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Multidisciplinary Approach Resulting in Improved Maternal Survival in Eisenmenger Syndrome: Prospective Study in a Tertiary Care Centre

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Abstract: ***Background:*** ***Pregnancy with Eisenmenger syndrome is a very rare disease with grave prognosis and mortality rate of 30-50% due to increased circulatory burden in gravid women. Availability of newer drugs, intensive care unit along with proper antenatal and postnatal care has reduced their morbidity and mortality. Early diagnosis and proper counselling of these patients for MTP could further reduce the overall mortality rate in these patients.*** ***Methods: This was a prospective study done in Obs & Gyne department of Lok Nayak Hospital, New Delhi on 7 pregnant women admitted with Eisenmenger syndrome from 2014-2017.*** ***Results: Only one out of seven patients died making the mortality rate of 14.28% in our study. Tab Furosemide and Sildenafil were the main drugs that were used in all patients. ICU care in postpartum period was required in 80% of cases. 80% of the patients delivered vaginally. MTP was done in 28.57% of the cases.*** ***Conclusions: Our multidisciplinary approach using obstetrician, cardiologist, intensive care unit, paediatrician along with prolonged hospitalisation, oxygen therapy, bed rest, use of furosemide, Sildenafil, judicious use of anticoagulants and extended postpartum care proves to be beneficial in the management of this high risk pregnancy. Vaginal delivery was found to be safer in these patients. MTP is also safer option and seems to be beneficial in these patients.***

Keywords: Eisenmenger syndrome, Congenital Heart defects, maternal mortality rate, Sildenafil, MTP in Eisenmenger syndrome

1. Abbreviations

Eisenmenger syndrome	ES
Congenital Heart defects	CHD
Atrial septal defect	ASD
Ventricular septal defect	VSD
Pulmonary Artery Hypertension	PAH
Hemoglobin	Hb
Hematocrit	HCT
NewYork Heart Association	NYHA
Fetal growth restriction	FGR
Low molecular weight heparin	LMWH
High dependency units	HDU
Neonatal intensive care unit	NICU
Bilevel Positive Airway Pressure,	BiPAP
continuous positive airway pressure	CPAP
Standard deviation	Stdev

2. Introduction

The development of Eisenmenger syndrome (ES) is defined as the development of pulmonary hypertension in response to a left-to-right cardiac shunt with consequent bidirectional or reversal (right-to-left) of shunt flow. Congenital heart defects that may result in Eisenmenger syndrome include ventricular septal defect (VSD), atrioventricular septal defect (AVSD) or atrioventricular canal defect (AVCD), patent ductusarteriosus (PDA), atrial septal defect (ASD), D-transposition of the great vessels, and surgically created aortopulmonary connections.

As a result of the right-to-left shunt, patients are chronically hypoxemic, hence cyanotic. ES gradually leads to progressive right ventricular (RV) failure with digital clubbing, cyanosis, dyspnea, edema, a loud pulmonary component of second heart sound on auscultation, right ventricular hypertrophy in electrocardiography, and arrhythmias. Eisenmenger syndrome is very rare in pregnant women with an incidence of about 3% in the pregnant patients with congenital heart defects.[1] The hemodynamic changes in pregnancy leads to increased circulatory burden in gravid patients which contributes to high maternal mortality rates (30–50%). [2-6] ES is class IV in the WHO pregnancy risk classes and is regarded as contraindication for pregnancy. According to some studies MTP is considered safer in these patients than any kind of delivery. [7] The major causes of death in these patients are right ventricular failure, pulmonary hypertension crisis, arrhythmias, thromboembolic events and preeclamsia. In recent era development of newer drugs, availability of intensive care unit along with proper antenatal and postnatal care has shown to reduce their morbidity and mortality. Various clinical studies in last 2 decades revealed that Pulmonary artery hypertension (PAH) specific therapies (prostanoids, endothelin receptor antagonists and phosphodiesterase-5 inhibitors, single or in combination) had significantly lowered the risk of death over a median follow-up of 4 years. [8] Some of these drugs like Sildenafil, epoprostenol, L-arginine, inhaled Nitric oxide has been tried on pregnant women with variable results. Lacassie et al used sildenafil 150 mg/day along with L-arginine 3 g/day and facemask nitric oxide 64 ppm, and reported significant reduction of PAH and Peripheral vascular resistance(PVR) and clinical improvement in woman with severe PAH due to Eisenmenger syndrome treated during pregnancy.[9] Cartago et al. reported two cases of ES patients treated with Sildenafil during pregnancy with good clinical outcome.[10] Chris et al. demonstrated the successful treatment of a woman with ES with intravenous epoprostenol.[11]

Most complications in these patients occur near term and in post-partum period and therefore extended post-partum hospital observation is suggested. [12]

