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Maternal Fetal Outcome In Microbial Invasion Of Amniotic Fluid In Premature Rupture Of Membranes.

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ABSTRACT

Premature rupture of membranes (PROM) is a frequent phenomenon that occurs in about 4% - 7%. However, the associated sequent problems are proportionally high. Almost two thirds of PROM are spontaneous, common risk factor young mother, multiple pregnancy, genital tract infection, previous preterm delivery. The complications range from induction of labour, caesarean section, fetal pulmonary morbidity and even mortality. To identify and quantify the risk factors and complications of premature rupture of membrane in pregnant women. 100 pregnant women diagnosed as PROM were examined for the physical signs. Detailed gynaecological and obstetric history was reported. Laboratory investigations included cervical swabs and posterior fornix swabs under aseptic conditions Drugs including types of antibiotics, Dexamethasone and tocolytics were also included. Results: The mean age of 100 patients was 28.9 years. Most of them, 66.1% of patients received antibiotics mostly Erythromycin. Dexamethasone was given for 32.1%. FTND accounted for 62% and PTND for 10% and Caesarean section was performed for 28%. The main indications for C/S were failed induction, in 50%, 11.8% were equally distributed between; macrosomia, previous scars, drained liquor, previous C/S, breech presentation. Only 1% of new born babies had complication. Conclusions and Recommendations: Further large studies should be done for more elaboration and analytical studies to quantify the strength of each risk factor. Strategy for management of PROM should be adopted for proper timing of induction, emergency caesarean intervention with ultimate goals of minimizing and or preventing maternal and fetal complications of disease.

Keywords: Amnioinfusion, Antibiotics, Biomarkers, fetal inflammatory response syndrome, high leak pre-PPROM, pregnancy, prognosis; steroids.

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INTRODUCTION

Preterm premature rupture of the fetal membranes (PROM) is associated with 30-40% of premature births and is an important cause of perinatal morbidity and mortality [1, 2]. It has been estimated that 10% of perinatal deaths are directly or indirectly attributable to PROM [3-5]. Limited data are available for India, but studies from other parts of the world have shown the etiology of the condition to be multifactorial. Infection has been cited as a major cause of membrane damage. There is growing evidence associating upper genital tract infections with PROM [6]. One possible mechanism by which infections might act is through ascension from the cervical/vaginal area and replication in the placenta, the decidua and the membranes [7, 8]. Another hypothesis is that several organisms that are commonly present in the vaginal flora, including group B streptococci, *S. aureus* and microorganisms that cause BV, secrete proteases that degrade collagen and weaken the fetal membranes leading to PROM. Researchers have postulated that PROM may be the result of direct bacterial insults that necrotize tissue leading to host-mediated auto destruction [9].

MATERIALS AND METHODS

This Prospective analytical study case-control study of 100 patients presenting with PROM at greater than 31 weeks of gestation were included in 2022 at Department of Obstetrics and gynecology, Government Ariyalur Medical College, Ariyalur, Tamil Nadu, India. The inclusion criteria were gestational age > 31 weeks; diagnosis of PROM confirmed by clinical finding of posterior vaginal pool, vaginal pH or ferning; cervical dilation of < 3 cms; singleton pregnancy; and clear liquor. Exclusion criteria included: woman in labour; mal-presentations; multiple gestation; medical disorders; and a history of cervical encirclage. Data were collected from all eligible participants who gave informed consent. A structured questionnaire collected data on socio demographic and medical variables. Collected biological specimens included liquor from the posterior fornix of the vagina and midstream urine. Dipstick urinalysis was performed (Multistix 10 SG, Bayer Diagnostics). If nitrites and leucocytes were found in the urine analysis, that patient's urine was also sent for culture. Vaginal fluids were cultured on three primary culture media: blood, chocolate and McConkey agar. Cultures were incubated at 37° Celsius for 24 hours. Wet preparation slides were also made from all swabs and examined for fungal elements. And a Gram stain film of all specimens was also examined for intracellular Gram-negative diplococci. Isolates that appeared as Gram variable coccobacilli oxidase negative and bacitracin positive were identified as *Gardnerella vaginalis*. Other significant isolates were identified by conventional methods. The *in vitro* sensitivity test of some of the isolates was determined in Muller-Hinton agar plates by standard method against Ampicillin (10 mg), Erythromycin (10 mg), Cloxacillin (5 mg), Gentamycin (10 mg) and Azithromycin (10 mg). Anaerobic facilities are lacking Gram stain was done for diagnosis of BV using Nugent's score.

