"A RANDOMISED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF THREE DIFFERENT METHODS OF MATERNAL HYDRATION FOR OLIGOHYDRAMNIOS"

By

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UNDER THE GUIDANCE

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ABSTRACT

AIMS

To compare efficacy of maternal hydration with oral water, 1L of Ringer lactate(RL) + 1L of 5% Dextrose(5%D) and 2L of 0.45% Normal saline (0.45% NS) in increasing AFI in patients with oligohydramnios.

MATERIALS AND METHODS

Patients who had been diagnosed as oligohydramnios (with AFI<8) by USG were included in the study. Detailed history of all the patients was taken and complete examination was done.

Totally 108 cases were allocated into 3 groups depending on the computer generated randomized table. Group 1(36) was given oral hydration i.e., 2L of water in 2 hours. Group 2(36) received 1L R.L+ 1L 5%Dextorse in 2 hours intravenously and Group 3(36) was given 2L 0.45%NS in 2 hours intravenously. AFI & Symphysiofundal height was assessed after 2 hours and 24 hours after the hydration therapy.

RESULTS

All the types of hydration therapy had significant increase in AFI and SFH at 2 hours and 24 hours. In group A mean increased from 4.91 ± 1.58(baseline) to 5.88 ± 1.86 and 6.49 ± 2.22 at 2hours and 24 hours respectively. Similarly in group B the mean increased from 4.98 ± 1.86 to 5.79 ± 1.89, 6.18 ± 2.23 at 2 and 24 hours respectively. In group C also these the mean value increased from 5.58 ± 1.31 to 7.32 ± 1.40, 8.32 ± 1.77 at 2 and 24 hours. There was significant increase in group C when compared to other two groups and there was no statistically significant difference

between group A and group B. There was significant rise in SFH in all the three groups at 2 hours and 24 hours. None of the patients had any major side effects.

CONCLUSION

Both oral and IV hydration with hypotonic solution increases the level of amniotic fluid in cases of oligohydramnios. But 0.45%NS was shown to be significantly better than oral hydration and IV hydration with RL+5%D. SFH can be used to assess the amount of amniotic fluid clinically whenever AFI by ultrasound is not feasible.

LIST OF ABBREVATIONS

AF	–	Amniotic fluid
AFV	–	Amniotic fuid volume
AFI	–	Amniotic fluid index
RL	–	Ringer lactate
5%D	–	5% Dextrose
0.45% NS	–	0.45% Normal saline
NS	–	Normal saline
FGR	–	Foetal Growth Restriction
USG	–	Ultrasonography
IV	–	Intravenous
L	–	Liter
SFH	–	Symphysiofunal height
LSCS	–	Lower segment cesarean section
NICU	–	Neonatal intensive care unit
ACE inhibitors	–	Angeotensin converting enzyme inhibitors

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INTRODUCTION

The amniotic fluid (AF) is a part of the fetus's life support system.[1] Amniotic fluid is produced after the amniotic sac is formed at about 12 days after conception. It is first made up of effusion provided by the mother's circulation and then around the 20th week fetal urine becomes the primary source. As the baby grows it will move with the help of the amniotic fluid. In the second trimester the baby will begin to breathe and swallow the amniotic fluid.[2] Amniotic fluid aids in the development of muscles, limbs, lungs and digestive system. Amniotic fluid also provides temperature stability, cushioning and its presence in the collapsed airways helps to stimulate lung development. The amniotic fluid volume is an important indicator of fetal wellbeing and also an important part of antenatal fetal surveillance.[1]

In some cases the amniotic fluid may be too low or too high. If the measurement of amniotic fluid is too low it is called oligohydramnios. Oligohydramnios is defined as amniotic fluid index (AFI) less than normal for that gestational age.[3] AFI below 8cm is borderline oligohydramnios and less than 5cm is known as oligohydramnios. The AFI more than 24 cm is called polyhydramnios. [4] The incidence of oligohydramnios is 8.5%-15.5%.[3] It can occur at any time during pregnancy, but it is most common during the third trimester. In 2005 Leeman et al. reported that oligohydramnios occurred in about 1 % to 5 % of pregnancies at term.[5] At term the average AF is approximately 750ml, but volume decreases rapidly after 40 weeks.[6] Postdated pregnancies are at risk of oligohydramnios because the AF can decrease by half once woman reaches 42 weeks gestation. Oligohydramnios can complicate 12% of pregnancies above 41 weeks of gestation.[2]

Oligohydramnios is caused by fetal urinary tract abnormalities, conditions causing, fetal growth restriction, uteroplacental insufficiency, drugs like prostaglandin inhibitors, ACE inhibitors, rupture of membranes.[7]

The common clinical findings are smaller symphysiofundal height, fetal malpresentations, undue prominence of the fetal parts and reduced amount of amniotic fluid on palpation.[2] Oligohydramnios is most consistently associated with FGR and the mechanism is probably uteroplacental insufficiency which explains the genesis of both fetal growth restriction and decreased liquor. Fetal hypoxia causes redistribution of cardiac output in favor of fetal brain and diverting the blood supply away from kidney and lungs. This results in decreased fetal urinary production and decreased lung secretions, which contribute the amniotic fluid volume.[8]

Oligohydramnios is also associated with other complications like pressure induced deformities like potter facies, pulmonary hypoplasia, congenital malformations, increased risk of cord compression, high rate of surgical delivery and meconium aspiration syndrome.[2,8] The risk of adverse perinatal outcome increases even in low-risk pregnancies when oligohydramnios is diagnosed after 40 weeks. Maternal Outcome is not affected adversely due to oligohydramnios. However, increased interventions like induction of labour and caesarean deliveries due to fetal growth restriction and preterm delivery indirectly increase maternal morbidity.[9]

Several treatment modalities have been suggested to restore amniotic fluid volume to its normal range and to reduce the perinatal mortality and morbidity. These include maternal hydration (oral and intravenous), amino acid infusion, omega 3 fatty acids, desmopressin, serial trans-abdominal amnioinfusions, intramniotic sealing techniques.[3,7,9-26] Some of these treatment modalities need hospital admission and surgical interventions which are associated with serious side effects.[16,21] An effective

medical therapy for oligohydramnios is very important for the fetus to grow normally to near term. Out of all, maternal hydration is a feasible method, cheap and devoid of serious side effects.

Many studies have proved that oral hydration therapy with water is better than IV therapy, [3] but IV has the advantage that a fixed amount of fluid can be infused at a relatively constant rate with ensured compliance.

Various fluids have been tried for maternal IV hydration like Normal saline, Ringer lactate, 0.45% Normal saline and 5%Dextrose.[13-18] Some authors studied only 5% D and some have studied only RL.[13,16] But hydration with 5% Dextrose has the theoretical risk of transient hyperglycemia, especially if it is given in post prandial period. Indian women, who are prone for diabetes mellitus, are at greater risk, especially if they are undiagnosed. Ringer lactate fluid has more sodium concentration hence combining these two fluids might reduce risk of hyperglycemia and the combination becomes more hypotonic. So, we decided to combine these two fluids.

One more fluid commonly used as hypotonic fluid in pediatric age group is 0.45%NS.[18] But its efficacy has not been tested widely for improving AFI. So, we wanted to study whether this hypotonic fluid will be effective in improving AFI.

Many patients diagnosed by other practitioners as oligohydramnios were already started on arginine granules and amino acids orally, so we decided to continue the treatment in all the three groups so that we can avoid bias.

Many studies have taken AFI at various timings like 1 hour, 1 ½ hour, 2 hours and 3 hours, 4 hours, 24 hours and 48 hours.[13,16-17,19-20,22-23] We have taken AFI at 2 hours and 24 hours as 1 hour will be too early for amniotic fluid to raise. So, Baseline AFI

was taken and repeated 2 hours after hydration. Repeat AFI was done at 24 hours as we wanted to know the duration of effect of hydration therapy.

So, in the present study we have compared the efficacy of maternal hydration with oral water, 1 L of RL+ 1 L of 5%D and 2 L of 0.45% NS over 2 hours.

OBJECTIVE OF THE STUDY

PRIMARY:

1. To compare efficacy of maternal hydration with oral water, 1L of Ringer lactate(RL) + 1L of 5% Dextrose(5%D) and 2L of 0.45% Normal saline (0.45% NS) in increasing AFI in patients with oligohydramnios.

SECONDARY:

1. To know the duration of effect of hydration therapy.
2. To know the increase in symphysiofundal height due to hydration therapy.
3. To know the side effects of each method.

REVIEW OF LITERATURE

Oligohydramnios is treated with various types of hydration therapies like oral, intravenous hydration.

Goodlin RC, et al (1983) found the relation between maternal plasma volume expansion and amniotic fluid volume. In this study amniotic fluid and maternal plasma volumes were estimated in high-risk obstetric patients who were suspected of being hypovolemic. Patients with intrinsic maternal or fetal disease were excluded from the study. There was good (P value is less than 0.001) correlation between maternal plasma volume expansion and amniotic fluid volume. In the presence of oligohydramnios, there is usually maternal hypovolemia, and vice versa. Oligohydramnios may be treated with vigorous maternal plasma volume expansion by fluids. They concluded that only if maternal plasma volume expansion is normal, there will be normal uterine perfusion, sufficient to provide amniotic fluid formation in normal amounts.[27]

Shere et al. (1990) accidentally found that hydration therapy increases amniotic fluid. A patient gravida 4, para2 with 35 weeks gestation with acute maternal hypovolemic situation with oligohydramnios without any medical history with prior normal amniotic fluid at 31 weeks, was treated with intravenous fluid hydration. Then they noted that there was immediate reaccumulation of normal amniotic fluid volume.[28]

ORAL HYDRATION

Acute oral hydration decreases maternal osmolality. This inturn causes the shift of water from mother to fetus. So, there will be decrease in fetal plasma osmolality which causes fall in fetal arginine vasopressin secretion, this leads to increase in fetal urine production and increase in amniotic fluid.[12]

Kilpatrick SJ et al (1991) studied the effect of maternal oral hydration in oligohydramnios. Pregnant women were divided into 2 groups, study group contained patients with oligohydramnios and control group had patients with normal amniotic fluid. Patients in both the groups were given hydration with 2 liters of water orally. It was found that there was increase in amniotic fluid volume up to 16% in women with normal amniotic fluid and upto 31% in women with oligohydramnios. [10]

Kilpatrick SJ et al. (1993) repeated a similar study on women with normal amniotic fluid, to prove that maternal oral hydration would increase the amniotic fluid (AF) index in pregnancies with normal amniotic fluid. Forty women with a normal AFI were randomized into 2 groups. In hydration group women drank 2 L of water and women in the control group drank only 100 mL of water. AFI was assessed 4-6 hours after treatment. The mean AFI in the hydration group increased significantly by 3.0 +/- 2.4 cm (P < or = .0001) whereas it declined significantly by 1.5 +/- 2.7 cm in the control group (P < or = .02). The maternal urine specific gravities also changed significantly i.e., in the hydration group decreasing and in the control group increasing (P < or = .0001). In the hydration group there was increase in the AF index by approximately 16%, whereas fluid restriction decreased the AFI by 8% in women with normal AFI. These findings support the data in the earlier study that maternal hydration increased the AFI by 31% in women with decreased AF and suggest that maternal fluid volume or osmolality may have a role in maintaining the AF volume.[20]

Ten women with third-trimester oligohydramnios (amniotic fluid index < or = 5 cm) and 10 controls with normal amniotic fluid volume (amniotic fluid index > 7 cm) were recruited prospectively for this study by Flack NJ et al. (1995). Patients were asked to drink 2 L of water over 2 hours. There was a significant reduction in maternal plasma ($p < 0.05$) and urine osmolality ($p < 0.0001$) in both groups after oral

hydration. Hydration increased amniotic fluid volume in women with oligohydramnios (mean change in amniotic fluid index 3.2 cm, 95% confidence intervals 1.1 to 5.3; $p < 0.02$) but not in those with normal amniotic fluid volume (mean change in amniotic fluid index -2.0, 95% confidence intervals -4.1 to +0.2). Hydration was associated with an increase in uterine artery mean velocity in the oligohydramnios group but not in controls, the hourly fetal urine production rate, however, did not increase in either group. There was no change in pulsatility index or in velocity in any of the fetal vessels studied in either group.[11]

A prospective randomized controlled trial was conducted on pregnancies complicated by idiopathic oligohydramnios by Tito Silvio Patrelli, et al to know the effect of maternal intravenous and oral hydration on the quantity of amniotic fluid. In this study Group A underwent 6 days of intravenous infusion of 1500 mL of an isotonic solution per day over 6 hours. An AFI measurement, a nonstress test, and a fetal biophysical profile were performed at 0 and 7 days which was compared with the control group(Group B) . Group A was randomized into subgroups A1 and A2 and were followed till birth. Subgroup A1 was prescribed home oral hydration therapy of 1500 mL/d and subgroup A2 2500 mL/d. They considered the AFI to compare the effectiveness of the therapy. In group A, the mean AFI ± SD at recruitment was 39.68 ± 11.11 mm and in group B, it was 126.92 ± 10.59 mm ($P < .001$). In group A, the mean AFI after 7 days was 77.70 ± 15.03 mm ($P < .001$) and in group B, it was unchanged. In subgroup A1, the mean AFI at birth was 86.21 ± 16.89 mm and in subgroup A2, it was 112.45 ± 14.92 mm ($P < .001$). It was concluded that in pregnancies complicated by isolated oligohydramnios, both oral and intravenous hydration therapy significantly improves the quantity of amniotic fluid.[7]

A study was conducted by Bhawna Malhotra et al, in department of obstetrics and gynaecology, AIMS, New Delhi on 100 subjects i.e., 50 subjects in each group. Hydration group was instructed to drink 2 L of water over 1hour and repeat AFI was done after 3 hours and in control group 50 subjects were allowed to drink only 100 ml of water. The mean AFI in hydration group increased significantly whereas it declined significantly in control group.[19]

Pragati Mishra et al conducted a prospective clinical trial to assess the effect of oral hydration therapy on amniotic fluid volume in isolated oligohydramnios (AFI <10) cases in third trimester. Total 137 women were selected over the period of four years. Hydration therapy in the form of 2 litres of water orally was given over 2 hours above the routine fluid intake and the change in AFI was reassessed after 3hours, 24hours and 48 hours. Cases were followed till delivery, noting intra-partum complications and perinatal outcome. Short term improvement in amniotic fluid volume was achieved after oral hydration therapy, which persisted into long term if hydration therapy was continued and had its favourable impact on perinatal outcome also. Mean pre-hydration AFI was 5.75 ± 1.59 at '0' Hour which increased to mean post-hydration AFI of 6.09 ± 1.65cm ($p=0.0836$) at 3 hour and 7.41 ± 1.46 cm ($p<0.0001$) at 24 hours. It suggests that oral hydration starts increasing the amniotic fluid within 3 hours and is maintained till 24 hours. Continuation of therapy further increased the amniotic fluid volume and at 48 hours mean amniotic fluid index was 8.06 ± 1.55 cm ($p<0.0001$). Except for the 3 hour change ($p=0.0836$) both 24 hour and 48 hour mean AFI was significantly improved ($p<0.0001$) from base line AFI with 95% confidence.[23]

A prospective, nonrandomized, interventional study was conducted by Fiat G et al (2003). 30 women with AFI < 10th percentile were included in study group and

30 women with AFI >10th percentile were included in control group. The women in both the groups were instructed to drink at least 2L of water daily and their AFI was evaluated before and 1 week after the initiation of oral hydration. AFI increased from 8.1 +/- 0.73 to 11.8 +/- 2.4 1 week later (P < .01) in 25 (83%) of the study subjects. But AFI was similar before and 1 week after oral hydration in all the controls. This study concludes that long-term maternal oral hydration seems to significantly increase the AFI in selected women with reduced fluid.[29]

Jignesh Kansaria, et al, have done a study, "Oligohydramnios and Maternal Hydration Therapy" to assess its effects on amniotic fluid volume. In the study 33 patients with oligohydramnios were advised maternal hydration therapy i.e., at least 2 litres of oral fluids in a day. Maternal hydration showed improvement in amniotic fluid volume (AFV) in 24 patients with oligohydramnios. They concluded that simple maternal hydration appears to increase amniotic fluid volume.[30]

Akter MD et al conducted a randomized controlled trial on 64 pregnant women from 32 to 35 weeks gestation, to determine the effect of oral hydration in women with amniotic fluid index (AFI) ≤ 5. Patients in Group A were instructed to drink 2 liters of water in 2 hours and from the next day extra 2 liters of water daily for 7 days. Group B women were allowed for routine water intake. AFI was done after 2 hours, 24 hours and 7 days of oral hydration therapy in both the groups. P values less than 0.05 was considered statistically significant. Pre-treatment mean AFI was 4.77 ± 0.42 (mean ± SD) vs. 4.80 ± 0.43 (mean ± SD) and post treatment AFI after 2 hours was 6.35 ± 0.65 vs. 4.81 ± 0.42 after 7 days was 7.08 ± 0.21 vs. 5.0 ± 0.20 in oral hydration group and control group respectively. They concluded that maternal oral hydration therapy significantly increases the AFI.[31]

INTRAVENOUS HYDRATION THERAPY

Umber A et al (2007), conducted a study on 50 women in 3rd trimester with oligohydramnios to determine the effect of acute intravenous maternal hydration on amniotic fluid volume. The Study group had 25 women with third trimester oligohydramnios and the control group had 25 women with normal amniotic fluid. Both the groups received IV hydration with 2 L 5%Dextrose in 2 hours. Specific gravity of urine and amniotic fluid index were noted before and after treatment. It was observed that amniotic fluid volume increased in both the groups. However, the percentage increase in mean AFI was 58.6% in the study group, which was significantly greater than the percentage increase of 28.4% in control group.[32]

Shivkumar PV, et al conducted a study to know the role of intravenous hydration and amino infusion in FGR and Oligohydramnios. Group A received no infusion and were kept on high protein diet. Group B received IV infusion of NS, RL, 5%Dextrose, in ratio of 2:1:2(5 pints) given on alternate days for 3 days in a week. Group C received amino acid drip 100ml twice daily on alternate days for 3 days in a week. Group D received amino acid drip 100ml twice daily on alternate days for 3 days in a week along with iv infusions of NS, RL, 5%Dextrose in ratio of 2:1:2(5 pints) given on alternate days for 3 days in a week. It was found that if IV fluids & IV infusion of amino acids, when given as a week regimen on alternate days, increased the short term AFI and also the foetal weight.[14]

A research was done by Mahnaz Shahnazi et al, to evaluate the effects of intravenous hydration on amniotic fluid volume. A single blind controlled clinical trial was conducted on 20 pregnant mothers with amniotic fluid index of lower or equal to 5 cm and gestational age of 37-41 weeks. The subjects were divided into two groups of case and control. The case group received one liter of isotonic saline during

30 minutes by the bolus method. Revaluations of amniotic fluid index in both groups were made 90 minutes after baseline measurement. Intravenous hydration therapy significantly increased the amniotic fluid index in the case group (mean change: 1.5 cm; 95%CI: 0.46 - 2.64; P = 0.01). The mean change of amniotic fluid index in the control group did not significantly increase (P = 0.06). The elevation of amniotic fluid index in the hydration group (32%) was significantly higher than the control group (1%) (P = 0.03).[22]

It is a prospective cohort study by Jorge Burgos et al, to analyse whether maternal intravenous fluid therapy prior to external cephalic version (ECV) increases the amount of amniotic fluid and the success rate of the procedure. 100 pregnant women with a breech presentation at term were administered with 2 L of hypotonic saline IV before the version attempt, compared to a control cohort of 100 pregnant women not given hydration treatment. Intravenous fluid therapy with 2 L of hypotonic saline prior to ECV was found to be an effective and safe technique for increasing the AFI. However, its use in ECV did not increase the success rate of the procedure. The mean increase in the amniotic fluid index (AFI) after intravenous maternal hydration was 3.75 ± 2.71 cm ($P < .01$).[33]

Magnna EF et al. studied the intravenous hydration therapy and observed a median change of 1.7 cm in the amniotic fluid index due to therapy.[34]

One more fluid commonly used as hypotonic fluid in pediatric age group is 0.45%NS[17] but its efficacy has not been tested widely for improving AFI.

