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Retrospective Study of Neonatal Outcomes with the Use of Magnesium Sulfate in Case of Preterm Labor

Dr. Melfa Dolly [a], ***Dr. Mithul. V. Mammen*** [b]

[a] *Pharm. D, Moradabad, 244001, Uttar Pradesh, India*
[b] *Pharm. D, Moradabad, 244001, Uttar Pradesh, India*

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ABSTRACT

BACKGROUND:

The use of magnesium sulphate for pregnancy toxemia or preterm labor was not widely accepted because the majority of reports over the last decade showed magnesium disturbances in the neonate. However, its use has been increased in order to prevent uterine contractions during preterm labor, and it is now a commonly used tocolytic drug. Recently, a few studies have indicated that the use of magnesium sulfate has a neuroprotective effect on the neonate, but it has some toxic effects when used for an extended period of time. The goal of this study is to assess the neonatal outcomes of preterm births, because it is still unclear how to describe the neonatal outcomes with the use of magnesium sulphate during preterm labor.

STUDY DESIGN:

Retrospective observational analysis was carried out in 63 neonates to figure out the effects of magnesium sulphate who were prematurely born. The outcomes were obtained and calculated in percentage.

RESULTS:

Out of 565 pregnancies, 75 were found to be preterm labor cases in which 63 patients were given magnesium sulfate making an incidence of 11.15% as preterm labor and preterm birth.

CONCLUSION:

The neonatal outcomes with the use of magnesium sulphate were found and shown the morbidity, mortality or complications. Early Admission in NICU promoted to prevent neonatal morbidity and mortality.

Keywords: Preterm labor, magnesium sulphate, neonatal morbidity, neuroprotection, neonatal outcome

1. INTRODUCTION:

Preterm birth is defined by WHO as all births before 37 completed weeks of gestation or fewer than 259 days since the first day of a woman's last menstrual period. Preterm labor can be categorized into three categories according to gestational age as extremely preterm (less than 28 weeks), very preterm (28-32weeks) and Late preterm (32-37weeks). Incidence is found between 5 to 10 %. Mostly babies born in late preterm birth is largely associated with the risk of respiratory difficulties. Late preterm delivery accounts for 9.1% in USA. Globally 15 million preterm babies are born every year. Among that, India accounts for approximately three million preterm births in a year. [1]

In 2010, an estimated 14•9 million babies (uncertainty range 12•3-18•1 million) were born preterm, 11•1% of all live births worldwide, ranging from about 5% in several European countries to 18% in some African countries. More than 60% of preterm babies were born in south Asia and sub-Saharan Africa, where 52% of the global live births occur. [2]

Preterm birth is the major cause of neonatal mortality, making it as the leading cause of baby's death in neonate and even in those babies who survive, are at risk of developing long term issues like neurodevelopmental deficits, such as cerebral palsy, cognitive dysfunctions.

Preterm labor is associated with neonatal morbidities and mortality. Babies are more prone to infections. A study conducted by McGuire W, Clerihew L, Fowlie PW over Infection in the preterm infant in 2004 revealed the systemic infection in preterm neonates fall in two categories. Early onset

infection occurs in the intrapartum period and presents in the first 48-72 hours after birth. It can be caused by Group B streptococci and Escherichia coli; Listeria monocytogenes across the placenta after the mother has eaten infected food.

Late onset infection usually acquired in hospital and clinically evident more than 72 hours after birth (usually after the first week of life). It can be caused by Gram positive microorganisms like staphylococcus and enterococci, fungal species like candida. Infections like Invasive fungal infection, Nosocomial infection, Sepsis, meningitis, candidiasis, and congenital infections like HIV can occur. Long term morbidities like CNS defects, cerebral palsy, chronic lung diseases, and cognitive dysfunction are also a serious problem. [3]

Use of magnesium sulfate in case of preterm labor:

Study basically focuses on neonatal outcomes with the use of magnesium sulfate which is administered to women undergoing early preterm labor reduces for neuroprotection in surviving neonates.

