Original Article

Risk factors and outcome of malformations of gastrointestinal tract in neonates in a tertiary care center in India

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ABSTRACT

Objective: The objective of the study was to determine the prevalence and associated risk factors of malformations of the gastrointestinal tract (MGIT) in neonates in a tertiary care hospital. **Methods:** We conducted a prospective, observational, case–control study on all intramural neonates till discharge/outcome for 1 year. Babies with MGIT diagnosed antenatally or postnatally were taken as cases and two consecutively born healthy babies were taken as controls. **Results:** Out of 25,116 live births, there were 41 cases of MGIT with a prevalence of 1.63 per 1000 live births. Tracheoesophageal fistula was the most common (39.02%), followed by anal atresia (24.39 %), esophageal atresia (9.46%), and mesenteric cyst (7.31%). Antenatally and postnatally, 16 (39.1%) and 25 (60.9%) cases were diagnosed, respectively. A significant association was observed between MGIT and lack of periconceptional iron/folic acid supplementation, birth weight <2.5 kg, maternal age >30 years, low socioeconomic profile, consanguinity, febrile illness in first trimester, and gender. The average time to onset of first feed and mean duration of hospital stay in babies with MGIT were 7 days and 14 days, respectively. **Conclusion:** Most MGIT can be diagnosed clinically and radiologically before/soon after birth and have a good outcome with timely surgical intervention. Pre-pregnancy counseling for periconceptional folic acid supplementation with screening ultrasonography, appropriate follow-up, and referral system should be developed for the management of these cases. A coordinated multidisciplinary approach for prevention, management, and rehabilitation of affected babies is required.

Key words: Birth defects, Malformations of the gastrointestinal tract, Neonates, Risk factors

Birth defects or congenital malformations have been variously defined as abnormalities of structure or function, including metabolism present from birth [1]. They are an important cause of mortality in neonates and under-5 children in low-middle-income countries like India with the reported overall prevalence between 1.6% and 4.1% [2-5]. Malformations of gastrointestinal tract (MGIT) are the third most common cause of congenital birth defects with an incidence of 38.37 per 10,000 [6] and the reported prevalence varying between 0.06% and 0.4% [7]. As per the National Neonatal Perinatal Data 2002, out of 9.2% mortality from congenital malformations, intramural and extramural gastrointestinal malformation proportion was 0.2% and 2.9%, respectively [8].

Various maternal and demographic risk factors such as advanced maternal age, prematurity, higher birth order, cigarette smoking, folic acid deficiency, and consanguinity in marriage are known to be associated with birth defects [2-5]. MGIT can be easily diagnosed with the help of simple modalities such as abdominal X-ray and contrast studies and has good outcome with timely surgical intervention. Till now, the literature available specifically for the incidence and association of MGIT with various risk factors is still insufficient. Timely diagnosis and appropriate management (preoperatively and postoperatively) can reduce mortality and morbidity to a great extent. The present study was, therefore, undertaken to determine the prevalence and associated risk factors of MGIT in neonates in a hospital.

Access this article online	
Received - 07 April 2021 Initial Review - 21 April 2021 Accepted - 15 May 2021	Quick Response code
DOI: 10.32677/IJCH.2021.v08.i05.004	

METHODS

This was a prospective, observational, case–control study conducted in the department of pediatrics in collaboration with the department of obstetrics and gynecology, at a tertiary care hospital in Delhi for the duration of 1 year from December 2014 to November 2015. Ethical clearance was obtained from the Institutional Ethical Committee. With an anticipated prevalence of 0.12% of MGIT [7,8], absolute precision taken as 0.045 with 95% confidence intervals, 28 cases of suspected MGIT were expected to occur. The population consisted of all live babies born in the hospital during the study period. The study group consisted of all

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intramural live neonates diagnosed with MGIT (either antenatally or postnatally) and followed till discharge/outcome. Two healthy babies born consecutively and having no MGIT were enrolled as controls for studying the risk factors. Written informed consent was taken from all the mothers of enrolled babies in a language understood by them. All the babies were examined at birth for the presence of any MGIT by clinical examination or by putting orogastric tube, for example, for anal atresia, tracheoesophageal fistula. Babies asymptomatic at birth were followed up till 48 h of birth/discharge to rule out the appearance of any signs and symptoms suggestive of MGIT such as failure to pass meconium by 48 h, abdominal distension, and gastric aspirates.

A predesigned questionnaire with demographic profiles and risk factors was utilized to interview the mothers of all babies. It consisted of particulars such as age, socioeconomic (SE) status, consanguinity, lack of folic acid supplementation; smoking, alcohol or tobacco abuse; any febrile illness with rash, comorbidities; bad obstetric history; or birth defects in previous babies. The details of all babies (cases and controls) such as birth weight, gender, gestation, and clinical details were recorded. Whenever there was one malformation, the baby was examined to rule out other malformations. Investigations done in support of diagnosis were abdominal X-ray: Erect view, ultrasound – abdomen, and contrast study of GIT, and other special investigations such as echocardiography to rule out cardiac, renal, vertebral, or any other congenital anomalies.

