

Maternal and fetal outcome in COVID 19 positive pregnant women with thyroid dysfunction

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Abstract

Background: Normally functioning thyroid glands are able to meet the increasing need for hormones during pregnancy and keep thyroid hormone levels within normal limits. However thyroid dysfunction in pregnancy can cause adverse maternal and fetal outcomes like pre-eclampsia and gestational hypertension, antepartum hemorrhage, anemia, preterm delivery, low birth weight and addition of SARS-CoV-19 infection can worsen the perinatal outcome. In present ambispective study, obstetric outcomes of 32 cases of COVID 19 positive pregnant women with thyroid dysfunction (Group A) were compared with 32 cases of COVID 19 negative pregnant women with thyroid dysfunction (Group B).

Results: Pregnancy induced hypertension (PIH) was the most common antepartum complication noted in both the groups (28.1% vs 12.5%). Group-A had 40.6% LSCS rate whereas it was 37.5% in group-B. Average period of gestation at delivery was 38 weeks in both the groups. The most common neonatal complication was low birth weight (9.4%) in both the groups. Group A was also associated with meconium aspiration syndrome (MAS) (9.4%), neonatal sepsis (6.2%) and transient tachypnoea of newborn (TTN) (3.1%). NICU admissions were 37.5% in group A while only 6.25% in group B. (p value <0.01). Most common indication for NICU admission was MAS (9.4%) in group A. It was observed that incidence of pregnancy induced hypertension (PIH) and neonatal complications including NICU admissions were increased in presence of both COVID 19 and thyroid disorder as compared to only thyroid disorder in pregnancy. Multi-disciplinary approach with more vigilant monitoring can help reduce perinatal morbidity and mortality.

Keywords: COVID-19; SARS-CoV-2; Thyroid dysfunction; Hypothyroidism; Hyperthyroidism; Pregnancy; Obstetric outcomes; PIH (pregnancy induced hypertension); NICU/nursery admission

1. Introduction

Thyroid dysfunction holds second place after diabetes mellitus amongst the most common endocrine disorders affecting women of childbearing age. Thyroid dysfunction encompasses overt hypothyroidism, subclinical hypothyroidism and hyperthyroidism. At least 2%-3% of pregnant women are affected by thyroid dysfunction. The prevalence of hypothyroidism in pregnancy is around 2.5% according to western literature¹. As per an epidemiological study of 11 cities from 9 states in India there is a high prevalence of hypothyroidism (13.13%) in India, majority being subclinical in pregnant women during the first trimester². Hyperthyroidism occurs in 0.2-0.3% of pregnant women and is most commonly associated with gestational transient thyrotoxicosis or grave's disease^{3,4}. The fetus until 10 to 12 weeks of gestation is dependent on supply of thyroxine (T4) from the mother and it is vital for fetal growth and neurocognitive development.

Thyroid dysfunction in pregnancy may be accompanied by both maternal and fetal complications. Hypothyroidism in pregnancy is associated with premature birth, fetal cardiac complications, stillbirth, abortion, low birth weight,

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increased frequency of cesarean delivery, placental abruption, preeclampsia and gestational hypertension, heart failure, thyroid storm, perinatal morbidity and mortality along with cognitive dysfunction.

The novel coronavirus disease 2019 (COVID-19) is caused by coronavirus 2 (SARS-CoV-2) and it led to severe acute respiratory distress syndrome making it a global public health crisis number one from 2019 to 2022. As per CDC, total 43,289,203 cases of COVID-19 were reported in united states till September,2021⁵. The total number of cases reported in India were 3,37,39,980 with 1.33% death rate⁶. During this crisis, pregnant women remained at increased risk of acquiring viral respiratory infection and developing severe pneumonia, acute respiratory distress syndrome, respiratory failure, multi-organ failure, septicemia, as compared to general population due to the physiologic changes in their immune and cardiopulmonary systems. It was hence observed that pregnant women who got infected with SARS-CoV-2 were associated with increased risk of maternal and perinatal morbidity and mortality. COVID 19 infection could be associated with perinatal outcomes such as preterm birth, premature rupture of membranes, fetal distress, increased cesarean deliveries, low birth weight, neonatal asphyxia, increased neonatal intensive care admissions, pneumonia, septicemia and mortality⁷.

