ORIGINAL PAPER

Risk factors related to omphalocele and gastroschisis

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Abstract

Omphalocele and gastroschisis are recognized as congenital malformations with a high mortality. Only 60% of children with such malformations survive until the end of the first year of age. It has been suggested that omphalocele and gastroschisis are associated with other congenital malformations, concerning the bones, the heart and the kidney. The aim of the present study is to determine the risk factors in 12 omphalocele and four gastroschisis cases diagnosed and surveyed in the last four years (November 2003–November 2007) at the Emergency County Hospital of Constanta. In 10 of the 16 cases of the studied group, the subjects resulted from spontaneous premature births. None of the cases in the studied group received the maximum APGAR score, values varying between 6 and 9. The average birth weight in the studied group is 2100 g, with values between 950 g and 2900 g. Maternal age is between 15–21-year-old. Average maternal age in cases of second-degree gastroschisis is 6.5 years younger than the witness population and in case of first degree is 5.8 years younger. 87.5% of children's mothers in studied group are first time pregnant, first time gestant. The mother's socio-economic status may be a risk factor on the occurrence of omphalocele and gastroschisis. 81.25% of children's mother in the studied group have no own income and half are single (mono-parental families). None of the studied cases had a history of congenitally malformed siblings, but half of the cases in the studied group associate congenital malformations of gastro-intestinal tract, locomotor system, kidneys and/or heart. The abdominal wall defect existing in gastroschisis is accompanied by the delay of the intestinal loops differentiation. In all cases of gastroschisis in the studied group, the thin intestine caliber is higher or equal to the one of the thick intestine, the intestinal loops remained outside the abdominal cavity have an aspect characteristic to the fifth month of fetal life.

***Keywords*:** omphalocele, gastroschisis, risk factors, malformations.

Introduction

The abdominal wall congenital malformations omphalocele and gastroschisis have a high mortality rate. Only 60% of children with such malformations survive by the end of the 1st year of age [1, 2].

Studies performed in the last decade show the frequent association of the abdominal wall congenital malformations – omphalocele and gastroschisis – with skeleton dysplasia, congenital diaphragmatic hernia, renal agenesis, as well as the association of omphalocele with trisomias 13, 18 and 21 [3–5].

Currently it is not known the exact certain cause of the forward abdominal wall congenital malformations, it is most probably an intrication of genetic and environment factors, the congenital malformation resulting from the intensity and the moment when these factors action [6].

The authors wish to identify the conditions favorable to the occurrence of abdominal wall congenital malformations: omphalocele and gastroschisis.

Material and Methods

This study concerns 16 cases of newborn with abdominal wall congenital malformations recorded at the Emergency County Hospital of Constanta, Pediatrics Surgery and Orthopedics Clinic: four cases of gastroschisis; twelve cases of omphalocele, among which eleven live newborn babies and one spontaneous aborted at 26 weeks (gestational age).

Study methods consisted of case history; the study of peculiar aspects and anatomical characteristics of malformed abdominal wall; the anatomical macroscopic study of the forward abdominal wall, by dissecting the cases ended in death – including the case of spontaneous abortion; retrospective study of omphalocele and laparoschizis cases reported in specialized literature.

Results

In Constanta County, there was a 10.3% birthrate recorded during November 2003–November 2007. During this time interval, 12 cases of omphalocele and four gastroschisis were recorded. The analysis of gender distribution revealed the predominant alteration of the male sex. One case of omphalocele from 16 in the studied group is female, the other 11 cases of omphalocele, as well as all the gastroschisis cases were male gender (Table 1).

None of the cases in the studied group were awarded maximum APGAR score, the values varying between 6 and 9 (Table 1). The fetal ailment existing at birth in IInd degree omphalocele and gastroschisis was expressed by reduced values of APGAR score. The Ist degree omphaloceles affected the newborn vital signs less than the IInd degree omphaloceles (Table 1).