The administration of MgSO4 necessitates a baseline maternal laboratory examination, which includes a complete blood count, a high sr.cr level, and Urine output larger than 30 ml/h, normal vital signs, and adequate mother mentation. Urine outflow should be closely checked and sustained at a rate of roughly 50 mL/h. Physicians opted to administer magnesium sulfate for neuroprotection in accordance with the larger randomized trial. [4]

A study conducted by Chollat C, Sentilhes L, Marret S for Fetal Neuroprotection by Magnesium Sulfate in 2018 described the magnesium sulphate mechanism of action in neuroprotective action From Translational Research to Clinical Application. Multiple mechanisms may underlie the neuroprotective impact of magnesium. Magnesium affects several pathways potentially involved in preterm brain injury. As a non-competitive NMDA receptor antagonist, magnesium prevents excitotoxic calcium-induced injury. Magnesium decreases extracellular glutamate under ischemic conditions, possibly reducing excitotoxicity. Magnesium limits calcium influx through voltage-gated channels, which may reduce the activation of apoptosis.

Magnesium also has anti-inflammatory properties as it reduces oxidative stress and reduces the production of pro-inflammatory cytokines interleukin-6 and tumor necrosis factor-α. Magnesium deficiency increases endothelial nitric oxide production, which can promote endothelial dysfunction. This could involve decreased calcium influx and activation of phagocytic cells, inhibition of neurotransmitter release, or inhibition of nuclear factor kappa B. Physicians opted to administer magnesium sulfate for neuroprotection in accordance with the larger randomized trial. [5]

This study basically focuses on analyzing the neonatal outcomes with the use of magnesium sulphate which was administered to women who undergone preterm labor in our hospital, as there is less number of studies available in India regarding the maternal use of magnesium sulphate to correlate the association of maternal effects and analyzing the neonatal outcomes with the drug. Our study aimed in assessing magnesium sulfate as a tocolytic agent which helps in preventing cerebral palsy and other neonatal birth deficits in case of preterm births and also to assess comorbidities occurred in neonates with the maternal use of the drug during preterm labor in the area of study.

2. MATERIALS AND METHODS:

A Retrospective observational study was conducted in the department of obstetrics and gynecology of Teerthanker Mahaveer medical college and research center which is a tertiary care hospital catering to the preterm cases covered in the area of study. The study was approved by the institutional research and ethics committee. The sample size was calculated by using Rao software was found to be 63. The study was conducted over a period of two months for the collected data of the past one year (from March 2019 to December 2020) wherein 63 women who had been provided with magnesium sulphate in case of preterm labor.

All antenatal women aged between 20-30 years, came to our hospital OPD or emergency that undergone labor before 34 weeks of gestational age are included in our study. All the preterm births were included in the study. The data of those who were included for the study were collected from the medical records department of the hospital, after obtaining permission for the same. Women above 35 weeks of gestational age and whose data are not clear are excluded. The results were analyzed and calculated in percentage method. Our study aimed at analyzing the neonatal effects along with the use of magnesium sulphate in case of preterm births and outcomes are measured in terms of birth weight, NICU admission- days of admission, Apgar score and complications.

Maternal sociodemographic details like age, of the participants were collected from the case sheets.

3. RESULTS:

Data Interpretation:

The observational study was conducted and the results obtained were given in tabulated form with the population size for each criterion considered calculated with the percentage. The figures of the same were illustrated.

Table 3.1: frequency, percentage and cumulative frequency distribution of sociodemographic profile of the women undergone preterm labor that were provided with magnesium sulphate.

Table 3.1: Maternal sociodemographic outcomes:

Age	Frequency (n=63)	Percentage (%)	Cumulative frequency

21-25 years	29	41.7	41.7
26-30 years	34	58.3	100.0
Area			
Rural	29	46	46
Urban	34	54	100.0
SocioEconomicClass			
Low class	7	11.1	11.1
Lower middle class	37	58.7	69.8
Upper class	1	1.6	71.4
Upper lower class	6	9.5	81.0
Upper middle class	12	19.0	100.0
Gestational Age (Period)			
25-27/6 weeks	20	31.9	31.9
28-30/6 weeks	23	36.7	68.6
31-33/6 weeks	20	31.4	100.0
Gravida			
Primigravida	14	22.2	22.2
Gravida 2	27	42.9	65.1
Gravida 3	17	27.0	92.1
Gravida 4	5	7.9	100.0

The majority of the patients i.e., 58.3% (n=34) enrolled in our study aged between 26-30 years of age and the rest 41.7% (n=29) patients were aged between 21-25 years of age. Maximum patients i.e., 54% (n=34) enrolled in our study belonged to urban area. Maximum number of patients i.e., 36.7% (23) undergone preterm at their 28th to 30th week of gestational age and among the total study population, 42.9% (n=27) undergone preterm at their gravida 2 where 58.7% (n=37) belonged to lower middle class.

