Prevalence of Neural Tube Defects (NTDs) In And Around Varanasi Region: Some Observations

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Abstract

Congenital anomalies are one of the primary causes of infant mortality and disability in the world. Neural Tube Defects (NTDs) are the most typical type of birth defect resulting from the failure of Neural tube closure. In this retrospective hospital-based study, the data of the children affected byneural tube defects (NTDs) were analyzed. Prevalence of Hydrocephalous, Myelomeningocele (MMC), Encephalocele, Lipo MMC, Meningocele, Spina Bifida Occulta among children with more or less than one year of age and their occurrence in males and females was studied. The frequency of occurrence of cases of neural tube defects was significantly less among all the congenital disabilities, i.e., 5% of total cases studied. The prevalence of myelomeningocele, hydrocephalous, and Encephalocele was higher than other types of NTDs. This study concludes that the prevalence of hydrocephalous and myelomeningocele in this area raises a concern to have more research of their etiology.

Introduction

Birth defects occur during intrauterine life, leading to structural or functional abnormalities that can be further detected during pregnancy, at birth, or later on at any stage of life. One or more factors may be responsible for them: genetic, infectious,nutritional, or environmental (WHO, 2020). Defects of the central nervous system (CNS) account for a high proportion of all the major birth defects; among them, Neural Tube Defects(NTDs) are majorly responsible for neonatal morbidity and mortality (Yilan, 2006;Smithells, 1976).

NTDs are severe defects of the CNS that result from the failure of closure of the Neural tube, which occurs between 22 to 28 days after conception (Santos et al., 2016). The brain and spinal cord formation start with the development of neural tubes during the embryogenic process of neurulation. It starts with thickeningthe dorsal surface ectoderm of the neural plate that folds up and fuses into the midline to create the neural tube. When the closure is not complete, the neuroepithelium remains exposed to the extra-embryonic environment and consequently subject to degeneration *in utero*,leading to the loss of neurological function at and below the level of that place. The severity and type of NTDs vary with the level of the body axis affected (Greene, 2010).

Classification

It can be done broadly as follows -

1. Defects affecting brain structure, such as anencephaly,encephalocele, and hydrocephalous.
2. Defects affecting spinal cord structure, such as meningocele, myelomeningocele, and other forms of spina bifida.

Anencephaly is a condition of complete or partial absence of the brain; it is also known as exencephaly or craniorachischisis.This defect leads to fetal deaths, stillbirths, or neonatal deaths. In encephalocele, the brain and meninges herniate through a skull defect, especially in the occipital region.Hydrocephalous is characterized by the buildup of cavities deep within the brain that puts pressure and can cause brain damage. Spina bifida is characterized by the failure of fusion of the vertebral arches of the spine (Mikic et al., 2011). Meningocele is a condition in which the protrusion contains abnormal meninges and cerebrospinal fluid. In myelomeningocele, the cystic protrusion contains elements of the spinal cord and nerves (Santos et al., 2016). NTDs were reported to be high among children born to women of lower socioeconomic status (Welderufael et al., 2011).

ETIOLOGY OF NTDs

Neural tube defects (NTDs) are considered to be caused by heterogeneous factors. With many years of etiological assessment, it has been established that the variation in the frequency of spina bifida and anencephaly rely upon several demographic factors, and they are as follows – Habitat, Sex, Ethnic groups, Mother age, Family history, Social status, Congruity that can be partially genetic and partially exogenic (Nasri et al. 2014).

Environmental pollution and occupational hazards are the key contributors to many congenital anomalies and neurotoxicity. They result in many structural and functional alteration which results in different birth defects in the child. Such chemicals and radiations exposure during organogenesis can adversely affect the growing embryo and cause mutagenic effects leading to chromosomal abnormalities and syndromes (Huynh et al., 2021). It has been reported that trihalomethane in water has an interaction with folate related genes that can have more negative effects on women who are not taking folic acid supplements during their pregnancy and are at a high risk of NTDs in the child born to them (Sallman et al. 2020). It has been well established till date that periconceptional and early gestational use of 0.4 mg folic acid can approximately prevent 50% of NTDs. The socio-economic status and its association with Neural tube defects have been reported to be higher in the lower socio-economic class, which is predicted to be caused by vitamin deficiency and imbalanced dietary habits of a mother. Another possible cause for prevalence inthe lower socioeconomic class could be the occupational exposure of parents to different kinds of harmful chemicals and substances (Ladipo-Ajayi et al., 2020).

Exposure of mothers during pregnancy to the organic and inorganic solvents of pesticides can be a vital contributor to the child suffering from NTDs, and those parents who are associated with farm and farming activities are more prone to it. A statistically significant association of spina bifida with xylene and anencephaly with benzene and mercury exposure has been reported. Relatively more attention is to be paid to drinking water contamination concerning NTDs. It includes the mineral constitution, hardness, inorganic and organic constituent, water nitrates and other heavy metals, and chemical disinfection by-products(Dolk and Vrijheid 2003; Server, 1995).

Inorganic impurities of water whose relation with NTDs has been studied include heavy metals (lead, cadmium, arsenic, chromium, barium, mercury, selenium, and silver) and other elements such as nitrates, nitrites, fluoride. Water hardness (total calcium and magnesium) has been reported as a contributor in NTDs in different ecological studies whereas a high level of nitrates has implied anencephaly.

Trihalomethanes (THM), i.e., Chloroform, bromoform and bromodichloromethane, and other chlorination byproduct have been associated with NTDs (Dolk and Vrijheid 2003; Costa et al. 2004).

Alcohol consumption, smoking, infection, and environmental pollution can be some other exogenous causing factors of NTDs. Environmental factors may play an essential role in the etiology of NTDs, which is considered to comprehend all non-genetic etiology, and it mainly includes mothers' age, illness, medications, uniformity, social class, and metabolic disorders (Blatter, 1994).

