The influence of chorionicity, amniocity and type of twins development on the twins pre-birth mortality and occurrence of congenital abnormalities in fetus from twin pregnancies

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Abstract

Background: The aim of the study was to assess the relationship between twins chorionicity and amniocity and prenatal mortality and occurrence of inborn defects as well the assessment of the connection between the type of twin development (symmetric, divergent) and the mortality and occurrence of congenital abnormalities.

Material and method: Material contained 606 twin pregnancies monitored and resolved in the II Clinic of Gynecology, Obstetrics and Neonatology of the Medical University in Wroclaw between years 1990-2010. Data concerning the pregnancies course was obtained from pregnancy files and obstetric histories. The analysis included the information about chorionicity, twins development type, antepartum death or asphyxia, presence of congenital abnormalities, incidence of twin-to-twin transfusion syndrome (TTTS). The statistical analysis was carried out by means of chi² test. The statistically significant rate was p < 0.01. Results: The examined group included 433 dichorionic diamniotic pregnancies DCDA (71.45%), 167 monochorionic diamniotic MCDA (27.56%), 5 monochorionic monoamniotic MCMA (0.83%) and 1 pregnancy of unestablished chorionicity. The congenital abnormalities were observed in 26 pregnancies (4.29%): 12 – DCDA, 13 – MCDA, 2 – MCMA. Symmetric development (defined as the mass difference between fetuses lower than 15%) concerned 397 fetuses (65.51%), divergent – 208 (34.32%), and in one case was impossible to evaluate (unseparated twins). 31 cases of twin-to-twin transfusion syndrome (TTTS) were diagnosed (5.12%). It was proven that in the group of MCDA fetuses the rate of congenital abnormalities and prenatal mortality were significantly higher than among DCDA twins. In case of divergent type of twins growth the incidence of inborn defects and mortality were higher than in twins of symmetric development type. Conclusions: Antepartum mortality is significantly higher in monochorionic than dichorionic twins. Congenital abnormalities are significantly more frequently observed in monochorionic twin fetus. In case of divergent development type the antepartum twin mortality is higher than in the symmetrical one. Inborn defects are significantly more often diagnosed among twins of the divergent development type. Antepartum twin mortality is higher in twins diagnosed with congenital abnormalities.

Key words: chorionicity, amniocity, pre-birth mortality, congenital abnormalities, twins

Introduction

Twin pregnancies in Europe account for 1-2% of all pregnancies [1, 2]. This percentage differs depending on world region and it ranges from 0.6% in Asia to 4% in Africa (in Nigeria as much as 1 in 11 pregnancies is a twin pregnancy) [1]. In Poland twin births make about 1% of all deliveries [3]. Once being obligatory Hellin’s rule (the appearance probability of a twin birth equals 1:80, triplet – 1:80 etc.) is currently out-of-date since multiple pregnancies occur more often [4]. The increase in the incidence of multiple pregnancies is associated with the use of assisted reproductive technology (in vitro fertilization – IVF, infertility hormone treatment), social transformation (late maternity), as well as change of environment conditions [1].

Regarding the mechanism of fertilization we distinguish mono- and dizygotic twins. 1/3 of twins being born are children originating from monozygotic pregnancies, 2/3 – dizygotic [5]. Monozygotic pregnancies arise from division of one egg cell fertilized by one sperm. Reasons of zygote division and development of two embryos are not completely clear. Setting free more than one egg cell during the ovulation is conditioned by raised FSH level in mother’s organism [1]. Where as dizygotic twin pregnancies arise when two separate ova are independently fertilized by two separate sperm resulting in two separate zygotes [6]. Furthermore the literature describes the phenomenon of overfertilization (superfecundation). It is the fertilization of two or more ova from the same cycle by sperm from separate act of sexual intercourse performed in time of 3-4 days [7].

The factors having influence on probability of increase of developing a dizygotic pregnancy are: race, mother age greater than 35 years, multiparity (3 and
more deliveries), increased body mass index (BMI) and height of mother, frequent sexual intercourses, history of multiple pregnancies and treatment with ovulation stimulation drugs [7, 8]. The highest rates of dizygotic twin pregnancies are observed among black race, less among the Caucasian and rarely among Asians. The influence on the higher frequency of monozygotic pregnancies is mainly associated with in vitro fertilization [9].

