



DRUG UTILIZATION STUDY IN COVID-19 POSITIVE CASES OF PREGNANCIES AND DELIVERIES

Tankala Divya., Madhuri D Kulkarni and Mirza Shiraz Baig*

Department of Pharmacology, Government Medical College, Aurangabad

ARTICLE INFO

Article History:

Received 4th August, 2021

Received in revised form 25th
September, 2021

Accepted 23rd October, 2021

Published online 28th November, 2021

Key words:

SARS-COV-2, COVID-19, Pregnancy,
SARS, Drug utilisation study,
Prescription pattern in Covid
deliveries, Covid in ANC, Covid
positive deliveries.

ABSTRACT

Background: Drug utilization research aims to expedite the rational use of drugs in population. Pregnancy is a distinct physiological condition, where careful consideration of the benefit to the mother and the risk to the foetus is required while prescribing drugs. Various drugs were administered in relation to covid 19 and pregnancy. The primary aim of this study is to assess drug utilization in patients with Covid positive pregnancies and deliveries in tertiary care hospital and to observe the side effects, safety, tolerability of drugs utilized in Covid 19 pregnant case.

Materials and methods: This is a retrospective, observational study, conducted in a tertiary care center over 14 months (March 2020 to May 2021). Case records of Covid positive pregnant women and deliveries were included in the study.

Results: A total of 407 pregnant women medical records were reviewed. The majority of them were within the age of 21-30 years.. Vitamins and minerals along with tablet Azithromycin were the most commonly prescribed drugs for Covid positive pregnancies and deliveries and were well tolerated by the patients.

Conclusion: In the present study all the drugs were prescribed by generic names. No drug from FDA pregnancy risk category X was prescribed. Some drugs were utilized from FDA category D for life threatening chronic illnesses, however the drugs prescribed to treat Covid-19 were well tolerated by the patients.

Copyright © 2021 Tankala Divya et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

The definition of drug utilization study by WHO states as “the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences.⁽¹⁾The principal aim of drug utilization research is to enable the rational use of drugs among general population. The rational use of drugs denotes that patients receive medicines suitable for their clinical needs, in doses that meet their individual requirements, for an adequate period of time, and at the lowest cost to them.⁽²⁾ Pregnancy is a condition characterized by natural suppression of the immune system. Various physiological changes in the immune and cardiopulmonary systems make pregnant women more susceptible to severe responses to respiratory viruses.⁽³⁾ Covid-19, a pandemic, caused by the SARS-CoV-2 spread globally in the last few months.⁽⁴⁾ Pregnant women belong to an exceptional group because of the physiological changes during pregnancy that make them more susceptible to the virus.⁽⁵⁾ The anatomical changes during pregnancy such as an increase in the transverse diameter of the thoracic cage and an elevated level of the diaphragm, decrease the maternal tolerance to hypoxia.⁽⁶⁾ The respiratory illnesses during pregnancy may lead to infectious morbidity and high maternal and or fetal mortality rates. It is currently unknown about the outcome in

pregnant women in response to covid-19 drug management, as to which drugs are beneficial with minimum risk and optimum tolerance.

The medical treatment of Covid-19 during pregnancy is a major problem for physicians due to potential adverse fetal and neonatal effects of different drugs.⁽⁷⁾ The safety (both maternal and fetal/neonatal) of testing drugs in pregnant women is cited as the greatest concern by physicians, researchers and pharmaceutical companies.⁽⁸⁾ While Covid-19 treatment plans vary across different countries, the WHO and the Centers for Disease Control and Prevention (CDC) guidelines are very general, and both advise to manage pregnant and paediatric patients with much attention. Data on the maternal and perinatal outcomes of pregnant women infected with the SARS-CoV-2 are limited to a handful of case reports and series. The sample sizes were small and the findings were diverse.⁽⁹⁾ The current paper attempts to unravel meaningful factors that may aid physicians in dealing with such issues and to discover significant phenomena that are specific to the pregnant women.⁽¹⁰⁾

Hence we are performing a retrospective, observational study to analyze the drugs used in Covid 19 pregnancies and their tolerability, efficacy and safety in pregnant women.

*Corresponding author: Mirza Shiraz Baig

Department of Pharmacology, Government Medical College, Aurangabad

Aims and Objectives

The primary aim was to study drug utilization in Covid positive deliveries in tertiary care hospital

MATERIAL AND METHODS

Study Design

Retrospective and Observational Study

Study Population

Case records of all COVID positive pregnancies and deliveries at Government medical college, Aurangabad during March 2020 to May 2021.

