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Oral Hydration Therapy for the Management of Very Preterm Preeclampsia.

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Background: *Therapies to stabilize clinical manifestations and prolong pregnancies to attain fetal viability in preeclampsia do not exist[1]. Antiangiogenic factor, Soluble fms-like tyrosine kinase1 (sFlt-1) induces preeclampsia-like phenotype in experimental models[2], and circulates at high levels in preeclampsia. Extracorporeal removal of circulating sFlt-1 by Dextran-sulfate apheresis reduces proteinuria and stabilizes blood pressure without apparent adverse effects on fetus and mother[1].Serum, Urine, and fractional excretion of sFlt-1 are much higher among severe preeclamptic women compared to mild pre-eclamptic controls[3]. Consuming plenty oral fluids and producing urine output more than 2500ml/24hrs, may significantly reduce clinical symptoms, and may help to continue pregnancies to viability, as enhanced sFlt1 renal excretion is possible.*

Methods*: In this case control study, twenty women with very preterm (<34wks) preeclampsia with hydration therapy was compared with gestational age matched twenty controls without intervention. Cases were advised to consume plenty oral fluids and produce a targeted urine output more than 2500ml/24hrs. Anti-hypertensive drugs, Nifidepin, T. Labetalol, and weekly Inj. Hydroxy progesterone were given. Mean arterial pressure, urine albumin dipstick, edema grade, serum sodium, and potassium were recorded at different gestational ages in both groups and compared. The number of weeks that pregnancy continued, birth-weights, RDS, NICU admission days, indications for termination of pregnancies, and take home babies, were recorded in both groups and compared. Amniotic Fluid Optical Density estimations (AFOD) were done at the time of termination of pregnancies in cases.*

Results: *Mean daily urine output was 3692±989ml in cases. Statistically significant reduction in blood pressure, albuminuria, edema, was observed in cases (P=0.000, 0.000, 0.000). Continuation of pregnancy in cases was 7.51±5.22wks, and in controls it was 1.38±1.18wks (P=0.000). Significant decrease in RDS, NICU admission days (P=0.000, 0.001), and increase in birth-weights and take home babies (P=0.000, 0.041) were observed in cases. No significant difference was observed in serum sodium, and potassium levels between two groups (P=0.201, 0.072). The Mean AFOD at termination of pregnancies in casas was 0.86±0.37*

Conclusion: *Oral hydration therapy with urine output 3962±989ml/24hrs helps to prolong very preterm pre-eclamptic pregnancies to term with good perinatal outcome.*

Keywords: *Oral Hydration therapy; Very preterm Preeclampsia.*

I. Introduction

Pre-eclampsia is a devastating human specific disorder of pregnancy. Large volume of evidence is cumulating to support the concept of immunological maladaptation for etiopathogenisis of Pre-eclampsia[4]. As there is no other way than the allogenic fetus to grow inside the uterus of the mother, the immunological interactions between maternal immune system and fetal proteins/cells at utero-placental bed, and also between maternal immune system and the deported fetal proteins/cells at different systems of the mother are inevitable[4].For the same reason Pre-eclampsia is not be preventable, and for the same reason the incidence of pre-eclampsia is constant, and not changing for many years all over the world[5]. Pregnancy induced adaptation mechanisms in maternal immune system to make it possible to sustain pregnancy till term. The immunological adaptation/ mal-adaptation activity in the mother depends on the degree of fetomaternal match/or mismatch[4], and also on the load of deported allogenic fetal cells/proteins in to the mother[6, 7].

Clinical manifestation of preeclampsia depends on the disturbed balance between angiogenic (VEGF and PLGF) and anti angiogenic (sFlt-1, and s. Endoglin) factors[8]. Immune mal-adaptation mechanisms results in excessive production of sFlt-1, and Sol. Endoglin, which leads to endothelial dysfunction both at uteroplacental bed and at different systems of the mother[4].Antiangiogenic factor Soluble fms-like tyrosine kinase1 (sFlt-1) induces preeclampsia-like phenotype in experimental models[2].There is uncontrolled predominance of anti

angiogenic factors in pre-eclampsia. Increasing levels of circulating sFlt-1 is observed with increasing severity of preeclampsia.

