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Recognizable Birth Defects Among Neonatal Admissions at a Tertiary Hospital in South Western Uganda: Prevalence, Patterns and Associated Factors

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Abstract:-

- ***Background.***

Birth Defects (BDs) are among the leading causes of infant mortality and morbidity globally. About 95% deaths from birth defects occur in middle and low income countries. However, there is still less comprehensive data about BDs in low resource settings. The prevalence and patterns of birth defects varies across different geographical regions and this may be reflective of variation in aetiological factors in different geographical regions.

- ***Study Objective.***

We determined the prevalence, patterns and associated factors of birth defects among neonates at admission at Mbarara Regional Referral Hospital(MRRH) in South Western Uganda.

- ***Methods.***

Between June 2023 and July 2023, we conducted a hospital based descriptive, cross sectional study among neonates being admitted to the neonatal unit at MRRH. We consecutively enrolled all neonates at the time of their admission. Parents of the neonates were interviewed using a structured questionnaire to collect social-demographic and clinical information. All the neonates had a structured physical examination for BDs by a paediatrician. Ultrasonography, cardiac echocardiography, X-ray, Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) were also done when indicated. Data from questionnaire was entered into REDCap, and exported to Stata 17 for cleaning and analysis. Clinical characteristics were described using means, frequency and proportions. We summarized the prevalence and patterns of birth defects using frequencies and percentages and performed a univariable and multivariable modified Poisson regression analysis to identify the factors associated with birth defects.

- ***Results.***

We enrolled 412 neonates at admission at MRRH with a mean age of 6.2 days. The prevalence of birth defects was 25% (n=103). The musculoskeletal system was the most affected (24.5%) followed by the Central Nervous System (15.6%). Factors significantly associated with birth defects were: maternal fertility medicine use (aPR = 2.50; 95% CI=1.16-5.38; P=0.005) and both paternal occupational risk exposure (aPR= 1.48; 95% CI=1.04-2.10; P= 0.005) and alcohol intake (aPR=1.47; 95% CI = 1.04-2.09; P=0.005).

- ***Conclusions***

The prevalence of birth defects was high among neonates at admission at MRRH. Maternal fertility medication, paternal occupational risk exposures and alcohol intake were significantly associated with birth defects among the neonates. We recommend clinicians to do routine comprehensive neonatal examinations at admission to identify birth defects.

Keywords:- *Birth Defects, Prevalence, Pattern, Associated Factors, Neonatal Admissions, MRRH Neonatal Unit.*

I. INTRODUCTION

Birth defects are also known as congenital abnormalities, congenital disorders or congenital malformations. World Health Organization (WHO) defines BDs as defects of function, metabolism and structure. Birth defects can exist at, or before birth and may present as single or multiple anomalies[1]. BDs can be categorized into both Major and Minor. Major refers to those that cause serious functional disability, social rejection and stigma (like hydrocephalus), fetal loss or even deaths. The minor, are those with minimal impact on clinical function but may have a cosmetic impact, e.g. pre-auricular pit. The long-term disability caused by BDs may be of significant impact to the child's well-being and development, but also on their families, health care systems and societies [2].

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WHO estimates that globally, over eight million children (6%) are born with serious birth defects annually. However, this figure may be exclusive of terminated pregnancies and still births[1] . Approximately, 270,000 newborns die during the first 28 days of life every year from congenital anomalies[1]. It is estimated that approximately 95% of the children who die from birth defects are from low and middle income countries [4]. Globally, variations in the prevalence of BDs have been reported among different geographical regions as well as time. In high income countries like the United States of America, United Kingdom, and China, BDs have been reported to affect 2-5% of all live births[3–6] . However, in the Middle East, a high prevalence of 7% was reported among consanguineous marriages [2,6,7]. In Africa, the few available studies on BDs have reported an incidence between 1.5% and 3%; Nigeria, Egypt, Kenya (KNH) and Uganda respectively [8–10]. However in Tanzania, Bugando Medical Centre reported a prevalence of 29% [11]. The incidence BDs in many developing countries might be underestimated due to the lack of birth defect registries. There are also additional challenges in diagnostic capabilities, unreliable medical documentation/records and lack of systematic BD follow-up examinations in post-natal period including adolescent clinics.

Generally, congenital anomalies that involve the CNS, cardiovascular and musculoskeletal systems have been reported to be the most common[1,12]. Epidemiological surveys of congenital anomalies in various parts of the world with different environment, socioeconomic status are likely to give out vital information on the prevalence, pattern and risk factors for congenital anomalies in different areas [13]. Although birth defects may be the result of one or more genetic, infectious, nutritional or environmental factors, about 50% of birth defects may not be linked to a specific cause[1]. Identification of causes of BDs is important in designing effective preventive strategies, especially for certain birth defects. However, in about 25% of congenital anomalies, the causes seem to be "multifactorial", indicating a complex interaction between genetic and environmental risk factors [21]. A wide range of environmental risk factors have been associated with the occurrence of congenital anomalies [21]. During pregnancy, exposure to certain drugs like phenytoin thalidomide, alcohol, cigarette smoking, certain environmental chemicals and high doses of radiation have all been implicated in the causation of congenital anomalies[14,15]. The occurrence of BDs has also been associated with advanced maternal and paternal age, parental consanguinity, increasing birth order and low birth weight [4,16]. Younger maternal age is associated with nervous and abdominal wall anomalies[17] . BDs have been also reported with increased frequency among low income earners. Majority (about 95%) of BDs have been reported to occur in middle and low income countries [4.] Maternal education especially to degree level has been reported as protective[18]. Inadequate folate intake both pre and peri-conception has been reported to be associated with neural tube and congenital heart defects[19].Some maternal infections like rubella, Cytomegalovirus, Toxoplasmosis are a significant risk factor for BDs [20]. The prevalence of BDs has been found higher in babies born to mothers with diabetes during pregnancy[21]. Certain occupational exposure or living near, or in, waste sites, smelters or mines may also be a risk factor for BDs [22].

