

## Indomethacin is Effective in Idiopathic Polyhydramnios with Better Fetal Outcome

SADAF ZAHRA SYED<sup>1</sup>, SANA ANSARI<sup>2</sup>, S. M. AFTAB<sup>3</sup>, SADIYA. BUTT<sup>4</sup>, SHAHID H. WARRIS<sup>5</sup>, AFSHAN MAZHAR<sup>6</sup>

<sup>1</sup>Assistant Professor, KEMU, Lady Willingdon Hospital, Lahore.

<sup>2</sup>Postgraduate Trainee, Lady Willingdon Hospital, Lahore.

<sup>3</sup>Assistant Professor Cardiology, KEMU, Mayo Hospital Lahore

<sup>4</sup>Woman Medical Officer, Lady Willingdon Hospital, Lahore.

<sup>5</sup>Associate Professor of Psychiatry & Behavioral Sciences, M. Islam Medical and Dental College, Gujranwala

<sup>6</sup>Senior Registrar, Lady Willingdon Hospital, Lahore.

Correspondence to Dr. Sadaf Zahra Syed Email: [draftabshah15@gmail.com](mailto:draftabshah15@gmail.com)

### ABSTRACT

**Aim:** To assess the Effectiveness of indomethacin in managing idiopathic polyhydramnios pregnancies and its effect on fetal outcomes.

**Study design:** Case control study:

**Place and duration of study:** Department of Obs and Gyne LWH / KEMU, Lahore from august 2017 to January 2018

**Methods:** 118 patients were included in this study; patients were divided into two groups A&B. each group had 59 patients. Group A was case group and group was B was control group having idiopathic polyhydramnios with clinical symptoms like abdominal discomfort and respiratory discomfort. group A was treated with indomethacin 25mg three times a day for a period of 04 weeks but not exceeding beyond 32 weeks of gestational age. Ultrasonography was done after 04 weeks of treatment to see the reduction in AFI and fetal echocardiography was done to see premature closure of ductus arteriosus.

**Results:** Total of 118 patients were enrolled in this study. In group A (cases), AFI decreased in 42 (71%) with use of indomethacin and maternal symptoms relieved in 52 (89%) cases. 40 (67.7 % delivered at terms in group A, 35 (59%) in group B, out of 59 new born babies, 37 required neonatal care from group A and 55 required neonatal care from control group B.

**Conclusion:** It is concluded from this study that indomethacin is effective in idiopathic polyhydramnios with better fetal outcome.

**Keywords:** Polyhydramnios, indomethacin, amniotic fluid index

---

### INTRODUCTION

Polyhydramnios also known as hydraminos indicate the “occurrence of an abundant amount of amniotic fluid comparative to the gestational age”. In normal pregnancy, the 95<sup>th</sup> percentile for the maximum volume of amniotic fluid is about 2200ml. The 95<sup>th</sup> percentile amniotic fluid index (AFI) at maximum fluid volumes for normal gestation is between 18 and 20cm<sup>1</sup>.

The incidence of abnormal intrauterine amniotic fluid volume (AFV) is reported in nearly 1 to 3% of pregnancies. An AFI value from 0 to 5cm that is labeled as low fluid, 5.1 to 18cm as normal AFI and >18cm as high fluid volume. Based on severity, 3 groups are formed, mild (AFI 25-30) moderate (30-35) and severe (AFI >35cm). Idiopathic polyhydramnios takes place in roughly “65%” of pregnancies having no obvious etiology. Both maternal and fetal outcome can be influenced by this condition. The maternal outcomes are ante partum hemorrhage, respiratory compromise, anomalous presentation, postpartum hemorrhage, uterine dysfunction and increase the operative intervention. Idiopathic polyhydramnios is independently associated with increased risks of morbidity<sup>2,3</sup>. Polyhydramnios affect both the mother and fetus in the number of ways and its presence must incite the exploration for the various fetal abnormalities. Aneuploidies

requires karyotyping while gross fetal anomalies can be diagnosed sonographically<sup>3</sup>.

- Congenital anomalies (14.5%): duodenal atresia, anencephaly and esophageal atresia.
- Premature labor: intracranial hemorrhage and acute respiratory distress syndrome.
- Others: placental abruption hypoxia secondary to cord prolapsed, prolonged labor due to malpresentation, large for gestational age and hydrops fetalis<sup>4</sup>.

