

Evaluation of Intravenous Maternal Hydration Therapy in Isolated Oligohydramnios: A Randomized Controlled Clinical Trial

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Background: Oligohydramnios has invariably been associated with adverse perinatal outcome such as fetal distress (ante/intra-partum fetal heart rate decelerations, meconium passage and cord compression). The current study aimed to determine the effects of intravenous maternal hydration on amniotic fluid volume in pregnancies above 34 weeks manifested with decreased amniotic fluid index (AFI).

Patients and methods: A randomized controlled clinical trial included 42 pregnant women who were diagnosed to have oligohydramnios by ultrasound. They attended Obstetrics and Gynecology Department at Mansoura University Hospitals from November 2019 to December 2021. The participants were divided into 3 groups: *Group A* with 14 women allocated to infusion of normal saline and Ringer's solution for 1 liter/day for 1 week, *Group B* with 14 women allocated to infusion of normal saline and Ringer's solution for 3 liter/day for 1 week, and *Group C* with 14 Fourteen women as a control group.

Results: The mean AFI in *Group A* before treatment was 4.54 (SD 0.58), in *Group B* was 4.46 (SD 0.54) and in *Group C* was 4.72 (SD 0.375), with no significant difference between the three groups (P1=0.692, P2=0.344 and P3=0.183), as P1: difference between group A and B, P2: Between group A and C and P3: difference between group B and C. There were statistically significant increases in AFI in *Group A* and *Group B* in comparison with the control group (P<0.05) after 48 hours and 1 week of hydration. However, no significant difference was recorded among Groups A and B as regards AFI.

Conclusion: Applying normal saline and Ringer's solution is safe and effective method on mothers with isolated oligohydramnios and gestational age above 34 weeks, and could eliminate the need to terminate the pregnancy before term, which has terrible consequences on the mother and the fetus.

Keywords: Amniotic fluid, Intravenous maternal hydration therapy, Isolated oligohydramnios.

INTRODUCTION

Amniotic fluid (AF) is an important part of pregnancy sac and helps fetal development. It has a number of important functions like the development of gastrointestinal tract, musculoskeletal system, and lung development, providing essential nutrients to the fetus and it has bacteriostatic properties ⁽¹⁾.

It also acts as a protective cushion for the fetus against the pressures placed on the abdomen, prevents attachment to the fetal membranes, and keeps the fetal temperature stable. In addition, it facilitates the fetal symmetrical growth and movement ⁽²⁾.

Many factors may affect the amniotic fluid index. The mothers' blood volume plays an important role in maintaining the amniotic fluid volume. Hydration status and maternal plasma osmolarity can also alter amniotic fluid volume ^(2,3). AFI is assessed by ultrasound where an AFI of 5.0 cm or less is defined as oligohydramnios. It was added to antepartum testing, to better identify fetuses at higher risk of poor perinatal outcome ⁽¹⁾.

Oligohydramnios, in the absence of premature rupture of membranes and fetal anomalies, is considered as a symptom of chronic reduction in placental function, which results in the reduction of fetal urinary output ⁽⁴⁾. It occurs in 3% to 5% of pregnancies at term ⁽⁵⁾. Sequel of chronic oligohydramnios may be responsible for problems such as Malpresentation, umbilical cord compression, concentration of meconium-stained liquor, difficult or failed external cephalic version, difficult ultrasound visualization of fetal parts,

pulmonary hypoplasia, fetal heart rate deceleration, increased chance of caesarean section (CS), non-reactive non-stress tests, intrauterine growth restriction (IUGR), congenital abnormalities, post-date pregnancy, and low Apgar scores ⁽⁶⁾.

In some cases, it may even be reduced to a few milliliters of viscous fluid which results in an increase in fetal death to 40-50 times of the rates among normal pregnancies ⁽⁷⁾.

Thus, researchers have been prompted to study the basic mechanisms and treatment options of the condition. Among a number of interventions that have been tried to improve the AFV are bed rest, and intravenous hydration therapy. Which are cost-effective, simple to accomplish, with fewer side effects, and do not require special techniques with successful outcome ^(1,8).