A randomized clinical trial was conducted by Linnli Yan-Rosenberg et al, comparing the effect of maternal intravenous hydration and placebo on the amniotic fluid index in third trimester oligohydramnios. 44 patients having AFI<6 were included in the study. Patients in study group were given IV 0.45% Normal saline at

rate of 1000 ml/hr for 2 hours. Patients in placebo group were given 0.45% NS at 10 ml/hour for 2 hours. Maternal age, parity, gestational age, birth weight in both the groups were not significantly different. The AFI was reassessed after 1 hour after the hydration. There was increase in AFI in both the groups. The changes in AFI did not significantly differ between the treatment and the placebo groups (1.2±2.1 vs 1.5±2.1, respectively; $p>0.05$).[17]

ORAL AND INTRAVENOUS HYDRATION THERAPY

A study was conducted by Doi S et al, to determine the effect of maternal hydration with IV isotonic fluid, IV hypotonic fluid, and oral water on amniotic fluid index (AFI) in women with oligohydramnios. Patients with low AFI and gestational age over 35 weeks without maternal complications were randomized into four groups (2 L/2 h IV isotonic fluid, 2 L/2 h IV hypotonic fluid, 2 L/2 h oral water, control). Eighty-four patients (n=21/group) completed the study without any maternal adverse effects. The mean increase in AFI after hydration was significantly greater in the IV hypotonic and oral water groups (2.8+/-1.9, $P < .001$; 3.8 +/-1.9, $P < .001$, respectively), but not in the IV isotonic group (0.5+/-1.1), compared with the control group (0.5+/-1.1). Maternal hydration with either IV hypotonic fluid or oral water increases AFI in oligohydramnios. Maternal osmotic change had direct impact on increasing amniotic fluid volume with short-term acute hydration.[35]

Umber A et al, conducted a study on 50 women in 3rd trimester with oligohydramnios Group A received IV hydration with 2 L 5%Dextrose in 2 hours. In Group B oral hydration was given 2 liters of water in 2 hours. In IV hydration group, the mean AFI increased from 3.2 cm to 7.7 cm and in oral hydration group, it increased from 3.2 to 7.5cm. However, the percentage increase in mean AFI was

58.6% in the intravenous hydration group, which was not significantly greater (P value>0.05) than the percentage increase of 58.4% in oral hydration group.[13]

A study was conducted by Nahid Lorzadeh , et al on 80 subjects who were divided into 4 groups . Group A: Control group receiving no suggestion in regards to fluid intake. Group B: Oral intake of 2 L/2 hours of water. Group C: IV infusion of 2 lit/2hours of isotonic fluid (Normal saline). Group D: IV infusion of 2L/2hours of hypotonic fluid (Ringer's solution). USG was performed twice, one before oral hydration therapy and the second, one hour after IV hydration. The mean AFI difference in 3 groups i.e., oral water, IV isotonic, IV hypotonic before and after intervention was significant ($p<0.0001$) but in control group this difference was not statistically significant.[16]

A comparative study was done by Prasanta C.Chandra, et al to study the effects of oral and intravenous hydration in oligohydramnios. Group A, consisted of 20 subjects who received oral hydration of 10-12 glasses per day, Group B included 30 women who were given intravenous hydration therapy with Ringer lactate 4000ml. Actual time between AFI assessment in Group A averaged 61.9+-11.7hours. In Group B, AFI was repeated after 45.1+-8.9 hours. They found that there was 2/3rds increase in amniotic fluid volume after oral intake as compared to less than half, after intravenous infusion with a P value of <0.05.[18]

In a study done by Shehzad B Momina et al included 113 patients in each group it was done to compare the efficacy of oral and I.V. hydration in management of third trimester oligohydramnios. Group 'A' received intravenous hydration i.e. two liters of 5% dextrose per day for 3 days and Group 'B' was treated with oral hydration i.e. administration of two liters of hypotonic solution (water) per day for 3 days, in addition to their normal routine fluid intake. AFI measurement was repeated

at 3rd day after hydration therapy. Baseline AFI of group A was 2.93±0.11 and group B was 2.92±0.10. AFI after hydration was recorded as 5.89 ± 0.374 in Group – A and 7.48 ± 0.303 in Group – B and P-value was < 0.05, which showed a statistical significant difference. Both oral and IV hydration were effective. But maternal oral hydration was more effective than intravenous hydration in patients.[3]

A Cocharane review was done by Hofmer GJ etal, in 2012 to assess the effects of maternal hydration on amniotic fluid volume. In this maternal hydration (oral or intravenous) was compared with no hydration. It was a review of four trials. Oral hydration of 2 liters of water over 2 hours was associated with increase in amniotic fluid. Intravenous hypotonic hydration at a rate of 1000ml/hour in women with oligohydramnios was associated with an increase in amniotic fluid volume. Isotonic intravenous hydration had no measurable effect.[15]

AMNIOTIC FLUID PHYSIOLOGY:

Amniotic Fluid serves a number of important functions in the development of the embryo and fetus. It cushions the fetus against physical trauma, allows for growth of the fetus, free from restriction or distraction by adjacent structures, provides for a thermally stable environment, allows the respiratory and gastrointestinal tract and musculoskeletal system to develop normally, and helps to prevent infection.[36]

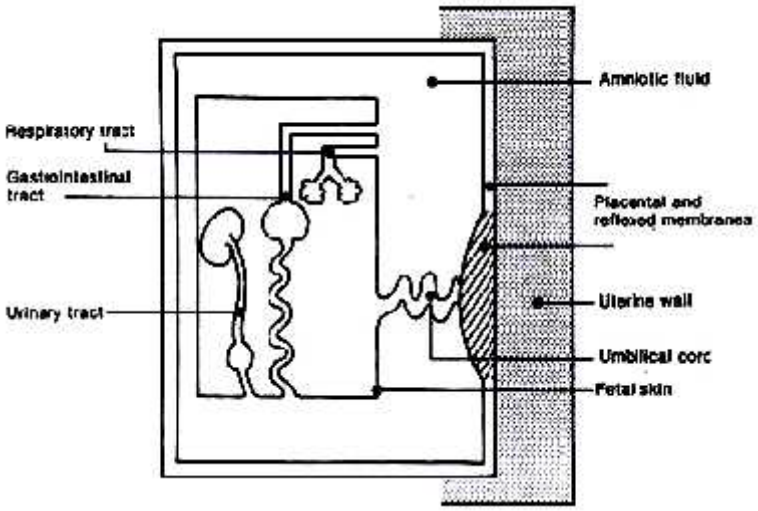


Figure 1: The major fetal and maternal amniotic structures involved in the formation and re- absorption of amniotic fluid.[37]

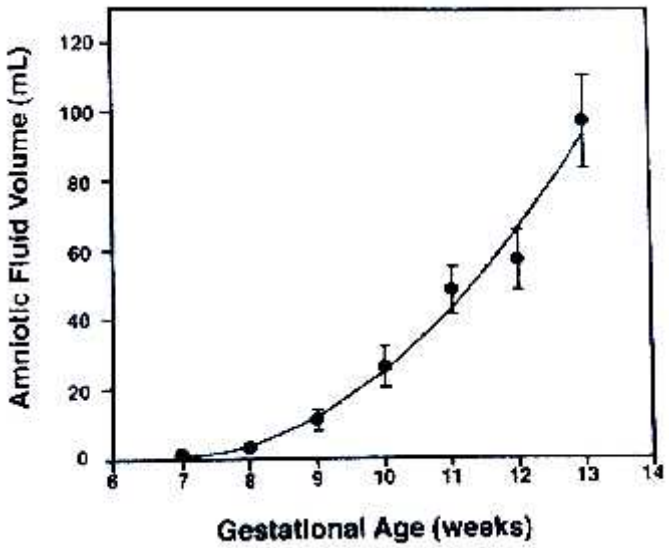


Figure 2 – Amniotic fluid volume in early pregnancy[37]

The regulation of amniotic fluid is a dynamic process. Various pathways are involved in formation and absorption of amniotic fluid. In early pregnancy the chorioamnion acts as a molecular sieve.[36] The two main pathways that are involved in amniotic fluid formation in initial half of pregnancy they are transmembranous and intramembranous pathways. Amniotic fluid increases rapidly in early pregnancy reaching 50 ml at 12 weeks.[37]

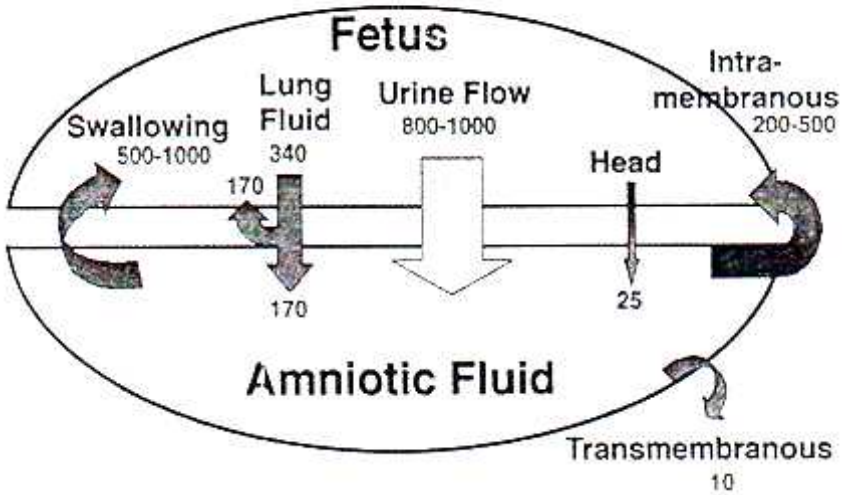


Figure 3 – Summary of water flow in and out of amniotic space in late gestation[37]

In the later half of the gestation, two primary sources of amniotic fluid are the fetal kidneys (fetal urine) and lungs (secretion from oro nasal cavities). The primary sources of amniotic fluid removal are the gastrointestinal tract (swallowing) and absorption into the fetal blood perfusing the surface of the placenta.[37]

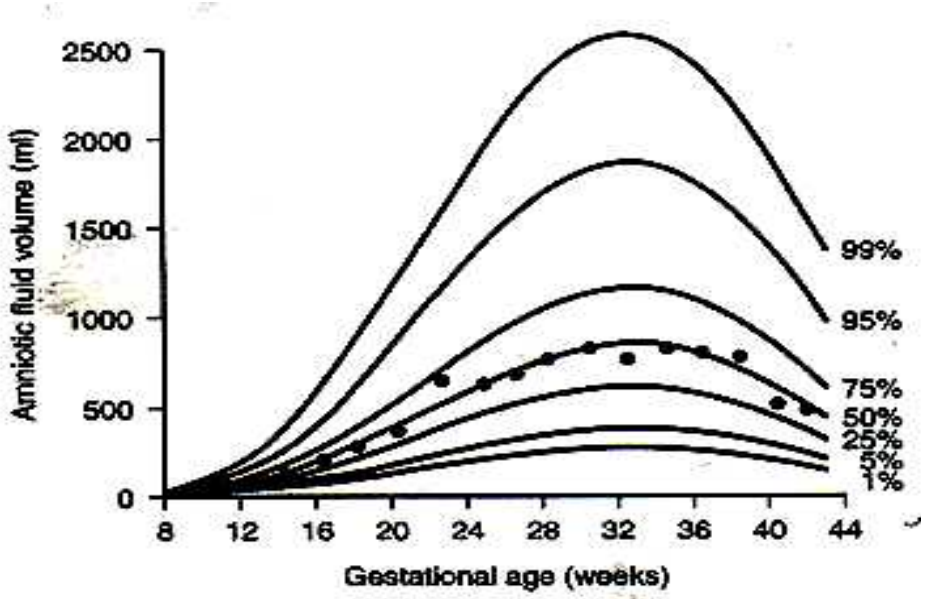


Figure 4 – Normogram showing Amniotic Fluid Volume at different gestational ages.[37]

Amniotic fluid in a same patient varies depending on the gestational age. It increases rapidly in the first half of pregnancy. The increase in amniotic fluid continues approximately till 32 weeks and it remains relatively constant in a range of 700-800ml from 32-39 weeks later declines gradually. From 40 weeks the amniotic fluid decreases progressively at the rate of 8% per week.[37]

ASSESSMENT OF AMNIOTIC FLUID VOLUME:

Various methods include:

1. **Clinical Assessment:**

- Measurement of symphysio fundal height
- Palpation to look for amount of liquor(fetal liquor ratio)

2. **Quantitative Assessment:**

Amniocentesis with instillation of inert chemical marker (paraaminohippurate) followed by determination of the marker. Though it is most accurate method of AFV assessment it is difficult to perform and is invasive.

3. **Semi Quantitative Assessment:**

a) **Subjective Assessment:** The relative amount echo free fluid areas are subjectively compared with the space occupied by the fetus and placenta by USG. It is simple and rapid method.

b) **Maximum Vertical Pocket (MVP):** This technique has evolved from the studies of Chamberlain et al. in which the single deepest uninterrupted pocket of amniotic fluid is measured by USG. Pocket > 2 cm is considered normal.[36]

c) **Amniotic fluid index (AFI):** In 1987, Phelan et al developed a semi quantitative sonographic assessment of the Amniotic fluid volume to be known as the Amniotic fluid index.[38] This measurement is based on the division of the gravid uterus into four quadrants using the external maternal landmarks of the umbilicus and linea nigra. The deepest amniotic fluid pocket in each quadrant, in a similar manner to the maximum vertical pocket, is measured. These four measurements are added together, and the sum is referred to as the Amniotic fluid index.[39]

d) **Two Diameter Pocket – TDP:** This method consists of identifying the deepest amniotic fluid pocket by ultrasound, measuring its vertical and horizontal dimensions, and then multiplying these values together.[40]

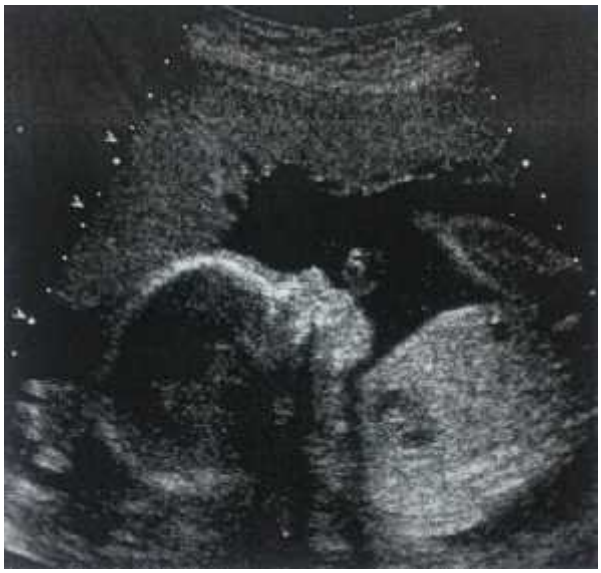


Fig. 5: Picture showing the normal Amniotic fluid with fetus and placenta.[37]

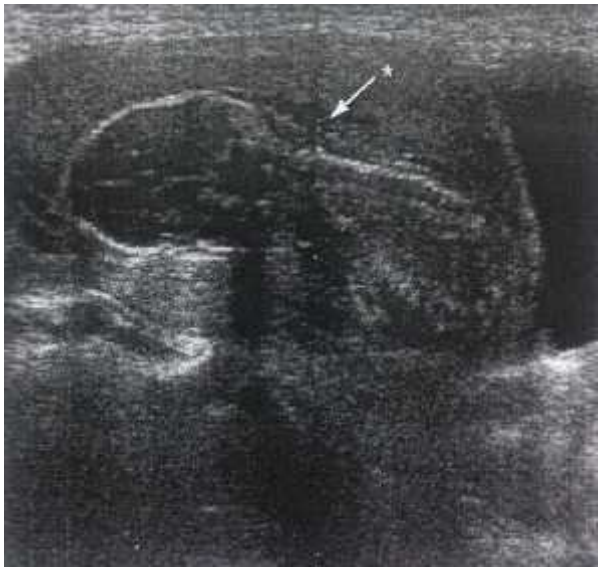


Fig. 6: Picture showing that fetus is "crowded" within the uterus with no amniotic fluid.[37]

Table no 1. Definitions of Oligohydramnios.[37]

Technique	Definition	Reference
USG	Single vertical pocket < 0.5cm	Mercer et al.
USG	Single vertical pocket < 1.0 cm	Manning, Hill, and Platt.
USG	Single vertical pocket < 2 cm	Manning et al.
USG	Single vertical pocket < 3 cm	Halperin et al.
USG	AFI < 5th percentile for gestational age	Moore and Cayle
USG	AFI < 5 cm	Phelan et al
USG	AFI < 7 cm	Dizon Townson et al
USG	AFI < 8 cm	Jeng et al
USG	Two diameter pocket < 15 cm	Magann et al

MANAGEMENT OF OLIGOHYDRAMNIOS

Various treatments have been tried to improve AFI like hydration therapy, amino acid infusion, amnioinfusion, omega 3 fatty acids and arginine granules, drugs like desmopressin. [3,7,9-26] Maternal hydration therapy has been suggested by many authors to restore amniotic fluid volume to its normal range and to reduce the associated perinatal morbidity and mortality.