Fetal outcomes in these patients are also poor with a high risk of spontaneous abortion, FGR growth restriction (FGR),

preterm birth, low-birth weight and congenital cardiac malformations.[5]

3. Methods

This was a prospective study done in Obs & Gyne department of Lok Nayak Hospital, New Delhi from 2014 - 2017 on pregnant women admitted with ES.Criteria for clinical diagnosis of Eisenmenger syndrome were cyanosis and clubbing of the fingernails, loud pulmonary component of the second heart sound on auscultation and right ventricular hypertrophy on chest X-ray and electrocardiogram. The diagnosis of Eisenmenger syndrome was confirmed by echocardiography showing bidirectional or reversal of the preexisting cardiac shunts. After admission, all patients were evaluated by multidisciplinary approach, consisting of obstetrician, cardiologist and anaesthetists. Complete general physical, cardiovascular, and obstetric examination were performed. New York Heart Association (NYHA) class was assigned. Laboratory investigations were undertaken. Patients were kept in HDU with intensive monitoring and oxygen therapy. Physical activity was restrained and cardiac drugs were started with cardiologist consultation. Hemodynamic measurements and blood gas analyses were carried out in all cases upon admission and during treatment. Ultrasound scans and cardiotocography (CTG) were performed to evaluate fetal status.

Seven patients (A-G) were admitted in the hospital from 2014-2017 with the diagnosis of Eisenmenger syndrome and all of them were recruited for the study. Descriptive statistics have been used for the purpose of analysis where mean and standard deviation has been calculated for the maternal and cardiac characteristics.

4. Results

Maternal characteristics (Table 1)

Out of seven patients three (**D, E, G**) of them were referred from other hospitals in view of Eisenmenger syndrome for better management. Three patients (**A, B, C**) were booked and had regular ANC follow up from 2nd trimester. Patient **F** was unbooked and came for MTP as she was counselled by cardiologist for the same.

Four patients (**A, C, D, E**) were admitted in third trimester, two of them (**B & G**) were admitted in second trimester for stabilisation as both of them presented in NYHA 3 in OPD. Patient **F** was advised MTP from cardiologist and was admitted in first trimester.

Majority of patients (57.14%) were primigravida. Two of them (**A, E**) were second gravida with one spontaneous abortion in first trimester. Patient **F** was a multiparous who had history of two vaginal deliveries and one spontaneous abortion in first trimester.

Patient **A** was diagnosed as CHD along with ES at 21 years of age and was started on tab furosemide. She was on regular follow-up since then. Patient **B** was diagnosed was diagnosed as CHD at 9 years of age and was diagnosed as ES at 16 years of age. She was on tab furosemide since 16 years of age and was on regular follow-up in cardiology department. She was started on tab dilitazem 30mg TDS at 22 years of age but was not taking it regularly till she got admitted to our department. Patient **C** was diagnosed as CHD at 21 years of age but was not started on any treatment. Patient did not follow-up after that. She was diagnosed as ES during 1st trimester of her pregnancy when she presented to physician in NYHA class IV. She was admitted in cardiology department and started on tab diltiazem (calcium channel blocker) 60 mg OD, tab furosemide and tab Sildenafil 12.5 mg TDS. She was stabilised and discharged to follow up in cardiology and ANC OPD. Patient was compliant and had regular follow- ups in cardiology and ANC OPD. She was started on tab warfarin 5mg and 3mg on alternate days in 2nd trimester for thromboprophylaxis. Patient **D** was diagnosed as CHD along with ES at 28 years of age and was started on tab furosemide but she left treatment on her own and did not follow-up further. Patient **E** was diagnosed as congenital heart disease along with ES at 13 years of age. She was started on tab Ditide (Benthiazide + Triamterene) but she stopped on her own and did not follow up further. Patient **F** was diagnosed as CHD at 22 years of age and was kept on conservative management. But patient was noncompliant and did not follow-up further. She was diagnosed as ES in the 2nd trimester of her previous pregnancy when she came to hospital with complaints of breathlessness and was started on tab furosemide, digoxin and tab sildenafil 25 mg TDS. Patient **G** was diagnosed as VSD at 1.5 years of age and as ES at 12 years of age and was started on tab sildenafil 12.5mg TDS and tab furosemide. She took treatment for 2 years and then left it on her own and did not follow up further.

Thus CHD was diagnosed during childhood in 3 (42.85%) of them while other 4 (57.14%) were diagnosed during adulthood. Five out of seven (71.4%) patients were diagnosed as Eisenmenger syndrome prior to their pregnancy. Only one out of seven (14.28%) patients was compliant for treatment and follow-up. Thus compliance for treatment and follow-up remain a big challenge in our patients.