### PATIENTS AND METHODS

A sample size of 118 patients fulfilling the criteria were enrolled in this study from department Gyne & Obs Unit-II Lady Willingdon Hospital, informed consent from patients were obtained for taking part in Study and using their data in Research.

All cases of pregnancy including primigravida and multigravida with idiopathic polyhydramnios with AFI more than 20, Gestational ages from 24 weeks to 32 weeks. Primi-gravid as well as multigravida patients. Following patients were excluded like Polyhydramnios with congenital anomalies incompatible with life e.g., neural tube defects, cardiac anomalies, gestational anomalies etc. gestational age more than 32 weeks in the case group.

Received on 13-06-2019

Accepted on 10-09-2019

**RESULTS**

A total of 118 patients were enrolled in this study (59 cases; 59 controlled) in this study, with idiopathic polyhydramnios pregnancy. The baseline characteristics of these patients were as follows:

1. The mean age of cases in Group-A and Group-B were 25.59 ± 4.79 years and 25.02 ± 3.90 years. Statistically this difference was not significant (P>0.05)
2. The mean gestational age at time of delivery in Group-A was 37.01±3.36 weeks and in Group-B was 36.33 ± 3.70 weeks with statistically higher mean gestational age in Group-A, p-value < 0.001.

In group -A the mean GPA was 2.36 ± 1.79, 1.19 ± 1.63 and 0.17 ± 0.46 while in group-B the mean GPA was 2.44 ± 1.56, 1.20 ± 1.32 and 0.24 ± 0.65 respectively. The mean GPA in both groups was statistically same, p-value > 0.05 The mean blood pressure and pulse rate in both groups were same, p-value <0.005.

The mean height, weight and BMI in Group-A were 1.50 ± 0.048, 72.66±9.40 and 32.32 ± 4.26 while mean height, weight and BMI in Group-B were 1.51±0.02, 62.36 ±2.83 and 27.48 ±1.49 respectively. The mean weight and BMI in Group-A was significantly higher, p-value <0.05.

The mean BSR at baseline in both groups was statistically same while the mean BSR at final follow up was significantly higher in Group-B compared to Group-A, p-value <0.001. The mean fetal heart rate in Group-A was 135.46 ± 3.76 and in Group-B was 135.56 ± 3.58 /minute the mean fetal heart rate was statistically same in both groups, p-value >0.05. The mean AFI at baseline in Group-A and Group-B was 23.92 ± 2.45 and 23.75 ± 1.78 and at final follow up the mean AFI was 19.05 ± 2.88 in Group-A and 24.71 ± 1.85 in Group-B respectively. The mean AFI at final follow up was significantly lower in Group-A then in Group-B, p-value <0.001.

In Group-A there were 18(30.5%) cases and in Group-B there were 45(76.3%) cases who had Tachycardia and 38(64.4%) cases in Group-A and 55(93.2%) cases in Group-B had Tachypnea, with significantly higher frequency of Tachycardia and Tachypnea in Group-B than Group-A, p-value <0.001. A total of 10(16.9%) in Group-A and 19(32.2%) cases in Group-B had meconium aspiration with insignificant difference, p-value >0.05. A total of 4(6.8%) cases had hypoglycemia and 1(1.7%) case had hyperglycemia in Group-A, with significantly higher hypoglycemia in Group-A, p-value <0.05. Hypothermia was developed in 22(37.3%) cases of Group-A and 41(69.5%) cases in Group-B with significantly higher cases in Group-B , p-value <0.001. Cases 2(3.4%) of Group-A and 1(1.7%) case of Group-B had hyperthermia, with insignificant difference, p-value >0.05. The mean birth weight (kg) in Group-A and Group-B were 3.05 ± 0.47 kg and 2.90 ± 0.39 kg. The mean APGAR score at 1 minute in Group-A was 5.53 ± 1.39 and in Group-B was 5.54± 1.11 and at 5 minutes the mean APGAR score in Group-A was 6.31±1.45 and 6.39 ± 1.20 in Group-B. The mean birth weight, APGAR score at 5 and 10 minute was statistically same in both groups, p-value >0.05. At first week of follow up, 37(62.7%) cases in Group-A and 55(93.2%) cases in Group-B with significantly higher frequency of need of neonatal care in group-B, p-value <0.001. Only 1(1.7%) cases in Group-A and 2(3.4%) cases in Group-B had asphyxia with no significant difference, p-value >0.05. There were 5(8.5%) cases in Group-A and 15(25.4%) cases in Group-B had Jaundice with significantly higher cases in group-B. Only 1(1.7%) case had intracranial hemorrhage in Group-B while none of the cases had in Group-A, p-value >0.05.

