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CLINICAL CHARACTERISTICS AND OUTCOME OF SARS COV-2 PATIENTS TREATED WITH FAVIPIRAVIR AT A PRIVATE OUTDOOR CLINIC IN WESTERN INDIA

General Medicine

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ABSTRACT

Background: Favipiravir received emergency authorisation in India to treat patients with mild Covid-19 illness. We designed this retrospective study to determine the outcome of SARS CoV -2 patients who received Favipiravir(FVP) at a private outdoor clinic.
Objective: (1) Outcome of Covid-19 patients treated with FVP (in terms of need for hospitalisation and days to clinical recovery). (2) To characterise clinical features of Covid-19 disease and the impact of comorbidities on outcome.
Methods: In this single centre retrospective, observational study, clinical outcome, presenting features and impact of co morbidities were studied in patients treated with Favipiravir. Patients included in the analysis were classified as having mild, moderate and severe categories of COVID 19 disease using Ministry of Health and Family Welfare (MoHFW) Covid-19 treatment guidelines. All patients had received FVP.
Results: 113 patients were evaluated with median age of 48. Overall, 95(84.07%) and 18 (15.9%) presented with mild disease and moderate or severe disease respectively. Of the 92 home isolated patients 40(43.4%) ,38(41.3%) and 14(15.2%) patients recovered in less than 7 ,7-14 days and more than 14 days respectively. Of the 18 admitted patient two (1.7%) succumbed to the disease. Patients with persistent fever, cough and chest pain more often required admission. Hospitalised patients were older and had Hypertension and Diabetes more often.
Conclusion: Most SARS CoV 2 patients reporting to our OPD and treated with FVP had mild disease and recovered within a fortnight in home quarantine. Clinical features of our patients matched those reported elsewhere and those with co morbidities had worse outcome (hospitalisation).

KEYWORDS

SARScoV2, Favipiravir

The world has been reeling under the SARS COV 2 pandemic since December 2020 and multiple drugs and combination therapies have been tried to combat the disease. Initial reports from China suggested that more than 80% of those infected with SARS-CoV-2 experience mild or moderate disease (1) and yet few studies to date have investigated therapeutic interventions in this population.

Favipiravir (FVP), an oral broad spectrum RdRp polymerase inhibitor was first approved by Japan in June 2020 for treating mild to moderate disease and subsequently got approval in several countries like Russia, China, India. FVP (prodrug) is a purine base analogue that is converted to active favipiravir ribofuranosyl-5B-triphosphate (favipiravir-RTP) by intracellular phosphoribosylation. It is a selective and potent inhibitor of RNA-dependent RNA polymerase (RdRp) in RNA viruses. Favipiravir binds to polymerase domains and prevents incorporation of nucleotides for transcription of the viral RNA which leads to chain termination and lethal viral mutagenesis (2,3,4). Early clinical studies from China have shown promising results in terms of reduction in viral load as well as improvement in clinical and radiological outcomes. (3)

In view of the pandemic, FVP got approved in various guidelines to treat mild to moderate cases of Covid 19. McCullough P. A. et al also studied Favipiravir in Early Ambulatory Treatment of SARS-CoV-2 Infection in mild cases. (5,6). An Indian study by Udwadia et al. showed early recovery in SARS CoV2 patients with Favipiravir in mild disease (7). We therefore decided to review our data on its use in cases presenting to our OPD.

METHODS

In this single centre retrospective observational study, FVP was prescribed to all consecutive patients who were RT PCR/rapid antigen test positive. The study period was from 15th October 2020 to 31st December 2020. Informed consent was taken. Primary outcome evaluated were Need of hospitalization and days to clinical recovery. Clinical recovery was defined as resolution of symptoms for 48 hours. Secondary objective was to characterise clinical features of Covid-19 disease and the impact of comorbidities on outcome.

Treatment: All patients who presented with mild disease to our OPD received FVP 1800mg/day on the first day and then 1600 mg/day for 6 days with other supportive treatment (paracetamol/oral rehydration therapy and multivitamins). Those with co morbidities like Diabetes, Hypertension, Coronary Artery disease and COPD were in addition given Aspirin(75mg/day), Atorvastatin (10 mg/Day) and Dabigatran (110 mg twice a day). Clinical recovery was defined as patients becoming clinically asymptomatic.