Generally, differences in sex exist in the ubiquity of NTDs, and more females are born than males with spina bifida (sex ratio 1/0.8), and for anencephaly, it extensively varies (sex ratio 1/0.45 to 1/1). Some studies suggest an association of NTDs with influenza infection, and women under the medications of analgesic and antidepressants are liable to have affected offspring. Maternal epilepsy and the use of antiepileptic drugs such as valproic acid increase the risk of spina bifida. In case of contraceptive use before pregnancy, some study suggests a child born with NTDs in case of women use drugs for ovulation induction (Wasserman et al. 1998; Sever, 1995).

This retrospective study aims to represent and analyzeNTD data-affected children and the prevalence of the types of NTDs in the Varanasi region.

Methodology

The data were taken from the Department of PaediatricsSurgery, Institute of Medical Sciences, Sir Sunderlal Hospital (BHU), Varanasi,from June 2011 to May 2017. Generally, all the cases reported cover eastern Uttar Pradesh; a total of 509 NTDs cases were identified out of 9178 congenital cases. The cases were also classified based on types of NTDs specified in this region, i.e., hydrocephalous, myelomeningocele (MMC), Encephalocele, lipo MMC, meningocele, spina bifida occulta.

The data obtained was represented through piecharts and graphs (Figs. 1 to 15), illustrating the percentage of total neural tube defect cases and their type in the Varanasi region.

Results

In this retrospective study, the frequency of occurrence of neural tube defects cases was much less among all the congenital defects, as shown in Fig.1. The prevalence of myelomeningocele, hydrocephalous, and encephalocele cases was higher than lipomyelomeningocele, spina bifida occulta, and meningocele shown in Fig.2. The sex ratio of occurrence of neural tube defects shows a significant difference among males and females, which is nearly double as shown in Fig.3. This analysis provides evidence that neural tube defects were diagnosed more in children above one year of age; the difference in rate is 4.5 times that of less than one year, as shown in Fig.4. In the individual years, data analysis from the year 2012-2016, the cases of NTDs seem to be declining per year with a 1 percent increase in the year 2013 (Figs. 5-15). Whereas in cases reported per year with different types of NTDs, a specific trend in the number of decrease in cases of NTDs is seen, no trend per year can be seen for any specific type of disorder. However, it can be drawn from the above data that Myelomeningocele (MMC) is the commonest encountered NTDs followed by Hydrocephalous in this region.

From Fig. 7, the prevalence of MMC in 2012 was found to be maximum, followed by hydrocephalous, Encephalocele, and others. The total congenital cased was 93%, whereas NTD was observed only 7% (Fig. 8). In 2015, the NTDs occurrence frequency for MMC and hydrocephalous was found to be the same (Fig. 13). Further, in 2016, MMC was found to be maximum as 26 (Fig. 15). Of the cases reported per year with different types of NTDs, no specific trend can be seen for any specific type of disorder. Nevertheless, it can be drawn from the above data that Myelomeningocele (MMC) is the commonest encountered NTDs followed by Hydrocephalous in this region.

Discussion

This study indicates that hydrocephalous and myelomeningocele are prevalent in this area, raising a concern to have more research of their etiology. The study area covers the region, which has a more rural and semi-urban population than urban with a larger population having lower socio-economic status, which could be a reason for unbalanced dietary intake that may be a cause of these many congenital defects. The result obtained represent more number of males affected by NTDs, which also raises concern to have more research about the presence or absence of a specific essential element and other necessary macro and micronutrients in the dietary habits of the pregnant women, which are leading to have these many neural tube defects (NTDs).

Additional attention must be given to the potential role of environmental and other occupational contributors in the etiology of NTDs in some specific populations. The different exposure and toxicity assessment approachesmust mark the effect on pregnant women and assess the risk of NTDs.Also, the additional concern must be taken for maternal and parental exposure to agricultural chemicals, pesticides, and other harmful solvents.

Concluding Remarks

The frequency of occurrence of neural tube defects cases was much less among all the congenital defects, i.e., 5% of total cases studied. The prevalence of myelomeningocele, hydrocephalous, and Encephalocele was higher than other types of NTDs. The study concludes that the prevalence of hydrocephalous and myelomeningocele in this area raises a concern to have more research of their etiology. The present study further concludes the prevalence of hydrocephalous (35%) and myelomeningocele (44%) in the Varanasi region, and we must widen the role of the environment in the etiology of congenital abnormalities as NTDs.

Declarations

Ethics approval and consent to participate: Not applicable

Consent to publication: Not applicable

Authors' contributions: The main investigator was Devendra Mohan, who designed the manuscript. The technical drafting of the manuscript was done by Praveen Kumar Tiwari and Markandeya, while Vaibhav Pandey, Shashank Shekhar Jha and Surendra Kumar Pandey helped in writing. Data collection was done by Ramkrishna Mishra, Pragati Shakya and Pawan Kumar Mishra. Moreover, Govind Pandey, Kapil Malviya and Sheo Prasad Shukla were advisors of the present research. All the authors have read and approved the manuscript.

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Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests" in this section.