Site of Study

Department of Obstetrics and Gynaecology at Tertiary Care Centre.

Sample Size

All case records of COVID positive deliveries during the corona pandemic, between March 2020 to May 2021

Informed Consent

As there is no direct involvement of the patients, informed consent is not applicable. Still a blanket consent is taken from Head of the department of Obstetrics and Gynecology. However data regarding Covid positive patients is kept confidential.

Inclusion Criteria

- All case records of Covid positive pregnancies and deliveries during the corona pandemic between March 2020-May2021 Can "pregnancies".

Exclusion Criteria

- Incomplete data entry case records were excluded from the study.

Study Procedure

- All case records coming under the inclusion criteria were studied.
- The case records were taken from the record section of the hospital after obtaining NO Objection Certificate from concerned department.
- All the details of the treatment given to the patients was recorded.
- Data so collected was tabulated and analysis was done accordingly.

Statistical Analysis

The data obtained is analyzed in Microsoft excel. The categorical data were expressed as a percentage.

Ethical Approval

The study was approved by the Institutional Ethics Committee of Government Medical College, Aurangabad, Maharashtra, India.

RESULTS

This study was conducted in the Obstetrics and Gynaecology department of a tertiary care teaching hospital in the Marathwada region of western India over 14 months (1st March 2020 to 31st May 2021). A total of 407 prescriptions

were studied. Observations of the study are presented in the form of different tables and figures.

The mean age of pregnant women was 25.1 years and the majority of them were within the age group of 21-30 years as described in Figure 1.

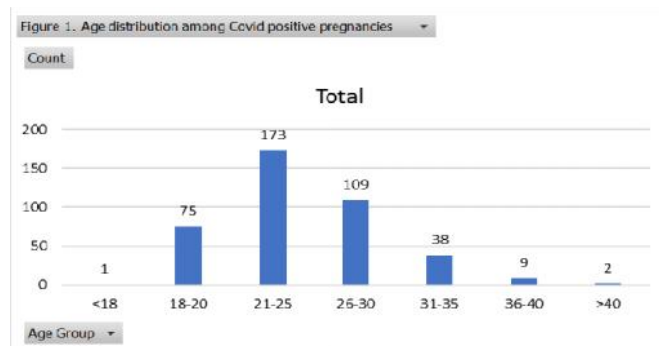


Figure 1 Age distribution among Covid positive pregnancies

Table 1 Trimester wise distribution of cases

Trimester	Total	Percentage
1 ST	16	4%
2 ND	20	5%
3 RD	285	70%
Postnatal	86	21%

Most of the Covid positive pregnant women had presented in the third trimester.

Table 2 Clinical details of cases

Clinical Presentation			
Symptom	Total no. of cases	Percentage	
Fever	78	19.16	
Cough	46	11.3	
Malaise/Bodyache	3	0.73	
Loss of smell/Taste	1	0.24	
Sore throat	4	0.9	
Chest pain/Shortness of breath	27	6.63	
Vomiting/Diarrhoea	1	0.24	
Pain abdomen	42	10.3	
Asymptomatic	225	55	

Table 3 Prescription details for Covid management

Sr No.	Drug name	Dosage form	Dose	Duration	Pregnancy cat Schedule
1	Vitamin C	Tablet	500MG BD	7 days	C
2	Ferrous Sulphate	Tablet	200MG BD	7 days	A
3	Folic Acid	Tablet	5MG BD	7 days	A
4	Calcium	Tablet	500MG BD	7 days	C
5	Zinc	Tablet	50MG BD	7 days	C
6	Vitamin D	Tablet	6000IU once a week	6 weeks	C
7	Azithromycin	Tablet	500MG OD	5 days	B
8	Hydroxychloroquine	Tablet	200mg BD	7 days	B
9	Cefixime	Tablet	200mg BD	7 days	B
10	Favipiravir	Tablet	200mg BD	5 days	-
11	Oseltamivir	Tablet	75 mg BD	7 days	C
12	Dalteparin	Injection	5000IU OD	7 days	B
13	Cefotaxim	Injection	1 gm IV BD	7 days	B
14	Augmentin	Injection	1.2gm IV BD	7 days	B
15	Ceftriaxone	Injection	1gm IV BD	7 days	B
16	Meropenem	Injection	1gm IV BD	7 days	B
17	Linezolid	Injection	600mg IV BD	7 days	C
18	Piperacillin+Tazobactam	Injection	4.5GM IV BD	7 days	B
19	Metronidazole	Injection	500mg IV BD	5 days	B
20	Remdesivir	Injection	100mgIV OD	5 days	-
21	Pantoprazole	Injection	40mg IV OD	7 days	B
22	Paracetamol	Tablet	500 mg OD	SOS	A

55% of covid positive pregnant women were asymptomatic at the time of presentation to the hospital. However they were admitted in hospital in view of better care. The details are presented in table 2. Fever was the common complaint among the symptomatic Covid positive women.