Among all these, simple maternal hydration has shown to increase amniotic fluid through reduction in maternal plasma osmolality which leads to a rise in AFI. Hydration can be either oral or IV. It is proved that any type of hydration therapy i.e., either oral or IV, has an effect on maternal plasma osmolality which inturn causes increase in amniotic fluid.[13]

Oral hydration is a means of transiently increasing amniotic fluid volume and is less invasive than amnioinfusion. Hydration with oral water reduces maternal plasma osmolality and sodium concentration, resulting in an osmotically driven maternal to fetal water flux. Increased placental blood flow volume, fetal urine output, and possibly decreased reabsorption of amniotic fluid via swallowing or intramembranous flow increases the amniotic fluid volume.[15]

Various fluids have been tried for maternal IV hydration like Normal saline, Ringer lactate, 0.45% Normal saline and 5%Dextrose, fructodex, amino acids. Among these fluids Normal saline(isotonic) has been shown to be not effective and hypotonic solutions like 5%Dextrose and Ringer lactate are effective in improving the AFI , but are less effective compared to oral hydration.

Fructodex solution is a combination of dextrose 5% and fructose 5%. Dextrose and fructose molecules readily pass the placental barrier and act as an energy source for the growing fetus and, hence, may be useful in growth-restricted fetuses. They are

also readily oxidized to carbon dioxide and water at the end of energy production. Carbon dioxide is readily excreted by maternal lungs and the remaining intravenous fluid acts like hypotonic solution which induces osmotic diuresis in even otherwise normal fetus and improves liquor.[25]

Amino acids, an important component of amniotic fluid, their concentration in AF can be improved with good maternal nutrition by intravenous amino acid infusion. In oligohydramnios with growth restriction, serum amino acids were found to be lower than those in normally grown fetuses. This indicates the possibility of intrauterine nutrient deficiency leading to oligohydramnios.[41] Amino acids cross the placenta by an active transport system and their concentration in the fetus are more than in the mother. Infusion of amino acids improved the AFI and its supplementation may be beneficial in the management of oligohydramnios to prolong the pregnancy for better neonatal outcome.[42]

Nitric oxide (NO) is an important regulator of placental perfusion, as it plays a role in placental vascular endothelial function. NO is synthesized by l-arginine/NO pathway from the physiologic precursor l-arginine by the stereospecific enzyme NO synthase. L-arginine is the only substrate for the production of NO.[43] NO diffuses into the underlying vascular smooth muscle cells and mediates vasodilatation and platelet stabilization by a cyclic GMP-dependent process.[15] NO-induced vasodilation in renal vessels may improve glomerular filtration rate (GFR) and thereby enhance fetal urine production. So, treatment with l-arginine may result in significant improvement in liquor.[25]

Transabdominal amnioinfusion is used to treat oligohydramnios with rupture of membranes and second trimester oligohydramnios.[22]This procedure is invasive and is associated with infections.

Desmopressin is an antidiuretic agonist. It causes increased reabsorption of water and increased the urine osmolality along with decreased urine amount with its effect by increasing the permeability of cell membrane. Due to the effects of this drug on plasma osmolality and volume, it is contraindicated in patients with cardiac, renal disease, blood pressure disorder and allergy to this medicine.[26]

MATERIAL AND METHODS

METHODS OF COLLECTION OF DATA:

SOURCE OF DATA:

Pregnant women admitted in BLDE UNIVERSITY'S, Shri B. M. Patil Medical College Hospital and Research Centre, Vijayapura.

PERIOD OF STUDY: December 2014 – June 2016.

SAMPLE SIZE:

Estimation of sample size:

Following formula is used to estimate the sample size for proposed project.

$$n = \frac{(Z_\alpha + Z_\beta)^2 \times 2 \times (SD)^2}{d^2}$$

Here, Z_α= Z value at level=99%

Z_β= Z value at level=85%

SD=Average standard deviations

d= Difference between the means

The mean and SD of Ringer lactate in a study conducted by Lorzadeh N et al[17] was 5.9 ± 0.94 and the mean and SD of oral water in a study conducted by Malhotra B et al[20] was 2.01 ± 3.73.

Considering the average SD 3, at 99% confidence level and 85% power in the study, 30 cases were studied in each group. To compensate for the dropouts, another 6 cases is included in each group. So, total of 36 cases were studied in each group.

Total sample size is 36+36+36=108

Procedure

All the patients who have been diagnosed with oligohydramnios (with AFI<8) by USG were studied. Detailed history of all the patients was taken and complete

examination was done. Patients were screened for anaemia (Hb %), DM (OGCT- oral glucose challenge test), Preeclampsia (Blood pressure charting, urine albumin).

INCLUSION CRITERIA:

1. Antenatal cases between 18years and 35 years
2. Gestational age from 28 -41 weeks
3. Singleton pregnancy
4. AFI<8cms
5. Intra uterine growth retardation with oligohydramnios
6. Unexplained oligohydramnios

EXCLUSION CRITERIA:

1. Hypertensive disorders in pregnancy
2. Pre-existing or gestational diabetes
3. Anaemia (Hb<8gm%)
4. Premature rupture of membranes
5. Multiple gestation
6. Cardiovascular disorder
7. Maternal pulmonary disorder
8. Oligohydramnios due to Fetal congenital anomalies
9. Patients on Non Steroidal Anti Inflammatory Drugs

After having met all the inclusion and exclusion criteria and obtaining written informed consent participants were allocated into three different treatment groups depending on the computer generated randomized table.

GROUP 1: Oral hydration i.e., 2L of water in 2 hours (hypotonic).

GROUP 2: 1L R.L+ 1L 5%Dextorse in 2 hours intravenously.

GROUP 3: 2L 0.45%NS in 2 hours intravenously.

USG was done and AFI was noted by Phelan method at

1) Admission (Before Hydration Therapy)
2) Repeated 2 hours after the hydration therapy
3) Repeated after 24 hours of the hydration therapy

Symphysiofundal height was noted at the time of admission and was repeated along with AFI i.e., 2hours and 24 hours.

COMPOSITION OF FLUIDS

RINGER LACTATE

Each 100 ml contains:

Sodium Lactate solution USP equivalent to Sodium lactate – 0.320 gm

Sodium chloride IP – 0.600 gm

Potassium chloride IP – 0.40 gm

Calcium chloride IP – 0.027 gm

Water for injection IP

5% DEXTROSE

Each 100 ml contains:

Dextrose anhydrous IP – 5.00 gm

Water for injection IP

0.45% NORMAL SALINE

Each 100 ml contains:

Sodium chloride IP – 0.45 gm

Water for injection

RESULTS AND OBSERVATIONS

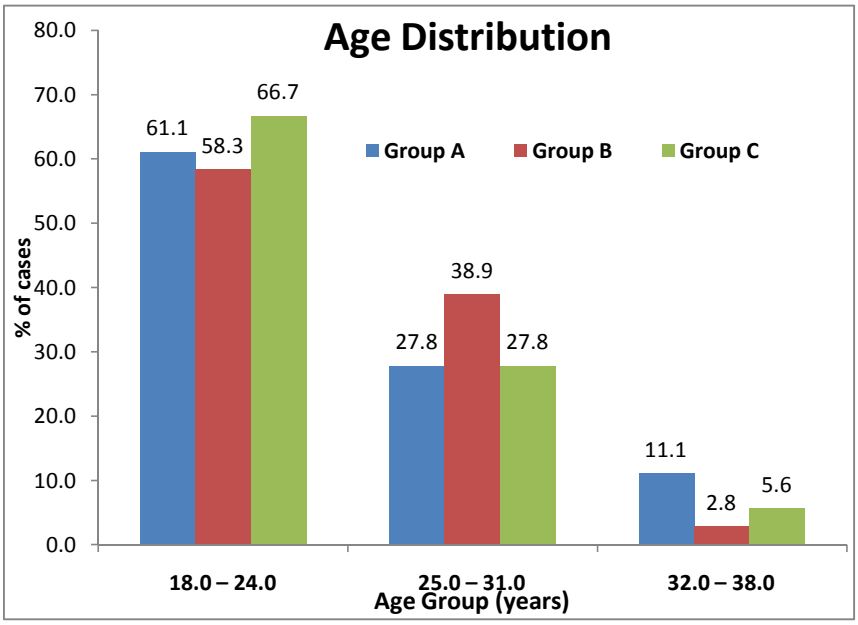
Table 2) The age distribution of the cases studied across three study groups.

Age (years)	Group A (n=36)		Group B (n=36)		Group C (n=36)		Inter Group Comparisons (P-value)		
							Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
	n	%	N	%	N	%			
18.0 – 24.0	22	61.1	21	58.3	24	66.7	0.288^{NS}	0.686^{NS}	0.549^{NS}
25.0 – 31.0	10	27.8	14	38.9	10	27.8	-	-	-
32.0 – 38.0	4	11.1	1	2.8	2	5.6	-	-	-
Total	36	100.0	36	100.0	36	100.0			

Values are n (% of cases). P-values by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1. The distribution of age of the cases studied did not differ significantly across three study groups (P-value>0.05 for all).



Graph 1) The age distribution of the cases studied across three study groups.

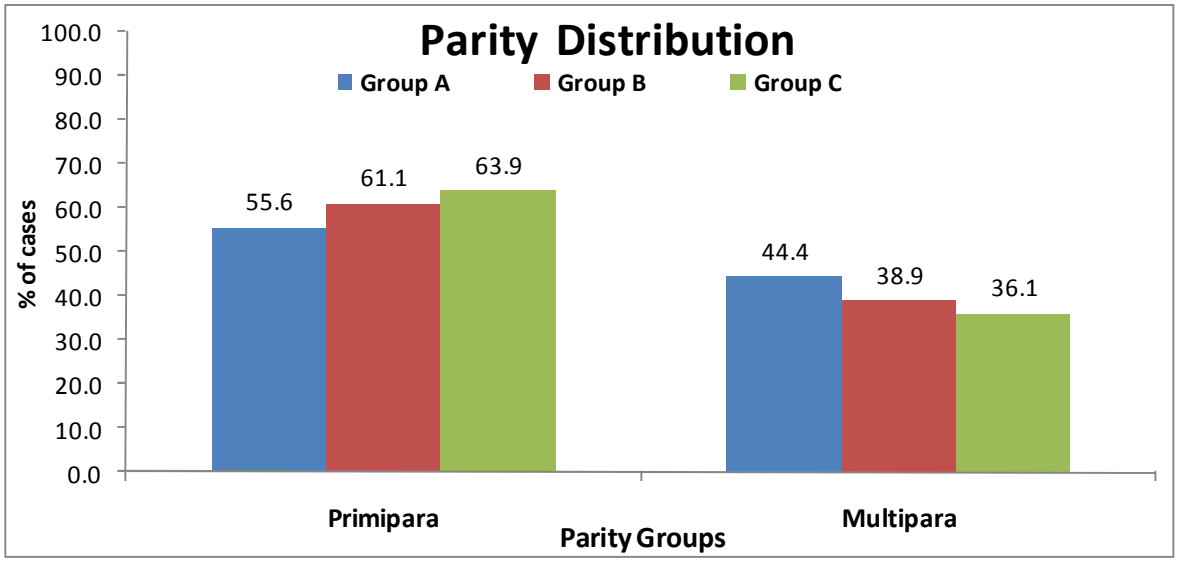
Table 3) The distribution of parity of the cases studied across three study groups.

Parity	Group A (n=36)		Group B (n=36)		Group C (n=36)		Inter Group Comparisons (P-value)		
							Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
	n	%	n	%	n	%			
Primipara	20	55.6	22	61.1	23	63.9	0.811^{NS}	0.631^{NS}	0.999^{NS}
Multipara	16	44.4	14	38.9	13	36.1			
Total	36	100.0	36	100.0	36	100.0			

Values are n (% of cases). P-values by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1. The distribution of parity did not differ significantly across three study groups (P-value>0.05 for all).



Graph 2) The distribution of parity of the cases studied across three study groups.

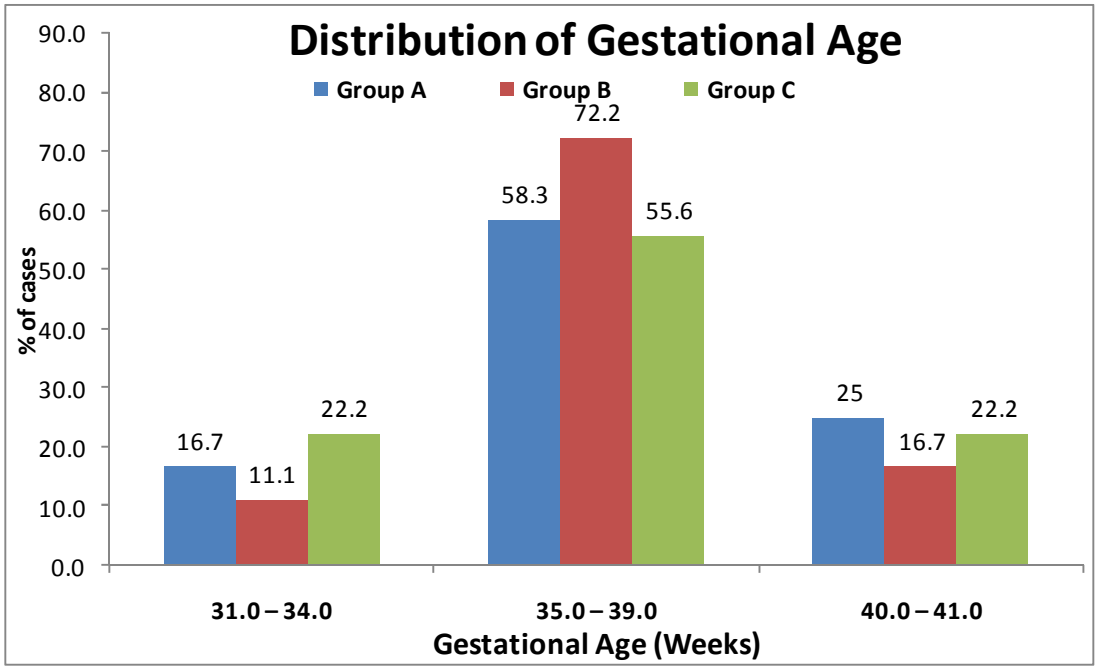
Table 4) The distribution of gestational age of the cases studied across three study groups.

Gestational Age (Weeks)	Group A (n=36)		Group B (n=36)		Group C (n=36)		Inter Group Comparisons (P-value)		
							Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
	n	%	n	%	n	%			
31.0 – 34.0	6	16.7	4	11.1	8	22.2	0.735^{NS}	0.767^{NS}	0.343^{NS}
35.0 – 39.0	21	58.3	26	72.2	20	55.6	0.322^{NS}	0.999^{NS}	0.220^{NS}
40.0 – 41.0	9	25.0	6	16.7	8	22.2	0.563^{NS}	0.999^{NS}	0.767^{NS}
Total	36	100.0	36	100.0	36	100.0			

Values are n (% of cases). P-values by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1. The distribution of gestational age did not differ significantly across three study groups (P-value>0.05 for all).



Graph 3) The distribution of gestational age of the cases studied across three study groups.

Table 5) The inter-group and intra-group comparison of systolic BP across three study groups.

Systolic BP (mmHg)	Group A (n=36)	Group B (n=36)	Group C (n=36)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	122.0 ± 3.3	122.9 ± 3.9	122.8 ± 4.4	0.999^{NS}	0.999^{NS}	0.999^{NS}
2-Hrs	124.2 ± 3.2	124.5 ± 4.5	124.9 ± 3.7	0.999^{NS}	0.999^{NS}	0.999^{NS}
24-Hrs	122.9 ± 3.1	123.1 ± 4.1	122.6 ± 4.2	0.999^{NS}	0.999^{NS}	0.999^{NS}
Intra-Group Comparison (P-value)						
Baseline v 2-Hrs	0.001^{***}	0.001^{***}	0.001^{***}			
Baseline v 24-Hrs	0.001^{***}	0.379^{NS}	0.463^{NS}			

Values are Mean ± Standard deviation (SD). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using paired't' test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

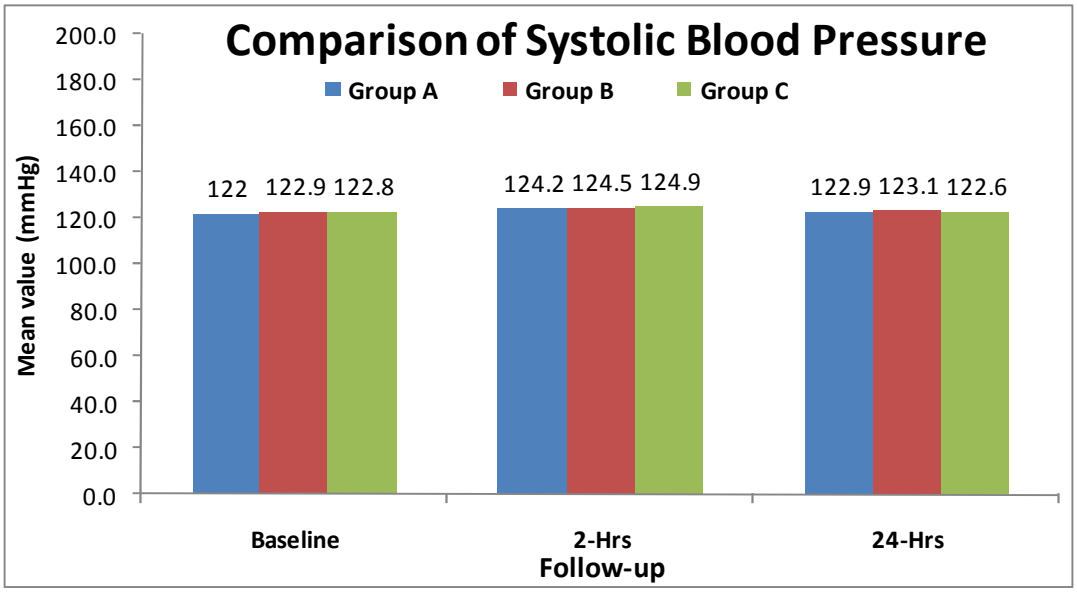
Comments:

1) **Inter-Group Comparison:**
    a. The average baseline systolic BP did not differ significantly across three study groups (P-value>0.05 for all).
    b. The average systolic BP at 2-Hrs did not differ significantly across three study groups (P-value>0.05 for all).
    c. The average systolic BP at 24-hrs did not differ significantly across three study groups (P-value>0.05 for all).

