EPIDEMIOLOGY OF CONGENITAL GASTROINTESTINAL ANOMALIES IN LIVE NEWBORNS IN TUZLA CANTON

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Objective The aim of this study was to evaluate the epidemiologic characteristics of gastrointestinal anomaly (GIA) in newborns in the Tuzla Canton.

Patients and methods We analyzed retrospectively the medical records of live newborns with GIA born at the Clinic of Gynecology and Obstetrics in Tuzla in the period from 1.1.1998 to 31.12.2007. A questionnaire was used to gather data on the mothers' age, gestational age, birth weight and presence of an anomaly. According to gestational age the patients were divided into two groups. The first group consisted of newborns born before the 37th week of gestation and the second group consisted of newborns with gestational age between 37-42 weeks. According to birth weight the patients were divided into 3 groups: eutrophic, hypertrophic and hypotrophic, and in relation to mothers' age they were grouped into 3 groups: from 16 to 20, from 21 to 35 and from 36 to 40 years.

Results During period in question 69 live newborns were registered with GIA. The lowest prevalence was $6.6/10^4$ in 2001 and the highest prevalence was $31.2/10^4$ in 2004. The most frequent GIA was congenital diaphragmatic hernia with a prevalence of $4.2/10^4$, and the rarest was omphalocele with a prevalence of $0.2/10^4$. There was no significant difference between male and female newborns with GIA. Of the total number of newborns with GIA, 58 or 84.1% were eutrophic, 32 or 46.4% were preterm's with average gestational age of $34,8\pm1,3$ weeks and of the total number of preterm newborns, 29 or 90.6% were eutrophic. Associated anomalies were most frequent with duodenal atresia (75.0%) and rarest in newborns with congenital diaphragmatic hernia (5.3%).

Conclusion The overall prevalence of GIA during the period in question was $15.3/10^4$. Newborns with GIA were equally distributed according to sex and most of them were born from mothers in the age group from 21 to 35 years. GIA in newborns in nearly half of cases were in preterm babies, but a high percentage were eutrophic.

In our study we noted a low association of GIA with other system anomalies.

Key words: Gastrointestinal anomalies ▪ Newborns ▪ Epidemiology ▪ Tuzla Canton

Introduction

Congenital anomalies are anatomical or functional aberrations from the normal spectrum, which are conditioned by genetic, chromosomal, infectious, chemical physical or other harmful agents during intrauterine development. They represent a significant cause of perinatal morbidity and mortality (1). Congenital GIA are associated in more than 50% of cases with other anomalies which complicate treatment of these patients (2, 3, 4). Even GIA are complicated by themselves and long term prognosis is related to the associated anomalies (5). Correct and timely diagnosis and appropriate treatment reduce morbidity, mortality and the occurrence of complications after operative treatment (6). Data on the epidemiological characteristics of congenital GIA in children in the Tuzla Canton are not known. Accordingly, it is not possible to plan programs for prevention, early diagnosis and treatment of these patients.

The aim of this study was to analyze the prevalence of GIA at live newborns in the Tuzla Canton, the distribution of anomalies in relation to the gender of newborns and mother's age, the association of congenital GIA with gestational age and birth weight and the association of GIA with other anomalies.

Patients and methods

The study was undertaken as an epidemiological analysis of GIA in live newborns born at the Clinic for Gynecology and Obstetrics, University Clinical Center, Tuzla over a 10 year period (January 1 1998 - December 31 2007)

Patients

In the period from 01.01.1998. to 31.12.2007. 45,070 live newborns were born at the Clinic for Gynecology and Obstetrics, University Clinical Center, Tuzla. In the same period 50,654 live newborns were born in the Tuzla Canton (7), which means that the live newborn population included in this study represent 89% of all live newborns in the Tuzla Canton. The study registered 69 live newborns born at the Clinic for Gynecology and Obstetrics, University Clinical Center, Tuzla with diagnosed and, with surgical treatment, confirmed GIA. During the period in question there were no live newborns born outside of the University Clinical Center, Tuzla that were referred to Department of Pediatric Surgery because of suspicion of GIA. According to gestational age, the live newborns were divided into two groups .The first group consisted of newborns with gestational age less than 37 weeks and the second group consisted of newborns with gestational age from 37 to 42 gestational weeks. According to birth weight (BW), the live newborns were divided into 3 groups: eutrophic (normal weight for gestational age; birth weight between 10th and 90th percentile), hypertrophic (heavy for gestational age; birth weight above 90th percentile) and hypotrophic (small for gestational age; bith weight less than 10th percentile). In relation to the mothers' age, the newborns were divided into 3 groups: the first group from 16 to 20, the second group from 21 to 35 and the third group from 36 to 40 years.