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Figures

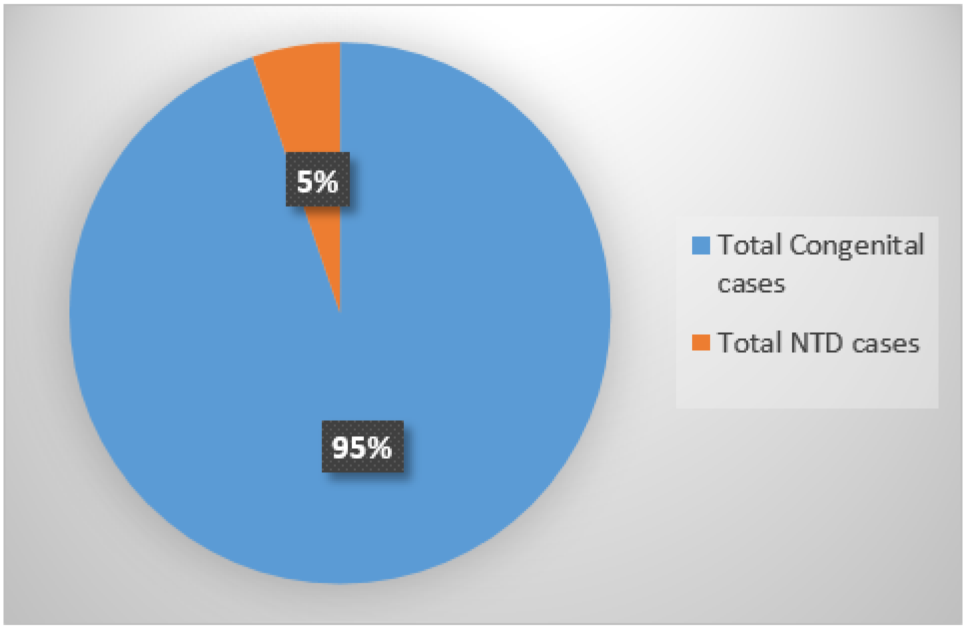

Figure 1

The pie chart depicts the percentage of occurrence of NTDs among all the congenital cases

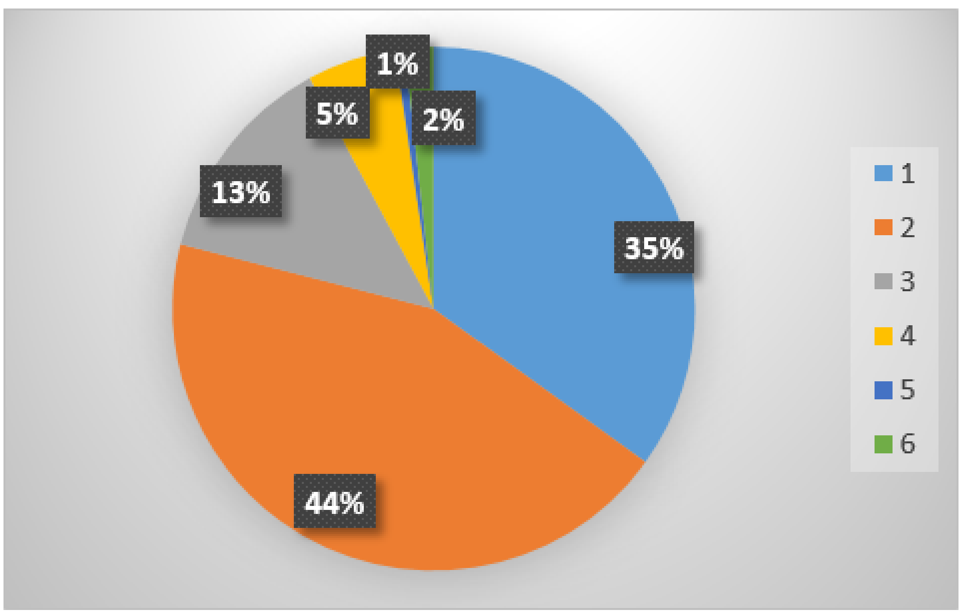

Figure 2

The pie chart depicts the percentage of occurrence ofdifferent NTDs; (1) Hydrocephalous; (2) MMC; (3) Encephalocele; (4) Lipo MMC; (5) Meningocele; (6) Spina Bifida Occulta