WHO and the Ministry of Health, Uganda recommend that all new born babies should have a detailed new born examination with in the first 48 hours of life. In 2010, the World Health assembly also passed a resolution calling up countries to prevent birth defects where necessary and also do surveillance registry for birth defects. Generally, prenatal diagnosis of BDs remains a challenge in low and middle income countries including focused routine new born assessments and rigorous follow-up systems for BDs [1,2]. The current study was therefore conducted in order to determine the prevalence, pattern and factors associated with BDs among neonates admitted at MRRH. Results of this study may provide vital base line information for further studies and public health measures.

II. METHODS

- *Study Design:*

We conducted a cross sectional hospital based study on 412 neonates admitted at Mbarara Regional Referral Hospital between June 2023 and July 2023.

- *Study Setting*

Mbarara Regional Referral Hospital (MRRH) is a government funded public hospital, situated in Mbarara city in south western Uganda, about 260 kilometers from Kampala, the capital city of Uganda. The hospital has an overall catchment population of over 4.5million people, and a 500-bed capacity. The hospital serves as a teaching hospital for Mbarara University of Science and Technology (MUST) and other tertiary health training institutions in the region. MRRH receives patients from all the districts of Ankole and Kigezi subregions in South Western Uganda, Toro and part of greater Masaka subregions in central Uganda. This hospital also provides services to patients from 2 refugee camps, (Nakivale, Oruchinga), who are from Rwanda, Burundi, Congo, Somalia, Sudan, Ethiopia. MRRH offers more specialized services in the region. The radiology department which offers free ultrasonography, x-rays services but Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) are done at subsidized prices compared to those in private settings. The hospital also offers specialized surgery: paediatric, neuro, orthopaedic, plastic and reconstruction, urology, cardiothoracic plus vascular surgery and general surgery. The hospital also offers oncology, cardiology and renal services.

The Paediatric ward is managed by a team of 10 pediatricians, 30 paediatric residents, 8 intern doctors and 10 nurses. The daily average total number of admissions to the paediatric ward is about 12 and of these, often more than 70% are newborns. The neonatal unit is staffed with 2 pediatricians, and 6 nurses. The nurses work in 8 hour shifts, and on average each shift has only one nurse. The unit has 3 intern doctors, 3 paediatric resident doctors on rotational basis. The neonatal unit functions as a level II unit, however

it also receives neonates that require advanced respiratory and cardiovascular support. The neonatal unit admits close to 3,000 neonates every year (60% of overall paediatric admissions), therefore approximately 250 sick neonates are admitted every month.

Of the neonates admitted to this neonatal unit, approximately two-thirds are born at MRRH and a third are out born. The neonatal unit has a 35-bed occupancy, divided into 4 sections, the high dependency unit (for both term and preterm babies), 2 units for stable preterm and term neonates, as well as a KMC unit, with 4 adult beds. The unit sometimes admits up to thrice its capacity, with neonates sharing infant warmers and cots. The neonatal unit currently has 14 phototherapy machines, 4 radiant warmers, 8 infusion pumps, 5 monitors. There is a supply of medical oxygen with oxygen cylinders, and 14 backup oxygen concentrators. The unit does not have a mechanical ventilator and Continuous Positive Airway Pressure machines (CPAP), but uses bubble CPAP with cold unblended oxygen, that is locally developed for neonates with respiratory distress syndrome. The services offered include provision of intravenous antibiotics (commonly ampicillin and gentamycin), intravenous fluids, phototherapy, nasal gastric tube feeding. Mothers feed their babies on a 2 hourly basis.

Neonates with major birth defects and require immediate surgery are initially stabilized from the neonatal unit in consultation with the paediatric surgical team and transferred to the paediatric surgery unit after their surgery. This paediatric surgical unit is about from 50 meters from the main pediatric ward. Post-surgery children are closely monitored by both the surgical and paediatric team.

➢ *Inclusion Criteria*

We included all neonates who were admitted to the Neonatal ward during the study period.

➢ *Exclusion Criteria*

Neonates who were severely ill and died at admission were excluded from the study.

➢ *Sample Size Estimation*

Using OpenEpi, Version 3, open source calculator—SSPropor , and basing on the prevalence of congenital birth defects as 26% from study conducted in a tertiary referral hospital in Tanzania (Mashuda et al., 2014), our sample size was 412 neonates.

➢ *Sampling Procedure*

Neonates were consecutively enrolled until the desired sample size was met. After a written consent was obtained from the mother by the research nurse, the nurse went on to collect parental data: socio-demographic, clinical information and exposure risk. All neonatal physical exams were done by the study paediatrician on weekly duty.

➢ *Study variables*

- *Exposure Variables:*

✓ *Maternal:*

Socio-demographic (age, marital status, level of education, occupation, pregnancy characteristics (number of antenatal care visits, illness during pregnancy, use of folic, parity) birth defects risk exposures (medications, radiation, alcohol and other illicit drugs) and family history of birth defects.

✓ *Paternal:*

Socio-demographics (age, level of education, occupation) birth defects risk exposures (medications, radiation, alcohol and other illicit drugs) and family history of birth defects.