Excessive or deficient maternal thyroid hormone levels have serious effects on the fetal and maternal outcomes at every stage of a pregnancy and with superimposed COVID-19 infection, the outcomes could worsen. One study conducted in non-pregnant population, suggested that abnormal thyroid dysfunction was more common in severe cases than mild/moderate cases of COVID 19 infections⁸. Studies assessing the impact of COVID 19 infection co existing with thyroid dysfunction on maternal and perinatal outcomes are limited.

This study aims to assess the maternal and perinatal outcomes in coexisting thyroid disorder with COVID-19 infection.

2. Materials and methods

This is a pilot ambispective cohort study which was conducted from January 2021 to September 2021 in the department of obstetrics and gynecology, Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi. After taking ethical clearance from the institute's ethical committee and obtaining informed consent a total of 64 patients were enrolled in this study. A total of 32 cases of COVID 19 negative antenatal women with singleton pregnancy with thyroid dysfunction in third trimester or post-delivery without any preexisting chronic medical disorders admitted between January to September 2021 were enrolled in GROUP B prospectively. The case records of COVID 19 positive patients from May 2020 onwards to January 2021 were reviewed retrospectively [from may 2020 to January 2021 the institute was completely dedicated to COVID 19 positive patients only] and enrolled in group A alongwith patients followed prospectively between January to September 2021 . (total of 32 cases in Group A)

The maternal and fetal outcomes in group A (COVID-19 positive cases with thyroid disorder) were compared with group B (COVID 19 negative cases with thyroid disorder) and data was analysed SPSS-PC-25 version.

A detailed obstetric history, trimester history, menstrual history, past history, history regarding symptoms of COVID 19 was taken of the cases followed by detailed general and physical examination. Necessary blood investigations like CBC, liver and kidney function tests, coagulation profile and inflammatory markers like CRP, LDH, serum ferritin, procalcitonin, d-dimer, interleukin-6, radiological investigations and RTPCR test for COVID 19 were done and patients were categorized into the severity of COVID-19 infection and were triaged accordingly. The ones with severe or moderate COVID-19 infection were admitted in either ICU or HDU (high dependency unit) and the ones with mild or asymptomatic COVID-19 infection were admitted in ward or labor room as per the obstetric complaints of the patient. Venous blood samples of 3ml were collected in plain vial for thyroid function test including S.TSH, free T3, Free T4 estimation and patients were diagnosed with thyroid disorder as per FOGSI 2019 guidelines (the trimester specific TSH cut off recommended are: 1st trimester 2.5 mIU/L; 2nd trimester, 3.0 mIU/L; 3rd trimester, 3.0 mIU/L)⁹.

Both mother and neonate were managed in a multi-disciplinary approach according to the guidelines laid down by the government.

The maternal and fetal outcomes like gestational age at delivery, mode of delivery, birth weight, APGAR score, any neonatal complication were observed and both mother and neonate were followed-up for 1 week to observe for adverse outcomes.

The data was analyzed and statistically evaluated using SPSS-PC-25 version. Depending on normality distribution, comparison of quantitative data between two group was tested by student 't' test or Man Whitney U test while for more than two groups comparison ANNOVA test or Kruskal Wallis H test was used. Statistical differences between the

proportions tested by chi square test or Fisher's exact test. 'P' value less than 0.05 was considered statistically significant.