General fluid needs increase during pregnancy, in order to support fetal circulation, amniotic fluid, and a higher blood volume. Individuals normally need 1–1.5 ml of water for each calorie consumed (e.g., a person eating a 2000-calorie diet would need 2000–3000 ml of fluid each day). Most pregnant women are advised to increase their caloric consumption by about 300 calories ⁽⁹⁾. Therefore, they would need at least 300 ml of additional fluid intake, so the current recommendation for water intake is drinking 8–10 glasses of water each day. Maternal hydration, above the recommended daily oral intake, may theoretically increase amniotic fluid volume by causing fetal diuresis and by improving

placental perfusion. An effective non-invasive method of increasing amniotic fluid volume (AFV) that may have several applications in obstetric practice⁽¹⁰⁾. Other studies suggested that oral and intravenous hydration may alter the amniotic fluid index in normal pregnancies and in oligohydramnios and thereby to reduce the associated perinatal morbidity and mortality. But the mechanism for this effect remains unclear^(11,12). Additional studies are needed to evaluate the effect of intravenous maternal hydration on unexplained oligohydramnios compared to a non-intervention group.

The aim of the current study was to determine the effects of intravenous maternal hydration on amniotic fluid volume in pregnancies above 34 weeks manifested with decreased amniotic fluid index.

PATIENTS AND METHODS

A randomized controlled clinical trial was conducted on 42 pregnant women who were diagnosed to have oligohydramnios by ultrasound and attended Obstetrics and Gynecology Department at Mansoura University Hospitals from November 2019 to December 2021.

Inclusion criteria:

Singleton pregnancy. Well established gestational age above 34 weeks. Intact membranes at the time of selection. Oligohydramnios AFI below 5. Normal Umbilical artery (UA) Doppler. A non-anomalous fetus.

Exclusion criteria:

Women at risk of fluid overloads such as those with cardiac disease, renal impairment, moderate or severe preeclampsia or hypertension (diastolic blood pressure >100 mmHg or proteinuria), diabetes with pregnancy, autoimmune disease and vascular disease. Rupture of fetal membranes. Multiple pregnancies. Post-term pregnancy.

Sample Size:

Sample size calculation was based on mean amniotic fluid index between 2 studied groups receiving different doses of hydration therapy 1500 and 2500 respectively retrieved from previous research⁽¹⁰⁾. Sample size calculation was based on student's t-test to compare between 2 means (86.21 and 112.45), and difference in standard deviation of 1.97. Using G*power version 3.0.10 to calculate sample size, with the total calculated sample size was 11 patients in each group, using student's t-test, 2-tailed, with α error = 0.05 and power = 90.0% and effect size = 1.56 and adding 20% to avoid attrition, then every studied group will include 14 with total sample size of 42 patient.

Group assignments:

A study sample of 42 pregnant women was randomized into three groups by opaque sealed envelope method, with **14 women in each group**:

- We put code number to every participant with the name and address kept in a special file.

- We hid the patient's name when we use the research.
- All participants had the recommended daily oral water intake.

Group A: Fourteen women allocated to infusion of (normal saline and Ringer's solution) for 1 liter/day for 1 week.

Group B: Fourteen women allocated to infusion of (normal saline and Ringer's solution) for 3 liter/day for 1 week.

Group C: Fourteen women as control group.

METHODOLOGY

All patients in this study were subjected to the following:

- I. History taking:** Personal (age, duration of the marriage, special habits), menstrual history, obstetric history, present history of any medical or obstetric problems, past history, and family history.
- II. Clinical examination:** General and obstetric examination.
- III. Investigational studies:**
 - **Laboratory investigation:** Complete blood picture, random blood sugar, liver function test, and kidney function test.
 - **Ultrasound study:** The ultrasound machine used was GE Logic F6 device, Trans-abdominal ultrasound was performed to all patients while the patient was in a slightly tilted position with the head of the bed raised 30 degrees and a small pillow under the right loin. Amniotic fluid index was first measured for all participants & then the participants were divided into three groups, the first one was given one liter of intravenous fluid (normal saline + Ringer's solution within 24 hr. for 7 days). The second group was given three liters of intravenous fluid (normal saline + Ringer's solution within 24 hr. for 7 days), and the third group was the control group. Then, amniotic fluid index was measured to all groups in the predetermined periods.
 - **Ultrasound examination done:**
 - (1) Measurement of fetal biometry including: Biparietal diameter (BPD), head circumference (HC), femur length (FL).
 - (2) Detection of congenital malformation.
 - (3) Umbilical artery (UA) Doppler.
 - (4) Amniotic fluid index measurement.

Procedure and intervention:

The amniotic fluid index was measured and cases with AFI below 5 were included. The measurement before the study was defined as the initial

amniotic fluid index and the outcome were measured after 48 hours, repeated after 1 week and after 2 weeks of the initial amniotic fluid index.

