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An Observational Study of Urinary Calcium Excretion in Nephrotic Children

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Abstract

Background: Hypocalcemia is a known entity in nephrotic syndrome. Does hypercalciuria contribute to this state, is investigated in our study.

Aims: To study the urinary calcium excretion during nephrotic range proteinuria and during remission in nephrotic children.

Design & Setting: This observational-cohort study was carried out in a tertiary care hospital in Northern India from July 2015 to June 2016.

Material & Methods: Eighty consecutive nephrotic patients (aged 2-14 years) with new onset nephrotic syndrome or relapse were enrolled. Eight patients were lost to follow up and 3 were excluded due to addition of calcium to their treatment. Urinary and blood samples of the patients were sent at initial enrollment, at remission and at completion of alternate day therapy. Urinary calcium to urinary creatinine ratio (UCa/UCr) at onset (of patients with initial episode) or relapse (in known cases of nephrotic syndrome) and during remission was compared.

Statistical Analysis: Analysis of variances (ANOVA) was applied for comparison among groups showing normal distribution and Kruskal-Wallis Test was used for parameters having non-Gaussian distribution.

Results: No statistically significant difference in the value of UCa/UCr was observed during onset/relapse, after remission and after stopping steroid therapy.

Conclusion: Urinary calcium excretion does not statistically vary during nephrotic range proteinuria and after it.

Keywords: Calciuria; Relapse; Remission; UCa/UCr ratio.

Introduction

Nephrotics characterized by heavy proteinuria, hypoalbuminemia, hyperlipidemia and edema, show a number of calcium homeostasis disturbances leading to abnormal bone histology such as hypocalcemia, reduced serum vitamin D metabolites, impaired intestinal absorption of calcium and elevated level of immunoreactive parathyroid hormone [2]. Total plasma calcium concentration is low, parallel to reduction of albumin level as calcium is partly albumin bound [9]. Serum calcium is reduced proportionately to fall in

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concentration of serum albumin during early stages and true hypocalcemia becomes evident later in course of disease [7]. Later is mainly attributed to loss of plasma proteins and mineral in urine and to steroid therapy [8]. Levels of both vitamin D binding protein and 25 hydroxy D_3 is lost in urine in patients with nephrotic syndrome (NS) [5]. Blood levels of 25 hydroxy D_3 has direct and significant relationship with levels of serum albumin and an inverse significant relationship with degree of proteinuria [10]. Systemic corticosteroids reportedly cause hypercalciuria by inhibiting osteoblastic activity and increasing osteoclastic activity in bone, as well as by increasing urinary calcium excretion from kidney [6]. However, exact biochemical basis for changes in levels of calcium in patients with NS remains speculative.

In this study we evaluated urinary calcium excretion during proteinuric and non proteinuric phases to observe the contribution of calciuria in causing decrease in level of calcium in these patients. We aimed to establish how much does the loss of ionic calcium which forms 45% of total calcium and is freely filtered contributes to decrease in calcium levels.

Material and Methods

The prospective cross sectional study was conducted at tertiary level hospital in Northern India over 12 months from July 2015 to June 2016. Eighty consecutive patients of nephrotic syndrome attending the hospital were enrolled for the study. The eligible candidates were 2-14 year old nephrotics with normal renal function. Those excluded were children with clinical evidence of malnutrition, systemic disease and inflammatory renal disease or those taking calcium or vitamin D supplementation 3 months prior to enrollment and during study period and those who received diuretics or any other drug altering calcium or vitamin D metabolism.

Written informed consent was obtained from all parents/guardian before enrolling the patients in study. The study protocol was approved by institutional ethical committee.

Detailed history and physical examination of each case was recorded systematically on a standard performa. Spot urine sample was tested by reagent strip to test for proteinuria. Blood and urine sample was obtained in morning following an overnight fasting at relapse/initial episode, remission and on stopping of steroid treatment. Three milliliter blood in and 10 ml sterile urine was sent to lab for serum albumin, lipid profile (total cholesterol, VLDL, HDL), serum urea, creatinine and serum ionized calcium. Non fasting second urine passed in the morning as collected in hydrated state for UP/UC and UCa/UCr estimation. Hypocalcemia was defined as ionized calcium level <4.5 mg/dl and hypercalciuria was defined as UCa/UCr >0.2.

Patients were treated according to ISPN protocol [8]. UCa/UCr was used to assess calcium excretion during relapse/first episode, remission and after stoppage of steroid. If any patient developed features of hypocalcemia during the study period then calcium was added to his treatment and he was excluded from the study. Data was entered in Microsoft Excel sheet and analyzed by Epi Info 7 software. Analysis of variances (ANOVA) was applied for comparison among groups showing normal distribution and Kruskal-Wallis Test was used for parameters having non-Gaussian distribution.

Results

Of 80 patients of nephrotic syndrome aged 2 to 14 years were enrolled, 8 patients were lost to follow up and 3 excluded from the study due to administration of calcium during follow up leaving 69 children whose data was analyzed (Fig. 1). There were 48 male and 21 female patients with 37 children between 2-5 years of age, 29 between 6-10 years and 3 patients between 11-14 years of age. Thirty patients were from rural background and 39 were from urban area. Mean ± SD height of the patients was 103.9 ± 23 cm, weight was 17 ± 6.3 kg and BMI was 15 ± 3.3 kg/m^2.

Forty three patients had prior steroid exposure and 26 were cases with no prior exposure to steroids. Out of 69 patient 35 did not require hospitalization and 34 required hospitalizations for causes like massive edema, infection and oliguria. Mean time to attain remission was 7.84 days. Fifty nine patients remitted on prednisolone alone but 10 patients required alternative drugs (7 were on levamisole, 1 on cyclophosphamide and 2 on calcineurin inhibitors). One patient was on long term alternate day therapy. Nine patients re-relapsed in the study period.

There was highly significant difference in the mean value of serum albumin during onset/relapse, remission and after stoppage of steroid therapy ($p < 0.001$). There was significant difference in mean value of VLDL, HDL and TG in initial episode/ relapse of nephrotic syndrome and after stopping steroid therapy ($p < 0.05$) and the corresponding

difference in value of total cholesterol was highly significant (p<0.001). There wasn't any significant difference in the mean value of serum urea and creatinine during onset/relapse, remission and after stopping steroid therapy (p>0.05). There was highly significant difference in the mean value of UP/UC during onset/relapse, remission and after stoppage of steroid therapy (p<0.001) (Table 1).

In patients with initial episode of nephrotic syndrome there was no significant difference in the mean value of UCa/UCr during onset, remission and after stopping steroid therapy (p >0.27). There was significant difference in the mean value of UCa/UCr during relapse, remission and after stopping steroid therapy in frequent relapsing and steroid resistant nephrotic syndrome (p value 0.022 and 0.016 respectively). However, with the combined data of all the subgroups, there was no significant difference in the mean value of UCa/UCr during onset/relapse, remission and after stopping steroid therapy (p>0.05) (Table 1). No correlation was foundbetween changes in values of serum albumin and UCa/UCr levels.

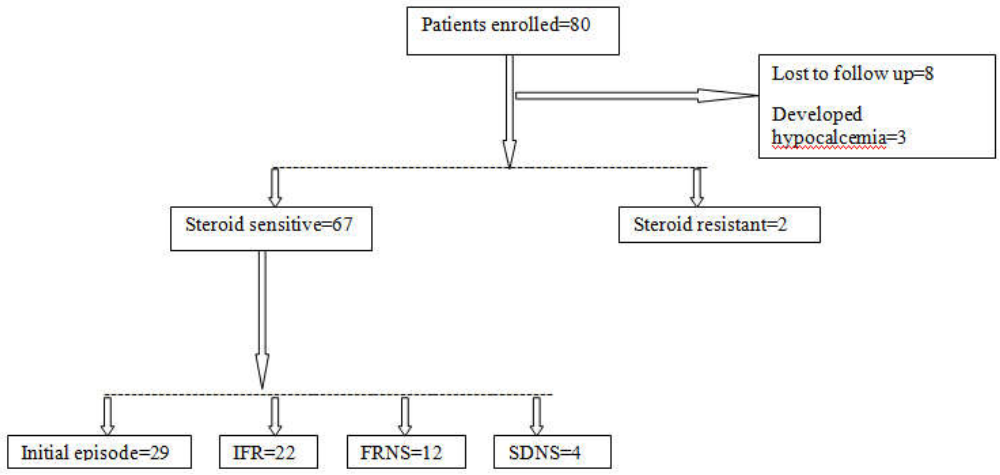

Fig. 1: Study cohort

IFR = Infrequent relapsers

FRNS = Frequently relapsing nephrotic syndrome

SDNS = Steroid dependant nephrotic syndrome

Table 1: Biochemical parameters in mean ± SD during onset/relapse (a), at remission (b) and after steroid therapy(c).

	(a)	(b)	(c)	p value
S.Albumin(g/dL)	2.4 ± 0.58	3.35 ± 0.52	3.85 ± 0.55	a vs. b <0.001 a vs. c <0.001
VLDL(mg/dL)	67 ± 39.7	55 ± 36.2	51.1 ± 29.9	a vs. b >0.05 a vs. c <0.05
HDL(mg/dL)	90.2 ± 33	77.2 ± 31	70.15 ± 33.3	a vs. b >0.05 a vs. c<0.01
Total cholesterol (mg/dL)	374 ± 179	304 ± 159	209 ± 86	a vs. b<0.05 a vs. c<0.001
S.Urea(mg/dL)	36 ± 26	32 ± 16	34 ± 16	a vs. b >0.05 a vs. c>0.05
S.Creatinine(mg/dL)	0.71 ± 0.18	0.72 ± 0.19	0.72 ± 0.18	a vs. b >0.05 a vs. c>0.05
UP/UCr	11.44 ± 6.7	2.28 ± 3.2	1.5 ± 2.6	a vs. b<0.001 a vs. b<.001
S.calcium(mg/dl) (ionized)	1.04 ± 0.16	1.23 ± 1.0	1.09 ± 0.56	a vs b >0.05 a vs c >0.05
UCa/UCr	0.55 ± 1.1	0.60 ± 1.68	0.53 ± .77	a vs. b>0.05 a vs. b>0.05

Discussion

We found no significant difference in the mean value of UCa/UCr during relapse, remission and after stopping steroid therapy ($p>0.05$). Also there was no significant difference in mean value of serum ionized calcium during relapse, remission and after completion of steroid therapy. Although blood calcium level was lower than normal it failed to reach statistically significant level. However, we did not find the calciuria significant.

Limitation of the study was that though we excluded the patients on calcium supplementation but the dietary intake of calcium and duration of sun exposure of different patients could have been different. Secondly although we aimed to measure urinary excretion but what proportion of it was due to corticosteroid therapy and what proportion was due to disease per se is difficult to demarcate. Thirdly vitamin D levels in patients at baseline and in remission were not available.