Extracorporeal removal of circulating sFlt-1 by dextran sulfate apheresis, reduces proteinuria, and stabilizes blood pressure without apparent adverse effects on fetus and mother[9, 1]. Urinary and fractional excretion of sFlt-1 is much higher among severe preeclamptic women when compared to mild pre-eclamptic, and normal pregnant controls[3].

In this preliminary study we tested the hypothesis that, consuming plenty of oral fluids and producing a targeted urine output of more than 2500ml/24hrs, may significantly reduce clinical symptoms and may also help to continue pregnancies to viability, as enhanced renal excretion of sFlt1 is possible.

Methods: In this case control study, pregnancy outcomes of twenty singleton early preterm pre-eclamptic women cases with hydration therapy were compared with twenty gestational age matched preeclamptic women controls that were treated conventionally without hydration therapy.

Exclusion: Women with severe preeclampsia, and complications of preeclampsia at first diagnosis were excluded from the study. Preeclampsia was diagnosed as per the standard criteria[10].
CRL or LMP Gestational ages were recorded (which ever available) at the time of first diagnosis of preeclampsia in both cases and controls. The gestational ages at the end of pregnancies in every woman were recorded in both cases and controls.

Grading of pedal edema was done based on dent depth and rebound time on pitting. (Source: Guelph General Hospital Congestive Heart Failure Pathway**).**
Grade 0: There is no detectable swelling of feet. **Grade 1:** There is a barely detectable 2mm depression that rebounds immediately. **Grade 2**: There is a 4mm deep pit that rebounds in few seconds .**Grade 3:** There is a 4mm deep pit that rebounds in 10 to 12seconds. **Grade 4:** There is 8mm deep pit that rebounds in more than 20 seconds.

Grading of albuminuria by Dipstick Test[11]; Patient was asked to collect random midstream urine sample in a 50 mL urine container for urine protein estimation by dipstick protein test. The dipstick analysis was done using the Uri plus 900 urinalysis stip. The following are the grades of proteinuria as provided by the manufacturers. **Grade 0=** absent; **Grade 1=**Trace= 15 to 30 mg/dL; **Grade 2=**1+= 30 to 100 mg/dL; **Grade 3=** 2+= 100 to 300 mg/dL; **Grade 4=** 3+= 300 to 1000 mg/dL; **Grade 5=** 4+= greater than 1000mg/dL.

Hydration therapy: Women in cases group were advised to take plenty of oral fluids and produce a targeted urine output of >2500ml/day. Women were advised to pass urine in to the given measuring jars, and were advised to measure the urine output at every voiding. Specially designed urine output charts were given to record the daily urine output **(Fig.1).**

Specially designed fluid output charts (Fig. 1): Each digit on the longitudinal column of the chart represents 100ml of urine output. The women were advised to measure the urine output at every voiding and were asked to record on this chart. If she passes 300ml of urine at one voiding, she colors 3 digits on the column. She repeats the same process every time she passes urine. This way she records total urine output from 7.00AM to 7.00AM next day (24hrs). She was advised to bring this chart at every antenatal visit to show the doctor. This graphical recording of urine output helps for easy monitoring of the urine output both by the patient and the doctor. Average daily urine output in every woman, and the Mean daily urine output of all women is shown **Table 2**.

In cases: The duration of pregnancy that could be continued from initial diagnosis to delivery was calculated. Retrospectively this period was divided in to 6 equal parts in every woman. Around these points of periods, recorded blood pressure, pedal edema grade, urine albumin dipsticks grade **(Table.1),** serum Na+, and serum K+ (**Table.2)** were considered for analysis. The average values of these parameters were calculated and shown in the **Table 1&2.** Mean Arterial Pressure (MAP) was calculated from average blood pressure in each case and shown in **Table.1**.

In controls: The duration of pregnancy that could be continued from initial diagnosis to delivery was calculated. Retrospectively this period was divided in to 4 equal parts in every woman. Around these points of periods, recorded blood pressure, pedal edema grade, urine albumin dipsticks grade **(Table.1)**, serum Na+, and serum K+ values (**Table.2)**were considered for analysis. The average values of these parameters were calculated and shown in the **Table1&2**. Mean Arterial Pressure (MAP) was calculated from average blood pressure in each woman and shown in **Table 1**.