2) Intra-Group Comparison:

a. In Group A, B and C the average 2-Hrs systolic BP was significantly higher compared to baseline Systolic BP (P-value<0.001 for all). But it not clinically significant.

b. In Group A, the average 24-Hrs systolic BP was significantly higher compared to baseline systolic BP (P-value<0.001). In Group B and C the average 24-Hrs systolic BP did not differ significantly compared to baseline Systolic BP (P-value>0.05 for all).



Graph 4) The inter-group and intra-group comparison of Systolic BP across three study groups.

Table 6) The inter-group and intra-group comparison of Diastolic BP across three study groups.

Diastolic BP (mmHg)	Group A (n=36)	Group B (n=36)	Group C (n=36)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	82.4 ± 4.1	81.2 ± 3.7	81.7 ± 4.2	0.596^{NS}	0.999^{NS}	0.999^{NS}
2-Hrs	81.8 ± 2.8	81.3 ± 3.3	82.1 ± 3.7	0.999^{NS}	0.999^{NS}	0.951^{NS}
24-Hrs	81.7 ± 2.5	81.4 ± 3.3	82.0 ± 3.5	0.999^{NS}	0.999^{NS}	0.999^{NS}
Intra-Group Comparison (P-value)						
Baseline v 2-Hrs	0.136^{NS}	0.899^{NS}	0.334^{NS}			
Baseline v 24-Hrs	0.177^{NS}	0.776^{NS}	0.493^{NS}			

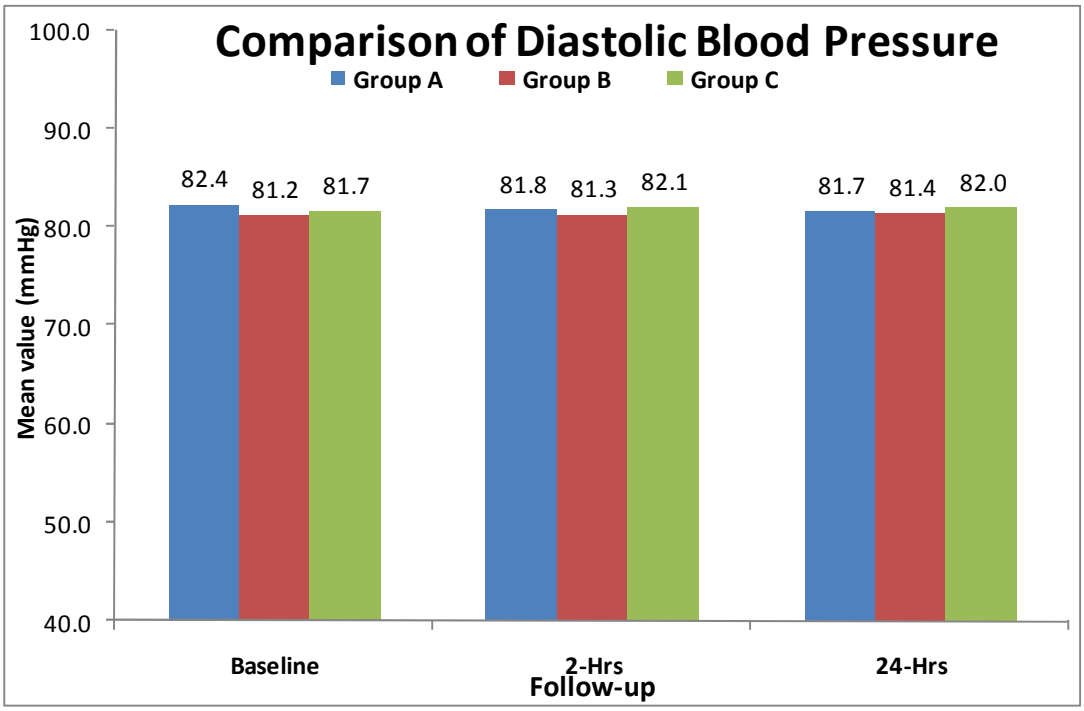
Values are Mean ± Standard deviation (SD). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using paired 't' test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Inter-Group Comparison:**
    a. The average baseline, 2-Hrs and 24-Hrs Diastolic BP did not differ significantly across three study groups (P-value>0.05 for all).

2) Intra-Group Comparison:

a. In Group A, B and C, the average baseline Diastolic BP did not differ significantly compared to 2-Hrs and 24-Hrs Diastolic BP (P-value>0.05 for all).



Graph 5) The inter-group and intra-group comparison of Diastolic BP across three study groups.

PRIMARY OUTCOME

Table 7) The inter-group and intra-group comparison of Amniotic fluid index (AFI) across three study groups.

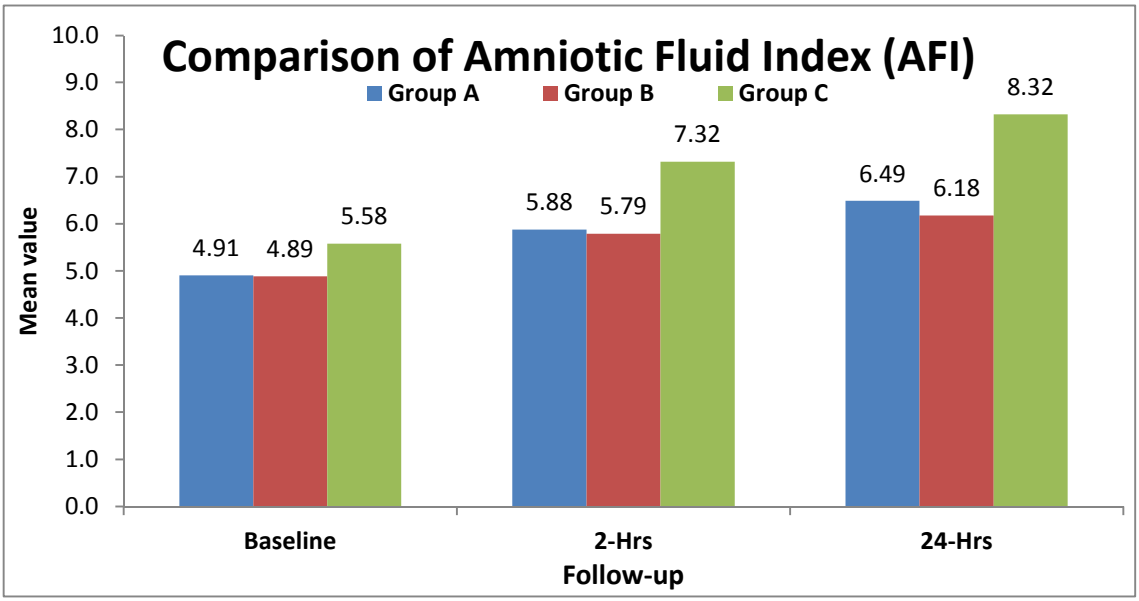
Amniotic fluid index (AFI)	**Group A (n=36)**	**Group B (n=36)**	**Group C (n=36)**	**Inter Group Comparisons (P-value)**		
				Group A v/s Group B	**Group A v/s Group C**	**Group B v/s Group C**
Baseline	4.91 ± 1.58	4.98 ± 1.86	5.58 ± 1.31	0.999^{NS}	0.198^{NS}	0.301^{NS}
2-Hrs	5.88 ± 1.86	5.79 ± 1.89	7.32 ± 1.40	0.999^{NS}	0.002^{**}	0.001^{***}
24-Hrs	6.49 ± 2.22	6.18 ± 2.23	8.32 ± 1.77	0.999^{NS}	0.001^{***}	0.001^{***}
Intra-Group Comparison (P-value)						
Baseline v 2-Hrs	0.001^{***}	0.001^{***}	0.001^{***}			
Baseline v 24-Hrs	0.001^{***}	0.001^{***}	0.001^{***}			
2-Hrs v 24-Hrs	0.001^{***}	0.001^{***}	0.001^{***}			

Values are Mean ± Standard deviation (SD). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using paired 't' test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Inter-Group Comparison:**
    a. The average baseline Amniotic fluid index did not differ significantly across three study groups (P-value>0.05 for all).
    b. The average 2-Hrs and 24-Hrs amniotic fluid index was significantly higher in group C compared to groups A and B (P-value<0.05 for all).
    c. The average 2-Hrs and 24-Hrs amniotic fluid index did not differ significantly between Groups A and B (P-value>0.05 for both).

2) **Intra-Group Comparison:**
    a. In Group A, B and C the average amniotic fluid index at 2-Hr and 24-Hrs was significantly higher compared to baseline amniotic fluid index (P-value<0.001 for all).
    b. In Group A, B and C the average amniotic fluid index at 24-Hrs was significantly higher compared to 2-Hrs amniotic fluid index (P-value<0.001 for all).



Graph 6) The inter-group and intra-group comparison of Amniotic fluid index (AFI) across three study groups.

Table 8) The comparison of persistence of oligohydramnios (AFI<8 cm) across three study groups after treatment.

Oligohydramnios (AFI<8 cm)	Group A (n=36)		Group B (n=36)		Group C (n=36)		Inter Group Comparisons (P-value)		
							Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
	N	%	N	%	n	%			
2-Hrs									
Yes	29	80.6	31	86.1	21	58.3	0.753^{NS}	0.072^{NS}	0.017^{*}
No	7	19.4	5	13.9	15	41.7			
24-Hrs									
Yes	24	66.7	23	63.9	11	30.6	0.999^{NS}	0.004^{**}	0.009^{**}
No	12	33.3	13	36.1	25	69.4			
P-value (Intra-Group	0.285^{NS}		0.055^{NS}		0.032^{*}				

Values are n (% of cases). P-values by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

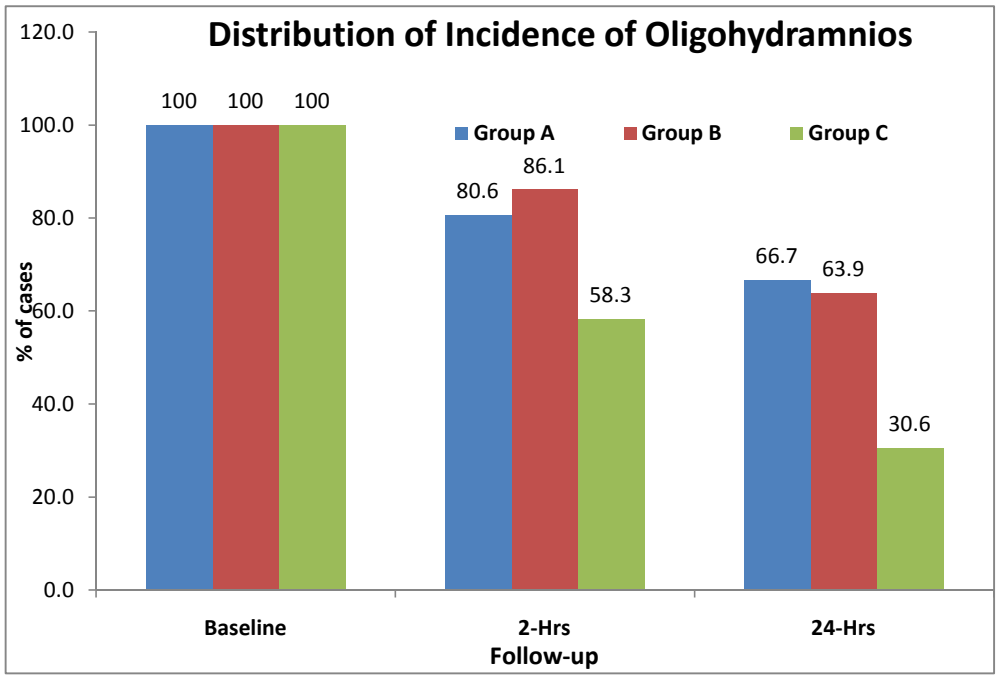
1. Inter-Group Comparison:
    a. The distribution of baseline oligohydramnios did not differ significantly across three study groups (P-value>0.05 for all).
    b. The number of cases of persistent oligohydramnios at 2-Hrs was significantly higher in Group B compared to Group C (P-value<0.05).
    c. The number of cases of persistent oligohydramnios at 24-Hrs was significantly higher in Groups A and B compared to Group C (P-value<0.01 for both).

2. Intra-Group Comparison:

    a. In Group A, the number of cases of persistent oligohydramnios at 24-hrs did not differ significantly compared to incidence of oligohydramnios at 2-Hrs (P-value>0.05).

    b. In Group B, the number of cases of persistent oligohydramnios at 24-hrs did not differ significantly compared to incidence of oligohydramnios at 2-Hrs (P-value>0.05).

    c. In Group C, the number of cases of persistent oligohydramnios at 24-hrs was significantly lesser compared to incidence of oligohydramnios at 2-Hrs (P-value<0.05). This shows that the effect was seen better in all groups.



Graph 7) The comparison of incidence of oligohydramnios across three study groups.

Table 9) The inter-group and intra-group comparison of Symphysiofundal height (SFH) across three study groups.

Symphysiofundal height (SFH)	Group A (n=36)	Group B (n=36)	Group C (n=36)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	32.7 ± 2.1	32.8 ± 1.8	32.8 ± 1.9	0.999^{NS}	0.999^{NS}	0.999^{NS}
2-Hrs	34.3 ± 2.2	33.6 ± 1.9	34.0 ± 1.9	0.473^{NS}	0.999^{NS}	0.999^{NS}
24-Hrs	33.8 ± 2.2	33.3 ± 1.9	33.9 ± 1.8	0.699^{NS}	0.999^{NS}	0.562^{NS}
Intra-Group Comparison (P-value)						
Baseline v 2-Hrs	0.001^{***}	0.001^{***}	0.001^{***}			
Baseline v 24-Hrs	0.001^{***}	0.001^{***}	0.001^{***}			
2-Hrs v 24-Hrs	0.005^{**}	0.001^{***}	0.312^{NS}			

Values are Mean ± Standard deviation (SD). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using paired 't' test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

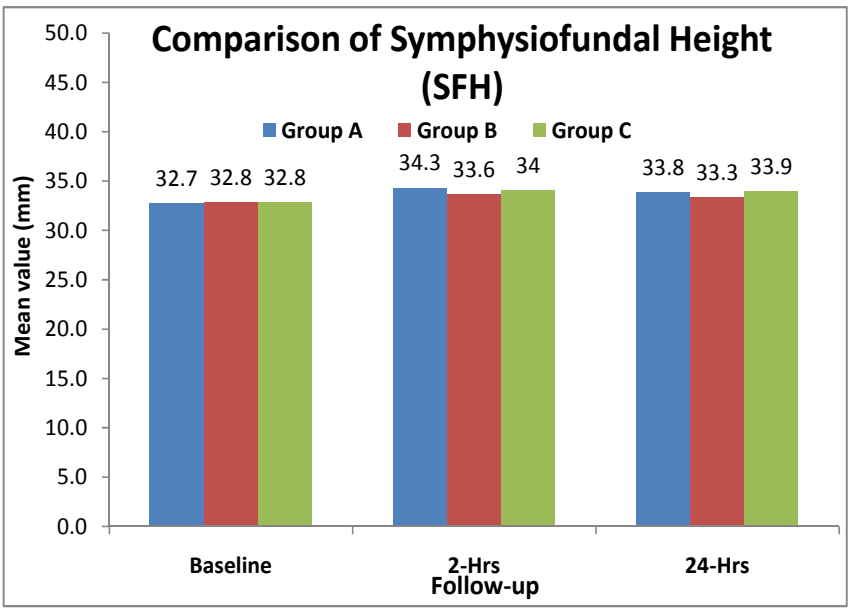
1) **Inter-Group Comparison:**

   a. The average baseline, 2-Hrs and 24-Hrs Symphysiofundal height did not differ significantly across three study groups (P-value>0.05 for all).

2) Intra-Group Comparison:

a. In Groups A, B and C the average Symphysiofundal height at 2-Hrs and 24-Hrs was significantly higher compared to baseline Symphysiofundal height (P-value<0.001 for all).

b. In Group A and B the average Symphysiofundal height at 24-Hrs was significantly higher compared to 2-Hrs Symphysiofundal height (P-value<0.01 for both).



Graph 8) The inter-group and intra-group comparison of Symphysiofundal height (SFH) across three study groups.

Table 10) The inter-group and intra-group comparison of Amniotic fluid index (AFI) among idiopathic oligohydramnios and FGR with oligohydramnios with any hydration.

