

Alteration of the amniotic fluid and neonatal outcome

*Enrico Volante, Dandolo Gramellini, Sabrina Moretti, Christine Kaihura,
Giulio Bevilacqua*

Department of Gynaecology, Obstetrics and Neonatology, University of Parma, Italy

Abstract. Quantitative and qualitative alterations of the amniotic fluid complicate 7% of the pregnancies. Polyhydramnios complicates 1-3% while oligohydramnios involves 3-5% of the pregnancies. The most common causes of polyhydramnios are fetal abnormalities, maternal diabetes and twin pregnancies, but are idiopathic in the 60%. Perinatal mortality has been reported to range between 10-30% while the risk of preterm birth reaches up to 22% in pregnancies complicated by polyhydramnios. The neonatal outcome, in cases where polyhydramnios is due to fetal-neonatal abnormalities, depends on the underlying pathology. Polyhydramnios due to defects in intestinal canalisation in particular, has been correlated to good neonatal prognosis. In our experience no early postoperative deaths occurred in a group of 16 newborns consecutively admitted to our unit in the last two years, with abnormalities of the gastrointestinal tract with need of surgery within the second week of life. Most cases of oligohydramnios are due to premature rupture of membranes, other causes are fetal abnormalities, such as urinary tract malformations, or chromosomopathies and drugs e.g. NSAID's. Oligohydramnios of mild entities is often associated to preterm birth, fetal growth restriction. In some cases of oligohydramnios, neonatal survival is highly conditioned by pulmonary hypoplasia which develops with rates that range between 13 and 21%. Neonatal prognosis is often disastrous in cases with severe oligohydramnios, which however could be improved by amnioinfusion, which restores an amniotic fluid volume sufficient in reducing the adverse environmental effects and in prolonging, where possible, pregnancy. Beside the quantity also the quality of the amniotic fluid may be related to the neonatal outcome. Finding of some inflammatory factors (interleukines) in the amniotic fluid seems to be significantly correlated to periventricular leucomalacia (PVL), cerebral paralysis and long-term neurological abnormalities, both in the preterm and term neonate. Therefore, increase of the cytokines in the amniotic fluid could give information not only of the infection but also regarding the risk of developing neurological sequelae in neonatal period. Diagnosis and therapy for pathologies that alter the amniotic fluid have progressed, however efforts have still to be made in the identification and search for those quantitative-qualitative alterations of the amniotic fluid, for their potential implications on neonatal outcome.

Key words: Amniotic fluid, polyhydramnios, oligohydramnios

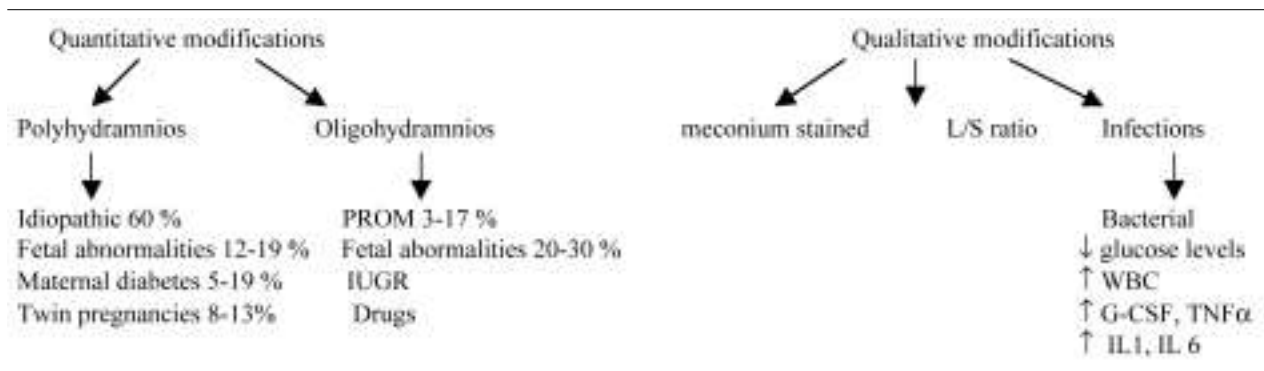
The fetus and the newborn cannot be considered as two distinct entities. Any situation that compromises the fetus' well-being e.g. alterations in the amniotic fluid quantities and properties, could influence the clinical status of the neonate at birth, and in severe cases, compromise its future.