Ultrasonographic assessment of zygosity is difficult and is characterized by a low predictive value. However it has clinical meaning, because it specifies the diagnostic investigation range in case of suspicion of genetic defect [3].

The other twin classification concerns their chorionicity and amniocity. Binovular twins are always dichorionic diamniotic (DCDA) and uniovular can be as well as mono- and dichorionic, depending on the time of division. If this division takes place in the first 3 days after fertilization DCDA twins develop; if between 4 and 8 day – they have a common chorion and two separate amnions (MCDA – monochorionic diamniotic). Divisions after the 8 day of development share a chorion and amnion (MCMA – monochorionic monoamniotic). After the 13 day there exists the danger of an incomplete fetus separation, incorrectly called conjoined or siamese twins [1, 10].

Nowadays the only reliable method diagnosing twin pregnancy is ultrasonographic examination. The number of pregnancy follicles in utero can be already evaluated in the 4 week of pregnancy. This examination shall be repeated after 3-4 weeks because of the “vanishing twin” phenomenon. It is a quite common phenomenon which occurs in the 20-50% of twin pregnancies, also known as fetal resorption. Vanishing twin is a fetus which dies in utero and is then partially or completely resorbed by the co-twin [11]. In the II trimester, death of one of fetuses does not result in its resorption, but mumification and flattening, also known as “fetus papyraceus” [12].

Fetus chorionicity can be determined already at 5 weeks after conception, but reliable assessment of amniocity cannot be made before the eighth week, when amnion membrane can be clearly visualized. The late second and third trimester are a real challenge for ultrasonographist, because defining amniocity and chorionicity must rely on following characteristics: chorion localization, sex, place of fetal membranes origin, their thickness and area [13].

In the 4-5th week of pregnancy chorion presents as a thick, hiperechogenic structure localized at the margin of the pregnancy sac. As DCDA pregnancies develop the chorion of both pregnancy sacs forms a picture similar to two rings (“two ring sign”). A picture of one pregnancy vesicle, in which two fetuses develop, is described as a “one ring sign” and indicates a monoamniotic pregnancy.

Visualizing four layers (2 amnions and 2 chorions) of the septum dividing the fetus and its thickness over 2 mm indicates monochorionic pregnancy, and measurement of the thickness over 5 mm characterizes dichorionic pregnancies [14]. In a monochorionic diamniotic pregnancy the septum composed of two amnion layers may not be seen in USG until the 8-10th week pregnancy. In dichorionic pregnancies thickness of the septum dividing the fetus is reduced in the course of pregnancy. Whereas in monochorionic pregnancies such changes in septal thickness are not observed [14].

Penetration of the chorion between the membranes in place of their implantation in the placenta is also a characteristic phenomenon of a dichorionic pregnancy – which is known as “lambda sign”. The lambda sign may not be visible in the second half of the pregnancy. Thin (< 2 mm), two-layer-septum attaching perpendicularly to the placenta, without chorion penetrating between amnions (“tau sign”) is typical for a monochorionic pregnancy. The meaning of the “tau sign” is reduced in the second half of the pregnancy, because in the course of dichorionic pregnancy the “lambda sign” changes and it imits of the “tau sign” [15].

On the basis of a study carried out by Bora and Bracero it can be concluded, that chorionicity defining should always take place in the first trimester of pregnancy [16, 17]. Results of examinations carried out in the second trimester of pregnancy and based only on the thickness of fetal membranes found their confirmation in a histopathological examination only in 77,3% cases, whereas USG examinations performed in the first trimester in 98%.

Fetuses from twin pregnancies have higher mortality rate and more frequent occurrence of various inborn defects than single fetus. It is generally accepted, that monochorionic twins have a higher rate of complications including lethal ones. Due to the large database concerning twins, which exists in II Department of Gynecology, Obstetrics and Neonatology of the Medical University in Wroclaw, we decided to look closer at this problem. An undoubted advantage of this database is the fact, that all of the analyzed pregnancies were led and finished in a one clinical center.

Not only chorionicity and amniocity were analyzed, but also frequency rate of congenital defects and antepartum deaths. The attention was paid to type of fetus
development, as well as to changes in particular twin groups, which have taken place for the last two decades.