Table 1: Maternal characteristics

Maternal characteristics	*Patient A*	*Patient B*	*Patient C*	*Patient D*	*Patient E*	*Patient F*	*Patient G*	*Mean (Range)*	*Stdev*
Age (years)	22	24	24	30	24	24	24	24.57 (22-30)	2.51
Registration	Booked	Booked	Booked	Referred	Referred	Unbooked	Referred	-	-
Gravida	2	1	1	1	2	4	1	-	-
Abortion	1	0	0	0	1	1	0	-	-
Parity	0	0	0	0	0	2	0	-	-
Live issue	0	0	0	0	0	1	0	-	
Age of patient when CHD diagnosed (years)	21	9	21	28	13	22	1.5	16.5 (1.5-28)	9.09
Diagnosed as ES •Before pregnancy	At 21 years of age	At 16 years of age	-	At 28 years of age	At 13 years of age	-	At 12 years of age	-	-
•During pregnancy	-	-	During 1st trimester	-	-	2nd trimester of Previous pregnancy	-		
•Postpartum	-	-	-	-	-	-	-		
Hospital admission in obstetric dept. (weeks of pregnancy)	31+6	24	34+4	37+5	28+1	8	13+3	-	-

Table 2: Cardiac characteristics

Parameters on admission	*Patient A*	*Patient B*	*Patient C*	*Patient D*	*Patient E*	*Patient F*	*Patient G*	*Mean (Range)*	*Stdev*
Hb (g/dl)	14.5	18	15.9	13.7	13.5	9.7	16	14.47 (9.7-18)	2.62
HCT (%)	44.9	52.5	46	42.2	45.2	32.5	48.5	44.54 (32.5-52.5)	6.22
Anatomic defect	PM VSD*	PM VSD*	PM VSD with DORV#	Inlet VSD with OS ASD^	PM VSD	ASD	PM VSD	-	-
Lesion diameter (cm)	3.4	3.7	1.7	1.6	1.8	3.1	1.5	2.40 (1.5-3.7)	0.96
EF (%)	60	60	60	60	60	60	60	60 (60-60)	0.00
SaO2 on room air (%)	80-85	85-90	80-90	80-90	75-80	80-90	80-85	83.57 (75-90)	3.18
ECG	RVH	RAD	RAD	Biventricular enlargement	RAD	RAD with RVH	RVH	-	-
X-Ray	Cardiomegaly	Cardiomegaly	Cardiomegaly & Homogenous opacity in left middle zone	Cardiomegaly	Cardiomegaly	NAD	NAD	-	-

PM VSD : Perimembranous VSD, OS ASD : Osteum secondum ASD, DORV: double outlet right ventricle, Standard deviation: Stdev

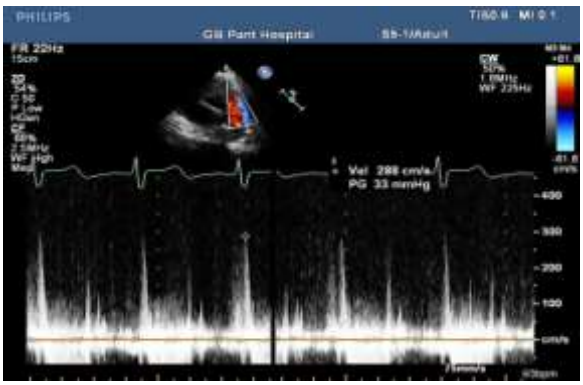

Figure 1: 2D Echo of patient E with doppler studies revealed bidirectional flow across the septal defect (ES).

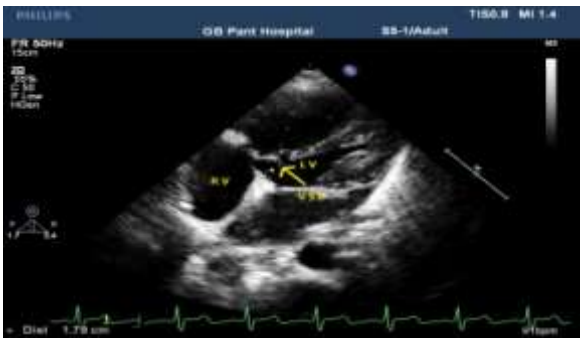

Figure 2: 2D Echo of patient E showing large peri-membranous ventricular septal defect of 18 mm size. Mean pulmonary artery pressure was 33 mmHg, suggestive of pulmonary artery hypertension.(RV- right ventricle, LV - left ventricle, VSD -ventricular septal defect).

Cardiac characteristics (Table 2)

Four (57.14%) patients had only VSD, one (14.28%) had only ASD, one (14.28%) of them had combination of VSD along with ASD while one (14.28%) patient had VSD with DORV. Thus VSD alone or in the combination was found to be the most common congenital lesion in these women.

Arterial oxygen saturation of hemoglobin during pregnancy was low in all the patients with the mean of 83.57 (std dev 3.18) % and range of 75-90%.Patient **E** who died had lowest SaO2 and maximum deviation from the mean for the parameter of SaO2.