- *Outcome Variables: Birth Defects*

➢ *Study Procedure*

All neonates at admission had a detailed structured physical examination (general and systemic head to toe) performed by the study paediatrician . During the study period, the research team had a paediatrician on duty on weekly basis who carried out the clinical assessments for birth defects. After a detailed physical examination, the paediatrician filled the findings into the questionnaire. The study team, composed of four paediatricians and 2 study nurses reviewed all study infants every morning to agree on physical findings of each neonate. Ultrasonography, X-ray imaging, cardiac echocardiography, CT and MRI were performed when required. For both CT and MRI, a fee waiver was sought from hospital but ultrasonography and x-rays were done free of cost at the study site. All radiological investigations had a report by the reviewing radiologist. Echocardiography was done by a paediatric cardiologist who was part of the study team. All neonates with significant phenotypic abnormality underwent a screening echocardiography. Our facility was unable to do Genetic studies, metabolic screening for Inborn errors of metabolism and viral serology for Rubella, Cytomegalo Virus (CMV), Herpes simplex.

The International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) Version for congenital malformations, deformations and chromosomal abnormalities was used to describe the patterns of birth defects. [34]. Neonates with multiple congenital anomalies were grouped depending on whether those anomalies qualified as a specific syndrome or not. Children with multiple birth defects that qualified as a specific syndrome were categorized into that syndrome. When no specific syndrome could be classified by those anomalies, all the organ systems involved were individually classified into the ICD-10 for congenital malformations.

➢ *Data Management and Statistical Analysis*

Data was entered in REDCap ™ database and exported to STATA version 17 statistical software for cleaning and statistical analysis. Descriptive statistics of the variables were presented using means and standard deviations for continuous variables and percentages for categorical variables. The prevalence of birth defects was reported as a percentage. The patterns of birth defects were summarized as frequencies and percentages. Univariable and multivariable modified Poisson regression analysis were used to assess the factors associated with birth defects among the children at admission. Factors with a $p < 0.1$ on univariable analysis were subjected to modified Poisson regression analysis. Crude (unadjusted) and adjusted prevalence ratios were calculated to quantify the strength of association between the factors and birth defects. The 95% confidence intervals were determined and the factors with a p-value of less than 0.05 were considered to have a significant association with birth defects.

➢ *Quality Control*

All the neonatal examinations were done by a Paediatrician using a structured questionnaire. The study team, composed of four paediatricians and 2 study nurses reviewed these neonates on a daily basis and made a consensus decision about the birth defects. A reference atlas, Smith's Pattern of Recognizable Human Malformations was also used. All anthropometric measurements were done following standard operating procedures using calibrated hospital equipment.

➢ *Ethical Approval*

Ethical approval was obtained from the MUST Ethics Review Board (MUST -2023-855) and both administrative and site clearance by the MRRH administration and the Department of Paediatrics and Child Health respectively.

III. RESULTS

➢ *Neonatal Characteristics*

Between June and July 2023, 412 neonates were enrolled. Of these, 51.9% were males, 47.8% females and 1 child (0.3%) had undetermined sex due to ambiguous genitalia. Their mean age was 6.2 days. About a third, were born preterm and only 3 (0.73%) were post term. Regarding their weights,180 (43.7%) were < 2.5 Kg, 230 (55.8%) were between 2.5 to 4 kg and 2 (0.5%) above 4 Kg. The mean weight of the neonates was 2.68kg. Majority (89.1%) were in the birth order of 1-4. Twenty-five (6.1%) neonates had a family history of BDs reported among other siblings. Only 5 (1.2 %) children had their BD detected by ultrasonography during the antenatal period. Of the 412 neonates enrolled, 103 had one or more BDs identified. Of the 103 neonates with BDS, 51 (49.5%) were males and 52 (50.5%) were females. Frequency of BDs was more with babies born via SVD as compared to CS 77(74.8%) vs 26 (25.2%).

Table 1 Neonatal Characteristics

Characteristic		**Birth defect**		**P-Value**
	Total (N=412)	**Yes (n=103)**	**No (n=309)**	
	n (%)	**n (%)**	**n (%)**	
Sex				0.465
Male	214 (51.9%)	50(48.5%)	164(53.1%)	
Female	197 (47.8%)	52 (50.5%)	145 (46.9%)	
Ambiguous genitalia	1 (0.3%)	1 (1.0%)	0	
Gestational age				0.234
Term	129 (31.3%)	28 (27.2%)	101 (32.7%)	
Preterm	283 (68.7%)	75 (72.8%)	208 (67.3%)	
Birth weight				0.670
<2.5 kg	180 (43.75)	40 (38.8%)	140 (45.3%)	
2.4-< 4.0kg	230 (55.8%)	63 (61.2%)	169 (54.7%)	
>4kg	2 (0.5%)	0	0	
Mode of delivery				0.936
SVD	345(83.7%)	77 (74.8%)	268 (86.7%)	
C-section	67(16.3%)	26 (25.2%).	41 (13.3%)	
History of birth defects among other siblings				0.291
Yes	25 (6.1%)	5 (4.9%)	20 (6.5%)	
No	387 (93.9%)	98 (95.1%)	289 (93.5%)	
BD detected by ANC ultrasonography				0.123
Yes	5 (1.2%)	5(4.9%)	0	
No	407 (98.8%)	98 (95.1%)	309	

➢ *Maternal Characteristics*

Maternal sociodemographic characteristics showed that majority (75.7%) of mothers were aged between 20 and 35 years, with 9.7% below 20 years and 14.8% above 35 years. All were of African race and 86.9 % were Christians. Fifty (9.7%) had education above tertiary level while 7.5% had not attained any formal education. Only10.7% of the mothers were not staying with the husbands. No history of consanguinity was reported. The majority (85.4%) of mothers had informal employment and two thirds (65.5%) were living way below the poverty line on less than 1.9 USD per day. Nearly all mothers (99.5%) attended antenatal

care(ANC) but only 69.7% had at least 4 or more ANC visits. Most mothers reported to have taken folic acid tablets during pregnancy although majority (76.7%) took it after the first trimester and only 6 (1.5%) mothers started it pre-conception.