**Background**

The aim of the study was to assess the relation between chorionicity and amniocity and prenatal mortality among twins and occurrence of inborn defects as well the assessment of connection between the prenatal mortality and the type of twin fetus development (symmetric, divergent) and occurrence of congenital abnormalities.

**Material and method**

Material contained 606 twin pregnancies monitored and resolved in the II Department of Gynecology, Obstetrics and Neonatology of the Medical University in Wroclaw in years 1990-2010. Data about the course of pregnancies was obtained from pregnancy files and obstetric histories. The analysis included the about chorionicity, the type of twins development, prenatal fetal death or asphyxia, presence of abnormalities and the incidence of twin-to-twin transfusion syndrome (TTTS).

The chorionicity was defined by means of USG examination performed in the first trimester of pregnancy. The result was based on the observation of following features: one or two ring sign, lambda sign or tau sign, the number of chorions and thickness of the septum between fetuses. Additionally, in the second trimester fetal sex and localization and number of placentas were assessed [7, 9, 16, 17, 18, 19].

The symmetric development of twins was defined as the mass difference between fetuses lower than 15% [18].

The following dependences were statistically analyzed with chi² test:

- antepartum mortality and chorionicity in twin pregnancies;
- mortality and type of twins development;
- occurrence of abnormalities and chorionicity in twin pregnancies;
- occurrence of abnormalities and type of twins development;
- occurrence of abnormalities and pre-birth mortality in twin pregnancies.

The mean age of mothers was 29.1 years (min 18, max 47).

In the examined group there were 283 primiparas (46.7%). By means of chi² test it was examined, whether there is a relationship between the prenatal mortality, occurrence of inborn defects, the type of development of twin pregnancy, the chorionicity and the fact, that the mother was a primipara.

**Statistical analysis**

The statistical analysis was based on the chi² test. p<0.01 was considered as a statistically significant value.

**Results**

Among the 606 twin pregnancies analyzed between the years 1990-2010 in the II Department of Gynecology, Obstetrics and Neonatology of the Medical University in Wroclaw there were 433 dichorionic diamniotic pregnancies DCDA (71.45%), 167 monochorionic diamniotic MCDA (27.56%), 5 monochorionic monoamniotic MCMA (0.83%) and 1 pregnancy of unestablished chorionicity (Fig. 1).

![Figure 1](image1.png)

**Fig. 1.** The frequency of intrauterine death of one of the fetuses in twin pregnancies in 1990-2010

![Figure 2](image2.png)

**Fig. 2.** The percentage of twins DCDA, MCDA and JKJO in the study group (DKDO – dichorionic diamniotic, MCDA – monochorionic diamniotic, MCMA – monochorionic monoamniotic, N – not specified)
The congenital abnormalities were observed in 26 cases (4.29%): 12 – DCDA, 13 – MCDA, 2 – MCMA (Fig. 2). Symmetric development was observed in 397 fetuses (65.51%), divergent – 208 (34.32%), and one case was impossible to evaluate (unseparated twins). There were 9 cases of congenital abnormalities in the group of symmetrically developed fetuses, whereas in the group of divergent development there were 16. Connections between occurrences of inborn defects and the type of fetal development and between the development type and pre-birth mortality were examined. In both cases this connection was statistically significant (p < 001).

The following congenital abnormalities were observed: amorphous fetus (1) (probably TRAP – twin reversed arterial perfusion syndrome), double-vessel umbilical cord (1), umbilical cord velamentous insertion (1), obstructive uropathy (1), esophageal atresia (1), unseparated fetus with one umbilical cord (1), epispadiasis (1), finger accretion (1), Down syndrome (1), meningocoele (1), club foot (1; in both fetus), umbilical hernia (2), hypospadiasis (2), heart defects (2), acrania (2), hydrocephalus (3) and other not described abnormalities (4). In the collected material prevailed defects concerning one of twins. Only in one pair were observed abnormalities of similar exacerbation in both fetuses – club feet. Interesting, that in our material, in 26 pregnancies with congenital abnormalities only one case of genetic defect was stated – Down syndrome.

Among monochorionic diamniotic twins 31 TTTS cases were diagnosed (5.1%).

Intrauterine death and simultaneous occurrence of defects concerned 5 fetuses (heart defect – 1, Down syndrome – 1, finger accretion – 1, hydrocephalus – 1, other – 1).

