Appropriate timing for performing abdominal ultrasonography and termination of observation follow-up for antenatal grades 1 or 2 hydronephrosis

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Abstract

**Background:** Most cases of antenatal Society of Fetal Urology (SFU) grades 1 or 2 hydronephrosis (HN) improve or resolve spontaneously with conservative treatment. However, there is no consensus on the duration of follow-up for grades 1 or 2 HN. The aim of this study was to determine the need for a continuous follow-up period and to propose a new follow-up protocol for children with antenatal grades 1 or 2 HN.

**Methods:** Subjects underwent ultrasonography examination according to the SFU classification. We retrospectively evaluated data from 112 patients with postnatal grade 1 HN and 69 with grade 2 HN diagnosed between January 2010 and December 2017. We examined the change in HN grades using serial ultrasonography. The Kaplan-Meier method was used to show the effect of HN grade on the rate of HN changes.

**Results:** The mean follow-up duration was 44.9 ± 36.4 months (range, 12–274 months). Initial SFU grade 1 HN disappeared in 47.0% of cases at 12 months, 66.4% at 24 months and 73.2% at 48 months. Initial SFU grade 2 HN improved in 74.7% of cases at 12 months, 88.3% at 24 months and 89.5% at 48 months. However, 14.6% of SFU grade 1 and 2.8% of SFU grade 2 cases increased in grade, and 99.3% of these cases worsened within the first 6 months. No cases with increased grade required pyeloplasty. Initial disappearance and later reappearance of HN occurred in 40.5% of SFU grade 1 and 2 cases. The mean duration of later reappearance was 39.1 ± 36.2 months (range, 12–137 months). No reappearance was detected after more than 1 year.

**Conclusions:** Ultrasonography within the first 6 months was necessary for management of children with antenatal grades 1 or 2 HN because some patients showed worsening. Thereafter, it was considered safe to increase the follow-up intervals for stable cases. Most cases resolved spontaneously; however, a few cases reappeared within 1 year. Therefore, ultrasonography after 1 year was necessary for children with HN that had spontaneously disappeared. The appropriate time to terminate follow-up was considered to be 1 year or more after HN disappearance was confirmed.

**Background**

Fetal hydronephrosis (HN) is the most common anomaly detected on antenatal ultrasonography, with an estimated prevalence of approximately 2–5.5% [1–3]. In most cases, HN is diagnosed in the absence of urinary tract obstruction, when the anteroposterior diameter of the renal pelvis is just above the normal range for gestational age [4]. Studies have shown that most cases of antenatal HN improve or resolve spontaneously with conservative treatment [2,3]. In a systematic review of seven articles, 98% of Society of Fetal Urology (SFU) grade 1 or 2 HN cases improved or resolved [5]. Additionally, in two prospective studies the resolution rates for SFU grades 1 and 2 were reported to be 98% –99% and 60–98%, respectively, [6,7]. However, some patients do not show improvement or show increase in the HN grade, and a few cases require surgery [8,9]. The detection and postnatal follow-up of persistent antenatal HN is
believed to help in the early recognition and prevention of progressive renal damage [3,10–12]. There is no consensus on the duration of follow-up for cases of grade 1 or 2 HN [13]. In patients with SFU grades 1 and 2 HN, a more abbreviated follow-up may be warranted and could save costs [14]. However, it has been pointed out that SFU grades 1 and 2 show different natural courses [7], and there is a concern whether similar follow-ups may be acceptable for SFU grades 1 and 2. The aim of this study was to examine the hypothesis that different follow-up periods may apply for SFU grades 1 and grade 2, and we propose a new follow-up protocol for children with antenatal SFU grade 1 or 2 HN.

**Methods**

*Patient characteristics*

Ultrasonography assessments of HN grade were performed according to the SFU classification [15]. We let patients hydrate and tested the patient's bladder when it was not full. All patients visited our institutions between 48 hours after birth and 1 month of age, and patients were divided in groups using the HN grade as a baseline. We retrospectively evaluated 112 grade 1 unilateral HN cases detected antenatal and 69 cases of with grade 2 unilateral HN. For all cases we used abdominal ultrasonography performed at our institutions between January 2010 and December 2017. Eleven patients were excluded due to repeated febrile urinary tract infections or hydroureter, symptomatic vesicoureteral reflux on voiding cystourethrography, or due to ureterovesical junction obstruction on magnetic resonance imaging.

*Follow-up surveillance*

Patients were followed up according to HN, and ultrasonography was performed once every 1–3 months. SFU grades were determined by the pediatric urologist responsible for the each patient. A single pediatric urologists (AN) reviewed all ultrasonography findings as a second reviewer. If the first urologists and the reviewer disagreed, the diagnosis of the reviewer was adopted to minimize inter- and intra-rater variability [16]. At the final evaluation, the term “resolved” was used to indicate a change in the SFU grade to grade 0; “improved” was used to indicate a decrease in the SFU grade by one or more levels, (as per definition this category also included all “resolved” cases); “no change” indicated no change from the initial SFU grade; and “worsened” indicated an increase in the SFU grade and included cases with temporary upgrade. In further follow-ups, another ultrasonography was performed for low (1–2) SFU grade HN, while renal nuclear medicine studies using dynamic scanning modes were performed for HN that progressed to a high (3–4) SFU grade [17]. Of the “resolved” cases, 42 cases were followed up for every 1 up to 6 months to examine whether HN would come back.