Methods

The medical records of live newborns with GIA born at the Clinic for Gynecology and Obstetrics were analyzed retrospectively. A questionnaire was used to gather data on mothers' age, gestational age, birth weight and the presence of an anomaly.

Gestational age was determined by the Petrussa score (8) and newborns were classified by means of the standards of live newborns intrauterine growth (9). The research was approved by the institutional ethical committee.

Statistical analysis

The prevalence rate was calculated as the number of live newborns with GIA per 10,000 live newborns. The prevalence trend was shown as an adjustable triennial mean. Standard methods of descriptive statistic were used in data analysis. The Chi-square test for trends was used for testing significances between samples. The hypothesis were tested at the level of significance of $\alpha=0.05$, i.e., the difference between the samples was significant if P<0,05. ArcusQuickStat software was used in statistical analysis (10)

Results

45070 live newborns were born at the Clinic for Gynecology and Obstetrics, University Clinical Center, Tuzla in the period from (January 1 1998 - December 31 2007). A total of 69 live newborns were registered with GIA (40 or 57.9% males, 28 or 40.6% females and 1 or 1.5% newborn with undetermined gender) or 0.15%. The lowest prevalence of GIA of $6.6/10^4$ was recorded in 2001 and the highest, of $31.2/10^4$ in 2004. The prevalence trend was shown as an adjustable triennial mean (Figure 1).
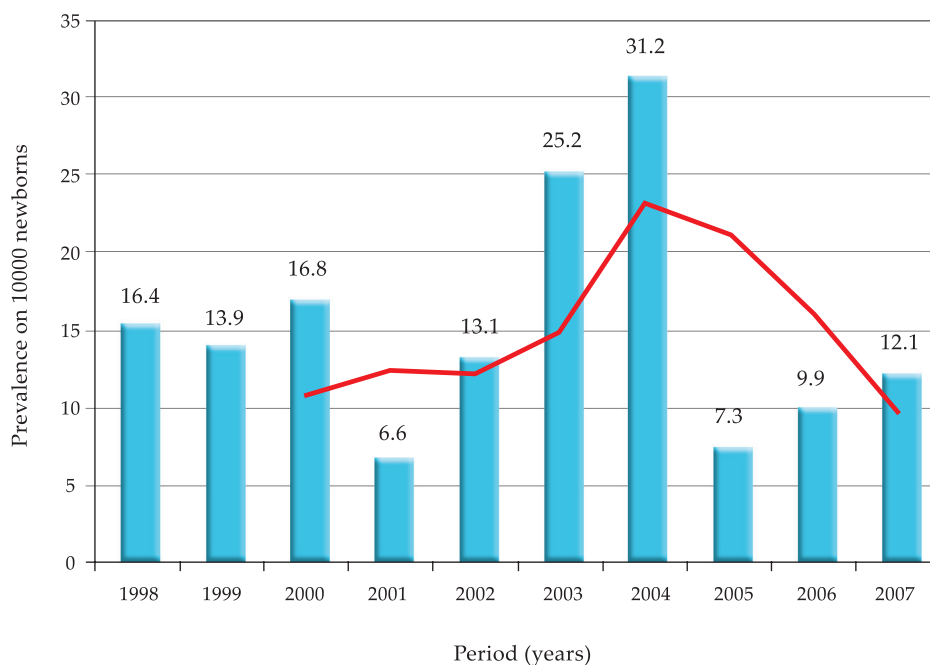

Figure 1 *Prevalence of gastrointestinal anomaly during examined period*

The prevalence of GIA by types of anomaly is shown in Table 1.

Congenital diaphragmatic hernia was the most common anomaly with a prevalence of $4.2/10^4$ live newborns, while omphalocele was rarest with a prevalence of $0.2/10^4$.

Table 2 shows that there was no statistically significant difference in the distribution of GIA in relation to gender in the sample examined (p=0.06). Newborns with GIA were sigificantly more often born by a mother in the 21-35 years age group (p<0.01). GIA were sigificantly higher in male live newborns born by mothers in the 21-35 years age group (p<0.03).

Table 1 The frequency of congenital gastrointestinal anomalies in relation to the type of anomaly

Type of gastrointestinal anomaly	Number	Prevalence*
Esophageal atresia	13	2.8
Duodenal atresia or stenosis	4	0.8
Atresia or stenosis of small intestine	9	2.0
Colonic atresia or stenosis	10	2.2
Congenital diaphragmatic hernia	19	4.2
Omphalocele	1	0.2
Gastroschisis	13	2.8
Total	69	15.3

*Per 10000 live newborns.