Statistical Analysis

Data were entered in MS Excel and analyzed using Stata 8.0 (Stata Corporation, College Station, TX). The primary outcome was PROM, analyzed as a binominal variable. In univariate analysis, χ^2 test and Fischer's exact test were used to assess the associations between PROM and categorical variables and t-test and the Wilcoxon rank sum test were used for continuous variables. Likelihood-ratio tests were used to determine the statistical significance of each variable. Associations, measured as odds ratio (OR) and adjusted for relevant confounding factors, were estimated using multivariate conditional logistic regression analysis. In the first model independent risk factors for PROM were identified. Variables significantly associated with PROM were tested and retained if they remained significantly associated with the outcome ($P \leq 0.05$) after inclusion of other potential predictors. All confidence intervals were calculated at the 95% level.

RESULTS

This study was done *In the Period from 1st January 2012-31st Dec 2012*, included 100 cases of PROM. Their mean age is 28.6 years, std. deviation is 5.9 years, median is 28 years and range is 17 - 42. Table 1 shows the age distribution of 100 cases of PROM. The majority were at the age group of 21 - 30. Table 2 shows the education distribution of 100 cases of PROM; where university education was the most frequent forming 39% followed by secondary level 31% and preparatory level 21%. Table 3 shows the occupation distribution of 100 cases of PROM; almost 75% were housewives. Table 4 shows the distribution of patients according to gravidity: primigravida were 48% followed by multi- para 46%,

nulipara was reported among abortions were only reported among 17%. Table 5 shows the distribution of duration and suspected causes of leakage where 83% occurred more than 24. hours and high percentage (43%) were due to unknown causes and 26% had previous PROM, 14% caused by itching and 12% by recurrent UTI. Table 6 shows the distribution of 100 PROM cases according to temperature where only 4% of them were feverish, 55% had pulse more than 80/minute and 10% of them had bp >120 mHg. Table 7 shows the distribution of patients according to type of treatment given to the mother where 66.1% have received antibiotics, 32.1% received dexamethazone and only 1.7% received tocolytics. Table 8 Gynecological examination .Table 9 shows the distribution of patients according to mode of delivery full term normal delivery occurred in 62% of cases followed by 28% for C/S and only 10% were post term normal delivery. Almost, 50% of C/S indication was failed induction and fetal distress along with slow fetal heart accounted 14.3%. Big size baby ac- counted for 3.6% similar to previous 2 C/S, old scar, leaked liquor. C/S were significantly different in age group < 22 years: all C/S reported compared to 77.8% reported vaginal delivery ($\chi^2 = 5$ o, P, 0.02). Only 4.8% who reported FTND had gestational age < 37 weeks compared to 39.3% who reported C/S with significant difference ($\chi^2 = 47$. P, 0.001).Table 10 shows Distribution according the isolated microorganism where *Candida albicans* was the most frequent accounting for 40% followed by G. Vaginal (25%) and antibiotic sensitivity was most frequently re- ported for Erythromycin accounting 21.7%, 17.4% for azithromycin and 15.9% for Ofloxacin. Table 11 shows the distribution of babies according to Apgar score and development of complications: Apgar score of % was the most frequent accounting for 79% followed by 4 accounting for 17% and only 1% complication had been reported.