All follow-up procedures were performed after obtaining informed consent form patients’ parents for clinical care. The clinical data were obtained in a retrospective study at after approval of study protocol by our institutional review board approval (approved by Ethical Committee of the Gamagori City Hospital, approval no. Gamabyo 500-4). All statistical analyses were performed using SPSS Statistics Ver. 22 (IBM, Armonk, NY, USA). Values are shown as mean ± SD (range minimum–maximum). Kaplan-Meier method
was used to show the effect of HN grade on the rate of HN changes and compared with the use of the log-rank test. All tests were 2-sided. A p-value of less than 0.05 was considered statistically significant.

Results

The mean follow-up duration was 44.9 ± 36.4 months (range, 12–274 months). Patient characteristics at baseline are shown in the table. The rate of time to resolution or improvement in SFU grades 1 or 2 was determined using the Kaplan-Meier method (Figure 1). Initial SFU grade 1 HN resolved in 47.0% of cases at 12 months, 66.4% at 24 months and 73.2% at 48 months. The median time to resolution was 14 months (95% confidence interval [CI] 9.49–18.51). Initial SFU grade 2 HN improved in grade in 74.7% of cases at 12 months, 88.3% at 24 months and 89.5% at 48 months. The median time to resolution was 14 months (95% CI 6.15–7.85). The rate of resolution of SFU grade 2 than in grade 1 (log-rank test, $\chi^2 = 14.679$, $P = 0.00013$). However, 14.6% of SFU grade 1 (15 cases) and 2.8% of SFU grade 2 (2 cases) increased in grade, including cases with temporary up-grade. Then, 99.3% of these cases worsened within the first 6 months, and only one case of SFU grade 1 worsened at 13 months. The rate of worsening for SFU grade 1 or 2 was determined using the Kaplan-Meier method (Figure 2). The rate of worsening of HN was significantly higher in SFU grade 1 than in grade 2 (log-rank test, $\chi^2 = 6.227$, $P = 0.013$). None of the patients underwent pyeloplasty due to deterioration of renal function. We followed up on 42 cases in which HN resolved. The mean additional follow-up duration was 39.1 ± 36.2 months (range, 12–137 months). Initial disappearance with later reappearance of HN occurred in 40.5% of patients (17 cases). The mean period before later reappearance of HN was 6.4 ± 3.5 months (range, 1–11 months). The rate of time to reappearance of HN was determined using the Kaplan-Meier method (Figure 3). No cases showed reappearance of HN after more than 1 year. After reappearance HN resolved again in 10 cases but remained in 7 cases with reappeared HN of SFU grade 1 or 2. However, none of the patients underwent pyeloplasty during the observation period.

Discussion

Most cases of antenatal HN improve or resolve spontaneously with conservative treatment [2,3]. However, some patients do not show improvement without treatment. Currently no consensus exists regarding the optimal schedule and duration of follow-up for patients with SFU grades 1 or 2 HN. It is unclear what neonates require postnatal evaluation, when postnatal evaluation for HN should start, for how long examinations should be carried out, and the duration of the follow-up [13].

The timing for postnatal resolution of HN is quite variable, occurring over the first few years of life. Despite variability in the underlying diagnoses, mild grades of HN generally show early resolution, with most cases of SFU grades 1 or 2 HN resolving within 12–18 months of age [18–20]. In our study, most cases of SFU grade 1 or 2 HN showed spontaneous improvement or resolution within 4 years. In particular, since SFU grade 1 HN resolves slower than grade 2, the follow-up period is likely to be longer in many cases. However, a small number of cases showed worsening from SFU grades 1 to 2 or from SFU
grades 2 to 3, and this worsening was mainly noted within 6 months of age in our study. A previous study reported the need for surgical intervention in a small percentage of cases of mild-grade HN cases [21]. In another previous report, of 225 kidneys with SFU grade 2 HN, 3 showed worsening of HN to a severe grade [159]. Furthermore, a study showed that SFU grade 3 cases that finally required surgery were identified during follow up [22] and it has been concluded that SFU grade 3 should be more closely monitored than SFU grade 2 [17]. We think that SFU grade 1 patients should undergo follow-up ultrasonography during the next 6 months to 1 year when the grade of HN may worse. After that, for stable cases, it is considered safe to stop close monitoring and increase follow-up intervals for once a year. On the other hand, according to our results, SFU grade 2 patients may worsen to high-grade HN at 6 months or less, so we consider necessary to perform serial ultrasonography. However, after that period, it will be possible to increase the follow-up interval, similar to what is done for SFU grade 1.