Table 3.2 showed the frequency , percentage and cumulative frequency of risk factors, leaking PV and maternal side effects observed in the study population.

Table 3.2: Maternal outcomes

Risk Factors	**Number(n) n=63**	**Percentage (%)**	**Cumulative frequency**
Pre -Eclampsia	36	57.1	57.1
Eclampsia	12	19.0	76.1
Gestational hypertension	8	12.7	88.8
Chronic hypertension	6	9.5	98.3
PIH	1	1.6	100.0
Leaking PV			
Present	8	12.7	12.7
Absent	55	87.3	100.0
Maternal side effects			
Hypotension	29	46.0	46.0
Diarrhea	7	11.1	57.1
Seizure	5	7.9	65
Confusion	4	6.3	71.3
Muscle weakness	9	14.3	85.6
Tachycardia	4	6.3	91.9
Hypoglycemia	5	7.9	100.0

Majority use of magnesium sulphate was observed in patents admitted with the risk factor of pre eclampsia i.e., 57.1% (n=36). Hypotension was observed in 29% (n=29) of the study population as the major maternal side effects recorded with magnesium sulphate use and 7.9% (n=5) patients were observed with seizure and the rest maternal side effects recorded was confusion(6.3%), diarrhea(11.1%),muscle weakness(14.3%), tachycardia(6.3%), hypoglycemia(7.9%).

Table 3.3 showed the frequency, percentage and cumulative frequency of neonatal outcomes like birth weight, birth weight category, gender, NICU admission, days of NICU admission, APGAR scores, and complications observed in the neonates.

Table 3.3: Preterm Neonatal outcomes with the maternal use of magnesium sulphate:

Neonatal outcome	**Number (n) n=63**	**Percentage (%)**	**Cumulative frequency**
Birth Weight(Kg)			
1	3	4.8	4.8
2	30	47.6	52.4
3	29	46.0	98.4
4	1	1.6	100.0
Birth Weight Category			
Low birth weight	35	55.6	55.6
Normal birth weight	25	39.7	95.2
Very low birth weight	3	4.8	100.0
Gender			
Male	34	54	54.0
Female	29	46	100.0
NICU Admission			
NICU	38	60.3	60.3
NORMAL	20	31.7	92.0
IUD	4	6.3	98.3
STILL BIRTH	1	1.6	100.0
Days of admission			
1-3 days			
0	33	52.4	52.4
1	7	11.1	63.5
2	19	30.2	93.7
3	4	6.3	100
4-6 Days			
0	55	87.3	87.3
4	4	6.3	93.7
5	1	1.6	95.2
6	3	4.8	100.0
APGAR Score			
<7 AT 1 MINUTE	38	60.3	
<7 AT 5 MINUTE	36	57.1	
Complications			
No complication	20	31.7	31.7
Respiratory distress syndrome	16	25.4	57.1
Neonatal death	5	7.9	65.0
Hypoglycemia	5	7.9	72.9
Hypotonia	5	7.9	80.8
Hyperbillirubineamia	3	4.8	85.6
Neonatal jaundice	3	4.8	90.4
IUGR	4	6.3	96.7
Hypocalcaemia	1	1.6	98.3
Sepsis	1	1.6	100.0

Birth weight measured for the total 63 neonates, out of where 35 (55.6%) neonates were found with less birth weight and were categorized under low birth weight category. NICU admission was required for 38 neonates (60.3%) who were born prematurely. Out of 63 neonates, 4 were found to be IUD (6.3%), and 1 were born still birth (1.6%) and the rest 31.7% (n =20) were born normal. Complications like respiratory distress syndrome 25.4% (n=16) which was the major complication found in the preterm neonates, neonatal death occurred for 5 neonates which makes 7.9% out of the total neonates. IUGR was observed in 6.3% (n=4) neonates. Rest accounted for complications like hypoglycemia 7.9% (n=5), hypotonia (n=5%), Hyperbillirubineamia 4.8% (n=3), neonatal jaundice 4.8.% (n=3), hypocalcaemia 1.6% (n=1) and 31.7% (n=20) neonates were born with no complication.