Amniotic fluid index (AFI)	Idiopathic oligohydramnios (n=85)	FGR with oligohydramnios (n=23)	Inter Group Comparisons (P-value)
Baseline	5.19 ± 1.57	5.01 ± 1.53	0.619^{NS}
2-Hrs	6.40 ± 1.86	6.06 ± 1.87	0.448^{NS}
24-Hrs	7.12 ± 2.29	6.54 ± 2.19	0.283^{NS}
Intra-Group Comparison (P-value)			
Baseline v 2-Hrs	0.001^{***}	0.001^{***}	
Baseline v 24-Hrs	0.001^{***}	0.001^{***}	
2-Hrs v 24-Hrs	0.001^{***}	0.002^{**}	

Values are Mean ± Standard deviation (SD). Inter-group comparisons are done using independent sample t test. Intra-group comparisons are done using paired 't' test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

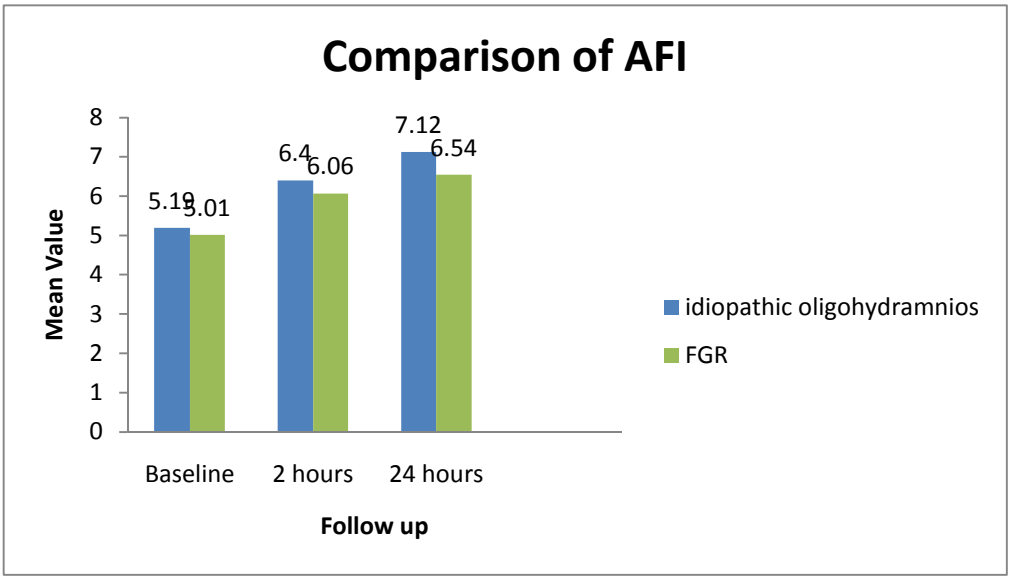
Comments:

1) **Inter-Group Comparison:**
    a. The average baseline, 2-hr and 24-Hrs Amniotic fluid index did not differ significantly across idiopathic oligohydramnios and FGR with oligohydramnios with any hydration (P-value>0.05 for all).

2) **Intra-Group Comparison:**

a. In both idiopathic oligohydramnios and FGR with oligohydramnios groups the average amniotic fluid index at 2-Hr and 24-Hrs was significantly higher compared to baseline amniotic fluid index (P-value<0.001 for all).

b. In idiopathic oligohydramnios and FGR with oligohydramnios groups the average amniotic fluid index at 24-Hrs was significantly higher compared to 2-Hrs amniotic fluid index (P-value<0.01 for all).



Graph 9) The inter-group and intra-group comparison of Amniotic fluid index (AFI) across idiopathic oligohydramnios and FGR with oligohydramnios with any hydration.

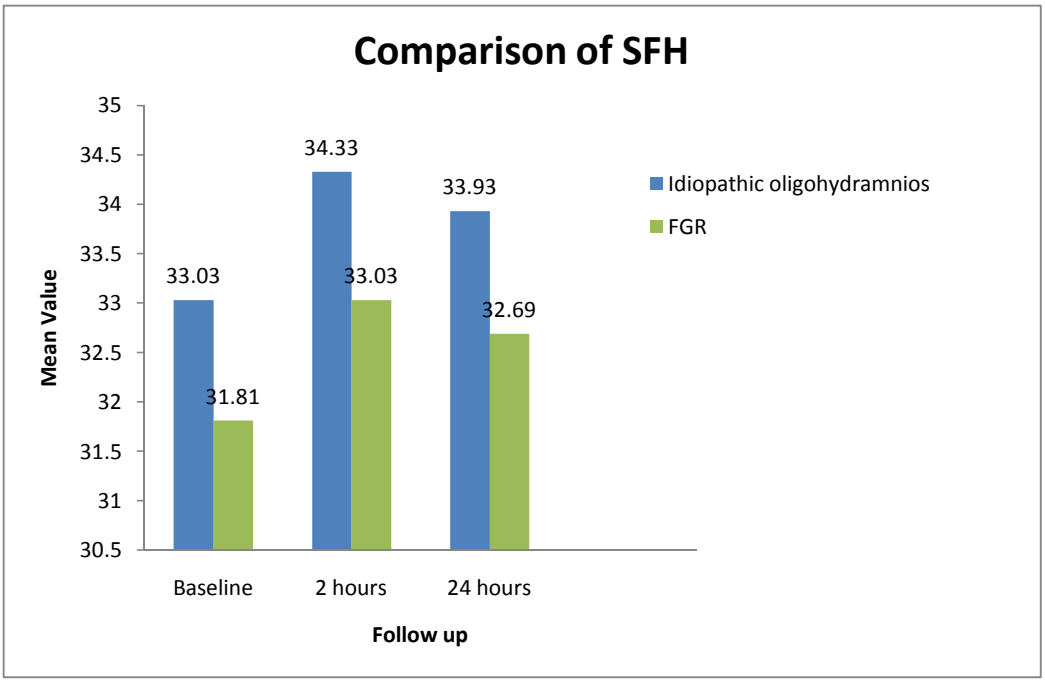
Table 11) The inter-group and intra-group comparison of Symphysiofundal height (SFH) across idiopathic oligohydramnios and FGR with oligohydramnios with any hydration.

Symphysiofundal height (SFH)	Idiopathic oligohydramnios (n=85)	FGR (n=23)
Baseline	33.03 ± 1.80	31.81 ± 2.11
2-Hrs	34.22 ± 1.82	33.03 ± 2.31
24-Hrs	33.93 ± 1.77	32.69 ± 2.29
Intra-Group Comparison (P-value)		
Baseline v 2-Hrs	0.001***	0.001***
Baseline v 24-Hrs	0.001***	0.001***
2-Hrs v 24-Hrs	0.001***	0.024*

Values are Mean ± Standard deviation (SD). Inter-group comparisons are done using independent sample t test. Intra-group comparisons are done using paired‘t’ test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1) **Intra-Group Comparison:**
    a. In idiopathic oligohydramnios and FGR with oligohydramnios groups the average Symphysiofundal height (SFH) at 2-Hr and 24-Hrs was significantly higher compared to baseline Symphysiofundal height (SFH) (P-value<0.01 for all).
    b. In idiopathic oligohydramnios and FGR with oligohydramnios groups the average Symphysiofundal height (SFH) at 2-Hrs was significantly higher compared to 24-Hrs Symphysiofundal height (SFH) (P-value<0.05 for all).



Graph 10)The inter-group and intra-group comparison of Symphysiofundal height (SFH) across idiopathic oligohydramnios and FGR with oligohydramnios with any hydration.

Table 12) The inter-group and intra-group comparison of Amniotic fluid index (AFI) across three study groups in idiopathic oligohydramnios.

Amniotic fluid index (AFI)	Group A (n=25)	Group B (n=31)	Group C (n=29)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	4.86 ± 1.62	5.05 ± 1.74	5.64 ± 1.26	0.999^{NS}	0.203^{NS}	0.443^{NS}
2-Hrs	5.81 ± 1.94	5.91 ± 1.87	7.44 ± 1.30	0.999^{NS}	0.002^{**}	0.003^{**}
24-Hrs	6.46 ± 2.29	6.32 ± 2.24	8.54 ± 1.64	0.999^{NS}	0.001^{***}	0.001^{***}
Intra-Group Comparison (P-value)						
Baseline v 2-Hrs	0.001^{***}	0.001^{***}	0.001^{***}			
Baseline v 24-Hrs	0.001^{***}	0.001^{***}	0.001^{***}			
2-Hrs v 24-Hrs	0.001^{***}	0.001^{***}	0.001^{***}			

Values are Mean ± Standard deviation (SD). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using paired 't' test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

Inter-Group comparison:

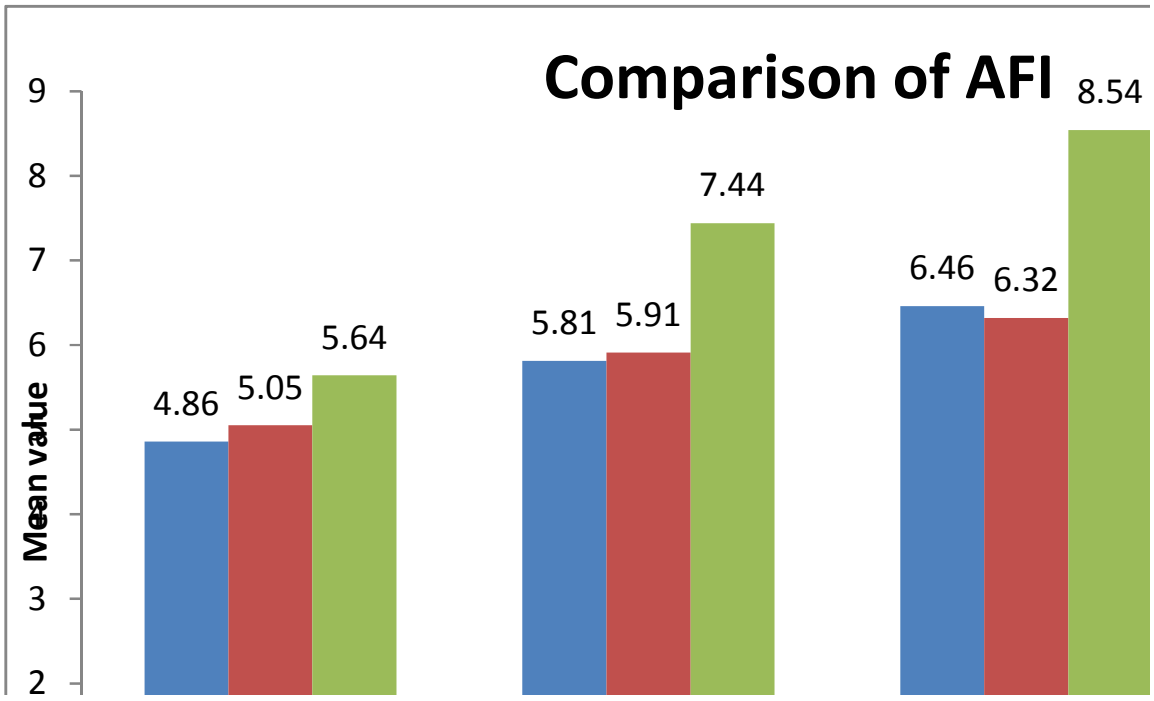
a. The average 2-Hrs and 24-Hrs amniotic fluid index was significantly higher in group C compared to groups A and B (P-value<0.05 for all).

b. The average 2-Hrs and 24-Hrs amniotic fluid index did not differ significantly between Groups A and B (P-value>0.05 for both).

Intra-Group comparison:

a. In Group A, B and C the average amniotic fluid index at 2-Hr and 24-Hrs was significantly higher compared to baseline amniotic fluid index.

b. In Group A, B and C the average amniotic fluid index at 24-Hrs was significantly higher compared to 2-Hrs amniotic fluid index.



Graph 11) The inter-group and intra-group comparison of Amniotic fluid index (AFI) across three study groups in idiopathic oligohydramnios.

Table 13) The inter-group and intra-group comparison of Amniotic fluid index (AFI) across three study groups in FGR with oligohydramnios.

Amniotic fluid index (AFI)	Group A (n=11)	Group B (n=5)	Group C (n=7)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Baseline	5.02 ± 1.56	4.52 ± 1.59	5.34 ± 1.59	0.999^{NS}	0.999^{NS}	0.999^{NS}
2-Hrs	6.04 ± 1.76	5.10 ± 2.13	6.81 ± 1.79	0.999^{NS}	0.999^{NS}	0.387^{NS}
24-Hrs	6.58 ± 2.15	5.26 ± 2.18	7.40 ± 2.12	0.801^{NS}	0.999^{NS}	0.313^{NS}
Intra-Group Comparison (P-value)						
Baseline v 2-Hrs	0.001^{***}	0.120^{NS}	0.001^{***}			
Baseline v 24-Hrs	0.001^{***}	0.168^{NS}	0.002^{**}			
2-Hrs v 24-Hrs	0.021^{*}	0.614^{NS}	0.041^{*}			

Values are Mean ± Standard deviation (SD). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. Intra-group comparisons are done using paired 't' test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

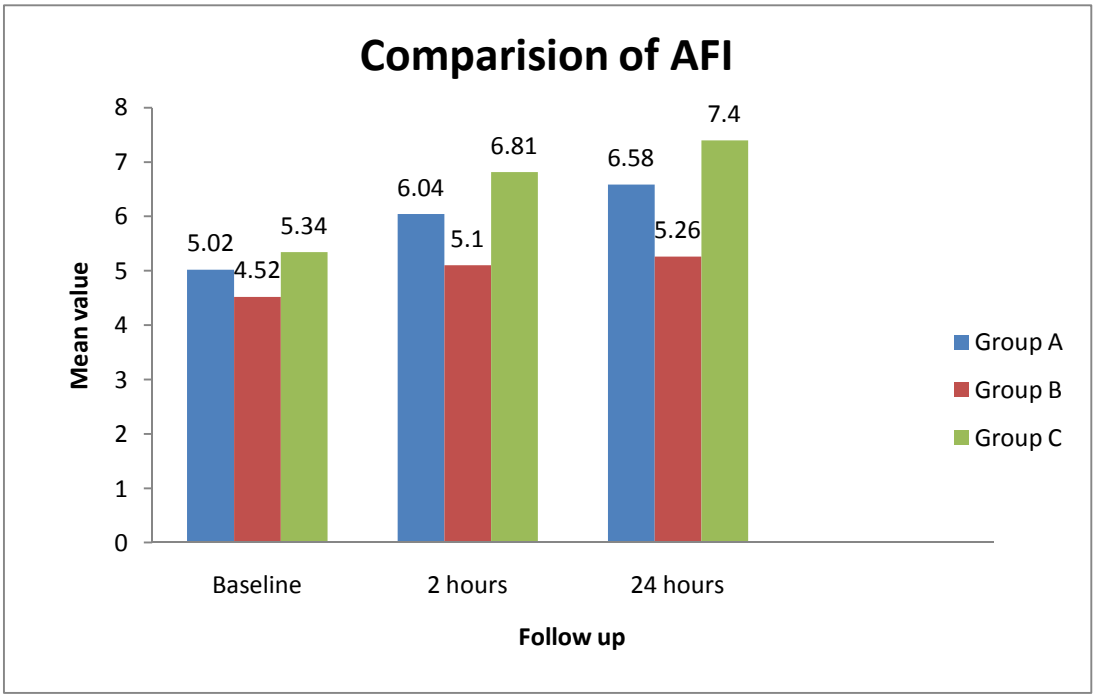
Inter-Group comparison:

a. The average 2-Hrs and 24-Hrs amniotic fluid index did not differ significantly between Groups A, B and C.

Intra-Group comparison:

a. In Group A and C the average amniotic fluid index at 2-Hr and 24-Hrs was significantly higher compared to baseline amniotic fluid index.

b. In Group B there was no significant difference in the average amniotic fluid index at 2-Hr and 24-Hrs compared to baseline amniotic fluid index.



Graph 12) The inter-group and intra-group comparison of Amniotic fluid index (AFI) across three study groups in FGR with oligohydramnios.

Patients whose AFI remained < 8cm after 24 hours after hydration, repeat hydration was given according to randomization table on the same patient. So, 1 patient received more than one type of treatment. 43 patients received only one type of hydration, 23 patients received hydration twice and 3 patients received hydration thrice. 2 patients who received one type of hydration and 2 patients who received two types of hydration could not be followed up (total 6 cases). So, we could study perinatal outcome of only 41 patients.

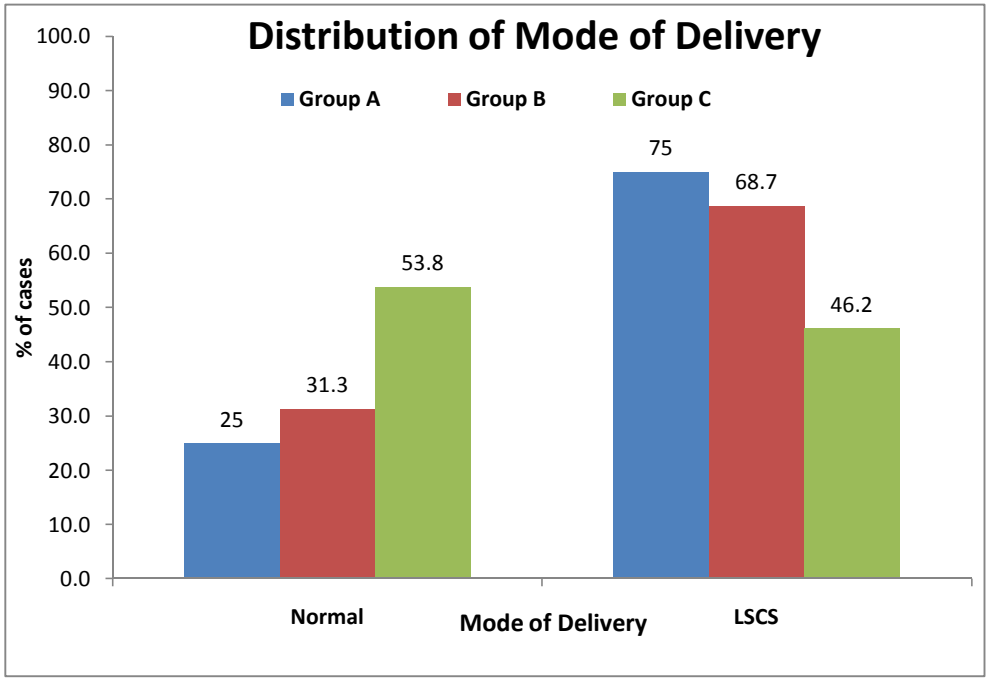
Table 14) The distribution of mode of delivery of the cases studied across three study groups.

