Concomitant COVID 19 Infection And NTDS: 68 Patient Case Series

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Abstract

Introduction: Documented articles have determined that viral illness during early pregnancy and several antiviral drugs are associated with an increased risk for neurodevelopmental congenital anomalies of the newborn. These include NTDs, the most common and severe malformations of spinal cord (spina bifida) or brain (anencephaly, encephalocele, hydrocephalus), which develop within 6 weeks of pregnancy with an incidence of one in 1000 neonates worldwide and they cause lifelong neurological complications. The aim of this study is to describe the clinical characteristics of simultaneous cases of COVID 19 in pregnant women with neural tube defects in their newborns.

Patient and methods: This is descriptive study case series including cases of Neural Tube Defects when their mothers were affected with COVID-19 infection that was reported in Zahko Maternity hospital. Those in the labour unit were enrolled in this study and the cases was collected during the period 1st January 2020 and 1st January 2022. The information collected through direct interview with the mothers through questionnaire includes the information about the socio-demographic, obstetrical history and history of COVID 19 infection, severity presence of fever and type of medication received.

Results: Regarding the general and obstetrical history of the patients, the current study revealed that the affected age group of mothers was as follows; 28 (41.2%) of them (26-30 years), and 15 (22.1) of them (> 35). Anemia and fever in the 1st trimester were found in 54 (79.4%) of them. Alcohol intake was reported in 2 (2.9%) of them, consanguinity in 19 (27.9%) of them, female newborns constituted 38 (55.9%), gestational diabetes mellitus in 1 (1.5%), diabetes mellitus in 6 (8.8%), and hypertension in 5 (7.4%). The drugs received during pregnancy, were as follows; antibiotics; all patients 100%; antihypertensive drugs received by 14 (20.6%), antipyretics 29 (42.6%), antacids 21 (30.9%), and antifungals 16 (23.5%).

Conclusions: the COVID19 infection may be blamed as a cause of NTDs, and further research about the pathophysiology is needed.

Keywords: Concomitant COVID 19 & Neural Tube Defects, Case Series of COVID 19 & Neural Tube Defects

Introduction

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), represents a global public health emergency with considerable morbidity and mortality. As of end of July 2022, 567 million people have already been infected globally by SARS-CoV-2 with more than 6.38 million death cases. [1]

It is greatly obvious that SARS-CoV-2 has infected both females and males in almost similar proportions. Epidemiological statistics reveal that comparatively more female have been infected with COVID in their active reproductive age (between 20 years to 49 years) [2].

Members of the coronavirus family are known to be responsible for severe complications during pregnancy, such as miscarriage, fetal growth restriction and congenital anomalies [3]. Only a few studies to date have reported, relatively higher rates of adverse birth outcomes in women affected by SARS-CoV-2 at late pregnancy [3]. Documented articles have determined that viral illness during early pregnancy and several antiviral drugs are associated with an increased risk for neurodevelopmental congenital anomalies of newborn [4]. These include NTDs, the most common and severe malformations of spinal cord (spina bifida) or brain (anencephaly, encephalocele, hydrocephalus), which develop within 6 weeks of pregnancy with an incidence of one in 1000 neonates worldwide and cause lifelong neurological complications [5]. The aim of this study is to describe the clinical characteristics of simultaneous cases of COVID 19 in pregnant women with neural tube defects in their newborns.

Patients and Methods

This study is a case series study of 68 cases of NTDs with COVID-19 infection. The study was conducted in Zakho Maternity hospital of 100 beds including the obstetrics and gynecology department, and daily number of outpatients in the gynecology and obstetrics was 120 patients and about 25-30 deliveries per day in the labour room. The hospital serves the population of Zahko with a 450 thousands population and 250,000 internally displaced persons from the Shinkal and Mousel cities and from Syria. The cases of NTDs where their mothers were affected with COVID-19 infection that were reported in Zahko hospital labour unit were enrolled in this study. The cases' data was collected during the period 1st Jan. 2020 to 1st Jan. 2022. The information was collected through direct interview with the mothers through questionnaires including the information about the sociodemographic, obstetrical history and history of COVID 19 infection, severity, presence of fever, and type of medication received. Verbal consent was taken from every mother enrolled in the study and they were informed about the aim and objectives of the study. Statistical analysis of the data was done using the Social Science Software package (SPSS) version 25. The data is presented using frequency and percentage; median and interquartile range was calculated and presented as the quartile percentile in a line graph.

