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ORIGINAL ARTICLE

Perinatal Outcome in Maternal COVID-19 infection at a Tertiary care Institute- A cross Sectional Study

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Abstract

Abstract COVID 19 pandemic is one of the biggest challenge to health system of developing as well as developed countries. Because of the novelty of the virus, limited data were available regarding perinatal outcome. The objective of this study is to find out the perinatal outcome in COVID-19 infected mothers who delivered during COVID Pandemic.

Methodology A cross sectional study was carried out at PCMC'S Post-Graduate Institute and YCM Hospital Pune (Maharashtra) from 1 May 2020 to 31 October 2021 which was a dedicated COVID hospital during COVID pandemic. A total of 362 maternity patients (including 5 twin pregnancies) having COVID 19 infection who gave birth to 367 Newborns were studied. Maternal COVID -19 infection was diagnosed either by RTPCR test or Rapid Antigen test. Demographic variables, maternal symptoms, labour and neonatal outcome were recorded. RT PCR of neonates at birth was performed. Data was analyzed statistically by using Epi Info Software.

Aim To analyze the perinatal outcome among COVID-19 infected mothers who delivered during Covid pandemic.

Objectives Study was conducted with the primary objective to analyze the labour outcome, maternal symptoms and secondarily to study maternal demographic profile and to compare disease severity during 1st and 2nd wave of COVID and to detect possibility of vertical transmission of COVID-19 in neonates of covid positive mothers.

Results 74.2% patients from young reproductive age (21–30 years age) were affected. All socioeconomic classes were affected. 61% patients were multigravida. Normal BMI was noted in 49.8%. 28.2% deliveries were preterm. Caesarean section rate was 50.5%. Following obstetric high risk factors were noted—anaemia in 34.2% followed by previous LSCS in 26.2% cases and preeclampsia in 18.7%

Overall 54.6% patients were asymptomatic while 45.4% were symptomatic. Symptomatology between 1st and 2nd wave showed statistical significance (p value < .05%) for mild, moderate and severe symptoms. Myalgia, cough, fever and fatigue were common presenting symptoms. 14% patients required ICU/HDU care. HDU/ICU requirement showed statistical significance (p value < .05) between 1st and 2nd wave. Overall maternal mortality was 1.1% (4 maternal deaths in 2nd wave) with no mortality in 1st wave.

96.4% were live births. Birth weight was more than 2.5 kg in 62% cases and 21.3% cases required NICU. Vertical transmission of COVID was seen in 1.1% cases.

Conclusion Pregnant patients with moderate and severe disease are at higher risk of perinatal complications. ICU/HDU management with multidisciplinary management may reduce morbidity and mortality. Neonatal affection due to COVID may not be severe but may increase prematurity due to iatrogenic intervention.

Keywords COVID-19 · SARS-CoV-2 · Perinatal Outcome · Neonatal Outcome · Preterm labour

Introduction

COVID-19 infection caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) has led to global public health crisis. Though initial reports during pandemic suggested that pregnant women were not at a higher risk of complications due to COVID-19 infection, previous two coronavirus outbreaks, severe acute respiratory syndrome

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coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) suggest that pregnant women are particularly susceptible to adverse outcome, including the need for intubation, admission to ICU, renal failure and death. [1, 2] This study aims to find out perinatal outcome in COVID-19 infected mothers who delivered during COVID pandemic.

Methodology

A cross sectional study was conducted from 1st May 2020 to 30th October 2021 at PCMC'S Postgraduate Institute and YCM Hospital Pimpri Pune (Maharashtra) which was declared as a dedicated COVID hospital during COVID pandemic. During this study period all pregnant women (antenatal, intrapartum, and postpartum) who were diagnosed to have COVID-19 infection by RT PCR / Rapid Antigen Test were admitted in institution. Only patients delivered after 28 weeks of gestation with COVID positive test were enrolled for the study.

Objectives

Primary

To analyze the perinatal outcome among COVID-19 infected mothers who delivered during covid pandemic (1st wave and 2nd wave of pandemic).

Secondary

1. To study the socio demographic profile of COVID-19 affected pregnant women delivered during study period.
2. To compare the maternal disease severity and clinical profile in 1st and 2nd wave of COVID-19 infection among intra partum cases.
3. To study fetal affection in COVID-19 positive patients.