The mean duration of NICU in Group-A was 0.53±0.72 and in Group-B was 1.36±1.57 respectively. The mean days of admission for neonatal care in Group-B was significantly higher than Group-A, p-value <0.001.

Table-1: Comparison of fetal heart rate in both groups

Study design	Mean	S.D	Minimum	Maximum
Group-A (n=59)	135.46	3.76	120.00	142.00
Group-B (11=59)	135.56	3.58	120.00	142.00
Total (11=118)	135.51	3.66	120.00	142.00

P value 0.881

Table 2: Comparison of Amniotic fluid at baseline and at final visit in both groups

	Study design	Mean	S.D	Minimum	Maximum	p-value
USG with AFI (Baseline)	Group-A (n=59)	23.92	2.45	19.00	30.00	0.669
	Group-B (n=59)	23.75	1.78	21.00	30.00	
	Total (n=118)	23.83	2.13	19.00	30.00	
USG with AFI (Final)	Group-A (n=59)	19.05	2.88	15.00	26.00	<0.001
	Group-B (n=59)	24.71	1.85	21.00	31.00	
	Total (n=118)	21.88	3.73	15.00	31.00	

Table 3: Comparison of neonatal outcome at birth in both study groups

	Study Groups		P value
	Group A	Group B	
Birth Trauma	0(0%)	0(0%)	--
Tachycardia	18(30.5%)	45(76.3%)	<0.001 **
Tachypnoea	38(64.4%)	55(93.2%)	<0.001 **
Meconium aspiration	10(16.9%)	19(32.2%)	0.054
Hypoglycemia	4(6.8%)	0(0%)	0.042*
Hyperglycemia	1(1.7%)	0(0%)	0.315
Hypothermia	22(37.3%)	41(69.5%)	<0.001 **
Hyperthermia	2(3.4%)	1(1.7%)	0.59

Table 4: Comparison of birth outcome at birth in both study groups

	Study design	Mean	S.D	Minimum	Maximum	p-value
Neonatal birth weight (kg)	Group-A (n=59)	3.05	0.47	2.00	4.20	0.059
	Group-B (n=59)	2.90	0.39	2.00	3.60	
	Total (n=118)	2.98	0.43	2.00	4.20	
Apgar score at 1 mint (at birth)	Group-A (n=59)	5.53	1.39	2.00	8.00	0.99
	Group-B (n=59)	5.54	1.11	2.00	7.00	
	Total (n=118)	5.53	1.25	2.00	8.00	
Apgar score at 5 mints (at birth)	Group-A (n=59)	6.31	1.45	2	9	0.731
	Group-B (n=59)	6.39	1.20	3	8	
	Total (n=118)	6.35	1.32	2	9	

Table 5: Comparison of neonatal outcome at 1<sup>st</sup>week of follow in both study groups

	Study Groups		P value
	Group A	Group B	
Need of neonatal care	37(62.7%)	55(93.2%)	<0.001
Asphyxia	1(1.7%)	2(3.4%)	0.55
Jaundice	5(8.5%)	15(25.4%)	0.014
Intracranial hemorrhage	0(0%)	1(1.7%)	0.315
Neonatal death	0(0%)	2(3.3%)	--
Need any surgery	0(0%)	0(0%)	--

Table 6: Comparison of Admission in Neonatal Care at 1<sup>st</sup>week of follow in both study groups

	Study design	Mean	S.D	Minimum	Maximum
Admission in neonatal care (1 week follow up)	Group-A (n=59)	0.53	0.72	.00	3.00
	Group-B (n=59)	1.36	1.57	.00	8.00
	Total (n=118)	0.94	1.28	.00	8.00

P value &lt;0.001

## DISCUSSION

In our study 118 patients were (59 cases and 59 control) were enrolled. The mean age of patients presented with polyhydramnios in this study was  $28.59 \pm 4.79$  years. This was similar to the study conducted by S Taskin<sup>2</sup> where mean age was 29 years. This comparison showed that polyhydramnios is a problem of peak reproductive age group. In our study the parity of the patients with polyhydramnios, 51% of the patients were multigravida and 49% patients were primigravida. The finding is in contrast to the study conducted by Anisa and colleagues<sup>5</sup> who found 78% multigravida.