Data for the study population in neonates were measured for (1) prevalence, risk factors, and clinical profile of GIT malformations, (2) morbidity in the form of duration of hospital stay and time to onset of first feed, and (3) mortality. The data were entered into MS EXCEL spreadsheet and analysis was done using Stata 14.0 Statistical software. Categorical variables were presented in numbers and percentages (%) and Chi-square test was used to compare frequencies. Stepwise multivariable logistic regression was used to assess the significant risk factors of GIT malformations after adjusting for confounding variables. The odds ratio (95% CI) was computed as summary measure. In this study, $p<0.05$ was considered statistically significant.

RESULTS

During the study period of 1 year, out of 25,116 live births, birth defects accounted for 308 cases with a prevalence of 12.26 per 1000 live births. Out of these, 41 (13.31%) cases were of MGIT with a prevalence of 1.63 per 1000 live births. The males and females were 48.78% and 43.90%, respectively, with male-to-female ratio of 1.1:1 (three cases not included due to ambiguous genitalia) (Table 1). In this study, out of 41 cases of GIT malformations, 16 cases (39.0%) were picked up on antenatal ultrasonography while 25 cases (60.9%) were diagnosed after birth. Out of 25 cases, 18 cases (72%) presented within 24 h of birth and rest after 24 h of birth.

In the sociodemographic factors, women more than 30 years were found to be at a higher risk for MGIT as compared to the control group, that is, 36.59% and 19.51%, respectively, the association being statistically significant (p=0.040). The mothers from lower socioeconomic status were more significantly associated with GI birth defects as compared to that in the control group with p=0.011. A higher proportion of women in the study group had a history of consanguineous marriage as compared to the control group (p=0.042). Similarly, a significant number of women in the study group did not receive periconceptional folate supplementation and iron as compared to the control group (p=0.0016) and higher proportion of women had a history of febrile illness in the first trimester as compared to the control group (p=0.016) (Table 1).

Among fetal factors, significant association was observed between male gender and low birth weight (LBW) babies <2500 g in study group when compared to control group (Table 1). On multivariate analysis, lack of periconceptional folic acid supplementation and baby birth weight below 2.5 kg, were observed to have an independent, significant association with the occurrence of MGIT (Table 2).

Among MGIT, tracheoesophageal fistula was the most common 16 (39.02%) anomaly followed by anal atresia 10 (24.39

Table 1: Sociodemographic and risk factors in a study and control group

Factors	MGIT (n=41)	Non-MGIT (n=82)	p value
Maternal factors			
Mother age			
Equal or <30	26 (63.4)	66 (80.4)	0.040
>30	15 (36.5)	16 (19.5)	
Socioeconomic status			
Upper	5 (12.2)	14 (17.0)	
(LM+UM)	12 (29.2)	43 (52.4)	
Lower	24 (58.5)	25 (30.4)	0.01
Obstetrical birth order			
1 and 2	15 (36.5)	38 (46.3)	0.57
3 and 4	17 (41.4)	30 (36.5)	
5 and more	9 (21.9)	14 (17.0)	
Consanguinity	4 (9.7)	1 (1.2)	0.04
Iron and folic acid	21 (51.2)	60 (73.1)	0.01
Tobacco	6 (14.6)	7 (8.5)	0.30
Smoking	7 (17.0)	8 (9.7)	0.24
Alcohol	2 (4.8)	1 (1.2)	0.25
Previous spontaneous abortion	9 (21.9)	10 (12.2)	0.15
Previous still birth	4 (9.7)	3 (3.6)	0.22
Exposure radiation	3 (7.3)	2 (2.4)	0.33
Febrile illness in the first trimester	5 (12.2)	1 (1.2)	0.01
Period of gestation (<37 weeks)	15 (36.5)	22 (26.8)	0.26
Fetal factors			
Birth weight <2500 g	14 (34.1)	9 (10.9)	0.002
Gender			0.02
Male	20 (48.7)	51 (62.2)	
Female	18 (43.9)	31 (37.8)	
Ambiguous	3 (7.3)	0 (0.0)	

MGIT: Malformations of gastrointestinal tract

Table 2: Results of multivariable logistic regression analysis: Risk factors of MGIT

