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AMNIOTIC FLUID INDEX AND FETAL BLADDER OUTLET OBSTRUCTION. DO WE REALLY NEED MORE?

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ABSTRACT

Purpose: With the constant advances in technology and expertise of prenatal diagnosis, necessity of early counseling in cases of bilateral obstructive uropathy has become of paramount importance. To better evaluate fetal renal function new biochemical (serum and urine) fetal markers have been introduced in the literature. However, they are only available at select centers and always requiring an invasive approach. Furthermore, paucity of normal controls sometimes makes interpretation of results difficult. Owing to this growing interest towards biochemical evaluation of fetal renal function, assessment of amniotic fluid, which is mostly expression of fetal urination, has progressively fallen into disrepute, and studies comparing the amount of amniotic fluid with renal function are scant.

Materials and Methods: In a 3-year period 28 cases of bilateral obstructive uropathy were seen prenatally at the Artemisia Medical Center. All cases were initially reviewed at 17 to 20 weeks of gestation when a distended fetal bladder with thickened wall and enlarged kidneys were visualized. At the same time ultrasonographic assessment of amniotic fluid was performed by calculating the amniotic fluid index. An amniotic fluid index less than the 25th percentile was considered below average and an index less below the 5th percentile was considered oligohydramnios, whereas an index between 50th and 75th percentiles was considered normal. All cases were subsequently evaluated for renal function up to age 1 year. Impaired renal function was defined as a serum creatinine greater than 1.2 mg/dl before age 1 year.

Results: Of the 28 cases 18 had an index of oligohydramnios (group 1) and 10 had a normal index (group 2). No significant variations were observed in amniotic fluid index at repeated consultations throughout pregnancy. Two cases in group 1 and 1 case in group 2 were lost to followup while in the other group 1 cases intrauterine death occurred. Bilateral obstructive uropathy was confirmed in all instances after birth as valves in 18 cases and urethral atresia in 3. Of the 12 surviving group 1 cases there were 3 neonatal deaths from severe lung hypoplasia, and in the remaining 9 cases mean serum creatinine at each evaluation before age 1 year was 1.3 ± 0.2 mg/dl. All patients in group 2 survived with a mean serum creatinine at each evaluation of 0.6 ± 0.1 mg/dl ($p < 0.05$).

Conclusions: Despite widespread use of prenatal biochemistry, evaluation of amniotic fluid by the amniotic fluid index remains a reproducible and inexpensive method to predict renal function in cases of bilateral obstructive uropathy of any origin. It retains its validity not only in severe, but also in milder reductions. Conversely, intact amniotic fluid mostly invariably predicts normal renal function at long-term evaluation. For a better understanding of the disease such information is to be promptly conveyed to the prospective parents at each prenatal consultation.

KEY WORDS: oligohydramnios, bladder neck obstruction, amniotic fluid

Congenital obstructive uropathy occurs approximately in 1 every 3,000 pregnancies and comprises a spectrum of pathological conditions, the most common being posterior urethral valves. Recently improvements in the expertise of sonographers and capability of the equipment have produced a significant increase in the detection rate of bladder outlet obstruction (BOO), which, in turn, has considerably raised interest toward in utero relief of obstruction. Such interest has also been boosted by the advances in fiberoptic technology with the possibility of antegrade endoscopic incision of valves in utero by fetal cystoscopy.[1] Results of different evaluations have been reported in terms of prenatal and postnatal mortality, and long-term renal function.[2] However, all of these studies have the limitation of few control cases, resulting in parameters of normal renal function (RF) to remain elusive.

Amniotic fluid (AF) has long been considered the first prognostic sign of RF deterioration since early in gestation, and fetal urine accounts for more than 80% of its production. The majority of authors consider oligohydramnios the primary indication to proceed with more invasive testing and, currently, oligohydramnios is considered per se the best predictor of adverse prognosis.[3] However, few studies have evaluated the role of AF as a single prognosticator of RF after birth, and most of them do not give information about the method of AF measurement or amount, which is only referred to as normal or oligohydramnios.

MATERIALS AND METHODS

The database at the Artemisia Medical Center, a tertiary referral center in fetal medicine, was reviewed for cases of

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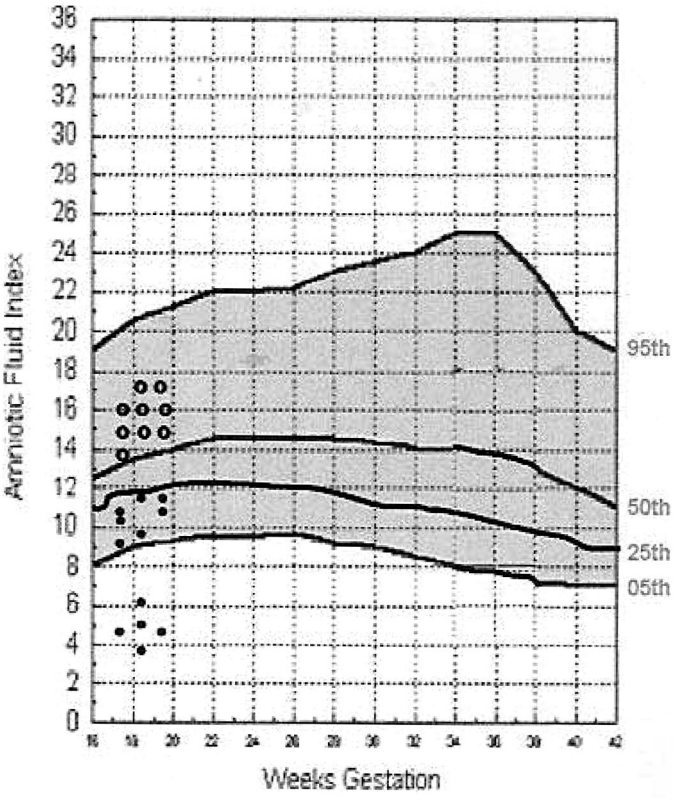
BOO seen between 1999 and 2002. Detailed ultrasonographic assessment included fetal gender, bladder wall thickening (3 mm or greater), presence of "keyhole" dilated upper urethra and presence of hydroureter and/or hydronephrosis. In each case AF was also evaluated by calculating the amniotic fluid index (AFI) according to Phelan et al.[4] Cases with significant intrauterine growth retardation where excluded from study as were those with abnormal karyotyping. Maternal hydration was accurately monitored before each consultation. All fetuses with suspected BOO were subsequently evaluated at regular intervals (approximately every 2 to 3 weeks).