A number of studies have pointed out the presence of hypocalcemia in nephrotic patients. Dasitania et al. in their study mention that hypocalcaemia is due to hypoalbuminemia, loss of vitamin D-binding protein in the urine and the use of steroid therapy [3]. Goldstein et al. studied Vitamin D metabolites and calcium metabolism in patients with nephrotic syndrome and normal renal function and found low ionized calcium [4]. The mechanism of hypocalcaemia is not evident. It is possible that low value of 25OHD results in low blood levels of other vitamin D metabolites, such as 1, 25-dihydroxyvitamin D [l,25-(OH)2D] and 24,25-(OH)2D3; a deficiency of these compounds may cause defective intestinal absorption of calcium (α) and resistance to the calcemic action of parathyroid hormone (PTH), resulting in hypocalcaemia [4].

But what contribution did hypercalciuria have in this state of hypocalcemia is to our knowledge seldom studied. Akil et al. did find increased renal calcium excretion with usage of oral prednisolone but their comparison group was patients with bronchial hyperactivity using inhalational steroids [1]. In another study Ayi Dilla et al. did a prospective study on calcium and vitamin D supplementation in children with frequently relapsing and steroid dependent nephrotic syndrome. In their study they found that urinary calcium/creatinine ratio progressively increased [11].

A state of hypocalcemia exists in patients of nephrotic syndrome. Calcium supplementation is still not recommended in asymptomatic patients on short term steroid therapy. Since there is no significant increase in calciuria during state of proteinuria, vitamin D deficiency may be the major contributor. Whether targeted Vitamin D supplementation is required in nephrotic during phase of heavy proteinuria may be investigated in further larger studies.

Conclusion

We know nephrotic patients during state of heavy proteinuria are hypocalcemic. However urinary excretion of calcium is not significantly altered during and after the state of proteinuria.

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Funding: None

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Original Research Article

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Neonatal Outcome in Babies Born to Mothers with PROM

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Abstract

Objectives: To know the incidence of neonatal complications following premature rupture of membranes more than 12 hours.To study the incidence of early onset sepsis following premature rupture of membranes more than 12 hours. To know the incidence of mortality among neonates born to mothers with PROM more than 12 hours. To know the incidence of neonatal infection in neonates born to mothers with history of PROM more than 12 hours who have not received antibiotics before labour.

Methods: Total 185 neonates born to mother's with PROM of more than 12 hours were evaluated in this study born in Sangameshwar Teaching Hospital and Basaveshwar General and Teaching Hospital attached to M.R. Medical College, Gulbarga. Clinical features like fever, feeding difficulties and respiratory distress were commonly encountered. Laboratory investigations like total count, band count, toxic granules and baby's blood culture were used for the diagnosis of sepsis.

Results: The present prospective study includes 185 cases of neonates born to mothers with PROM of more than 12 hours duration. The incidence of PROM was 4.12%, Respiratory distress syndrome was the most commonest clinical manifestation 35 (18.91%) followed by septicemia 28 cases (15.14%) and pneumonia 3 cases (1.62%). The incidence of septicemia was 15.14%. Most common organisms isolated in blood culture of neonates were Klebsiella in 13 cases (40.6%), Staphylococcus 10 cases (31.3%), E.coli 6 cases (18.8%) and Pseudomonas 3 cases (9.4%). There was strong correlation between maternal genital flora and bacterial isolates of baby's blood culture. The incidence of neonatal deaths was 1.08% of 15.14% of early onset septicemic neonates.

Conclusion: PROM is a high risk Obstetric condition, active management is needed to enable delivery within 18 hours of PROM and it offers better neonatal outcome

Keywords: Premature rupture of membranes; Early onset septicemia; Pneumonia; Respiratory distress syndrome.

Introduction

Pre mature rupture of membranes (PROM) is defined as rupture of membranes before onset of labour. When this occur before 36 wks of gestation it is called preterm PROM [1].

Premature rupture of fetal membranes occurs in approximately 10% of all pregnancies and preterm PROM as been estimated at 3%-4.5% of all deliveries [2].

The etiology of PROM seems to be multifactorial, several predisposing factors like black race, low

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socioeconomic group, smoking, history of PROM in previous pregnancies, vaginal bleeding, multifetal pregnancy and polyhydromnios may play role in PROM [3].

The fetal and neonatal morbidity and mortality risks are significantly affected by severity of oligohydromnios, duration of latency, gestation at PROM.

The most significant maternal risk is intrauterine infection which increases with the duration of rupture of membranes.

The complication of PROM for the infants are preterm delivery, infection (pneumonia, sepsis), pulmonary hypoplasia, limb and body deformity, umblical cord compression, abruption and cord prolapse [2].

Neonatal sepsis is clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in 1st month of life.

Neonatal sepsis can be classified into two major categories depending upon the onset of symptoms.

Early onset sepsis; it presents within 72 hours of life and infants usually presents with respiratory distress and pneumonia, the source of infection is maternal genital tract and labour room [4]. Early onset sepsis occurs due to ascending infection following rupture of membranes or during passage of baby through infected birth canal [5].

The important part of PROM management is accurate assessment of gestational age, pulmonary maturity and presence or absence of sepsis.

The most common fetal morbidity associated with preterm PROM is respiratory distress syndrome and is related primary to gestational age at delivery. It may be advantageous to prolong pregnancy in order to reduce the risk of gestational age dependent morbidity.

In current scenario PROM is managed aggressively by preventing infection, delaying the delivery until fetal lung maturity and active intervention by induction of labour if longer preventable.

The knowledge of neonatal complication in relation to PROM and its effect on neonates is essential to reduce neonatal morbidity and mortality.

Diagnosis of early onset sepsis, close observation for early signs of sepsis, aggressive evaluation and early treatment has decreased the incidence of early onset sepsis associated with PROM. The present study was undertaken to evaluate newborns born to mothers with PROM for early onset sepsis. Neonatal outcome has also been evaluated in the prospective study.

Fetal and Neonatal Outcome: management of PROM has undergone intensive change in the resulting in significant alterations in the risks for morbidity and mortality in the fetus and neonate. Categories of major significance of fetal and neonatal outcome include:

a. Fetal and neonatal infections.
b. Fetal Growth.
c. Perinatal asphyxia.
d. Neonatal RDS.
e. Congenital anomalies.
f. Perinatal mortality.

Materials and Methods

This is a prospective study conducted from December 2013 to May 2015 in Sangameshwar Hospital and Basaveshwar Teaching and General Hospital, attached to M.R. Medical College, Gulbarga.

Selection of Cases

All neonates born to healthy mothers with PROM more than 12 hours during their hospital stay were studied in this study.

A detailed history was taken including age, parity, Obstetric history of the mother with emphasis on exact time of rupture of membranes, duration history and antibiotics before labour were evaluated. Detailed birth history including resuscitation details, Apgar score and gestational age assessment were evaluated.

In examination of the neonate the pulse rate, respiratory rate, CFT and temperature were noted followed by systemic examination. Required investigations are done for the neonate and followed during their hospital stay.

Inclusion criteria

All neonates born to healthy mothers with PROM more than 12 hours.

Exclusion criteria

1. Antepartum hemorrhage
2. Toxemia of pregnancy

3. Medical disease in mother other than infection.
4. Meconium aspiration syndrome.
5. Major congenital malformations.
6. Neonates with hyaline membrane disease.

Following investigations were carried out:

- Hb% was estimated by automated analyzer.
- Total leukocyte count (TLC) estimated by automated analyser.
- Differential leucoyte count (DLC) done by peripheral smear.
- Band count estimated by peripheral smear.
- Toxic granules estimated by peripheral smear.
- CRP semi quantitive estimation by latex agglutination technique.
- Blood culture and sensitivity.
- Urine analysis, urine culture and sensitivity (if required).
- Chest x-ray (if required).
- CSF analysis and head ultrasound (if required).

Cervical swab from selected mothers with PROM of more than 12 hours who have not received antibiotics before labour for culture.

The present study is undertaken to know the incidence of PROM, to know incidence of early onset septicemia and mortality among neonates born to mothers with PROM more than 12 hours and also to know the incidence of neonatal infection in neonates born to mothers with history of PROM more than 12 hours who have not received antibiotics before labour.

Results

In this study, there were 4452 pregnant women who delivered out of which 185 were complicated with premature rupture of membranes (4.155%).

Table 1: Incidence of premature of rupture of membranes

	Total number of delivery	Number of PROM	Percentage
Present study	4452	185	4.12

The total number of neonates included in this study 185. (Table 1).

Table 2: Distribution of cases according mode of delivery

Mode of delivery	Number of Cases	Percentage
Normal vaginal delivery	62	33.51%
Caesarean section	123	66.49%
Total	185	100%

This table 2 shows that 62 (33.51%) neonates are delivered by normal vaginal delivery and 123 (66.49%) were delivered by caesarean section (Fig. 1).

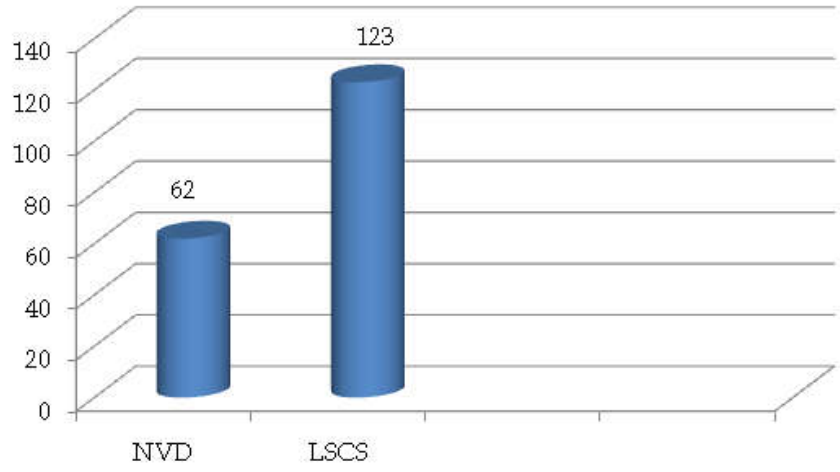

Fig. 1: Distribution of cases according mode of delivery

Table 3: Distribution according to gestational age

Gestational age	Number of Cases	Percentage
<37 weeks	55	29.73%
>37 weeks	130	70.27%
Total	185	100%

This table 3 shows that out 185 cases 55 (29.73%) were of < 37 weeks and 130 cases (70.27%) were gestational age more than 37 weeks (Fig. 2).