Table 2 Distribution of gastrointestinal anomaly in relation to newborn gender and mothers age

Age of mother (years)	Newborns with gastrointestinal anomalies							
	Total		Male		Female		Undetermined	
	n	%	n	%	n	%	n	%
16-20	15	21.8	8	53.3	7	46.7	-	
21-35	53	76.8*	32	60.4**	20	37.7	1	1.9
36-40	1	1.4	-	-	1	100.0	-	
Total	69	100.0	40	57.9***	28	40.6	1	1.5

*χ^2test 6.391, df=1, p=0.01 in relation to mother's age; **χ^2 test 4.654, df=1, p<0.03 in relation to females; *** χ^2 test 3.559, df = 1, p = 0.06 in relation to females.

Table 3 Distribution of newborns with gastrointestinal anomaly according to gestational age in relation to birth weight

Weeks of gestation (n; $\overline{x}\pm SD$)	Newborns with gastrointestinal anomalies						
	n (%)	Hypotrophic		Eutrophic		Hypertrophic	
		n (%)	PM (g; $\overline{x}\pm SD$)	n (%)	PM (g; $\overline{x}\pm SD$)	n (%)	PM (g; $\overline{x}\pm SD$)
<37 (34.8±1.3)	32 (46.4)	3 (9.4)	1723 ±208	29 (90.6)**	2472 ±458	-	-
37-42 (38.6±1.1)	37 (53.6)*	6 (16.2)	2430 ±462	29 (78.4)***	3245 ±353	2 (5.4)	4000±282
Total	69 (100)	9 (100)	2194 ±519	58 (84)	2870 ±574	2 (2.9)	3750±636

BW=Birth weight; *χ^2 test 0.464, df =1, p=0.5 in relation to prematures; **χ^2 test 39.063, df=1, p< 0.0001 in relation to hypotrophic newborns; ***χ^2 test 0.973, df=1, p= 0.32 in relation to hypo-and hypertrophic newborns.

Table 3 shows the average gestational age and average birth weight values for newborns with GIA. In the group of preterm newborns there was a statistically significant number (p<0.0001) of eutrophic newborns, while in the group of term newborns there was no significant difference (p=0.32) in distribution between eutrophic, hypotrophic and hypoertrophic newborns.

In newborns with esophageal atresia associated anomalies were recorded in 5 or 38.5% of cases: in two cases cardiac anomaly and in three cases cheilognatopalatoschisis, syndactyly and Down's syndrome. In 3 or 75% of cases of newborns duodenal atresia or stenosis was associated with cardiac anomaly, Down syndrome and urinary tract anomaly. One newborn (10%) with anorectal atresia or stenosis had associated urinary tract anomaly. One patient with congenital diaphragmatic hernia had associated cheilognatopalatoschisis. In 5 or 38.5% of cases newborns with gastroschisis had associated anomalies, urinary tract anomaly in two patients and small intestine atresia at 3 patients.

Discussion

The overall prevalence of GIA in our study during the period in question was $15.3/10^4$ and was higher than the prevalence recorded in Iran ($10/10^4$) and Saudi Arabia ($13/10^4$) in similarly designed studies (11, 12). The prevalence of $15.3/10^4$ in a Danish study (13) was identical to our result, but this study included stillborns, spontaneous abortions after 20 weeks of gestation and induced abortions. Since our study included only live newborns, with the inclusion of stillborns, the prevalence would have different values. Congenital diaphragmatic hernia was the most common anomaly with a prevalence of $4.2/10^4$ live newborns, while omphalocele was the rarest with a prevalence of $0.2/10^4$. The prevalence of esophageal atresia in our study was not significantly different from the prevalence noticed in the USA (14). The prevalence of duodenal atresia was half the prevalence found in a study from Japan (15). The prevalence of small intestine atresia or stenosis was similar to the results of studies from Australia and Great Britain (16, 17).

The prevalence of omphalocelle was 10 times lower than in studies from Iran (11) and Italy (18). This latter study reports a prevalence of gastroschisis of $0.6/10^4$ which is 4 times lower than that recorded in our study. A study conducted in Iran (11) on 37.951 live newborns, noted the prevalence anorectal anomaly of $5.0/10^4$, which is higher than the prevalence recorded in our study ($2.2/10^4$). The prevalence of anorectal anomalies in our study was three times lower than the prevalence found in a study from Saudi Arabia (12). In studies from Denmark (13) and Iran (11) prevalence values of congenital diaphragmatic hernia were recorded ($2.7/10^4$ and $1.0/10^4$, respectively) which were significantly lower than the prevalence in our study. This heterogeneity could be explained by the geographical (19) and racial (11) differences between mentioned studies. However, it should not be forgotten that nutritional (20) and environmental factors (12, 21) can also influence the prevalence of GIA in some areas. In our study the connection between these factors and GIA prevalence was not analyzed, so future research should pay attention to that. Besides standardization of the collection of epidemiological data on congenital anomalies, the design of these studies should be unified. This could be helpful in a comparison of GIA prevalence between different regions for the purpose of a better understanding of patterns of GIA occurrence and possibly an understanding of their causes.