A statistical analysis was done by using chi square test to find the p value and the results obtained were given below.

Table 3.4: Assessment of association between sociodemographic outcomes with neonatal complications.

NEONATAL COMPLICATIONS	*SOCIODEMOGARPHIC OUTCOMES*						
	AREA			*Value*	*df*	*P value*	
	RURAL	*29*	*Pearson Chi-Square*	*9.178a*	*9*	*0.421(NS)*	
	URBAN	*34*	*Likelihood Ratio*	*10.189*	*9*	*0.335*	
HYPERBILLRUBIN-EAMIA	*TOTAL*	*63*	*N of Valid Cases*	*63*			
HYPOCALCAEMIA	***SOCIO-ECONOMIC CLASS***						
	LOW	*7*		*Value*	*df*	*P value*	*63*
HYPOGLYCEMIA	*LOWER MIDDLE*	*37*	*Pearson Chi-Square*	*32.230a*	*36*	*0.649(NS)*	
HYPOTONIA	*UPPER*	*1*	*Likelihood Ratio*	*32.308*	*36*	*0.645*	
IUGR	*UPPER LOWER*	*6*	*N of Valid Cases*	*63*			
NEONATAL DEATH	*UPPER MIDDLE*	*12*					
NEONATAL JAUNDICE	*TOTAL*	*63*					
	GRAVIDA						
NO COMPLICATION	*PRIMIGRAVIDA*	*14*		*Value*	*df*	*P value (Asymp. Sig. (2-sided)*	
RDS	*GRAVIDA 2*	*27*	*Pearson Chi-Square*	*25.858a*	*27*	*0.526(NS)*	
SEPSIS	*GRAVIDA 3*	*17*	*Likelihood Ratio*	*28.501*	*27*	*0.386*	
	GRAVIDA 4	*5*	*N of Valid Cases*	*63*			
	TOTAL	*63*					

(p<0.05 significant level; S-significant; NS- not significant)

No statistical relationship was assessed between sociodemographic outcomes with the magnesium sulphate usage in preterm women.

Table 3.5: Assessment of maternal outcomes with neonatal complications.

NEONATAL COMPLICATIONS	***MATERNAL OUTCOMES***					
	LEAKING PV					
	Absent	*55*		*Value*	*df*	*P value*
HYPERBILLRUBIN-EAMIA	*Present*	*8*	*Pearson Chi-Square*	*40.562a*	*9*	*0.000 (S)*
	Total	*63*	*Likelihood Ratio*	*30.973*	*9*	*0.000*
HYPOCALCAEMIA			*N of Valid Cases*	*63*		
HYPOGLYCEMIA	*RISK FACTORS*					
HYPOTONIA	*PIH with fetal distress*	*1*		*Value*	*df*	*P VALUE*
IUGR	*Chronic hypertension*	*6*	*Pearson Chi-Square*	*47.691a*	*36*	*0.092(NS)*
NEONATAL DEATH	*Eclampsia*	*12*	*Likelihood Ratio*	*34.822*	*36*	*0.525*
NEONATAL	*Gestational hypertension*	*8*	*N of Valid Cases*	*63*		

JAUNDICE	*Pre eclampsia*	*36*				
NO COMPLICATION	*TOTAL*	*63*				
RDS						
SEPSIS						
	ESTABLISHED/ADVANCED PRETERM					
	Advanced	*3*		*Value*	*df*	*P value*
	Established	*60*	*Pearson Chi-Square*	*2.638a*	*9*	*0.977(NS)*
	total	*63*	*Likelihood Ratio*	*3.637*	*9*	*0.934*
			N of Valid Cases	*63*		
	MATERNAL SIDE EFFECTS					
	Confusion	*4*		*Value*	*df*	*P VALUE*
	Diarrhoea	*7*	*Pearson Chi-Square*	*57.201a*	*54*	*0.357 (NS)*
	Hypoglycaemia	*5*	*Likelihood Ratio*	*49.925*	*54*	*0.632*
	Hypotension	*29*	*N of Valid Cases*	*63*		
	Muscle weakness	*9*				
	Seizures	*5*				
	Tachycardia	*4*				
	Total	*63*				