Table 4: Distribution of cases of according to birth weight

Weight in grams	Number of Cases	Percentage
<1500	3	1.62%
1500-2500	62	33.51%
>2500	120	64.87%
Total	185	100%

The analysis shows that out of 185 neonates 3 (1.62%) cases weighing <1500 gms, 62 (33.51%) cases were weighing between 1500 and 2500 gms and 120 cases (64.87%) weighing >2500 gms. (Table 4 and Fig. 3)

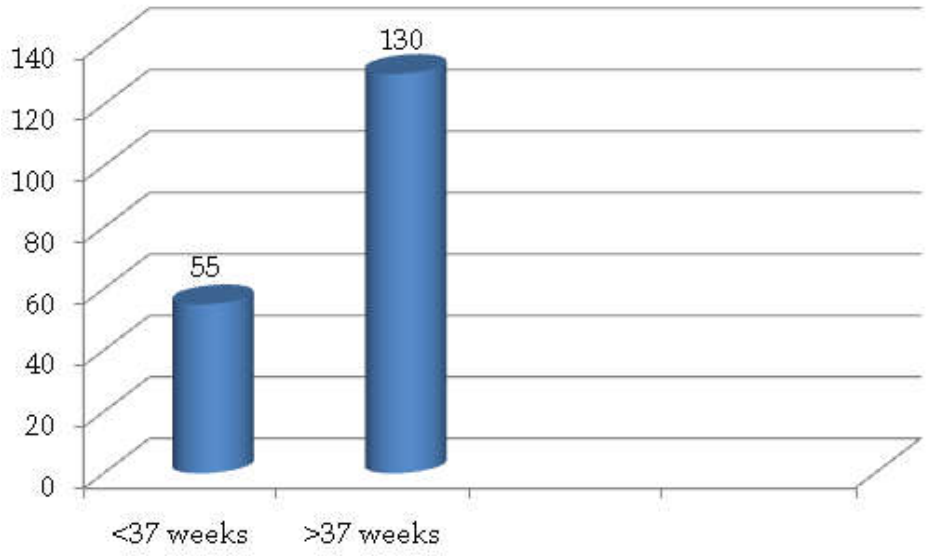

Fig. 2: Distribution according to gestational age

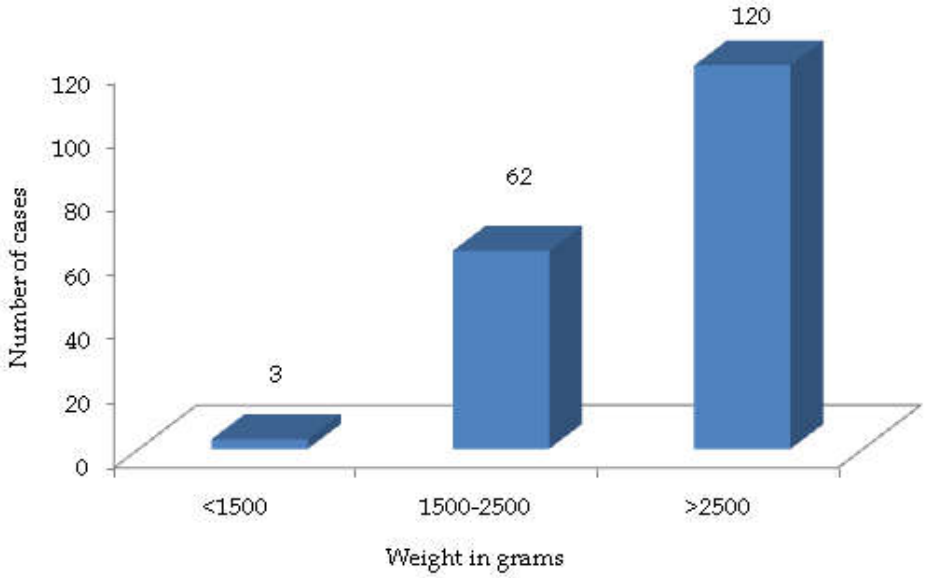

Fig. 3: Distribution of cases of according to birth weight

Table 5: Sex wise distribution of neonates

Sex	No of Cases	Percentage
Male	82	44.32%
Female	103	55.68%
Total	185	100%

The analysis of the present study shows that out of 185 neonates 82 (44.32%) were males and 103 (55.68%) were females (Table 5 and Fig. 4).

Table 6: Distribution of cases according to duration of PROM

Duration in hours	Number of Cases	Percentage
12-18 hrs	91	49.19%
18-24 hrs	40	21.62%
24-48 hrs	36	19.46%
>48 hrs	18	9.73%
Total	185	100%

The analysis shows that out of 185 mothers 91 (49.19%) had PROM of 12-18 hrs duration, 40 (21.62%) had 18-24 hrs, 36 (19.46%) had PROM 24-48 hrs and 18 (9.73%) had >48 hrs of duration (Table 6 and Fig. 5).

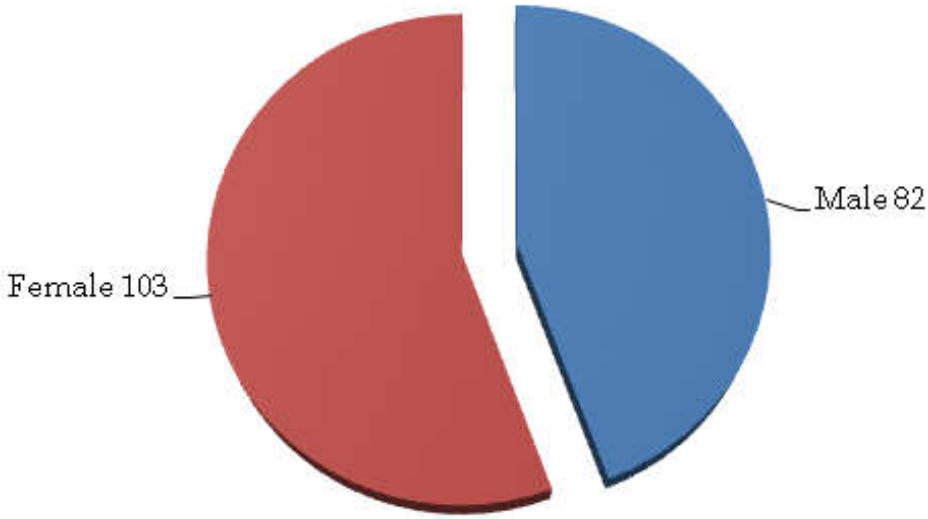

Fig. 4: Sex wise distribution of neonates

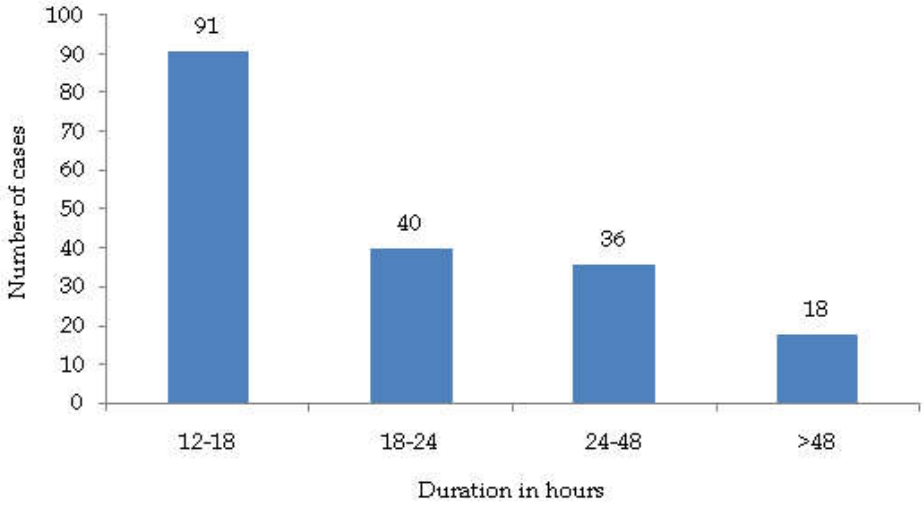

Fig. 5: Distribution of cases according to duration of PROM

Table 7: Distribution of cases according to cervical swab culture

Organisms	Number of Cases	Percentage
Klebsiella	22	11.89%
Staphylococcus	15	8.10%
E.Coli	13	7.02%
Pseudomonas	3	1.62%
No growth	132	71.35%
Total	185	100%

Cervical swab culture and sensitivity was done in all the cases with PROM. Out 185 cases 53 (28.63%) had growth on the cervical swab culture. Out of 185 cases Klebsiella was grown in 22 (11.89%) cases, Staphylococcus growth was seen in 15 (8.10%) cases, E.coli was grown in 13 (7.02%) cases and Pseudomonas was isolated in 3 cases (1.62%) (Table 7 and Fig. 6).

Table 8: Distribution of cases according to neonatal morbidity

Type of morbidity	Total cases	Percentage
R.D.S	35	18.92%
Septicemia (EOS)	28	15.14%
Pneumonia	3	1.62%
Meningitis	0	0
NEC	0	0
Asymptomatic	119	64.32%
Total	185	100%

Morbidity was seen in 66 (35.68%) out of 185 cases. This table shows that out 185 cases 35 cases (18.98%) had respiratory distress syndrome, it is the commonest morbidity in present study. The next commonest being. Septicemia (EOS) seen in 28 cases (15.14%) (Table 8 and Fig. 7).

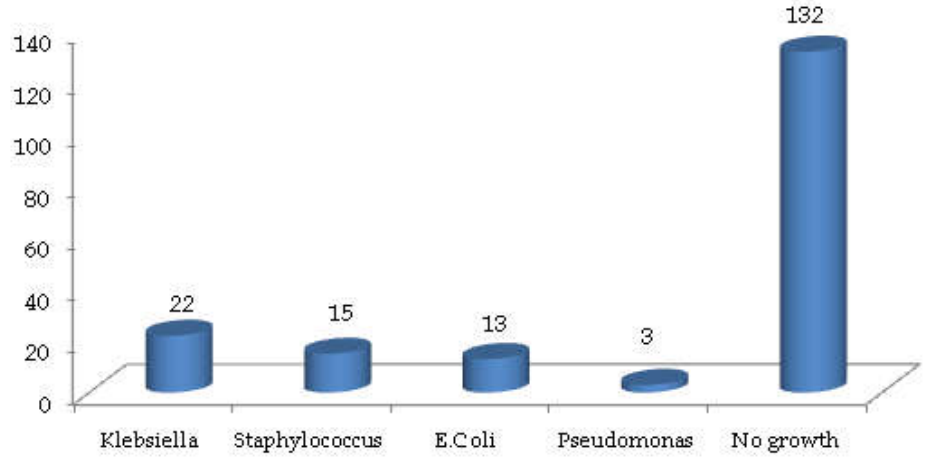

Fig. 6: Distribution of cases according to cervical swab culture

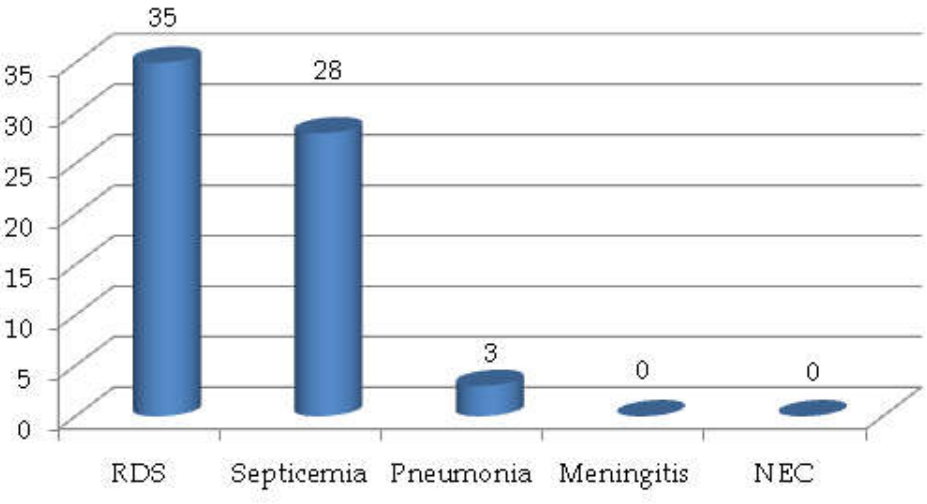

Fig. 7: Distribution of cases according to neonatal morbidity

Table 9: Distribution of cases according gestational age and neonatal morbidities