Quantitative and qualitative alterations of the amniotic fluid have been distinguished, the earlier re-

presented by alterations in the volume and these complicate 7% of the pregnancies while the latter are given by modifications in the amniotic fluid composition (markers of pulmonary maturity, meconium stained fluid, bacteria, cytokines) (Table 1).

Polyhydramnios complicates 1-3% of the pregnancies while oligohydramnios involves 3-5% of the pregnancies; most cases moreover are of mild entities,

Table 1. Alterations in the amniotic fluid



and when observed at term, rarely lead to severe neonatal sequelae. On the contrary, cases with severe oligohydramnios, or polyhydramnios, that present in the second-third trimesters could lead to high rates of perinatal morbidity and mortality, both as a result of alterations in the amniotic fluid volume or secondary to an underlying pathology.

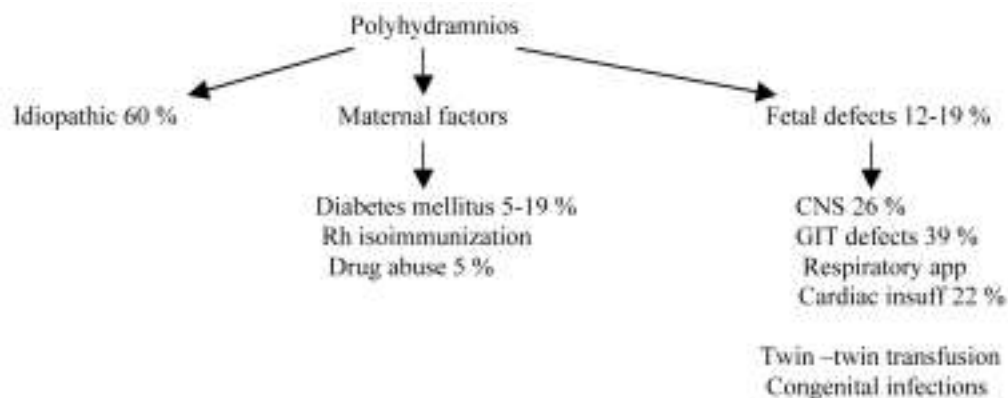
The most common causes of polyhydramnios are summarised in table 2. Amongst the possible causes, one that is worth mentioning is drug-abuse in pregnancy. Infact, some authors report an incidence of polyhydramnios (AFI >24 cm) on the average of 3.9% in normal controls with respect to 28,6% in a group of 63 drug-addicted pregnant women. An explanation of this could be the depression of the central nervous system which could in turn lead to reduction in swal-

lowing, while hypoxia could alter the “production-reabsorption” cycles of the amniotic fluid. Some of the “idiopathic” polyhydramnios, about 5%, according to some authors could actually be of this kind (1).

As regards to neonatal outcomes in pregnancies complicated by polyhydramnios, perinatal mortality has been reported to range between 10-30% while the risk of preterm birth reaches up to 22%.

However in those cases of idiopathic polyhydramnios, no increase in preterm birth, low birth weight and low Apgar scores at 5 min, in admission to the intensive care unit or in the perinatal mortality were observed compared to those born from pregnancies with normal amniotic fluid volume, although higher incidences of fetal malpresentation, of cesarean sections and of macrosomia were reported (2).

Table 2. Volume abnormalities: polyhydramnios



Finding of polyhydramnios in diabetic patients has decreased remarkably due to increased control, and conversely, cases of isoimmunization are now rare.

In cases where polyhydramnios is due to fetal-neonatal abnormalities, the outcome depends on the underlying pathology.

Polyhydramnios due to defects in intestinal canalization in particular, has been correlated to good neonatal prognosis. In our experience no early postoperative deaths occurred in a group of 16 newborns consecutively admitted to our unit in the last two years, with abnormalities of the gastrointestinal tract with need of surgery within the second week of life. In these cases, as in all the cases with abnormalities diagnosed in utero, the prenatal counselling is extremely important as the planning of delivery in a tertiary care centre, with a neonatal intensive care unit and a pediatric surgery.

In the neonates born from pregnancies complicated by oligohydramnios the prognosis is poor and the mortality rate reach value of up to 76%.

Most cases of oligohydramnios are related to premature rupture of membranes, and therefore at risk of foetal infections with all the associated complications linked to infection, or to either foetal abnormalities, or chromosomopatias (Table 3). Oligohydramnios is often associated to preterm birth, fetal growth restriction, with a higher risk of adverse outcomes given by a higher rate of fetal distress and of meconium stained fluid, and pulmonary hypoplasia (3) (Table 4).