Table 2 Maternal Characteristics

Characteristic			Birth defect		P- Value
		Total (N=412)	Yes (n=103)	No (n=309)	
		n (%)	n (%)	n (%)	
Maternal age (years)					0.950
	<20	39 (9.5%)	9 (8.7%)	30 (9.7%)	
	20-34	311 (75.7%)	79 (76.7%)	232 (75.3%)	
	≥35	61 (14.8%)	15 (14.6%)	46 (14.9%)	
Level of education					0.430
	Below Primary level	240 (58.3%)	54 (52.4%)	186 (60.2%)	
	Secondary Level	122 (29.6%)	35 (34.0%)	87 (28.2%)	
	Tertiary Level	50 (12.1%)	14 (13.6%)	36 (11.6%)	
Parity					0.260
	I-1V	367 (89.1%)	95 (92.2%)	272 (88%)	
	≥V	45 (10.9%)	8 (7.8%)	37 (12.0%)	
Prior abortion					0.950
	No	309 (75.0%)	77 (74.8%)	232 (75.1%)	
	Yes	103 (25.0%)	26 (25.2%)	77 (24.9%)	
Birth defect among other children					0.910
	No	387 (93.9%)	97 (94.2%)	290 (93.9%)	
	Yes	25 (6.1%)	6 (5.8%)	19 (6.1%)	
Preconception folate use					0.018*
	No	406 (98.5%)	99 (96.1%)	307 (99.4%)	
	Yes	6 (1.5%)	4 (3.9%)	2 (0.6%)	
Family planning use pre- pregnancy					0.170
	No	269 (65.3%)	73 (70.9%)	196 (63.4%)	
	Yes	143 (34.7%)	30 (29.1%)	113 (36.6%)	
Fertility medicines use					0.069
	No	407 (98.8%)	100 (97.1%)	307 (99.4%)	
	Yes	5 (1.2%)	3 (2.9%)	2 (0.6%)	
Number of ANC visits					0.760
	<4	125 (30.3%)	30 (29.1%)	95 (30.7%)	
	≥4	287 (69.7%)	73 (70.9%)	214 (69.3%)	
Maternal chronic disease					0.580
	No	351 (85.2%)	86 (83.5%)	265 (85.8%)	
	Yes	61 (14.8%)	17 (16.5%)	44 (14.2%)	

- *Maternal Risk Exposures and BDs*

A third of the mothers had occupational teratogenic exposure which mainly included chemicals used in farming like herbicides and pesticides. Radiation exposure was minimal (2.2%) with mostly x-ray radiations. Only 9.7% of the mothers used illicit drugs just before or during pregnancy e.g. alcohol, tobacco.

Table 3 Maternal Risk Exposures and BDs

Characteristic			Birth defect		P- Value
		Total (N=412)	Yes (n=103)	No (n=309)	
		n (%)	n (%)	n (%)	
Maternal occupational exposure					0.310
	No	269 (65.3%)	63 (61.2%)	206 (66.7%)	
	Yes	143 (34.7%)	40 (38.8%)	103 (33.3%)	
Radiation Exposure					0.850
	No	403 (97.8%)	101 (98.1%)	302 (97.7%)	
	Yes	9 (2.2%)	2 (1.9%)	7 (2.3%)	
Illicit drug use					0.120
	No	372 (90.3%)	89 (86.4%)	283 (91.6%)	

Characteristic			Birth defect		P- Value
	Yes	40 (9.7%)	14 (13.6%)	26 (8.4%)	
Chronic medication exposure					0.490
	No	360 (87.4%)	88 (85.4%)	272 (88.0%)	
	Yes	52 (12.6%)	15 (14.6%)	37 (12.0%)	
*$p < 0.05$					

➢ *Paternal Characteristics*

The average paternal age was 32 years with a majority (96.8%) below 50 years. Most fathers had informal employment. Very few fathers (2.2%) were reported to have dysmorphic features and only 12% of the fathers reported positive family history of birth defects. More than a third of the fathers reported alcohol use and nearly a third had occupational teratogenic exposure to one or more: herbicides, pesticides, paints, industrial pollutants, petroleum and by-products.