Ministry of Health and Family Welfare (MoHFW) COVID-19 treatment guidelines (8) was used to categorise mild, moderate and severe covid-19 illness. The patients followed up for at least 4 weeks were included. At our clinic all patients were counselled about the disease and home isolation rules and were educated to self-monitor their symptoms, temperature, vitals and oxygen levels by pulse oximeter and blood sugars in case of diabetes and report them daily to us by mobile short message service. Video consultation was scheduled every third day or as needed in case of clinical worsening. Patients were instructed to report immediately in case of persistent high fever, breathlessness, extreme fatigue and oxygen saturation less than 94%. Patients were subjected to routine laboratory investigations on presentation and were repeated on day 7, 10 and 14, including a complete blood count, renal functions, C-Reactive Protein (CRP), D dimer levels, transaminases and Serum Ferritin. All patients were physically examined on Day 14 of their illness. The data was analysed with Fisher Exact test where proportions were compared and t test when testing means. $p<0.05$ was taken as significant.

RESULTS

A total of 113 patients were included in the analysis. Of these, 92(84.07%) had mild covid-19 illness and were managed at home. 18(15.9%) patients (Fig 1) progressed quickly to moderate to severe illness needing hospital admissions. Total 3 patients were lost to follow up.

Table 1 Demographic And Baseline Characteristics Of Patients

Total Pt No 113		
Male	64 (56.63%)	
Female	49(43.36%)	
	Mean Median	
Age	49 +18.41 49	
Clinical features		
Sore throat		113(100%)
Fever	107(94.69%)	
Cough	95(84.07%)	
Anosmia		41(36.28%)
Ageusia		36(31.85%)
Dyspnoea		35(30.97%)
Chest pain		34(30.08%)
Co-morbidities		
Hypertension 63(55.75%)		

Diabetes 42(37.16%)
CAD(Coronary Artery Disease) 10 (8.84%)
COPD(Chronic Obstructive Pulmonary Disease) 9(7.96%)
Others

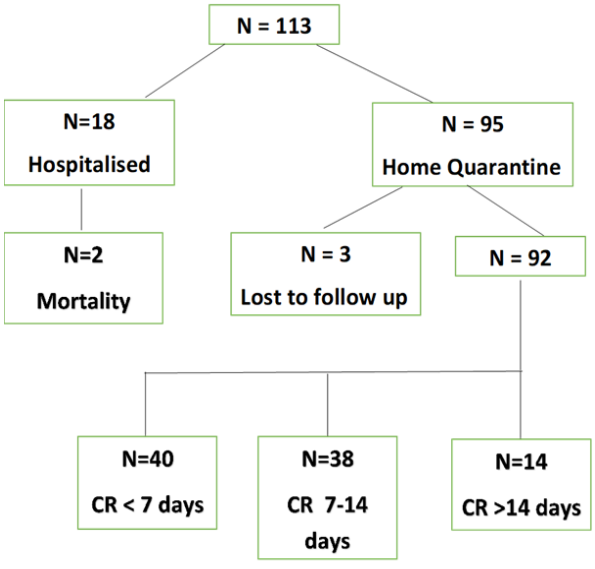
(Others included Acute Myeloid Leukaemia (AML) Carcinoma, Chronic Kidney Disease(CRF), Diabetic nephropathy, Dyslipidaemias, patients with seizures, Myasthenia Gravis, Primary Sjogren's and Subarachnoid Haemorrhage(SAH)

Amongst home isolated patients, just more than half of these (51.5%) had comorbidities. They had more cough and dyspnoea, a higher CRP and creatinine than those without co morbidities (Table 2).

Table 2 Home Isolation N=95

	Co morbidities	No comorbidities	p value
	N=49(51.5%)	n=46(48.4%)	
Male	30(61.2)	22(47.4)	0.0881
Female	19(38.7)	24(52.1)	0.0881
Age	57+14.08	34+12.5	<0.0001
Fever	48(97.9)	40(86.9)	0.0054
Cough	30(65.2)	30(65.2)	<0.0001
Sore throat	49(100)	46(100)	1
Anosmia	15(30.6)	23(50)	0.0093
Ageusia	11(30.6)	21(45.6)	0.0415
Dyspnoea	14(14)	4(8.6)	0.0004
S.Creatinine >1.4	10 .0+21.5	2+5	0.0006
(0.7 – 1.3 mg/dl)			
CRP	*12.0+15.5*	*4.9+4.7*	*0.0027*
(1- 0.6 mg/L)			
D-Dimer	479.5+64	285+206	0.0552
(0.00-500 ngFEU/ml)			
Ferritin	151.8+25	93.2+119	0.157
(21.8 -274 ng/mL)			
LDH	211.8+88.8	229.8+124.5	0.4167
(140 -280 U/L)			

They also had more loss of smell and taste. 40(43.4%) patients showed recovery in less than 7 days, 38(41.3%) patients recovered between 7 to 14 days while 14(15.2%) patients had persistent symptoms beyond 14 days(Fig 1)