Inclusion Criteria

1. All women who were diagnosed to have COVID-19 infection by RT PCR/ Rapid Antigen Test and delivered during the study period. (Covid positive at the onset of labour or at the time of LSCS)
2. All maternity cases delivered after 28 weeks were included in the study

DATA COLLECTION TOOL.

Demographic data	Age, BMI, Socio-economic Status
Clinical presentation & need for ICU with duration	Symptomatology on admission, oxygen saturation at presentation, duration of hospitalization/ ICU stay, admission to death interval
Obstetric History	Gravida, parity, gestational age at presentation, postpartum status, obstetric high risk
Intra Partum and Neonatal details	Indication and mode of delivery (if applicable), newborn weight, RT-PCR of newborn, NICU admission, morbidity and mortality
Medical History	Co-morbidities, symptoms at presentation, clinical findings
Treatment	As per ICMR/Government of India Guidelines
Maternal outcome	Stable/discharged/died

Exclusion Criteria

Patient admitted with COVID-19 infection however referred to other institutes were not included in the study because of non-availability of records related to outcome. Refusal of consent for participation in the study.

Technique/ Methodology

We conducted a prospective, single-center, cross sectional study at PCMC'S PGI and YCM Hospital, Pune (tertiary teaching hospital) which was a dedicated Covid Hospital during the study period. Sample size was all intrapartum women diagnosed to have SARS-CoV-2 infection admitted and delivered in this hospital during the study period of 18 months. An informed consent of the admitted intrapartum women was taken for participation in study. Data was collected in standard format as mentioned in the data collection tool. In cases where patient was not able to give consent due to medical reasons, access to medical records was requested. Ethics committee was requested for waiver off the consent in such cases. Variables such as maternal demographic details, symptomatology on presentation, maternal morbidity and mortality, maternal high risk, perinatal outcome such as mode of delivery, NICU admission requirement, neonatal morbidity and mortality were tabulated and data analyzed statistically.

Table 1 Maternal Sociodemographic Variables

	1st Wave N1 = 276	2nd Wave N2 = 86	Total N = 362	Percentage (%)	*P* Value
Maternal age					
< 20 yrs	29	16	45	12.4	*P* > .05 Not significant
21 – 25 yrs	120	36	156	43.0	
26 – 30 yrs	88	25	113	31.2	
31 – 35 yrs	28	07	35	9.7	
> 35yrs	11	02	13	3.7	
TOTAL	276	86	362		
Body mass Index					
< 18.5	30	17	47	13	*P* > .05 Not significant
18.5–24.9	142	38	180	49.8	
25–29.9	86	27	113	31.2	
> 30	18	04	22	6	
Socioeconomic status (modified kuppuswamy scale)					
Upper class	18	08	26	7.2	*P* > .05 Not significant
Upper Middle	34	12	46	12.8	
Lower middle	88	28	116	32	
Upper lower	72	20	92	25.4	
Lower class	64	18	82	22.6	
Gestational age *					
28 – 31.6 wks	16	02	18	5	*P* > .05 Not significant
32 – 34.6 wks	18	05	23	6.4	
35 – 36.6wks	50	11	61	16.8	
> 37wks	192	68	260	71.8	
Parity					
Primi	105	36	141	39	*P* > .05 Not significant
Multi	171	50	221	61	
TOTAL	276	86	362		

Ethical aspect.

Institutional Ethics Committee approval was obtained and confidentiality of the data was maintained throughout the study.

Statistical analysis

Statistical analysis was done using Epi-info7 software.

Data collection

Data were collected in uniform, consistent and reliable manner by trained qualified doctors with the use of standard proforma. Key variables as mentioned in the data collection tool were documented.

Results

Table 1 shows among women infected with COVID-19 74.2% women were in the young reproductive age group (21–30). Women belonging to all socioeconomic classes were infected. 61% of these women were multigravida. Normal BMI was noted in 49.8%.