Operative repair was not required for any case in our study. Since there were no surgeries, we initially believed that the follow-up interval could be increases. However, our study showed that there is a high probability that HN will reappear soon after it disappears. This reappearance of HN is therefore a new important finding to help answer the question of whether it is sufficient to confirm the first disappearance of HN at the end of follow-up. In our study, once HN disappeared for more than 1 year, no case had reappearance of HN. It has been suggested that the follow-up may be terminated if no reappearance is detected for more than 1 year. In our study, there were 7 cases that showed no improvement after they reappeared. In this study, no patient had been submitted to surgery, but at this time it was only possible to describe the some natural history of the cases. New prospective studies are needed to determine the complete natural history of HN cases.

Chertin et al. reported that 50% of cases requiring surgical intervention underwent surgery within the first 2 years, and almost all cases underwent surgery within the first 4 years [23]. These authors recommended evaluation every 3–6 months during the above-mentioned period [23]. Some authors have proposed that further evaluation is unnecessary for SFU grades 1 or 2 [14, 24]. Others have advised serial ultrasonography until decrease in grade or resolution of HN, or until patients are old enough to communicate symptoms of renal colic [25, 26]. Based on the above results, we propose that the follow-up is terminated when there is a confirmation that HN disappeared and did not return for 1 year, or when low grade HN remains stable for more than 4 years (at this time patient will be old enough to communicate symptoms), while the follow-up interval is increased.

Our study had some limitations. This was a retrospective study. Additionally, follow-up indications were not standardized across the participating physicians. The evaluation grade of HN was based on the SFU classification only; anterior-posterior diameter measurement [27] and UTD classification [28] were not performed. Furthermore, in this cohort we may have included not only ureteropelvic junction obstruction but also other complicating malformations, including asymptomatic vesicoureteral reflux because we do not routinely perform voiding cystourethrography or magnetic resonance imaging in asymptomatic HN patients. The SFU grading system has problems with inter- and intra-rater variability [16, 29]. We tried to minimize the problems by adopting a second single reviewer for all ultrasonography findings; however,
the reliability problem for grades 2 and 3 remains [16, 30]. Further studies are needed to overcome these limitations and confirm the findings of the present study.

Conclusions

Ultrasonography within the first 6 months was necessary for the management of children with SFU grades 1 or 2 HN because some patients showed worsening. Thereafter, it is considered safe to stop close follow-up and increase the follow-up interval for stable cases. Most cases of perinatal SFU grades 1 or 2 HN resolved spontaneously with conservative treatment. However, a few cases reappeared within 1 year. Therefore, ultrasonography after 1 year was necessary in children with HN that spontaneously disappeared. The appropriate time to terminate follow-up was considered to be 1 year or more after the disappearance was confirmed.

Declarations

Ethics approval and consent to participate: The patients’ parents were fully informed of the disease, examinations, and complications, and were required to sign a written informed consent form before undergoing any procedures. All study protocols were approved by the Ethical Committee of the Gamagori City Hospital (approval no. Gamabyo 500-4). The requirement for research consent was waived due to the study’s retrospective nature of the study.

Consent for publication: Not applicable.

Availability of data and material: The datasets used and/or analyzed during the current study are available from the first author or the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors’ contributions: Conception and design: AN and YH; enrollment of patients and acquisition of data: AN, KM, and HN; drafting of the manuscript: AN, KM, and YH; statistical analysis: AN and HK; analysis and interpretation of data: TK, SK, and TM; supervision: TY. We confirm that all authors have read and approved the final manuscript.

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List Of Abbreviations

CI: confidence interval
HN: hydrenephrosis
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**Tables**

Due to technological limitations, the tables are only accessible as a download in the supplementary files section.
Figures
Figure 1

Time to resolution or improvement for hydronephrosis grades 1 or 2. Kaplan-Meier method. Points displayed as crosses show censored cases. The upper table in this figure shows the number of affected patients at risk at each observational point. The lower table in this figure shows the rate (%) of resolution or improvement of hydronephrosis at each observational point. The rate of resolution or improvement of hydronephrosis is shown for grades 1 and 2 over time.
hydronephrosis was significantly higher in grade 2 than in grade 1 (log-rank test, \( \chi^2 = 14.679, P = 0.00013 \)).
Time to worsening for hydronephrosis grades 1 or 2. Kaplan-Meier method. Points displayed as crosses show censored cases. The upper table in this figure shows the number of affected patients at risk at each observational point. The lower table in this figure shows the rate (%) of worsening of hydronephrosis at each observational point. The rate of worsening of hydronephrosis was significantly higher in grade 1 than in grade 2 (log-rank test, $\chi^2 = 6.227$, $P = 0.013$). There were 14.6% of grade 1 and 2.8% of grade 2 cases increased in grade. Then, 99.3% of these cases worsened within the first 6 months, only one case of grade 1 worsened at 13 months over the study period.

Figure 2
Figure 3

Time to reappearance of hydronephrosis. Kaplan-Meier method. Points displayed as crosses show censored cases. The upper table in this figure shows the number of affected patients at risk at each observational point. The lower table in this figure shows the rate (%) of reappearance of hydronephrosis at each observational point. No cases showed reappearance of hydronephrosis after more than 1 year.

Supplementary Files
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- newnewHNtable.pdf