Most commonly prescribed drugs for Covid 19 management in pregnancy and their pregnancy category has been summarized in Table 3. However the drugs Favipiravir and Remdesivir have not been assigned any pregnancy category yet.

Table 4 Other drugs used

Sr no.	Drug name	Dosage form	Dose	Duration	Category (Schedule)
1.	Labetalol	Tablet	200MG	3-4days	C
2.	Magnesiumsulphate	Injection	4 GM	1 day	D
3.	Levipil	Injection	500MG	2 days	C
4.	Thyronorm	Tablet	25-50MCG	Lifelong	A
5.	Diclofenac	Tablet	50MG	1-2 days	D

Apart from being Covid positive, some females suffered from other conditions like Preeclampsia, Eclampsia. Only 1 female during the study received category D drug, MgSo4, as described in table 4.

Table 5 Pattern of drugs utilised among Covid positive pregnant women

Class of Drugs	Drug Name	No.of Encounter	Total	Percentage
Vitamins and minerals	Vitamin C 500mg	407	2442	70%
	FSFA	407		
	Folic acid	407		
	Vitamin d3	407		
	Zinc	407		
	Calcium	407		
Antibiotics	Azithromycin	407	507	14.5%
	Augmentin	2		
	Cefotaxim	19		
	Metronidazole	47		
	Ceftriaxone	23		
	Cefixime	1		
	Piperacillin+tazobactam	6		
	Meropenem	1		
	Linezolid	1		
	Dalteparin	7		
Anticoagulants	Enoxaparin	2	9	0.25%
	Pantoprazole	407	407	11.65%
Antacids	Levipil	2	2	0.05%
Anti epileptics	Mag sulphate	1	12	0.34%
	Labetalol	11		
Antihypertensive s	Hydroxychloroquine (HCQ)	1	1	0.02%
	Favipiravir	16	24	0.7%
Antivirals	Remdesivir	6		
	Osetamivir	2		
Nsaids	Diclofenac	2	80	2.3%
	Paracetamol	78		
Hormonal Supplements	Thyronorm	9	9	0.25%
	Total drugs		3493	100%

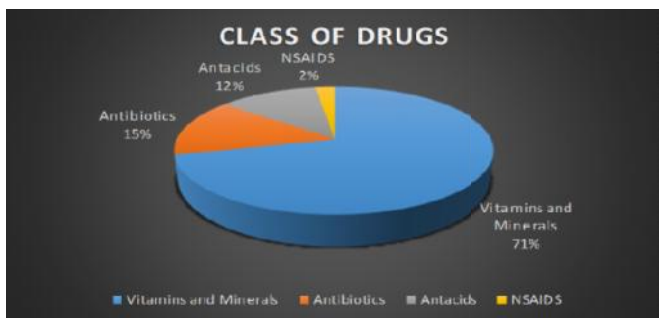


Figure 2 Class of drugs prescribed

Vitamins and minerals constitutes 70% of the total number of prescribed drugs followed by antibiotics (15%).

Table 6 FDA Category of drugs

Sr no.	FDA Category	No.of Patients Received The Drug	Percentage
1	A	901	25.8
2	B	923	26.42%
3	C	1644	47.06%
4	D	3	0.08%
5	Not assigned	22	0.62%
T	TOTAL	3493	100%

Overall majority of the prescriptions had drugs from Category C as detailed in table 6

Table 7 Total number of drugs prescribed per patient

Sr No.	Number of Drugs	No.of Patients	Percentage
1	8	326	80.1
2	9	24	5.9
3	10	46	11.3
4	11	6	1.47
5	12	4	1.0
6	13	1	0.24
Total		407	100

Polypharmacy was practised during treatment of patients. A minimum of 8 drugs per encounter and a maximum of 13 were prescribed to the Covid positive pregnant women as detailed in Table 7.

Table 8 Drugs prescribed by generic and brand names

Type of Prescription	Number (%)
Generic	100
Brand	0

All the drugs were prescribed by generic names, the brand name was not used in any of the prescriptions as mentioned in table 8.

Table 9 Adverse events

Local	Nil
Systemic	Nil

There were nil adverse events noted with the prescribed drugs during the study period as noted in table 9.

