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Congenital heart defects in children with Gastro-intestinal malformations

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Background. Congenital malformations of the gastrointestinal (GI) tract are common birth defects detected in the neonatal period and usually present with signs of GI obstruction which at times can be life threatening. Anorectal malformations are among the more frequent congenital anomalies. The co-occurrence of congenital heart defect (CHD) along with GI malformation can significantly affect the natural history of either defect.

Purpose — to study the prevalence of GI malformations in children with CHD and study the risk factors.

Materials and methods. A total 100 patients of GI malformations were enrolled out of which 66 (66%) were males and 34 (34%) were females. All patients with any GI malformations (anorectal malformation, tracheoesophageal fistulae, anterior abdominal wall defects) presenting to Neonatal Intensive Care Unit (NICU), Paediatric Cardiac unit, Pediatric and Pediatric surgery outpatient department (OPD) as well as Inpatient department (IPD) between October 2019 to October 2021 were included in study. A detailed history and examination was done followed by echocardiography and the prevalence of CHD among GI malformation was observed and risk factors were studied.

Results. Most common GI anomaly was anorectal malformation (71%) followed by tracheoesophageal fistula (17%), CHD was seen in 14 children. Most common heart defect was ventricular septal defect (VSD) (43%) followed by patent ductus arteriosus (PDA) (36%) and atrial septal defect (ASD) (14%). Among cases with anorectal malformation, CHDs was seen in 10% and the most common defect was VSD (43%). Forty one percent of cases with tracheoesophageal fistula had CHDs with PDA (57%) being the most common underlying defect. Functional heart defects were present in 28 children of GI malformations.

Conclusions. The coexistence and severity of CHD in patients with GI malformation can have prognostic implications. Thus, early cardiac evaluation should be performed in every case of GI malformation, preferably with echocardiography. This is likely to help in the risk stratification as well as management of such children.

The study was performed in accordance with the principles of the Declaration of Helsinki. Study is approved by Ethical Committee of the Institution. Informed consent of patients was obtained for the study.

No conflict of interests was declared by the authors.

Keywords: children, gastrointestinal malformation, congenital heart defect, tracheoesophageal fistula, anorectal malformations, ventricular septal defect.

Вроджені вади серця в дітей з вадами розвитку шлунково-кишкового тракту

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Вступ. Вроджені вади розвитку шлунково-кишкового тракту (ШКТ) є поширеними вродженими дефектами, які виявляються в неонатальному періоді та зазвичай супроводжуються ознаками шлунково-кишкової непрохідності, які інколи можуть бути небезпечними для життя. Аноректальні вади розвитку належать до найчастіших вроджених аномалій. Поєднання вродженої вади серця (ВВС) із вадою розвитку ШКТ може істотно вплинути на природний перебіг будь-якої вади.

Мета — вивчити поширеність вад розвитку ШКТ в дітей з ВВС та виявити фактори ризику.

Матеріали та методи. Усього залучено 100 пацієнтів із вадами розвитку ШКТ, із них — 66 (66%) хлопчиків і 34 (34%) дівчинки. Усіх пацієнтів із будь-якими вадами розвитку ШКТ (аноректальні вади розвитку, трахеостравохідні нориці, дефекти передньої черевної стінки), які надходили до відділення інтенсивної терапії новонароджених, дитячого кардіологічного відділення, амбулаторного відділення дитячої та дитячої хірургії, а також стаціонарного відділення в період із жовтня 2019 року до жовтня 2021 року, включили в дослідження. Проведено детальний анамнез і обстеження з подальшою ехокардіографією, виявлено поширеність ВПС серед вад розвитку ШКТ, вивчено фактори ризику.