3. Results

Table 1 Sociodemographic features of study subjects

Age in Years	Group A (n=32)		Group B (n=32)		P value
	No	%	No	%	
20-24 years	4	12.5	11	34.4	
25-29 years	12	37.5	11	34.4	
30-34 years	13	40.6	9	22.5	
35 years and above	3	9.4	1	2.5	
Mean age in years	28.81 +/- 4.65		26.66 +/- 3.94		
GRAVIDA					
PRIMI	10	31.2%	11	34.4%	0.86
G2	11	34.4%	12	37.5%	
>/=	11	34.4%	9	28.1%	
EDUCATION					
Illiterate	2	6.25%	4	12.5%	0.17
Primary	8	25%	14	43.7%	
Secondary	14	43.5%	11	34.5%	
Higher secondary	8	25	3	9.4%	
Already on thyroid treatment					
No	6	18.8%	5	15.6%	0.74
Yes	26	81.2%	27	27%	
Type of Thyroid Disorder					
Hyperthyroidism	2	6.2%	2	6.2%	1.0
Hpothyroidism	30	93.8%	30	93.8%	
Overt	7	23.3%	11	36.7%	0.25
Subclinical	23	76.7%	19	63.3%	

In both the groups 93.8% cases (n=30) had hypothyroidism and 6.2% (n=2) had hyperthyroidism. Both the groups had more or less equal distribution of overt and subclinical hypothyroidism. With 23.3% and 36.7% cases of overt hypothyroidism in group A and group B respectively.

Table 2 Impact of COVID 19 infection on group A subjects (n=32)

Severity of COVID 19 on admission	No	%
Asymtomatic	19	59.4%
Mild	13	40.6%
Moderate	0	0

Severe	0	0
Symptoms:		
Cough	12	37.5%
Sore Throat	12	37.5%
Fever	10	31.3%
Myalgias	6	18.8%
Headache	4	12.5%
Anosmia	7	21.9%
Others	4	12.5%
Day since symptom onset:		
Nil	19	59.4%
1-2	2	6.25%
3-5	7	21.9%
6-7	1	3.12%
>7	3	9.37%

In Group-A which includes COVID-19 positive pregnant female with thyroid disorder, majority of cases were asymptomatic 59.4% (n=19) and 40.6% (n=13) had mild COVID illness.

Table 3 Antepartum complications with various thyroid dysfunctions in study subjects

Antepartum Complications	Group A		Group B		P value	
	Hyperthyroidism (n=2)	Hypothyroidism (N=30)	Hyperthyroidism (n=2)	Hypothyroidism (n=30)	P value	
Anemia	0	4 (13.3%)	0	2 (6.7%)	0.67	
PIH	1	8 (26.7%)	0	4 (13.3%)	0.33	
SGA	0	2 (6.7%)	0	0	0.49	
GDM	0	2 (6.7%)	2	2 (6.7%)	1.0	
IHCP	0	3 (10%)	0	3 (10%)	1.0	
FGR	0	1 (3.3%)	0	2 (6.7%)	1.0	
PROM	0	1 (3.3%)	0	0	1.0	
Preterm Labour	0	2 (6.7%)	0	2 (6.7%)	-	
Antepartum Complications with Hypothyroidism in both groups:						
Antepartum Complications:	GROUP A	GROUP A	GROUP B	GROUP B	P value for SC	P value for overt
	Subclinical (n=23)	Overt (n=7)	Subclinical (n=19)	Overt (n=11)		
Anemia	2 (8.7%)	2 (28.6%)	1 (5.3%)	1 (9.1%)	1.0	0.52
PIH	5 (21.7%)	3 (42.9%)	3 (15.8%)	1 (9.1%)	0.70	0.24

SGA	2 (8.7%)	0	0	0	0.49	1.0
GDM	2 (8.7%)	0	1 (5.3%)	1 (9.1%)	1.0	1.0
IHCP	2 (8.6%)	1 (14.3%)	1 (5.3%)	2 (18.1%)	1.0	1.0
FGR	0	1 (14.3%)	0	2 (18.1%)	1.0	1.0
PROM	1 (4.3%)	0	0	0	1.0	1.0
Preterm labour	2 (8.7%)	0	2 (10.5%)	0	1.0	1.0

Pregnancy induced hypertension (PIH) was the most common antepartum complication noted in group-A (28.1%, n=9). Other complications like anaemia (12.5%), Small for gestational age (6.2%), Gestational Diabetes mellitus GDM (6.2%), IHCP (9.3%), Fetal growth restriction (3.1%), preterm premature rupture of membranes (3.1%) and preterm labour (6.2%) were also noted. In Group-B (n=32), most common antepartum complication was PIH (12.5%) and GDM (12.5%). Other complications like IHCP in 9.3% cases, anaemia, FGR and preterm labour were noted in 6.2% cases each.