Obstetric complications (Table 4)

Preterm delivery was seen in two out of five (40%) patients who continued their pregnancy Patient **B** was diagnosed as early onset FGR at 30 weeks of gestation and was followed with serial biometry and fetal Doppler scans. Dexamethasone cover was given for fetal lung maturity. At 34+4 weeks absent diastolic flow was found in umbilical artery and elective caesarean was done. Patient **E** went into spontaneous labour at 28+6 weeks and delivered vaginally. Patient **F** (G 4 P2L1A1) had history of one abortion in first trimester followed by full term vaginal delivery which was taken by dai at home, she didn't have any intrapartum or postpartum complication but baby expired few hours after birth. During her third pregnancy she was diagnosed as ES in 2nd trimester and was admitted in hospital. She went into labour at 33+6 weeks and had preterm vaginal delivery. Thus she had history of one neonatal death and preterm delivery.

FGR and associated oligohydraminos was seen in 3 patients (**B, C, D**).PIH and DVT although are known complications in pregnancy with ES, was not seen in any of our patients.

Table 3: Maternal clinical profile

Clinical profile	*Patient A*	*Patient B*	*Patient C*	*Patient D*	*Patient E*	*Patient F*	*Patient G*	*Number of patients (n) Percentage of patients (%)*
Breathlessness	Y	Y	Y	Y	Y	Y	Y	7 (100)
NYHA	II	III	II	II	IV	II	III	NYHA II: 4 (57.14) NYHA III: 2 (28.57) NYHA IV:1 (14.28)
Palpitation	N	N	Y	N	Y	N	N	2 (28.57)
Cough	Y	Y	Y	Y	Y	N	N	5 (71.14)
Hemoptysis (history)	Y	Y	N	Y	Y	N	N	4 (57.14)
Recurrent URI(history)	Y	Y	Y	Y	Y	Y	Y	7 (100)
Cyanosis	Y	Y	Y	Y	Y	Y	Y	7 (100)
Clubbing	Y	Y	Y	Y	Y	Y	Y	7 (100)
Edema	Y	Y	Y	N	N	Y	Y	5 (71.14)
Y:Yes, N:No								

Table 4: Obstetric complications

Obstetric complications	*Patient A*	*Patient B*	*Patient C*	*Patient D*	*Patient E*	*Patient F*	*Patient G*	*Number of patients (n) Percentage (%)*
Repeated abortions	N	N	N	N	N	N	N	0
Preterm delivery	N	Y (Iatrogenic)	N	N	Y (spontaneous)	NA	NA	2/5 (40)
Previous stillbirth/Early neonatal death	N	N	N	N	N	Y	N	1 (14.28)
Oligohydraminos and associated FGR	N	Y	Y	Y	N	NA	NA	3/5 (60)
PIH	N	N	N	N	N	NA	NA	0
DVT	N	N	N	N	N	N	N	0
Fetal echo	Normal	Normal	Normal	Normal	Not done	NA	NA	-
Y: Yes, N:No, NA : Not applicable, PIH: Pregnancy induced hypertension, DVT: Deep vein thrombosis								

Table 5: Management of Pregnant Women with Eisenmenger Syndrome

Management	*Patient A*	*Patient B*	*Patient C*	*Patient D*	*Patient E*	*Patient F*	*Patient G*
Cardiac drugs	Tab furosemide Tab diltiazem 30mg TDS was added in postpartum	Tab furosemide Tab diltiazem 30 mg TDS (increased further to 60 mg TDS)	Tab furosemide Tab diltiazem 60 mg OD	Tab furosemide	Tab furosemide Tab metoprolol	Tab furosemide Tab digoxin	Tab Furosemide
Sildenafil therapy	20 mg TDS	20 mg TDS	12.5 mg BD	25mg TDS	25 mg TDS	25mg TDS	25mg TDS
Antithrombotic therapy	Not given	Inj LMWH	Tab warfarin 5mg and 3mg on alternate days, Shifted to LMWH at 36weeks	No	Tab warfarin 2 mg OD Stopped when patient started c/o spotting P/V off and on	No	No
Gestational age (weeks) at delivery/MTP	37+3	34+5	39+2	37+5	28+6	8	18+6
Onset of labour	Spontaneous	Elective termination	Spontaneous	Spontaneous	Spontaneous	NA	NA
Mode of delivery/MTP	Vaginal (Vacuum)	Elective caesarean	Forceps	Vaginal (vacuum)	Vaginal	Suction & Evacuation (MTP)	Medical method (MTP)
Indication for caesarean /MTP	-	FGR with absent diastolic flow	-	-	-	ES	GCA
Monitoring	Noninvasive	Noninvasive	Noninvasive	Noninvasive	Noninvasive	Noninvasive	Noninvasive
Anaesthesia /analgesia	Inj morphine	Epidural anaesthesia	Epidural Analgesia	Inj morphine	Inj morphine	iv sedation & paracervical block	Inj morphine
Oxytocic drugs	Yes	Yes	Yes	Yes	yes	-	-
Blood lossin intrapartum period/ abortion	~400 ml	~ 500ml	~ 700ml	~ 450ml	Massive PPH 1.2 litre	~100ml	~150ml