Results

Table 1 shows the general and obstetrical history of the patients. the current study revealed that the affected age group of mothers was as follows; 28 (41.2%) of them (26-30 years), 15 (22.1) of them (> 35). Anemia and fever in the 1st trimester were found in 54 (79.4%) of them. Alcohol intake was reported in 2 (2.9%) of them, consanguinity in 19 (27.9%) of them. Female newborns constituted 38 (55.9%), with GDM in 1 (1.5%), DM in 6 (8.8%), and Hypertension in 5 (7.4%).

The drugs received during pregnancy, are as follows; Antibiotics, all patients 100%, Antihypertensive drugs were received by 14 (20.6%), Antipyretics 29 (42.6%), Antacid 21 (30.9%), and Antifungal 16 (23.5%), as in Table 2.

The current study revealed that vaccination status of 6 (8.8%), infection in 2nd trimester in 30 (44.1%), infection in 1st trimester 29 (42.6%). It also revealed mild infection occurred in 51 (75%), moderate in 15 (22.1%), and severe in 2 (2.9%) as in Table 3.

The median (interquartile range (IQR)) of hemoglobin level was 10 (9.55-10.65), the median (IQR) of CRP was 19(9.45-81.5). The median (IQR) of D-Dimer was 300 (208.5- 700), the median (IQR) of S. Ferritin was 301(134-416.5), and median (IQR) of blood sugar was 118(99-143.5), as shown in Table 4.

Table 1. The general and obstetrical history of the patients

		Frequency	Percent
Age	<20 years	6	8.8
	21-25	10	14.7
	26-30	28	41.2
	31-35	9	13.2
	> 35	15	22.1
Anemia	Yes	54	79.4
	No	14	20.6
Fever in 1st Trimester	Yes	54	79.4
	No	14	20.6
Alcohol Intake	Yes	2	2.9
	No	66	97.1
Consanguinity	Yes	19	27.9
	No	49	72.1
Gestational Diabetes Mellitus	Yes	1	1.5
	No	67	98.5
Baby Sex	Male	30	44.1
	Female	38	55.9
Diabetes Mellitus	Yes	6	8.8
	No	62	91.2
Hypertension	Yes	5	7.4
	No	63	92.6

Table 2. The Drugs received during pregnancy

		Frequency	Percent
Antihypertensive drug	Yes	14	20.6
	No	54	79.4
Drug for febrile illness	Yes	29	42.6
	No	39	57.4
Antacid	Yes	21	30.9
	No	47	69.1
Antibiotic	Yes	68	100
Antifungal	Yes	16	23.5
	No	52	76.5
	Total	68	100