Morbidity	Gestation age in weeks			Total Cases
	< 34	34-37	> 37	
RDS	11 (5.95%)	17 (9.19%)	7 (3.78%)	35 (18.91%)
Septicemia	4 (2.16%)	10 (5.41%)	14 (7.57%)	28 (15.14%)
Pneumonia	0	1 (0.54%)	2 (1.08%)	3 (1.62%)
Meningitis	0	0	0	0
NEC	0	0	0	0
Total	15 (7.66%)	28 (15.14%)	23 (12.43%)	66 (35.68%)

Out of 185 cases 66 cases (35.68%) had morbidity. In that 66 cases (35.68%) 43 cases were born before 37 weeks. So neonatal morbidity was common in preterm babies. Out of 35 cases of RDS (18.91%), 28 cases (15.14%) were of preterm gestation. Septicemia was more common in preterm babies. X2 = 27.5, P < 0.001. There was highly significant difference in morbidity among preterm (<37 weeks) and term(>37weeks). Out of 55 cases with gestational age less than 37 weeks 43 cases (78.18%) had morbidity (Table 9 and Fig. 8).

Table 10: Neonatal morbidity in relation to duration of PROM

Complication	PROM 12-18 hrs	PROM 18-24 hrs	24-48 hours	>48 hours
RDS	00(00.00%)	20(10.81%)	05(2.70%)	10(5.41%)
Septicemia	00(00.00%)	6(3.24%)	15(8.11%)	7(3.78%)
Pneumonia	00(00.00%)	0(0.00%)	02(1.08%)	1(0.54%)
Total	00(00.00%)	26(14.05%)	22(11.89%)	18(9.73%)

This table 10 shows that as PROM increases incidence of EOS. Thus if duration of PROM is more than 24 hours, the incidence of septicemia was 11.9% as compared to 3.24% incidence when duration was less than 24 hours. But when duration of PROM was less than 24 hours R.D.S was common. X2 = 27.5, P < 0.001 highly significant. Morbidity is more in the neonates with longer duration of PROM. It is statistically significant (Fig. 9).

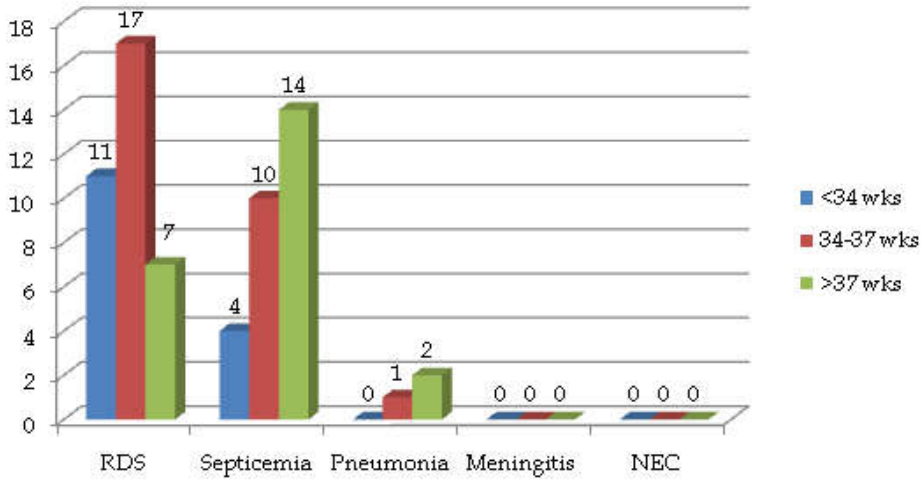

Fig. 8: Distribution of cases according gestational age and neonatal morbidities

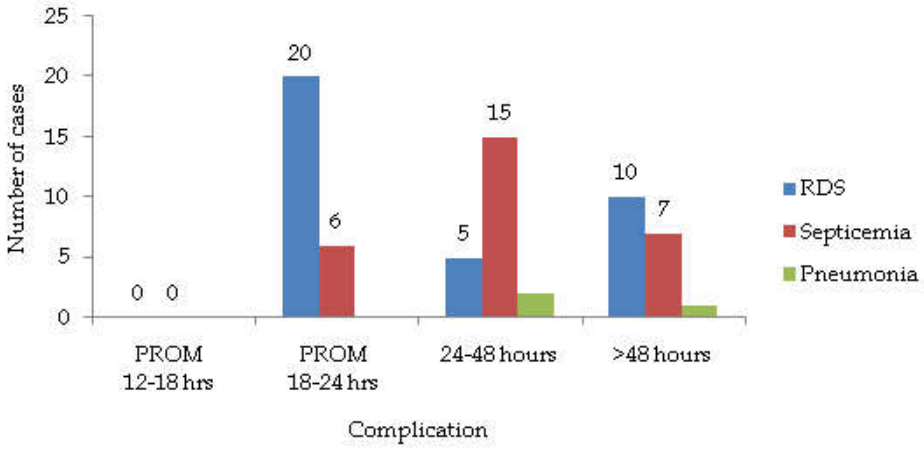

Fig. 9: Neonatal morbidity in relation to duration of PROM

Table 11: Distribution of neonatal deaths according to duration of PROM

Duration in hours	Live Cases		Deaths		Total	
	No	%	No	%	No	%
12-18	91	49.19	00	00	91	49.19
18-24	40	21.62	00	00	40	21.62
24-48	35	18.91	1	0.54	36	19.46
>48	17	9.19	1	0.54	18	9.73
Total	183	98.91	2	1.08	185	100

Analysis shows that out of 185 neonates with history of PROM two case (1.08%) died, out of which 1 case died duration of 24-48 hours and another case died duration of > 48 hours (Table 11 and Fig. 10).

Table 12: Distribution of cases in relation to leucocyte counts

Variable	Number of cases	Percentage
WBC (cells/cumm)		
<5000	17	9.19%
5000-20000	147	79.46%
> 20,000	21	11.35%
Total	185	100%

Normal WBC count was taken as a range between, 5000-20,000/cum (Steigbiggel et al.) [47]. The analysis shows that out of 185 cases 17 (9.18%) had leucopenia and Leucocytosis was observed in 21 cases (11.35%) (Table 12 and Fig. 11).

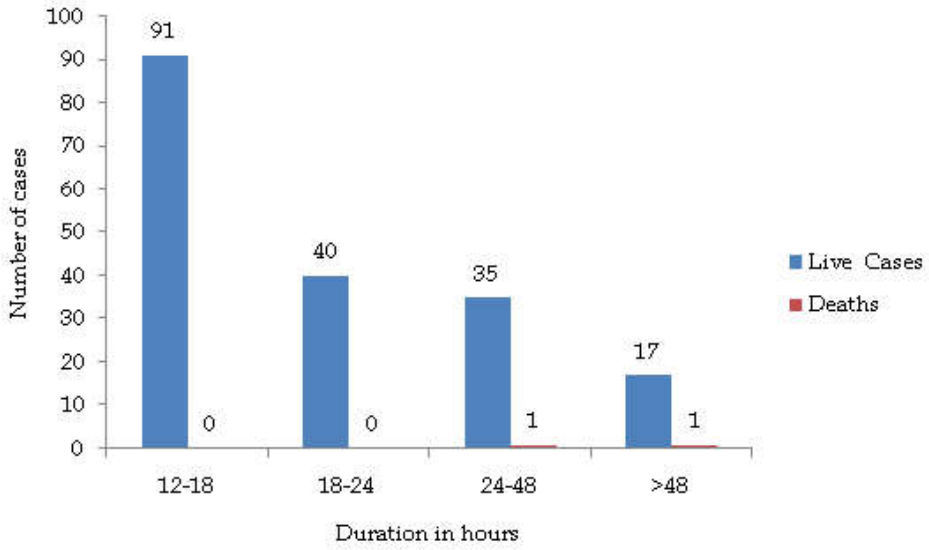

Fig. 10: Distribution of neonatal deaths according to duration of PROM

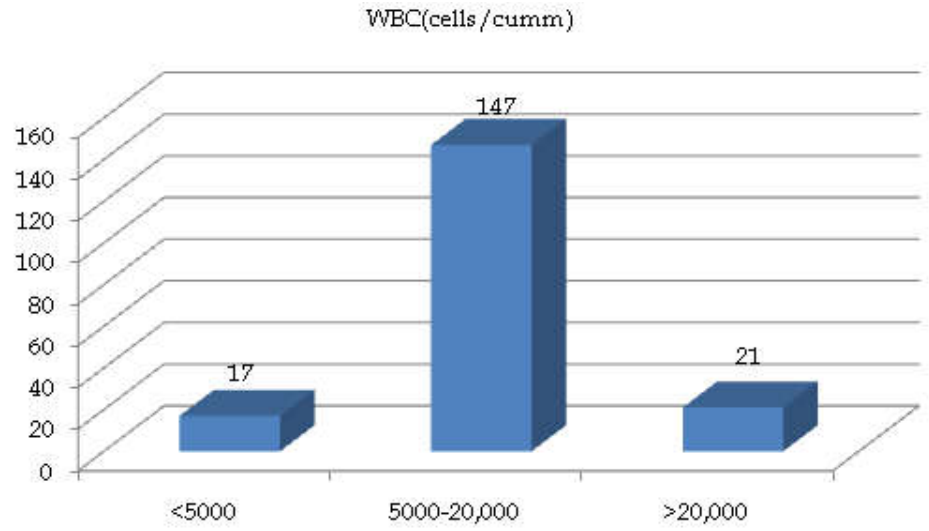

Fig. 11: Distribution of cases in relation to leucocyte counts

Table 13: Distribution of cases according to their CRP results

Variable	Number of cases	Percentage
CRP		
Positive	57	30.81%
Negative	128	69.19%
Total	185	100%

In the present study out of 185 cases C-reactive protein was positive in 57 cases (30.81%) and negative in 128 cases (69.19%) (Table 13 and Fig. 12).