Table 6: Maternal and Foetal outcome

Parameters in postpartum/postabortal phase	*Patient A*	*Patient B*	*Patient C*	*Patient D*	*Patient E*	*Patient F*	*Patient G*
Hb% (hematocrit)	12.9 (36.8)	13.4 (40.8)	11.8 (36.4)	14.9 (39.2)	5.5 (16.8)	9.4 (31.4)	15.5 (46.9)
Transfusions	Nil	Nil	Nil	Nil	3 unit WB and 4 unit FFPs	nil	Nil
Tachycardia Intrapartum/during abortion Immediate Postpartum/postabortal	90-96 85-90	90-98 86-96	90-100 84-94	88-98 84-94	120-130 110-114	80-88 86-96	80-90 88-96
ECG	NSR	NSR	NSR	NSR	Ventricular arrhythmia on day 3	NSR	NSR
SaO2	80-85	80-85	80-90	80-90	70-80	80-90	80-85
ICU stay (days)	10	8	1	0	2	0	0
Maternal survival	Survived and discharged	Survived and discharged	Survived and discharged	Survived and discharged	Death	Survived and discharged	Survived and discharged
Duration of hospital stay(days)	60	119	41	16	8	7	59 days
Fetal outcome Baby weight (gms) Apgar	 2580 9, 9, 9	 1355 9, 9, 9	 2170 9, 9, 9	 2355 9, 9, 9	 650	 _	 200 gm

Management and fetomaternal outcome (Table 5 and 6)

Patient **A** was admitted at 31+6 weeks of gestation for safe confinement. She was already on tab furosemide and Sildenafil 20 mg TDS since her pregnancy was diagnosed. She went into spontaneous labour at 37+3 weeks; patient was monitored throughout using noninvasive techniques, injection morphine was used for labour analgesia and second stage of labour was cut-short by vacuum. Blood loss was average. Baby weight was 2580 gm and Apgar of 9, 9, 9. Intrapartum and immediate postpartum period was uneventful. From day 3 of delivery patient started having tachycardia and difficulty in breathing and saturation started to fall to 60-70%, she was shifted to ICU and was initially

kept on BiPAP and tab diltiazem 30 mg TDS was started for rate control but saturation didnot improve and finally patient was kept on CPAP. Patient improved gradually and weaned off from CPAP to BiPAP to oxygen mask and shifted back to HDU after 10 days of stay in ICU. Total duration of hospital stay was 60 days and finally discharged with the healthy baby.

Patient **B** was admitted at 24 weeks of gestation as she presented in OPD in NYHA III. Tab Sildenafil 20mg TDS was started after cardiologist consultation. At 29 weeks of gestation, LMWH was started for thromboprophylaxis as her hematocrit was persistently more than 52.5%. Caesarean section was done under epidural anaesthesia at 34+4 weeks of gestation for FGR with absent diastolic flow in umbilical artery. Post-placental Copper T was inserted for further contraception. Baby weight was 1355 with Apgar of 9, 9, 9. Intrapartum and immediate postpartum period was uneventful. She was shifted to ICU for monitoring after caesarean section with epidural catheter insitu. Her SaO2 was between 80-85 % in the immediate post-op period. Antibiotic coverage was given in pre and post-op period. LMWH was restarted 12 hours after the surgery. On day 3 she started having difficulty in breathing and her SaO2 started falling and was between 75-80%. Her chest X-ray was done which showed cardiomegaly along with nonhomogenous opacity. Physician referral was taken and was started on nebulisation with ipratopium and budesonide, iv furosemide 40 mg BD and antibiotics were continued. She was kept on BiPAP for 3days and then was gradually

weaned off to oxygen mask. Her ICU stay was for 8days after-which she was transferred, back to ward. Vasodilator agents, tab Tadalafil 20 mg TDS and Ambrisentan 5 mg BD were added on day 6, tab warfarin was started on day3, stitch removal was done on day 10. Her baby was admitted in NICU for 40 days in view of low birth weight and sepsis. Baby was discharged on day 45, with weight of 1600 grams. Her duration of hospital stay was 119 days. The delay in discharge was due to baby as baby was admitted in NICU for 37 days as baby was both premature and had FGR. Finally patient was discharged along with the healthy baby and counselled to follow up regularly.