Factors	Odds ratio	p value	95% C.I. for odds ratio	
			Lower	Upper
Mother age >30 years	1.79	0.45	0.38	8.36
Socioeconomic status				
Upper	1	0.05		
(LM+UM)	0.17	0.11	0.02	1.50
Lower	0.98	0.98	0.13	7.08
Consanguinity	22.24	0.56	0.00	775968.98
Iron and folic acid	5.46	0.024	1.25	23.88
Febrile illness >38°C	61.08	0.22	0.079	47176.05
IV fluid	73.23	0.0002	7.57	708.52
Antibiotics	4.81	0.02	1.25	18.45
Birth weight <2500 g	6.68	0.02	1.24	35.87

MGIT: Malformations of gastrointestinal tract

%) and esophageal atresia 4 (9.76%). Rest were mesenteric cyst 3 (7.31%), omphalocele and ileal atresia 2 (4.88%) each, and 1 (2.44%) case each of meconium cyst, intestinal atresia, duodenal atresia, and Hirschsprung's disease. Six (14.6%) out of the 41 MGIT cases were syndromic babies.

In this study, out of 41 cases of MGIT, 8 (19.6%) were sick and not operated on because of comorbidities (four from asphyxia, three from prematurity, and one was syndromic who left against medical advice). Thirty-three babies (80.4%) were operated on, out of which, 13 died intra- or postoperatively. Twenty babies were discharged and kept under follow-up. Out of 41 babies of MGIT, 20 (48.7%) died (both operated and non-operated). Seven (35%) died due to prematurity, 6 (30%) due to associated birth defects, 4 (20%) due to asphyxia, and 3 (15%) due to sepsis/shock. Average time to onset of first feed and mean duration of hospital stay in babies with MGIT were 7 days (range 3–14 days) and 14 days (standard deviation of 7 days; ± 2 S.D.), respectively.

DISCUSSION

Our work was designed to study the prevalence, spectrum, associated risk factors (both mother and baby), and outcome of neonates born with MGIT in a hospital. Although so far, many studies have analyzed risk factors associated with birth defects, very few have looked specifically for MGIT.

The prevalence of MGIT was 1.63 per 1000 live births (0.16%) in the present study. Various other studies have shown prevalence ranging from 0.72 to 2.3 per 1000 live births [2,7,9]. Observed lower rate of 0.16% reflects the picture of only those high-risk population which delivered at hospital whereas community-based studies analyze a larger stratum of society with varying SE status, which has been implicated as a possible risk factor for MGIT [10-12]. Other factors which can affect the reported prevalence of MGIT are differences in geographical locale, environmental factors, genetic factors, racial background, nutrition, and social-economic differences and timing of discharge. Babies discharged early from postnatal ward in busy hospitals may not capture true prevalence as many MGIT may present in the 1st week of life.

As seen in literature, our study observed a higher proportion of males being affected by MGIT as compared to females, that is, 48.78% and 43.90%, respectively, with male: female ratio of 1.11:1. The association with females of more than 30 years was also observed in accordance with other studies.

Lower SE status was observed as a significant risk factor for MGIT in our study as seen in literature [4]. This could be because our hospital caters to referred cases from large population belonging to the lower SE status. The present study observed the lack of periconceptional folic acid supplementation as a statistically significant risk factor for MGIT as seen in 63.5% of women who delivered neonates with birth defects [4]. Lower SE status is generally associated with poor literacy; a combination of the two factors leads to lack of antenatal supervision and periconceptional folic acid supplementation, hence predisposing to birth defects. These observations emphasize the significance of periconceptional maternal counseling for folic acid supplementation, especially in women on anti-epileptics, or those with a history of NTDs and GI birth defect in previous births and endorse the need for strategies for food fortification with folic acid at national level, for example, significant association of consanguinity was seen with MGIT as seen with birth defects in various other studies [4,5,13-15].

In the present study, all consanguineous marriages were from Muslim community, which reflects the difference in marital habits among different ethnic groups. Our study did not observe any significant association between MGIT and maternal comorbid conditions unlike other studies in which diabetes, hypertension, and hypothyroidism showed a positive association with congenital malformations [16]. This could be because of very small sample size in each variable in our study.

Among fetal factors, LBW babies (<2500 g) were an independent significant risk factor on multivariate analysis with MGIT. Similar observations were seen with birth defects association in other studies [2]. However, no association was seen with prematurity contrary to other studies done previously [5,13] probably because of small size of the present study. Tracheoesophageal fistula was the most common MGIT (39.02%), followed by anal atresia (24.39%), esophageal atresia (9.46%), and other defects. Various studies reported imperforate anus, intestinal atresia, and TEF as the most common MGIT [7,9,17].

Evaluation of the prevalence and spectrum of MGIT and the associated risk factors would help the health-care authorities in planning preventive strategies at various levels. By the development of a population-based surveillance program to capture GI birth defects, countries can gain a better understanding of the burden and risk factors for these conditions and plan facilities for referral of such infants to higher centers in an optimal and timely manner. The prevalence estimates can be used to evaluate any current prevention or clinical management programs

and provide a basis for epidemiological research. This could go a long way for improvement of families, societies, and nation.