(p<0.05 significant level; S-significant; NS- not significant)

Association of leaking PV with neonatal complications can be seen in table 3.5. No statistical relationship was found between neonatal complications and maternal side effects with magnesium use.

Table 3.6: assessment of neonatal outcomes with neonatal complications.

NEONATAL COMPLICATIONS	*NEONATAL OUTCOMES*					
HYPERBILLRUBIN-EAMIA	*GENDER*					
	Female	*29*		*Value*	*df*	*P VALUE*
HYPOCALCAEMIA	*Male*	*34*	*Pearson Chi-Square*	*12.868a*	*9*	*0.169(NS)*
HYPOGLYCEMIA	*Total*	*63*	*Likelihood Ratio*	*15.088*	*9*	*0.089*
			N of Valid Cases	*63*		
HYPOTONIA	*BIRTH WEIGHT CATEGORY*					
IUGR	*LBW*	*35*		*Value*	*df*	*P VALUE*
NEONATAL DEATH	*NBW*	*25*	*Pearson Chi-Square*	*26.272a*	*18*	*0.094(NS)*
	VLBW	*3*	*Likelihood Ratio*	*19.773*	*18*	*0.346*
NEONATAL JAUNDICE	*TOTAL*	*63*	*N of Valid Cases*	*63*		
	APGAR SCORE (1 MIN)					
NO COMPLICATION		*Value*	*df*	*P VALUE*		
RDS	*Pearson Chi-Square*	*112.714a*	*63*	*0.000 (S)*		
	Likelihood Ratio	*87.625*	*63*	*0.022*		
SEPSIS	*N of Valid Cases*	*63*				
	APGAR SCORE (5 MIN)					

		Value	*df*	*P VALUE*		
	Pearson Chi-Square	*217.085a*	*81*	*0.000(S)*		
	Likelihood Ratio	*153.684*	*81*	*0.000*		
	N of Valid Cases	*63*				
	NICU ADMISSION					
	IUD	*4*		*Value*	*df*	*P VALUE*
	NICU	*38*	*Pearson Chi-Square*	*126.000a*	*27*	*0.000(S)*
	NORMAL	*20*	*Likelihood Ratio*	*109.655*	*27*	*0.000*
	STILLBIRTH	*1*	*N of Valid Cases*	*63*		
	TOTAL	*63*				
	NICU ADMISSION (1-3 DAYS)					
		Value	*df*	*P VALUE*		
	Pearson Chi-Square	*146.494a*	*27*	*0.000(S)*		
	Likelihood Ratio	*121.828*	*27*	*0.000(S)*		
	N of Valid Cases	*63*				
	NICU ADMISSION (4-6 DAYS)					
		Value	*df*	*P VALUE*		
	Pearson Chi-Square	*126.000a*	*27*	*0.000(S)*		
	Likelihood Ratio	*59.048*	*27*	*0.000*		
	N of Valid Cases	*63*				

(p<0.05 significant level; S-significant; NS- not significant)

Table 3.6 showed a statistical relationship between neonatal complication with the low Apgar scores at 1 and 5 min, in NICU admission in case of complications for 1-3 days and 4-6 days where the p value obtained is p=0.000 which is <0.05 showing a significant relationship between the usage of magnesium in preterm labor.