Table 2 shows that overall 54.6% patients were asymptomatic while 45.4% were symptomatic. Symptomatology between 1st and 2nd wave showed statistical significant difference (P Value <.05%) for (mild, moderate and severe). Myalgia, cough, fever and fatigue were common presenting symptoms.14% patients required ICU/HDU care. HDU/ICU requirement showed statistical significance. (P Value <.05%) between 1st and 2nd wave. Overall maternal mortality was 1.1% (4 deaths). All maternal deaths occurred in 2nd wave with no mortality in 1st wave (Table 3). 28.2% deliveries were preterm. Common obstetric high risk factors noted were anaemia in 34.2%

Table 2 Symptomatology, Maternal Morbidity and Mortality

	1st Wave N1 = 276		2nd Wave N2 = 86		Total N = 362	Percentage(%)	
	Number	Percentage (%)	Number	Percentage (%)			
1Asymptomatic	185	67	13	15.1	198	54.6	$P < .05$ Statistically significant
2. Symptomatic	91	33	73	84.9	164	45.4	
*Distribution of Symptoms among the Symptomatic cases (N3 = 164)							
Fever	34	12.3	62	72	96	26.5	
Cough	48	17.3	50	58.1	98	27.0	
Myalgia	60	21.7	48	55.8	108	29.8	
Fatigue	56	20.2	28	32.5	84	23.2	
Diarrhoea	05	1.8	12	13.9	17	4.6	
Anosmia	40	14.4	08	9.3	48	13.2	
Dyspnea	08	6.5	32	37.2	40	11.0	
Chest pain	01	0.36	16	18.6	17	4.6	
Loss of taste	38	13.7	30	24.8	68	18.7	
*Each Symptom is considered separately and one patient had more than one (2–5 Symptoms in one case have been noted)							
Severity of disease							
Asymptomatic	185	67	13	15.1	198	54.6	$P < .05$ Statistically significant
Mild	64	23.1	49	56.9	113	31.3	
Moderate	20	7.3	16	18.7	36	10	
Severe	07	2.6	08	9.3	15	4.1	
2 ICU/HDU admission	27	9.7	24	27.9	51	14	$P < .05$ Statistically significant
3] Maternal mortality	00	00	04	4.6	04	1.1	$P < .05$ Statistically significant

Table 3 Obstetric High Risk Factors

	1st Wave	2nd Wave	Total	Percentage (%)
No High Risk Factor				
Preterm Labour	84	18	102	28.2
1 Anemia	98	26	124	34.2
2 Preeclampsia	54	14	68	18.7
3 IUGR	09	02	11	3.0
4 Prev LSCS	82	13	95	26.2
5 Twins	02	03	05	1.4
6 DM/GDM	01	02	03	0.8
7 APH	01	00	01	0.3
8 PPH	06	02	08	2.2
Few patients had more than one Obstetric High Risk associated in one case				

followed by previous LSCS in 26.2% cases and preeclampsia in 18.7% (Table 4). Caeserian section rate was 50.5%. Neonatal outcome showed live birth were 96.4%, birth weight was more than 2.5 kg in 62% cases and 21.3% cases required NICU. Vertical transmission of COVID was seen in 1.1% cases.

Discussion

COVID-19 pandemic caused by SARS-CoV-2 virus posed a biggest challenge to health system of developing as well as developed countries. Because of the novelty of this virus, limited data were available regarding maternal and perinatal outcome. Initial reports [3, 4] didn't show any increased adverse effect of COVID-19 on pregnant women; however, there is emerging evidence which shows higher risk of severe disease and increased Intensive Care Unit (ICU) admissions in pregnant women when compared to non-pregnant women [5, 6]. This study describes the perinatal outcome in a tertiary care maternity unit which was a dedicated COVID center during COVID-19 pandemic.

In our study (Table 1), 80.9% COVID affected pregnant women were in the age group of 21–34 years. 12.3% cases were below the age of 20 years and 3.7% cases were above