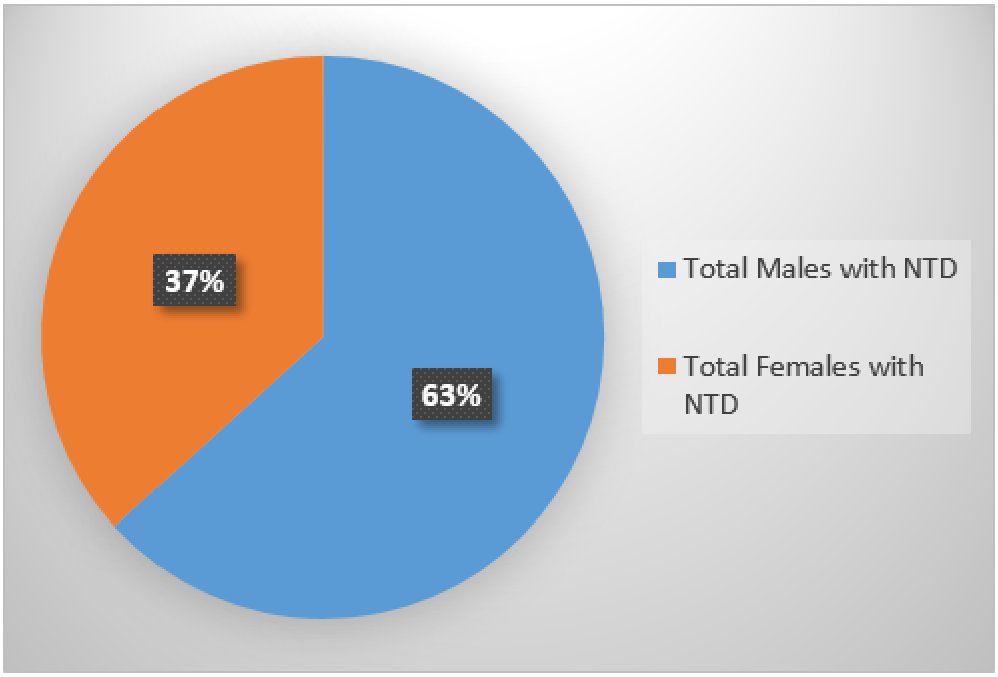

Figure 3

The pie chart depicts the percentage of males and females affected with NTDs

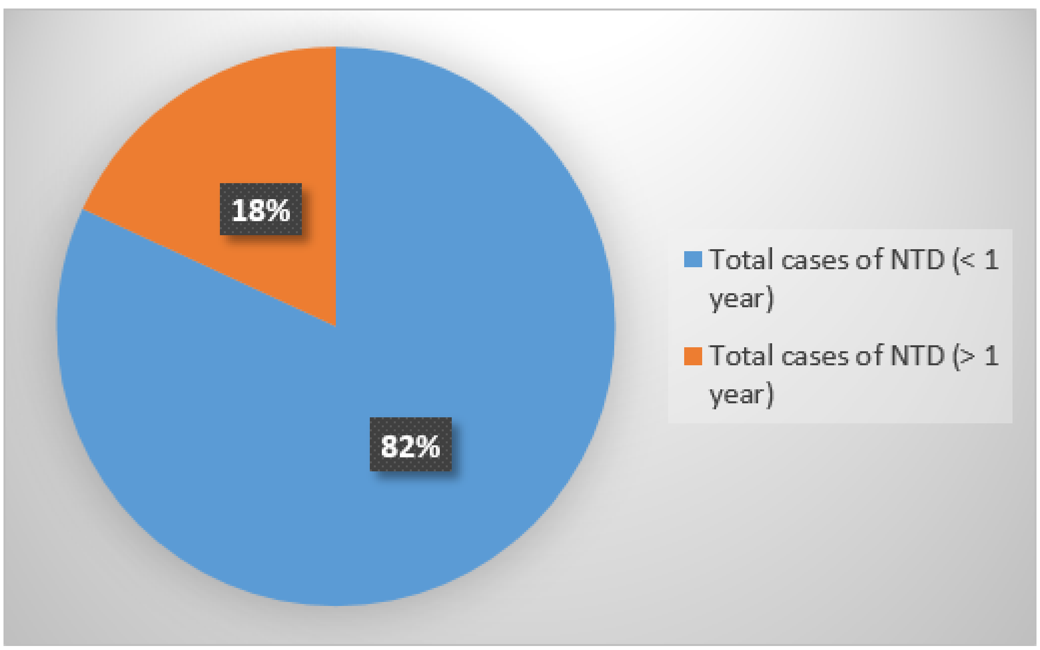

Figure 4

The pie chart represents the age of children affected with NTDs