AFOD (Amniotic Fluid Optical Density) estimations were done for AF samples collected at the time of termination of pregnancies in cases[12, 13 and 14]and shown in **Table 3.** The reasons for termination of pregnancies were recorded in both cases and controls and shown in the **Table 2**. Neonatal outcomes like development of RDS, birth weights, NICU admission days, take home baby at discharge were recorded in both cases and

controls and shown in the **Table 3**. Blood pressure was controlled with Cap Nifidepine, and T. Labetelol in adequate doses at required intervals in both cases and controls. For women in cases group, Inj. Hydroxy progesterone caproate 250mg IM weekly was given up to 24wks. After 24wks, 500mg IM weekly was given till delivery. Antenatal steroids were given whenever needed.

Statistical comparison was done with independent samples 't' test by using SPSS 2007 software, and a P value <0.05 was considered significant. Informed and written consent was obtained from all subjects who participated in this study. This study confirms to the standards of declarations of Helsinki.

Table: 1 Outcomes of comparative study of very preterm preeclampsia with Hydration therapy (cases) and without Hydration therapy (controls)

S.L NO	G.A at first detected Wks.		G.A at delivery Wks.		Preg. Continued for wks.		Average MAP		Average edema Grade	
	Cases	controls	Cases	controls	Cases	Control	Cases	controls	Cases	controls
1	32.28	26	39.14	30.56	6.85	4.57	100.06	119.33	0.33	1.75
2	33.85	33.85	38.85	31.85	5	0.85	100.76	119.5	0.33	2
3	33	32.14	38.14	32.85	5.14	0.71	106.53	117.33	0.33	0.85
4	33.71	31.14	37.42	32.00	2.71	0.71	101.93	119.16	0.83	0
5	33.28	32.71	36.26	33.71	3.14	1	105.86	111.66	1	1.16
6	31.71	26	35.56	28.00	3.85	2	108.83	130.83	0.66	2.75
7	22.43	33.14	37.42	34.00	15	0.71	95.06	88	0.33	2.5
8	21.57	34.28	37.71	34.85	16.14	0.57	101.73	117.33	0.16	0.75
9	26.28	33.43	35.85	34.28	9.57	0.85	110.1	104	0	0
10	33	30	36.28	31.00	3.28	1	112.93	119.83	0	0
11	31.85	27	36.28	28.00	4.42	1	102.4	117.58	0	2.75
12	21.43	34	37.85	34.85	16.42	0.85	100.06	115	0	1.75
13	33.14	31.71	39.56	32.28	6.42	0.57	101.5	118.5	0.33	1.5
14	33.43	31.14	35.00	32.00	1.71	0.85	112.06	115.66	0.16	0
15	21.14	29.28	38.71	31.42	17.57	2.14	99.86	121.16	0.33	0.75
16	33.71	27	37.56	29.00	4.85	2	95.86	121.66	0.16	1.75
17	29	32	36.56	33.14	7.57	1.14	100.76	120.16	0	2
18	32.28	32.14	36.42	33.00	4.14	0.85	108.73	116.83	1	1.25
19	31.85	33.28	35.71	34.14	3.85	0.85	108.73	106	0.83	2
20	20.71	27	27.85	31.56	7.14	4.57	123.53	120.33	0.16	2
M± St.d	**29.38 ± 5.00**	**30.71 ± 2.74**	**36.71 ± 2.45**	**32.12 ± 2.06**	**7.51 ± 5.22**	**1.38 ± 1.18**	**104.86 ± 6.72**	**115.99 ± 8.65**	**0.35 ± 0.33**	**1.38 ± 0.90**
Sig. P. Value. 2.tailed		**0.303**		**0.000**		**0.000**		**0.000**		**0.000**

Results: The Mean daily urine output in cases was found to be 3692 ± 989ml.
The Mean gestational age that pre-eclampsia first detected in cases was 28.13±7.53wks, and in controls it was 30.71± 274wks (P=0.162).

In cases group, pregnancies could be prolonged more towards term (36.71±2.4wks) when compared to women in control group (32.12±2.06wks); P. Value: 0.000.

In cases group, pregnancies could be prolonged more towards term (36.71±2.4wks) when compared to women in control group (32.12±2.06wks); P. Value: 0.000.

Mean gestational weeks that pregnancies could be continued in cases was 7.51±5.21wks, and in controls it was1.39±1.18wks (P=0.001).