Table 4 Labour and Neonatal Outcome

	1st Wave N1 = 276	2nd Wave N2 = 86	TOTAL N1 = 362 N2 = 367 N3 = 351 N4 = 77	Percentage (%)	
Term Vs. Preterm (N1 = 362 Covid positive Mothers)					
Term delivery G.AGE > 37	192	68	260	71.8	*P* > .05 Not Significant
Preterm delivery G.AGE < 37 weeks	84	18	102	28.2	
Mode of delivery (N1 = 362 Covid positive Mothers)					
Vaginal delivery	121	53	174	48	P < .05 Statistically significant
Caesarean delivery	151	32	183	50.5	
Instrumental delivery	04	01	05	1.5	
Neonatal Outcome (N2 = 367*) (*Includes 5 cases of twins hence 362 mothers giving birth to 367 Newborn)					
Live Birth	268	83	351	95.6	*P* > .05
Not Significant					
Still Birth	10	06	16	4.4	
Birth weight (N2 = 367)					
< 1.5	17	05	22	5.9	*P* > .05 Not Significant
1.5–2	24	12	36	10	
2–2.5	57	25	82	22.3	
> 2.5	180	47	227	61.8	
Neonatal RTPCR Results (N3 = 351 Live Birth)					
RTPCR Positive	3	1	4	1.1	*P* > .05 Not significant
NICU Requirement (N3 = 351 Live Birth)					
Yes	58	19	77	22	*P* > .05 Not significant
No	207	67	274	78	
Neonatal death (N = 351)	02	01	03*	0.85	
Reasons for NICU admission (N4 = 77 NICU admitted babies)					
(N = 351)	n1 = 58	n2 = 19	n1 + n2 = 77	Percentage(%) (22%)	
Prematurity	22	8	30	8.6	
Hyperbilirubinaemia	11	4	15	4.3	
Birth Asphyxia	5	1	6	1.7	
#TTNB	9	3	12	3.4	
Meconium Aspiration Syndrome	8	2	10	2.7	
Neonatal Sepsis	3	1	4	1.3	

*2 Neonatal deaths in 1st wave were due to prematurity with neonatal sepsis (Both had COVID RTPCR swab Negative). 1 Neonatal death in 2nd wave was due to extreme prematurity with birth asphyxia # Transient Tachypnea of newborn

35 years. UK Obstetric Surveillance System (UKOSS) Marian Knight et al. [7]) a national population-based cohort study of 427 pregnant women reported that 1% were below 20 years, 58% between 20–34 years and 41% were above 35. BMI was normal (18.5–24.9) in 49.8%, while 31.2% were overweight BMI (25–29.9). In UKOSS study, BMI was normal in 31%, 35% were overweight and 34% were obese. In our study, out of 362 women 39% were primipara and 61% were multipara. Most women were in lower middle socioeconomic class (32%) followed by 25.4% in upper lower class.

Most of the women who delivered during COVID infection were above 37 weeks (71.8%), while 16.8% were between 35 and 36.6 weeks, 6.4% were between 32–34.6 weeks and 5% were between 28 and 31.6 weeks.UKOSS study [7] showed that 5% pregnant women were below 22 weeks, 14% were between 22–27 weeks, 15% were between 28–31 weeks, 25% were between 32–36 weeks, 33% were beyond 37 weeks and 7% were peripartum. However, our data exclusively includes women who had delivered with COVID infection while UKOSS study includes all

pregnant women with SARS-Co-V2 infection irrespective of delivery.

In our study (Table 2), 54.6% patients were asymptomatic. Majority of pregnant women who were infected with SARS-CoV-2 were asymptomatic. The PregCOV-19 Living Systematic Review reporting on universal screening in pregnancy estimated 74% (95% CI 51–93) of women were asymptomatic [8], while study from USA reported that 86% of women who were admitted in labour and tested positive for SARS-CoV-2 were asymptomatic [9]. When comparison was done between 1st and 2nd wave for symptomatic (33% Vs 84.9%) and asymptomatic (67% Vs15.1%) patients, statistically significant difference was noted (P Value < 0.05) in the current study.

Among the presenting symptoms, myalgia was noted in 29.8% cases, cough in 27% cases, fever in 26.5% cases, fatigue in 23.2% cases and loss of taste in 18.7% cases in our study. Most symptomatic women experience only mild or moderate cold/flu-like symptoms [10]. Till 29th Nov 2020 PregCOV-19 systematic review [8] included over 64,000 pregnant women worldwide with suspected or confirmed COVID-19. In this review, the most common symptoms of COVID-19 in pregnant women were cough (41%) and fever (40%). Less frequent symptoms were dyspnoea (21%), myalgia (19%), loss of sense of taste (14%) and diarrhoea (8%). Pregnant women with COVID-19 were less likely to have fever or myalgia than non-pregnant women of the same age. The PRIORITY (Pregnancy CoRonavirus Outcomes RegIsTry) ongoing prospective cohort study of pregnant women from the US [11] noted most prevalent first symptoms in infected women were cough (20%), sore throat (16%), myalgia (12%) and fever (12%). Among 594 symptomatic women in this group, one-quarter had persistent symptoms 8 or more weeks after onset.