Table 4 Paternal Characteristics

Characteristic			Birth defects		P-Value
		Total (N=412)	Yes (n=103)	No (n=309)	
		n (%)	n (%)	n (%)	
Paternal age (years)		32.40 ±8.17	32.05 ±8.45	32.52±8.08	0.620
Paternal age (years)					0.630
	<50	399 (96.8%)	99 (96.1%)	300 (97.1%)	
	≥50	13 (3.2%)	4 (3.9%)	9 (2.9%)	
Paternal occupation					0.860
	Formal	74 (18.0%)	18 (17.5%)	56 (18.2%)	
	Informal	336 (82.0%)	85 (82.5%)	251 (81.8%)	
Paternal dysmorphic features					0.560
	No	403 (97.8%)	100 (97.1%)	303 (98.1%)	
	Yes	9 (2.2%)	3 (2.9%)	6 (1.9%)	
Paternal alcohol use					0.053
	No	257 (62.4%)	56 (54.4%)	201 (65.0%)	
	Yes	155 (37.6%)	47 (45.6%)	108 (35.0%)	
Paternal smoking					0.780
	No	394 (95.6%)	99 (96.1%)	295 (95.5%)	
	Yes	18 (4.4%)	4 (3.9%)	14 (4.5%)	
Paternal radiation exposure					0.420
	No	365 (88.6%)	89 (86.4%)	276 (89.3%)	
	Yes	47 (11.4%)	14 (13.6%)	33 (10.7%)	
Paternal occupational exposure					0.120
	No	293 (71.1%)	67 (65.0%)	226 (73.1%)	
	Yes	119 (28.9%)	36 (35.0%)	83 (26.9%)	
Paternal chronic medication use					0.490
	No	375 (91.0%)	92 (89.3%)	283 (91.6%)	
	Yes	37 (9.0%)	11 (10.7%)	26 (8.4%)	
Paternal history of birth defects					0.790
	No	363 (88.1%)	90 (87.4%)	273 (88.3%)	
	Yes	49 (11.9%)	13 (12.6%)	36 (11.7%)	
*$p < 0.05$					

➢ *Prevalence of Birth Defects Among Neonates Admitted at MRRH*

During the study period (June, 2013 to July 2013), a total of 412 neonates were enrolled in the study. Of these, 103 were diagnosed with one or more BDs, representing an overall prevalence of 25.0% (95% CI 0.21-29.4).

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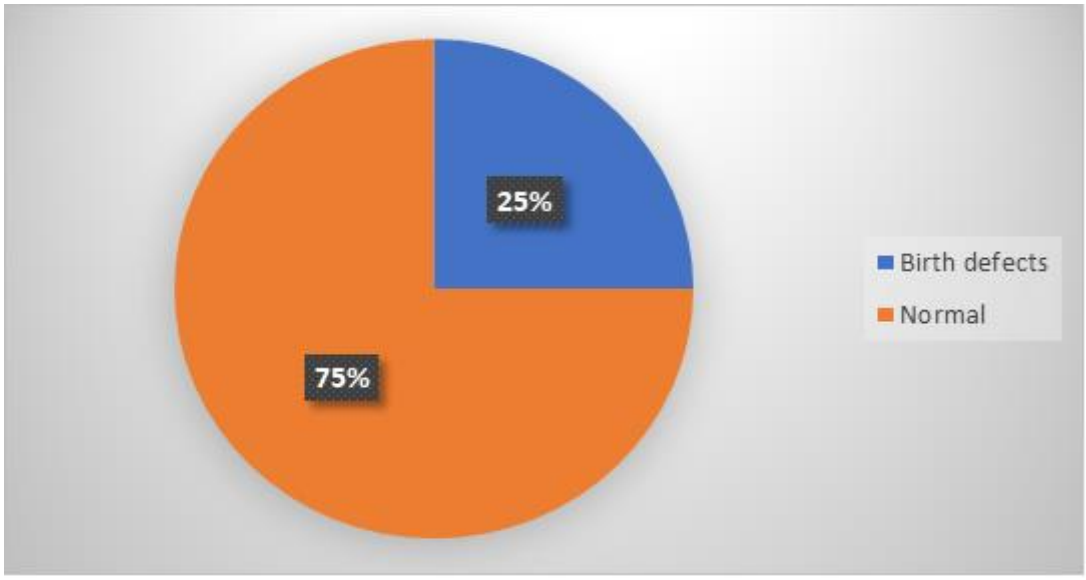

Fig 1 Prevalence of Birth Defects Among Neonates Admitted at MRRH (n=412)

➢ *Distribution of BDs Among the Neonates*

Out of 412 neonates enrolled, 103 had BDs. Of the 103 neonates, 65 (63.1%) had single defects while 38 (36.9%) had multiple. This brought the total number of birth defects to be 147. Of these, 75 (51.02%) were major and 74 (49.08%) minor. The commonest types of birth defects identified were in the musculoskeletal 24.5%, CNS 15.6 %, Cardiovascular (CVS) 11.6 % and Genital 10.9%.

Table 5 Distribution of Birth Defects according to ICD-10 (WHO Version 2017) n=103

ICD code	Birth defect	Number	Percentage
Q00-Q007	**Congenital malformations of the nervous system**		
	Spina Bifida meningocele	8	
	Hydrocephalus	8	
	Meningoencephalocele	4	
	Anencephaly	1	
	Hydranencephaly	1	
	Encephalocele	1	
		23	**15.6%**
Q10-Q18	**Congenital malformations of the eye, ear, face and neck**		
	Cystic hygroma	1	
	Microtia	1	
	Microphthalmos	1	
	Congenital cataract	2	
	Ear pit	6	
		11	**7.5%**
Q20-Q28	**Congenital malformations of the circulatory system**		
	Ventricular Septal Defect	8	
	Atrial Septal Defect	4	
	Patent Ductus Arteriosus	2	
	Coarctation of Aorta	1	
	Truncus arteriosus	1	
	Patent Foramen Ovale	1	
		17	**11.6%**
Q30-Q34	**Congenital malformations of the respiratory system**		
	Laryngotracheomalacia	4	
	Congenital lobar emphysema	1	
	Choanal atresia	1	
		6	**4.1%**
Q35-Q37	**Cleft lip and cleft palate**		
	Cleft lip and palate	4	
	Cleft palate	3	