Mean arterial pressure that was observed in cases was 104.86±6.72mmHg, and in controls it was 115.99±8.65 mmHg (P=0.000).

Mean edema grade that was observed in cases was 0.34±0.33, and in controls it was 1.37±0.91 (P=0.000).

Urine albumin dipstick grade that was observed in cases was 0.63±0.62, and in controls it was 2.15±0.46 (P=0.000).

Mean serum sodium levels that was observed in cases was 139.77±2.66mmol/L, and in controls it was 138.48±1.60mmol/L (P=0.072).

Mean serum potassium levels that was observed in cases was 4.09.77±0.15mmol/L, and in controls it was 3.97±0.38mmol/L (P=0.201).

In cases group 19 pregnancies could attain completion or near completion of fetal functional maturity, and the Mean AFOD value at the end of pregnancies was 0.86±0.37.

Table: 2. Outcomes of comparative study of very preterm preeclampsia with (cases) and without (controls) Hydration therapy. Continuation of Table 1

S.L NO	Average urine dipstick- grade		Average S. Na^+ levels m.eq/dil		Average S. K^+ levels m.eq/dil		Average daily urine output	Indication for Termination of pregnancy	
	Cases	Control	Cases	controls	Cases	controls	Cases	Cases	Controls
1	0.66	2	138.11	138.82	4.29	3.75	4276	Spont .labo	Severe PIH, OL. Amnios.
2	0.83	2	137.35	138.6	4.09	3.45	5607	Spont .labo	Reduced FM, OL.Amnios.
3	0.16	2	140.86	140.97	3.96	3.82	4400	O. Amnio	Severe PIH, pre c/s
4	0.5	1.5	149.28	141.8	3.99	4.02	2443	Spont.labo	Eclampsia
5	0.16	2	138.9	137.67	3.87	4.15	3011	Spont.labo	OL.Amnio, F. Distress
6	2.1	2.5	140.65	138.5	4.26	4.95	3834	O.Amnio	Gross ped.ede. Pleu effu.
7	0.66	2.75	142.23	136.92	**4.1**	4.32	5258	Spont.labo	Eclamp., OL.Amnio, IUGR
8	0.16	2.5	139.36	137.9	4.06	4	5400	PROM	Imminent Eclampsia
9	0.16	1.5	137.08	137.77	4.26	3.87	2936	Spont.labo	Imin. Eclampsia, OL.Amni.
10	1.83	2.25	138.31	138.27	4	4.12	3396	Spont.labo	mminent Eclampsia
11	0.33	2.75	139.76	140.1	3.99	4.6	2908	Spont.labo	Imminent Eclampsia
12	0.33	2.75	140.68	137.97	4.15	4.47	3720	O.Amnio	Reduced FM, OL.Amnios
13	0.33	1.25	140.76	140.02	3.99	3.87	3646	Spont.labo	Severe PIH
14	0.33	2	140.01	138.62	4.07	4.1	2706	Spont.labo	Eclampsia, pre c/s
15	0.16	2	137.91	138.15	4.18	3.67	5164	Spont.labo	Imminent Eclampsia
16	1	2.5	140.68	135.52	4.07	3.7	3076	Spont.labo	Eclampsia, OL.Amnios
17	0.16	2.75	137.26	135.22	4.11	3.47	2932	PROM	Eclampsia.
18	0.5	2	138.01	139.75	4.13	3.67	3012	O.Amnio	Severe PIH
19	2	1.5	138.45	137.7	4.51	3.8	3200	O.Amnio	Imminent Eclampsia
20	0.33	2.5	139.76	139.4	3.82	3.67	2926	Pl. Abrupt.	Severe PIH, OL Amnios
M± St.d	**0.63 ± 0.62**	**2.15 ± 0.46**	**137.77 ± 2.66**	**138.48 ± 1.60**	**4.09 ± 0.15**	**3.97 ± 0.38**	**3692.55 ± 989.07**		
Sig. 2 tailed P. Value		**0.000**		**0.074**		**0.201**	.		

In cases group only one baby developed mild RDS for shorter duration, where as in controls group 10 babies (out of 14 survived) developed RDS (P=0.000).

Mean NICU admission days in cases group was 0.00±0.00 days, and in controls group it was 8.36±7.04 (P=0.000).