Mode of delivery	**Group A (n=12)**		**Group B (n=16)**		**Group C (n=13)**		**Inter Group Comparisons (P-value)**		
							Group A v/s Group B	**Group A v/s Group C**	**Group B v/s Group C**
	N	%	N	%	N	%			
Normal	3	25.0	5	31.3	7	53.8	0.999^{NS}	0.226^{NS}	0.274^{NS}
LSCS	9	75.0	11	68.7	6	46.2			
Total	12	100.0	16	100.0	13	100.0			
P-value (Intra-Group)	0.083^{NS}		0.134^{NS}		0.782^{NS}				

Values are n (% of cases). P-values by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1. Inter-Group comparisons:
    a. The distribution of mode of delivery did not differ significantly across three study groups (P-value>0.05 for all).
    b. Though not significant apparently more number of patients had normal delivery in group C (25%, 31.3%, 53.8% in group A, group B, group C respectively).
2. Intra-Group Comparisons:
    a. In each study group, the distribution of mode of delivery did not differ significantly (P-value>0.05 for all three groups).



Graph 13) The distribution of mode of delivery of the cases studied across three study groups.

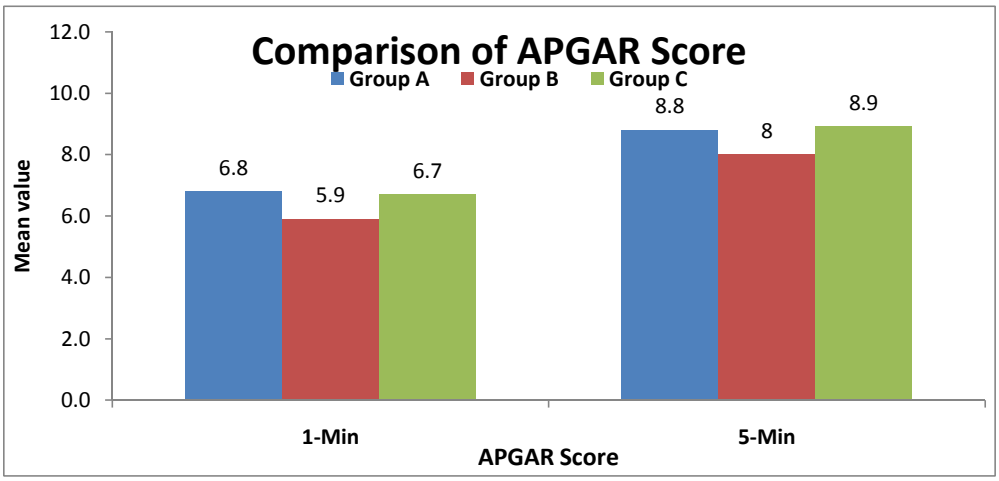
Table 15) The inter-group comparison of APGAR Score across three study groups.

APGAR Score	Group A (n=12)	Group B (n=16)	Group C (n=13)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
1-Min	6.8 ± 0.6	5.9 ± 1.6	6.7 ± 0.8	0.139^{NS}	0.999^{NS}	0.253^{NS}
5-Min	8.8 ± 0.6	8.0 ± 1.5	8.9 ± 0.6	0.115^{NS}	0.999^{NS}	0.096^{NS}

Values are Mean ± Standard deviation (SD). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1. The average APGAR score at 1-min did not differ significantly across three study groups (P-value>0.05 for all).
2. The average APGAR score at 5-min did not differ significantly across three study groups (P-value>0.05 for all).



Graph 14) The inter-group comparison of APGAR Score across three study groups.

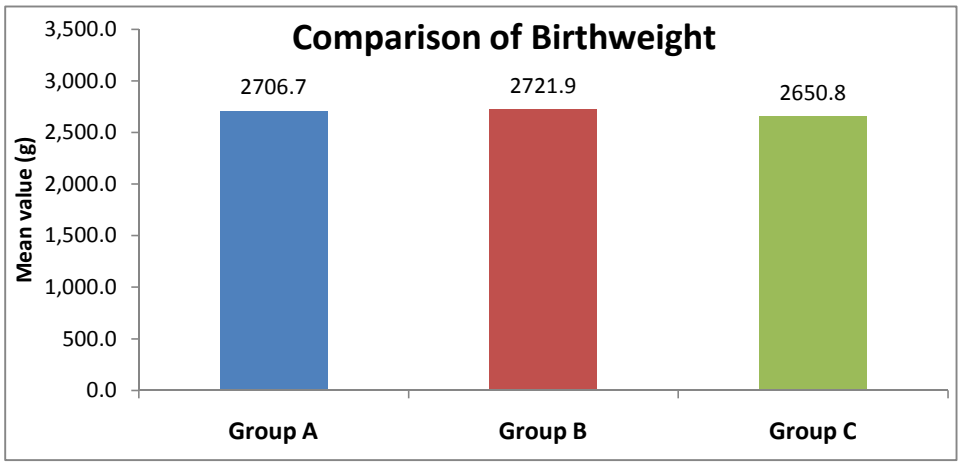
Table 16) The inter-group comparison of Birthweight across three study groups.

Parameter	Group A (n=12)	Group B (n=16)	Group C (n=13)	Inter Group Comparisons (P-value)		
				Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Birthweight (g)	2706.7 ± 444.1	2721.9 ± 218.7	2650.8 ± 260.5	0.999^{NS}	0.999^{NS}	0.999^{NS}

Values are Mean ± Standard deviation (SD). Inter-group comparisons are done using one-way analysis of variance (ANOVA) with Bonferroni's Post-Hoc test for multiple group comparisons. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1. The average birthweight did not differ significantly across three study groups (P-value>0.05 for all).



Graph 15) The inter-group comparison of Birthweight across three study groups.

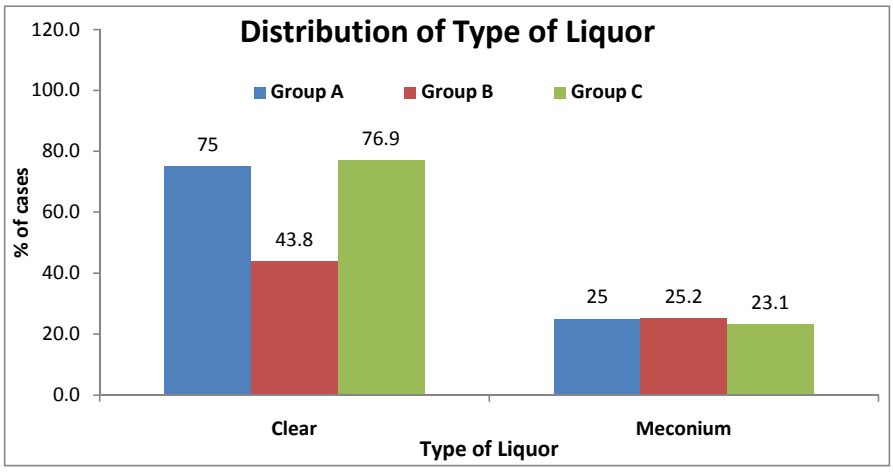
Table 17) The distribution of type of liquor across three study groups.

Type of liquor	Group A (n=12)		Group B (n=16)		Group C (n=13)		Inter Group Comparisons (P-value)		
							Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
	n	%	N	%	n	%			
Clear	9	75.0	7	43.8	10	76.9	0.136^{NS}	0.999^{NS}	0.130^{NS}
Meconium	3	25.0	9	56.2	3	23.1			
Total	12	100.0	16	100.0	13	100.0			

Values are n (% of cases). P-values by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1. The distribution of type of liquor did not differ significantly across three study groups (P-value>0.05 for all).
2. More number of cases in group B had meconium stained liquor compared to group A and C, though it was not statistically significant.



Graph 16) The distribution of type of liquor across three study groups.

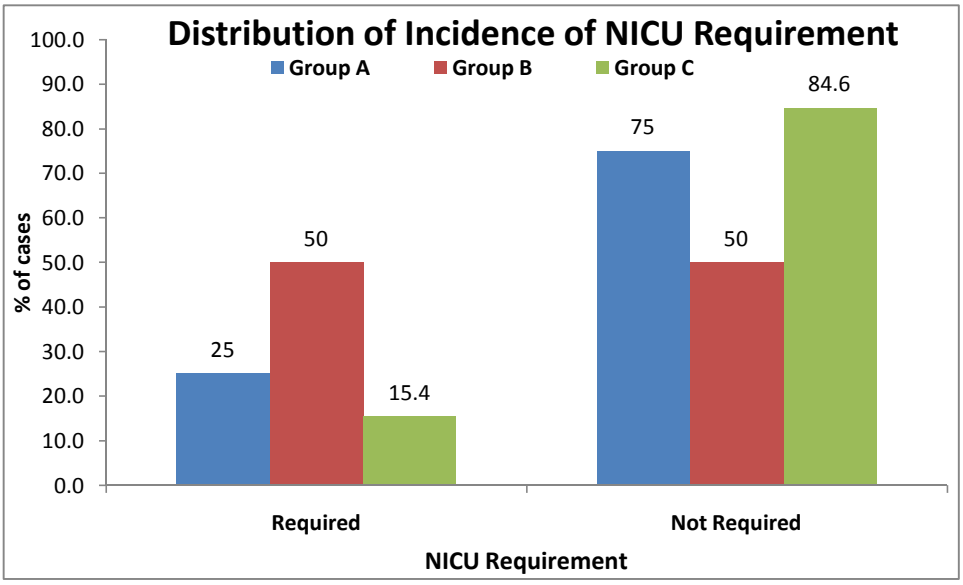
Table 18) The distribution of incidence of NICU requirement across three study groups.

NICU Requirement	Group A (n=12)		Group B (n=16)		Group C (n=13)		Inter Group Comparisons (P-value)		
							Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
	n	%	n	%	n	%			
Required	3	25.0	8	50.0	2	15.4	0.253^{NS}	0.645^{NS}	0.114^{NS}
Not Required	9	75.0	8	50.0	11	84.6			
Total	12	100.0	16	100.0	13	100.0			
P-value (Intra-Group)	0.083^{NS}		0.999^{NS}		0.013^{*}				

Values are n (% of cases). P-values by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

1. Inter-Group Comparisons:
    a. The distribution of number of babies requiring NICU did not differ significantly between three Study Groups (P-value>0.05 for all).
2. Intra-Group Comparisons:
    a. In Group C, the number of babies requiring NICU was significantly lesser (P-value<0.05).



Graph 17) The distribution of incidence of NICU requirement across three study groups.

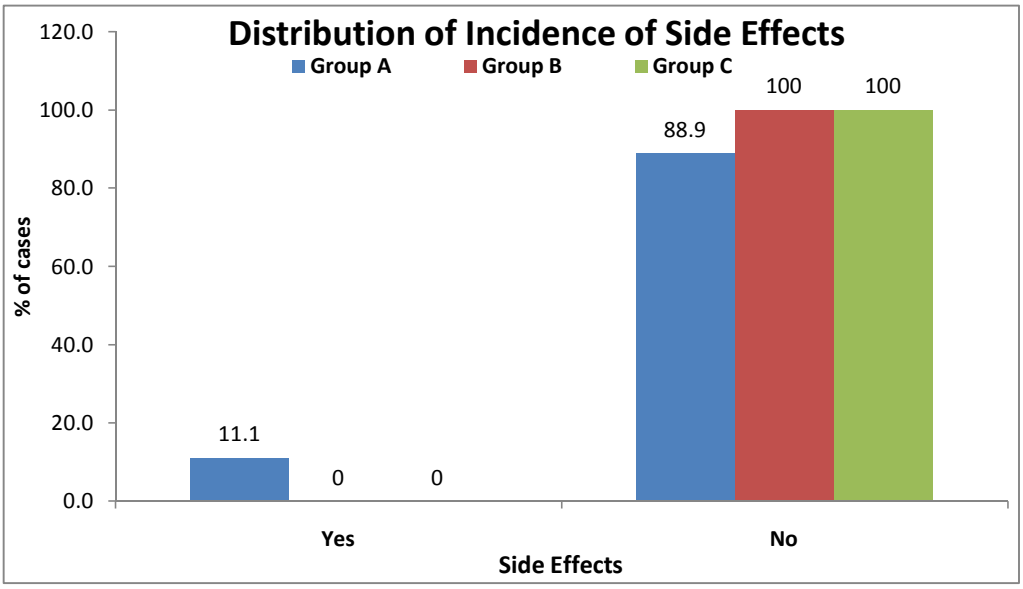
Table 19) The distribution of incidence of side effects across three study groups.

Side Effects	Group A (n=36)		Group B (n=36)		Group C (n=36)		Inter Group Comparisons (P-value)		
							Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
	n	%	n	%	n	%			
Yes	4	11.1	0	0.0	0	0.0	0.115^{NS}	0.115^{NS}	0.999^{NS}
No	32	88.9	36	100.0	36	100.0			
Total	36	100.0	36	100.0	36	100.0			
P-value (Intra-Group)	0.001^{***}		0.001^{***}		0.001^{***}				

Values are n (% of cases). P-values by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001. NS: Statistically Non-Significant.

Comments:

a. Out of all the patients only 4 patients in oral group had nausea. None of the patients in group B and C had any complications.



Graph 18) The distribution of incidence of side effects across three study groups.

DISCUSSION

Oligohydramnios is defined as AFI less than normal for that gestational age. Amniotic fluid volume is derived from the difference in the inflow and outflow of fluid from the amniotic space. Amniotic fluid is maintained in a dynamic equilibrium. Amniotic fluid volume is an important parameter in the assessment of fetal wellbeing.

In this study we have compared 3 types of hydration therapy i.e., oral hydration, intravenous hydration with RL+ 5%D, intravenous 0.45%NS. As giving arginine and amino acid oral supplements was routine practice among practitioners, many patients were already on such medication when the diagnosis of oligohydramnios was made. So, we decided to continue such treatment in all the groups to avoid the bias. The idea behind our study was to know the type of hydration which increases AFI better when compared to other therapies.

In our study 108 patients were studied and there was no significant difference in the baseline parameters like age, parity, gestational age, blood pressure, AFI and symphysiofundal height.

Parameters	**Group A (n=36)**	**Group B (n=36)**	**Group C (n=36)**	**P-value**
Maternal age (years)	22.9 ± 4.1	23.9 ± 4.2	23.4 ± 4.1	0.658^{NS}
Parity	1.44 ± 0.50	1.39 ± 0.49	1.36 ± 0.49	0.768^{NS}
Gestational age (weeks)	37.4 ± 2.6	37.1 ± 2.0	36.8 ± 2.9	0.596^{NS}
Systolic BP	122.0 ± 3.3	122.9 ± 3.9	122.8 ± 4.4	0.557^{NS}
Diastolic BP	82.4 ± 4.1	81.2 ± 3.7	81.7 ± 4.2	0.427^{NS}
AFI	4.9 ± 1.6	4.9 ± 1.7	5.6 ± 1.3	0.130^{NS}
Symphysiofundal height (mm)	32.7 ± 2.1	32.8 ± 1.8	32.8 ± 1.9	0.988^{NS}

Table 20) Baseline characteristics of the cases studied across three study groups.

AUTHOR	GA	AFI(cm)
Present study	30 – 41 weeks	< 8
Umber A[13]	28 – 42 weeks	≤ 5
Shehzad B Momina[3]	28 – 42 weeks	< 5
Nahid Lorzadeh[17]	35 – 41 weeks	≤ 5
Linnli Yan Rosenberg[18]	37 – 42 weeks	< 6
Pragati M[24]	28 – 42 weeks	<10

Table 21 – Comparison of gestational age and AFI with present study and other studies

Many studies have taken different range of gestational ages in their studies. As early as 28 weeks of gestation was included and as late as 42 weeks were also included in the studies done by Umber A, Shehzad B M, Linnli Y R. In the present study we have taken from 28 – 41 weeks but no cases could be recruited before 30 weeks. No pregnancy was allowed to continue beyond 41 weeks as active intervention was done as per our hospital protocol. Oligohydramnios has been defined in various ways by various authors. But, most of them consider AFI less than 8 cm as borderline oligohydramnios and AFI less than 5 cm as oligohydramnios. Pragati M has taken AFI <10 cm, Chelmow D has taken ≤ 8cm, Linnli Y R has taken AFI< 6 and few authors Shehzad, Nahid, Umber have taken AFI less than 5 cm. In the present study we have included all patients with AFI less than 8cm.

According to the present study, all the three hydration groups A, B, C have shown statistically significant improvement in AFI both at 2 hours and 24 hours compared to baseline AFI. This study has also proved that patients receiving 0.45%NS showed good improvement over other two types of hydration both at 2 hours and 24 hours.

In group A, mean increased from 4.91 ± 1.58(baseline) to 5.88 ± 1.86 and 6.49 ± 2.22 at 2hours and 24 hours respectively and the increase was statistically significant at both 2 hours and 24 hours with p- value of 0.001. Similarly in group B the mean increased from 4.98 ± 1.86 to 5.79 ± 1.89, 6.18 ± 2.23 at 2 and 24 hours respectively. In group C also the mean value increased from 5.58 ± 1.31 to 7.32 ± 1.40, 8.32 ± 1.77 at 2 and 24 hours.

When we compare group A and group B there was no statistically significant difference (p value of 0.999). But when we compare group A and group C the p-value is 0.002 and 0.001 at 2 hours and 24 hours which shows that there was statistically significant improvement in AFI in patients of group C. The p-value at 2 hours and 24 hours is 0.001, 0.001 respectively when we compare group B and group C. So patients in group C showed significant increase in amniotic fluid when compared to other two groups.

As there are no similar studies in literature, we have compared the results of the individual group in the present study with other studies.

So far there is only one study on 0.45%NS conducted by Linnli Yan Rosenberg. But the results are not similar to present study. The study included 44 patients having AFI<6. Patients in study group were given IV 0.45% Normal saline at rate of 1000 ml/hr for 2 hours. Patients in placebo group were given 0.45% NS at 10 ml/hour for 2 hours. The AFI was reassessed after 1 hour after the hydration. The changes in AFI did not significantly differ between the treatment and the placebo groups (1.2±2.1 vs 1.5±2.1, respectively; p>0.05).[18] But, in the present study the increase in AFI was statistically significant. It may be because the effect might take more than 1 hour to increase AFI and here the AFI was assessed just after 1 hour.

Many of the previous studies have shown that the oral hydration is better than IV hydration. Even the Cochrane review in 2010 had concluded that oral hydration is better.[16] But in our study 0.45%NS was showed to be better than oral hydration. Though oral hydration is easy, simple and cheap, it depends on the patient's compliance. If the patient does not drink water properly the effect may not be seen.