Table 4 Association of TSH level with Antepartum Complications

Antepartum Complications	GROUP A TSH LEVEL			GROUP B TSH LEVEL			P VALUE FOR TSH<4	P VALUE TSH 4-10
	<4 (n=18)	4-10 (n=13)	>10 (n=1)	<4 (n=10)	4-10 (n=21)	>10 (n=1)		
Anemia	1 (5.6%)	3 (23.1%)	0	0	2 (9.5%)	0	1.0	0.34
PIH	4 (22.2%)	3 (23.1%)	1(100%)	3 (30%)	1 (4.7%)	0	0.67	0.13
OTHERS	5 (16.7%)	5(15.45%)	0	3 (30%)	7(33.3%)	0	1.0	0.76
NONE	8 (44.4%)	2 (15.4%)	0	4 (40%)	11(52.4%)	1(100%)	1.0	0.06

Even with serum TSH level 4-10 mIU/L or more than 10 mIU/L, the occurrence of antepartum complications were more or less same in both the groups.

Table 5 Obstetrical Outcome in study subjects

MODE OF DELIVERY	GROUP A (N=32)		GROUP B (N=32)		P VALUE
	No.	%	No.	%	
NVD	19	59.4	20	62.5	0.76
LSCS	13	40.6	12	37.5	
Indications of LSCS	GROUP A (N=13)		GROUP B (N=12)		
	No.	%	No.	%	
CPD	2	15.4	0		0.0
DTA	1	7.7	0		0.0
Failed Induction	1	7.7	1		7.7
Fetal Distress	6	46.1	5		38.5
Uncontrolled GHTN	1	7.7	0		0.0
Arrest of descent of head	1	7.7	1		7.7

Not willing for TOLAC	1	7.7	0		0.0	
Previous 2 LSCS	0	0.0	2		15.4	
Breech	0	0.0	1		7.7	
Previous LSCS with Scar Tenderness	0	0.0	1		7.7	
Transverse Lie	0	0.0	1		7.7	
POSTPARTUM COMPLICATIONS	GROUP A (N=32)		GROUP B (N=32)		P VALUE	
	NO	%	NO	%		
Nil	30	93.8	30	93.8	1.0	
PPH	2	6.2	2	6.2		
POG at Delivery	GROUP A		GROUP B			
	Hyperthyroidism (n=2)	Hypothyroidism (n=30)	Hyperthyroidism (n=2)	Hypothyroidism (n=30)	P value	
<34 weeks	0	0	0	0	-	
34-34+6 weeks	0	3(10%)	0	5(16.7%)	0.70	
37-39+6 weeks	1	22(73.3%)	2	20(66.7%)	0.57	
>=40 weeks	1	5(16.7%)	0	5(16.7%)	1	
Median POG in weeks at delivery	38.96+/-1.25		38.62+/-1.49			
POG at delivery	Group A		Group B		P sub-clinical	P overt
	Subclinical (n=23)	Overt (n=7)	Subclinical (n=7)	Overt (n=11)		
<34 weeks	0	0	0	0	-	-
34-36+6 weeks	3(13.0%)	0	2(10.5%)	3(27.3%)	1	0.24
37-39+6 weeks	18(78.2%)	4(57.1%)	14(73.7%)	6(54.5%)	0.72	1
>=40 weeks	2(8.7%)	3(42.8%)	3(15.8%)	2(18.2%)	0.64	0.32

Group-A had 40.6% LSCS rate whereas LSCS rate was 37.5% in group-B. In group-A, most common indication was fetal distress (46.1%). Other indications were Cephalo-pelvic disproportion (15.4%), Deep transverse arrest (7.7%), failed induction (7.7%), uncontrolled gestational hypertension (7.7%), arrest of descent of head (7.7%) and not willing for TOLAC (7.7%).