Neonatal prognosis is often disastrous in cases with severe oligohydramnios, which however could be

improved by amnioinfusion, which restores an amniotic fluid volume sufficient in reducing the adverse environmental effects and in prolonging, where possible, pregnancy.

These therapeutic procedures have to-date become of routine use in many centres, and many studies report higher rates in pulmonary hypoplasia, of both perinatal and neonatal mortality and of abnormal neurological outcomes in control groups compared to those amnioinfused (4-5).

In our experience the amnioinfusion reduce perinatal mortality and morbidity: in 80 pregnancies with severe oligohydramnios, 35 treated with amnioinfusion versus 45 conservatively treated ones, the incidence of neonatal deaths is lesser (5% vs. 33%; $p < 0.05$) in the amnioinfused group and the cases of cerebral haemorrhage $> 2^\circ$ or periventricular leukomalacia were more frequent in the no-amnioinfused group (7 out of 27 vs. 0 out of 15; $p < 0.05$) (6).

In oligohydramnios, neonatal survival is highly conditioned by pulmonary hypoplasia which, in cases with severe reduction in the amniotic fluid volume, can reach the frequency of 21%. The ethio-pathogenesis of this severe neonatal respiratory disease seems related to the compression of the ribcage, absence of respiratory movements, loss of pulmonary amniotic fluid, reduced perfusion of the fetal lungs though diagnosis in-utero of this pathology remains a challenge.

It however seems to be possible with the aid of clinical data, fetal biometry and velocimetry, to diagnose this pathology with a 100% positive predictive value, an accuracy of 93% and a sensibility of 71% (6).

Table 3. Volume abnormalities: oligohydramnios

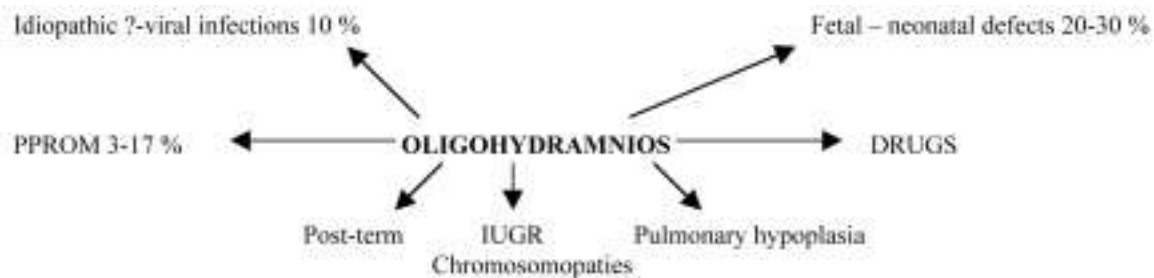


Table 4. Prenatal diagnosis of pulmonary hypoplasia

Clinical information	Fetal biometry	Doppler velocimetry
-Prom occurring ≤ 20 wks of pregnancy -Oligohydramnios lasting ≥ 8 wks -AFI ≤ 1 cm	- AC $< 5^{\circ}$ P - ratio between fetal abdominal/thoracic circumference $< 5^{\circ}$ P	- PSV, TAV, EDV $< 5^{\circ}$ P

Some drugs such as NSAID's taken during pregnancy for tocolysis or only taken as painkillers can give, in some patients other than oligohydramnios, important neonatal adverse effects. Their effect infact on the fetal kidney (reducing the urinary excretion) has been well established, and is prescribed in cases with polyhydramnios. Less defined, are the possible effects on fetal tubulogenesis and glomerulogenesis which could give severe consequences. Inappropriate or prolonged use, therefore could infact lead to renal failure in neonates as reported in literature (7, 8).

We report a case referred to us 8 days after birth with a diagnosis of acute renal failure. From the mother's history, we learnt that she had taken nimesulide for 28 days with the development of oligohydramnios at 32 weeks of pregnancy. At one year the child is still under treatment for chronic renal failure (9).

Besides the quantities also the quality of the amniotic fluid may be related to the neonatal outcome.

Amongst the alterations in amniotic fluid composition, are the alterations in the L/S ratio to-date of reduced importance following the routine use of prenatal corticosteroids and supplementary surfactant in the prevention and therapy of neonatal respiratory distress syndrome.