Technique of US:

Amniotic fluid index:

The uterus was divided into four quadrants by using the umbilicus as one reference point dividing the uterus into upper and lower halves, and the linea nigra was then used to divide the uterus into right and left halves. A convex transducer was then placed on the maternal abdomen along the longitudinal axis of the mother, with the transducer head being perpendicular to the floor in each of the four uterine quadrants.

The vertical diameter of the largest amniotic fluid pocket, in each uterine quadrant once identified, was measured. The measurements obtained from each uterine quadrant were summed up to represent the amniotic fluid index.

Amniotic fluid index ≤ 5 cm was labeled as low amniotic fluid volume, while amniotic fluid index ≥ 5.1 to 20 cm was labeled as normal amniotic fluid volume and amniotic fluid index ≥ 20 cm was labeled as high amniotic fluid volume. We were careful to maintain a perpendicular relationship of ultrasound transducer to the floor to avoid falsely enlarged amniotic fluid pocket. We extended the ultrasound evaluation to the lateral margins of the uterus to guard against erroneous inadequate amniotic fluid volume impression, as adequate amniotic fluid may be located in the flanks of the supine patient. For each amniotic fluid index, the mean of two measurements was used for analysis.

Technique of the study:

Assessment of patient for inclusion and exclusion criteria was done. Full history and examination were done to avoid selection bias. All patients were selected from Obstetrics and Gynecology Department of Mansoura University Hospitals. Sealed envelope method was used to randomize patients into the 3 groups.

All patients had a startup ultrasound examination to verify the initial amniotic fluid index at the beginning of the study. Patients in *Group A* were given total 1 liter per day of (500 ml normal saline and 500 ml ringer's solution) and patients in *Group B* were given a total of

3 liters per day of (1500 ml normal saline and 1500 ml ringer's solution).

Patients were examined by ultrasound after 48 hours in groups A and B to measure the increase or the decrease of the AFI after starting the intravenous infusion. Repeated ultrasound was done after 1 week ± 1 day after the initial assessment of the AFI. Another ultrasound was done after 2 weeks ± 1 day after the initial assessment (1 week ± 1 day after intravenous infusion has stopped) to allocate any difference in the AFI after stopping the intravenous hydration.

Ethical consent:

An approval of the study was obtained from Mansoura University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 20 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Qualitative data were represented as frequencies and relative percentages.

Chi square test (χ^2) and Fisher's exact test to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean, standard deviation (SD) and median (minimum and maximum). Data were tested for normal distribution using Kolmogorov-Smirnov test. Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data) and Mann Whitney U test for non-parametric data. One Way ANOVA test was used to compare more than 2 independent groups of normally distributed data with Post Hoc and Kruskal Wallis test for non-parametric data. Paired t test was used to compare between 2 studied periods. P value < 0.05 was considered significant.