ILLUSTRATIONS:

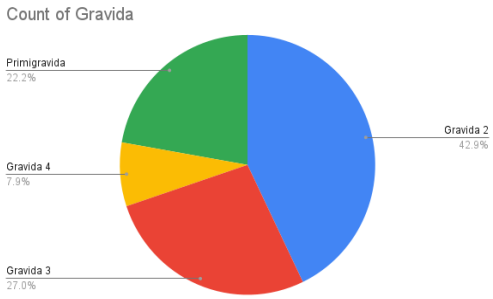

Fig 3.1.1: Gravida at the time of labor

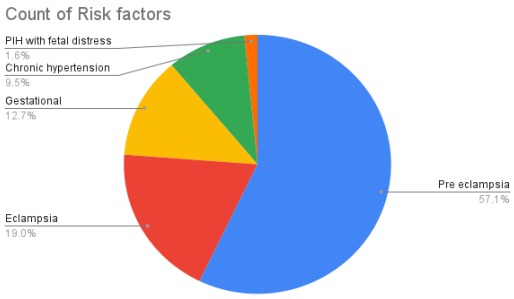

Fig 3.2.1: Count of risk factors

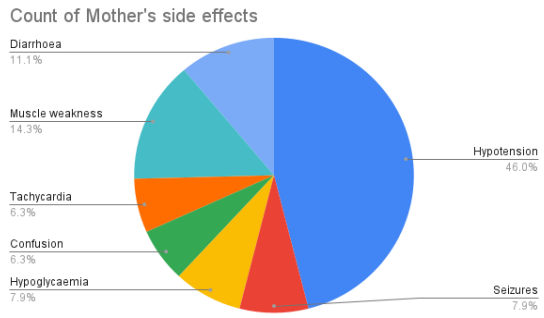

Fig 3.2.2: Maternal side effects

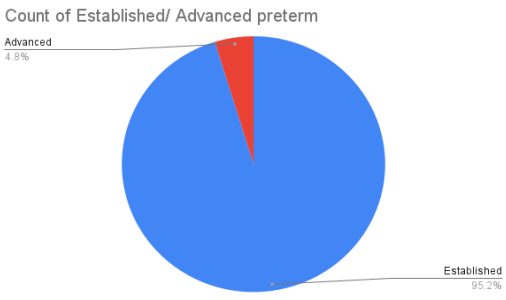

Fig 3.2.3: Count of Established/advanced preterm labor

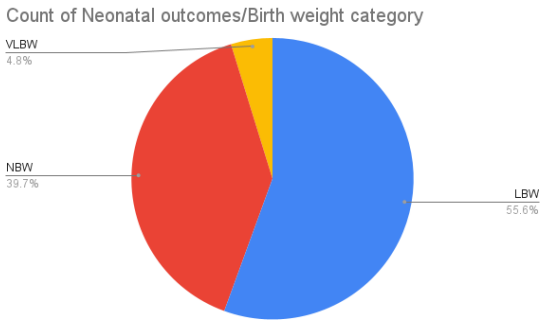

Fig 3.3.1: Birth weight category

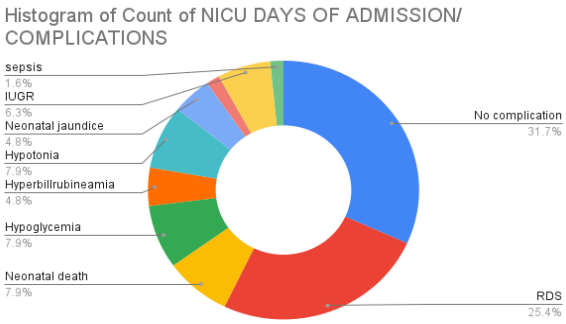

Fig 3.3.2: Complications observed in NICU admission

DISCUSSION:

The study was conducted to assess the neonatal outcomes in preterm births with the maternal use of magnesium sulfate. This study had shown the incidence of 11.15 % as preterm birth among the total deliveries in the hospital.

Table 3.1 shows the maternal sociodemographic details where the percentage of age, locality, gestational age and gravida of the study population were calculated. Study population under the age criteria between 26-30 years shown 58.3% of preterm labor. Gestational period from 28-30/6 weeks showing 36% were most accountable for the preterm labor observed from the study.