Результати. Найпоширенішою аномалією ШКТ була аноректальна мальформація (71%), за якою слідувала трахеостравохідна нориця (17%), ВПС спостерігалися в 14 дітей. Найчастішою вадою серця був дефект міжшлуночкової перегородки (43%), за яким слідували відкрита артеріальна протока (36%) і дефект міжпередсердної перегородки (14%). Серед випадків аноректальної мальформації ВПС зустрічалися в 10%, а найчастішим дефектом був дефект міжшлуночкової перегородки (43%). 41% випадків із трахеостравохідною фістулою мали ВПС, із відкритою артеріальною протокою — 57%, що є найчастішим основним дефектом. Функціональні вади серця виявлені у 28 дітей із вадами розвитку ШКТ.

Висновки. Співіснування і тяжкість ВПС у пацієнтів із вадами розвитку ШКТ можуть мати прогностичне значення. Отже, у кожному випадку вади розвитку ШКТ слід проводити ранню кардіологічну оцінку, переважно за допомогою ехокардіографії. Це може допомогти в стратифікації ризику, а також у веденні таких дітей.

Дослідження проведено відповідно до принципів Гельсінської декларації. Дослідження схвалено Локальним етичним комітетом установи. На проведення дослідження отримано інформовану згоду пацієнтів.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: діти, вада розвитку шлунково-кишкового тракту, вроджена вада серця, трахеостравохідний свищ, аноректальні вади розвитку, дефект міжшлуночкової перегородки.

Introduction

All organ systems within the body can be affected by congenital anomalies (CA). The cardiovascular system is the most common system followed by musculoskeletal and genitourinary system [23] whereas in another study, the most commonly affected system was gastrointestinal (GI) system followed by musculoskeletal system [5]. Congenital heart defects (CHDs) affect approximately 5 to 10 per 1000 live births while the occurrence of GI malformations has been reported to be between 1.3 to 1.8 per 1000 live births. The most frequent GI malformation is anorectal malformations (ARM) with an incidence of 1 in 2000 live births [12]. Other GI anomalies include tracheoesophageal fistula (TEF) and anterior abdominal wall defects with an incidence of 1 in 3000–4500 live births [4] and 5 per 10000 live births respectively [20].

The co-occurrence of CHDs along with GI malformations is commonly described with about 20% of patients with major GI malformations can have an associated CHD, particularly amongst those with recognised syndromes [6,17,25].

The study is **aimed** to look into the burden of CHD in these patients so that early measures can be instituted. The spectrum of CHD is also important to know as an innocuous small restrictive ventricular septal defect (VSD) or a patent foramen ovale (PFO) will not have much of an effect as compared to a complex cyanotic heart disease. Similarly a duct dependent circulation is an equal emergency as an obstructed ARM which require tacking of both the conditions simultaneously and coordination of both the specialities.

The purpose of the study — to study the prevalence of GI malformations in children with CHD and study the risk factors.

Materials and methods

This is a cross sectional observational study in which first 100 patients with GI malformation presenting to our hospital were included in the study and incidence of CHD was observed among those children.

Sample size: It is calculated by the formula $4pq/l^2$ where 'l' is an absolute error, 'p' is a prevalence known from earlier studies, 'q' is a 100 minus 'p', 'l' is an allowable error (taken here as 10%). The size of study is N=95.16. If we add 5% non-response rate, the total sample size is 99.66 (~ 100).

All the patients coming to the hospital with any GI malformations were first screened by history (including maternal risk factors) and examination followed by echocardiography. Informed consent was taken before screening. The prevalence of CHD among GI malformations was calculated. Risk factors associated with GI malformations with or without CHD was alsostudied.

Place of Study. Neonatal Intensive Care Unit (NICU), Pediatrics & Pediatric surgery outpatient & ward, Pediatric Cardiac unit — Department of Pediatrics, Jawaharlal Nehru Medical College, AMU, Aligarh.

Inclusion criteria. All patients with any GI abnormality (ARM, TEF, anterior abdominal wall defects, anomaliesassociated with any syndromes).

Exclusion criteria. Parents not giving consent.

Outcome measures

Primary outcome measures. Prevalence and spectrum of CHDs in children with GI malformations.

Secondary outcome measures. Risk factors in children associated with GI malformations with orwithout CHDs.