AUTHOR	GA	METHOD	REASSESSMNET OF AFI	MEAN VALUE	P value
Present study	30-41 weeks	2L of water in 2 hours	2 hours 24 hours	5.88 ± 1.86 6.49 ± 2.22	0.001* 0.001*
Akter MD[31]	32-35 weeks	2L of water in 2 hours in first 24 hours Extra 2 L of water every day after first 24 hours	2 hours 7 days	6.35 ± 0.65 7.08 ± 0.21	<0.05 <0.05
Pragati Mishra[24]	28-42	2L of water in 2 hours	3 hours 24 hours 48 hours	6.09 ± 1.65cm 7.41 ± 1.46 cm 8.06 ± 1.55 cm	0.0836(NS) <0.0001* <0.0001*
Fait G[29]		2L of water daily	7 days	11.8 ± 2.4	<0.01*
Flack NJ[11]		2L of water in 2 hours	After hydration	3.2 cm	< 0.02

Table 22 – Comparison of effects of oral hydration in present study and other studies

Here we have compared the results of oral hydration with other studies. Studies have reassessed AFI at various intervals. Few studies have reassessed immediately after hydration and few have assessed after 2 hours, 3 hours, 24 hours,

48 hours, 7 days. In a study done by Pragati Mishra AFI was reassessed at 3 hours, 24 hours and 48 hours and this shows that the duration of increase in AFI was seen even after 48 hours.[24] Few studies have given continuously for 7 days and reassessed AFI afte 7 days. In our study AFI showed statistically significant increase in AFI starting from 2 hours to 24 hours.

Both RL and 5%D have been studied separately by many authors as hypotonic solutions and have shown increase in AFI. Patients receiving 5%D are at increased risk of hyperglycemia which can be dangerous in undiagnosed gestational diabetes mellitus. RL contains less sodium concentration compared to NS. The combination of RL and 5%D makes the fluid more hypotonic without the risk of hyperglycemia. So, we combined both RL and 5%D to have additive effect in increasing AFI.

But there are no studies in which both RL and 5%D are given among patients of a single group, the results are compared separately for both 5%D and RL in group B.

A study conducted by Umber et al concluded that maternal intravenous hydration (2L of 5%D) as well as oral hydration (2L of water) in 2 hours increases AFV in women with oligohydramnios. Mean change in amniotic fluid index was 4.5 cm ± 1.25 in intravenous hydration group and the mean change in Amniotic fluid index was 4.3 ± 1.23 in oral hydration group. There was no statistically significant difference in between both groups with P value > 0.05.[13] In the present group both group A and group B had increased AFI. But there was no statistically significant difference in between both groups.

Shehzad B Momina conducted a study on 226 women, out of which half were given 5%D and the other half were given oral hydration. The study concluded that oral hydration is more effective than intravenous hydration (5%D) in patients with

oligohydramnios. Results reveal a significant increase in AFI after hydration in both groups, but it was found that oral hydration more effective as it was 88.5% in oral hydration group while 48.67% in intravenous group.[3] But in our study the effect of RL+5%D was equal to oral hydration. This shows that combining RL and 5%D might increase the effectiveness.

According to the study conducted by Chandra et al, patients were given oral hydration of 10-12 glasses per day in group A and in group B intravenous hydration therapy with Ringer lactate 4000ml was given, 62.5% and 44.0% demonstrated improved indices after oral and intravenous hydration, respectively. Mean change in amniotic fluid index in intravenous was + 0.6 and in oral hydration it was + 0.7. Both the groups had increase in amniotic fluid volume, but neither appears to be particularly advantageous over the other.[19]

In a study conducted by Nahid Lorzadeh, patients were randomized into 4 groups, control group receiving no hydration, oral hydration group, intravenous isotonic fluid (NS) hydration group, intravenous hypotonic fluid(Ringers solution) hydration group. AFI was found to be increased in all the three treatment groups. But the mean increase in AFI was significantly greater in oral hydration group (6±1.99) compared to other groups. There was mean increase in IV isotonic (5.3±0.7), IV hypotonic (5.9±0.94) hydration groups when compared to control group (4.8±0.6).[17]

Out of 108 cases, 85 cases were idiopathic oligohydramnios and 23 cases were associated with FGR. Among idiopathic oligohydramnios all the three groups had significant improvement in AFI at both 2 hours and 24 hours compared to baseline. There was no significant difference in between group A and B. But group C showed statistically significant improvement in AFI at both 2 hours and 24 hours when compared to other two groups. Among FGR cases, group A and group C showed

significant increase in AFI at 2 hours and 24 hours. But in group B there was no significant difference at 2 and 24 hours. But there was no significant difference among the three groups. May be the sample size in each group is too less to show the difference. Both idiopathic oligohydramnios and FGR with oligohydramnios groups showed significant improvement in AFI at 2hours and 24 hours with any type of hydration therapy.

Symphysiofundal height is another parameter which was not studied by anybody. Assessment of AFI daily by USG may not be feasible in all the settings. So, we wanted to know whether the increase in the amount of liquor can be assessed clinically by noting the increase in SFH. In the present study the average SFH at 2 hours and 24 hours was significantly higher compared to baseline. But there was no significant difference among three groups. This proves that SFH also increases as the amount of liquor increases. So, if USG is not available or if it cannot be done frequently, SFH can also be used to see the effect on amount of liquor, which can be more objective than assessing the amount of liquor subjectively by palpation.

Patients whose AFI remained < 8cm after 24 hours after hydration, repeat hydration was given according to randomization table on the same patient. So, 1 patient received more than one type of treatment. 43 patients received only one type of hydration, 23 patients received hydration twice and 3 patients received hydration thrice. 2 patients who received one type of hydration and 2 patients who received two types of hydration could not be followed up (total 6 cases). So, we could study perinatal outcome of only 41 patients.

	Group A v/s Group B	Group A v/s Group C	Group B v/s Group C
Mode of delivery (vaginal delivery Vs LSCS)	0.999^{NS}	0.226^{NS}	0.274^{NS}
APGAR(1 min)	0.139^{NS}	0.999^{NS}	0.253^{NS}
APGAR(5 min)	0.115^{NS}	0.999^{NS}	0.096^{NS}
Birthweight	0.999^{NS}	0.999^{NS}	0.999^{NS}
Meconium	0.136^{NS}	0.999^{NS}	0.130^{NS}
NICU requirement	0.253^{NS}	0.645^{NS}	0.114^{NS}

Table 23 – Comparison of perinatal outcome among 3 groups (P value)

The perinatal outcome did not vary significantly among the three groups. It may be due to less number of patients in each group. But apparently the outcome was better in group C though not significant. May be studies with more number of patients in each group will be able to show the difference.

There was increase in systolic blood pressure statistically in all the three groups but it was not clinically significant as the increase was only by 0.9 to 2.2 mm of Hg .No other clinically significant side effects of fluid overload were seen. Out of 108 patients 4 patients had nausea among oral hydration group, where as in other 2 groups patients did not experience any side effects. Thus, nausea can be the limitation for effectiveness of oral hydration as patient may not drink the required amount.

LIMITATIONS

1. Sample size is small in each group.
2. No cases with gestational age <30 and >41 weeks could be studied.
3. Oligohydramnios with antenatal complications were not included except FGR.
4. The duration of effect of hydration therapy beyond 24 hours was not studied.
5. Effect of left lateral position was not assessed.
6. There was no control group as it was not possible ethically when many studies have proved that hydration increases AFI.
7. Arginine and amino acid supplements also might have had their effect on improvement in AFI, but the effect was equal in all the groups as it was a randomized control trial.

CONCLUSION

Our study strongly suggests that maternal hydration status has a definite role in amniotic fluid regulation. All hydration therapies increased AFI at 2 hours and 24 hours.

In our study, 0.45%NS has significantly proved its efficacy over RL+5%D and oral hydration in treatment of oligohydramnios after 2 hours as well as 24 hours of hydration therapy. On the other hand RL+ 5%D and oral hydration have found to increase in AFI with no significant difference in rise in AFI among both. Symphysiofundal height increased significantly at 2 hours and 24 hours for all the groups. This suggests that it can be used for clinical assessment of increase in liquor where USG is not available. Both idiopathic oligohydramnios and FGR with oligohydramnios showed significant improvement with any type of hydration. But in idiopathic oligohydramnios 0.45%NS proved to be better than oral and RL+5%D. In cases of FGR with oligohydramnios oral and 0.45%NS were effective, but sample size is too less to generalize the statement.

Oral hydration seems to be easy, feasible and non-invasive method of choice among various types of hydration in oligohydramnios and can be an option in patients with mild oligohydramnios. Additional benefit of water being cheaper, easily available and patient can easily be managed at home on OPD basis with regular follow up with no major complications.

But in our study 0.45% NS has shown a better efficacy than oral hydration and RL+5%D. Though it needs IV access and needs supervision, it can be a good choice for patients with severe oligohydramnios (idiopathic or FGR). Also there is surety that patient has received hydration unlike oral hydration.

None of the patients had any major side effects. Nausea was seen in 4 patients in oral hydration group and was managed conservatively.

In our study all three treatment options had no complications for fetus and had good neonatal outcome and lesser NICU admissions. Patients receiving 0.45%NS had better perinatal outcome than other two groups though not statistically significant.

SUMMARY

Oligohydramnios is an obstetrical complication. It may cause fetal complications like cord compression, intrauterine growth restriction, musculoskeletal abnormalities such as facial distortion and clubfoot, pulmonary hypoplasia, meconium aspiration syndrome. It directly does not cause any maternal complications. But maternal morbidity is associated with operative vaginal delivery and caesarean section.

All the types of hydration therapies can be used in treatment of oligohydramnios. In our study 108 cases were divided into 3 groups. Out of all 0.45%NS showed good improvement in AFI at 2 hours and 24 hours compared to other two groups (oral hydration group and RL+5%D group). Oral and RL+5%D groups have also shown significant increase in AFI when compared to baseline AFI. Both idiopathic oligohydramnios and FGR with oligohydramnios showed similar response to any type of hydration, but 0.45%NS was better in cases of idiopathic oligohydramnios. Hydration therapy showed good improvement in AFI in unexplained oligohydramnios when compared to oligohydramnios with FGR. SFH can be used to assess increase in liquor clinically when USG is not feasible.

So, 0.45%NS is a sound option for treatment of oligohydramnios as it is found to be most effective among the three types of hydration. Still oral hydration can be an option in treatment of mild oligohydramnios because of its patient compliance.

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ANNEXURE-I

ETHICAL CLEARANCE

Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. 5414
Date 24/11/14
BLDE U's Shri B.M. Patil Medical College

B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 22-11-2014 at 3-30pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title "A randomized controlled trail to compare the efficacy of three different methods of maternal hydration for oligohydraminios"

Name of P.G. student Dr. Abhigna. V.
Dept of OBG.

Name of Guide/Co-investigator Dr. Neelamma Patil
Associate professor of OBG.

for
DR.TEJASWINI VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE- II

BLDE UNIVERSITY'S SRI BM PATIL MEDICAL COLLEGE VIJAYAPUR-586103

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH:

I the undersigned…… s/o. D/o. W/o……aged……years ordinarily resident of……. do here by state/ declare that Dr…….. of ……. Hospital has examined me thoroughly on…… at …….. and has explained to me in my own language……. that I am suffering from ……..disease (condition) and this disease/ condition mimic following diseases…….. Further Doctor…….informed me that he/ she is conducting dissertation/ research titled "A Randomised Controlled Trial To Compare The Efficacy Of Three Different Methods Of Maternal Hydration For Oligohydramnios" under guidance of Dr…….requesting my participation in the study. I will be given either oral or intravenous fluids to increase amount of liquor amni and serial USGs will be done to note the change in the amount of liquor amni.

Doctor has also informed me that, during conduct of this procedure few adverse effects like fluid overload and electrolyte imbalance may be encountered. The complications are very rare but are not anticipated. They are usually treatable but in rare circumstance may prove fatal in spite of anticipated diagnosis & best treatment

made available. Further Doctor has informed me that my participation in this study help in evaluation of results of the study which is a useful reference for treatment of other similar cases in near future, and my baby outcome may also be improved if the treatment is found to be useful.

The Doctor has also informed me that information given by me, observations made/ photographs/ video graphs taken upon me by the investigator will be kept secret and not accessed by the person other than me or my legal hirer except for academic purposes.

The Doctor did inform me that though my participation is purely voluntary based on information given to me, I can ask any clarification during the course of treatment/ study related to Diagnosis, Procedure of treatment, result of treatment or prognosis. At the same time I have been informed that I can with draw from my participation in this study at any time if I want or investigator can terminate me from study at any time from the study but not the procedure of treatment & follow up unless I request to discharge.

In view of anticipated/ unexpected complications during the course of study, that I will be treated free of cost, as explained by the investigator.

After understanding the nature of dissertation or research, Diagnosis made, mode of treatment I the under signed smt…….under my full conscious state of mind I agree to participate in the said research/ Dissertation.

Signature of patient:

Signature of Doctor:

Witness 1.

2.

Date:

Place:

ANNEXURE-III

PROFORMA

RANDOMISED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF THREE DIFFERENT METHODS OF MATERNAL HYDRATION FOR OLIGOHYDRAMNIOS

Name: **IPNo:**

Age: **Case.no:**

Address: **Occupation:**

DOA: **Contact no:**

DO Study: **Mobile:**

Chief complaints: **Residence:**

History of present pregnancy:

Gestational age at diagnosis of oligohydramnios:

H/o prior hydration treatment: YES ☐ NO ☐

Any other treatment for oligohydramnios: YES ☐ NO ☐

If yes (drug/dosage/duration)

Obstetrics history:

Married Life:

Obstetric Score:

H/O oligohydramnios in previous pregnancy: YES ☐ NO ☐

Treatment taken for oligohydramnios: YES ☐ NO ☐

if yes details(drug/dosage/duration):

Menstrual History

LMP: EDD BY USG

EDD: I TRIMESTER:

POG: II TRIMESTER:

III TRIMESTER:

Corrected EDD: POG:

Corrected POG:

Past History:

Family History:

Personal History:

General Physical Examination

PR: BP: RR: TEMPERATURE:

Thyroid**:**

Pallor / icterus / cyanosis / clubbing / oedema / lymphadenopathy:

Systemic Examination

CVS:

RS:

Per Abdomen

Fundal height(GA):

Presentation:

Symphysiofundal height(cms):

FHS:

Fetal liquor ratio (clinical):

Moderate oligohydramnios:

Severe oligohydramnios:

INVESTIGATIONS

Hb%**:**

OGCT**:**

URINE ROUTINE:

TORCH (IF done already)**:**

USG**:**

BPD: PLACENTA

FL: POSITION:

AC: GRADE:

EFW:

FGR(YES/NO):

DOPPLER(If done):

OUTCOME MEASURES:

AFI:

Before :	
After 2hours :	
After 24hours :	

SYMPHYSIOFUNDAL HEIGHT:

Before :	
After 2hours :	
After 24hours :	

CHANGE IN VITALS

Treatment	PR	BP	RR	OEDEMA
Before				
After 2 hours				
After 24 hours				

SIDE EFFECTS

Vomiting: YES ☐ NO ☐

Headache: YES ☐ NO ☐

Allergic reactions: YES ☐ NO ☐

Any other

If yes, treatment given:

REMARKS:

KEY TO MASTER CHART

SLNO	serial number
B	booked
UB	unbooked
GA	gestational age
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
AFI	Amniotic fluid index
SFH	symphysiofundal height
MOD	Mode of delivery
VD	Vaginal delivery
CS	Cesarean section
B wt	Birth weight
AG 1	Apgar at 1 minute
AG2	Apgar at 5 minutes
NICU	Neonatal intensive care unit
MS	Mother side

