

Neural Tube Defects Trend, is COVID19 Responsible for Increased Rates?

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ABSTRACT

Background: many studies reported the association between NTDs and maternal fever, infection like toxoplasma, rubella and cytomegalovirus, this study aimed to give the trend of the NTDs in Zakho and find if it was related to new epidemic of COVID19.

Patient and method: This is study have two lines 1st studying the trend of the prevalence of NTDs depending on the health directorate statistics from Jan. 2013 to December 2021. The 2nd is a case series of 18 case of NTDs with COVID19 infection that reported in Zakho Maternity hospital labour unit.

Results: The prevalence of NTD ranged from 32 during 2013 to 35 during 2017 per 10000 births, with sudden n increase to 53 per 10000 births during 2021. The case series study of 18 patient with NTDs and COVID19 infection done to uncover our doubt about the relation of COVID19 infection and NTDs. The general characteristics of mothers had baby with NTDs show that mean age of mothers was (30.5 ± 7.5) most of them from Zakho 12 (66.7%), followed by Shingar 4(22.2%). Only 2(11.1%) they married their consanguinity. Female sex of the affected baby was the common 10(55.6%), the male: female ratio was 0.8:1. Fever during the 1st trimester reported among 15(83.3%) of the patients, most of the mothers had mild COVID19 infection 14(77.8%), and 4(22.2%) had moderate severity, the antibiotics and vitamin supplement was reported among 13(72.2%).

Conclusions

There were increased prevalence of the NTDs in Iraq during the new epidemic COVID19 period.

Keyword: NTDs, maternal hyperthermia, COVID19 infection

INTRODUCTION

Neural tube defects (NTDs) are a major group of severe congenital anomalies that are associated with substantial mortality, morbidity, and long term disability, as well as emotional, psychological, and economic costs[1] In 2020 about 3129 fetuses with congenital anomaly was reported in Iraq of these Anencephaly and similar malformation 4.48 %, Other congenital malformations of spinal cord 4.48%, Spina bifida 2.79 of the total congenital anomalies[2]

Neural tube defects (NTDs) are serious birth defects, which result from the failure of the neural tube to close in the cranial region, or more caudally along the spine by the 28th day of gestation. Human NTD are relatively common and both complex and heterogeneous in genetic origin[3]

Infants born with anencephaly die within a few hours or days of birth, while those with spina bifida have lifelong disabilities with varying degrees of paralysis, hydrocephalus, requiring ventriculoperitoneal shunting, and neurogenic bladder and rectum with incontinence of urine and stools. Motor weakness in form of paraparesis or paraplegia was present in (84%) babies and sensory deficit was present in 44% babies. Bowel and bladder dysfunction was present in 48% of cases. Ventriculitis was the most common associated morbidity (38%). Meningomyelocele (MMC) repair was the most commonly performed primary surgery (33%) followed by Ventriculoperitoneal (VP) shunt repair (24%).[4] More than half of the patients with spina bifida and encephalocele (51%) are handicapped and cannot move around, while 21% can walk independently. Spina bifida associated damage to the spinal cord produces severe disabilities requiring extensive medical, surgical, and multidisciplinary care [5].

Neural tube defects caused by genetic and environmental factors, other contributing factors like immune dysregulation, diabetes, obesity, folic acid antagonists, dihydrofolate reductase inhibitors, Amniotic bands disrupt neural tube development, and maternal hyperthermia and socioeconomic status [6]. The environmental factors include factors stress, hypervitaminosis A, radiation, infectious disease like Cytomegalovirus, rubella, toxoplasmosis, and toxic wastes from landfills within 3 km, also contributes to some extent[7] Therefore it's important to know if the new epidemic of COVID19 is a risk factor or associated with increased incidence of NTDs. This study aimed to find the trend of the NTDs in Zakho city and present the case series of cases of NTDs with COVID19 infection.

PATIENT AND METHOD

This is study have two lines 1st collecting the data from the Zakho health directorate regarding the incidence of cases with neural

tube defects and total number of births were collected. The 2nd line is a case series of 18 case of NTDs with COVID19 infection. The study conducted in Zakho Maternity hospital of 100 bed including the obstetrics and gynecology department, daily outpatient in the gynecology and obstetrics was 120 patient and about 25-30 delivery per day in the labour room the hospital serves the population of Zakho 450,000 thousands population and 250000 internally displaced person from the Shinkal and Mousel cities and from Syria.

The statistical data of NTDs was collected from the planning department of the Zakho health directorate from Jan. 2013 to December 2021. The total prevalence of NTDs was calculated by dividing the number of cases of NTDs cases by the total number of births during that year, and multiplying by 10,000. The 2nd is a case series study of 18 case of NTDs and their mother were affected with COVID19 infection that reported in Zakho hospital labour unit.

The information collected include the information about the sociodemographic, obstetrical history and history of COVID 19 infection, severity presence of fever, type of medication received.

RESULTS

The prevalence of NTD ranged from 32 during 2013 to 35 during 2017 per 10000 birth, with sudden n increase to 53 per 10000 births during 2021, as shown in figure 1.



Figure 1: The incidence of NTDs in Zakho

The case series study of 18 patient with NTDs and COVID19 infection done to uncover our doubt about the relation of COVID19 infection and NTDs. The general characteristics of mothers had baby with NTDs show that mean age of mothers was (30.5 ± 7.5)

most of them from Zakho 12(66.7%), followed by Shingar 4(22.2%).