At each consultation AFI was calculated by the same sonographer. Fetuses with AFI <25th percentile according to Moore and Cayle[5] were group 1 while those with AFI between 50th and 75th percentiles were group 2. AFI <5th percentile was considered oligohydramnios, AFI <25th percentile was considered below average and AFI <50th percentile was considered normal AF. Surviving cases were subsequently evaluated after birth at the Bambino Gesu' Children's Hospital for RF at regular intervals up to age 1 year. Impaired RF was defined as serum creatinine (Scr) greater than 1.2 mg/dl before age 1 year.

RESULTS

In a 3-year period 28 cases of BOO were seen prenatally at the Artemisia Medical Center. All cases were initially reviewed at 17 to 20 weeks of gestation when a distended fetal bladder with thickened wall and enlarged kidneys were visualized. There were 18 cases in group 1 and 10 in group 2. No significant variations were observed in AFI percentile at repeated consultations throughout pregnancy. Two cases in group 1 and 1 in group 2 were lost to followup, while in other 4 cases in group 1 intrauterine death occurred. Fetal autopsy confirmed BOO in all 4 cases, urethral atresia in 3 and posterior urethral valves (PUV) in 1. BOO was also confirmed in all cases after birth, PUV in 18 and urethral atresia in 3.

Of the remaining 12 group 1 cases there were 3 neonatal deaths from severe lung hypoplasia (in retrospect all 3 cases had AFI below the 5th percentile) and 9 had a mean Scr at each evaluation of 1.3 ± 0.2 mg/dl. Of these 9 cases AFI was <5th percentile in 2 and between 5th and 25th percentiles in 7. All patients in group 2 survived with a mean Scr at each evaluation of 0.6 ± 0.1 mg/dl ($p < 0.05$, see figure). None of the surviving patients required diversion nor did they experience urinary tract infections.



Amniotic fluid index at initial evaluation of fetuses with normal RF (○) and impaired RF (●).

DISCUSSION

The presence of AF throughout gestation enables normal development of fetal respiratory and urinary tracts, and continued fetal growth in a nonrestricted, sterile and thermally controlled environment. Following keratinization of the fetal skin at approximately 22 weeks of gestation AF is considered to be a result of fetal urination approximating 30% of fetal body weight daily.[6] In addition, studies on acute phase proteins in fetal life have demonstrated that, since the function of clearing waste products in pregnancy is handled principally by the placenta, the main function of fetal kidneys only remains that of supplementing the production of AF.[7] This is the reason why we made a direct comparison between AF amount and RF after birth.

Not surprisingly, necessity of accurate selection of candidates for in utero treatment has prompted numerous clinical studies based on the assessment of fetal RF. To date, such assessment mostly relies on different biochemical markers such as electrolytes (calcium and sodium) and light chain major histocompatibility antigens (beta-2 microglobulin).[8] Similar studies have also been attempted in fetal serum by studying molecules, such as cystatin C and beta-2 microglobulin itself, which do not cross the placental barrier.[9] In addition, other groups have proposed an ultrasound guided technique of renal biopsy which would theoretically allow precise definition of the extent of renal damage in obstructed and dysplastic kidneys.[10]

A comparison between different amounts of AF and RF has only been reported for fetal renal anomalies. Carr et al, in their review of 7 infants with prenatally diagnosed hyperechoic kidneys and normal AF, noted that Scr levels remained normal for a 3-year period but provided no information regarding the definition of normal AF or ultrasonographic thresholds.[11] Similarly, Muller et al, in a study on bilateral renal hypoplasia and cystic kidneys, reported 1 case of normal RF at 1 year of those with oligohydramnios while the remaining cases had normal AF.[12] On the other hand, evaluation of AF and RF in fetuses with BOO is usually biased since the majority of such evaluations are made after in utero treatment when oligohydramnios is considered a prerequisite by most urologists.

McLorie et al reported on 12 candidates for vesico-amniotic shunting, of whom 9 were actually treated in utero with 6 alive at birth.[13] However, only 3 subjects had a creatinine clearance greater than 70 ml per minute at a mean followup of 42 months and, interestingly, only 1 patient was more than 50th percentile for height and weight. In another series of 14 shunted fetuses with PUV only 3 exhibited intact RF at age 1 year.[14] From these large series it appears clear that, irrespective of any other fetal evaluation (such as ultrasonographic findings or urinary electrolytes) few fetuses with oligohydramnios will develop normal RF later in life.

Our data on obstructive uropathy confirm these findings and enable us to identify 3 diagnostic categories: 1) subjects with AFI <5th percentile who are likely to die (3 of 5 in our series), 2) subjects with AFI between 5th and 25th percentiles who will survive but will have impaired RF (7 of 9) and 3) patients with intact AF who will survive with good RF (10 of 10 cases). Although this a limited experience, we believe