A study was conducted in 2013 by López, P. O., &Bréart, G. in Chile, to assess some sociodemographic characteristics of the maternal population over time, and their possible association to rates of preterm birth concluded that risk of preterm birth remained higher in groups of mothers: <18 and >38 years of age; without a partner; primiparas and grandmultiparas. However, global increase in preterm birth was not explained by the modification of socio demographics characteristics of maternal population. Some socio demographic characteristics remained associated with preterm birth over time. Rates of preterm birth increased in overall population, especially during the third period (2001-2008). In the same time, characteristics of maternal population changed: significant increase of extreme reproductive ages, significant decrease in parity and increase in mothers living without a partner. [6] Our study showed that there is a no association between sociodemographic characteristics and neonatal complications.

Table 3.2 shows the maternal outcomes observed after the administration of magnesium sulphate in case of preterm labor. Maternal outcomes with respect to factors like risk factors, leaking PV, mother's side effects were calculated. 58.1% of the preterm labor occurred due to Preeclampsia and the rest were associated with Eclampsia (17.7%), Gestational Hypertension (12.9%), Chronic Hypertension (9.7%), and PIH (1.6%). Observed side effects in the study population with the use of magnesium sulphate were Hypotension, Diarrhea, Seizure, Confusion, Muscle Weakness, Tachycardia, and Hypoglycemia where 47.5% was associated with Hypotension.

A systemic review study conducted by Bain ES, Middleton PF, Crowther CA in 2013 for assessing the maternal adverse effects of different antenatal magnesium sulphate regimens for improving maternal and infant outcomes quantified an association between iatrogenic overdose of magnesium sulphate and life-threatening consequences and concluded that appropriate administration of antenatal magnesium sulphate was not shown to be associated with serious maternal adverse effects, though an increase in 'minor' adverse effects and treatment cessation was shown. [7]. Although, there is no statistical relationship, our study is also an another evident for maternal a undergoing minor adverse effects if appropriate usage of magnesium is provided.

Preterm neonatal outcomes were discussed in Table 3.3:

At our center, the highest morbidity incidence was found with RDS which accounts for 25.4% of the preterm neonates. Neonatal death rate was found to be 7.9%. The study showed 61.3% of the neonates were admitted in NICU after birth when the APGAR score calculated at 1 minute(60.3%) and 5 minutes(57.1%) was found to be <7 and associated with other complications like neonatal jaundice(4.8%), IUGR(6.3%), hypocalcaemia(1.6%), Hyperbillirubineamia(4.8%), hypoglycemia(7.9%), sepsis(1.6%), Hypotonia (7.9%).

A study conducted by Girsen AI, Greenberg MB, El-Sayed YY, Lee H, Carvalho B, Lyell DJ in 2015 revealed the association between antenatal magnesium sulphate treatment in case of pre eclampsia and NICU admission of the exposed neonates who had <7 APGAR scores at 1 and 5 minutes.

A retrospective cohort analysis was conducted by Abbassi-Ghanavati M, Alexander JM, McIntire DD, Savani RC, Leveno KJ in 2012 for evaluating the effects of magnesium on the newborns. Their study revealed that a total of 6654 women with preeclampsia were treated with intravenous magnesium sulfate as described; 88 (6%) of the infants were diagnosed with hypotonia. Lower 1-minute and 5-minute Apgar scores, intubation in the delivery room, admission to special care nursery, and hypotonia were all significantly increased as maternal serum magnesium concentrations increased before birth. [8][9]. This study also revealed that there is an association between low Apgar scores to the neonatal complications.

Significance of the study was assessed by calculating the p-value using chi square test for neonatal outcomes with sociodemographic and maternal outcomes.

A statistically significant was found between Leaking PV with neonatal complications with the use of magnesium sulphate with a p value 0.000(<0.05).

Association between <7 Apgar scores at less than 1 minute and 5 minutes was found. [8]

An association between NICU admission stay for 1 to 3 days and 4 -6 days was found with the p- value of p=0.000. our study showed a large number of NICU admission was between 1 to 3 days.

CONCLUSION:

Preterm birth risk factors can be minimized through adolescent health education, contraception counseling, and birth spacing. Preventing premature labor by intervening early in the prenatal period for other possible risk factors. The cost of a NICU stay was not considered in the study, but it is still significant. although the study shown the neonatal mortality, the early intervention of neonatal morbidities have reduced the long term defects and increase in mortality rate by timely treatment provided in our center.

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