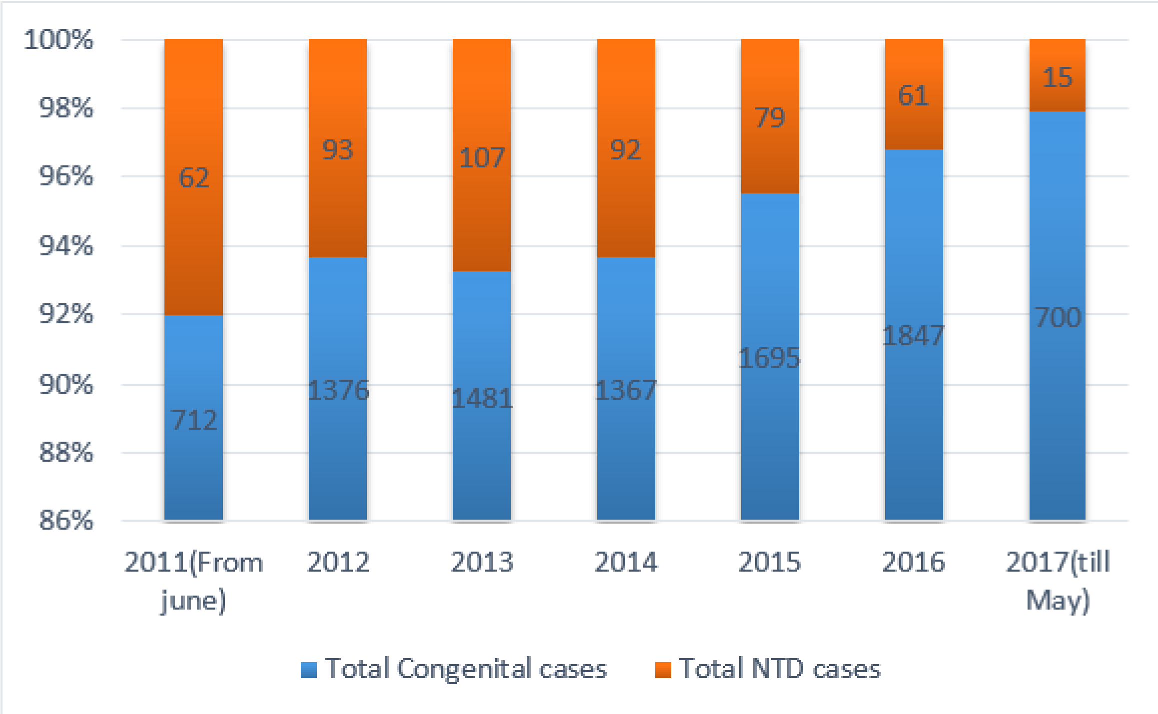

Figure 5

The graph shows the percentage of occurrence of NTDs from 2011 to 2017

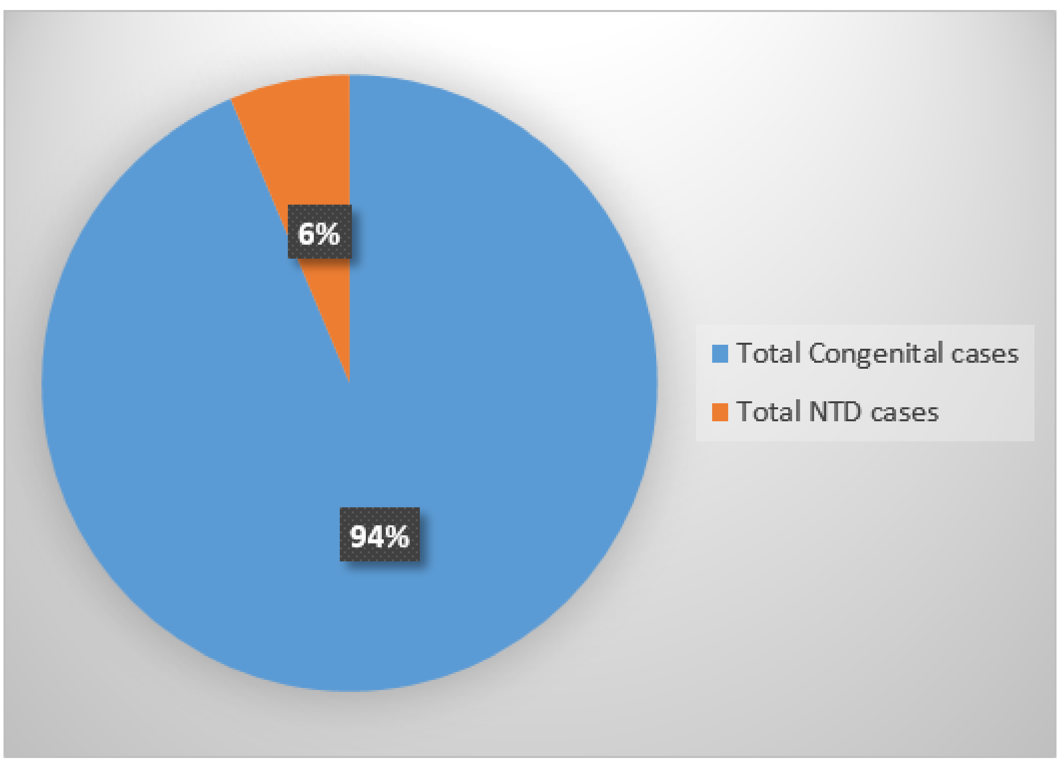

Figure 6

The pie chart depicts the percentage of occurrence of NTDs out of other congenital diseases in the year 2012