Patient **C** was admitted at 34+4 weeks for safe confinement and warfarin was switched over to LMWH at 36 weeks of gestation. She went into spontaneous labour at 39+2 weeks of gestation, epidural analgesia was given during active labour and patient was monitored throughout the labour through noninvasive techniques via multiparameters monitors, labour progressed well and second stage of labour was cut short using outlet forceps. Baby weight was 2170 gms with the apgar of 9, 9, 9. In immediate postpartum period patient was stable, and her SaO2 was between 80-90%. Patient was shifted to ICU for observation and was kept on venti mask. Her ICU stay was uneventful and was shifted back to the ward after 24 hours of observation. Total duration of hospital stay was of 41 days and patient was finally discharged with the healthy baby.

Patient **D** also went into spontaneous labour at 37+5 weeks of gestation, labour progressed well, injection morphine was used as analgesics, patient was monitored throughout using noninvasive techniques via monitors, second stage of labour was cut-short by vacuum and she delivered a baby of weight 2355 with apgar 9, 9, 9.Post delivery hematocrit was 39.2% and patient was stable with SaO2 of 80-90% and PR between 88-98 bpm. Total duration of hospital stay was 16 days and she was discharged with her baby.

Patient **E** was referred from private hospital in view of placenta previa with ES. She was admitted there with complaints of bleeding per vaginum (BPV) and was managed conservatively. Patient was in NYHA IV when admitted to our hospital but there was no BPV, cardiology referral was taken and was started on Tab sildenafil 20mg TDS, metoprolol extended release 12.5 OD, Tab warfarin 2 mg OD and tab furosemide 40 mg OD. From day 3 of admission she started having spotting PV off and on and warfarin was stopped. On day 6 of admission she started having excessive BPV, uterine contractions also settled for which she was prepared for LSCS, by the time she was shifted to OT, crowning was seen at a the OT table, delivery conducted and a female baby of 650 gms delivered, baby didn't cry after birth and was intubated and shifted to NICU. Patient had atonic PPH after delivery, uterine massage done uterotonics started but bleeding was not controlled so balloon tamponade done along with vaginal packing, one unit PCV started.Total blood loss was approximately 1.2 litres. Her PR was between 120-130 bpm during intrapartum period and saturation was between 70-80%.She was shifted to ICU for observation. Post delivery her Hb was 5.5gm% (HCT 16.8%) and 2unit of PCV and 4 units of FFPs were transfused. After all transfusions her Hb was 7.4 gm%. In ICU she was initially kept on ventimask and saturation was 70-75 % so she was put on rebreathing mask with reservoir bag following which her SaO2 increased to 75-85%. and her pulse rate was between 110-120 bpm. Balloon tamponade and vaginal pack was removed on day 2 of delivery. Approximately 36 hours after delivery patient went in right ventricular failure with pulmonary oedema and was intubated in view of falling saturation. During intubation patient had cardiac arrest, cardiopulmonary resuscitation was done and she revived and was kept on mechanical ventilation. She had multiple episodes of ventricular bigeminy and had further 3 episodes of cardiac arrest and could not be revived after last arrest. Baby also expired on day 2 due to RDS.

Patient **F** was counselled by cardiologist regarding high risk of pregnancy and advised MTP. She came to our hospital for MTP and was admitted at 8 weeks of gestation. Anaesthetists and cardiologists opinion was taken. She was already on tab furosemide, digoxin and Sildenafil and same were continued. MTP was done by suction and evacuation under intravenous sedation and paracervical block. During procedure patient was monitored throughout using non invasive monitors. SaO2 was between 80-90%. Blood loss was ~ 100 ml and post procedure Hb was 9.4 gm% (HCT 31.4%). Total duration of hospital stay was 7 days and patient was discharged after that.

Patient **G** was referred from a district hospital in view of ES. Patient was admitted at 13+3 weeks as she had complaints of breathlessness and was in NYHA III.Cardiologists opinion was taken and dose of Sildenafil was increased to

25mg TDS and tab furosemide was continued. She developed fever and was diagnosed as LRTI and was treated with a course of antibiotics. Her GCA scan showed hydrocephalus with bone dysplasias. Patient and her relatives were prognosticated and second trimester MTP was planned. Anaesthetist's opinion was taken. Medical management was planned and patient was given mifepristone 200 mg followed by misoprostol. Fetus of 200gm along with placenta was expelled after 2 doses of 100mcg of misoprostol instilled vaginally 6 hours apart. Blood loss was average ~ 150 ml. Post abortal Hb was 15.5gm% (HCT 46.9%). PR was between 80-90 bpm during contractions and between 88-96 after abortion. SaO2 was maintained between 80-85%. Total duration of hospital stay was 59 days.

