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2-DG as an adjunctive treatment in covid-19

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Abstract
Background: COVID-19, the pandemic in recent years which had a global detrimental effect over the mankind and healthcare system. There is no specific treatment for as of now. Antivirals, antibiotics. Steroids and multiple pharmaceutical strategies were tried in treatment of COVID-19.As per the clinical trials, viral infected cells and glucose metabolism were targeted for the treatment of COVID-19 with 2-Deoxy D glucose. 2-DG has been given the Emergency Use Autherisation as an adjunctive therapy along with standard of care in hospitalized patients. It acts by inhibition of viral replication and by inhibition of cytokine release.
Aim: To study the role of 2-DG as an adjunct to proposed standard of treatment in COVID-19 patients.
Materials and Methods: It is a cross sectional observational study conducted at Kamineni Academy of Medical Sciences and Research Centre, Hyderabad.
Results: We have observed that there is declined RR and early weaning of oxygen support in patient of COVID-19 with 2 Dg as an adjunctive modality. There was significant decrease in Oxygen support after administration of 2-DG. In the study among subjects who recovered mean day of administration of 2-DG drug was 6.00 ± 1.512 days and among subjects who expired was 7.33 ± 2.646. However there was no significant difference in Day of administration of first dose of 2-DG with respect to outcome.
Conclusion: In this study we have observed significant benefits in mortality outcomes and oxygen requirements in patients receiving 2-DG along with standard care of management.

Keywords: 2DG, mortality, covid-19, oxygen support, cytokines

Introduction
Novel corona virus disease caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) emerged in December 2019 (COVID-19) in a cluster of patients in Wuhan, China, which has been designated a worldwide pandemic. As of 10 September 2021, there have been 223,022,538 confirmed cases of COVID-19 worldwide, including 4,602,882 reported deaths (WHO, 2021) [5]. Pharmacological therapies of proven efficacy in corona virus disease 2019 are still lacking with no proven antiviral treatment. COVID -19 in obligatorily dependent on glucose metabolism for replication in host. Thus, a disrupted glucose metabolism and metabolic derangement in diabetes may be an intrinsic cellular strategy that favors SARS-CoV-2 pathogenesis [2]. If the cells take up the 2DG in place of glucose, then the pathogenesis will be dampened. We have observed the effects of 2DG as adjunctive modality with standard management in patients with COVID-19 pneumonia with oxygen requirement.

Methodology
It is a cross sectional observational study conducted at Kamineni Academy of Medical Sciences and Research Centre, Hyderabad.
Sample size-24 subjects
Inclusion criteria: Patients of active COVID-19 pneumonia on oxygen support Exclusion criteria: COVID-19 infected persons who are not requiring the oxygen support.
24 cases of COVID-19 patients treated were with standard care of treatment along with 2-DG for 5 days and observed the outcome and compared with various parameters. In our study we have observed the respiratory rate, oxygen requirement and outcome, before and after giving 2-DG.

Results

We have observed that there is declined RR and early weaning of oxygen support in patient of COVID-19 with 2 Dg as an adjunctive modality. Mean RR before 2-DG was 27.96 ± 4.611cpm and after 2-DG administration was 26.00 ± 9.478cpm. There was no significant decrease in Respiratory rate after 2-DG administration. In the study before 2-DG, 100% of them were on Oxygen support and after 2-DG, 66.7% were on oxygen support. There was significant decrease in Oxygen support after administration of 2-DG. In the study among subjects who recovered mean day of administration of 2-DG drug was 6.00 ± 1.512 days and among subjects who expired was 7.33 ± 2.646. However there was no significant difference in Day of administration of first dose of 2-DG with respect to outcome.

Table 1: Profile of subjects

		Frequency (n = 24)	%
Age	<40 years	4	16.7%
	41 to 50 years	5	20.8%
	51 to 60 years	9	37.5%
	>60 years	6	25.0%
Gender	Female	7	29.2%
	Male	17	70.8%

In the study majority were in the age group 51 to 60 years (37.5%). 70.8% were males and 29.2% were females

