoring in Diabetic Patients.

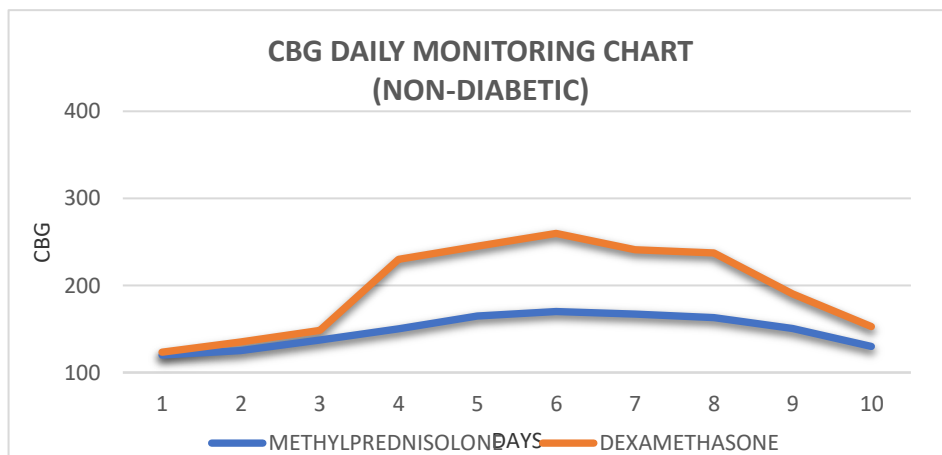


Figure 7: CBG Monitoring in Non-Diabetic Patients.

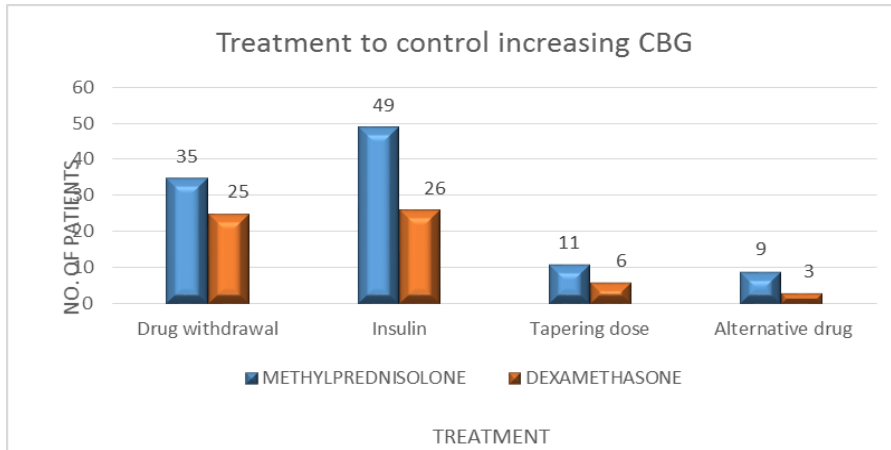


Figure 8: Measures to Control Corticosteroid Induced Hyperglycaemic Effect.

Health care practitioners have seen the corticosteroid use in covid therapy as a glimmer of hope and have started using these drugs more frequently than ever in clinical practice. The fear of mortality in the short term has overridden the concern of adverse long-term consequences with steroid use.

We evaluated the efficacy of the corticosteroids (Dexamethasone and Methylprednisolone) by comparing the length of ICU stay. Since the patients in Covid ICU were on oxygen support, we determined the days taken by the patient to attain normal oxygen saturation (without oxygen support). So we considered length of ICU stay as important criteria in our study.