Among dead fetuses, in 3 of them, the symmetric development type was described, in 22 the divergent one. In 7 cases TTTS syndrome occurred. In 5 pregnancies the death of fetus localized closer to the uterus fundus was accompanied by the asphyxia of fetus localized in its lower segment.

In years 1990-2000 193 twin pregnancies were registered, in three of them one of fetus was dead before birth (1.6%). In years 2001-2010 413 twin pregnancies were registered, in 22 of them (5.3%) the pre-birth death of one fetus was observed (Fig. 4).

It was proved, that in the MCDA group congenital abnormalities were significantly more often and pre-birth mortality was higher than in the DCDA group. In case of divergent development type of fetus occurrence of congenital defects was more often observed and mortality was higher than in twins of symmetric development type.

No relationship was detected between age of mother and occurrence of abnormalities in fetus, fetus death, twins development type and chorionicity in twin pregnancies. However, the mean age of women, whose children showed congenital abnormalities, was almost two years lower (27.31 vs 29.18) than in women, who bore children without inborn defects.

It was demonstrated, that twins statistically more often are characterized by the divergent development type when their mother is a primipara. In children of primiparas the frequency of pre-birth death, occurrence of divergent development type and monochorionicity was similar to children of mothers being in second or next pregnancy.
Discussion

Monozygotic twinning seems to be an anomaly in itself, with increased number of spontaneous abortions and congenital structural defects. After 30 weeks of pregnancy both monozygotic and dizygotic twins’ rate of intrauterine growth is slower than the growth of singletons. It is believed that the development of twins in early pregnancy is biochemically programmed so that they are more mature compared to singletons in the same gestational age [1, 19-21]. Besides, intrauterine conditions (reduced space in the uterus, the deterioration of efficiency of utero-placental unit) make the twins unable to grow as fast as fetuses from single pregnancies. The incidence of growth disorders in multiple pregnancies is significantly higher than in singleton pregnancies and fetal growth is determined by their genetic potential and placenta capacity [18]. Therefore, it is advisable to use from 28th week of pregnancy separate centile ranks for twin pregnancies, which is very important for the qualification to category SGA (small for gestational age) [18, 20]. Readiness to contraction of the uterus appears after 34 weeks in a twin pregnancy, in a triplet – after 32 weeks [20].

In our material we analyzed 606 cases of twin pregnancies 71.45% were dichorionic and 28.38% monochorionic. This data is similar to results reported by other research centers (eg. dichorionic 79.9%, monochorionic 20.1% in Baghdadi et al. [22]).

Congenital abnormalities were observed in 26 pregnancies (4.29%): 12 dichorionic, 13 monochorionic diamniotic and 2 monochorionic monoamniotic. We do not have data about zygosity of twins. But it is known monozygotic twins are affected by 2-3 times greater risk of birth defects than dizygotic [1]. The heart defects are the most common congenital malformation [23], however this was not observed in our study. Among 26 cases of reported defects, heart defects were diagnosed only twice (8%). In twin pregnancies with an inborn defect, there has been diagnosed only one case of genetic defect - Down syndrome. What is interesting, we observed no association between mother’s age and the incidence of birth abnormalities in fetuses. Mothers of children with defects were on average almost two years younger than mothers of children without defects (0.01 < p < 0.05).

We found that congenital abnormalities occur more frequently among twins with divergent than symmetric type of development; the divergent type also have increased prenatal mortality. There is also relationship between type of development and chorionicity of twins (p < 0.01). Among monochorionic twins divergent type of development was significantly more common. Divergent type of development is significantly more often seen among primiparas (p < 0.01). Similar findings were presented by Murakami [24] who recommended more careful care for women whose first pregnancy is a twin pregnancy.

Analyzing only twins from DCDA group we found that there is a statistically significant association between mortality and divergent type of development. A similar dependence is not observed in the group of monochorionic twins, so only dichorionic twins with divergent type of development is a negative factor.

The frequency of intrauterine fetal deaths in developed countries is 0.3-0.4% [25]. In Poland in 1999-2008 prenatal mortality for newborns weighing more than 500 g was 5.08 %. In Lower Silesia, 4.9 % stillbirths was observed for the same age group in the same period of time [26]. For twin pregnancies, frequency of intrauterine death of one fetus is estimated at 0.5-6.8% [27].