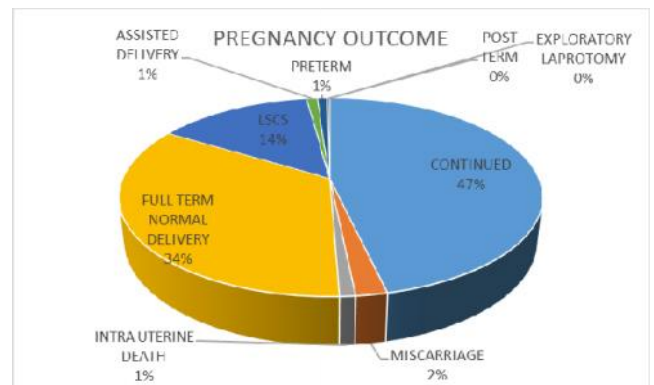


Figure 2 Pregnancy outcome

Majority of the Covid positive pregnancies were continued and discharged successfully from the hospital, however 1% preterm deliveries and 1% intrauterine deaths were reported as seen in Figure 2

DISCUSSION

- The present study reflects the general trend of drug prescription among cases of Covid positive pregnancies and deliveries.

- A total of 407 case records were observed and analysed from March 2020 to May 2021.
- Our study showed an overall maximum number of patients between the age group of 18-30 years (26.04%) followed by 31-40 years (25%), as this is the reproductive age group.
- Most women admitted due to COVID-19 were in the third trimester of pregnancy when they tested positive, similar to the observation made in a study done by Engjom.⁽¹¹⁾
- The most common symptoms reported by pregnant and recently pregnant women with suspected or confirmed COVID-19 were fever (34.6%) and cough, comparable to a study done by John.⁽¹²⁾
- All the patients received nutraceuticals. A study done by Pinar Bahat⁽¹³⁾ supports the increased supplementation of micronutrients to pregnant women as it is advantageous during COVID infection.
- Every COVID positive pregnant woman received Tablet Azithromycin 500mg as a primary antibiotic and was well tolerated by the patient similar to a study done by Giampreti.⁽¹⁴⁾
- Polypharmacy was practised while prescribing treatment due to uncertainty of drugs benefitting COVID positive pregnant women. However as there is no definite drug for COVID infection, repurposed drugs were prescribed to pregnant women. Minimum of 8 drugs were prescribed to the patients with mild to moderate symptoms.
- Apart from medications, oxygen saturation levels were maintained above 95%, and optimum hydration was maintained. Mostly the cases were treated in wards, and the critical cases were admitted in ICU.
- There were mild to nil adverse reactions in pregnant women who received the drugs prescribed in the hospital.
- Preterm delivery was seen in just 1 % of the deliveries and assisted deliveries done in 1 % of the pregnant women. However no conclusion can be made with regard to COVID infection as there was no comparison group. But the study done by Enjong⁽¹¹⁾, concluded higher rate of preterm deliveries in COVID infected patients.
- At present, there is insufficient evidence to conclude any correlation between spontaneous preterm labor and COVID-19 infection in pregnancy in our study. Total 11 females succumbed to COVID-19, out of which 8 died in the month of April 2021, indicating the severity of COVID-19 infection during the second wave.
- Specific actions pregnant women can take include not skipping prenatal care appointments, limiting interactions with other people as much as possible, taking precautions to prevent COVID-19 infection when interacting with others, having supply of adequate medicines, and talking to their health care provider about how to stay healthy during the COVID-19 pandemic.⁽¹⁵⁾

Strength of the Study

It is the first study in our institute as well as in Marathwada region for assessing the drugs utilized in the management of COVID positive cases of pregnancy, in view of their side effects, tolerability, safety and efficacy.

Limitations of the Study

The retrospective design of the study determines the limitations.

Follow up of data to evaluate the outcome was not done and in some cases, no data was available after discharge of patient particularly of foetal outcome.

Effect of drugs on maternal quality of life during the treatment was not assessed.

CONCLUSION

In view of the limited cases of the study, various drugs utilized for the management of COVID 19 positive cases of pregnancies and deliveries were safe, tolerable, effective, and gave a positive outcome.

Further research including Randomized controlled trials, are needed for special drugs like Remdesivir, Tocilizumab, Hydroxychloroquine, Favipiravir.