Ethical considerations. Study is approved by Ethical Committee of the Institution.

Data analysis. The study was analysed statistically by means of the SPSS 20 (for Windows). Chi Square test was used to compare any significant difference in the prevalence of CHD among different groups of GI anomaly and also to find the relation with incidence of CHD and various maternal risk factors. Logistic regression analysis was used to study the association of risk factors with GI malformation and CHD.

Results

A total of 100 children with GI malformation were studied in which 14 children were found to have CHD. Out of the total 100 patients, there were 66 (66%) males and rest were females. Those children with CHDs (i.e. 14) were taken as cases and without CHDs were taken as controls 86. The profile of various CHD was evaluated in these cases. ARM was the most common GI malformation followed by TEF in both the genders. Out of the total 14 children who were found to have CHDs, 10 (71.4%) cases were males while females constituted 4 (28.5%) cases. There was male preponderance in various cases of CHD.

A total of 71 (71%) children had ARM of whom 7 (10%) had CHD (Table 1).

TEF was found to be the second most common GI malformation constituting a total of 17 (7%) children of whom 7 (41.2%) had CHDs. No CHD was found in patients of omphalocele and conge-

Table 1

Spectrum of various gastrointestinal malformation according to gender

Diagnosis	Male	Female	Total
Anorectal malformation	45 (63.3%)	26 (36.6%)	71 (100%)
Tracheoesophageal fistula	13 (76.4%)	4 (23.5%)	17 (100%)
Congenital Hypertrophic Pyloric Stenosis	5 (83.3%)	1 (16.6%)	6 (100%)
Atresia	1 (33.3%)	2 (66.6%)	3 (100%)
Omphalocele	2 (66.6%)	1 (33.3%)	3 (100%)
Total	66 (66%)	34 (34%)	100 (100%)

Table 2

Spectrum of various CHDs according to gender

Diagnosis	Male	Female	Total
VSD	4 (66.7%)	2 (33.3%)	6 (100%)
ASD	2 (100%)	0 (0.0%)	2 (100%)
PDA	3 (60%)	2 (40%)	5 (100%)
Cor triatriatum	1 (100%)	0 (0.0%)	1 (100%)
Total	10 (71.4%)	4 (28.5%)	14 (100%)

nital hypertrophic pyloric stenosis (CHPS). The most common CHD detected was VSD seen in 6 (43%) patients followed by PDA in 5 (36%) patients and ASD in 2 (14.2%) patients.

There were 28 (28%) patients of functional heart defect, most common was PFO 19 (19%) followed by Pulmonary Artery Hypertension (PAH) in 8 (8%). There was a child with ventricular hypertrophy present along with ARM (Table 2).

Risk factors for CHD in children with GI malformation

The association of various risk factors with the occurrence of CHD among children with GI malformations was studied. The risk factor studied were associated with CHD from the past studies [6,9,19]. The data was retrieved from the history which was recorded in a predesigned proforma and from the maternal records. Various risk factors studied are shown in Table 3 and on univariate analysis the risk factor found to be significantly associated with CHD are history of maternal diabetes and hypertension. Maternal diabetes (OR=11.455; 95% CI 1.719 to 76.305) and maternal history of preeclampsia (OR=16.800; 95% CI 2.723 to 103.647) were found to be significantly associated with CHD. However, maternal age, paternal age, febrile illness during the 1st trimester, bad obstetric history, obesity, alcohol consumption, smoking, drug intake during the 1st trimester were not found to be significantly associated with the risk of CHDs in their babies. Maternal intake of multivitamin and folic acid was not found to be protective against CHD (Table 3).

Discussion

There was male preponderance both in children with GI malformation with or without CHD. Similar studies also showed male preponderance in children with GI defect [9,17,19,23]. The study subjects included 62 (62%) term and 38 (38%) preterm deliveries. 70 children were delivered by normal vaginal route while 30 children were caesarean deliveries.