RESULT

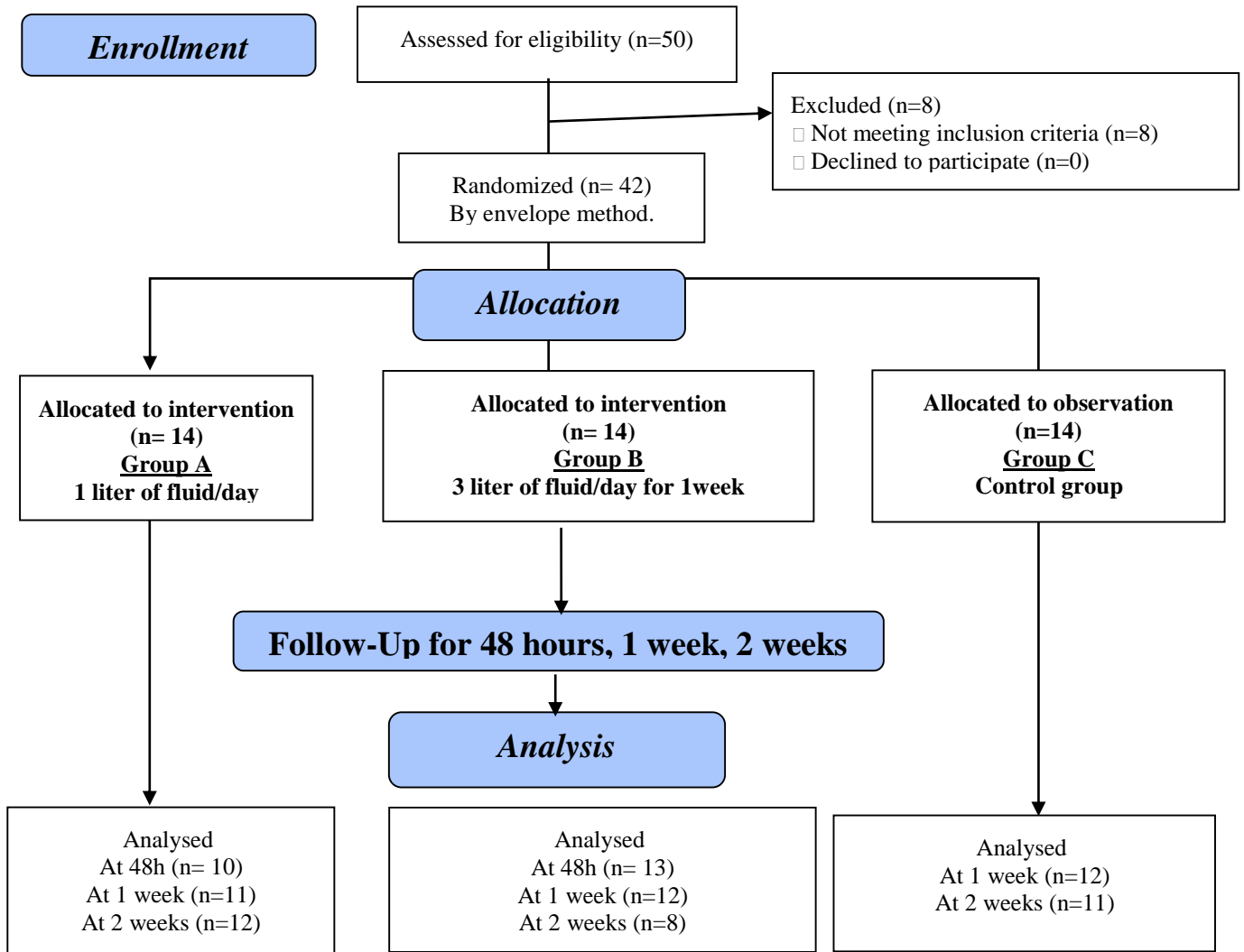


Figure (1): Consort flow chart showing study design.

The mean ages of the included cases were 28.29, 24.78 and 24 years for groups A, B and control respectively. Furthermore, the median (range) for gravidity was 4 (1-7), 3 (1-5) and 3 (1-8) for groups A, B and C respectively, with no statistically significant difference between the three groups (P1=0.061, P2=0.153 and P3=0.687). The median for parity had also no statistically significant difference between the three groups (P1=0.102, P2=0.098 and P3=0.962), as P1: difference between group A and B, P2: Between group A and C and P3: difference between group B and C (**Table 1**).

Table (1): Socio-demographic characteristics and obstetric history of the studied groups.

Variable	Group A N=14	Group B N=14	Group C N=14	Test of significance	Within group significance
Age /years mean ± SD	28.29 ± 4.14	24.78 ± 4.49	24 ± 5.02	F=3.49 P=0.04*	P1=0.049* P2=0.017* P3=0.651
Gravidity Median (range)	4 (1-7)	3 (1-5)	3 (1-8)	KW=3.87 P=0.144	P1=0.061 P2=0.153 P3=0.687
Parity Median (range)	2 (0-4)	1(0-3)	1 (0-3)	KW=3.64 P=0.162	P1=0.102 P2=0.098 P3=0.962

F: One Way ANOVA test, KW: Kruskal Wallis test, P1: difference between group A & B, P2: Between group A& C, P3: difference between group B&C. *Statistically significant, χ^2 : Chi-Square test.

The mean random blood sugar (RBS) was 99, 103 and 105 (mg/dl) for groups A, B and C respectively. Mean hemoglobin was 10.28 for *Group A*, 10.3 for *Group B* and 11.15 for the control group. Mean platelet level for *Group A* was 215 while it was 249.64 in *Group B* and 217.71 in *Group C*. The hematocrit value was 33.79, 32.26 and 33.33 for groups A, B and C respectively. In addition, the mean white blood cell count (WBC) for the included cases was 8.61 for *Group A*, 10.17 and 9.57 for groups B and C respectively. Neither of the previously studies parameters showed statistically difference between the study groups ($p > 0.05$) (**Table 2**).

Table (2): Laboratory findings of the studied groups.