Table 14: Distribution of CRP Results according to duration of PROM

Duration of PROM	CRP Positive	CRP Negative
12-18 hrs	3 (1.62%)	88 (47.57%)
18-24 hrs	11 (5.95%)	29 (15.68%)
24-48 hrs	26 (14.05%)	10 (5.41%)
>48 hrs	17 (9.19%)	1 (0.54%)
Total	57 (30.81%)	128 (69.19%)

In the present study out of 185 cases C-Reactive Protein was positive in 57 cases (30.81%), out of which CRP was positive in 3 (1.62%) cases in 12-18 hrs, 11 (5.95%) cases in 18-24 hrs, 26 (14.05%) cases in 24-48 hrs and 17 (9.19%) cases in >48 hrs (Table 14 and Fig. 13).

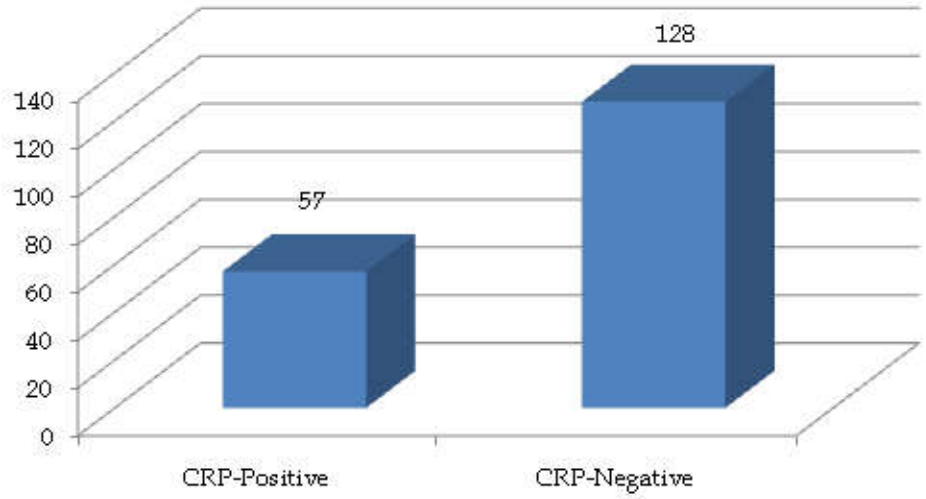

Fig. 12: Distribution of cases according to their CRP results

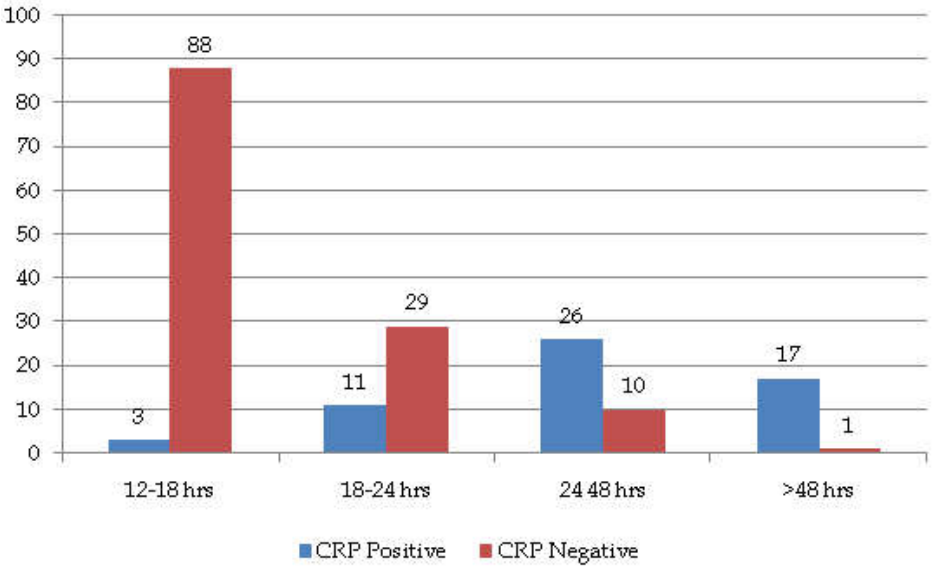

Fig. 13: Distribution of CRP results according to duration of PROM

Table 15: Distribution of cases according to their blood culture

Blood culture	Number of cases	Percentage
Positive	32	17.30%
Negative	153	82.70%
Total	185	100%

The analysis shows that out of neonates born to healthy mothers with PROM of more than 12 hours 32 cases (17.30%) had growth in blood culture (Table 15 and Fig. 14).

Table 16: Organisms isolated in blood culture

Organism	Live		Death		Total	
	No	%	No	%	No	%
Klebsiella	12	37.5	1	3.1	13	40.6
Staphylococcus	9	28.1	1	3.1	10	31.2
E.coli	6	18.8			6	18.8
Pseudomonas	3	9.4			3	9.4
Total	30	93.8	2	6.2	32	100

The analysis shows that was Klebsiella most common organism causing sepsis 13 cases (40.6%) out 32 cases. Out of 32 cases 2 (6.2%) case died due to Klebsiella and Staphylococcal septicemia (Table 16 and Fig. 15).

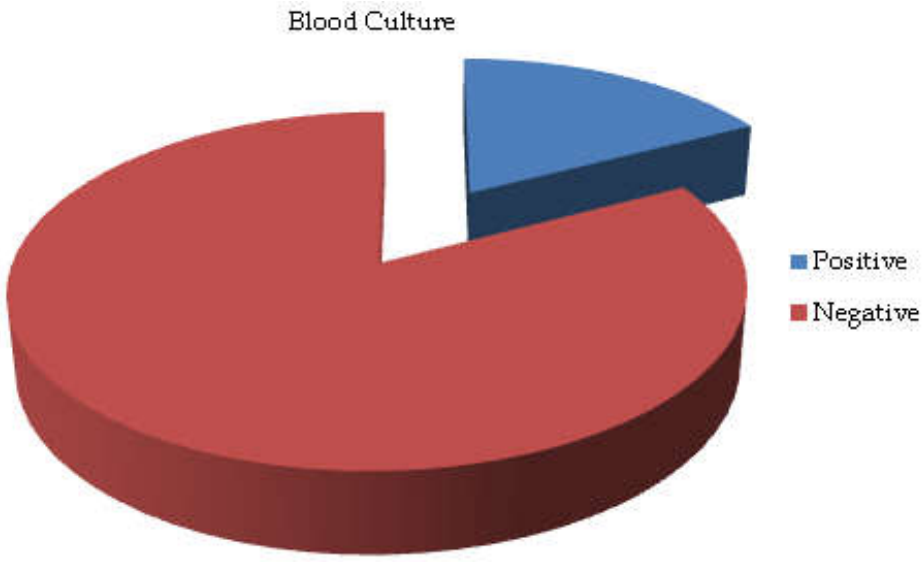

Fig. 14: Distribution of cases according to their blood culture

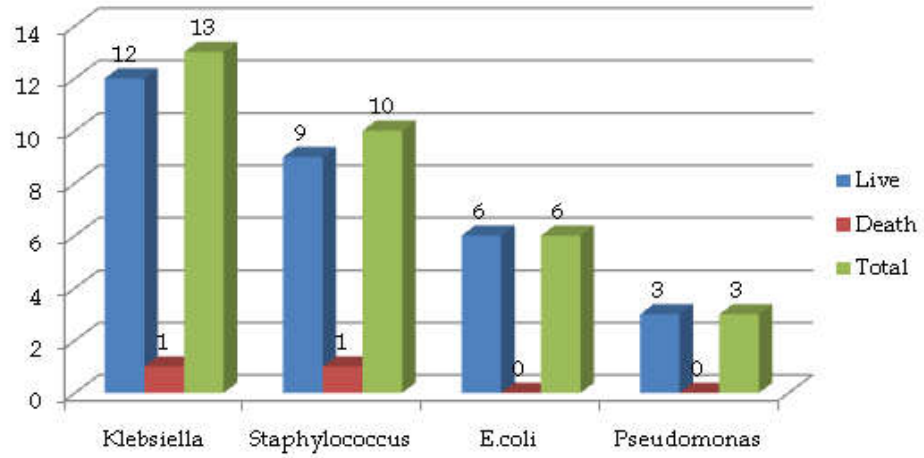

Fig. 15: Organisms isolated in blood culture

Table 17: Organisms isolated according to duration of PROM

Organisms	PROM 12-18 hrs	18-24 hrs	24-48 hrs	>48 hrs	Total
Klebsiella	0	2 (6.25%)	6 (18.75%)	5 (15.63%)	13 (40.63%)
Staphylococcus	0	2 (6.25%)	6 (18.75%)	2 (6.25%)	10 (31.25%)
E.coli	0	1 (3.13%)	3 (9.38%)	2 (6.25%)	6 (18.75%)
Pseudomonas	0	0	3 (9.38%)	0	3 (9.38%)
Total	0	5 (15.63%)	18 (56.25%)	9 (28.13%)	32 (100%)

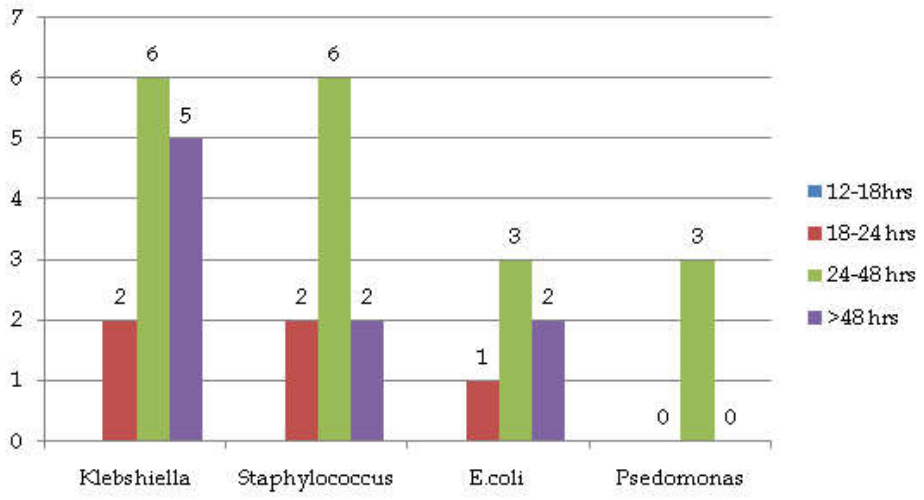

Fig. 16: Organisms isolated according to duration of PROM

The analysis shows that Klebshiella was most common organism causing sepsis and 6 cases were isolated from 24-48 hrs of duration of PROM, Staphylococcus was isolated next common organism causing sepsis and 6 cases were isolated from 24-48 hrs of duration of PROM (Table 17 and Fig. 16).

Discussion

This was a prospective study conducted from December 2013 to May 2015. The analysis of present study shows that 4452 pregnant women have delivered, out of which 185 (4.12%) were complicated with PROM.

Table 18: Incidence of Premature rupture of membranes.