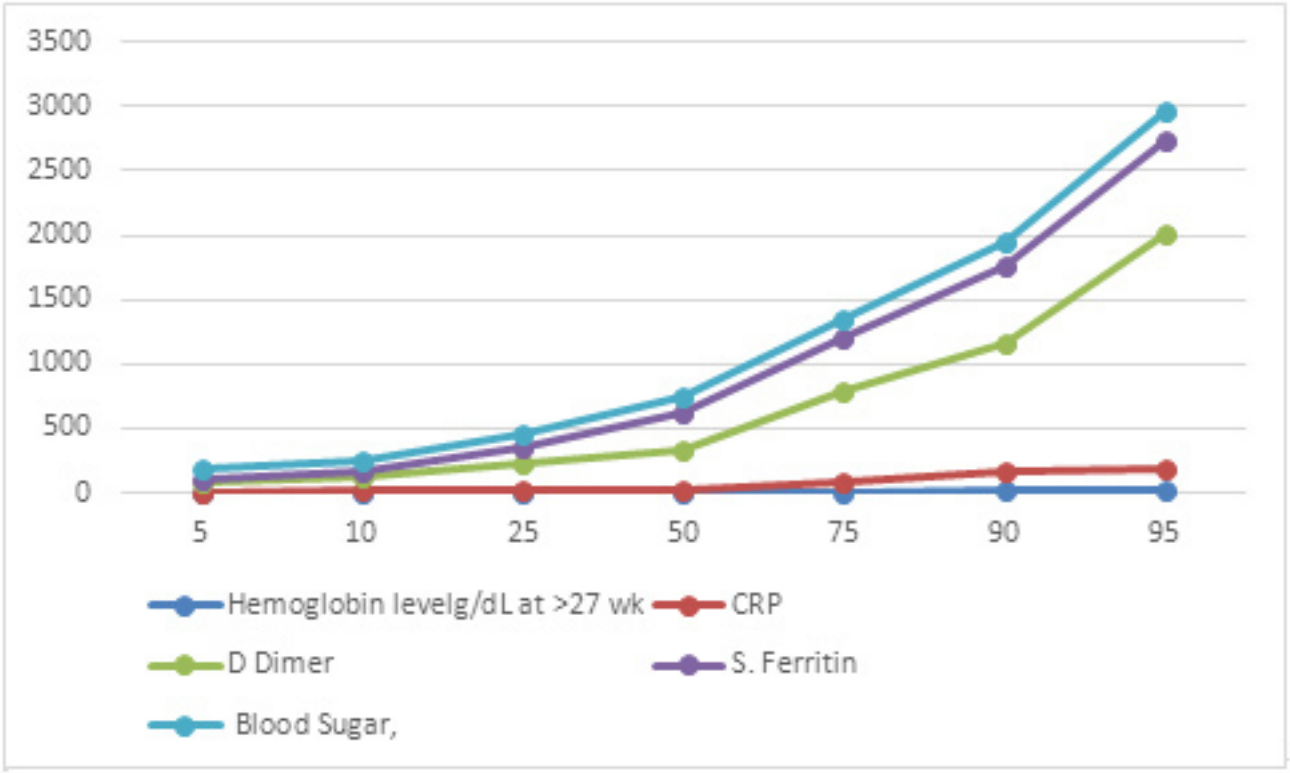
Table 3. The COVID 19 infection characteristics

COVID 19 Characteristics		Frequency	Percent
Vaccination Status	Yes	6	8.8
	No	62	91.2
Trimester of Infection	1st Trimester	29	42.6
	2nd Trimester	30	44.1
	3rd Trimester	9	13.2
Severity of COVID	Mild	51	75
	Moderate	15	22.1
	Severe	2	2.9

Table 4. The biochemical and hematological findings of COVID-19 patients with NTD

	Median (IQR)
Hemoglobin level g/dL at >27 wk	10 (9.55-10.65)
CRP	19 (9.45-81.5)
D Dimer	300 (208.5- 700)
S. Ferritin	301 (134-416.5)
Blood Sugar	118 (99-143.5)

Figure 1. The percentile distribution of biochemical and hematological markers of the COVID-19 affected pregnant women with NTD.



Discussion

The current study revealed that the affected age group of mothers is as follows; 28 (41.2%) of them were 26-30 years, 15 (22.1%) of them were > 35, and there was consanguinity in 19 (27.9%) of them. Kitova in 2013 found that the prenatal ultrasound diagnosis of NTDs with risk factors such as maternal age >35 years, and consanguinity should be targeted in the search for lower-than-normal fetal weight and abnormalities of the excretory tract and the adrenal glands [6]. According to Hamamy H et al, Al-Ani ZR, & Murshid W R, the Middle East Arab countries reveal some of the highest rates of consanguineous marriages in the world with first cousin marriages being more prevalent (25-30%) of all marriages. Among Arabs and other Middle East countries, due to consanguinity there are adverse reproductive outcomes and increase in rates of congenital malformations [7,8]. In the Middle East and Saudi Arabia increased consanguinity resulted in the appearance of spina bifida, anencephaly and hydrocephalous offspring [9].