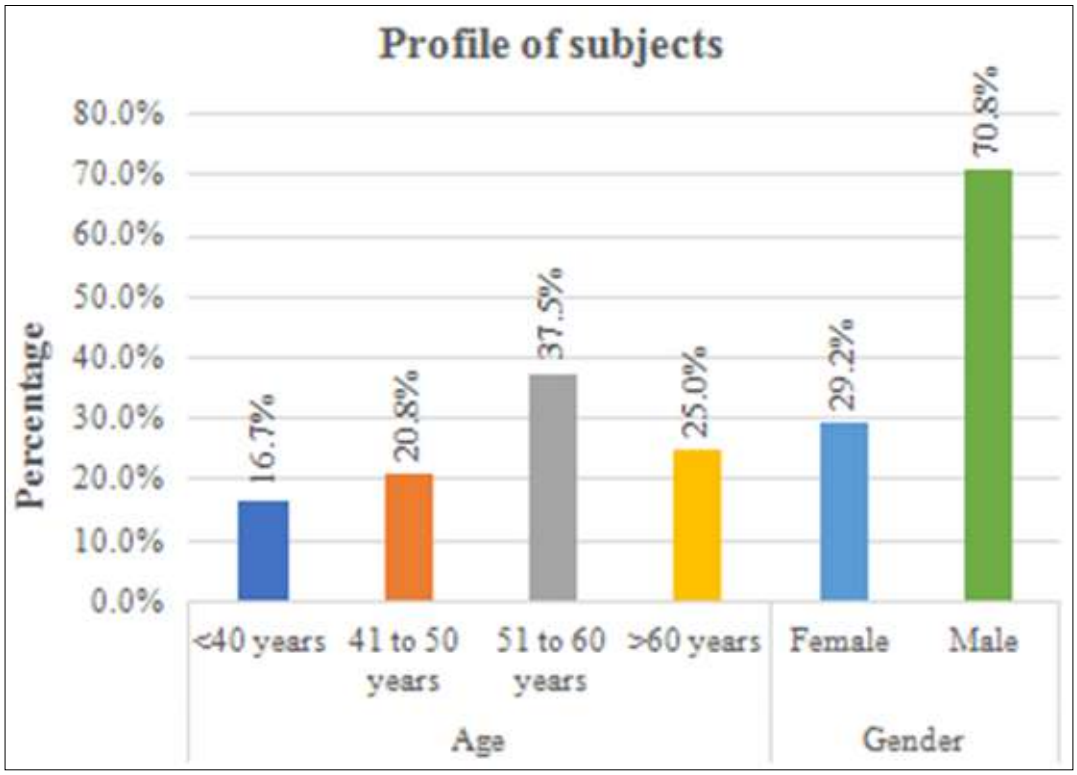

Fig 1: Bar diagram showing profile of subjects

Table 2: Oxygen support before and after 2DG administration

			Count	%	P value
Oxygen Support	Before 2DG	Yes	24	100.0%	
	After 2DG	No	8	33.3%	
		Yes	16	66.7%	0.005*

Wilcoxon Signed Ranks Text

In the study 2DG, 100% of them were on Oxygen support and after 2DG, 66.7% were on oxygen support. There was significant decrease in Oxygen Support after administration of 2DG