Table 1 – *Gender and APGAR score in studied group*

Case no.	Congenital malformation	APGAR score	Gender
1.	*IInd degree O*	7	Male
2.	*IInd degree O*	7	Male
3.	*Ist degree O omphalocele*	Spontaneous abortion at 26 weeks	Male
4.	*Ist degree O*	9	Female
5.	*Ist degree O*	9	Male
6.	*Ist degree O*	9	Male
7.	*Ist degree O*	8	Male
8.	*Ist degree O*	8	Male
9.	*Gastroschisis*	6	Male
10.	*Ist degree O*	8	Male
11.	*Gastroschisis*	7	Male
12.	*Gastroschisis*	7	Male
13.	*Ist degree O*	9	Male
14.	*Ist degree O*	9	Male
15.	*Gastroschisis*	7	Male
16.	*Ist degree O*	9	Male

O – omphalocele.

In 10 cases from the total 16 cases of the studied group, the subjects were premature spontaneous births, five cases were born on term, one case of Ist degree omphalocele was spontaneously aborted at the age of 26 weeks.

The average weight in the studied group was 2100 g with values between 950 g and 2900 g (Table 2). The reduced weight was associated with the presence of prematurity criterion.

Table 2 – *Fetus weight in the studied group compared to normal population*

Category	Minimum weight [g]	Maximum weight [g]	Average weight [g]
IInd degree omphalocele	2050	2750	2400
Ist degree omphalocele	950	2900	2250
Gastroschisis	2150	2400	2265
Studied group	950	2900	2100
Normal population	950	4200	3250

The maternal age in the studied group varied between 15 and 21-year-old, with the most reduced value in the most severe case of omphalocele (Table 3).

Table 3 – *Maternal age in the studied group and in the normal population*

Category	Minimum maternal age [year-old]	Maximum maternal age [year-old]	Average maternal age [year-old]
IInd degree omphalocele	15	21	18
Ist degree omphalocele	16	21	18.7
Gastroschisis	19	21	20
Studied group	15	21	19
Normal population	15	49	24.5

Average maternal age in the cases of IInd degree omphalocele was 6.5 years younger than the average maternal age of witness population (Table 3). Average maternal age in cases of Ist degree omphalocele was 5.8 year younger than the average maternal age of the witness population. In the studied group, seven from the 16 mothers were single and nine were married. Only three mothers from the studied group of malformed babies were employed having their own constant income, all the others 13 (81.25%) being homemakers. Fourteen mothers from the total 16 were I-para I-gesta (87.5%); only two mothers were II-para II-gesta.

The most frequent malformations associated with the omphalocele in the studied group were those of the gastro-intestinal tract (stomach, thin intestine, large intestine) and the locomotor system, followed by the congenital malformations of the kidney, heart, and cephalic extremity (Table 4).

Table 4 – *Plurimalformative associations and maternal age in the studied group*

Case no.	Malformation	Associate malformation	Maternal age [year-old]
1.	*IInd degree omphalocele*	Absent	15
2.	*IInd degree omphalocele*	Absent	20
3.	*Ist degree omphalocele*	Macrocephaly, syndactyly, polydactyly	21
4.	*Ist degree omphalocele*	Absent	19
5.	*Ist degree omphalocele*	Absent	18
6.	*Ist degree omphalocele*	Absent	21
7.	*Ist degree omphalocele*	Ventricular septal defect	20
8.	*Ist degree omphalocele*	Bilateral varus equine foot	16
9.	*Gastroschisis*	Stomach partially situated outside the abdominal cavity	20
10.	*Ist degree omphalocele*	Microcephaly. Congenital warped leg. Merged kidneys. Atrophied left urethra. Left mega-urethra	18
11.	*Gastroschisis*	Thin intestine caliber bigger than the one of the large intestine	20
12.	*Gastroschisis*	Thin intestine loops calibers equal to the ones of the large intestine	19
13.	*Ist degree omphalocele*	Varus equine of the left foot	21
14.	*Ist degree omphalocele*	Left kidney hypoplasia	18
15.	*Gastroschisis*	Thin intestine caliber bigger than the one of large intestine	21
16.	*Ist degree omphalocele*	Metatarsus adductor of the left foot	16

The anatomical study emphasized the omphalocele exclusively containing intestinal loops in Ist degree omphalocele cases (Figure 1) and omphalocele containing intestinal loops, liver and other viscera in IInd degree omphalocele cases (Figure 2).