Mean Birth weight of babies in cases group was 2.54±0.76kg, and in controls group it was 1.68±0.53kg (P=0.000).

In cases group, one IUFD occurred and 19 mothers could take their babies home. In control group, 6 IUFDs occurred and only 14 mothers could take their babies home (P=0.041).

Indication for termination of pregnancies: In control group women, pregnancies were terminated for eclampsia in 4, imminent eclampsia in 6; sever PIH in 5, fetal distress in 1, oligo amnios in 8, IUGR in 1,

reduced F.M in 2, and gross edema all over the body and pleural effusion and ascites in 1 woman. In cases group, 12 women went in for spontaneous labor. In 5 women oligo amnios, 2 women PROM, and in 1 woman placental abruption were the indications for termination of pregnancies. These results show that very significantly better pregnancy outcomes in cases group when compared to controls group.

The compliance of the women to take plenty of oral fluids and produce the targeted urine output was very good. Women consumed more fluids and produced more urine output than the given target of 2500ml/24hrs. None of the women developed the signs of over hydration.

Table: 3. Outcomes of comparative study of very preterm preeclampsia with (cases) and without (controls) Hydration therapy, continuation of Table 1 and 2.

S.L NO	AFOD at Termination of pregnancy	RDS		NICU admission days		Birth weight Kg		Take home baby	
	Cases	Cases	controls	Cases	controls	Cases	Controls	Cases	controls
1	0.87	0	IUFD	0	IUFD	2.7	1.4	1	0
2	1.2	0	1	0	18	3.1.	1.48	1	1
3	0,98	0	1	0	0	3.1	2.4	1	1
4	1.6	0	1	0	12	2.7	1.6	1	1
5	1.02	0	1	0	8	2.6	2.2	1	1
6	0.6	0	IUFD	15	IUFD	1.45	0.5	1	0
7	0.96	0	1	0	10	3.85	1.8	1	1
8	Mec.st.liq	0	1	0	10	3.7	1.9	1	1
9	1.5	0	0	5	0	2	2.39	1	1
10	0.75	0	IUFD	0	IUFD	3.1	0.92	1	0
11	1.1	0	IUFD	5	IUFD	1.65	0.8	1	0
12	0.96	0	0	2	0	2.35	2	1	1
13	0.95	0	1	0	12	3	2.1	1	1
14	1.07	0	1	5	18	2	1.5	1	1
15	0.90	0	1	0	15	3.2	1.7	1	1
16	1.07	0	IUFD	0	IUFD	2.51	1,4	1	0
17	0.47	1	1	0	14	2.86	1.8	1	1
18	1.12	0	0	0	0	2.5	2.1	1	1
19	0.6	0	0	14	0	1.55	2.4	1	1
20	Blood stain	IUFD	IUDF	IUFD	IUFD	0.9	1.4	0	0
Mean ± St.d	**0.86 ± 0.37**	**0.000 ± 0.000**	**0.712 ± 0.469**	**0.000 ± 0.000**	**1.689 ± 0.533**	**2.541 ± 0.763**	**1.689 ± 0.533**	**0.950 ± 0.223**	**0.70 ± 0.470**
Sig.2tailed P. Value			**0.000**		**0.001**		**0.000**		**0.000**

II. Discussion

The clinical features of Pre-eclampsia occur due to immunological mal-adaptation between maternal immune system and fetal proteins and trophoblastic tissues at fetomaternal interphase, and also between maternal immune system and deported micro chimeric fetal DNA, fetal proteins, and trophoblastic tissues at different systems of the mother[4]. Degree of clinical manifestation depends on degree of feto-maternal mismatch, and also on deported nonself protein load in the mother[6, 7]. Maternal immune system undergoes adoptive changes to accommodate the allogenic fetus, and this is the real 'Key' of nature which is responsible to preserve the human species[4]. Preeclampsia results due to the failure of this accommodation mechanism at any stage of pregnancy.

Similarities between preeclampsia and other immunological disorders: Atypical presentation is the hallmark of immunological disorders. If we observe immunological disorders like SLE, scleroderma, rheumatic

fever, neuro syphilis, all of them are atypical in their clinical presentations. They need multiple criteria (major, minor or their combinations) for their diagnosis. Similar atypical presentations are also seen in preeclampsia[4].