Only 2(11.1%) they married their consanguinity and 16(88.9%) their husband is not their relatives. Female sex of them affected baby was the common 10(55.6%), also the male was 8 (44.4%), the male: female ratio was 0.8:1.

Table 1: The general characteristics of the mothers

		Frequency	Percent
Age mean \pm SD		30.5 \pm 7.5	
Residency	zakho	12	66.7
	shingar	4	22.2
	syria	1	5.6
	musel	1	5.6
Husband is Consanguinity	yes	2	11.1
	No	16	88.9
Baby Sex	Male	8	44.4
	Female	10	55.6
Total		18	100

The obstetrical history show that alcohol was taken by 2(11.1%) of the patients, iron and folic acid supplementation received by 17(94.4%), antihypertensive drugs received by 4(22.2%), polyhydramnios 12 (66.7%), other congenital anomalies was reported by 1(5.6%) and was congenital heart anomalies as shown in table 2.

Table 2: The obstetrical history of mothers of the

Obstetrical History	Frequency	Percent
Alcohol Intake	2	11.1
Iron and folic acid supplementation	17	94.4
GDM*	0	0
Antihypertensive Drug	4	22.2
Drug for Febrile Illness	9	50
Oligohydramnios	0	0
Polyhydramnios	12	66.7
other anomalies/ heart disease	1	5.6

GDM: gestational diabetes mellitus

Fever during the 1st trimester reported among 15(83.3%) of the patients, most of the mothers had mild COVID19 infection 14(77.8%), and 4 (22.2%) had moderate severity, the antibiotics and vitamin supplement was reported among 13(72.2%), and only 2(11.1%) of the cases were vaccinated.

Table 3: The characteristics of COVID19 infection among the patients

		Frequency	Percent
Fever in 1st Trimester	yes	15	83.3
	No	3	16.7
Severity of COVID19	mild	14	77.8
	moderate	4	22.2
Treatment Used for COVID19	antibiotic and vitamin	13	72.2
	vitamin	5	27.8
Vaccination Status	yes	2	11.1
	No	16	88.9
Total		18	100

DISCUSSION

The trend of NTDs was increasing from 27 per 10,000 in 2014 to 53 per 10000 birth in 2021 the sudden jump in incidence noticed in 2020. We tried to find in other studies if they noticed the same increase in prevalence unfortunately we didn't found except for a systemic review in Africa that found the pooled prevalence of NTDs from a meta-analysis of 37 publications from the African region in 1990 and 2020.

The prevalence of NTDs was reported as 50.71 (95% CI 48.03, 53.44) per 10,000 births, in the study the researcher noticed heterogeneity in the prevalence and not taken into the account the variability of the prevalence in the last years of new epidemic of COVID19 that may change the incidence of NTDs [8].

A systematic review done in 2016 including 160 full text manuscripts and reports from 75 countries demonstrated that : Africa; 11.70 per 10,000 birth (95% CI 5.20, 75.40); Eastern Mediterranean: 21.90 per 10,000 birth (95% CI 2.10, 124.10) [9]. The reported values in 2016 was lower that reported in our study and in Africa in 2021. I was higher than what reported in Turkey by Çaylan N et al that studied the prevalence from 2014-2019 and found it (27.5 per 10,000 births)[10]. The case series study of 18 patient with NTDs and COVID19 infection done to uncover our doubt about the relation of COVID19 infection and NTDs. The general characteristics of mothers had baby with NTDs show that only 2(11.1%) they married their consanguinity and 16(88.9%) their husband is not their relatives. previous literature found that The prevalence of NTDs is 11.5/1000 total in children born to consanguineous parents, whereas it is 4.3/1000 total births in children of non-consanguineous parents which support the genetic role in disease [11,12]. This finding indicate that among those case series the cause is related to factor other than genetic predisposition. In current study the fever during the 1st trimester reported among 15(83.3%) of the patients, Hassan AM. In Egypt[13] 2021 found that 7.8% of the NTDs cases had infection, and Al-Musawi KM in Iraq[14] found that 60% of congenital anomalies their mothers had infection. Sunitha T et al [15] emphasized that maternal infection with toxoplasmosis represented an important role in having neonate with congenital anomalies .

Likewise, Egyptian studies done by Aly E and Abd-Manaf M in Egypt [16] found that taking drugs during pregnancy, and having infections considered risk factors that increase the incidence of CAs. Similarly, other study implemented in Saudi arabia by Mohammed A, et al [17] demonstrated that maternal disease as DM, the presence of fever due to infections, and medications misuse during pregnancy were maternal risk factors for congenital anomalies. COVID-19 infection during early pregnancy is projected by the United States of America Centers for Disease Control to alter fetal development, likewise other respiratory coronaviruses via the adverse effects of maternal inflammatory response on the fetus and placenta[18] increase in the activities of inflammatory cytokines, most especially IL-6, IL-17, and IFN- γ , in pregnant women with SARS-CoV-2 infection may disrupt fetal brain development, hence increasing the risk of neurodevelopmental disorders in their offspring[19]

CONCLUSIONS

There were increased prevalence of the NTDs in Iraq during the new epidemic COVID19 period, therefore more research is needed for exploring the relation between COVID19 infection and NTDs.

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Conflict of interest: Non

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