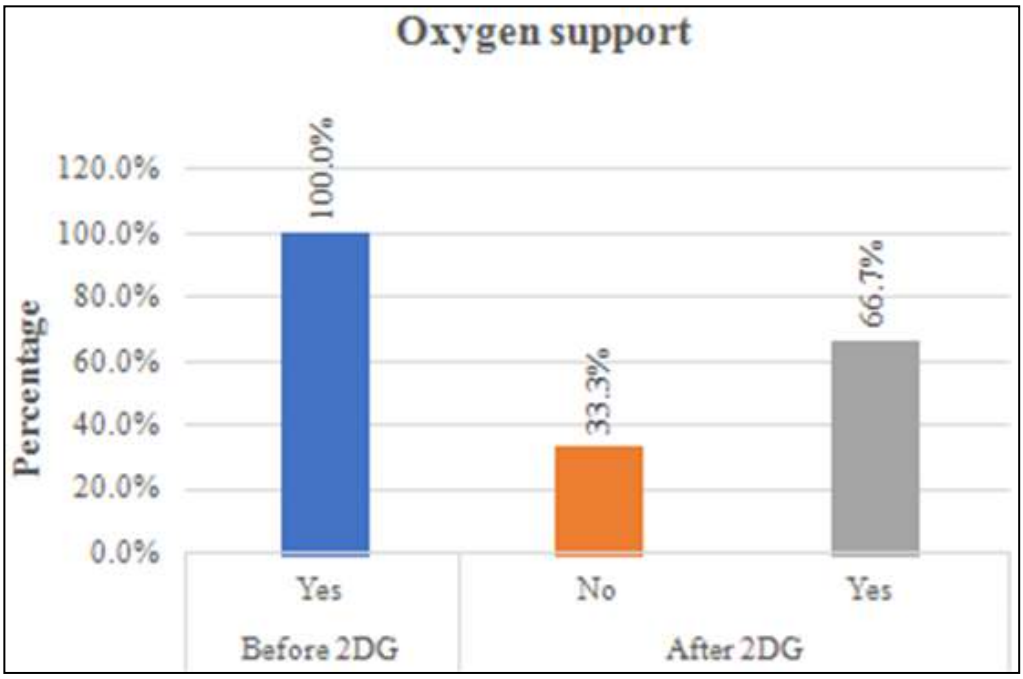

Fig 2: Bar diagram showing Oxygen support before and after 2DG administration

Table 3: Amount of Oxygen used before and after 2DG administration

		N	Mean	SD	P value
Oxygen	Before 2DG	24	79.75	21.977	0.521
	After 2DG	16	74.56	30.100	

Paired Samples Text

In the study before 2DG mean oxygen required was 79.75 + 21.977 liters and after 2DG administration, mean oxygen required decreased to 74.56 + 30.100 liters. There was no significant decrease in oxygen requirement after 2DG

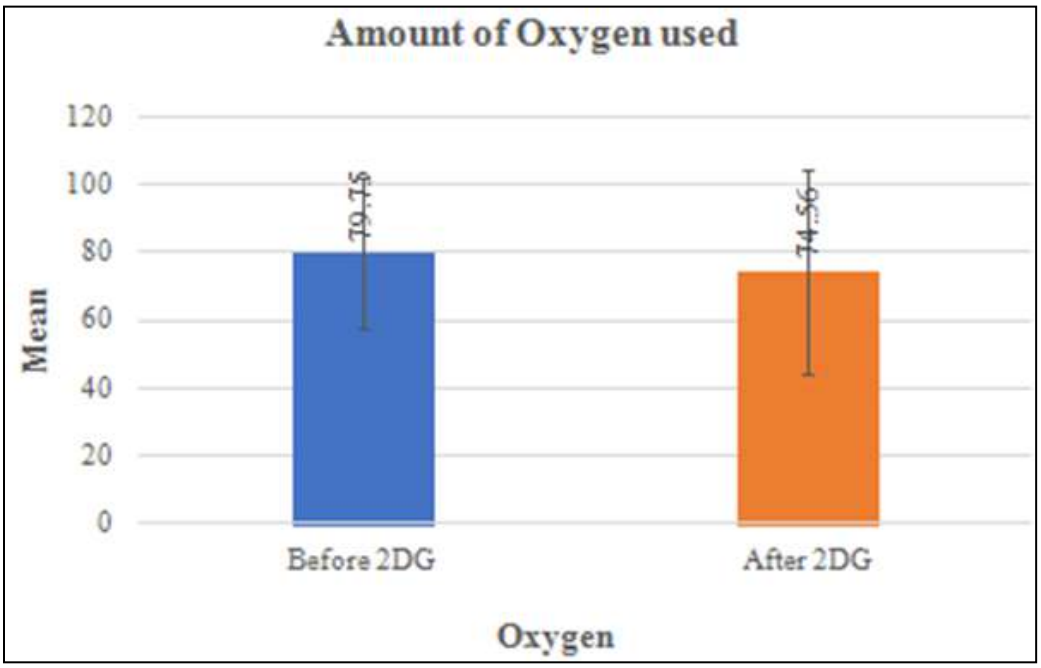

Fig 3: Bar diagram showing amount of oxygen used before and after 2DG administration

Table 4: Respiratory rate before and after 2DG administration

		N	Mean	SD	P value
Respiratory Rate	Before 2DG	24	27.96	4.611	0.219
	After 2DG	24	26.00	9.478	

Paired Samples Text

Mena RR before 2DG was 27.96 + 4.611cpm and after 2DG administration was 26.00 + 9.478cpm. There was no significant decrease in respiratory after 2DG administration