Among the symptomatic patients (45.4%) disease severity was mild in 31.3%, moderate in 10% and severe in 4.1% in our study. In a study of 1,219 patients, Metz et al. noted that 47% cases were asymptomatic, 27% had mild symptoms 14% cases had moderate symptoms 8% cases had severe symptoms and 4% cases were critical. 4.8% required ICU admission in this study. Center for Disease Control and Prevention data [13] demonstrate an increased risk of death from COVID- 19 and ICU admission among pregnant patients compared with non-pregnant patients. In our study, overall 14% patients required ICU/HDU admission as 2nd wave of COVID was more severe. Statistically significant difference was noted for ICU/HDU admissions when comparison was made between 1st and 2nd wave of COVID (9.7% Vs 27.9%).

Among 362 COVID maternity patients overall maternal mortality was 1.1% which was seen exclusively in 2nd wave of COVID (4.6%)while maternal outcome in 1st wave was good with zero mortality in 1st wave. Two registries such as PAN COVID (Pregnancy and Neonatal outcome in COVID 19) from UK reported maternal deaths in 0.5% and American Academy of Pediatrics (AAP) Section on Neonatal–Perinatal Medicine (SONPM) National Perinatal COVID-19 Registry-USA reported maternal deaths in 0.5% Mullins et al. [14]. Maternal death rate was 0.3% (3/1,000 patients with COVID-19) as reported by Metz et al [12]. In a study of 871 patients including antenatal, intrapartum and postpartum obstetric patients, author has reported maternal mortality of 1.03% due to COVID at the same institution [15].

Common obstetric high risk factors noted (Table 3) were anaemia in 34.2%, previous LSCS in 26.2% cases and preeclampsia in 18.7%. Preterm deliveries in our study were 28.2%, either spontaneous or iatragenic due to obstetric intervention (pre-eclampsia, eclampsia, SGA, or medical indication secondary to severity of COVID disease especially in moderate or severe disease). Such decisions of premature termination of pregnancy due to severity of COVID infection was taken by a multidisciplinary team involving treating obstetrician, pulmonologist and intensivist. Torri D et al., reported preterm births among patients with severe–critical illness in 83% of cases as compared with 61% in patients with mild–moderate illness and 49% in patients who were symptomatic ($P < 0.001$ for trend across severity for indicated delivery among preterm births). Of those induced preterm, COVID-19 was the primary indication for induction of labor in 3%[12].

A systematic review by Yee J et al. quoted, preterm delivery rate of 29%, a strikingly high number compared to the norm[16], which was reported to be between 5 and 18%[17]. Past research in pregnant patients on *coronaviridae* outbreaks, namely severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), showed that the proportion of pregnant patients who experienced preterm delivery were 29% and 32%, respectively, which were approximately similar to the ratio in pregnant COVID-19 patients [18]. Other obstetric factors observed in our study such as anaemia, previous LSCS, preeclampsia were already existent before diagnosis of COVID and didn't show clinical relevance for association with COVID-19, however preterm labour prevalence was higher in our study which may have some association with clinical course of COVID-19. UKOSS study states that preterm birth is more common amongst symptomatic pregnant women with COVID-19 and were higher than in asymptomatic women (19 and 9%, respectively)[7] Higher prevalence of preterm in our study correlated with these studies.

Table 4 shows Caeserian section rate in our study was 50.2% in pregnant women with COVID-19. In literature, around 64% caeserian rate has been noted for COVID 19 infection [18], this rate reaching 93% in China[19]. Majority of COVID-19 infections in pregnancy occur in the

third trimester [20, 21] with 15% requiring hospital admission[22], the increased cesarean rate could be partially justified. However, many patients with non-severe disease are being delivered using the C-section route; experts consider that early delivery, even in non-severe cases is beneficial for the subsequent treatment and outcome of COVID-19. This has led to an increase in the rate of preterm deliveries (21–31%), of which only few are related to spontaneous preterm labor and preterm premature rupture of membranes, while the rest are thought to be iatrogenic [21]

The timing of delivery depends on obstetric factors and clinical deterioration. Vaginal delivery is not contraindicated in patients with COVID-19. In the case of a critically ill patient, cesarean section is the most appropriate mode when emergent delivery is required. Cesarean section is the preferred mode of delivery in a case of preterm pregnancy with critical COVID-19 pneumonia [23].