5. Discussion

Pregnancy with Eisenmenger syndrome is a very rare disease with grave prognosis and mortality rate of 30-50% due to increased circulatory burden in gravid women. Therefore, ES is regarded as an absolute contraindication for pregnancy and patients should always be counseled to not to get pregnant. [13] Even if patient gets pregnant MTP is considered safer in these patients. [7] We performed MTP in two (28.57%) of our patients and both of them were discharged after 5 days of close observation. We could not find any previous study on outcome of MTP done in Eisenmenger syndrome.MTP done in our study was successful in both the patients. Thus we conclude that MTP is also safer option and seems to be beneficial in these patients. It is suggested that early diagnosis and proper counselling of these patients for MTP could further reduce the overall mortality rate in these patients.

In our study we found that four (57.14%) patients had only VSD, one (14.28%) had only ASD, one (14.28%) of them had combination of VSD along with ASD while one (14.28%) patient had VSD with DORV. Thus VSD alone or in the combination was found to be the most common congenital lesion in these women. This finding was in correlation with other studies which states that the type of cardiac defect is important, as only a small percentage of patients with unrepaired atrial septal defects develop ES, compared to higher percentages of patients with unrepaired ventricular septal defects and complete atrioventricular septal defects.[14]

Routine investigations done in all patients showed raised haemoglobin and haemoglobin concentration in all patients except patient F. An increase in haemoglobin levels in patients with cyanotic heart disease is a compensatory response in order to increase the blood oxygen carrying capacity. Although particular cut-off is not defined for haemoglobin and haemoglobin concentration in these patients, in the presence of systemic oxygen saturations of 80–85%, haemoglobin of 19–24 $g \cdot dL^{-1}$ is usually observed. [15, 16]. Maximum haemoglobin concentration in our study was 52.5%.Complications of erythrocytosis was not seen in any of our patient and venesection was not required in any of our patient. According to various studies venesections should only be performed in patients with severe hyperviscosity symptoms in the presence of very high haematocrit (>65%).[17] Studies have also reported that Erythrocytosis in cyanotic patients is often associated with decrease in platelet count, at times, white cell counts. This was observed in only one of our patient (A) where erythrocytosis was associated with thrombocytopenia.

All patients after admission were evaluated by cardiologists and started on various cardiac drugs. Drugs used in our study were diuretic (Furosemide), calcium channel blocker (Diltiazem) beta-blocker (metoprolol), digoxin and Sildenafil. Diuretic was started in all patients as it helps in symptomatic relief of congestion.

Calcium channel blocker (Diltiazem) was used in three (A, B, C) of our patients.It is a vasodilator and helps in decreasing pulmonary artery pressure. According to studies there is a small group (about 12%) of patients with a vasoreactive form of pulmonary hypertension in whom decrease in pulmonary pressure is observed after vasodilator administration. (Vasoreactivity is defined by a decrease of the mean pulmonary pressure of at least 10 mmHg to less than 40 mmHg). Calcium channel blocker at high doses is the recommended treatment for this group. This group has a good prognosis and uncomplicated course of pregnancy.[18, 19].Our patients also responded well to this drug and it seems an effective drug for the management of these patients.

Sildenafil is a phosphodiesterase inhibitor and has been demonstrated to treat PHTN. It reduces breakdown of cyclic guanosine monophosphate breakdown, making pulmonary vascular smooth muscle more sensitive to endogenous nitric oxide. It was used in all of our patients in various doses. It reduces ventilation perfusion mismatch and hypoxia. Of the PDE5 inhibitors studied, Sildenafil has the greatest selectivity for the pulmonary circulation and arterial oxygenation.[20] Various studies have proven Sildenafil to improve maternal clinical outcome.[21] We also found it to be promising drug for the management of this high risk pregnancy.

An important cause for morbidity and mortality in ES is thromboembolic phenomenon resulting from a hypercoagulable state. [22] For these reasons we considered the use of anticoagulant therapy in our patients. But it could be used in only two (B, C) patients in whom it was continued in postpartum period also. Patient A was not started on any anticoagulant as she had nose bleed three times during her admission and also because she always had thrombocytopenia throughout her pregnancy. Patient D was a referred case and was admitted with labour pains, so was not started on any anticoagulants. Patient E was also started on oral anticoagulants but stopped when she started complaining of pain and spotting per vaginum. These patients are at increased risk for peripartum deep venous thrombosis as well as pulmonary embolism due to polycythemia, venous congestion, and procoagulant state of pregnancy. Thus it is a common practice to give anticoagulation therapy although no prospective studies have proved the efficacy of this treatment. [18]They are at increased risk of bleeding also and therefore controversy remains whether to start or not start anticoagulation therapy in these patients. [23].Out of five patients who wished to

continue pregnancy, four patients survived and out of these four, two had received and two didn't receive anticoagulation. None of these patients had either thrombotic or hemorrhagic complications. So survival benefit or effectiveness of anticoagulation cannot be elucidated from our study and needs further study with a larger study population.