Concept of multiple systemic involvements with unequal severity: In all these immune disorders, multiple systems are involved but their involvement is not of same severity. One of the systems might be

leading and other organ systems might be lagging behind with different degrees of severity of involvement. In this process, some of the systems might not get involved or skipped. Similar pattern of multi systemic

involvement and skipping of involvement of systems is also seen in preeclampsia[4]. In a preeclamptic woman with multisystem involvement with unequal severity, if pregnancy continues further, the dysfunctions in all organ systems progress further and results in multi organ dysfunction syndrome which leads to maternal death[15]. There is every need to consider this fulminant disease as similar to that of a running mismatched blood transfusion. Timely termination of pregnancy helps to prevent maternal death[4].

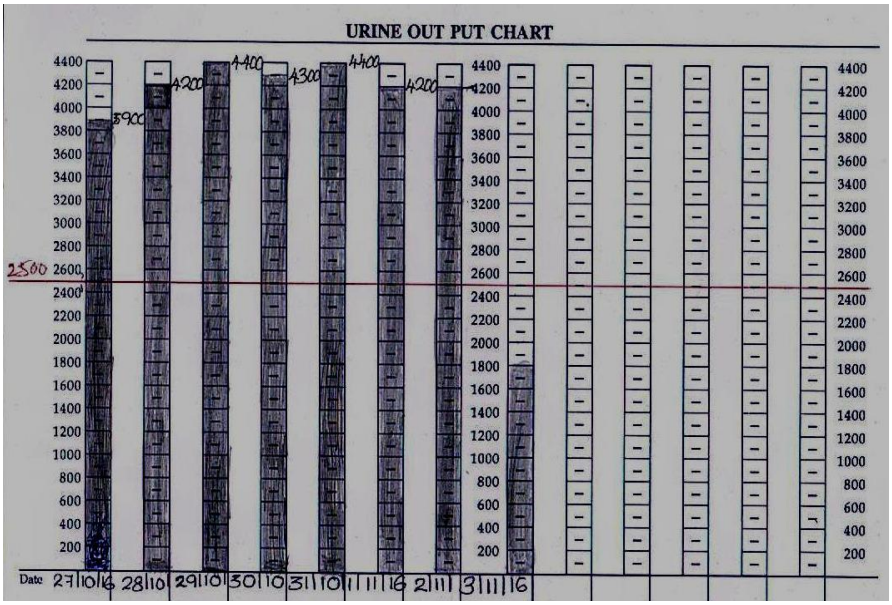

Figure1: Specially designed urine output chart. Each digit on the column measures 100ml of urine output.

Clinical manifestations in preeclampsia are due to disruption of balance between angiogenic (VEGF and PLGF) and anti angiogenic(sFlt-1, and s. Endoglin) factors[8]. There is uncontrolled predominance of anti angiogenic factors in pre-eclampsia[9].Immune mal-adaptation mechanisms results in excessive production of sFlt-1, and Sol. Endoglin at uteroplacental bed and also at different systems of the mother which leads to endothelial dysfunction[4].Antiangiogenic factor, Soluble fms-like tyrosine kinase1 (sFlt-1) induces preeclampsia-like phenotype in experimental models[2].Ravi Thadhani et al. reported, **e**xtracorporeal removal of circulating sFlt-1 by Dextran-sulfate apheresis reduces proteinuria and stabilizes blood pressure without apparent adverse effects on fetus and mother. By repeated Dextran-sulfate apheresis they could continue pregnancies for a variable period of 7 to 21days[9].

But Dextran-sulfate apheresis procedure is costly, cumbersome, risky, and not within the reach of every pre-eclamptic women. Continuous research is going on all over the world to develop simpler technique or drug to counter or remove the effect of sFlt-1, and help to prolong pregnancies to attain fetal viability.

Antiangiogenic factor sFlt-1 is excreted by kidney. The urinary, and fractional excretion of sFlt-1 is much higher among severe preeclamptic women compared to mild pre-eclamptic controls[3].Consuming plenty oral fluids and producing a targeted urine output more than 2500ml/24hrs was tried in this study to reduce the clinical features of preeclampsia and continue pregnancies to viability, as enhanced renal sFlt1 excretion is possible.