MASTER CHART

SL NO	NAME	AGE	GROUP	B/UB	PARITY	GA	SBP	DBP	AFI	SFH	SBP(2HRS)	DBP(2HRS)	AFI(2HRS)	SFH(2HRS)	SBP(24hrs)	DBP(24hrs)	AFI(24HRS)	SFH(24HRS)	MOD	B WT	AG 1	AG 5	LIQUOR	NICU/MS	side effects
1	jayashree	21	B	b	primi	36	118	78	6	27	120	80	7	27.5	122	80	7	27	FTVD	2.25	7	9	clear	ms	nil
2	parveen hf	20	C	b	primi	40	120	84	7	36	122	82	8	39	120	82	8.4	37	FTVD	2.5	7	9	meconium	nicu	nil
3	jayashree	21	A	b	primi	36	120	80	7	27	122	82	8.2	28	122	82	8	28.6	FTVD	2.25	7	9	clear	ms	nausea
4	deepa b	19	C	b	primi	34	130	84	2	31	132	80	3.4	32.2	132	80	3.2	31.6	LSCS	2.1	5	7	meconium	nicu	nil
5	deepa b	19	A	b	primi	34	128	86	3.2	31.6	130	84	1.5	33.4	128	84	1	30	LSCS	2.1	5	7	meconium	nicu	nil
6	kavita mb	22	C	b	primi	40	118	78	5	35	120	80	7	35.4	120	80	7.6	35	LSCS	2.7	7	9	meconium	ms	nil
7	bhagyashree s	22	A	b	g2p1l1	40	124	86	3	32	122	82	4.5	34	124	82	4.2	32.4	LSCS	2.2	7	9	clear	ms	nil
8	bhagyashree	22	C	b	g2p1l1	40	126	84	4.2	32.4	124	86	6	32.6	126	86	7	32.8	LSCS	2.2	7	9	clear	ms	nil
9	kavita s	30	B	b	g2p1l1	37	120	80	3	34	122	86	3.8	34.4	120	86	4.2	34	FTVD	2.8	7	9	meconium	ms	nil
10	bharati vr	25	B	b	primi	36	122	82	5	33	126	84	6	33.6	122	84	5.4	33	LSCS	2.3	7	9	clear	nicu	nil
11	bharati vr	25	A	b	primi	36	122	84	5.4	33	124	82	6	34	122	82	6.2	34	LSCS	2.3	7	9	clear	nicu	nil
12	bharati vr	25	C	b	primi	36	120	84	6.2	34	124	84	7.4	35	120	84	8.2	36	LSCS	2.3	7	9	clear	nicu	nil
13	renuka	26	C	b	g3p2l1d1	37	112	78	7	32.8	118	80	8.4	34.2	112	82	8.6	34	LSCS	2.3	5	9	meconium	ms	nil
14	archana rb	22	A	b	g2p1l1	40	122	84	4	33	116	82	5.2	36	122	80	5.6	35	LSCS	2.4	7	9	clear	ms	nil
15	archana rb	21	B	b	g2p1l1	40	122	80	5.6	35	120	84	6	35.8	120	86	6.2	35	LSCS	2.4	7	9	clear	ms	nil
16	siddamma vn	25	A	b	primi	38	122	88	4	36	124	80	5.2	38	122	82	5.6	36	LSCS	3.1	7	9	clear	ms	nil
17	kavita sn	30	B	ub	g2p1l1	37	124	80	4	34	128	82	4.8	35	122	84	5.2	34	FTVD	2.8	7	9	clear	ms	nil
18	siddamma vn	25	A	b	primi	38	120	86	5.6	36	124	84	7	37.6	126	82	7.6	37	LSCS	3.1	7	9	clear	ms	nil
19	kavita sn	30	C	ub	g2p1l1	37	122	84	5.2	35	122	86	7.6	36.4	125	82	8.2	36	FTVD	2.8	7	9	clear	ms	nil
20	shashikala	20	C	b	primi	38	120	82	4	34	122	80	6	35	120	82	7.8	35.2	FTVD	2.5	7	9	clear	ms	nil
21	sunanda b	22	B	ub	primi	40	122	86	6	34.6	124	84	7	35	122	84	7.8	34.8	LSCS	3.06	7	9	clear	ms	nil
22	parvati iy	30	C	b	g4p2l2a1	35	130	84	7	32	128	80	8.6	33.6	128	84	9	34	LSCS	2.2	7	9	clear	ms	nil
23	shoba tc	20	B	b	primi	40	128	80	7	33	130	82	8.2	34	128	82	8.2	33.4	LSCS	2.45	7	9	clear	ms	nil
24	jayashree HS	22	B	b	primi	39	124	68	3	33	126	70	4	33.8	124	72	3.8	33	LSCS	2.6	5	7	meconium	nicu	nil
25	farzana ag	21	A	b	primi	36	122	82	2	32	124	78	3.2	34	122	76	2.8	32..6	LSCS	2.5	7	9	clear	ms	nil
26	farzana ag	21	B	b	primi	36	120	80	2.8	32.6	122	82	3.2	33	120	80	1.8	33	LSCS	2.5	7	9	clear	ms	nil

27	jayashree jn	18	B	b	primi	34	116	74	2.5	31	120	78	3.5	32	116	80	3.8	31.8	FTVD	2.9	7	9	clear	ms	nil
28	jayashrre jn	18	A	b	primi	34	118	76	3.8	31.8	122	78	4.8	33	118	78	5.4	33.6	FTVD	2.9	7	9	clear	ms	nil
29	shantabai k	30	B	b	g3p1l1a1	36	124	82	5	35	122	80	6.4	36	120	80	6.6	36.4	LSCS	3.2	7	9	clear	ms	nil
30	shantabai k	30	B	b	g3p1l1a1	36	122	80	6.6	36.4	126	82	7.6	37	122	84	8	36.6	LSCS	3.2	7	9	clear	ms	nil
31	radha vd	21	A	b	g2p1l1	38	118	78	7	34	120	80	8.2	36	120	82	8.4	35	FTVD	3	7	9	clear	ms	nil
32	yashoda cj	24	C	b	g3p2l1d1	38	130	86	7	34.4	132	88	9	35	128	84	10.4	34.4	LSCS	2.8	7	9	clear	ms	nil
33	devamma bs	30	C	b	g2p1l1	36	122	80	6	34	128	84	9	35.6	122	86	11	35	LSCS	2.8	7	9	clear	ms	nil
34	siddamma rh	20	C	ub	primi	40	124	82	5	34	126	82	6.8	35	122	82	7.2	35.4	LSCS	3.3	7	9	clear	ms	nil
35	lakshmi rl	19	A	b	primi	39	122	84	5	32	122	82	6.2	34	124	84	6.4	34	LSCS	2.74	7	9	clear	ms	nil
36	siddamma rh	20	A	ub	primi	40	124	86	7.2	35.4	124	84	8.2	37	124	84	9	37.4	LSCS	3.3	7	9	clear	ms	nil
37	lakshmi rl	19	C	b	primi	39	120	84	6.4	34	122	82	8	35	120	82	8.8	34	LSCS	2.74	7	9	clear	ms	nil
38	pavakka	20	C	b	g4p3l1d2	40	120	84	4	31	126	84	6	32	120	84	7	32.4	LSCS	2	5	7	clear	ms	nil
39	pavakka	20	A	b	g4p3l1d2	40	122	86	7	32.4	124	84	8	34.5	126	84	9	34	LSCS	2	5	7	clear	ms	nil
40	savitri	25	A	ub	g3p2l2	41	126	80	5.4	35	126	82	6.4	36.2	126	82	6.8	35	FTVD	3.5	7	9	clear	ms	nil
41	savitri	25	C	ub	g3p2l2	41	124	86	6.8	35	128	88	8	35.5	124	88	9	35	FTVD	3.5	7	9	clear	ms	nil
42	chandrakala pk	22	B	b	g3p2l2	35	122	84	6	33	122	84	7	33.6	122	84	8.2	34	FTVD	2.84	5	7	meconium	nicu	nil
43	nethra sv	32	A	b	primi	31	120	84	5	28	126	84	6.2	30	120	86	6.6	29	LSCS	3.1	7	9	clear	ms	nil
44	nethra sv	32	C	b	primi	31	122	82	6.6	29	124	82	8.4	30.2	124	84	10.2	30.4	LSCS	3.1	7	9	clear	ms	nil
45	yasmin	23	C	b	g2p1l1	37	128	70	7	34	122	74	9	35	122	76	11	35	LSCS	2.86	7	9	clear	ms	nil
46	savita rr	22	B	b	primi	40	118	78	4	34.2	120	76	5	35.5	120	76	6.2	34	LSCS	2.94	7	9	clear	ms	nil
47	renuka	25	B	b	g2p1l1	39	120	84	4	34	122	82	5	34.6	120	78	5.8	34	LSCS	2.8	7	9	clear	ms	nil
48	renuka	25	A	b	g2p1l1	39	120	84	5.8	34	122	82	7.4	36	120	84	8.2	35	LSCS	2.8	7	9	clear	ms	nil
49	nethra sv	32	A	b	primi	37	126	82	6.8	35	128	84	8	36.8	126	82	10	36	LSCS	3.1	7	9	clear	ms	nil
50	navasad ha	23	C	b	g6p3l3d2a2	33	124	84	7	31	126	82	9	32	124	82	11	32							nil
51	bhagirathi cm	31	B	b	g2p1l1	40	122	80	7	32	122	82	8.2	33	122	84	9	32.6	LSCS	2.5	7	9	clear	ms	nil
52	bibijan rn	19	A	b	primi	39	120	78	3	33	124	80	3.5	34.2	120	84	3	34	LSCS	2.6	7	9	clear	ms	nil
53	pooja a n	20	B	b	primi	37	124	84	6	34	126	82	7	35	124	82	8	34.2	LSCS	3	5	7	meconium	nicu	nil
54	kalavati ph	19	B	b	primi	36	122	80	1.5	32	124	78	2.2	33.2	122	76	1	32.6	LSCS	2.6	7	9	meconium	nicu	nil
55	renuka ca	25	A	b	g2p1l1	36	120	78	3.9	32	122	78	5.2	34	120	76	6	33	FTVD	2.4	7	9	clear	ms	nil
56	renuka ca	25	A	b	g2p1l1	36	122	76	6	33	122	78	7	34	122	80	8	33	FTVD	2.4	7	9	clear	ms	nil
57	jyothi sk	22	C	b	g2a1	39	116	74	3	33	120	74	4.4	34	116	74	5.4	32.6	LSCS	2.6	7	9	meconium	nicu	nil
58	jyothi sk	22	B	b	g2a1	39	114	78	5.4	33.6	110	76	4	33	116	80	4	33	LSCS	2.6	7	9	meconium	nicu	nil

59	ashwini pb	21	B	b	primi	37	120	80	6	32	118	82	7	33	118	82	6.4	33	LSCS	2.7	7	9	meconium	nicu	nil
60	pavitra vk	27	B	b	g2p1l1	36	126	82	2	32	128	80	2	33	126	84	2	32.6	LSCS	2.5	7	9	meconium	nicu	nil
61	jayashree st	32	C	b	primi	30	122	86	6	30	124	86	8	32	120	86	10	32	FTVD	2.8	7	9	clear	ms	nil
62	kavita t	26	A	b	g2p1d1	38	112	72	5	33	120	78	6.2	34	114	80	7.2	33.6	LSCS	2.4	7	9	clear	ms	nausea
63	kamalabai	32	A	b	g4p3l2da	39	120	84	4	34	122	82	3	33.5	120	84	3	33	LSCS	2.7	7	9	meconium	nicu	nil
64	laxmi sw	20	C	b	primi	31	130	88	3	28	132	86	4.4	30	130	82	5.2	29.6	LSCS	2.9	7	9	clear	ms	nil
65	dhanashree kh	22	B	b	primi	38	128	88	7	34	130	86	8	35	128	86	8.2	35	FTVD	2.6	7	9	clear	ms	nil
66	laxmi sw	20	C	b	primi	31	130	86	5.2	29.6	132	84	7.6	31	132	84	8.4	32	LSCS	2.9	7	9	clear	ms	nil
67	ramiza ag	20	C	b	primi	35	120	84	3	30	122	82	3.5	31	124	80	3	30	LSCS	1.8	7	9	clear	nicu	nil
68	ramiza ag	20	A	b	primi	35	122	84	3	30	122	82	2.5	30	122	80	2	30	LSCS	1.8	7	9	clear	nicu	nil
69	ramiza ag	20	B	b	primi	35	122	82	2	30	122	80	1.5	31	122	80	1.5	30	LSCS	1.8	7	9	clear	nicu	nil
70	rohini nh	29	A	b	primi	36	120	86	6	33	124	84	7.4	34	122	84	8.4	33	LSCS	2.7	7	9	clear	ms	nil
71	rohini nh	29	B	b	primi	37	124	86	4	33	126	84	5	33.6	124	84	5.4	33	LSCS	2.7	7	9	clear	ms	nil
72	rohini nh	29	C	b	primi	37	122	84	5.4	33	126	82	7	34.4	122	80	8	35	LSCS	2.7	7	9	clear	ms	nil
73	arti ab	24	B	b	primi	34	130	80	6.6	30	128	82	7.4	31	132	82	8.2	30.6							nil
74	jayashree sp	33	A	b	primi	36	120	86	5	32	130	86	6.1	34.5	120	84	7	33	LSCS	2.6	7	9	clear	ms	nil
75	jayashree sp	33	B	b	primi	36	122	84	7	33	128	88	7.8	34	122	86	8.2	33	LSCS	2.6	7	9	clear	ms	nil
76	savita rp	22	C	b	primi	40	116	78	5	34	120	80	7	35	116	82	8.6	35.6	FTVD	2.9	7	9	clear	ms	nil
77	kaveri mh	24	C	b	primi	37	122	86	5	32	128	84	6.6	33	122	82	7.6	33	LSCS	2.9	7	9	meconium	nicu	nil
78	nandini sk	23	C	b	primi	34	126	78	5	31	126	80	7	32.6	122	80	8	33	FTVD	2.8	7	9	clear	ms	nil
79	kaveri mh	24	C	b	primi	37	122	76	7.6	33	124	78	8.8	34.6	124	74	9.6	34	LSCS	2.9	7	9	meconium	nicu	nil
80	lakshmi hy	25	B	b	g2p1l1	36	120	84	6	33	122	82	7	34	122	82	8	33.8	LSCS	3	7	9	clear	ms	nil
81	shahinaz	22	A	ub	g3p2l2	40	122	78	3	34	124	80	4	35.5	124	80	5	35	LSCS	3.2	5	7	meconium	nicu	nil
82	lakshmibai rh	20	A	b	primi	39	122	76	5	34	126	78	6	36	124	78	7.2	34.6	FTVD	2.9	7	9	clear	ms	nil
83	lakshmibai rh	20	C	b	primi	39	126	70	7.2	34.6	128	72	8.8	36	122	72	10	35	FTVD	2.9	7	9	clear	ms	nil
84	veena vt	26	B	b	g4p2l1d1a1	34	120	84	3	29	122	82	4	30	120	82	4.8	29.8							nil
85	veena vt	26	C	b	g4p2l1d1a1	34	118	82	4.8	29.8	120	82	6.4	31.4	116	80	8	32.8							nil
86	prabhavati sc	26	C	b	primi	37	128	80	6	33	122	82	7	34	128	82	7.8	33	LSCS	2.8	7	9	meconium	ms	nil
87	yallawwa sh	18	C	b	primi	32	126	84	6	29	126	84	7.8	31	124	86	9	31	PTVD	2.3	5	7	clear	nicu	nil
88	prabhavati sc	26	B	b	primi	37	130	78	7.8	33	132	76	8.2	33	132	74	8.8	33	LSCS	2.8	7	9	meconium	ms	nil
89	vijayalakshmi mk	20	B	b	primi	37	126	80	4	34	130	80	5	35	124	82	6.2	34	FTVD	2.4	3	5	meconium	nicu	nil
90	bharati rn	19	A	b	primi	39	122	86	4	33	124	82	5.2	35	126	80	6.4	35	FTVD	2.7	7	9	clear	ms	nil

91	bharati rn	19	C	b	primi	39	122	84	6.4	35	124	82	8	36.6	122	82	9	37	FTVD	2.7	7	9	clear	ms	nil
91	nirmala sn	20	A	b	g2p1l1	34	120	84	7	32	126	84	8.2	33.4	122	82	9.4	33	LSCS	1.6	7	9	clear	nicu	nil
93	veena vr	19	B	b	primi	34	130	86	5	30	132	82	6	31	132	80	6.4	30.8							nil
94	veena vr	19	A	b	primi	34	128	84	6.4	30.8	128	82	7.8	31.8	126	82	9	32.6							nausea
95	surekha	29	B	b	g2p1l1	39	122	80	7	34	122	80	8	35	122	80	9	34.8	FTVD	2.86	7	9	clear	ms	nil
96	sukanya ss	20	B	b	primi	35	126	86	6.5	32	126	82	7.4	33	126	80	8	34	PTVD	2.6	2	5	meconium	nicu	nil
97	shruti ma	20	C	b	primi	40	120	80	5	34	124	86	7.6	35	120	84	7.6	34.8	LSCS	3.16	7	9	clear	ms	nil
98	shruti ma	20	A	b	primi	40	122	84	7.6	34.8	130	82	8.6	36	124	82	9	36	LSCS	3.16	7	9	clear	ms	nil
99	najarparvin m	25	B	b	primi	39	130	84	6	34	132	80	7.2	35.6	132	78	8.4	36	LSCS	2.9	5	7	meconium	ms	nil
100	bhagirati js	20	A	b	g2p1l1	38	126	82	4	34	124	84	5.4	35.4	126	82	6.8	36	LSCS	2.38	7	9	clear	ms	nil
101	kamalakshi ks	24	B	b	g2p1l1	41	122	82	5	33	126	84	6	34	122	84	6.6	34	LSCS	2.5	7	9	clear	ms	nil
102	kamalakshiks	24	A	b	g2p1l1	41	120	84	6.6	34	124	82	7.6	35.6	120	80	8.4	35	LSCS	2.5	7	9	clear	ms	nil
103	rekha bt	18	B	b	primi	38	122	80	4	33.6	126	82	5.2	34.2	124	82	6	34	FTVD	2.56	7	9	clear	ms	nil
104	rekha bt	18	C	b	primi	38	124	78	6	34	130	80	8	35	124	84	9	35	FTVD	2.56	7	9	clear	ms	nil
105	renuka rs	22	C	b	g2a1	38	130	84	5	33	132	88	7	35	128	86	8.6	35.8	FTVD	3	7	9	clear	ms	nil
106	jyothi sp	21	A	b	g2p1l1	36	122	88	5	32	122	86	6	34	124	86	7.8	34.8	FTVD	3	7	9	clear	ms	nil
107	bharati ga	25	A	b	g3p2l1d1	39	120	84	2	32.6	124	86	3.4	34	122	84	4.4	35	LSCS	2.64	7	9	meconium	ms	nil
108	gurudevi ac	25	A	b	primi	40	126	76	6	34	124	74	7.4	35	126	78	8.2	35.8	FTVD	2.76	7	9	clear	ms	nausea

A Randomization Plan

from

http://www.randomization.com

1. GROUP B
2. GROUP C
3. GROUP A
4. GROUP C
5. GROUP A
6. GROUP C
7. GROUP A
8. GROUP C
9. GROUP B
10. GROUP B
11. GROUP A
12. GROUP C
13. GROUP C
14. GROUP A
15. GROUP B
16. GROUP A
17. GROUP B
18. GROUP A
19. GROUP C
20. GROUP C
21. GROUP B
22. GROUP C
23. GROUP B
24. GROUP B
25. GROUP A
26. GROUP B
27. GROUP B
28. GROUP A
29. GROUP B
30. GROUP B
31. GROUP A
32. GROUP C
33. GROUP C
34. GROUP C
35. GROUP A
36. GROUP A
37. GROUP C
38. GROUP C
39. GROUP A
40. GROUP A
41. GROUP C
42. GROUP B
43. GROUP A
44. GROUP C
45. GROUP C

46. GROUP B_____
47. GROUP B_____
48. GROUP A_____
49. GROUP A_____
50. GROUP C_____
51. GROUP B_____
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95. GROUP B_____
96. GROUP B_____

97. GROUP C_____
98. GROUP A_____
99. GROUP B_____
100. GROUP A_____
101. GROUP B_____
102. GROUP A_____
103. GROUP B_____
104. GROUP C_____
105. GROUP C_____
106. GROUP A_____
107. GROUP A_____
108. GROUP A_____

108 subjects randomized into blocks of

36 36 36

To reproduce this plan, use the seed 16546