In our study, ARM was found to be the most common GI malformation 71 (71%) followed by TEF 17 (17%), CHPS 6 (6%), atresia 3 (3%) and omphalocele which was similar studies by R.K. Gokhroo et al. [9], H. Olgun et al. [17] also found ARM to be the most common GI malformation (74.41%) and (34.5%) respectively followed by TEF. U.A. Orun et al. [19] conducted similar study and found cases of ARM to be the most common (43.2%) followed by atresia of stomach, ileal atresia and colonic atresia (21%) and TEF (18.3%).

The association between GI malformation and CHD is increasingly being recognized. The most popular theory for the association of GI malformation and CHD is early failure of midline mesodermal embryogenesis [14,22], the incidence of CHD can be in range of 16.5–28.5% in patients with GI malformations [8,10,17,27]. The prevalence of CHD is reported to be as high as 65% in patients of GI malformation accompanied with syndromes [10]. R.M. Tulloh et al. [25] documented 20% incidence of CHD in patients with GI malformations. A study by G. Chehab et al. [3] from Lebanon found the prevalence of cardiac anomalies

Table 3

Analysis of various risk factors for congenital heart disease in gastrointestinal malformation children on applying logistic regression analysis

Maternal risk factors	Variable taken	Degree of freedom	P value	Odd's ratio	Confidence interval	
					Lower limit	Upper limit
Maternal age	<30 yrs	1	0.697	0.729	0.148	3.584
	⩾30 yrs					
Paternal age	<30 yrs	1	0.068	6.964	0.869	55.842
	⩾ 30 yrs					
History of multivitamin and folic acid intake in the 1st trimester	absent	1	0.750	0.830	0.264	2.607
	present					
Preeclampsia (PIH)	present	1	0.002	16.800	2.723	103.647
	absent					
Maternal diabetes	present	1	0.012	11.455	1.719	76.305
	absent					
Febrile illness during the 1st trimester	present	1	0.794	0.750	0.086	6.505
	absent					
Obesity	present	1	0.073	3.120	0.901	10.805
	absent					
Bad obstetric history	present	1	0.127	2.440	0.775	7.678
	absent					
History of drug intake	present	1	0.740	1.238	0.351	4.363
	absent					

in 40 (38%) patients out of 105 patients with GI malformation while in a similar study by U.A. Orun et al. [19], the incidence of CHD was found to be 28.5%.

We found that the prevalence of CHD was 14% in children with GI malformation which was similar to studies conducted by I.A. Schierz et al. [23] and H. Olgun et al. [17] who have found the prevalence of CHD to be 15.5% and 17.9% respectively.

H. Olgun et al. [17] found out that the incidence of CHD in ARM, TEF and omphalocele was 15.9%, 23.7% and 28.6% respectively. Similarly, A.J. Thompson et al. [24] stated the similar incidence in ARM, TEF and omphalocele as 23%, 12% and 19% respectively. We found that the incidence of CHD in these anomalies was 10%, 41.2%, however no case of omphalocele (total of three cases) was associated with CHD during the study period.

In present study, the incidence of CHD was high among patients with TEF. This is in agreement with other studies conducted by R.K. Gokhroo et al. [9] and U.A. Orun et al. [19] where the risk of having CHD is highest among children with TEF.

R.K. Gokhroo et al. [9], H. Olgun et al. [17] and U.A. Orun et al. [19] found ASD to be the most common CHD in children with GI defect. In our study, VSD was found to be the most common CHD which is in agreement with the study done by I.A. Schierz et al. [23], other studies also found a similar spectrum of CHD [4,11]. Although patients of TEF can have various types of CHDs but VSD, PDA and ASD are the commonly seen in that order. In the present study, the most common CHD in TEF patients was found to be PDA followed by VSD.

Ingrid Ann Schierz et al. [22] found the prevalence of functional heart defect in 23 (32.4%) newborns. The most common functional heart anomaly was PFO 19 (82.6%) followed by hypertrophic obstructive cardiomyopathy (HOCM) 4 (17.3%) and PDA 3 (13%) cases.

