ORIGINAL ARTICLE

Neurological and Urological Malformations in Infant of Diabetic Mother at Tertiary Care Hospital; A Single Center Experience

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Abstract

Background: Congenital anomalies mostly affecting the central neurological, urological, circulatory, and skeletal systems occur in the infant of diabetic mothers.

Objective: This study was conducted to evaluate the neurological and urological malformations in the infant of a diabetic mother presenting at the NICU and causality department of NICH Karachi Pakistan.

Methods: It was a cross-sectional study conducted at NICH Karachi, from July 2022 to October 2022. Infants born to diabetic mothers were enrolled in the study and neurological and urological malformations were determined with the help of radiography which was performed by a pediatric radiologist who has had expertise in his field for more than 15 years.

Results: A total of 126 infants of diabetic mothers were included in this study. The age range of infants was 0-28 days. 1.58% of infants had neurological malformation. One infant had spina bifida occulta and other had mylomeningocele. 5% of infants were found to have urological malformations. 4 (3.2%) had a malformation of multicystic dysplastic kidney, 1 (0.8%) had agenesis and 1 (0.8%) had enlarged kidney syndrome.

Conclusion: The present study analyzed a lower frequency of neurological and urological problems among infants of diabetic mothers. However, the frequency is low but it causes a great burden with serious outcomes. Therefore, proper screening is recommended for infants of diabetic mothers to detect these malformations.

Keywords: *Diabetes mellitus, gestational diabetes, pre-gestational diabetes, congenital neurological, urological malformations.*

INTRODUCTION

The most prevalent endocrine illness that causes complications during pregnancy is diabetes mellitus (DM), which affects 3 to 10% of pregnancies on average [1]. Obstetric problems, congenital abnormalities, and neonatal morbidity are all more likely to occur during pregnancy in women with diabetes mellitus. Pregnant women with diabetes are said to have a 2- to 11-fold increased risk of congenital abnormalities compared to pregnant women without diabetes [2]. Although the exact mechanism linking diabetes to congenital abnormalities is not fully understood, hyperglycemia is thought to be a key factor [3].

Congenital anomalies mostly affecting the central neurological, circulatory, and skeletal systems occur in infants of diabetic mothers (IDM) [4, 5]. Neonates of diabetic mothers seem to have several anomalies more frequently than those of non-diabetic mothers [6].

Pregestational diabetes mellitus (PGDM) is more likely to cause malformations than gestational diabetes mellitus (GDM), particularly in patients whose blood sugar levels were abnormally high at the time of conception and in the first few weeks of pregnancy because maternal insulin does not cross the placenta and fetal insulin is not produced until the eighth week of development [5].

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Received: November 20, 2022; Revised: December 22, 2022; Accepted: January 04, 2023
DOI: https://doi.org/10.37184/lnjpc.2707-3521.5.18

Population-based research revealed that, as compared to the general population, infants of diabetic mothers have a fivefold higher prevalence of cardiovascular malformations, as well as a more than twofold higher rate of neural tube defects and urinary tract abnormalities [7-9]. Babies of diabetic mothers have been noticed to have an increased prevalence of several particular abnormalities: transposition of great vessels, holoprosencephaly, double outlet right ventricle and truncus arteriosus, preaxial polydactyly, renal agenesis/dysgenesis, anencephaly, anotia or microtia, and longitudinal limb defects [8].

Studies revealed varying percentages of congenital anomalies. Nasri *et al.* reported 183 malformed babies born to diabetes mothers were found among the 289,365 births, bilateral renal agenesis or dysgenesis (0.06%), and hemivertebrae (4%), along with neural tube diseases (anencephaly 9%, encephalocele 2.6%, meningomyelocele 3.5%, holoprosencephaly 0.9%) and vertebral anomalies (hemivertebra) (4%), were the most significant birth malformations [10]. Tinker *et al.* study reported pregestational diabetes among 0.6% of mothers having healthy infants and 2.5% among mothers with infants having any malformations. Gestational diabetes during the index pregnancy was reported by 4.7% of mothers of healthy infants and 5.3% of mothers of infants with malformations. Pregestational diabetes was associated with strong, statistically significant odds ratios (range, 2.5–80.2) for 46 of 50 birth defects

considered. Sacral agenesis showed the largest odds ratio. For holoprosencephaly, longitudinal limb deficiency, heterotaxy, truncus arteriosus, atrioventricular septal defect, and single ventricle complete greater than 10-fold increased risk was also observed. For gestational diabetes, statistically, significant odds ratios were fewer (12 of 56) and of smaller magnitude (range, 1.3-2.1; 0.5 for gastroschisis) [11].

There are still few studies on the impact of maternal PGDM and GDM on neurological malformations. Limited evidence suggests that the risk of neurological malformations in the IDM may be increased [12, 13]. Research has been done on neurological anomalies in IDM, with the majority of studies to date concentrating on perinatal outcomes and physical development [14, 15]. Due to the dearth of information on congenital defects among Pakistani children of diabetic mothers. To learn more about neuro-urological malformations in children born to diabetes mothers, this study was carried out in a tertiary care hospital, the National Institute of Child Health (NICH).