	F.Nili and AA. Shams Ansari	Adentunji o Adenji and Oluse o Atanda	Present Study
Total number of delivery	2357	2340	4452
Number of PROM	163	92	185
Percentage	6.91%	3.91%	4.12%

F. Nili and AA. Shams Ansari study found the incidence of PROM was 6.91% [2]. According to Adentunji o Adenji and Oluse o Atanda [8] study found the incidence of PROM was 3.91% [60]. The present study incidence of PROM is 4.12%, which is consistent with Adentunji o Adenji and Oluse o Atanda.

Total of 185 neonates were included in this study, born in Sangameshwar Hospital and Basaveshwar General and Teaching Hospital.

Table 19: Distribution of cases according to mode of delivery

Mode of delivery	Kifah Al-Q Qa & Fatin Al-Awayshah study	Sanyal and Mukherjee study	F.Nili and AA. Shams Ansari study	Present study
Normal vaginal delivery	54%	87%	34.4%	33.51%
Caesarean section	20%	13%	65.6%	66.49%

In Sanyal and Mukherjee study 87%cases are delivered by vaginal route and 13% are delivered by LSCS [11]. F. Nili and AA.Shams Ansari study 34.4% are delivered by vaginal route and 65.6% are delivered by LSCS [2]. In the present study Caesarean section was found to be the commonest

mode of Delivery 64.49%, which is consistent with F. Nili and AA.Shams Ansari study.

Table 20: Comparison of cases according to gestational age

Gestational age in weeks	Woranart et al.	Kifah Al-Q Qa & Fatin Al-Awayshah study	Danforth	Present study
<37	42.3%	62%	30%	29.73%
>37	57.69%	38%	70%	70.27%

Kifah Al-Q Qa & Fatin Al-Awayshah study found that incidence of PROM Was more in preterm gestation [7].

According to Danforth 70% of cases of PROM occurred at term and 30% of PROM occurred at preterm [6].

The present study shows increase in incidence of PROM in term gestation. These results are consistent with Danforth [6].

Table 21: Comparison according to Birth weight

Weight in grams	Woranart et al.	Shubeck F et al.	Present study
<2500	28.84%	24.8%	35.13%
>2500	71.15%	75.2%	64.87%

Shubeck F et al. study incidence of PROM was more in babies weighing less than 2500 gms (24.8%) [9].

In the present study the incidence of PROM was more in babies weighing more than 2500 gms (64.87%) but this is due to fact that the total number of babies weighing >2500 gms were more in the sample. Similar results were observed in Woranart et al study [10].

Table 22: Comparison of Cases according to sex

Total number of cases studied	Woranart et al. (n=5, 182)	Present study (n=185)
Males	53.96%	44.32%
Females	46.04%	55.68%

In the present study out of 185 cases 44.32% were males and 55.68% were female.

Table 23: Comparison according to the duration of PROM

Duration	Muhammad Matloob Alam et al.	Priscilla Frenette et al.	Present Study
<24 hrs	63%	52.2%	70.8%
24-48 hrs	29%	28.4%	19.5%
>48 hrs	8%	19.4%	9.7%

In Muhammad Matloob Alam et al. study 63% cases had PROM of <24 hrs duration, 29% cases had PROM of 24-48 hrs and 8% cases had PROM of >48 hrs [12].

In Priscilla Frenette et al. study 52.2% % cases had PROM of <24 hrs duration, 28.4% cases had PROM of 24-48 hrs and 19.4% cases had PROM of >48 hrs [13].

In the present study 70.8% cases had PROM of <24 hrs duration, 19.5% cases had PROM of 24-48 hrs and 9.3% cases had PROM of >48 hrs, which is consistent with Muhammad Matloob Alam et al. study.

Table 24: Comparison according to cervical swab culture

Organism	Asinidi A Asindi et al.	Kodakay and Telang	Gibbs and Duff	Present study
Klebsiella	13%	11%	0	11.89%
Staphylococcus	24%	6%	0	8.10%
E. Coli	0	20%	8%	7.02%
Pseudomonas	11.3%	0	0	1.62%

Kodakay and Telang study isolated E.coli in 20% cases, Klebsiella 11% cases and Staphylococcus in 6% cases [14].

Gibbs and Duff study found growth of E.coli in 8% of cases [16].

In the present study commonest organisms isolated was Klebsiella (11.89%) followed by Staphylococcus (8.10%) and E.coli (7.02%) and Psuedomonas (1.62%).

Table 25: Comparison according to neonatal morbidity

Morbidity	Nili and AA Shams Ansari	Anjanadevi and Reddy Devi	Anjana Devi	Present study
RDS	33.3	18.3%	-	18.92%
Septicemia	5.5	53.8%	11.5%	15.14%
Pneumonia	2.5	-	5.8%	1.62%
Meningitis	0	-	2.9%	0

Anjana Devi and Reddy Devi et al. found neonatal infection in 53.8% cases and RDS in 18.3% [17].

Anjana Devi et al. found septicemia in 11.5%, pneumonia in 5.8% and meningitis in 2.9% cases [18]. In the present study RDS was seen in 18.92% cases, septicemia in 15.14% cases and pneumonia, in 1.62% cases.

Table 26: Neonatal morbidity in relation to gestation

Morbidity	Gestation in weeks	
	<37 weeks	>37 weeks
RDS	15.14%	3.78%
Septicemia	8.58%	7.57%
Pneumonia	0.54%	1.08%
Meningitis	0%	0%

Merenstein GB and Weisman LE observed that when PROM is accompanied with prematurity the incidence of proven sepsis is 4-6% [19].

In the present study neonatal morbidity was more among preterm neonates with PROM.

Table 27: Neonatal morbidity in relation to duration of PROM

Complication	<24 hrs			>24 hrs		
	Nili and sham study	Taylor study	Present study	Nili and sham study	Taylor study	Present study
Septicemia	18.4%	1.3%	3.24%	15.3%	13.3%	11.89%
Meningitis	0	0		0	0	
Pneumonia	1.2%	0	0.54%	2.5%	0	1.08%

F Nili and AA Shams Ansari observed that the risk of pneumonia and mortality were much higher in group with > 24 hrs of PROM. Taylor claimed that as latent period increased from 12 hours to more than 24 hours neonatal infection rate also increase from 1.3% to 13.3% [20]. The present study shows that complications are more as the duration of PROM increases.

Table 28: Neonatal deaths according to duration of PROM

Duration in hours	Live	Deaths
12-18 hrs	49.19%	0
18-24 hrs	21.62%	0
24-48 hrs	18.91%	0.54%
>48 hrs	9.19%	0.54%

Analysis from the present study shows that mortality in neonates born to mothers with PROM is directly related to the duration of PROM. F. Nili and A.A. Shams Ansari observed that mortality in one group with PROM <24 hrs is less than mortality in one group with PROM > 24 hours [2].

Table 29: Cases according to their leucocyte count

Variable	Kifah Al-Q Qa & Fatin Al-Awayshah study	Present study
<5000	41.7%	9.19%
5000-20000	58.3%	79.46%
>20,000	0	11.35%

Kifah Al-Q Qa & Fatin Al-Awayshah observed leucopenia in 41.7% cases and 58.3% cases had leucocyte count between 5000 – 20000 cells/cumm [7]. The present study analysis shows that 9.19% of the neonates had leucopenia Leucocytosis was observed in 11.35% cases.

Table 30: Cases according to CRP results

Variable	Kifa AlQa & Fatin Al-Awayshah study	Present study
CRP Positive	21.7	30.81%
CRP Negative	78.3	69.19%

In the present study CRP positive in 30.81% of cases. These results are consistent with observations made by Kifah AlQa Qa and Fatin Al-Awayshah in their study [7].

Table 31: Organisms isolated in Baby's blood culture

Organism	Asinidi A Asindi et al.	Shubeck et al.	Present study
Klebsiella	13%	14%	40.6%
Staphylococcus	-	50%	31.2%
E.coli	-	-	18.8%
Pseudomonas	11.3%	4%	9.4%
Coagulate negative Staphylococcus	29%	-	0

Shubeck et al. observed growth of Staphylococcus in 50% of cases followed by Klebsiella in 14% of cases and Pseudomonas in 4% of cases [9]. Asindi A Asindi et al. isolated coagulate negative Staphylococcus in 29% cases, Klebsiella in 13% and Pseudomonas in 11.3% cases [15].

In the present study Klebsiella (40.6%) was the most common organism causing sepsis followed by Staphylococcus (31.2%), E.coli (18.8%) and Pseudomonas (9.4%).

Summary

The present prospective study includes 185 cases of neonates born to mothers with PROM of more than 12 hours duration delivered in Sangameshwar Hospital and Basaveshwar General and Teaching Hospital attached to M.R. Medical College, Gulbarga from December 2013 to May 2015.

1. Incidence of PROM is 4.12%.
2. 44.32% were males and 55.68% were females.
3. 33.51% of the total neonates were born by normal vaginal delivery and 66.49% were delivered by cesarean section.
4. 49.19% of the cases had Premature rupture of membranes of 12-18 hrs duration,

21.62% cases had Premature rupture of membranes of 18-24 hrs, 19.46% Premature rupture of membranes and 9.73% cases had Premature rupture of membranes of more than 48 hr.

5. Most common organism isolated in maternal genitalia by cervical swab culture was Klebsiella (11.89%) followed by Staphylococcus (8.10%), E.coli (7.02%) and Pseudomonas (1.62%).
6. RDS was the most common clinical manifestation (18.92%) followed by septicemia (15.14%) and pneumonia 1.62%.
7. Out of 185 cases 64.32% neonates were asymptomatic and 35.68% were symptomatic.
8. Neonatal morbidity was more common in preterm babies. RDS was the Commonest clinical presentation in these babies.
9. The incidence of septicemia was 8.3%.
10. The incidence of septicemia was more in Premature rupture of membranes of longer duration.
11. The incidence of neonatal deaths was 1.08% out of 185 neonates born to mothers with PROM of more than 12 hours duration.
12. CRP was positive in 30.81% of cases.
13. Out of 185 cases 9.19% had leucopenia and 11.35% had leucocytosis.
14. Most common organisms isolated in blood culture were Klebsiella followed by, Staphylococcus E.coli and Pseudomonas.
15. There was a correlation between organisms isolated from maternal genital tract and baby's blood.

Conclusions

- Premature rupture of membranes is a high-risk Obstetric condition. Active management is needed to enable delivery within 18 hrs of premature rupture of membranes as it offers better neonatal outcome.
- Premature rupture of membranes though common in term patients, is not responsible for increased maternal and fetal morbidity and mortality in them.
- Premature rupture of membranes is responsible for increased perinatal morbidity among preterm neonates.
- Morbidity increases as the duration of premature rupture of membranes increases.
- There was a strong correlation between organisms isolated from maternal genital tract and organisms isolated from blood in babies with early onset sepsis.
- Advances in care of preterm babies may reduce the perinatal mortality following premature rupture of membranes, the ultimate solution lies in prevention of premature rupture of membranes before term.