Patients who continued pregnancy in our study, four out of five (80%) of them delivered vaginally. During labour, patients were kept in propped up position, with continuous monitoring and oxygen therapy, labour analgesia was given either by epidural analgesia or by intravenous morphine. Antibiotic prophylaxis was given half hour before estimated time of delivery and second stage of labour was cut short by instrumental delivery Immediately after delivery, injection furosemide and morphine was given to all to prevent volume overload and pulmonary edema. Only one (20%) patient (B) had undergone elective cesarean section under epidural anesthesia. Due to limited studies, the ideal mode of delivery in ES patients is controversial.[6, 24] Compared with cesarean delivery, although vaginal delivery is associated with less risk of hemorrhage, infection and venous thromboembolism, vaginal delivery is associated with increased basal cardiac output and increased output with every uterine contraction, which promotes cardiac arrhythmia and worsens heart failure. Advantages of elective cesarean delivery include that it can be planned well in controlled settings and presence of senior staff can be ensured. Adverse hemodynamic effects of bearing down are overcome in caesarean section. In some studies because of the greater stability of hemodynamics, CS is considered to be safer than vaginal delivery. [25, 26] In our study all three (A, C, D) patients had uncomplicated intrapartum period during vaginal delivery. Thus intensive monitoring along with good labour analgesia, instrumental delivery to cut-short second stage of labour and post delivery diuretics to prevent circulatory overload proves vaginal delivery to be safer in these patients.

Patient (E) who died after vaginal delivery had many other contributory factors for her mortality and so safety of mode of delivery cannot be defined for her.She had massive PPH and had persistent tachycardia both during intrapartum and postpartum period which proved to be ominous for her. It has been studied that any hypovolumia resulting from blood loss or hypotension from a vasovagal response to pain or persistent tachycardia can result in sudden death in patients with ES. [27]. She also had lowest oxygen saturation during pregnancy, intapartum and in postpartum period and had ventricular arrhythmia on postpartum day 3.This is also was a ominous sign as study by Kempny et al and Narayanswami Sreeram showed that mortality was higher in patients with lower oxygen saturation and in cases of absence of sinus rhythm.[28, 29]

Post partum period in these patients is very crucial and needs extra vigilance and intensive care. The majority of deaths among pregnant patients with ES occur in the peri-partum period, mainly within the first month from delivery. [12] During delivery, both systolic and diastolic blood pressures are markedly increased during contractions because of compression of the abdominal aorta by the uterus, resulting in an increase in peripheral vascular resistance. Furthermore, temporary increase in venous return due to relief of caval compression and the additional blood shifting from the contracting uterus into the systemic circulation result in additional hemodynamic stress leading to increase pulmonary hypertension and right heart failure. Therefore careful monitoring and supportive treatment during this period is needed to prevent development of right heart failure. Four out of five (80%) patients needed ICU care in their postpartum period. Period of stay varied from 1-10 days. Thus extended postpartum care is recommended in these patients and patients should be asked to be in regular follow-up till 6 months of delivery.

ES in pregnancy presents an increased risk of fetal complications such as stillbirth, FGR and preterm delivery. [5] Our study also supports these findings and suggests that fetal complications are common in pregnancy with ES patients.

The reported incidence of maternal mortality according to various studies is 30-50% and major causes of which are right ventricular failure, pulmonary hypertension crisis, arrhythmias and thromboembolic events.[2-6] In our study, only one patient died making the maternal mortality rate of 14.28% which is quite lesser than the reported incidence of 30-50%.Thus our multidisciplinary approach seems to be improve maternal survival in patients with ES. Need of NICU and paediatrician support is equally important in view of high risk of prematurity and FGR. Various other studies also support the multidisciplinary approach in the management of such patients for successful maternal and fetal outcome. [30, 31]

6. Conclusion

Our multidisciplinary approach using obstetrician, cardiologist, intensive care unit, paediatrician along with prolonged hospitalization, oxygen therapy, bed rest, use of furosemide, calcium channel blockers, Sildenafil and judicious use of anticoagulants and intensive care in postpartum period seems to beneficial in the management of this high risk pregnancy. Out of 7 patients there was only one mortality in our centre making the incidence of 14.28 % which is quite lesser than the reported incidence of 30-50%. It is also obvious that apart from antenatal period, postpartum period in these patients is also very crucial and needs focussed vigilance and intensive care. Vaginal delivery was found to be safer in these patients.MTP is also safer option and seems to be beneficial in pregnancy with ES. We found that lower SaO2, persistent tachycardia, any hypovolumia / hypotension, arrhythmias had poor prognosis as patient who died in our group had all these complications. But proper correlation of these parameters with the morbidity and mortality needs extensive study with more number of patients which remains the limitation of our study.

7. Conflict of interest

There is no conflict of interest.

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