Variable	Group A N=14	Group B N=14	Group C N=14	Test of significance	Within group significance
RBG (mg/dl)	99 ± 4.84	103.86 ± 7.7	105 ± 5.88	F=3.62 P=0.036*	P1=0.047 P2=0.015 P3=0.632
HB (gm/dl)	10.28 ± 1.21	10.31 ± 0.74	11.15 ± 1.39	F=2.56 P=0.09	P1=0.948 P2=0.053 P3=0.061
Hematocrit (%)	33.79 ± 3.55	32.26 ± 2.69	33.33 ± 2.35	F=0.795 P=0.460	P1=0.22 P2=0.696 P3=0.404
Platelet (10 ³ /mm ³)	215.86 ± 6.78	249.64 ± 10.09	217.71 ± 8.23	F=0.774 P=0.468	P1=0.275 P2=0.952 P3=0.302

F: One Way ANOVA test, P1: difference between group A & B, P2: Between group A& C, P3: difference between group B&C. *Statistically significant.

The mean levels of serum albumin were 3.45 (SD 0.59), 3.63 (SD 0.27) and 3.25 (SD 0.64) for groups A, B and C respectively (P1=0.366, P2=0.591 and P3=0.303). Serum creatinine mean values were 0.575 (SD 0.06) for *Group A*, 0.60 (SD 0.06) for *Group B* and 0.60 (SD 0.0) for *Group C* (P1=0.317, P2=0.590 And P3=1.0). AST mean values were 28.58 (SD 8.77), 22.64 (SD 7.65) and 22.5 (SD 2.12) for groups A, B and C (P1=0.092, P2=0.335 and P3=0.983) (**Table 3**).

Table (3): Comparison of liver function test among studied groups.

Variable	Group A N=14	Group B N=14	Group C N=14	Test of significance	Within group significance
Serum albumin (g/L)	3.45 ± 0.59	3.63 ± 0.27	3.25 ± 0.64	F=0.781 P=0.470	P1=0.366 P2=0.591 P3=0.303
Serum creatinine (mg/dl)	0.575 ± 0.06	0.60 ± 0.06	0.60 ± 0.01	F=0.563 P=0.577	P1=0.317 P2=0.590 P3=1.0
AST (U/L)	28.58 ± 3.77	22.64 ± 3.65	22.5 ± 2.12	F=1.70 P=0.2066	P1=0.092 P2=0.335 P3=0.983
ALT (U/L)	22.16 ± 5.52	22.45 ± 4.45	20.5 ± 3.53	F=0.067 P=0.935	P1=0.922 P2=0.757 P3=0.718

F: One Way ANOVA test, P1: difference between group A & B, P2: Between group A& C, P3: difference between group B&C. *statistically significant, AST: aspartate aminotransferase, ALT: alanine aminotransferase

The mean values of gestational age in the three groups were 35.86, 36.31 and 36.59 weeks for group A, B and C respectively. Neither of the previously discussed parameters was found to be significant between the three groups ($p > 0.05$). The mean weight was 2541.07 in *Group A*, 2736.21 in *Group B* and in *Group C* was 2907.86 with no statistically difference between A and B (P1=0.213). The mean head circumference was 36.02, 36.19 and 35.99 weeks with no statistically significant difference between the three groups. Femur length for *Group A* was 36.41 weeks while it was 36 for *Group B* and 36.79 for the control group. Neither of the previously studied parameters was statistically different between the study groups ($p > 0.05$) (**Table 4**).

Table (4): Ultrasound findings of the studied groups.

US	Group A N=14	Group B N=14	Group C N=14	Test of significance	Within group significance
Gestational age/weeks	35.86 ± 1.35	36.31 ± 0.99	36.59 ± 1.08	F=1.45 P=0.248	P1=0.309 P2=0.100 P3=0.515
Newborn WT (gm)	2541 ± 430.01	2736.2 ± 445.28	2907.8 ± 339.37	F=2.83 P=0.07	P1=0.213 P2=0.02 P3=0.272
Head circumference/ cm	36.02 ± 1.55	36.19 ± 1.14	35.99 ± 1.02	F=0.108 P=0.898	P1=0.716 P2=0.950 P3=0.670
FL (cm)	36.41 ± 1.31	36.03 ± 1.39	36.79 ± 1.77	F=0.905 P=0.413	P1=0.510 P2=0.500 P3=0.186

F: One Way ANOVA test, P1: difference between group A & B, P2: Between group A& C, P3: difference between group B&C. *Statistically significant

The mean resistive index in *Group A* before treatment was 0.618 (SD 0.036), in *Group B* it was 0.605 (SD 0.042) and 0.601 (SD 0.025) for *Group C* with no significant difference between the three groups (P1=0.318, P2=0.209 and P3=0.791) (Table 5).

Table (5): Comparison of PI and RI among the studied groups.