The current study revealed that the anemia and fever in the 1st trimester were found in 54 (79.4%) of them. Molloy AM et al 2014 directly investigated the impact of iron and with mixed results [10].

The current study found that hypertension was found in 7.4%. This is lower than the study of Mazur L et al in 2011 that revealed that 41.5% patients were hypertensive [11]. Mpembeni R et al found that maternal hypertension and maternal fever during pregnancy were identified as risk factors for NTDs [12].

The current study revealed that DM was found in 8.8%. This is supported by Mary R. Loeken who found that maternal diabetes increases the risk for neural tube, and other, structural defects. The mother may have either type 1 or type 2 diabetes, but the diabetes must be existing at the earliest stages of pregnancy, during which organogenesis occurs [13]. This was also explained by Salbaum JM, 2010, who found that maternal diabetes during pregnancy is a well-known teratogen that increases the risk for birth defects, such as neural tube defects (NTDs) [14]. Schaefer Graf et al., 2000 found that the incidence and severity of diabetic pregnancy induced malformations are

correlated with poor glycemic control [15]. Ray, J.G et al 2007 found that there is a higher associated risk of NTD in the presence of features of maternal obesity and pre-pregnancy diabetes mellitus. In the presence of at least one feature of metabolic syndrome (maternal obesity and pre-pregnancy diabetes mellitus) in pregnancy, the risk of NTD was nearly doubled. In the presence of two or more features, it was six times higher. Inclusion of hsCRP as a metabolic syndrome feature attenuated these risk estimates considerably [16].

As the current study revealed that antipyretics 29 (42.6%), and alcohol intake was reported in 2 (2.9%) of them, the affected age groups of mothers are as follows; 28 (41.2%) of them (26-30 years), 15 (22.1) of them (> 35), and fever found in 79.4% of mothers. This goes with Abay Mulu, et al who found that alcohol consumption, maternal lack of education, maternal hyperthermia and disease, maternal antipyretic use, maternal age <20 and 31-35, were associated with tincreasing the risk of NTDs [17]. The current study revealed that antibiotics were taken by all patients 100%; this indicates habitual and misuse of antibiotics. Ailes EC, et al found that peri-conceptional exposure to some antibiotics might increase the risk for certain birth defects [18].

The current study found that female newborns constituted 55.9%. This is similar to results of Edris Y et al 2020 found that female newborns constituted 53.1% of all the NTDs. Edris Y et al 2020 also found that mothers of more than 35 years constituted 8.8% of the sample which is lower than our study results [19]. The current study found that consanguinity in (27.9%) of the sample which is lower than Nuzhat Nauman et al in 2016 who found that 60 % of couples were consanguineous with a neural tube pregnancy as compared to 45% in controls [20].

The current study found that all 68 newborns of mothers were affected by COVID 19 during pregnancy during the first 2 years of the pandemic. This is supported by Mrudula Phadke, et al who found that COVID-19 disease produced devastating effects on many aspects of women's health. COVID-19 disease has a direct effect by itself, treatment used, and indirect effects on women and offspring. Lockdowns, loss of jobs, decrease in salaries, migration, supply chain disruption, inadequacy and inaccessibility of foods, inadequate distribution of iron folic acid tablets to antenatal women will all possibly influence women [21]. Documented articles have determined that any viral illness during early pregnancy and several antiviral drugs are associated with an increased risk for neurodevelopmental congenital anomalies of new-born [22,23]. Muzumdar D et al reported 26 cases of NTDs during this COVID 19 period [24]. This is supported by a study of Khan MSI, et al. who found that COVID-19 may result in long-lasting congenital anomalies of infants either by infection or by therapeutic maneuver [25]. Blakeway et al, 2022, found no significant difference in rates of adverse pregnancy outcomes in vaccinated and unvaccinated pregnant women were observed [26]. Furthermore, an article done by Ruderman et al. found no association between COVID-19 vaccination during early pregnancy and congenital fetal abnormalities [27]. Published literature determined the developing body of evidence suggesting that COVID-19 vaccination in pregnancy does not alter perinatal outcomes [28–35].

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