Table 1: Age Distribution

Age	No.	%
≤20	4	4
21 - 30	61	61
31 - 40	31	31
>40	4	4
Total	100	100

Table 2: Level Of Education

Level of Education	Number	%
Illiterate	2	2
Preparatory	21	21
Primary	7	7
Secondary	31	31
University	39	39
Total	100	100

Table 3: Occupation

Occupation	Number	%
Housewife	75	75
Employer	22	22
Student	3	3
Total	100	100

Table 4: Obstetrics History

Gravity	Number		%
Primi	48		48
2 - 4	46		46
≥5	6		6
Parity	Number		%
Nullipara	52		52
1 - 4	44		44
≥5	4		4
Abortion	Number		%
No abortion	80		80
One	15		15
Two	5		5
Total	100		100

Table 5: Duration Of Leaking Hours And Complications

Duration of leaking hours	Number	%
≤24	17	17
>24	83	83
Suspected causes of leaking	Number	%
Unknown	43	43
Previous PROM	26	26
Underling causes of Itching	14	14
Recurrent UTI	12	12
Polyhydramnios	1	1
Unstable lie	1	1
Cervical incompetence	1	1
Antepartum hemorrhage	1	1
Fever	1	1
Total	100	100

Table 6: Physical Signs

Measurement of Temperature	Number	%
≤37°C	96	96
>37°C	4	4
Measurement of Pulse/minute	Number	%
≤80	45	45
>80	55	55
Systolic Blood Pressure	Number	%
≤120 mmHg	90	90
>120 mmHg	10	10
Total	100	100

Table 7: Shows The Distribution Of Patients According To Type Of Treatment Given To The Mother

Type of Treatment	Number	%
Antibiotic	39	66.1
Dexamethasone	19	32.2
Tocolytic	1	1.7
Total	59	100

Table 8: Gynaecological Examination

Fundal Level	Number	%
Corresponds to Date	77	77
Decreased	23	23
Vulval Examination	Number	%
Normal	92	92
Abnormal	8	8
Vaginal Examination	Number	%
Normal	90	90
Abnormal	10	10
Cervical Examination	Number	%
Normal	99	99
Abnormal	1	1
Total	100	100

Table 9: Shows the distribution of patients according to mode of delivery full term normal delivery

Mode of Delivery	Number	%
FTND	62	62
PTNVD	10	10
C/S	28	28
Indication of C/S	Number	%
Failed Induction	14	50
Fetal Distress	4	14.3
Slow Fetal Heart	4	14.3
Big Size Baby	1	3.6
Previous Scar	1	3.6
Drained Liquor	1	3.6
Previous 2 C/S	1	3.6
Breech Presentation	2	7.2
Total	100	100

Table 10: Showed The Microorganism Isolated From Leaking Water

Microorganism Isolated from Leaking Water	Number	%
<i>Candida albicans</i>	8	40
<i>Gardenella vaginalis</i>	5	25
<i>Staphylococcus aureus</i>	2	10
<i>Streptococcus pyogenes</i>	2	10
CONS	2	10
<i>Streptococcus pneumonia</i>	1	5
Total	20	100
Type of Antibiotic	Number	%
Erythromycin	15	21.7
Azithromycin	12	17.4
Ofloxacin	11	15.9
Gentamycin	9	13
Ampicillin	6	8.7
Cloxacil	6	8.7
Cefuroxime	5	7.3
Chloramphenicol	5	7.3
Total	69	100

TABLE 11: SHOWS THE DISTRIBUTION OF BABIES ACCORDING TO APGAR SCORE AND DEVELOPMENT OF COMPLICATIONS

Apgar Score	Number	%
0	1	1
4	17	17
5	79	79
Not Recorded	3	3
Complication	Number	%
Yes	1	1
No	99	99
Total	100	100

DISCUSSION

The mean age of the patients was 28.6 years with singleton pregnancy with similar age in studies done by Alhussini in Egypt and Saudi Arabia, the cases of the Pakistani study done by Noor S. were younger” 15 - 25 years” [10, 11]. Premature PROM was reported among 10% of the cases in this study which is more or less comparable to PPRM reported by Noor was 9.5% because of younger age as well as low socioeconomic class compared to findings of Smith G and Tahir *i.e.* 2.3% and 5.4% respectively [10, 12]. The gestational age more than 36 weeks was reported in 83% of the study subjects with >92% with early booking and only 6% were hospitalized for more than a week. Almost 83% of the patients reported leakage more than 24 hours. Primi gravidity was reported among 48% and Nulliparity was reported among 52% of the study subjects which are comparable to studies done in the region by al Hussein, Noor and Tahir [10, 11, 13] demonstrating high frequency of PROM among nulliparous women compared to parous ones The most frequent suspected causes of PROM in the study were previous PROM, itching, recurrent UTI accounting for 26%, 14%and 12% respectively 43% were of unknown causes. polyhydrominous. Unstable lie, cervical incompetence, Antipartum haemorrhage and fever were the least reported causes and each was 1%. Maternal infection was the most frequent cause of PROM in the study done by Modena in Italy 2004 [14] as well as smoking of the pregnant women and Cocaine intake which is the case in our study at all. But, Asindi reported high frequency of infections with CONS in Saudi Arabia and 24% of the mothers were colonized and 31% of their babies [15]. Mercer in his recent expert view