Groups	Group A N=14	Group B N=14	Group C N=14	Test of significance	Within group significance
PI	0.951 ± 0.07	0.940 ± 0.07	0.919 ± 0.054	F=0.845 P=0.437	P1=0.651 P2=0.272 P3=0.414
RI	0.618 ± 0.036	0.605 ± 0.042	0.601 ± 0.025	F=0.910 P=0.411	P1=0.318 P2=0.209 P3=0.791

F: One Way ANOVA test, P1: difference between group A & B, P2: Between group A& C, P3: difference between group B&C. *Statistically significant.

The mean AFI in *Group A* before treatment was 4.54 (SD 0.58) and in *Group B* it was 4.46 (SD 0.54) with no significant difference between the two groups (P1=0.692) and the mean AFI in the control group was 4.72 (SD 0.375) with no statistically significant difference between groups A and C (P2=0.344) and between B and C (P3 = 0.183). The mean AFI in *Group A* after 48 hours of hydration was 5.35 (SD 0.76) with statistical significant difference from the base line value P1=0.001* and it was 6.78 (SD 1.12) after 1 week of continuous daily hydration with significant difference from the pretreatment value (P2<0.001*) and reached mean of 6.83 (SD 1.72) after 2 weeks with P3=0.009* from baseline, In *Group B* there were significant difference in AFI after 48 hours, 1 week and 2 weeks from the baseline values (P1=0.004*, P2=0.001* and

P3=0.021* respectively). Meanwhile, in group C the AFI after 1 week was 4.39 (SD 0.43) and after 2 week was 4.33 (SD 0.50) with significant difference from baseline values P2=0.001* and P3=0.006* respectively.

Comparing within group significance between groups A and B at 48 hours and 1 week after treatment and after another week of stopping hydration there was no statistically significant difference P1=0.314, P1=0.139 and P1=0.406 respectively. But statistically significant differences were found between groups A and C at 1week and 2 weeks (P2=0.002* and P2=0.027*) and between groups B and C also at 1week and 2 weeks (P3<0.001* and P3=0.002* respectively) (Table 6).

Table (6): Comparison of amniotic fluid findings during follow up among the studied groups

Variable	Group A N=14	Group B N=14	Group C N=14	Test of significance	Within group significance
Baseline	4.54 ± 0.58	4.46 ± 0.54	4.72 ± 0.375	F=0.972 P=0.387	P1=0.692 P2=0.344 P3=0.183
48 hours	5.35 ± 0.76	5.86 ± 1.41	4.91 ± 0.0	F=0.716 P=0.500	P1=0.314
1 week	6.78 ± 1.12	7.84 ± 1.62	4.39 ± 0.43	F=12.63 P<0.001*	P1=0.139 P2=0.002* P3<0.001*
2 weeks	6.83 ± 1.72	7.79 ± 1.81	4.33 ± 0.50	F=6.38 P=0.002*	P1=0.406 P2=0.027* P3=0.002*
Comparison of change in AFI from 1 st follow up (Paired t test)	P1=0.001* P2<0.001* P3=0.009*	P1=0.004* P2=0.001* P3=0.021*	P1=... P2=0.001* P3=0.006*		----
% of change	% ₁ =17.81% % ₂ =49.3% % ₃ =50.4%	% ₁ =31.4% % ₂ =75.8% % ₃ =74.7%	% ₁ =4.0% % ₂ =6.9% % ₃ =8.3%		

F: One Way ANOVA test, P1: difference between group A & B, P2: Between group A & C, P3: difference between group B&C. *Statistically significant.

DISCUSSION

In the current study, we included 14 cases in each group with a total of 42 participants (pregnant women with isolated oligohydramnios above 34 week of gestation) AFI was assessed by ultrasound where an AFI of 5.0 cm or less is defined as oligohydramnios. The mean ages of the included cases were 28.29, 24.78, 24 years for the rehydration groups A, B and control group respectively. Also, 13 cases were multi-gravida in *Group A*, whereas only 5 cases were primi-gravida in *Group B* and 10 cases were multi-gravida in *Group C* and the median for parity was 2 (0-4) for *Group A*, 1 (0-3) for *Group B* and 1 (0-3) in *Group C*.

The mean gestational age of the included cases in the present study was 35.86 in *Group A*, 36.31 in *Group B* and 36.59 weeks in *Group C*, with no statistically significant difference between the three groups. There was also no significant statistical difference between the three groups in bi-parietal diameter, head circumference and femur length. The mean fetal weight was 2541.07, 2736.21, and 2907.86 gm. in groups A, B and C respectively with significant increase in *Group C* compared to *Group A*.