*C R = Clinical Recovery

Figure 1 Schematic diagram of patient disposition

Out of these fourteen patients, eight patients had cough, nine had dyspnoea on routine activities and six had severe generalised weakness. Patients with comorbidities had higher baseline CRP ,d dimer and NLR and subsequently at Day 7 & Day 14 they still had higher median values as compared to patients with no co morbidities(.Fig 2)

Fig 2 Investigations in patients with and without comorbidities at basline,7th and 14th day

Twenty one (22.8%) of the home quarantined patients were given oral corticosteroids and low molecular weight heparin for 3 days in view of persistent high grade fever after 7 days of illness.

Hospitalised patients were more often males, were older and had comorbidities like Hypertension (83%) and Diabetes (66.6%) especially uncontrolled glycemia (Table 3)) more often than those who were managed in home isolation. All hospitalised patients had fever, cough and most of them also had chest pain (83.3%) and dyspnoea (88.8%) (Table 3). We did not see any major side effects of FVP.

Table 3 Home Isolation Versus Hospitalised Patients (N=113)

	Home Isolation	Hospitalised	P value
	n=95(84.03%)	n=18(15.92)	
Male	52(54.7)	13(72.2)	0.0184
Female	43(45.6)	5(27.7)	0.0184
Age	46.34+17.79	63.7+15.35	0.0002
Fever	88(92.5)	18(100)	0.014
Cough	76(80)	18(100)	0.0001
Sore throat	95(100)	18(100)	1
Anosmia	38(40)	3(16.1)	0.0002
Ageusia	32(33.6)	3(16.1)	0.0051
Dyspnoea	18(18.9)	16(88.8)	<0.0001
Chest pain	18(18.9)	15(83.3)	<0.0001
Hypertension	47(49.4)	15(83.3)	<0.0001
Diabetes	29(30.5)	12(66.6)	<0.0001
CAD	4(4.2)	6(33.3)	0.0001
(Coronary Artery Disease)			
COPD	7(7.36)	2(11.1)	0.4594
(Chronic Obstructive Pulmonary Disease)			

DISCUSSION

Majority of patients (84.07%) recovered in home isolation with FVP and supportive therapy. Clinical features of our patients compared with those reported elsewhere (9,10,11). While the proportion of patients with co morbidities were significantly higher in those who needed hospitalisation, even amongst the home isolated, those with co morbidities had more symptoms of cough and dyspnoea and a higher CRP on presentation. Those with anosmia had a better prognosis as seen in other studies (11). Just about less than half in the home quarantined group recovered within a week.

The results of our study are comparable to other studies. Udwadia et al (7) showed early recovery with FVP. The clinical phenotype of our patients matched those reported in other studies. McCullough P. A et al have also described the benefits of early FVP in ambulatory patients. (5.6) Tian et al study also had 73.3% mild cases and the most common symptoms at the onset of illness were fever (82.1%), cough (45.8%), fatigue (26.3%), dyspnoea (6.9% (11) Other studies have also shown similar presentations of Covid 19 disease. A review by Singhal et al also confirms similar presentation in Indian patients. (9) As expected, the patients with co morbidities had more severe baseline symptoms like cough, dyspnoea and fever, significantly higher baseline NLR, d Dimer, CRP and creatinine values. Mithal et al also showed that patients with comorbidties like Hypertension and Diabetes had severe disease and delayed recovery which is similar to our study. (12) Almost 15.2 % patients had persistent symptoms of generalised weakness, cough and dyspnoea beyond 14 days. It was noted that all of them had at least one or more co morbidities which is comparable to other studies. (13.14.15)

It was observed that 15% required admission and there was mortality of 1.7% which is comparable to other studies. (16). Amongst the hospitalised, were higher proportion of patients in the > 60 age group and co morbidities (12).

The limitation of our study is that it is a retrospective observational analysis, all the patients were given FVP and so there was no control arm, it is a single centre study and the patient numbers are small. There can be many confounding factors like other treatments affecting the outcome. In the comparison of patients with or without comorbidities, difference of age may be the major confounding factor.

To conclude, most SARS CoV 2 patients reporting to our OPD and treated with FVP had mild disease and recovered in home quarantine. Few needed hospitalisations and these were in the higher age group, with co morbidities and had higher baseline levels of NLR, CRP and D- Dimer throughout the disease course. Therefore, timely and early use of FVP might lead to a milder disease course and lesser need for hospitalisation More data with larger number of patients from multiple centres and a control arm (with no anti virals) is needed to validate our observations.

Conflict of interest None

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