The present study indicates that the Multivitamins along with tablet Azithromycin were the most commonly prescribed drugs for COVID positive pregnancies and deliveries in this hospital. All the drugs were prescribed by generic names. Supplementation of micronutrients during the pandemic could be beneficial during pregnancy for prevention of infection. A large scale investment in research and development of corona virus vaccines and therapeutic drugs is needed as pregnant women are a group that cannot be ignored in drug development.

Acknowledgement

Authors would like to thank Dr. Shrinivas Gadappa, Professor and Head, Department of Obstetrics and Gynaecology, Government Medical College, Aurangabad for assistance in the study.

Funding: No funding sources

Conflict of interest: None declared

References

1. Sharma N, Jhanwar A. Study of drug utilization pattern in gynecology department of tertiary care hospital of Rajasthan, India. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2018 Jun 27;7(7):2650-4.
2. Chaudhari A, Aasani D, Trivedi H. Drug utilization study in antenatal clinic of Obstetrics Gynaecology Department of a Tertiary Care Hospital attached with Medical College. *Indian Journal of Pharmacy and Pharmacology*. 2021 Feb 15;3(4):186-91.
3. Global interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium from FIGO and allied partners: Information for healthcare professionals - Poon - 2020 - *International Journal of Gynecology & Obstetrics* - Wiley Online Library [Internet]. [cited 2020 Dec 30]. Available from: <https://obgyn.onlinelibrary.wiley.com/doi/full/10.1002/ijgo.13156>
4. Favilli A, Mattei Gentili M, Raspa F, Giardina I, Parazzini F, Vitagliano A, *et al.* Effectiveness and safety of available treatments for COVID-19 during pregnancy: a critical review. *J Matern Fetal Neonatal Med*. 2020 Jun 7;1-14.

5. Kwon J-Y, Romero R, Mor G. New Insights into the Relationship between Viral Infection and Pregnancy Complications. *Am J Reprod Immunol*. 2014 May;71(5):387–90.
6. O'Day MP. Cardio-respiratory physiological adaptation of pregnancy. *Semin Perinatol*. 1997 Aug;21(4):268–75.
7. Zhao X, Jiang Y, Zhao Y, Xi H, Liu C, Qu F, *et al*. Analysis of the susceptibility to COVID-19 in pregnancy and recommendations on potential drug screening. *Eur J Clin Microbiol Infect Dis*. 2020 Jul 1;39(7):1209–20.
8. Sheffield JS, Siegel D, Mirochnick M, Heine RP, Nguyen C, Bergman KL, *et al*. Designing Drug Trials: Considerations for Pregnant Women. *Clin Infect Dis*. 2014 Dec 15;59(Suppl 7):S437–44.
9. Thomas B, Pallivalapila A, El Kassem W, Tarannum A, Al Hail F, Rijims M, *et al*. Maternal and perinatal outcomes and pharmacological management of Covid-19 infection in pregnancy: a systematic review protocol. *Systematic Reviews*. 2020 Jul 18;9(1):161.
10. Yee J, Kim W, Han JM, Yoon HY, Lee N, Lee KE, *et al*. Clinical manifestations and perinatal outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. *Scientific Reports*. 2020 Oct 22;10(1):18126.
11. Engjom H, Aabakke AJM, Klungsøyr K, Svanvik T, Äyräs O, Jonasdottir E, *et al*. COVID-19 in pregnancy—characteristics and outcomes of pregnant women admitted to hospital because of SARS-CoV-2 infection in the Nordic countries. *Acta Obstetrica et Gynecologica Scandinavica* [Internet]. 2021 Apr 22 [cited 2021 Jul 21];n/a(n/a). Available from: <https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/aogs.14160>
12. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, *et al*. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020 Sep 1;370:m3320.
13. Yalcin Bahat P, Aldikactioglu Talmac M, Bestel A, Topbas Selcuki NF, Aydin Z, Polat . Micronutrients in COVID-19 Positive Pregnancies. *Cureus* [Internet]. [cited 2021 Jun 5];12(9). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7515144/>
14. Giampreti A, Eleftheriou G, Gallo M, Butera R, Contessa G, Faraoni L, *et al*. Medications prescriptions in COVID-19 pregnant and lactating women: the Bergamo Teratology Information Service experience during COVID-19 outbreak in Italy. *Journal of Perinatal Medicine*. 2020 Nov 1;48(9):1001–7.
15. Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD, *et al*. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–June 7, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Jun 26;69(25):769–75.

How to cite this article:

Tankala Divya *et al* (2021) ' Drug Utilization Study in Covid-19 Positive Cases of Pregnancies and Deliveries ', *International Journal of Current Medical and Pharmaceutical Research*, 07(11), pp 6028-6032.