In group-B, the most common indication was fetal distress (38.5%). Others indications were, previous 2 LSCS (15.4%), failed induction (7.7%), arrest of descent of head (7.7%), breech (7.7%), previous LSCS with scar tenderness (7.7%), transverse lie (7.7%). Not many post-partum complications were noted in either group. Both the groups had 2 cases of post-partum haemorrhage each (6.2%). While most of the deliveries occurred between 37 to 39+6 weeks in both the groups, 10% and 16.7% had late preterm delivery in group- A and group B respectively. No delivery was noted before 34-week period of gestation. Mean period of gestation at delivery was almost 38 weeks in both the groups.

Table 6 Neonatal outcomes in study subjects

	Group A		Group B		P value for hypothyroidism	
Birth Weight (gm)	Hyperthyroidism (n=2)	Hypothyroidism (n=30)	Hyperthyroidism (n=2)	Hypothyroidism (n=30)		
<2500	1	2 (6.7%)	0	3 (10%)		1
2500 - 3000	1	14 (46.7%)	2	11 (36.7%)		0.43
>3000	0	14 (46.7%)	0	16 (53.3%)		0.60
Mean Birth weight (gm)	2929.84±374.88		2770.38±480.892		0.28	
Birth weight(gms)	Group A		Group B		P value for subclinical hypothyroidism	P value for overt hypothyroidism
	Subclinical Hypothyroidism (n=23)	Overt Hypothyroidism(n=7)	Subclinical Hypothyroidism (n=19)	Overt Hypothyroidism (n=11)		
<2500	1 (4.3%)	1 (14.2%)	1 (5.3%)	2(18.2%)	1	1
2500 - 3000	11 (47.8%)	3 (42.8%)	7 (36.8%)	4(36.4%)	0.47	1
>3000	11 (47.8%)	3 (42.8%)	11 (57.9%)	5(45.5%)	0.51	1
APGAR SCORE (0,1,5 minutes)	Groups					
	Group A (n=32)			Group B (n=32)		
9,9,9	32 (100%)			32 (100%)		
Less than 9,9,9	0			0		
RTPCR report of neonates in Group A	Group A (n=32)					
COVID-19 negative	32 (100%)					
COVID-19 positive	0					
NICU admission	Groups				P value	
	Group A (n=32)		Group B (n=32)			
	12 (37.5%)		2 (6.25%)		<0.01	
Indication for NICU admission	Group A (n=32)		Group B (n=32)			
RDS	0		1 (3.1%)			
TTN	1(3.1%)		0			
Sepsis	2 (6.2%)		0			
MAS	3 (9.4%)		1(3.1%)			

Low Birth weight	1 (3.1%)	0	
Observation	5 (12.5%)	0	
Neonatal Complications	Group A (n=32)	Group B (n=32)	
RDS	0	1 (3.1%)	
TTN	1(3.1%)	0	
Sepsis	2 (6.2%)	0	
MAS	3 (9.4%)	1(3.1%)	
Low Birth weight	3 (9.4%)	3 (9.4%)	
	Group A	Group B	

Neonatal complications in subclinical versus overt hypothyroidism	Subclinical Hypothyroidism (n=23)	Overt Hypothyroidism (n=7)	Subclinical Hypothyroidism (n=19)	Overt Hypothyroidism (n=11)
RDS	0	0	0	1 (9.1%)
TTN	0	1 (14.2%)	0	0
Sepsis	2 (8.7%)	0	0	0
MAS	2 (8.7%)	1 (14.2%)	0	0
Low Birth weight	1 (4.3%)	1 (14.2%)	1 (5.3%)	2 (18.2%)

Low birth weight was noted in 9.4% of neonates in group-A out of which 6.75% were associated with maternal hypothyroidism and 3.1% with maternal hyperthyroidism. While in group B, 9.4% neonates of low birth weight were noted all of which were associated with maternal hypothyroidism. All the neonates in both the groups had an APGAR score of 9,9,9 at 0,1 and 5 minutes. 28.1% of thyroid disorder with COVID 19 positive pregnancy were associated with neonatal complications whereas only 15.6% pregnancy had neonatal complications in COVID 19 negative with thyroid disorder group. The most common complication was low birth weight (9.4%) in both the groups.