		7	**4.7%**
Q38-Q45	**Congenital malformations of the digestive system**		
	Ankyloglossia (tongue tie)	7	
	Imperforate anus	1	
	Oesophageal atresia	1	
	Bifid tongue	1	
	Hirschsprung	1	
	Duodenal atresia	1	
	Biliary atresia	1	
	High arched palate	1	
		14	**9.5%**
Q50-Q56	**Congenital malformations of genital organs**		
	Hypospadias	8	
	Epispadias	3	
	Chordae	1	
	Micropenis	1	
	Imperforate hymen	1	
	Labial hypertrophy	1	
	Ambiguous genitalia	1	
		16	**10.9%**
Q60-Q64	**Congenital malformations of the urinary system**		
	Renal agenesis	1	
	Polycystic kidney	1	
	Ectopic kidney	1	
		3	**2.0%**
Q65-Q79	**Congenital malformations and deformities of the musculoskeletal system**		
	Talipes equinovarus	14	
	Polydactyly	7	
	Gastroschisis	5	
	Omphalocele	2	
	Syndactyly	1	
	Clinodactyly	1	
	Craniosynostosis	1	
	Pectus excavatum	1	
	Pectus carinatum	1	
	Genu Varum	1	
	Osteogenesis imperfecta	1	
	Arthrogryposis	1	
		36	**24.5%**
Q80-Q89	**Other congenital malformations**		
	Sacral dimple	1	
	Epidermolysis dystrophica	1	
	Hereditary lymphedema	1	
	Neurofibromatosis unspecified	2	
	Foetal alcohol syndrome	2	
		7	**4.8%**
Q90-Q99	**Chromosomal abnormalities, not elsewhere classified**		
	Downs Syndrome	6	
	Patau syndrome	1	
		7	**4.8%**

- *Factors Associated with Birth Defects Among Neonates Admitted at MRRH*

- *Maternal Factors Associated with Birth Defects Among Neonates Admitted MRRH*

The maternal factors that were significantly associated with BDs were use of fertility medicine and informal employment. Mothers on fertility medication had 2.4 times increase in the likelihood of having neonates with BDs aPR 2.5 CI [1.16,5.38] P-value 0.020. However, mothers who had informal employment were less likely to have children with birth defects compared to those with formal employment a PR:0.55 CI [0.31,0.96] P-value= 0.037. (Table 6).

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Table 6 Maternal Factors Associated with Birth Defects Among Neonates Admitted MRRH

Variables		Birth defect		Unadjusted analysis		Multivariable analysis	
		Yes (n=103)	No(n=309)	cPR (95% CI)	P-value	aPR (95% CI)	P-value
		n (%)	n (%)				
Maternal age (years)							
	<20	9 (8.7%)	30 (9.7%)	0.91[0.49,1.66]	0.756	0.78[0.39,1.57]	0.487
	20-34	79 (76.7%)	232 (75.3%)	Ref.		Ref.	
	>34	15 (14.6%)	46 (14.9%)	0.97[0.60,1.56]	0.894	1.01[0.60,1.71]	0.956
Marital status							
	Married	89 (86.4%)	279 (90.3%)	Ref.		Ref.	
	Unmarried	14 (13.6%)	30 (9.7%)	1.32[0.82,2.10]	0.252	1.58[0.96,2.61]	0.073
Level of education							
	None	9 (8.7%)	22 (7.1%)	1.35[0.73,2.48]	0.336	1.75[0.77,3.98]	0.181
	Primary	45 (43.7%)	164 (53.1%)	1.33[0.91,1.95]	0.140	1.18[0.59,2.38]	0.640
	Secondary	35 (34.0%)	87 (28.2%)	1.30[0.78,2.18]	0.317	1.46[0.81,2.64]	0.211
	Tertiary	14 (13.6%)	36 (11.7%)	Ref.		Ref.	
Employment							
	Formal	21 (20.4%)	39 (12.6%)	Ref.		Ref.	
	Informal	**82 (79.6%)**	**270 (87.4%)**	**0.67[0.45,0.98]**	**0.043***	**0.55[0.31,0.96]**	**0.037***
Parity							
	I	39 (37.9%)	94 (30.4%)	1.23[0.86,1.74]	0.254	1.15[0.79,1.68]	0.455
	II-IV	56 (54.4%)	178 (57.6%)	Ref.		Ref.	
	≥V	8 (7.8%)	37 (12.0%)	0.74[0.38,1.45]	0.384	0.62[0.27,1.39]	0.245
Prior abortion							
	No	77 (74.8%)	232 (75.1%)	Ref.		Ref.	
	Yes	26 (25.2%)	77 (24.9%)	1.01[0.69,1.48]	0.948	1.02[0.69,1.50]	0.918
Birth defect among other children							
	No	97 (94.2%)	290 (93.9%)	Ref.		Ref.	
	Yes	6 (5.8%)	19 (6.1%)	0.96[0.46,1.97]	0.906	0.86[0.40,1.85]	0.703
Conception mode							
	Assisted	1 (1.0%)	1 (0.3%)	2.01[0.49,8.13]	0.328	1.35[0.47,3.87]	0.577
	Natural	102 (99.0%)	308 (99.7%)	Ref.		Ref.	
Fertility medicines use							
	No	100 (97.1%)	307 (99.4%)	Ref.		Ref.	
	Yes	**3 (2.9%)**	**2 (0.6%)**	**2.44[1.17,5.10]**	**0.018***	**2.50[1.16,5.38]**	**0.020***
Number of ANC visits							
	<4	30 (29.1%)	95 (30.7%)	0.94[0.65,1.37]	0.758	0.99[0.68,1.45]	0.963
	≥4	73 (70.9%)	214 (69.3%)	Ref.		Ref.	
Radiation Exposure							
	No	89 (86.4%)	283 (91.6%)	Ref.		Ref.	
	Yes	14 (13.6%)	26 (8.4%)	0.89[0.26,3.05]	0.849	1.11[0.71,1.73]	0.648
Illicit drug use							
	No	101(98.1%)	302 (97.7%)	Ref.		Ref.	
	Yes	2 (1.9%)	7 (2.3%)	1.46[0.92,42.32]	0.105	1.05[0.27,4.00]	0.968