The mean gestational age in our current study was found to be  $28.50 \pm 1.31$  weeks similar to the mean gestational age at presentation with polyhydramnios studied by Dorlejinet al<sup>6</sup> which was  $31 \pm 4.9$  weeks.

In the study of Naser and Colleagu<sup>1</sup> idiopathic polyhydramnios was further classified into mild polyhydramnios (AFI 25-30) which accounted for 84% and moderate polyhydramnios (AFI 30.1-35cm) in 16%. There were no cases with severe polyhydramnios (AFI >35cm). In our study, maximum cases were with mild polyhydramnios and no case of severe polyhydramnios were found. This shows that in case of Idiopathic polyhydramnios excluding Multiple gestation and Diabetes Mellitus the chance of getting AFI >35cm is rare.

Indomethacin is believed to reduce the normal PGs activity that is mediated by kidney vasculature.<sup>7</sup> Treatment was started between 24 and 32 weeks of gestation with symptomatic polyhydramnios as studied by Shrestha<sup>8</sup> and Abhyankar<sup>9</sup> in our study, Indomethacin was used for four weeks in between same gestational age with absence of congenital anomaly and AFI greater than 20cm with symptoms associated with polyhydramnios such as

abdominal discomfort and respiratory problems. In our study, a dosage of 25mg of Indomethacin was administered, three times a day per oral capsule form, which is the same as that used by Shrestha<sup>8</sup>. Most of the patients tolerated drugs well and no side effects seen in the mothers similar to Shrestha<sup>8</sup> and Abhyankar<sup>9</sup> study.

In our study, showed no ductal constriction was seen after 4 weeks of use of Indomethacin on echocardiography as in case reported by Tracan<sup>10</sup> in which there was no ductal constriction and it was recommended to use the drug at gestational age less than 32 weeks. The frequency of Indomethacin medicated fetal ductal narrowing inclines as gestational age progresses.

In our study mean gestational age of delivery in the study and control group was  $37.0 \pm 3.36$  weeks and  $36.33 \pm 3.70$  weeks with statistically higher mean gestational age in Group A (Study). Whereas in study by Soghra and Rezaei<sup>11</sup> the mean duration of gestation in case and control group was " $38 \pm 1.33$ " and " $34 \pm 2.93$ " weeks correspondingly. This study and current study both show statistically higher mean gestational age in Indomethacin induction group. In the current study, 75% delivered by spontaneous vertex delivery (SVD) in study group and 60% delivered by spontaneous vertex delivery in control group. It is comparatively less as in study by Cabrolet al<sup>12</sup> where 87.7% delivered vaginally. Caesarean section rate was 25% in the case group, 40% in the control group. They were mostly due to malpresentation, fetal distress, meconium, abruption, vaginal leaking in the control.

Fetal outcome noted in terms of fetal weight was statistically same in both groups which was from 2000 grams to 4200 grams in study group and 2000 grams to 3600 grams in control group. Results are similar to the study by Cabrolet al<sup>12</sup> where birth weight was within the range of

2750 to 3600 grams was noted. Both the groups had about 21 % low birth weight where as in study conducted by Cheng et al<sup>13</sup> 32% of the babies were with low birth weight.

In the current study, 81 % cases had 5 or above Apgar score at 1 minute, similar to study of Cabrolet al<sup>12</sup> and in 85% cases 7 or above Apgar score in 5 minutes. 15% of cases were with less than 7 apgar score in 5 minutes similar to the study by Chen et al<sup>13</sup> in which 11.1 % had <7 apgarscore in 5 minutes.