MATERIALS AND METHODS

Neonates from the emergency and NICU departments of the National Institute of Child Health, Karachi, were included in this descriptive cross-sectional study from July 2022 to October 2022, using a non-probability consecutive sampling technique after taking permission from ethical committee IERB-28/2021.

This cross-sectional study included all neonates between the ages of 0 and 28 days of both sexes who were born to diabetic mothers after taking written consent from parents. PGDM refers to mothers who are known to have DM before conception, and GDM refers to mothers who acquire glucose intolerance while pregnant. IDM was classified as a child born to a mother who had GDM or had previously developed diabetes before this pregnancy. According to American Diabetic Association Guideline reference, GDM was identified [16]. The study excluded neonates with severe hypoxia or neonatal sepsis, as well as those whose mothers had a history of chronic kidney disease, chronic liver disease, heart failure, tuberculosis, autoimmune disease, or drug use other than insulin or hypoglycemic medications for diabetes. Using the WHO sample size calculator, a sample size of 126 was determined, with a confidence level of 95%, absolute precision of 5%, and frequency of 3.5% for meningomyelocele among IDM [11].

Demographic information included age, gestational age at birth, gender, and other relevant details recorded in the pre-designed questionnaire. The type of diabetes mellitus, OGTT/HbA1c results, and medical therapy received were evaluated in the mother's prenatal record. Each neonate to a diabetic mother underwent a thorough examination by a pediatrician, followed by radiography as an ultrasound brain and spine was performed on all neonates included in the study. Any abnormality picked on it was further discussed with the neonatologist and radiologist and then MRI or CT scan was advised accordingly.

The data were analyzed using SPSS version 23.0. The frequency and percentage of qualitative characteristics such as gender, diabetes type, and congenital deformity type were calculated.

RESULTS

A total of 126 infants of diabetic mothers were included in this study. The age range of infants was 0-28 days. Nearly a quarter of the infants were delivered through vaginal delivery (n=34, 27%) whereas the remaining were cesarean section deliveries (n=92, 73%). Around three-fourths of children were born to mothers who had gestational diabetes (n=96, 76%). The majority of the mothers were on non-insulin therapy (n=113, 89.7%). Table **1** displays the socio-demographic and clinical features of recruited infants.

Table 1: Descriptive statistics for sociodemographic and clinical features of infants.

Demographic and Clinical Features	Groups	Frequency	Percentage
Age	0-15 days	118	94
	16-28 days	8	6
Gender	Female	50	40
	Male	76	60
Mode of Delivery	SVD	34	27
	LSCS	92	73
Gestational Age	Pre-Term	14	11
	Full Term	112	89
Birth Weight	Less than 2.5	1	1
	2.5-3.5	29	23
	More than 3.5	96	76
Parity	Primary Gravida	52	41
	Multi Gravida	64	51
	Grand Multi Gravida	10	8

Fig. (1) depicts the frequency of neurological malformation. One infant had spina bifida occulta and

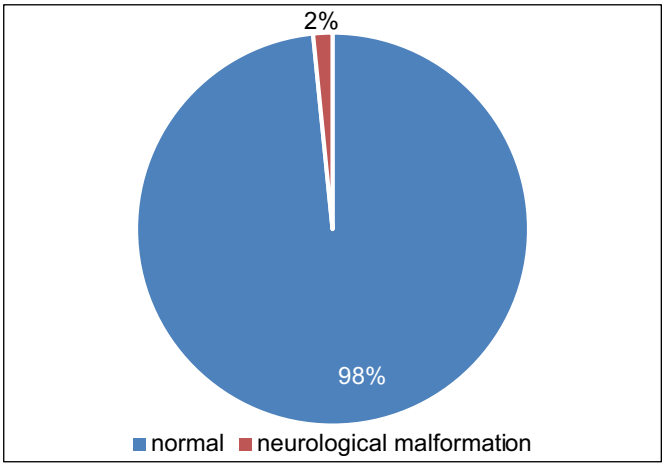

Fig. (1): Frequency of neurological malformation.

other had mylomeningocele. Both of the infants with neurological infants were born to mothers having pre-gestational diabetes.

Fig. (2) displays the frequency of urological malformation. 4 (3.2%) had a malformation of multicystic dysplastic kidney, 1 (0.8%) had agenesis and 1 (0.8%) had nephromegaly. Out of 6 infants with urological malformation, 4 were born to mothers having pre-gestational diabetes and 2 were born to mothers with GDM.