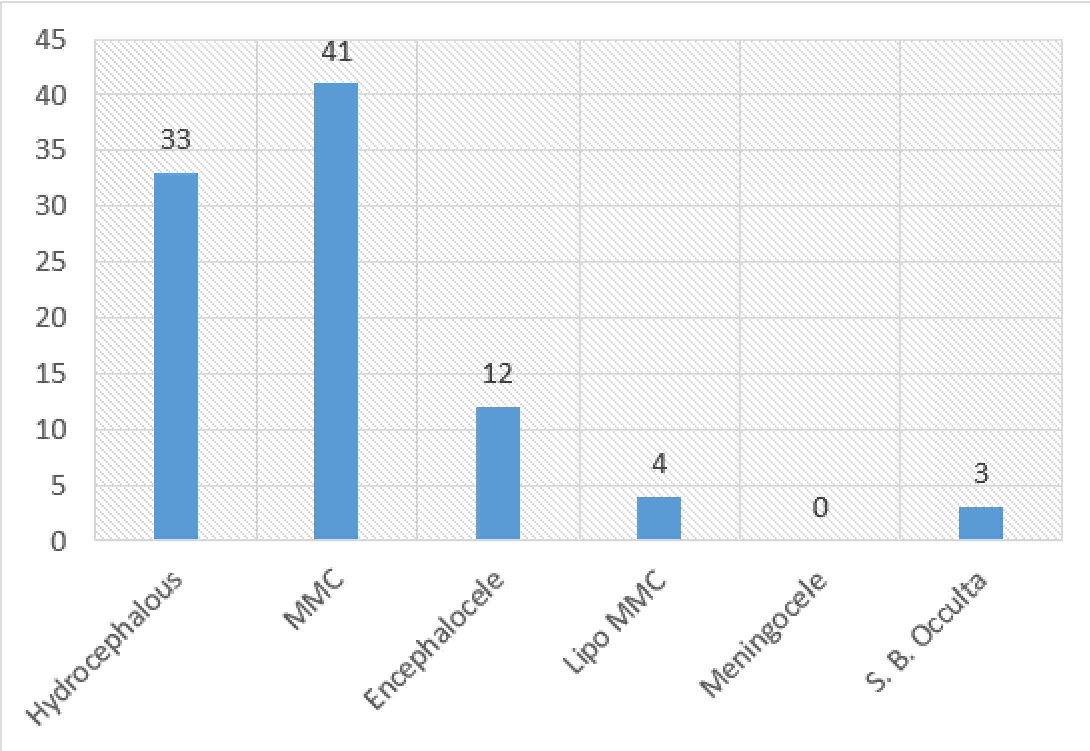

Figure 7

Graphical representation of various NTDs occurrence frequency in the year 2012

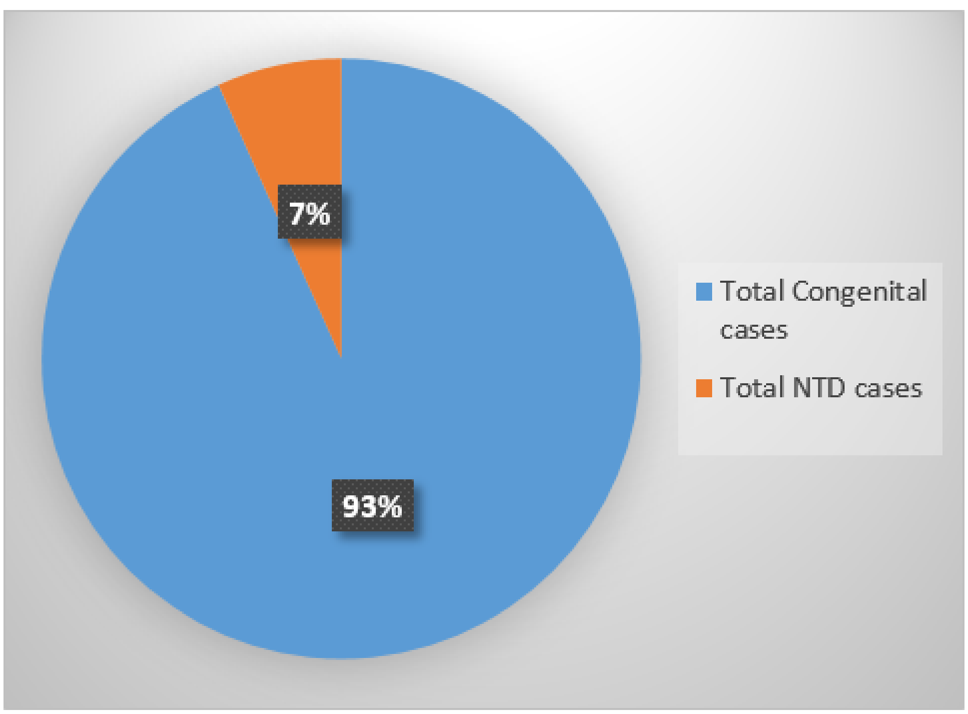

Figure 8

The pie chart depicts the percentage of occurrence of NTDs out of other congenital diseases in the year 2013

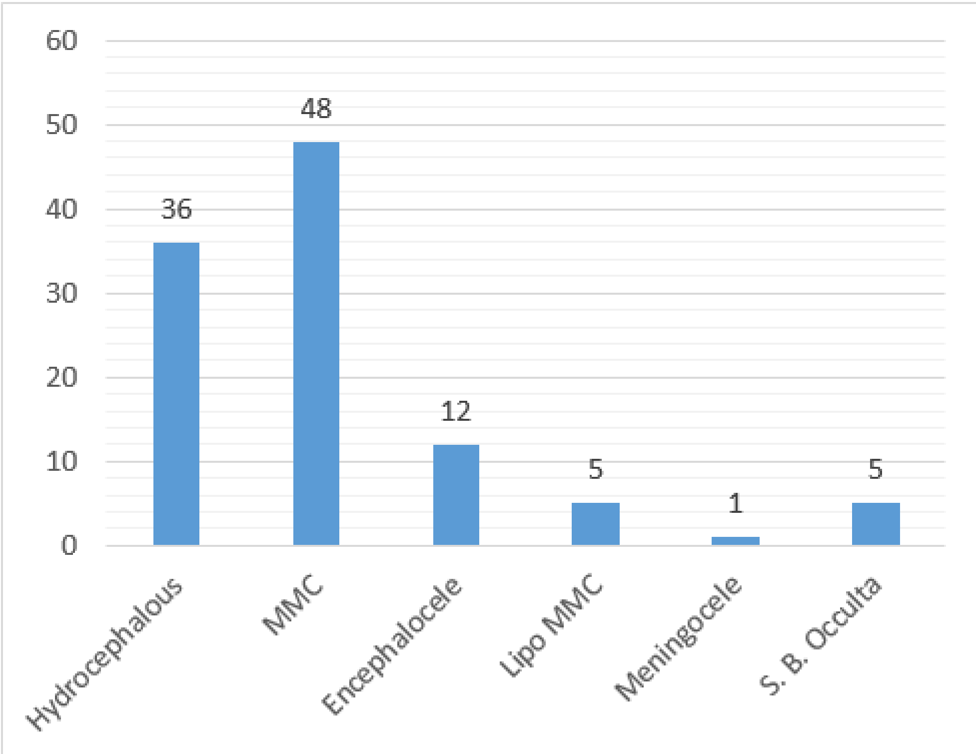

Figure 9

Graphical representation of various NTDs occurrence frequency in the year 2013

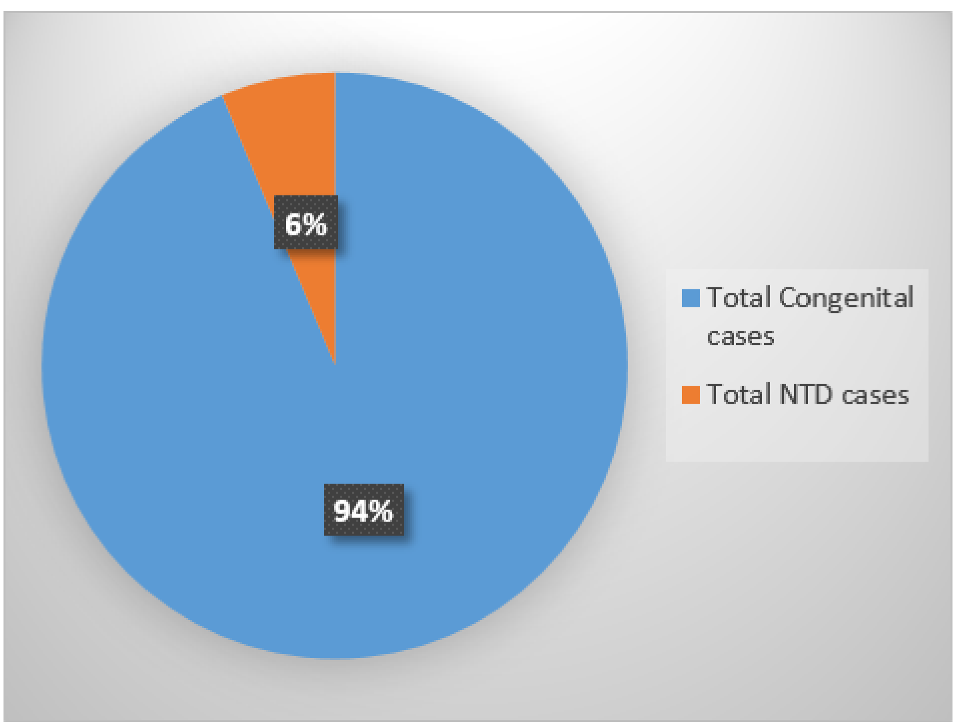

Figure 10

The pie chart depicts the percentage of occurrence of NTDs out of other congenital diseases in the year 2014