All our interventional cases had pretreatment investigation to ensure their safety and to avoid selection bias, we did random blood sugar test for all participant with mean of 99 in *Group A*, 103.86 in *Group B* and 105 in *Group C*, the serum albumin, serum creatinine, AST and ALT were also investigated to all interventional cases, the mean serum albumin ranged from 3.63 to 3.25 in the three groups, the mean serum

creatinine ranged from 0.575 to 0.60. In the interventional groups, AST and ALT mean ranged from 28.58 to 22.64 and from 22.16 to 22.45 respectively. There were no significant differences between all groups.

In the three groups the mean values of pulsatility index were 0.951, 0.940, and 0.919 in groups A, B and C respectively and the mean of the resistant index ranged from 0.618 to 0.601 in the three groups with no statistically significant difference found in between the three groups.

In this study, the mean AFI in group A before treatment was 4.54 and in *Group B* it was 4.46 with no significant difference between the two groups (p=0.692), and the mean AFI for *Group C* was 4.72 with no significant difference between groups A and C (P=0.344) and between groups B and C.

The percent of amniotic fluid index change in *Group A* was about 17.81% of increase after 48 hours of 1 liter of fluid administration per day from the baseline before intervention (P1=0.001*) and about 49.3% of increase after one week of intervention for the same group in relation to the baseline AFI (P2<0.001*), these percent of change remained nearly unchanged after one week of discontinuing the intervention (50.4%) P3=0.009*.

The amniotic fluid index changed in *Group B* after 48 hours of intervention by 31.4% when compared to the pretreatment baseline values (P1=0.004*), and increased by 75.8% after one week in relation to the baseline (P2=0.001*), but when we compared the AFI

in the same group after stopping the intervention for one week later in relation to the baseline, it nearly remained unchanged and was about 74.7% of increase ($P_3=0.021^*$).

Meanwhile in *Group C* the mean amniotic fluid index before starting hydration was 4.72 and when reassessed after one week it was 4.39 with a 6.9% drop ($P_2=0.001$) and 8.3% change after two weeks from the baseline ($P_3=0.006^*$).

The change of AFI in *Group A* who had 1 liter of fluids per day was statistically significant after 48 hours of hydration and after one week of continuous hydration ($P_1=0.001^*$ and $P_2<0.001^*$ respectively) and remained nearly constant after that with significant difference after another week from stopping the intervention ($P_3=0.009^*$) in relation to pretreatment values. *Group B* also had manifested change in the AFI after 48 hours of hydration as the mean AFI changed from 4.46 before hydration to 5.86 after 48 hours ($P_1=0.004$) and reached mean of 7.84 after one week of continuous hydration ($P_2=0.001^*$), and after that it remained nearly stable around 7.79 after stopping hydration for one week (p value $P_3=0.021^*$).

The mean AFI in *Group A* after 48 hours of treatment was 5.35 and in *Group B* it was 5.86 with no statistically significant difference between the two groups ($p=0.314$). There was also no statistically significant difference between the values of AFI after one week of intervention in *Group A* in relation to *Group B* ($P_1=0.139$) indicating that the daily amount of fluid administered did not make significant statistical difference between both groups (A and B), which is consistent with the conclusion reached by **Gizzo et al.** ⁽¹³⁾ in his meta-analysis that the effect of hydration therapy is time dependent rather than daily dose dependent.

In comparing both groups A and B in relation to the control group (*Group C*) we found significant statistical difference in amniotic fluid index between groups A and C after one week, and this significant difference was also demonstrated between groups B and C after one week of hydration in relation to *Group C* that had a decrease of AFI by 6.9% after one week with a statistical significant difference between both groups ($P_3<0.001^*$).

Measuring the effect of daily intravenous hydration for 7 days in our study, we found that when we stopped the intervention after one week the mean AFI remained stable in both groups A and B with no statistically significant difference between both groups after two weeks from the baseline ($P_1=0.406$). On the other hand, there were significant statistical difference between groups A and C $P_2=0.027^*$ after one week of stopping hydration, and significant difference between groups B and C also after the same period ($P_3=0.002^*$). In contrast, **Malhorte and Deka** ^(14, 15) did not find any persistent improvement in AF volume after IV isotonic fluid for one day. The persistence of significant

improvement in quantity of AF after cessation of hydration therapy, which represents a good advantage of the current study, may be related partially to change and improvement of the maternal personal history of insufficient fluid intake that may explain some cases of isolated oligohydramnios. Also, presence of hypotonic fluid may probably lead to long-established physiological homeostasis between maternal and fetal side in establishing a correct fetal AF volume.