Meconium aspiration syndrome (MAS) was noted in 9.4% cases with COVID 19 positive group. Neonatal sepsis was noted only in 6.2% COVID 19 positive group with thyroid disorder. 3.1% case of transient tachypnoea of new born (TTN) was noted in COVID 19 positive group.

Other than low birth weight, COVID 19 negative group with thyroid disorder was associated with respiratory distress syndrome RDS (3.1%) and MAS (3.1%)

Overall overt hypothyroidism was associated with 27.7% neonatal complications while subclinical hypothyroidism was associated with 14.3% neonatal complication rate.

Group A was associated with 37.5% NICU admission while group B was associated with only 6.25% NICU admissions. It is a significant finding with p value <0.01. Most common indication for NICU admission was MAS (9.4%) in group A.

4. Discussion

Normally functioning thyroid glands are able to meet the increasing need for hormones during pregnancy and keep thyroid hormone levels within normal limits. Excessive or deficient maternal thyroid hormone levels are known to have serious effects on the fetal and maternal outcomes at every stage of a pregnancy. With co-existing COVID-19 infection, the outcomes could be more adverse.

In current study, pregnant women with COVID-19 illness were more commonly complicated with pregnancy induced hypertension (PIH) (28.1% vs 12.5%). The cause of it may be explained as in hypothyroidism there is increase in

peripheral vascular resistance and arterial stiffness due to effect on the vascular smooth muscle cells because of vasoconstriction in absence of vasodilatory T3 hormone and presence of COVID 19 infection worsens the scenario¹⁰. Similar results were observed in studies conducted by Mahajan et al¹¹ and Nayak H et al¹² in July 2021 and July 2020 respectively.

There was increased incidence of anemia and GDM in the group with COVID 19 with thyroid disorder (Anaemia with group A: 12.5% ,GDM in group A : 6.2%). The increased cases of anaemia with COVID 19 can be because COVID 19 pandemic resulted in limitations in availability of antenatal care and inadequate iron and folic acid supplementation which added on to the pre-existing burden of nutritional anaemia in India. Studies conducted pertaining to the incidence of anemia and GDM with thyroid disorders such as by Gupta et al.¹³, Sahu et al.¹⁴ and Sreelatha S et al.¹⁵ showed increased incidence of these conditions in patients with thyroid dysfunction.

9.3% preterm birth was noted in COVID 19 positive with thyroid disorder group while 15.6% cases of preterm birth were noted in COVID -19 negative group. 18.7% cases of post-dated birth were noted in group A and 16.7% in group B.

All the cases belonging to asymptomatic to mild COVID category can be the reason for no significant rise in preterm deliveries.

Slight increase in post-dated birth in COVID 19 positive cases can be because early on in COVID 19 pandemic active interventions like induction or augmentation were delayed due to no adequate data available on how the general condition of women will respond but soon guidelines were in place and all interventions were done as per obstetric interventions. Systematic Review (PregCOV-19), 2020 estimated the overall rate of preterm birth to be 17% and spontaneous preterm birth 6%¹⁶.

In present study, even though COVID 19 pandemic being a novel and unknown territory LSCS were performed only for obstetric indications and normal vaginal delivery was the preferred route of delivery. Cesarean section rate was 40.6% in thyroid disorder with COVID-19 positive group. While it was 37.5% with thyroid disorder without COVID 19 infection group. Similar results were noted in a study conducted by Nayak H et al.¹² (2020) which had 50% LSCS rate in COVID positive group and 47 % in COVID negative group (47%). Mainly during early part of pandemic when proper protocols were not made, risk of increased exposure during vaginal delivery, delay due to time needed to put on personal protective equipment and transport of patients via the red corridor to the operation theatre could increase risk of fetal morbidity and mortality which caused a shift towards elective LSCS or low threshold for LSCS. This resulted in initial increased cesarean section rates in a lot of COVID related studies.