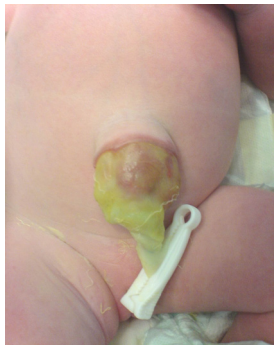

Figure 1 – *First-degree fetal omphalocele covered with a translucid, transparent, amniotic membrane. Intestinal wall defect 3 cm. The umbilical cord is inserted at the base*

The intestinal loops were contained in a translucid, amniotic sac (Figure 1). The umbilical cord was inserted centrally in the sac (Figure 3) or inserted at the base (Figure 2). The dimensions of the abdominal wall defect varied between 3.9–5 cm in the laparoschizis cases and 2.9 cm to 4.1 cm for the Ist degree omphalocele.

The shape of the abdominal wall defects in the gastroschisis cases were vertical opening zone situated sideways from the umbilicus at 1–1.4 cm.

The size of the abdominal wall defects varied between 2.9 cm for the Ist degree omphalocele up to 8 cm for the IInd degree omphalocele.

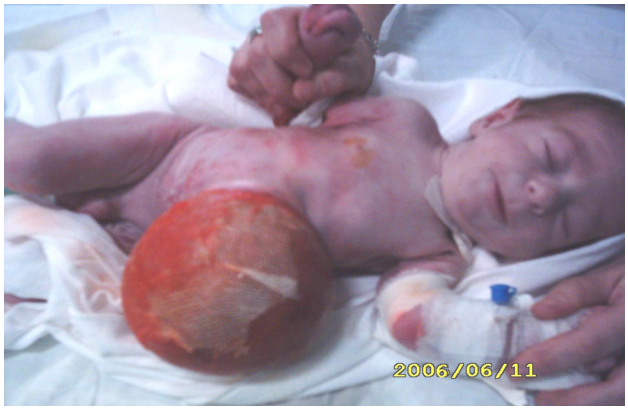

Figure 2 – ***Second degree omphalocele. Umbilical sac torn at birth, omphalocele diameter 15 cm, intestinal wall defect 8 cm. umbilical sac contains intestinal loops, liver, other viscera.***

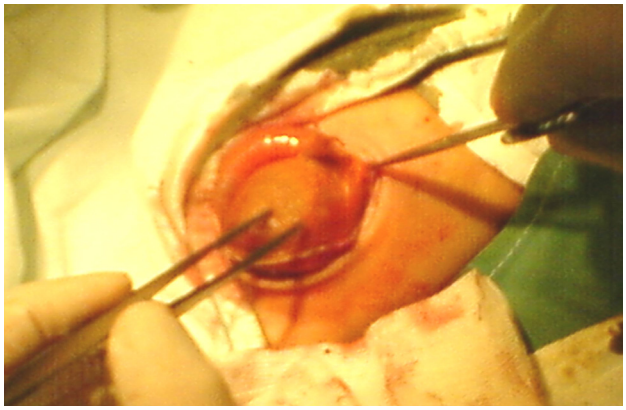

Figure 3 – ***First degree omphalocele. Central inserted umbilical cord. Intact sac of the omphalocele, 3.5 cm diameter. The sac contains intestinal loops. The umbilical ring is wide open.***

Although the present days there is not yet known the exact cause of gastroschisis, the anatomical alterations observed in the studied group suggest the existence of a delayed middle intestine development, which trigger delay in the forward abdominal wall. In all gastroschisis' cases from the studied lot, the thin intestine caliber was bigger or equal to the one of the large intestine (Figure 4). The non-differentiated aspect of intestinal loops left outside the abdominal cavity, were characteristics normal for the 5th month of fetal life, suggesting the delay in the intestine development (case no. 9, Figure 4).

Upon abdominal wall dissection there was increased adherence of teguments to subcutaneous, the two pillars of the superficial inguinal orifice was disposed almost horizontally, the superficial fascia belt was well represented over-umbilicus and almost absent under-umbilicus. The straight abdominal muscles was more adherent to the pod in their over-umbilicus area.

The umbilicus fascia and umbilicus fibred ring was absent on the abdominal wall affected by omphalocele

The Ist degree omphalocele displayed cover tissue with modified macro- and mesoscopic, at the same time maintaining the sub-cutaneous cell tissue, the cutaneous nerve branches and vascularization.