In 25 pregnancies (4.13%) intrauterine fetal death was diagnosed. All these cases concerned death of only one fetus. Intrauterine death and simultaneous occurrence of defects concerned 5 fetuses (heart defect – 1, Down syndrome – 1, finger accretion – 1, hydrocephalus – 1, other – 1).

Among 25 cases of intrauterine deaths, 40% concerned DCDA pregnancies, 52% – MCDA and 8% – MCMA.

According to the world literature, 50-70% cases of intrauterine deaths of one fetus concerns MCDA twins [28], and perinatal mortality of MCDA twins is 2-3 times higher than DCDA [29, 30]. In our study mortality of MCDA twins was almost 4 times higher than DCDA twins (DCDA 2.3%, MCDA and MCMA together – 8.7%). Among dead fetuses, 16 were localized closer to uterus fundus; in 5 of such pregnancies the death of fetus localized closer to the uterus fundus was accompanied by the asphyxia of fetus localized in its lower segment. Intrauterine fetal death of one twin, not only increases the risk of death or illness (intestinal atresia) of the second twin, but the long-term complications such as cerebral palsy or learning disability, especially when it concerns monozygotic pregnancy, extremely if it is monochorionic [31].

Number of twin births in the II Department of Gynecology, Obstetrics and Neonatology of the Medical University in Wroclaw increased. They reasons were discussed in the introduction: broad use of assisted reproductive technology (in vitro fertilization – IVF, infertility hormone treatment), late maternity, change of environ-
ment conditions. In years 1990-2000 193 twin pregnancies were registered, in three of them one of fetus was dead before birth (1.6%). In years 2001-2010 413 twin pregnancies were registered, in 22 of them (5.3%) the pre-birth death of one fetus was observed. This increase in mortality can be explained by the increasing age of pregnant and worsening environmental conditions.

Basing on our observations, we have shown that there is a statistically significant relationship between chorionicity and twin antenatal mortality ($p < 0.05$) – mortality was higher in monochorionic twins. This relationship is consistent with the common opinion. But also contradictory opinions can be found. For example, Baghdadi et al. [22] in their work did not find this relation. The main objection against earlier works is that analyzed cases were not monitored in the same hospital during whole pregnancy and infant care. Our study fulfills this condition, also the analyzed group is more numerous than Baghdadi’s research group (606 vs 238). Our observation confirms the study by Glinianaia et al. [30]. However, Hack et al. basing on analysis of 651 pregnancies in the years 1907-1938 presumed that modern obstetrics is more effective in reducing mortality in only dichorionic twins [32]. Basing on the above considerations we believe that the definition of chorionicity in the first trimester of pregnancy is very important for the proper monitoring and resolution of a twin pregnancy.

Another problem concerning dicorionic twins is twin-to-twin transfusion syndrome (TTTS). In the literature TTTS is mentioned as one of the main causes of intrauterine death or medical intervention [15, 22].

Among monochorionic diamniotic twins 31 TTTS cases were diagnosed. In 7 cases it was accompanied by intrauterine death of one twin. In more than half of the cases of intrauterine death of one monochorionic fetus TTTS was diagnosed. In Mahony’s et al. study TTTS concerns most of observed monochorionic fetuses [29].

In the case of death of one of the twins, specialist medical consultation, an individual management plan as well as psychological support for parents is necessary. Pregnancy in such situation should be monitored at 3rd reference center for perinatal care. Chorionicity and any possible defects should be confirmed. Conservative treatment is recommended for up to 37 weeks of pregnancy, unless there are other indications requiring earlier resolution of pregnancy. There are no contraindications to vaginal birth in the case of death of one of the fetuses. Histopathological examination of dead fetus and the placenta is recommended. Living child should be under long-term medical care [31, 33].

Conclusions
Antepartum mortality is significantly higher in monochorionic than dichorionic twins. Congenital abnormalities are significantly more often diagnosed in monochorionic twin fetus than dichorionic. In case of divergent development type the antepartum twin mortality is higher than in the symmetrical one. Inborn defects appear significantly more often among twins of the divergent development type. Antepartum twin mortality is higher in twins diagnosed with congenital abnormalities. Divergent type of development concerns more frequently primiparas than multiparas. Divergent type of development affects the antenatal mortality of dichorionic twins, but this relation is not observed in case of monochorionic twins.

References