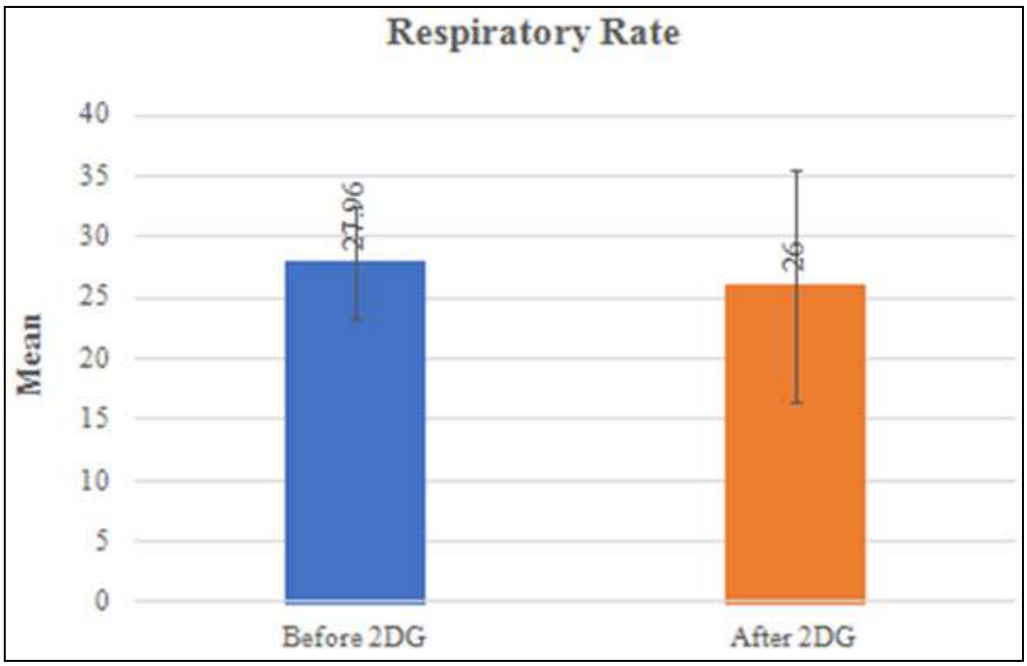

Fig 4: Bar diagram showing respiratory rate before and after 2DG administration

Table 5: Outcome distribution

		Count	%
Outcome	Discharged	15	62.5%
	Expired	9	37.5%

In the study 62.5% were discharged and 37.5% expired.

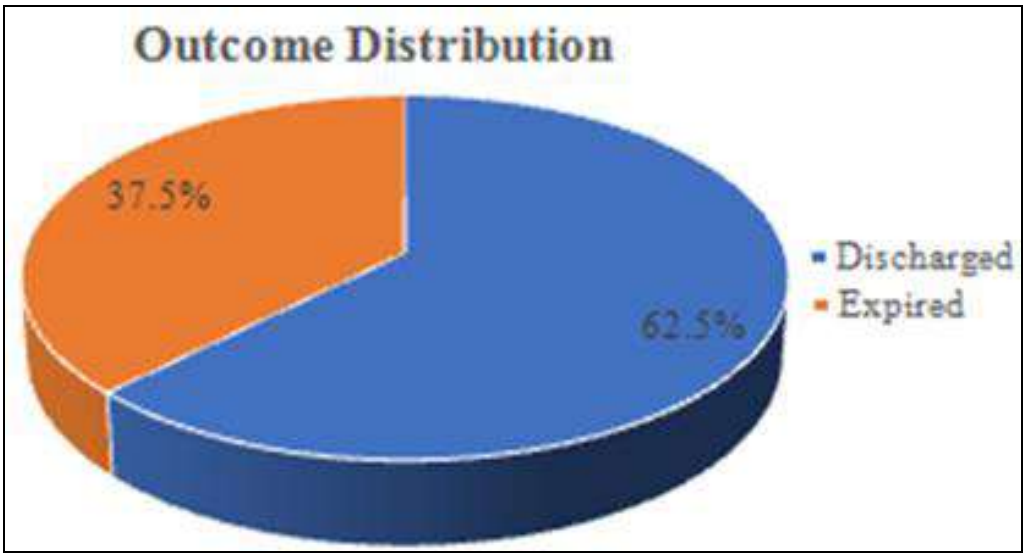

Fig 5: Pie diagram showing outcome distribution

Table 6: Mean day of administration of first dose of 2DG with respect to outcome

			Day of administration of first dose of 2DG		
		N	Mean	SD	P value
Outcome	Expired	9	7.33	2.646	0.128
	Recovered	15	6.00	1.512	

In the study among subjects who recovered mean day of administration of 2DG drug was 6.00 + 1.512 days and among subjects who expired was 7.33 + 2.646. However there was no significant difference in day administration of first dose of 2DG with respect to outcome.