2003 concluded that PROM is a multifactorial in nature, and chorionic infection or inflammation appear to play important role in the aetiology of preterm PROM specially in early gestational age. He also reported decreased membrane collagen content that increased with the gestational age and was associated with the pathogenesis of the condition [16]. Our study agree with the findings of Mercer in the suspected causes of PROM like prior conditions, uterine distension, infections, cervical incompetence and ante partum haemorrhage but he reported cigarette smoking, amniocentesis, and prior cervical conization. The swabs were done for the studies subjects showed that only 8% of the endocervical swabs were positive and 23% of the posterior vaginal fornix with similar findings from the study done by AlHussani in Assuit, Egypt 2012 who reported positive culture among cases of PROM significantly higher than among their matched control and the presence of significant association with the educational level, residence and education [10]. The most frequent microorganism in the current study was *Candida albicans* forming 40% followed by *Gardnerella vaginalis* for 25% and CONS for 10% like *Staphylococcus aureus* and *Streptococcus pyogenus*. Although, the current study findings are in consistence with the done by Alhussani in Egypt they are not comparable to the findings of the study done by Asindi in Saudi Arabia who reported the frequency of CONS as high as 31% and *Candida* was the least frequent organism [10, 15]. On the contrary, Karat et al. 2006 in case control study reported rates of microorganisms in cases of PROM and their matched controls as: 16% - 28% for *Staph aureus*, 8% - 19% for *Candida albicans*, and 3.3% - 20% for *E. coli* these non-matched results could be explained by the variability of sociodemographic characteristics, educational levels and racial origins [17]. Dexamethasone was administered to 32.2% of the subjects aiming to decreasing perinatal morbidity and mortality, this procedure is consistence with the guidelines subjected by Harding JE as a result of his meta analysis that concluded reduced risk of RDS and IVH and necrotising enterocolitis among those receiving corticosteroids versus no administration as all physicians caring for pregnant women should understand the dosing and indications for corticosteroid administration during pregnancy [18]. The most widely used and recommended regimens include intramuscular dexamethasone (Decadron) 6 mg every 12 hours for two days [19]. Other centers use intramuscular betamethasone (Celestone) 12 mg every 24 hours for two days, The National Institutes of Health recommends administration of corticosteroids before 30 to 32 weeks' gestation, assuming fetal viability and no evidence of intra-amniotic infection. Use of corticosteroids between 32 and 34 weeks is controversial [14]. Tocolysis was only conducted in 2.7% of the cases. Limited data are available to help to determine whether tocolysis is effective in the management of PROM, Tocolytic therapy can prolong latent period by inhibition of uterine contraction but did not prove to improve neonatal survival. The mode of delivery of the cases was as follow 62% by FTNVD and 10% by PTNV, Caesarean section was indicated for 28% of cases 50% of the indications were due to failure of induction, 14.3% were reported equally to fetal stress and slow fetal heart rate, 3.6% of cases was reported for six indications; macrosomia, old scar, breech presentation, previous 2 S/C, drained liquor a. The rates in this study were similar to what was reported by Elsalmani and his colleagues in Iran 2002, where 28.06% were subjected to C/S with higher rate among nullipara compared to Multipara [20]. Noor in Pakistan reported 14% rate of C/S [11]. The highest reports rates for C/S were reported in developing countries.

CONCLUSION

Although the results of the study reinforce the notion that early detection and aggressive treatment of lower reproductive tract infections may lead to better outcomes in women at risk for PROM, there is still a great deal of research needed to fully explicate the biologic processes of the fetal membranes. especially with regards to exogenous risk factors such as nutritional deficiencies and infection.

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