➢ *Paternal Factors and Association with BDs Among Neonates Admitted at MRRH.*

Both paternal alcohol use and occupational teratogenic exposure (herbicides, pesticides, mining, paint petroleum and by-products) were the factors significantly associated with having neonates with BDs. Each of them increased the likelihood of having a neonate with birth defects by 1.47 and 1.48 respectively. Although not statistically significant, advanced paternal age above 50 years had clinical significance and had an increased aPR: 2.18, CI [0.75,6.32], P-value 0.151. (Table 7)

Table 7 Paternal Factors and Association with BDs Among Neonates Admitted at MRRH

Variables		Birth defect		Unadjusted analysis		Multivariable analysis	
		Yes (n=103)	No(n=309)	cPR (95% CI)	P-value	aPR (95% CI)	P-value
		n (%)	n (%)				
Paternal age (years)							
	<50	99 (96.1%)	300 (97.1%)	Ref.		Ref.	
	≥50	4 (3.9%)	9 (2.9%)	1.24[0.54,2.86]	0.613	2.18[0.75,6.32]	0.151
Paternal occupation							

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	Formal	18 (17.5%)	56 (18.2%)	Ref.		Ref.	
	Informal	85 (82.5%)	251 (81.8%)	1.04[0.67,1.62	0.862	1.46[0.88,2.40]	0.140
Family dysmorphic features							
	No	91 (88.3%)	277 (89.6%)	Ref.		Ref.	
	Yes	12 (11.7%)	32 (10.4%)	1.10[0.66,1.85]	0.709	1.17[0.47,2.93]	0.734
Paternal alcohol use							
	No	56 (54.4%)	201 (65.0%)	Ref.		Ref.	
	Yes	**47 (45.6%)**	**108 (35.0%)**	**1.39[0.99,1.94]**	**0.052**	**1.47[1.04,2.09]**	**0.030***
Paternal smoking							
	No	99 (96.1%)	295 (95.5%)	Ref.		Ref.	
	Yes	4 (3.9%)	14 (4.5%)	0.88[0.37,2.14]	0.785	0.76[0.28,2.06]	0.591
Paternal occupational exposure							
	No	67 (65.0%)	226 (73.1%)	Ref.		Ref.	
	Yes	**36 (35.0%)**	**83 (26.9%)**	**1.32[0.94,1.86]**	**0.112**	**1.48[1.04,2.10]**	**0.029***
cPR: crude prevalence ratio; aOR: adjusted prevalence ratio; CI: confidence interval; *$p < 0.05$;							

IV. DISCUSSION

We set out to study the prevalence, patterns and associated factors of birth defects among neonates at admission at Mbarara Regional Referral hospital.

➢ *Prevalence of BDs among children at admission at MRRH*

The prevalence of birth defects recorded in this study among neonates at admission at MRRH was 25%. This prevalence is high compared to reports from many other countries. Lower prevalence rates have been reported from many other countries; United Kingdom (Glasgow City) 3.24% [3], Sweden 3. 4% [5], India (BSMMU), 3.68% [23], Iran 1.87% [24]Kenya [8], Egypt 2.5% [9] and Nigeria 2.8% [5] and that from Entebbe in Uganda 7.6% [10]

The high prevalence in our study is comparable with that in reports from Kenya (Kenyatta National Hospital) and Tanzania (Bugando Medical Center) of 19.4%[25] and 29% respectively [11]. The high prevalence of BDs among neonates at admission reported by our study could be explained by the wide catchment area beyond the official designation and receiving many referrals since MRRH offers more specialized services in the region. Detection rates for birth defects could have been higher in our study since all neonatal examinations were structured and also done by paediatricians as opposed to many other studies that used midwives. Additionally, beyond clinical evaluation, some BDs were identified using imaging studies and ultrasonography.

The studies that reported a lower prevalence compared to that of our study could be due to differences in methods and population. An earlier study in Entebbe, Uganda had reported a lower prevalence probably because of the restricted catchment area. However, a lower prevalence of 66.2/1000 births was also reported by a hospital based birth defects surveillance among 4 major hospitals in Kampala [33]. This also reported a lower prevalence that could be explained by differences in both the study methods and data collection. Many studies have used However, regional variations in BD prevalence have been also reported in other countries like; Nigeria 6.3% [26], 4.4% [27], 1.75% [28] and Kenya: PMH 1.94% [29]. and KNH 2.8% [8]. This would suggest that the prevalence of BDs is likely to differ with time and geographical region.