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Outcome of Kangaroo Mother Care in Low Birth Weight Babies (Preterm/Iugr)

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Abstract

Aims and objectives: To identify changes in the specific parameters (anthropometry, hypothermia, hypoglycaemia, sepsis) of neonates receiving 'KMC". To identify feeding patterns and sleep pattern in babies receiving KMC. To determine Mother's perception during KMC.

Methods and Material: It is a prospective case study, studying the outcome of Kangaroo Mother Care given to babies (32-40 weeks), weighing 1.5-2 kg born by normal vaginal delivery in Basaveshwar and Sangameshwar Teaching and General Hospital, Gulbarga.

Results: Our study group of 150 neonates included males more than females, SGA more than AGA, late preterm more than early preterm and term neonates. Neonates body temperature significantly increased after KMC. A significant increase in respiratory rate, decrease in heart rate and increase in oxygen saturation was seen in neonates receiving KMC in our study. Our study recorded a higher proportion of neonates achieving transition from predominant expressed breast milk consumption (paladai or wati) to predominant direct breastfeeding during hospital kangaroo mother care. Also all infants were on exclusive breast feeding at follow up and on were on regular supplements. Behavioral state of the babies before and during KMC was studied using modified BRASELTON behavioral assessment scale and it found that there was increased deep quiet sleep state (80%) during KMC. The mean crying state was found to be less during KMC(4%). There was significant mean weight gain of 20 gm/day during hospital KMC and during follow up, also babies with KMC had better weekly length increment. Maternal acceptance of KMC was good and concurred with other studies. (85.3%) mothers in our study strongly agreed that KMC provides warmth to the babies. 88% mothers felt that their baby is secure and majority of them felt that baby sleeps better and that it improves the weight of the baby. All the mothers were able to practice KMC at home and no adverse events were reported. The response of the family and/or the father was supportive.

Conclusion: KMC promoted an improvement in body temperature, thereby contributing towards improvement of thermal control, decreased heart rate, increased peripheral oxygen saturation, improvement of tissue oxygenation and improved breathing rate, which brought greater respiratory comfort to the newborns. Thus, KMC promoted beneficial physiological changes for low-weight PTNBs and contributed significantly to their physiological control.

Kangaroo mother care accelerates growth pattern in LBW babies and reduces hospital stay. By promoting kangaroo mother care, exclusive breast feeding was ensured in LBW babies.

Kangaroo mother care had a protective effect on morbidities like hypothermia, sepsis and apnea. It is superior alternativeto conventional method of care in institutions with limited resources.

Keywords: Kangaroo mother care; Anthropometry; Physiological changes.

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Introduction

Some 20 million neonates are born each year, because of either preterm birth or impaired prenatal growth, mostly in less developed countries [1]. The important birth outcomes related to LBW include both neonatal death and post neonatal death, short-term morbidities such as hypothermia, hypoglycaemia, respiratory distress syndrome, infections and necrotizing enterocolitis, and long-term morbidities such as blindness, deafness, hydrocephaly, mental retardation, and cerebral palsy [2]. LBW and preterm birth are thus associated with high neonatal and infant mortality and morbidity. Of the estimated 4 million neonatal deaths, preterm and LBW babies represent more than a fifth. Therefore, the care of such infants becomes a burden for health and social systems everywhere [1].

In most countries, the use of incubators is standard for thermal care of LBW babies. However, "***incubator care***" is not widely available in developing countries, especially outside of large cities. Even in the limited cases where incubator care is available, the use of this method can be very challenging. Problems such as poor maintenance, power outages and lack of replacement parts reduce the number of available, functional incubators. In addition, excess demand resulting from too many LBW newborns and insufficient machines results in many babies sharing an incubator. This practice, along with inadequate disinfection of incubators, can lead to increased infection rates. Untrained or poorly trained health personnel or insufficient staff available on a 24-hour basis can also impact the quality of incubator care provided in these settings. Since it largely excludes the participation of the mother, incubator care can also lead to decreased breastfeeding and maternal-newborn bonding. Given the cost of incubators and the operational and programmatic challenges, making incubator care available and accessible to the majority of families of LBW babies is simply not an option in most developing countries. Fortunately, there is an alternative approach for providing thermal care for and improving survival of LBW infants that is both effective and affordable—namely, ***Kangaroo Mother Care,*** or ***KMC*** [3].

KMC method was developed in the 1970´s in Colombia by neonatologists Edgar Rey Samaria and Hector Martinez Gomez, in response to overcrowded neonatal care units. This method includes three main components: 1) skin-to-skin contact—a newborn baby is kept in a prone position between the mother's breasts several hours a day; 2) exclusive on-demand breastfeeding; and 3) early hospital discharge with appropriate follow-up [4]. In addition, the baby is colonized by the mother's commensal organisms reducing the risk of nosocomial infections especially in a hospital environment. KMC can be started after birth as soon as the baby is clinically stable, and can be continued at home until the baby is stronger and begins to wriggle out which is often around the time the baby would have been born if they had been full term [5]. The most recent definitions of KMC: 'a standardized, protocol-based care system for preterm and/or LBW infant, based on skin-to-skin contact between the preterm baby and the mother. It is a conceptually simple, elegant technique in which the role of kangaroo healthcare providers is basically to teach, coach, offer expert counselling, and closely monitor the mother infant dyad. It is not "alternative" medicine but a scientifically sound, multilevel intervention [6].

However, kangaroo mother care (KMC) is an effective way to meet baby's needs for warmth, breastfeeding, protection from infection, stimulation, safety and love [1].

In our tertiary care hospital, with 30% preterm and LBW neonates being born each year and many cases being referred from peripheral centres, care of these newborns are a challenging task. Hence this study is undertaken to evaluate role of KMC in premature and LBW neonates.

Materials and Methods

Source of Data

A prospective case study will be carried out in babies (32–40 weeks), born through normal vaginal delivery weighing between 1.5–2.0 kg born in Basaveshwar Teaching & General Hospital and Sangameshwar hospital attached to M.R. Medical College, Gulbarga.

Method of Collection of Data (including sampling procedure if any):

In this prospective case study,

Cases - Babies (32–40 weeks), born through normal vaginal delivery weighing between 1.5–2.0 kg born in Basaveshwar and Sangameshwar Teaching & General Hospital receiving KMC.

KMC group: Mothers in the KMC group will be explained in detail about KMC adoption in the presence of their family. KMC will be initiated

as soon as the baby is stable. The mothers will provide skin to skin contact using a specially tailored Kangaroo bag made of soft flannel cloth. The mothers will be encouraged to keep the baby in KMC as long as possible during the day and night with a minimum period of one to two hours at a time. When the baby is receiving intravenous fluids, mother will provide kangaroo care seated in a comfortable chair placed close to the baby's cradle. Once the baby is on full feeds, she provides kangaroo care on the reclining cot in the semi upright position with the help of pillows.

Anthropometry:

Babies will be weighed naked on an electronic weighing scale (Conweigh Electronic weighing scale - accuracy of ± 5 g) immediately after birth and subsequently daily till discharge. The weighing machines were calibrated daily with 5 g standard weight. The length will be measured at birth, on discharge and on each follow-up visit by using an infantometer.

Head circumference (HC), chest circumference (CC), and foot length will be measured by standard methods at birth, on discharge and on each follow-up visit with a non-stretchable tape. All measurements will be carried out by the same clinician.

Modified Braselton Behavioral Assessment Scale (1984) is used for the assessment of behavioral state and they are graded as follows;

Deep quiet sleep state (DQS) (score-6)- closed eyes, with no eye or body movement, little or no response to noise or stimuli Active sleep state (ASS) (score-5) -movement of extremities, stretching of limbs body, changes offacial expression, eyes closed with eye movement and started with noise ordisturbance.

Drowsy state (DS) (score-4)- eyes opened or closed and if eyes open, appearing glazed and unfocussed, quiet, startle present or slow movement of extremities.

Quiet alert state (QAS) (score-3)- eyes opened, bright and interested in their surrounding and the presence of minimal body movements.

Active alert state (score-2)(AAS)- being, fussy, restless, opened eye, movement of face, handsand legs. Crying state (score-1)(CS)- continuous cry (lusty cry), red face and presence of movement of hands and legs.

Feeding: All babies were exclusively breastfed and those unable to take direct breastfeeds were given expressed breast milk by nasogastric tube or using a pallada or sterile wati and spoon. Feeding practice were noted before KMC, at discharge and at follow up. Trained nursing assistance was provided whenever required. They were also supplemented with calcium (100 mg/kg/d), phosphorus (50 mg/kg/d) and multivitamin supplements.

Monitoring: Neonates vital parameters [temperature with clinical thermometer, respiratory rate and heart rate by clinical examination and oxygen saturation with pulse oxymeter were monitored twice a day till discharge. Babies will be monitored for hypothermia, hypoglycemia, sepsis, feeding problem and other morbidities. Babies who develop a life threatening event like convulsions, hypothermia, and severe sepsis will be considered as critically ill and will be temporarily withdrawn from the KMC group. Babies requiring phototherapy will also be temporarily withdrawn from KMC group.

Discharge and follow up: Babies will be discharged when they show a weight gain of 10-15 g/kg/d for three consecutive days, are feeding well, maintaining temperature without assistance and the mother is confident of caring for her baby. They were followed up in OPD at post menstrual age of 40 weeks in preterm babies or at chronological age of 6 weeks in term SGA babies for compliance with KMC, anthropometry and morbidity and mortality.

Mother was advised about personal care, diet, benefits of the procedure for herself and was adequately supported with KMC pouch to carry newborn. Mothers in the KMC group will be interviewed on a pre-structured questionnaire to assess the acceptability and feasibility of KMC in the hospital and at home.

Inclusion Criteria

1. Mothers availability at the time of Data collection.
2. Mothers with Low Birth – Weight babies (1.5–2.0 kg).
3. Mothers willing to participate.

Exclusion Criteria

1. Babies less than 1.5 or more than 2.0 kg.
2. Babies delivered by caesarean section requiring NICU, critically ill, ventilator care, inotropic support, with chromosomal or life threatening congenital anomalies.
3. Mothers not willing to participate.

Sample Size and Design

This is a prospective case study which will be done over a period of one and half years and a minimum of 150 babies will be taken. The number of cases may increase depending on the availability in our hospital

Statistical Methods

- Data was entered using MS Excel 2007.
- Data imported to SPSS 17.0 version software.
- Descriptive statistics was used to analyse non parametric tests. Chi square tests was used to asses significant difference between 2 groups and $p<0.05$ was considered significant.
- Student 't' test was used to compare 2 groups of continuous data. $p<0.05$ was considered significant and $p<0.001$ was considered highly significant.

Results

Table 1: Distribution of Neonates According to Sex

Sex	No	%
Male	100	66.67
Female	50	33.3
Total	150	100

Table 1 shows Male babies were more than Females.

Table 2: Distribution of Neonates According to Gestational Age and Weight Appropriatness for GA.