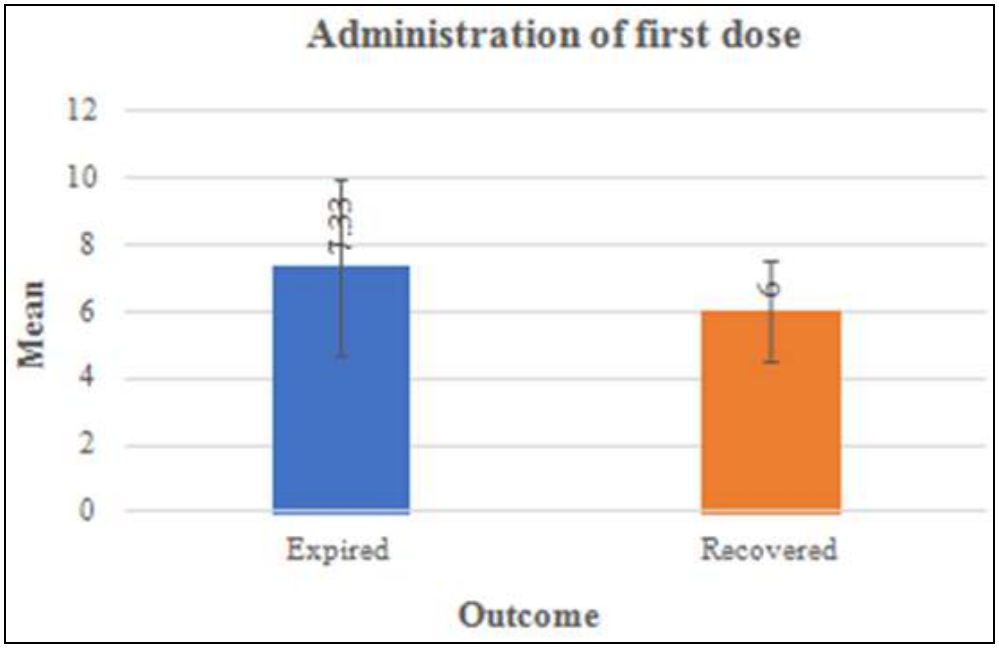

Fig 6: Bar diagram showing mean day of administration of first dose of 2DG with respect to outcome

Discussion

Viruses alter the host cell metabolism in order to make optimal conditions for their rapid and efficient replication and spread. One key particular example is the enhanced uptake of important nutrients such as glucose to support metabolic signaling, i.e., aerobic glycolysis, a primary pathway of glucose metabolism and its by-products for biosynthetic reactions. Being the obligate parasites, viruses are dependent on host-cell machinery to glycosylate their own proteins in the process of replication/multiplication [4]. The increased glucose metabolism imposed by sustained hyperglycemia may enhance SARS-CoV-2's entry and subsequent replication, as well as an exacerbated immune response in individuals with diabetes [1]. The increased glucose metabolism imposed by sustained hyperglycemia may enhance SARS-CoV-2's entry and subsequent replication, as well as an exacerbated immune response in individuals with diabetes [2]. Thus, a disrupted glucose metabolism and metabolic derangement in diabetes may be an intrinsic cellular strategy that favors SARS-CoV-2 pathogenesis. If the cells take up the 2DG in place of glucose, then the pathogenesis will be dampened. This is consistent with the altered innate immune response and excessive inflammatory cytokine production, the so-called "cytokine storm in severe COVID-19. 2-DG blocks SARS-CoV-2 replication in a colon epithelial carcinoma cell line [3]. The metabolic transcription factor hypoxia-inducible factor-1α (HIF-1α) is a master regulator of glycolysis and HIF-1αlevels and activity as well as target genes are strongly induced in SARS-CoV-2 infected monocytes consistent with elevated HIF-1α in blood monocytes isolated from critical COVID-19 patients [1]. The elevated influx of 2DG into cancerous cells has long been exploited as a diagnostic tool to identify and image cancers in patients by monitoring the preferential uptake of a 2DG-related compound, 18F-2-deoxyglucose, via positron emission tomography scan. These effects of 2-DG are used in patients of COVID-19 and the effects observed are early weaning of oxygen in this sample. In our study we have observed administration of 2 DG in patients infected with COVID-19 who are on proposed standard treatment with early weaning off from oxygen support 66.7% of sample, though the sample size is inadequate.

Conclusion

In this study we have observed significant benefits in mortality outcomes and oxygen requirements in patients receiving 2-DG along with standard care of management. As the sample size is 24.we need some more studies with 2-DG, substantiate and justify the use of this drug as an adjunctive modality.

Acknowledgment

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