The results obtained by the macro- and mesoscopic anatomical study of the abdominal wall in the cases of Ist degree omphalocele, IInd degree omphalocele and gastroschisis revealed a lack of differentiation and development of all abdominal wall layers, both those of ectodermal origin (tegument layer), as well as mesenchymal layers (subcutaneous, muscular-aponeurotic and serum).

At the Ist degree omphalocele, the sac was usually intact (Figures 1 and 3) and at the IInd degree omphalocele, the sac was torn upon birth (Figure 2).

The abdominal wall integrity was severely affected in gastroschisis (Figures 4 and 5) and IInd degree omphalocele (Figure 2) cases in which abdominal cavity was less developed, with reduced dimensions and the intestinal loops and other abdominal viscera were outside abdominal cavity.

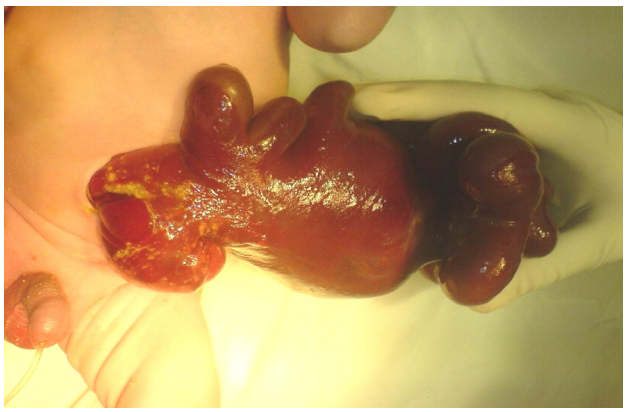

Figure 4 – ***Gastroschisis. Non-differentiated thin intestine. The diameter of the duodenum is bigger than the diameter of the large intestine.***

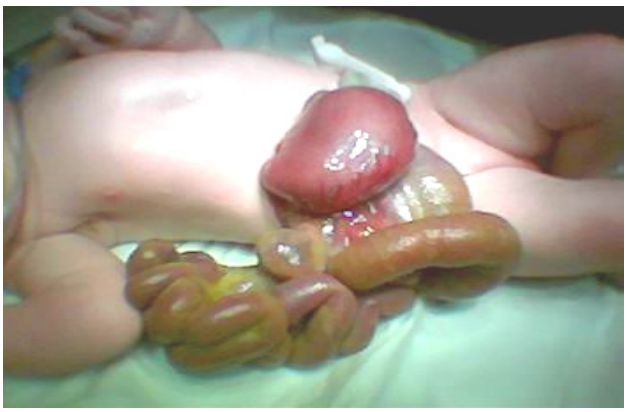

Figure 5 – ***Gastroschisis. Stomach partially situated outside the abdominal cavity, as well as the duodenal loop, the thin intestine loops, the ascendant and transverse colon, until to the spleen flexure.***

Discussion

The results obtained in the present study are confirmed by the EUROCAT [7] report from 2005 that shows an average frequency of 2.52 every 10 000 births for omphalocele and 0.94 every 10 000 births for gastroschisis in Europe during 1980–1990. In a study performed on a period of three decades, Rickham is reporting the frequency of 1/6000 births for omphalocele, 1/30 000 births for gastroschisis. Studies recently published by the *Birth Defects and Development Incapacity National Center, Disease Control and Prevention Center of Atlanta, Georgia, USA*, emphasize the equal alteration of different racial, ethnic groups.

The premature spontaneous births that characterize the cases from our study is conformed by the specialty literature that assesses that one third of omphalocele cases and more than half of gastroschisis' cases are premature [8, 9].

Statistic studies performed in the last 50 years reveal the importance of maternal age in the occurrence of abdominal wall congenital malformations. In a study published by Yang T *et al.* [10], the existence of a significantly younger maternal age is emphasized in 82 cases of omphalocele and 81 of laparoschizis in comparison to the normal population [8, 10, 11]. Abdominal wall congenital malformations' frequency in relation to the maternal age observed in the USA (Yang P *et al.*) reveals that the highest frequency of congenital abdominal wall defects is recorded at the youngest mothers under 20-year-old.