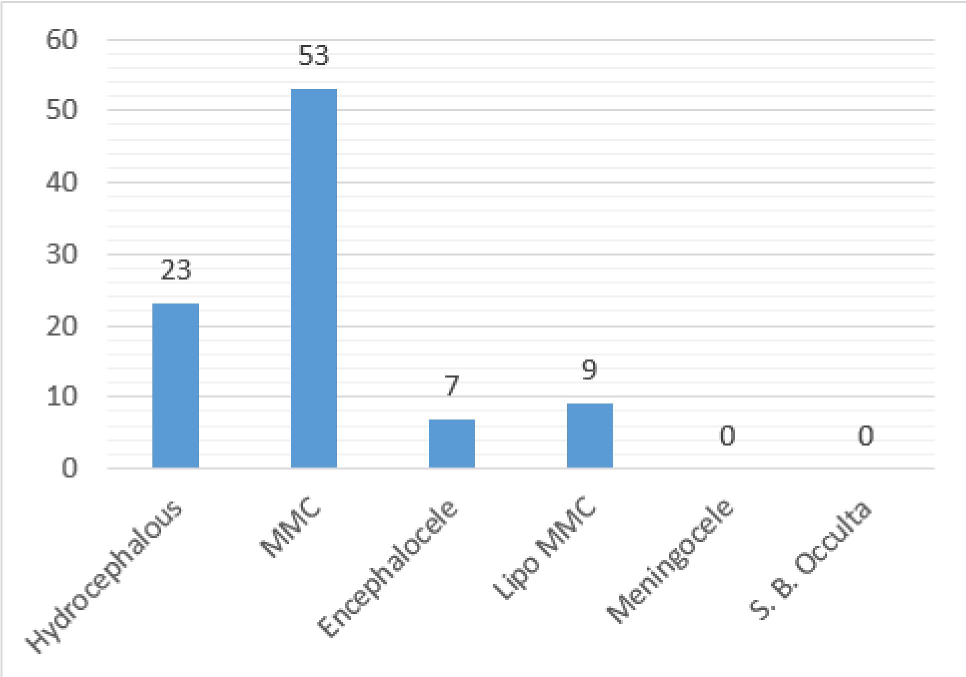

Figure 11

Graphical representation of various NTDs occurrence frequency in the year 2014

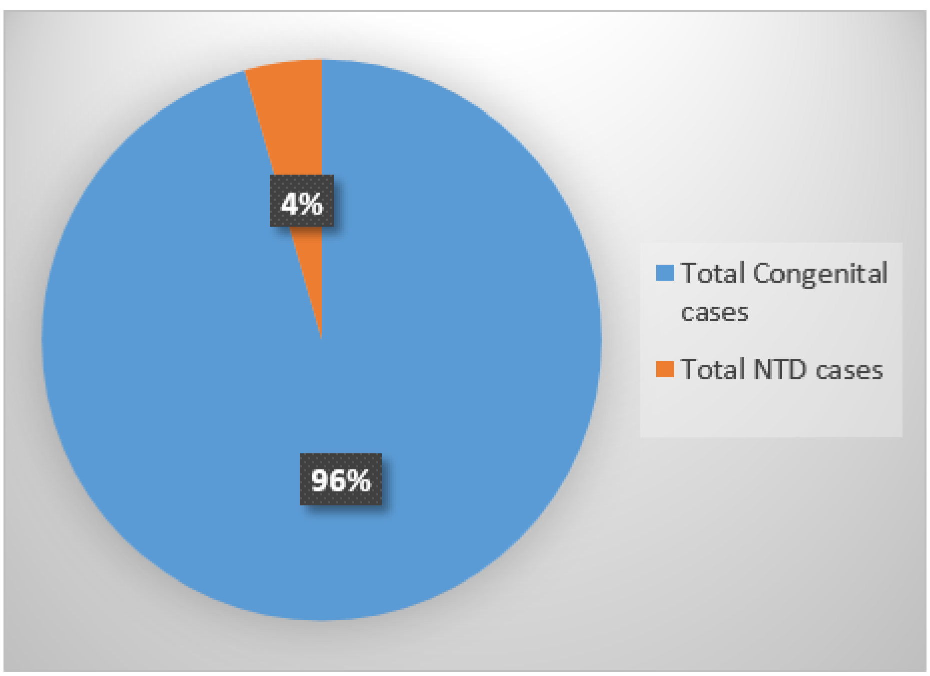

Figure 12

The pie chart depicts the percentage of occurrence of NTDs out of other congenital diseases in the year 2015