This study has certain limitations also. This being a hospital-based study, the observations may not be extrapolated to the general population. Malformations are an important cause of still births; however, still births were not included which may have resulted in low prevalence of MGIT. Furthermore, autopsies were not performed in early neonatal deaths which may have missed few MGIT. Since the duration of hospital stay of most newborns was 48 h, babies who presented later may have been missed.

CONCLUSION

MGIT can be diagnosed clinically and radiologically before/soon after birth and have good outcome with proper and timely surgical intervention. Pre-pregnancy counseling for periconceptional folic acid supplementation with screening ultrasonography, appropriate follow-up, and referral system should be developed for the management of these cases. A coordinated multidisciplinary approach for prevention, management, and rehabilitation of affected babies is required.

REFERENCES

1. World Health Organization. The Global Burden of Disease: 2004 Update. Geneva: World Health Organization; 2008. Available from: https://www.who.int/healthinfo/global_burden_disease/2004_report_update/en. [Last accessed on 2021 May 31]
2. Taksande A, Vilhekar K, Chaturvedi P, Jain M. Congenital malformations at birth in Central India: A rural medical college hospital based data. Indian J Hum Genet 2010;16:159-63.
3. Obu HA, Chinawa JM, Uleanya ND, Adimora GN, Obi IE. Congenital malformations among newborns admitted in the neonatal unit of a tertiary hospital in Enugu, South-East Nigeria--a retrospective study. BMC Res Notes 2012;5:177.
4. Raza MZ, Sheikh A, Ahmed SS, Ali S, Naqvi SM. Risk factors associated with birth defects at a tertiary care center in Pakistan. Ital J Pediatr 2012;38:68.
5. Al Bu Ali WH, Balaha MH, Al Moghannum MS, Hashim I. Risk factors and birth prevalence of birth defects and inborn errors of metabolism in Al Ahsa, Saudi Arabia. Pan Afr Med J 2011;8:14.
6. World Health Organization. Regional Office for South-East Asia. Birth Defects in South-East Asia: A Public Health Challenge: Situation Analysis. World Health Organization; 2013. Available from: https://www.apps.who.int/iris/handle/10665/204821. [Last accessed on 2021 May 31]
7. Kumar A, Singh K. Major congenital malformations of the gastrointestinal tract among the newborns in one of the English Caribbean countries, 1993-2012. J Clin Neonatol 2014;3:205-10.
8. National Neonatal-Perinatal Database (NNPD) Network, India, 2002-2003, NNPD, New Delhi. Available from: https://www.newbornwhocc.org/pdf/nnpd_report_2002-03.pdf. [Last accessed on 2021 May 31]
9. Golalipour MJ, Mobasheri E, Hoseinpour KR, Keshtkar AA. Gastrointestinal malformations in Gorgan, North of Iran: Epidemiology and associated malformations. Pediatr Surg Int 2007;23:75-9.
10. Oztarhan K, Gedikbasi A, Yildirim D, Arslan O, Adal E, Kavuncuoglu S, *et al*. Prevalence and distribution of congenital abnormalities in Turkey: Differences between the prenatal and postnatal periods. Congenit Anom 2010;50:221-5.
11. Dolk H, Loane M, Garne E. The prevalence of congenital anomalies in Europe. Adv Exp Med Biol 2010;686:349-64.
12. Abdi-Rad I, Khoshkalam M, Farrokh-Islamlou HR. The prevalence at birth of overt congenital anomalies in Urmia, Northwestern Iran. Arch Iran Med 2008;11:148-51.
13. Naoom M, ALSaadi Y, Yassin BG, Matloob H. Congenital anomalies among newborns admitted in tertiary hospital; Iraqi experience. J Facult Med Baghdad 2013;55:106-10.
14. Rittler M, Liascovich R, López-Camelo J, Castilla EE. Parental consanguinity in specific types of congenital anomalies. Am J Med Genet 2001;102:36-43.
15. Becker SM, Al Halees Z, Molina C, Paterson RM. Consanguinity and congenital heart disease in Saudi Arabia. Am J Med Genet 2001;99:8-13.
16. Ordóñez MP, Nazer J, Aguila A, Cifuentes L. Association between congenital malformations and chronic diseases of the mother. Med J Chile 2003;131:404-11.
17. Asindi AA, Al-Daama SA, Zayed MS, Fatinni YA. Congenital malformation of the gastrointestinal tract in Aseer region, Saudi Arabia. Saudi Med J 2002;23:1078-82.

Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Gupta S, Kumar K, Gupte N, Bagga D, Pandey RM, Chellani H. Risk factors and outcome of malformations of gastrointestinal tract in neonates in a tertiary care center in India. Indian J Child Health. 2021; 8(5):190-193.