In our current study, women who were treated with hydration therapy (cases) produced a Mean daily urine output of 3962 ± 989ml, and pregnancies could be continued for8.61 ± 7.79wks. In control group pregnancies could be continued only for 1.39±1.18wks (P=0.001).

In cases group 19 pregnancies could attain completion or near completion of fetal functional maturity, which was confirmed by mature or near mature AFOD values at the end of pregnancies[13,14, and 15]. Only one baby developed milder RDS for shorter duration. All other 18 babies were fully functionally mature and did not develop RDS. In control group, among 14 babies that survived, 10 babies were functionally premature and developed RDS (P=0.000). In this group AFOD estimations were not done because 6 women had IUFDs, and eight women had scanty liquor with meconium staining.

In cases group none of the babies were admitted to NICU (Mean:0.00±0.00 days), and in control group all 14 babies were admitted to NICU, and the number of days required was 8.36± 7.04 days (P=0.000). Mean Birth weight of babies in cases group was 2.54± 0.76kg, and in controls group it was 1.68± 0.53kg (P=0.000).
In cases group, the clinical features like Mean arterial pressure, Mean edema grade, Mean urine albumin dipstick grade were under well control when compared to control group (P=0.000).

In cases group, only one IUFD occurred and 19 mothers could take their babies home. In control group, 6 IUFDs occurred and only 14 mothers could take their babies home (P=0.041).

In cases group, none of the women developed severe preeclampsia or eclampsia. Whereas in control group, 4 women developed eclampsia, 6 women developed imminent eclampsia, and in 5 women there was sever preeclampsia.

Indication for termination of pregnancies: In cases group 12 women went in to spontaneous labor. In 5 women oligoamnios, in 2 women PROM, and in 1 woman Placental abruption were the indications for termination of pregnancies. In control group, pregnancies were terminated for eclampsia in 4, imminent eclampsia in 6; sever PIH in 5, fetal distress in 1, oligoamnios in 8, and IUGR in 1,and reduced F.M in 2, and gross edema all over the body and pleural effusion and ascites in 1 woman

In cases group the Mean serum sodium and potassium levels were 139.77±2.66mmol/L and 4.09.77± 0.15mmo/L respectively. In controls group the Mean serum sodium and potassium levels were 138.48±1.60mmol/L and 3.97±0.38mmol/L respectively. There is no statistically significant difference in serum sodium and potassium levels between cases and controls (P=0.072, P=0.201). These results show that Hydration therapy do not produce electrolyte imbalance.

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As progesterone is known for its immunomodulatory effect on pregnancy[16], we have given weekly Inj. Hydroxy progesterone caproate in cases as mentioned in the methods.
All the results of this study show that oral hydration therapy is very safe, effective, and prevents the severity and complications of preeclampsia and helps to continue pregnancies to viability.

Likely mechanism for Hydration therapy: The pathophysiology of preeclampsia is associated with diminished blood volume, hemo-concentration with raised hematocrit, vasospasm, and diminished organ and uteroplacental perfusion. All these effects are due to endothelial dysfunction secondary to raised antiangiogenic factor sFlt-1in maternal blood. In hydration therapy, fluids continuously enter vascular compartment from gastro intestinal tract. This results in increased blood volume and hemo-dilution. This increased blood volume results in increased renal, uteroplacental, and other organ perfusion. This results in increased excretion of antiangiogenic factor sFlt-1 through large quantity of urine output. This helps to reduce of blood levels of sFlt-1, which in turn results in reduction of endothelial dysfunction. By all these mechanisms, Hydration therapy breaks the vicious cycle of pathophysiology of preeclampsia. This could be reason for our excellent results of hydration therapy for preeclampsia. The compliance of the women to take plenty of oral fluids and produce the targeted urine output was very good. Women consumed more fluids and produced more urine output than the given target, and none of them developed the signs of over hydration.

Limitations for this study: In this study we hypothesized that increased sFlt-1excretion occurs with increased urine output. We should have done sFlt-1 estimation both in blood and urine before, during, and after the study. As this facility of sFlt-1 estimation is not available at our institution we could not do it. Further studies are needed with sFlt-1estimation to evaluate the results of our study.

III. Conclusion

Hydration therapy is the first of its kind in the literature of preeclampsia. This is a simple, easily practicable, and very effective intervention which does not costs anything to the patient. Hydration therapy helps to continue pregnancies to viability, avoiding the deleterious effects of preeclampsia on the mother and the fetus. Further research is needed with sFlt-1 estimation to confirm our results by multicentrec randomized control trials.