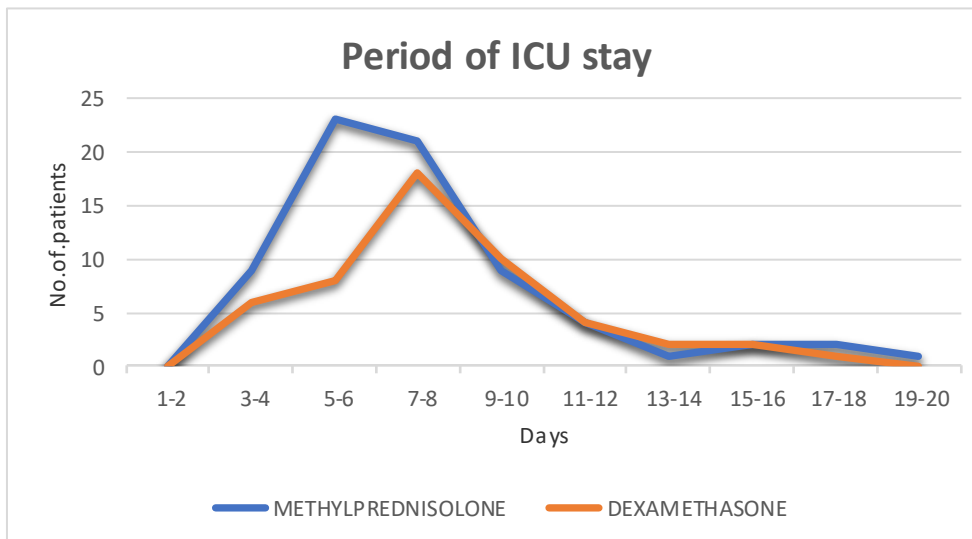


Figure 9 represent the length of hospital stay.

The mean value of **length of ICU stay** in Dexamethasone treated group was **8.27±3.4** and the p value was 0.023. The mean value of length of ICU stay in Methylprednisolone treated group was **7.6±3.5** and the p value was less than 0.0001. Normality of Length of hospital stay (Dexamethasone and Methylprednisolone group) was assessed with the Shapiro-Wilk test. Alpha risk was set to 5% ($\alpha = 0.05$). "Statistical analysis was performed with the online software EasyMedStat (www.easymedstat.com; Neuilly-Sur-Seine; France)."

On observing the mean value of length of ICU stay in both drugs (Dexamethasone and Methylprednisolone), we conclude that **Methylprednisolone treated group had shorter ICU stay than Dexamethasone treated group.**

Table 3: Comparing length of ICU stay in both the Drugs

Treatment Group	n	Mean	SD	P-Value
Dexamethasone	51	8.27	± 3.42	0.02390
Methylprednisolone	72	7.6	± 3.5	< 0.0001

Two sample t-test assuming equal variances is used to test the null hypothesis and find out whether statistically significant or not. Since p-value is greater than alpha 0.05 deviation, the null hypothesis is **not statistically significant** and the null hypothesis is not rejected.

Table 4: Two Sample t-Test Assuming Equal Variances

t-Test: Two-Sample Assuming Equal Variances		
	<i>Variable 1</i>	<i>Variable 2</i>
Mean	8.27451	7.541667
Variance	10.72314	12.27993
Observations	51	72
Pooled Variance	11.63663	
Hypothesized Mean Difference	0	
df	121	
t Stat	1.173806	
P(T<=t) two-tail	0.242778	
t Critical two-tail	1.979764	

Variable 1: Period of ICU Stay in Dexamethasone Treated group.

Variable 2: Period of ICU Stay in Methylprednisolone Treated group.

Case fatality rate is an epidemiological tool used to measure the fatality among the individuals in a treatment group. We used this tool to assume the reduced mortality in covid intensive patients after the implement of corticosteroids in covid therapy. We measure the case fatality rate for both the treatment group and compared them to report the better choice of drug. The case fatality rate of Dexamethasone treated group was 21.5% and Methylprednisolone treated group was 12.5%. Hence, **Methylprednisolone has less fatality rate than Dexamethasone.**