The effect of maternal intravenous hydration on amniotic fluid index in this study is consistent with that described by **Patrelli et al.** ⁽¹⁰⁾ who evaluated the effect of 1500 ml of intravenous isotonic hydration per day for 6 days only. His study included a total of 137 cases who were divided randomly (66 cases with isolated oligohydramnios allocated to the intravenous hydration group and 71 normal pregnant women without oligohydramnios in the control group). The mean age of the included cases was 26.1 and 25.3 years for intervention and non-intervention groups respectively ($p >0.05$) with the mean gestational age of included cases at recruitment was 31.5 weeks in the interventional group and 31.4 weeks for the control group ($p >0.05$) ⁽¹⁰⁾. He also described the results in another way whereas the mean AFI (SD) at recruitment was 39.68 (SD 11.11) mm in *Group A*, compared to 126.92 (SD 10.59) mm in the control group ($P <0.001$). The mean AFI increased to 77.70 (SD 15.03) mm after 6 days of therapy in *Group A* (overall $P <0.001$) but was unchanged in *Group B* (control group). In our study, unfortunately, we did not follow up the intervention group except for only one week after discontinuation of hydration therapy but **Patrelli et al.** ⁽¹⁰⁾ randomly subdivided *Group A* into subgroups A1 and A2, similar in baseline characteristics, according to different daily home water intake volumes into subgroup A1 with daily intake of 1500 mL and subgroup A2 2500 mL/d. and continued their follow up till delivery.

Furthermore, our results as regards the improvement in AFI after prolonged IV hydration are in agreement with that obtained from a randomized controlled trial done by **Cicily et al.** ⁽¹⁾. They recruited 136 singleton pregnant females with gestation age >34 weeks with oligohydramnios who were subsequently randomized into an intervention group that received 1 liter of hypotonic solution (ringer lactate) I.V given daily for 5 days only and control group. In his research, with IV hydration therapy, mean increase in AFI was 4 cm and minimum duration needed for improvement was one week. Also, in the same way like **Patrelli et al.** ⁽¹⁰⁾, all cases were followed-up till delivery to evaluate changes in AFI as well as maternal and perinatal outcomes where he concluded that IV hydration therapy showed significant improvement in the maternal and fetal outcomes. The main criticism for **Cicily et al.** ⁽¹⁾ study is that the intervention group was heterogeneous with different causes of oligohydramnios rather than the

isolated (idiopathic) type in both current study and that of **Patrelli et al.** ⁽¹⁰⁾.

The documented usefulness of maternal hydration to improve AFI in the current study is also supported by the systematic review and meta-analysis done by **Gizzo et al.** ⁽¹³⁾ where the authors concluded that maternal hydration is simple, safe, mostly well-tolerated and inexpensive therapy that may possess potential clinical usefulness in obstetric care. They, also, concluded that combination of IV and oral hydration is more effective than oral and lastly IV one with the use of hypotonic more superior to isotonic fluid and duration of therapy not less than 2 weeks (a time dependent therapy more than dose dependent) of daily amount more than 1500 ml. However these conclusions based on weak evidence as most studies had heterogeneity in patient selection criteria, sonographic diagnostic criteria, implementation of different hydration protocols and outcomes measured. Thus further studies are mandatory to reach sound conclusions ⁽¹³⁾.

The limitations of current study were the small sample size that was conducted in a single center. Also, lack of long-term follow up (more than two weeks) of amniotic fluid quantity and how long time the improvement of AF volume remains and necessity of further attempts to keep suitable AF volume until delivery, effect of hydration therapy on prolongation of pregnancy, mode of delivery beside our data lacks documents of important maternal and perinatal outcomes. Unfortunately, most of limitations beyond our scope of study were attributed to catastrophic event of COVID-19 pandemic and its effects upon ordinary medical services.

In conclusion, after one week of continuous daily hydration with different amounts of fluid intravenous hydration had manifestly changed the amniotic fluid index in cases of isolated oligohydramnios in pregnant women above 34 weeks of gestation. The amount of fluid administered did not make significant difference after 48 hours of hydration and after one week. The increase after one week of continuous hydration was more than that after 48 hours and it remained stable for another week when the hydration was stopped. Applying this safe and effective method in mothers with oligohydramnios and gestational age of above 34 weeks can eliminate the need to terminate the pregnancy before term which has terrible consequences on the mother and the fetus.

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