Finding of some inflammatory factors (interleukines) in the amniotic fluid seems to be correlated long-term neurological abnormalities.

Yoon and Romero demonstrated that the increase of the inflammatory factors in the amniotic fluid is significantly correlated to periventricular leucomalacia (PVL) and cerebral paralysis, both in the preterm and term neonate (10).

Therefore, the increase of the cytokines in the amniotic fluid could give information not only of the infection but also regarding the risk of developing neurological sequelae in neonatal period (11). Infact

the neurological damage is not directly due to the infection but it seem due to the inflammatory reaction of the foetus, with release of interleuchines (IL6, IL8, tumor necrosis factor) which cross the hematoencephalic barrier, altering the white matter and preventing the differentiation of the precursors of the oligodendrocytes and astrocytes, which promotes apoptosis and impairment of the oligodendrocytes (12, 13).

Diagnosis and therapy for pathologies that alter the amniotic fluid have progressed, however efforts have still to be made in the identification and search for those quantitative-qualitative alterations of the amniotic fluid, for their potential implications on neonatal outcome.

References

1. Panting-Kemp A, Nguyen T, Castro L. Substance abuse and polyhydramnios. *Am J Obstet Gynecol* 2002; 187-3: 602-5.
2. Panting-Kemp A, Nguyen T, Chang E, Quillen E, Castro L. Idiopathic polyhydramnios and perinatal outcome. *Am J Obstet Gynecol* 1999; 181-5: 1079-82.
3. Banks EH, Miller DA. Perinatal risks associated with border line amniotic fluid index. *Am J Obstet Gynecol* 1999; 180-6: 1461-3.
4. Locatelli A, Vergani P, Di Pirro G, Doria V, Biffi A, Ghiaini A. Role of amnioinfusion in the management of premature rupture of membranes at < 26 weeks' gestation. *Am J Obstet Gynecol* 2000; 183-4: 878-82.
5. Ogunyemi D, Thompson W. A case controlled of serial transabdominal amnioinfusions in the management of second trimester oligohydramnios due to premature rupture of membranes. *Eur J Obstet Gynecol Reprod Biol* 2002; 102-10: 167-72.
6. Gramellini D, Piantelli G, Delle Chiaie L, Rutolo S, Vadora E. Amnioinfusion in the management of oligoydramnios. *J Perinat Med* 1998; 26: 293-301.
7. Ludy JAM, Tbbael D, Rbben SGF, de Krijger RR, de Ridder MAJ, Wladimiroff JW. Prenatal prediction of pulmonary hypoplasia: Clinical, biotric, and Doppler velocity correlates. *Pediatrics* 2002; 109: 250-8.

8. Peruzzi L, Gianoglio B, Porcellini MG, Coppo R. Neonatal end stage renal failure associated with maternal ingestion of cyclo-oxygenase type 1 selective inhibitor Nimesulide as tocolytic. *Lancet* 1999; 354: 1610.
9. Norwood V, Morham SG, Smithies O. Post-natal development and progression of renal dysplasia in cyclo-oxygenase -2 null mice. *Kidney Int* 2000; 58: 2291-300.
10. Magnani C, Moretti S, Volante E, Bevilacqua G. Nimesulide ed insufficienza renale neonatale. *La Pediatria Medica e Chirurgica* 9° Congresso nazionale SIN Napoli 21/24 maggio 2003: 162.
11. Khanthou M, Fotopoulos S, Mouchtouri A, Lipsou N, Zika I, Sarafiudou J. Inflammatory mediators in perinatal asphyxia and infection. *Acta Paediatr* 2002; 448 (suppl): 92-7.
12. Yoon BH, Romero R, Park JS, et al. Fetal exposure to an intra-amniotic inflammation and development of cerebral palsy at the age of three years. *Am J Obstet Gynecol* 2000; 182: 675-81.
13. Gomez R, Romero R, Grezzi F, Yoon BH, Mazor M, Berry SM. The fetal inflammatory response syndrome. *Am J Obstet Gynecol* 1998; 179: 194-202.
14. Yoon BH, Park C-W, Chaiworapongsa T. Intrauterine infection and development of cerebral palsy. *BJOG* 2003; 110 (20): 124-7.

Correspondence: Enrico Volante, MD

Tel: 0039 0521 702436

Fax: 0039 0521 702542

E-mail: evolante@unipr.it