Competing interest statement: We all authors declare that we do not have any conflict of interest in this research work.

References

[1]. Thadhani R,Kisner T, Hagmann H et al, Pilot study of extracorporeal removal of soluble fms-like tyrosine kinase 1 in preeclampsia;Circulation. 2011 Aug 23; 24(8):940-50

[2]. Camille E. Powe, AB.Richard, J. Levine, et al Preeclampsia, a disease of the maternal endothelium: the role of anti-angiogenic factors and implications for later cardiovascular disease. Circulation. 2011 Jun 21; 123(24): 10.1161

[3]. Buhimschi CS[1], Magloire L, Funai E, et al. Fractional excretion of angiogenic factors in women with severe preeclampsia.Obstet Gynecol. 2006 May; 107(5):1103-13

[4]. Samartha Ram H. Sai Samyukta I. Padmapriya A,Preeclampsia and Eclampsia: A consequence of Immunological maladaptation. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS); 2279-0861.Volume 14, Issue 11 Ver. III (Nov. 2015), PP 20-32

[5]. C. R. Leitch, A. D. Cameron, J. J. Walker; The changing pattern of eclampsia over a 60-year period; BJOGA. August 1997 Volume 104, Issue 8 Pages 917–922.

[6]. V.J. Faber, F.J. Klumper, et al. Severe pre-eclampsia and HELLP syndrome after massive fetomaternal hemorrhage following blunt abdominal trauma. Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health.Volume 1, Issues 3–4, July– October 2011, Pages 197–199.

[7]. Holzgreve W, Ghezzi F, Di Naro E, Maymon E, Gänshirt D, Hahn S. Disturbed fetomaternal cell traffic in preeclampsia. ObstetGynecol 1998; 91: 669–72

[8]. Mitsuko Furuya, KentaroKurasawa, KiyotakaNagahama, et al. Disrupted Balance of Angiogenic and Antiangiogenic Signaling in Preeclampsia; Journal of Pregnancy Volume 2011 (2011), Article ID 123717, 10 pages

[9]. Ravi Thadhani, Henning Hagmann, WiebkeSchaarschmidt et al. 'Removal of Soluble Fms-Like Tyrosine Kinase-1 by Dextran Sulfate Apheresis in Preeclampsia' J Am SocNephrol 27: 903–913, 2016. doi: 10.1681/ASN.2015020157

[10]. [Guideline] American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy. Hypertension in pregnancy.Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy.Obstet Gynecol. 2013 Nov. 122 (5):1122-31. [Medline].

[11]. Sapna V. Amin, Pratap Kumar, and Muralidhar V. Pai 'Quantifying Proteinuria in Hypertensive Disorders of Pregnancy' International Journal of Hypertension; Volume 2014 (2014), Article ID 941408, 10 pages.

[12]. Ram S et al Amniotic fluid optical density at spontaneous onset of labor and its correlation with gestational age, birth weight, functional maturity and vernix caseosa of new born. Calicut Medical Journal 2009; 7(4) Vol 7 Issue 4 2009.
S.H.Ramet al Calicut Medical Journal 2009; 7(4):e2 - Dr. Pankaj Desai

[13]. Samartha Ram H, Sandhya Ram S, Individualised Term for Each Fetus: From Surge in Amniotic Fluid Optical Density (AFOD). http://ispub.com/IJGO/18/1/14784

[14]. Samartha Ram H., Shankar Ram H S., Sandhya Ram S et al. Correlation between Amniotic Fluid Optical Density (AFOD) and functional maturity status of the newborn at caesarean delivery in GDM. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS); 2279-0861.Volume 13, Issue 5 Ver. III. (May. 2014), PP 00-00

[15]. T. Lee-Ann Hawkins, Mark A. Brown, George J. Mangos, et al. Transient gestational hypertension: Not always a benign event: Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health 2 (2012) 22–27

[16]. Julia Szekeres-Bartho; Progesterone-mediated immunomodulation in pregnancy: its relevance to leukocyte immunotherapy of recurrent miscarriage; Review. Immunotherapy; September 2009, Vol. 1, No. 5, Pages 873- 882, DOI 10.2217/imt.09.54