Table 5: Patient Status

	NO. OF PATIENTS	
	DEXAMETHASONE (n=51)	METHYLPREDNISOLONE (n=72)
RECOVERED	40	63
DECEASED	11	9

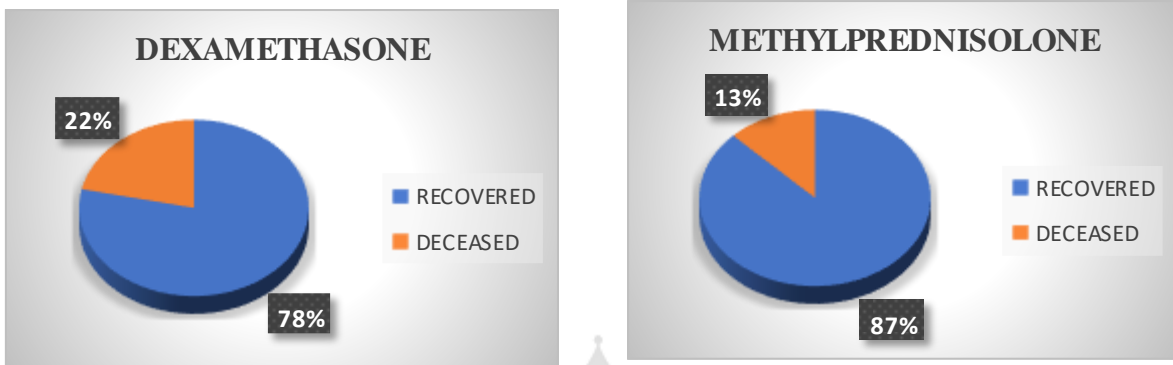


Figure 10: Patient Status.

Case fatality rate = Total. No. of New Deaths due to a certain disease

$$\frac{\text{(at a period of 6 months)}}{\text{Total. No. of Incident Patients with this disease}} \times 100$$

(at a period of 6 months)

$$\text{Case fatality rate} = \frac{20}{123} \times 100$$

Case fatality rate = 19.41%

$$\text{Case fatality rate of Dexamethasone treated group} = \frac{11}{51} \times 100$$

Case fatality rate = 21.56%

$$\text{Case fatality rate of Methylprednisolone treated group} = \frac{9}{72} \times 100$$

Case fatality rate = 12.5%

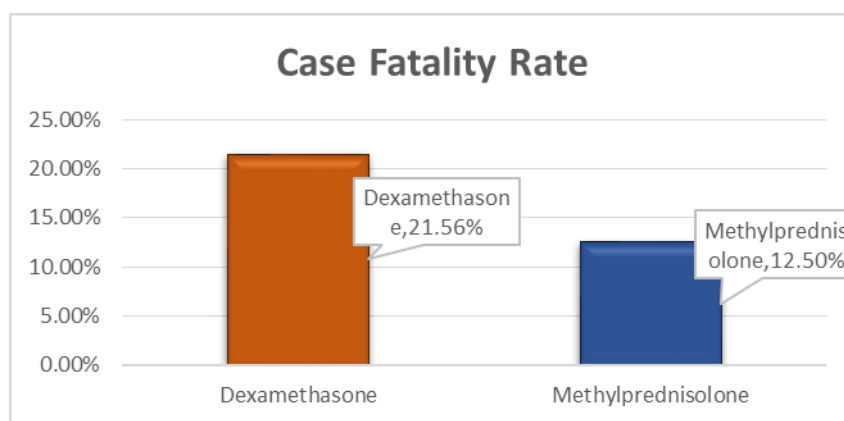


Figure 11: Case Fatality Rate

CONCLUSION:

In summary, we have presented the comparison of effectiveness of dexamethasone & methylprednisolone drugs in intensive care patients with covid-19 and also presented the management of corticosteroid induced Hyperglycemia in COVID ICU patients. In our observational study, out of that 123 patients 72 patients received Methylprednisolone & 51 received Dexamethasone. Since there is no standard drug to treat COVID, corticosteroids were used in alternative. Corticosteroids have significant anti-inflammatory and anti-fibrotic effects, which may play an important role in reducing pulmonary infection and in advanced stages of COVID-19. In our comparative study between methylprednisolone and dexamethasone drugs, we estimated the effectiveness by calculating the mean length of ICU stay. By comparing the mean length of ICU stay in both treatment groups, Methylprednisolone treated group has shorter length of ICU stay than Dexamethasone treated group. Methylprednisolone achieves higher lung tissues-to-plasma ratios than Dexamethasone. Patients treated with Methylprednisolone attained normal SpO₂ level earlier than with Dexamethasone. Methylprednisolone is chosen for its intermediate acting effect over Dexamethasone which has long acting effect. But in very severe condition like 'cytokine storm' Dexamethasone is chosen because of its Glucocorticoid activity (anti-inflammatory & immune suppressant property) which is 5 times more potent than Methylprednisolone.

Corticosteroids commonly causes Drug Induced Hyperglycemia. In the case of Corticosteroid induced Hyperglycemia, the mean value of CBG level is measured and compared between both treatment groups. Dexamethasone results in higher increase of CBG level in both diabetic and non-diabetic patients than Methylprednisolone. This is due to the long acting effect and higher potency. Though Dexamethasone produce more hyperglycemic effect, it

serves as a lifesaving drug in severe condition and its high blood sugar level is managed by tapering doses and appropriate anti-hyperglycaemic drugs & insulin.

Methylprednisolone has less case fatality rate when compared with Dexamethasone treated group in our study. From all the observations, we conclude that Methylprednisolone has better effectiveness and better choice of drug in Covid-19 ICU patients when compared with Dexamethasone based on the severity of the infection and patient characteristics. This study will be helpful to know the drug of choice in treating COVID intensive care patients and also useful for management of corticosteroid induced hyperglycemia in COVID ICU patients.

ETHICAL CLEARANCE:

This prospective study was approved by Institutional Human Ethics Committee, Number: IHEC/872/2022 and permitted by Member Secretary, Institutional Human Ethics Committee, Government Cuddalore Medical College & Hospital (RMMCH), Annamalai University. The registration number of IEC is EC/NEW/INST/2020/1249. Patient Informed Consent form were obtained. Since, human participants were involved in this investigation.

ACKNOWLEDGEMENT:

The authors would wish to extend their gratitude to Department of Medicine and Medical Records Department.

FUNDING:

None of the authors received funding to conduct this study nor the submission of this manuscript.

AUTHOR CONTRIBUTION:

Conceptualization and methodology including data collection: VVP, HRB, BBV, CKD; Writing - original draft preparation and literature search: VVP, HRB, BBV; Writing – Review and Supervision: CKD. The final manuscript has been read and approved by all the authors.

CONFLICT OF INTEREST:

The authors affirm that the publishing of this paper is free of conflict of interest.

REFERENCES:

1. Timing of corticosteroids impacts mortality in hospitalized COVID-19 patients Amit Bahl, Steven Johnson, Nai-Wei Chen Internal and emergency medicine 16 (6), 1593-1603, 2021 https://scholar.google.com/scholar?hl=en&as_sdt=0%2C5&q=hospitalization+of+covid+19+with+corticosteroids&oq=hospitalization+of+covid+19+with+corticosteroid#d=gs_qabs&t=1657166106319&u=%23p%3DUGA3_LGR3IwJ
2. The efficacy of corticosteroids therapy in patients with moderate to severe SARS-CoV-2 infection: a multicenter, randomized, open-label trial Article number: 245 (2021) <https://respiratory-research.biomedcentral.com/articles/10.1186/s12931-021-01833-6>
3. Dexamethasone in the Treatment of COVID-19: Primus Inter Pares? Vasiliki Romanou, Evangelia Koukaki, Vasiliki Chantziara, Panagiota Stamou, Alexandra Kote, Ioannis Vasileiadis, Antonia Koutsoukou and Nikoleta Rovina J. Pers. Med. 2021, 11(6), 556 <https://www.mdpi.com/2075-4426/11/6/556>
4. Health ministry adds steroid dexamethasone in COVID-19 treatment protocol updated on : June 27 2020 https://m.timesofindia.com/india/health-ministry-adds-steroid-dexamethasone-in-covid-19-treatment-protocol/amp_articles/76659845.cms
5. Beasley MB. Acute lung injury-from cannabis to COVID. Mod Pathol. 2022 Jan;35(Suppl 1):1-7. Doi: 10.1038/s41379-021-00915-6. Epub 2021 Sep 9. PMID: 34504310; PMCID: PMC8428494.
6. Diagnosis and Management Considerations in Steroid-Related Hyperglycemia in COVID-19: A Position Statement from the Endocrine Society of India Sambit Das,* Ashu Rastogi,1,* K. V. S. Harikumar,2,* Deep Dutta,3 Rakesh Sahay,4Sanjay Kalra,5 Sujoy Ghosh,6 Sushil K. Gupta,7 Kaushik Pandit,8 P. K. Jabbar,9 Suresh Damodaran,10 V. Sri Nagesh,11 Shehla Sheikh,12 S. V. Madhu,13 and Ganapathi Bantwal14 Indian J Endocrinol Metab. 2021 Jan-Feb; 25(1): 4–11. Published online 2021 Jul 21. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8323636/#__ffn_sectitle
7. World Health Organisation. WHO coronavirus (COVID-19) dashboard: situation by region, country, territory & area. World Health Organisation. 2021. Accessed July 8, 2021. <https://covid19.who.int/table>
8. World Health Organization. Coronavirus disease (COVID-2019) situation reports. 2020. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>
9. All India Institute of Medical Sciences, New Delhi National e-ICU on COVID-19 management. Updated on 01/09/2020 https://www.mohfw.gov.in/pdf/AIIMS_eICUsFAQs01SEP.pdf
10. World Health Organisation. COVID-19 significantly impacts health services for noncommunicable diseases. World Health Organisation. 2020. Accessed June 27, 2021. <https://www.who.int/news/item/01-06-2020-covid-19-significantlyimpacts-health-services-for-noncommunicable-diseases>
11. A living WHO guideline on drugs for covid-19. BMJ 2020;370:m3379. <https://doi.org/10.1136/bmj.m3379>
12. World Health Organisation. WHO coronavirus (COVID-19) dashboard: situation by region, country, territory & area. World Health Organisation. 2021. Accessed July 8, 2021. <https://covid19.who.int/table>
13. World Health Organization. Coronavirus disease (COVID-2019) situation reports. 2020. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>
14. All India Institute of Medical Sciences, New Delhi National e-ICU on COVID-19 management. Updated on 01/09/2020 https://www.mohfw.gov.in/pdf/AIIMS_eICUsFAQs01SEP.pdf
15. World Health Organisation. COVID-19 significantly impacts health services for non-communicable diseases. World Health Organisation. 2020. Accessed June 27, 2021. <https://www.who.int/news/item/01-06-2020-covid-19-significantlyimpacts-health-services-for-noncommunicable-diseases>
16. Coronavirus Update (Live): 30,157,437 Cases and 947,034 Deaths from COVID-19 Virus Pandemic—Worldometer [Internet]. Worldometers.info. 2020 [cited 10 November-2020]. Available from: <https://www.worldometers.info/coronavirus/?zarsrc=130>.
17. Therapeutics and COVID-19 <https://www.who.int/teams/health-care-readiness/covid-19/therapeutics>
18. World Health Organization. Global Surveillance for human infection with coronavirus disease (COVID-19). [https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-\(2019-ncov\)](https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov))

19. A living WHO guideline on drugs for covid-19. BMJ 2020;370:m3379.<https://doi.org/10.1136/bmj.m3379>