Low birth weight was noted in 9.3% cases with COVID 19 positive with thyroid disorder. Similar to 7.9 % of low birth weight neonates born to pregnant women with COVID-19 infection in a meta-analysis published by Bellos I et al.¹⁷ .In current study overall rate of low birth weight with hypothyroidism (n=60) seen was 8.3%. Gupta M et al.¹³ (2017) showed 19.2% low birth weight in overt hypothyroidism cases and 11.2% low birth weight rate with subclinical hypothyroidism.

In present study, all the neonates in both the groups had an APGAR score of 9 at 0 minute, 9 at 1 minute and 9 at 5 minutes. Similar results were seen with study conducted by Dulek H et al.¹ (2019) in which no significant difference was noted in APGAR score between thyroid disorders and euthyroid state.

All the neonates were tested for SARS-CoV-2 infection with RTPCR test. And all the neonates tested negative for COVID 19. Similar to Schwartz A et al.¹⁸ (2020) which did not find vertical transmission in their studies on pregnant women with COVID-19.

In present study, COVID 19 positive patients with thyroid disorder is associated with 28% cases of neonatal complications out of which 9.45% cases were of low birth weight and MAS (meconium aspiration syndrome) was present in 9.4% cases. 6.2% cases (n=2) of neonatal sepsis by staphylococcus aureus were noted. Repeated per vaginal examinations or some other source of hospital acquired infection was thought to be reason for the above. A review of perinatal outcomes with COVID 19 published by Salem D et al.⁷ (2021) found preterm birth (39%), fetal distress (43%), intrauterine growth retardation (10%), miscarriage (2%), and perinatal death (7%) had similar results. A Study by Nayak H et al.¹² (2020) showed 17.9% NICU admission rate in COVID-19 positive pregnancy mainly due to low birth weight, low APGAR score, neonatal seizures, meconium aspiration syndrome and ABO incompatibility.

The NICU admission rate noted in the COVID 19 positive with thyroid disorder group was 37.5% while it was only 6.25% in the COVID 19 negative group with thyroid disorder. The high NICU admission noted was in part because in the

initial phase of COVID-19 pandemic, neonates were admitted in the nursery in view to isolate the neonate from mother and reduce the risk of transmission of SARS-CoV-2 from mother to neonate.

In current study, overall neonatal complications were 18% with hypothyroidism. Overt hypothyroidism was associated with 22.2% neonatal complications and 11.9% with subclinical hypothyroidism. The results were similar to Sahu M et al.¹⁴ (2010) study that showed 11% neonatal complications with overt hypothyroidism and 22% neonatal complications with subclinical hypothyroidism.

5. Conclusion

In this observational study it was observed that incidence of pregnancy induced hypertension (PIH) in mothers and neonatal complications including nursery admissions were increased in presence of both COVID 19 and thyroid disorder as compared to only thyroid disorder in pregnancy. A multi-disciplinary approach with institutional standard practice protocols (SOPs) in place including more frequent maternal and fetal monitoring in antepartum, intrapartum and early postpartum period can produce largely favorable maternal and fetal outcomes.

The strength of the study is that no such study had been conducted at that time to assess the effect of co-existing COVID-19 infection and thyroid disorder with pregnancy outcomes. The limitation was the small sample size and it was a single centre observational study. Large scale multi-centre study is recommended to have more robust data on the matter.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all the individual participants included in the study.