In the present study, the functional heart defect was present in 28 out of 100 patients of GI malformation. The most common being PFO seen in 19 out of 28(67.8%) patients followed by PAH with TR 8 (28.5%) while ventricular hypertrophy was present in 1(3.5%) patient only.

Risk factors

1. Maternal age. In our study, we didn't find significant association of occurrence of cardiac anomalies in children with digestive tract malformation with maternal age. However, study done

by A. Miller et al. [15] found advanced maternal age >35 years was associated with increased prevalence of CHDs.

2. Paternal age. We found no significant association of occurrence of heart disease in GI malformation children with paternal age. In contrast, A.F. Olshan et al. [18] and Z.H. Lian et al. [13] found that the occurrence of CHD is higher with advancing paternal age.

3. Intake of multivitamin and folic acid. In the present study, intake of multivitamin and folic during first trimester had no protective role against CHD in the study subjects. In a study done by Shaad Abqari et al [1], mother who had taken multivitamin and folic acid during the 1st trimester had reduced risk of having CHDs in comparison to those who didn't take it in general population.

4. Maternal diabetes. Significant association was found between maternal diabetes and CHD (OR=11.455; 95% CI 1.719–76.305) in children with GI malformation. Similar findings were reported by Dabelea et al where he found diabetes in mothers was associated with increased risk of cardiac anomalies [7].

5. Preeclampsia. In the present study, association of pregnancy induced hypertension with CHD in patients with GI malformation was found to be significant (OR=16.800; 95% CI 2.723–103.647). Nathalie et al found similar findings in their patients with preeclampsia [16].

6. Febrile illness during the trimester I. There was no significant association found between febrile illness during the trimester I and CHD in patients with GI malformation, however a study in general population from the same centre [1] has found a significant association of CHD with febrile illness during the trimester I.

7. Smoking and alcohol intake. No case with maternal history of smoking and alcohol intake during the study period was found, but a study by Zhongyuan [28] found no association between smoking and alcohol intake with CHD in GI children, however, Sadia et al. found an association of smoking with increased risk of CHDs [21].

8. Bad obstetric history. A study from our centre in 2016 [1] in general population found significant association of CHDs with bad obstetric history but in this study no significant relationship between bad obstetric history and CHD in children with GI malformation was found.

9. Drug intake during the trimester I. We didn't find significant association of CHD with intake of drug during the trimester I in children with GI malformation. Shaad Abqari et al. [1] also reported the same findings and documented no significant association of CHD with intake of drug during the trimester I.

The study was undertaken in patients with GI malformation to assess the prevalence and spectrum of CHD in these children and also to assess the risk factors in patients with GI malformation with or without cardiac anomalies. The incidence of CHD in GI malformation patients was found to be high as compared to general population. The child can have a simple lesion like VSD or PDA or sometimes may be associated with complex cyanotic or obstructive heart defect like a case of cortriatriatum in a child with ARM.

The co-occurrence of CHD along with GI malformations can significantly affect the natural history of the defect. Association of a significant heart defect can have a long term implications in the operative and post-operative course of the malformations having prolong intensive care unit stay which further adds cost of treatment. As almost all patients of GI malformations require early surgical intervention, they should be evaluated for the presence of CHD at the earliest opportunity which may improve post-operative prognosis.

The association of various risk factors (though the sample size is not large enough) with occurrence of CHD will enable us to investigate further on lines of modifiable risk factors during pregnancy and helps in the prevention of the defect.

Conclusions

There have been limited studies on the topic of association of CHD in patients with GI malformation. This study tries to fill the gap in literature regarding the prevalence and the risk factors in these patients. The occurrence of CHD in patients with GI malformation was found to be high as compared to general population.

The presence of coexisting CHD is an important prognostic factor in patients with GI malformation. Therefore every patient of GI malformation warrants cardiac evaluation.

Limitation of study. Since the study recruited fewer numbers of patients, so the power of the study is low. Risk factors were assessed on questionnaire based performa rather than documented evidence.

No conflict of interests was declared by the authors.

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