In our study there was no significant difference in GIA distribution in relation to gender. In similar studies from Iran (10) and India (5) there also were no significant differences in gender distribution of congenital GIA, indicating that the distribution of GIA is equal between the genders. The analysis of prevalence of GIA in relation to the mothers' ages showed that there was a significantly higher prevalence of congenital anomalies in newborns born by mothers aged from 21 to 35 years. Similar results were found by Cho et al., in 2001 (22). This age group represents the largest general obstetric population in a proportion of 83.3% (23). The proportion of eutrophic newborns with GIA in our study was 58 or 84.1%, while 32 or 46.4% newborns were born prematurely with an average gestational age of 34.8 ⯑ 1.3 weeks. The proportion of eutrophic newborns in the group of premature newborns was 29 or 90.6%. Similar results were reported by Escobar et al., (3) and Cohen-Overbeek et al., (24) who found that newborns with upper intestinal obstruction were premature, but within the normal birth weight range.

In a study conducted in Ireland (25) the birth weight values were almost identical to values from our study and the gestational age of 37 weeks was the bottom line of the normal gestational age range. However, Eggink et al (26) reported in 2006 that newborns with gastroschisis in their study were premature and they had lower birth weight. The results of our study show that newborns with GIA were premature in almost half the cases, but a high percentage were eutrophic.

Associated congenital anomalies in our study were noted in the highest percentage in newborns with duodenal atresia (75.0%), esophageal atresia and gastroschisis (38.5%), and in the lowest in newborns with congenital diaphragmatic hernia (5.3%). The frequency of cardiac anomalies, Down's syndrome and skeletal anomalies in a report by Spitz (2) was similar to the frequency of those anomalies found in our study. In a study from the USA (3) Down's syndrome was associated with duodenal atresia in 27%, cardiac anomalies in 51% and urinary tract anomalies in 8.9% of cases. The percentage of the association of Down's syndrome with duodenal atresia was similar to our results. The higher percentage of cardiac and urinary anomalies registered in this study compared to our results can be explained by the insufficient diagnostics at

our institution and the small sample. In a 20-year retrospective postmortem analysis of 130 newborns with congenital diaphragmatic hernia Brownlee et al., (27) discovered the existence of other associated anomalies in 82 newborns (63%). The most frequent anomalies were cardiac (23%), gastrointestinal and abdominal wall anomalies (21.5%) and neural tube defects (19.2%). A study from Australia (28) found some associated anomalies in 54% of newborns with congenital diaphragmatic hernia. In our study only one patients (5.2%) had a skeletal anomaly associated with congenital diaphragmatic hernia, which again indicates the insufficient diagnostics and the exclusion of stillborns. There were rare congenital anomalies associated with gastroschisis, but the most frequent were intestinal atresia in 25% and criptorchismus in 31% of cases (29). The results from our study are similar to the data mentioned above. The relatively small sample or insufficient diagnostics possibly affected the number of other anomalies associated with GIA.

Study limitations

Some limitations were found during the conduct of the study. The study was conducted on a relatively small sample and no stillborns or abortions were included in the study. Additionally, our institution has limited ca-pabilities for diagnostics of associated anomalies. All the above may affect our results, which should be viewed with consideration of these limitations. Future studies should address this problem over a longer period, with a larger sample and the inclusion of stillborns, and fetuses from spontaneous and induced abortions. Additionally, diagnostics must be improved in the prenatal and postnatal period.

Conclusion

The overall prevalence of GIA during the period in question was $15.3/10^4$. The lowest prevalence was $6.6/10^4$ in 2001 and the highest prevalence was $31.2/10^4$ in 2004. Newborns with GIA were equally distributed according to sex and most of them were born by mothers in the 21 to 35 year age group. GIA were found in preterm in newborns in nearly half the cases, but a high percentage were eutrophic. In our study we noted a low association of GIA with other system anomalies, which is most likely a consequence of the insufficient diagnostics of congenital anomalies in newborns at our institution.

Conflict of Interest: The authors declare that they have no conflict of interest. This study was not sponsored by any external organisation.

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