➢ *Patterns of BDs*

The most common BDs among neonates at admission at MRRH were those of the musculoskeletal system, followed by those of the central nervous system. This finding was similar to those reported in studies in Entebbe, Uganda [10] Kenya [8], Egypt[30] , India[23] and Mexico[31] . Musculoskeletal system anomalies may be relatively more visible externally with more ease of identification as compared to those of internal organ systems like the respiratory. However, some studies recorded higher incidence of CNS anomalies; Mwanza; Tanzania [11] and cleft lip/palate in Zambia [32].

Of the musculoskeletal system birth defects, Talipes Equino Varus (TEV) was the commonest followed by polydactyly and gastroschisis. This is comparable to reports Uganda [10] and Kenya [8], where Talipes Equino Varus were the leading BDs. However, another study in Uganda [33]among hospitals in Kampala, reported genital anomalies to have predominated with hypospadias commonest. The difference in pattern and prevalence of birth defects indicates that they vary over time and with geographical location.

➢ *Factors Associated with BDs.*

The current study specifically focused on the maternal and paternal factors associated with BDs. Among the maternal factors, fertility medicine use was significantly associated with BDs in their newborns. This could be due to the fact that mothers on fertility medication may be relatively older in age having taken variably long periods of time to achieve the pregnancy. These mothers could also have had previous miscarriages that could signal presence of chromosomal abnormalities. They could also have an underlying disease for their infertility with also potential to cause BDs like the TORCHES. However, also common fertility medications like clomiphene have been associated with BDs in some studies including; congenital heart disease, Downs syndrome, oral clefts, spina bifida [34–36].

Maternal informal employment was found to be protective from BDs among their newborns in our study. However, we were unable to find any other study with similar report. This could be due to the fact that about 80% of mothers were in informal employment also majority were from rural settings. Many were also involved in farming as compared those in formal employment and were also working in polluted towns and cities. In our geographic area, there are more industries in the urban areas. Also, mothers in rural setting were more likely to feed on their self-grown vegetables and fruits as compared to mothers in formal employment who are more likely to buy vegetables and fruits from markets. Many farmers in our setting are using variable amounts of herbicides and pesticides; more than 90% used WEED MASTER, a herbicide on local market. Maternal education to degree level has been cited as protective factor for BDs in UK [18]but in our study, less than 15% of mothers had reached tertiary level of education.

Maternal smoking and alcohol consumption have been reported as significant risk factors for the occurrence of BDs including congenital heart diseases and orofacial clefts[15,37,38] although both were not significant in our study. However, underreporting by mothers could have occurred due to fear of blame for the occurrence of BDs.

Advanced maternal age has been linked to increased risk of BDs by many studies including those in Kenya, Tanzania and India respectively[8,43,44] however, this was not significant in the current study. This could have been due to the fact that majority (about 85%) of mothers in our study were less than 35 years of age but also maternal under reporting of their age is another possibility.

The paternal factors that were significantly associated with BDs included; alcohol intake and occupational chemical exposure. Several studies have indicated paternal alcohol use especially pre conceptual to be associated with BDs like clefts. These have been both in animal and human models [39,40]. Paternal alcohol consumption biologically increases the risk of genetic and epigenetic sperm anomalies [41]. In mice, offspring of fathers exposed to alcohol have a number of placenta-related difficulties, including increased fetal growth restriction, enlarged placentas, and decreased placental efficiency.

Paternal occupational exposures to: herbicides, pesticides, paint, petroleum and by products, industrial pollutants and mining were significantly associated with BDS. Majority of the fathers in our study were in informal employment (farmers, painters, saloon, motor cycle riders, factory labourers) and many were more likely to be exposed to teratogens: herbicides, pesticides paints, petroleum and by-products and industrial pollutants. Paternal occupation has been associated with BDs in their off springs in some other studies [22,42].

- *Strengths*

Our study site is the major referral Hospital in the geographical setting, with a big catchment area and variable population making the results representative. Data was collected by a team of paediatricians as compared to many other studies that mainly used midwives, nurses to identify BDs.

Our study could have identified more BDs through diagnostic imaging, ultrasonography and echocardiography as compared to many others whose identification method was only clinical.

Traditionally, studies on BDs have described maternal risk factors only but our study looked at the association paternal factors as well.

The prospective study design, unlike many other studies that used data from medical records to estimate birth defect prevalence and faced variable challenges including incomplete documentation, lack of details, inaccurate coding.

V. LIMITATIONS

Limited investigative capacity especially, genetic, metabolic studies and Viral serology especially for Rubella, Herpes and CMV.

Ascertainment bias could have affected our results due to fear by mothers of freely reporting about their social habits. Recall bias could have affected the risk exposure variables and also denial from parents due to fear of blame for occurrence of the BDs.

The study duration was short and this could have reduced the opportunity to study the seasonal variability of birth defects.

VI. CONCLUSIONS

The prevalence of birth defects among neonates at admission at MRRH was high (One among four).

The musculoskeletal was the commonest organ system affected by birth defects.

Maternal use of fertility medicines and both paternal alcohol intake and occupational exposure were the factors that were significantly associated with birth defects among neonates at admission at MRRH.

RECOMMENDATIONS.

Clinicians should routinely and comprehensively assess for BDs among neonates at admission.

Strengthening community Sensitization especially about modifiable risk for BDs like: paternal alcohol intake and occupational exposure.

Mothers on fertility medication should have early antenatal screening for BDs.

Developing a birth defect registry for the hospital for improved documentation and planning.

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- *Authors Contributions*

KP, MO, KS, KO, KL and ND conceived the idea, KP was the principal investigator. The team wrote the proposal and also participated in data collection. TL contributed to the methods section and did data analysis. KP and MO wrote the initial draft of the manuscript. All authors proof read the final manuscript.

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