In the cases, babies transferred to neonatal intensive care unit (NICU) in study group, were 62.7% and in the control, 93.2%. In Chen et al<sup>13</sup> study, 18.6% babies were admitted to NICU. There was significant difference in Indomethacin and non-Indomethacin group polyhydramnios pregnancy. The mean duration of NICU admission in case group was 0.53±0.72 and in control group was 1.36± 1.57. The mean days of admission for neonatal care in control group was significantly higher. In the current study, Early neonatal death occurred in 2 out of 59 cases which was in contrast to the study by Cabrol et al<sup>12</sup> where 12.5% of babies died early in their life. However in control group about 4 out of 59 had early neonatal death.

Though, all of the cases in whom treatment was monitored antenatally, delivered normal healthy neonates, yet several studies recommend that Indomethacin must only be utilized in symptomatic hydramnios cases in whom maternal safety supersedes concerns of fetal safety.

## CONCLUSION

When polyhydramnios diagnosis is confirmed, an assessment of feto-maternal factors is suggested which at least, must incorporate a thorough ultrasound assessment and diabetes screen. Prostaglandin synthetize inhibitors, however seems to be effective and convenient mode of treatment for polyhydramnios. The risk and benefit ratio may depend on the clinical judgment. Indomethacin should be used only in cases of symptomatic hydramnios, Indomethacin proved to be an effective treatment in reducing amniotic fluid index and relief of maternal pressure symptoms. Thus it may indirectly help in prolonging pregnancy.

It affect the gestational age at delivery and prevents preterm labour, improves birth weight, Apgar score,

decrease the need of resuscitation and also decrease the need of NICU admission. Study concluded that Indomethacin is effective in relief of maternal symptoms as well results into the better fetal outcomes.

## REFERENCES

1. James DK, Steer PJ, Al. High Risk Pregnancy. Beall MH, Beloosesky R and Ross MG. Abnormalities of amniotic fluid volume. 4<sup>th</sup> edition. United Kingdom. Saunders. 2011; (1):2003.
2. Taskin S, Pabaccu EG, Kanmaz G, Kahraman K, Kurtay G. Perinatal outcomes of idiopathic polyhydramnios. *Interventional Medicine and Applied Science* 2013;5(1):21-5.
3. Rajjah P. Variety of polyhydramnios. *emedicine* 2006; (1): 1-9.5
4. Dutta DC, Text book of Obstetrics. Multiple Pregnancy. Hydramnios and abnormalities of placenta and cord. 1<sup>st</sup> Edition. India. 2016; (1):214-17.
5. Hamza A, Herr D, Solomayer EF, et al. Polyhydramnios: Causes, Diagnosis and Therapy. *2013*; (1): 16-21.
6. Anisa F, Shamshad, Danish N. Frequency, causes and outcome of. *Gomal J Med Sci* 2008; 6(1): 106-9.
7. Dorlejin DMJ, Cohen-Overbeek TE, Groenendaal F, Bruinse HW, Stoutenbeek P. Idiopathic polyhydroamnios and postnatal findings. *J Matren Fetal Neonat Med* 2009; 22(1):315-20.
8. Boyd RL. Polyhydroamnios and Oligohydroamnios. *Am J Obset Gynecol* 2008; 190(1):7-13.
9. Shrestha A, Chawla CD. Role of Indomethacin in 111 polyhydramnios. *Srilanka Journal of Obstetrics and Gynaecology* 2013; 35(2):50-2.
10. Abhyankar S, Salvi VS. Indomethacin Therapy in Hydroamnios. *J Postgrad Med* 200; 46(1):176-8.
11. Tracain A, Gurakan B, Yildirim S, Ozkiraz S, Bilezikci B. Persistent pulmonary hypertension in premature newborn after 16 hours of antenatal indomethacin exposure. *J Perinatal Med* 2004; 32(1):98-9.
12. Soghra R, Rezaei S. The effect of indomethacin therapy on reducing the amniotic fluid index (AFI) in moderate to severe polyhydramnios. *Iranian J Obstet Gynecol Infertil* 2008; 11(1): 55-60.
13. Cabrol D, Jannet D, Pannier E. Treatment of symptomatic Polyhydroamnios with indomethacin. *Eur J Obset Gynecol Reprod Biol* 1996; 66(1):11-5.
14. Chen KC, Liou JD, et al. perinatal outcomes of polyhydroamnios without associated congenital fetal anomalies after the gestational age of 20 weeks. *Chang Gung Med J* 2005; 28(1):222-8.