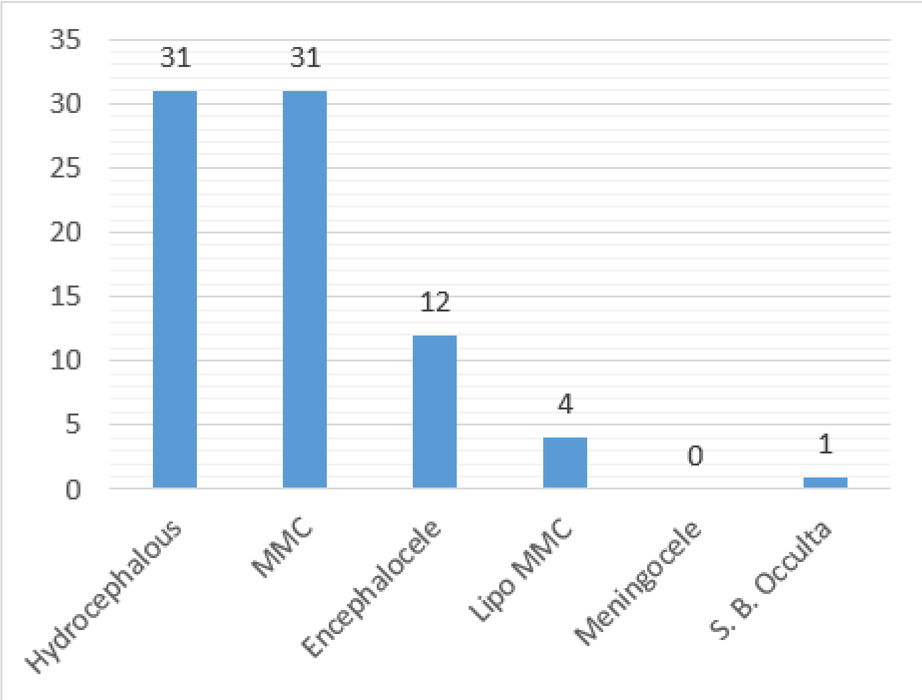

Figure 13

Graphical representation of various NTDs occurrence frequency in the year 2015

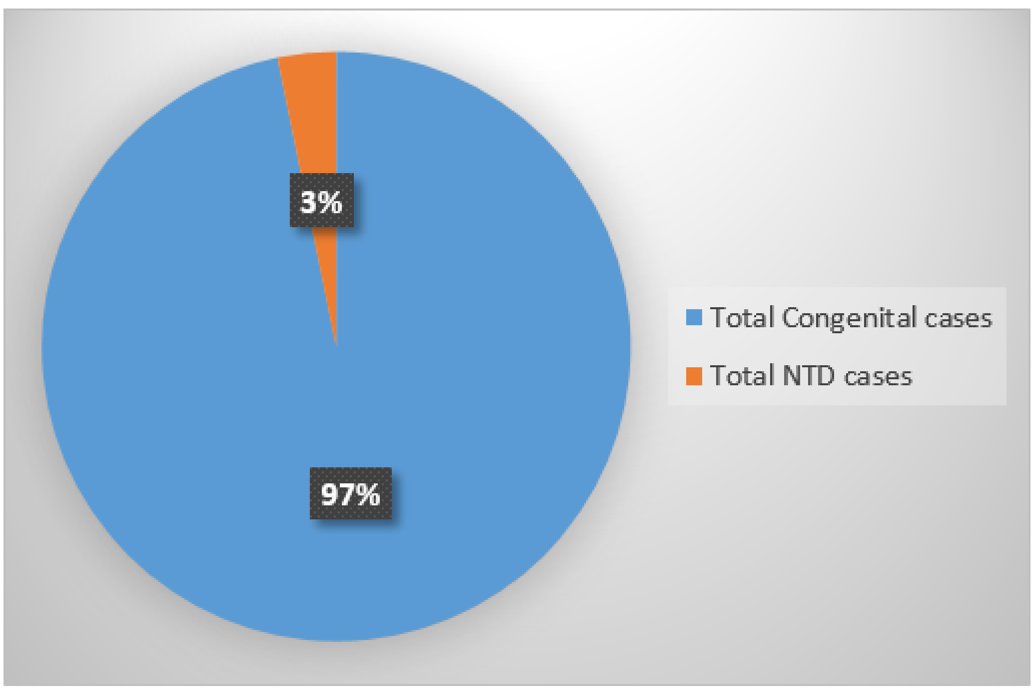

Figure 14

The pie chart depicts the percentage of occurrence of NTDs out of other congenital diseases in the year 2016

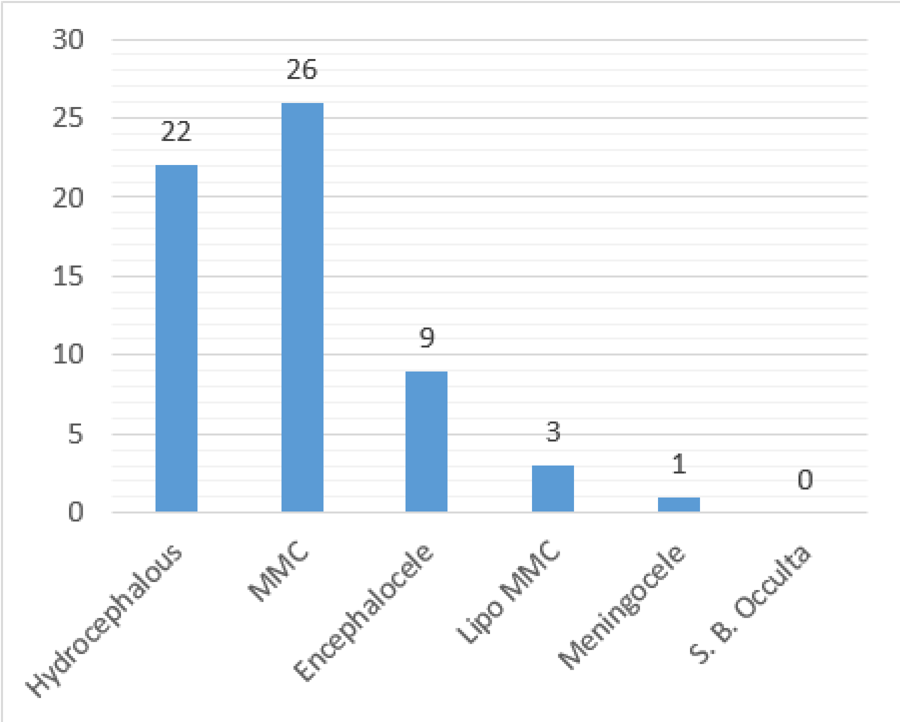

Figure 15

Graphical representation of various NTDs occurrence frequency in the year 2016