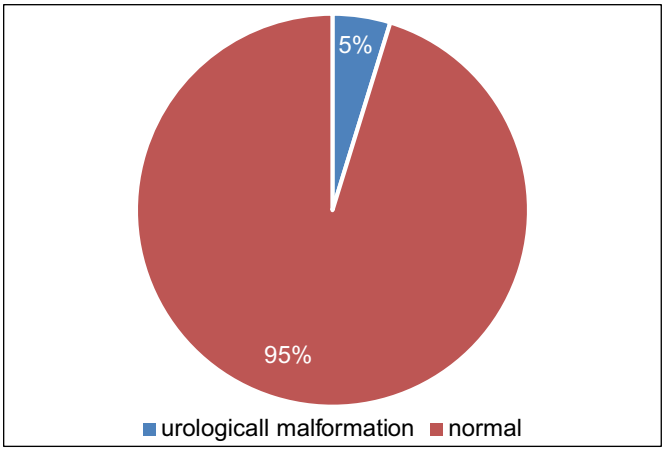

Fig. (2): Frequency of urological malformation.

DISCUSSION

A silent killer that can afflict anyone at any age is diabetes mellitus. Currently, the prevalence of diabetes among women of reproductive age is rising globally [17, 18]. There appears to be a correlation between rising DM prevalence and rising Gestational DM prevalence [19]. Since the nineteenth century, there has been speculation that women with diabetes mellitus may have a higher risk of having children who have congenital defects6. Congenital abnormalities (CAs) can result from a variety of factors, including placental malfunction and hormonal changes, in the offspring of diabetic mothers [17]. Diabetes has teratogenic consequences on a variety of organ systems. Cardiovascular, genitourinary, musculoskeletal, and other deformities have been observed in all research on congenital defects in children of diabetic mothers [6]. Between 5 and 10% of children of diabetic mothers experience significant malformations globally [19]. Over the past 25 years, the incidence of congenital abnormalities has not decreased despite better therapy [6].

Newborn hypoglycemia in IDMs after birth poses a danger for neonatal nervous system injury as well [20]. The present study found a low prevalence (1.58%) of malformation in our sample including neural defects of spina bifida occulta and mylomeningocele. A population-based study from the USA evaluating congenital anomalies among infants of diabetic mothers reported that out of a total of 293498 diabetic mothers' neonates, 0.72% had a congenital anomaly of the central nervous system [21]. Taslima investigated the congenital anomalies among the babies of mothers with uncontrolled diabetes and demonstrated several central nervous system anomalies including hydrocephalus (12.6%), meningocele (7.4%), and anencephaly (10.5%) [20]. The frequency of neurological malformation in this study was quite higher than the neurological malformation seen among infants of healthy mothers (0.8% *versus* 0.98%)

A similar study from Egypt reported that out of 100 studied IDM, 5% had congenital neurological problems including anencephaly (2%), encephalocele (1%), hydrocephalus (1%), and meningocele (1%) [22]. In contrast to our study findings, an Indian study reported none of the IDM had any neurological difficulty [23]. Another similar study from Libya demonstrated that 9.2% of cases had anomalies either sacral agenesis (1.7%) or ultrasound-detected problems (7.5%). The latter included dilated lateral ventricle (5%), hydrocephalus (1.7%), and brain edema (0.8%) [24]. The difference in the incidence of different neurological issues could be attributed due to different management for glycemic control and different approaches to overall pregnancy management among the different populations.

In experimental models, maternal hyperglycemia is linked to decreased glomerular filtration rate, increased blood pressure, microalbuminuria, and fewer nephrons in the offspring [25]. In this study, 5% of the total sample had urological malformation which included malformation of the multicystic dysplastic kidney (3.2%), agenesis (0.8%), and enlarged kidneys (0.8%). Ahmad *et al.* reported that low prevalence of 2% for renal problems and observed only the problem of renal agenesis in their study [22]. Mali and Muliya reported congenital kidney malformation among 1% [23].

The current study shared a single-center experience and analyzed a small sample size. Additionally, the study was a cross-sectional design which allowed researchers to examine how infants would ultimately fare in terms of neurological and urological issues. As a result, it was impossible to infer that the results applied to the entire Pakistani population. Future research examining the pattern of glycemic control during pregnancy and at the time of conception with a bigger sample size may help to further explain the prevalence of congenital malformations.

CONCLUSION

The present study analyzed a lower frequency of neurological and urological problems among infants of diabetic mothers. However, the frequency is low but it causes a great burden with serious outcomes. Therefore, proper screening is recommended for diabetic mothers to detect these malformations.

ETHICS APPROVAL

The study was commenced after taking approval from the hospital ethics committee (IERB-28/2021) and was

conducted according to the guidelines of the Declaration of Helsinki.

CONSENT FOR PUBLICATION

Written informed consent was taken from parents/ guardians before enrolment of their children into the study.

DATA AVAILABILITY STATEMENT

The data set may be acquired from the corresponding author upon a reasonable request.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

AUTHORS' CONTRIBUTION

SBA and MK: study conceptualization, SBA and K: methodology and proposal writing, SBA, MS: data collection, data analysis, and interpretation, SBA and K: Original draft preparation, SBA: writing review and editing. All authors read and approved the final draft of the manuscript for publication.

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