In our study, live birth and still birth were 95.6% and 4.4% respectively. Neonatal death rate was 0.85%. (Table 4) Birth weight distribution of 367 newborns delivered in 1st and 2nd wave showed, birth weight was more than 2.5 kg in 61.8% cases while birth weight was between 1.5–2.5 kg in 32.3% cases and 5.9% newborn had birth weight less than 1.5 kg. There was no statistical difference ($P > 0.05$) in the birth weight of newborns in 1st and 2nd wave of COVID Pandemic. Vertical transmission rate in our study was 1.1% among the 351 live born babies. Author has reported vertical transmission rate of 0.99 in the study of 201 women at the same institute [24]. Possibility of vertical transmission of COVID-19 has been proposed in previous studies, timing and rate of transmission needs to be determined [25]. According to a systematic review by Lamouroux, there was no evidence of vertical transmission [26]. The relative risk and proportion of neonatal infection by intrauterine transmission of SARS-CoV-2 from either transplacental or ascending infection, acquiring infection during labor and delivery, or following delivery from the mother, other individuals or the environment remain unknown [27]

In a systematic review of 33 studies by Yang Z involving 83 neonates delivered to SARS-CoV-2 infected mothers, three neonates were positive by RTPCR at 16, 36, 72 h of birth and another six had elevated virus specific antibodies[28]. Zeng L reported that three out of 33 neonatal covid infections were due to possible vertical transmission[29]. In a review by Pettirosso E of sixty articles, nineteen neonates were reported to be SARS-CoV-2 positive after birth which was confirmed by reverse transcription polymerase chain reaction of nasopharyngeal swab [31].

NICU admission was required for seventy seven newborns (22% cases) and reasons for the admission were prematurity—in thirty newborns (8.6%), hyperbilirubinaemia—fifteen cases (4.3%), Transient Tachypnea of Newborn in twelve cases (3.4%) and meconium aspiration in ten cases (2.8%). In the UKOSS study [7] sixty seven (25%) of 265 liveborn infants were admitted to a neonatal unit, 50 (75%) of whom were preterm, including 23 (34%) who were less than 32 weeks' gestation.

In our study, overall 3 neonatal deaths were noted (0.85%) among 351 live born babies. 2 neonatal deaths in 1st wave were due to prematurity with neonatal sepsis and one neonatal death in second wave was due to extreme prematurity with birth asphyxia. All 3 were COVID-RTPCR negative. PAN-COVID and AAP-SONPM registry reported neonatal death in 0.3% cases[14] In a study done by MK Nayak et al. on 165 neonates, death rate was 3%. [31]

Strength and Weakness

This study was conducted in a dedicated COVID hospital providing tertiary care maternity facility as per National Task force guidelines for COVID-19. Reliable primary source data was available for the study. Comparison of perinatal outcome in 1st and 2nd wave was reflected in the current study.

Comparable data of non COVID deliveries during same study period were not available as exclusively COVID maternity facility was provided at the study institution. Hence, comparison of results with non COVID sample was not possible.

Conclusion

Pregnant patients with moderate to severe disease are at higher risk of perinatal complications. ICU/HDU management with multidisciplinary management may reduce morbidty and mortality. Neonatal affection due to COVID may not be severe but may increase prematurity due to iatragenic intervention.

Recommendation: COVID patients with moderate to severe disease require institutional management with multidisciplinary review. Involvement of intensivist, chest physician and physiotherapist may help to guide the timing of delivery so that operative intervention such as caeserian section can be done in selected cases thus reducing iatrogenic prematurity.

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Authors Contributions MA ST RB NS were all involved in all steps of this research work, including conception, design, supervision of data collection, data analysis and write up of the manuscript. All authors

have approved the final manuscript. Conception and design of experiments: MA ST. Performed the experiments: MA ST RB NS Analysed the data: MA ST. Contributed materials/analysis tools: MA ST RB NS Wrote the paper: MA ST.

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