References

- [1] Dulek H, Vural F, Aka N, Zengin S. The prevalence of thyroid dysfunction and its relationship with perinatal outcomes in pregnant women in the third trimester. *North Clin Istanbul*. 2019 Sep 2;6(3):267–72.
- [2] Dhanwal DK, Bajaj S, Rajput R, Subramaniam KAV, Chowdhury S, Bhandari R, et al. Prevalence of hypothyroidism in pregnancy: An epidemiological study from 11 cities in 9 states of India. *Indian J Endocrinol Metab*. 2016;20(3):387–90.
- [3] Wémeau J, Klein M, Sadoul J-L, Briet C, Vélayoudom-Céphise F-L. Graves' disease: Introduction, epidemiology, endogenous and environmental pathogenic factors. *Ann Endocrinol*. 2018 Dec 1;79(6):599–607.
- [4] López-Muñoz E, Mateos-Sánchez L, Mejía-Terrazas GE, Bedwell-Cordero SE. Hypothyroidism and isolated hypothyroxinemia in pregnancy, from physiology to the clinic. *Taiwan J Obstet Gynecol*. 2019 Nov 1;58(6):757–63.
- [5] CDC. COVID Data Tracker [Internet]. Centre for Disease Control and Prevention. 2020 [cited 2021 Oct 1]. Available from: <https://COVID.cdc.gov/COVID-data-tracker>
- [6] #IndiaFightsCorona COVID-19 [Internet]. MyGov.in. 2020 [cited 2021 Oct 1]. Available from: <https://mygov.in/COVID-19/>
- [7] Salem D, Katranji F, Bakdash T. COVID-19 infection in pregnant women: Review of maternal and fetal outcomes. *Int J Gynecol Obstet*. 2021;152(3):291–8.
- [8] Wang W, Su X, Ding Y, Fan W, Zhou W, Su J, et al. Thyroid Function Abnormalities in COVID-19 Patients. *Front Endocrinol*. 2021 Feb 19;11:623–79.
- [9] Good clinical practice advice: Thyroid and pregnancy. [cited 2021 Oct 14]; Available from: <https://obgyn.onlinelibrary.wiley.com/doi/10.1002/ijgo.12745>

- [10] W. X. Chen LYT, W. X. Chen LYT. Relationship between subclinical hypothyroidism during pregnancy and hypertensive disorder complicating pregnancy and its poor prognosis. *Clin Exp Obstet Gynecol*. 2020 Feb 15;47(1):111–6.
- [11] Mahajan NN, Pophalkar M, Patil S, Yewale B, Chaaithanya IK, Mahale SD, et al. Pregnancy Outcomes and Maternal Complications During the Second Wave of Coronavirus Disease 2019 (COVID-19) in India. *Obstet Gynecol*. 2021 Oct;138(4):660–2.
- [12] Nayak AH, Kapote DS, Fonseca M, Chavan N, Mayekar R, Sarmalkar M, et al. Impact of the Coronavirus Infection in Pregnancy: A Preliminary Study of 141 Patients. *J Obstet Gynecol India*. 2020 Aug 1;70(4):256–61.
- [13] Gupta M, Pandotra P, Jindal M, Jamwal G, Goraya s. P s, Gupta V. Comparative study of feto-maternal outcome in clinical and subclinical hypothyroidism. *Int J Reprod Contracept Obstet Gynecol*. 2017 Apr 27;6:1909-21.
- [14] Sahu MT, Das V, Mittal S, Agarwal A, Sahu M. Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. *Arch Gynecol Obstet*. 2009 May 13;281(2):215.
- [15] Sreelatha S, Nadagoudar S, Asha DL. The study of maternal and fetal outcome in pregnant women with thyroid disorders. *Int J Reprod Contracept Obstet Gynecol*. 2017 Aug 1;6(8):3507–14.
- [16] 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(1):3320-8.
- [17] Bellos I, Pandita A, Panza R. Maternal and perinatal outcomes in pregnant women infected by SARS-CoV-2: A meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2021 Jan 1;256:194–204.
- [18] Schwartz DA. An Analysis of 38 Pregnant Women With COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes. *Arch Pathol Lab Med*. 2020 Mar 17;144(7):799– 805.