The decreased maternal age constitutes a strong risk factor in the occurrence of abdominal wall congenital malformations. Most authors underline the importance of maternal age in producing forward abdominal wall congenital malformations. The study performed at the *University of South Florida* between 1982–2000, revealed an average maternal age of 21.8 years for gastroschisis and 27.2 years for omphalocele. There is a certain association between maternal age and gastroschisis [11]. The young maternal age ≤20-year-old is statistic significant associated with the increased risk of gastroschisis. For this age group, there is a constant, statistic significant increase of gastroschisis cases in Norway, from 0.5/10 000 in 1967 to 1.3/10 000 in 1975, up to 2.9/10 000 in 1999, while at the same time period, the frequency of omphalocele is maintained to 2.1/20 000 births [12].

The mother's social-economic status may be a risk factor in the occurrence of omphalocele and gastroschisis; in the studied group, seven mothers from all 16 are single and nine are married. Only three mothers from the studied group of malformed babies have their own constant income, a result comparable to the data reported in 2004 by the *Medical Birth Register of Norway* [13], where 7% of the babies with congenital malformations of the abdominal wall (omphalocele and gastroschisis) belong to mono-parental families between 1967–1999.

The results obtained in our study as well as the studies published EUROCAT [7] and the *University of South Florida* in 2004 confirms the predominant alteration of the male sex in cases of omphalocele and gastroschisis.

The literature describes the association of the I-para status with higher frequency of omphalocele [6, 8].

Taking multivitamins during pregnancy seems to influence the occurrence of abdominal wall congenital malformations: omphalocele and gastroschisis. In the studied group, none of the mothers of children with omphalocele or laparoschizis did receive multivitamins during pregnancy. The importance of this particularity is confirmed by the studies published by the *Congenital Malformations Study National Center and the Disease Control and Prevention Center in Atlanta, Georgia, USA*. These studies have evaluated the connection between mothers using multivitamins and the frequency of the omphalocele at 72 children with congenital omphalocele and 3029 children without congenital malformations, born between 1968–1980 in a metropolitan area. Comparing cases in which no multivitamins during pregnancy were used with cases where multivitamins were used in the last trimester of pregnancy, it was revealed the statistic significant increased frequency of omphalocele (as single malformation, as well as in association with other malformations). The same study shows that the use of multivitamins during pregnancy is associated with a reduction of 60% of the risk of symptomatic omphalocele.

The high incidence of the intact sacs of the Ist degree omphalocele cases is comparable to the remarks of Driver CP *et al.* [14] and the results obtained by Marc and Rowe, who assess that 80–90% of omphalocele cases display intact sac.

The study of congenital malformations of the abdominal wall performed in the USA, at the *University of South Florida* between 1982–2000, emphasized the existence of plurimalformative associations at 76% of omphalocele cases and 23% of gastroschisis cases. In the studied group, half of omphalocele cases and all the four cases of gastroschisis associate other congenital malformations, but none of the studied cases has a history of siblings with congenital malformations. The omphalocele as an isolated congenital malformation, "non-syndrome", is one sporadic malformation, in which the recurrence risk is deemed negligible [3, 6]. This result is confirmed by the studies published by Pride in England, stating that the omphalocele is generally considered as a sporadic malformation with a negligible recurrence risk. EUROCAT report for the period 1980–1990 shows the presence of multiple congenital malformations at 54% of omphalocele cases and the existence of isolated, single malformation in 79% of laparoschizis cases.

Conclusions

The young maternal age at birth, and the low socio-economic level are the main maternal risk factors associated to pregnancy that can contribute to the increased occurrence of omphalocele and gastroschisis. One third of the children from the studied group belong to mono-parental families.

The obtained results emphasize the association between young maternal age and occurrence of omphalocele and gastroschisis. At the same time, in the studied lot, the most severe cases of omphalocele are noticed at the youngest mothers.

Omphalocele and gastroschisis mainly affect male children of I-para and I-gesta mothers. Both omphalocele and gastroschisis are associated with premature birth and low birth weight.

Omphalocele of smaller dimensions displays intact sac, unlike giant omphalocele, where the sac is torn at birth.

The defect of abdominal wall existing in gastroschisis is accompanied by the delayed differentiation between intestinal loops.

The obtained results contribute to the identification of factors favoring to the occurrence of forward abdominal wall malformations, but do not show the existence of a specific teratogenic factor.

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