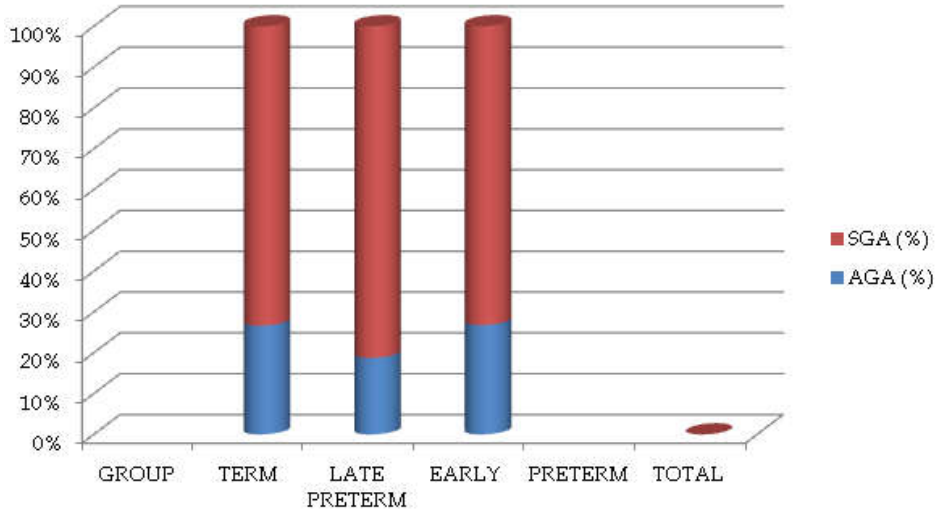
Group	AGA (%)	SGA (%)	Total (%)
Term	8	22	30 (20%)
Late Preterm	12	52	64 (42.6%)
Early Preterm	15	41	56 (37.3%)
Total	35 (23.3%)	115 (76.6%)	150

Table 2 shows in decreasing order of frequency neonates studied were late preterm, early preterm and term. SGA were more than AGA. Among SGA late preterm were majority and AGA early preterm were majority (Graph 1).

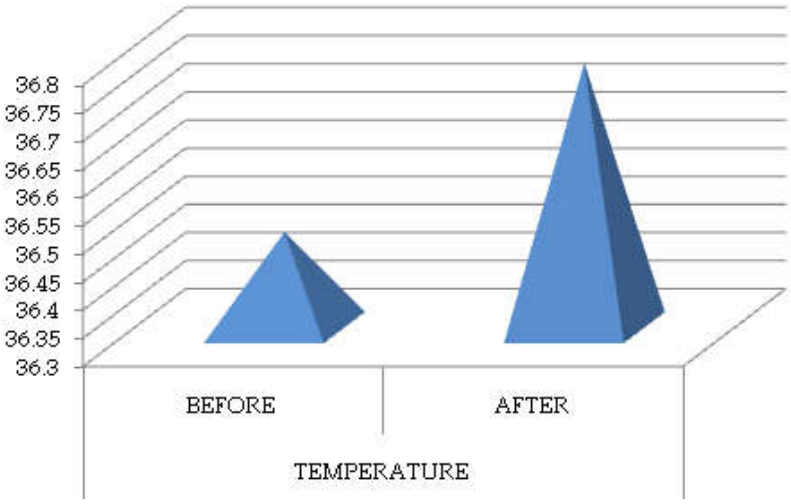
Table 3: Vitals of Neonates Before and After KMC.

Vitals		Mean	Std. Deviation
Temperature	Before	36.47	.17
	After	36.77	.24
Respiratory Rate	Before	38.24	20.91
	After	42.8	16.48
Heart Rate	Before	135.92	40.07
	After	128.57	45.78
Saturation	Before	94.92	1.44
	After	97.18	.69

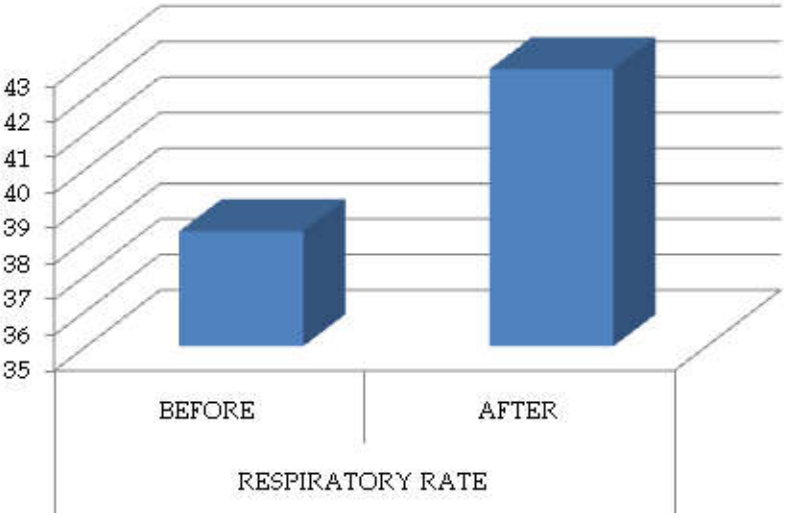
Table 3 evaluating vitals showed after KMC, newborns axilllary temperature raised by 0.280 celsius, respiratory rate increased by 5/min, heart rate decreased by 8/min, saturation increased by 2% (Graph 2-5).



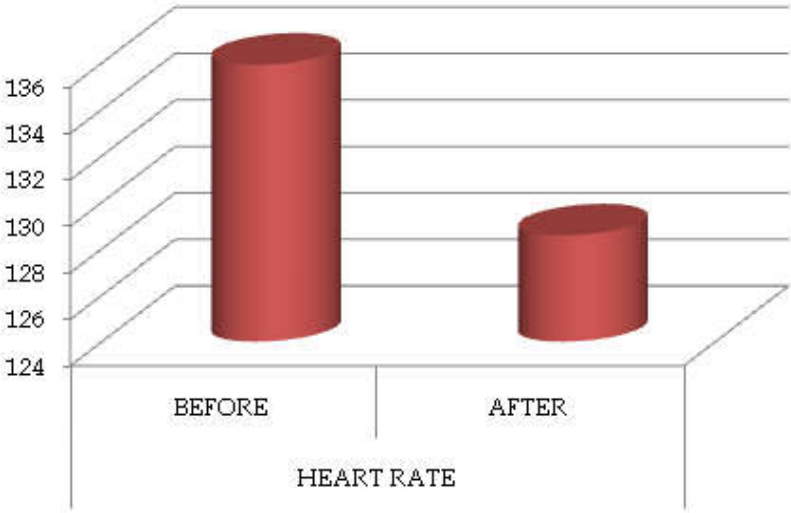
Graph 1: Distribution of Neonates According to Gestational Age and Weight Appropriatness for Gestational Age.



Graph 2: Temperature of Neonates Before and After KMC.

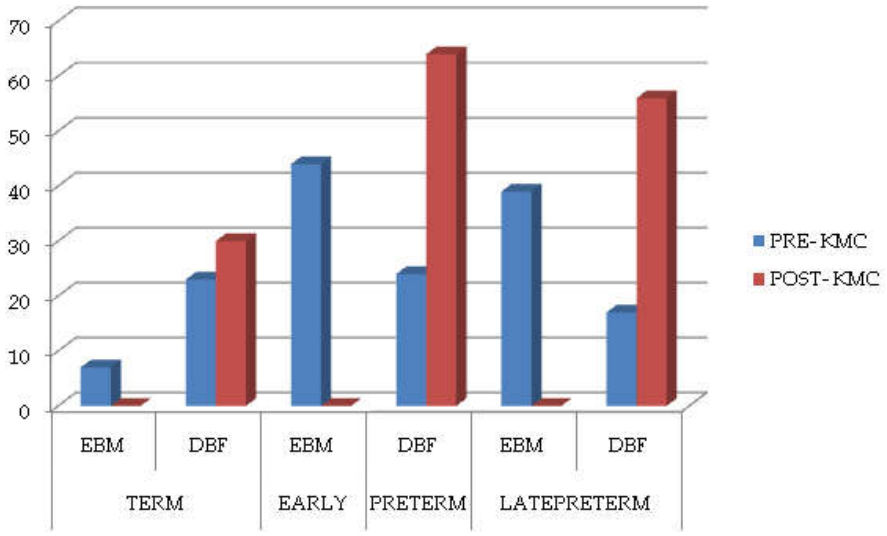


Graph 3: Respiratory Rate of Neonates Before and After KMC.



Graph 4: Heart Rate of Neonates Before and After KMC.

Graph 5: Saturation of Neonates Before and After KMC.

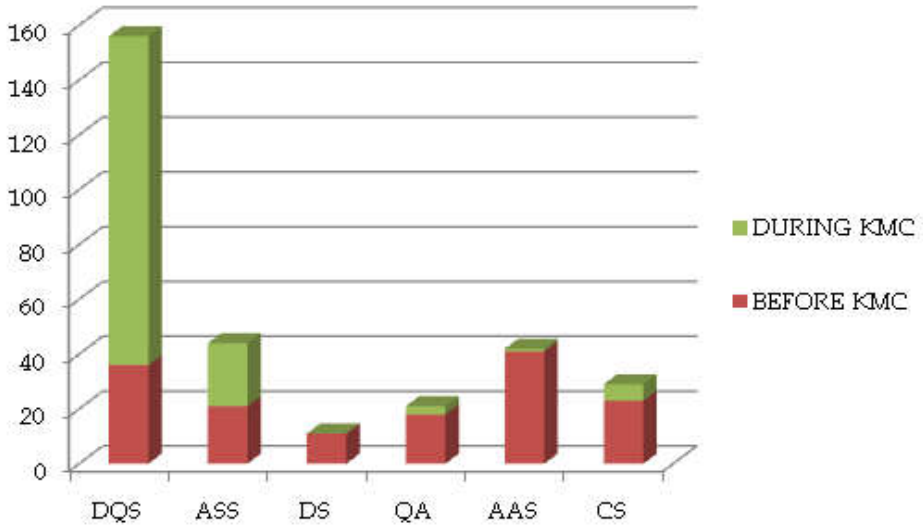


Graph 6: Feeding Method of Neonates Before and After KMC

Table 4: Feeding Method of Neonates Before and After KMC.

Group	Feeding Method	PRE- KMC	Post- KMC
Term	EBM	7	0
	DBF	23	30
Early Preterm	EBM	44	0
	DBF	24	64
Latepreterm	EBM	39	0
	DBF	17	56

Table 4 shows expressed breast milk was the predominant mode of feeding among early preterm and late preterm before KMC, which shifted to predominant direct breastfeeding after KMC (Graph 6).



Graph 7: Behavioural State of Babies During KMC

Table 5: Behavioural State of Babies During KMC

Behavioural State	DQS	ASS	DS	QA	AAS	CS
Before KMC	36 (24%)	21 (14%)	11 (7.3%)	18 (12%)	41 (27.3%)	23 (15.3%)
During KMC	120 (80%)	23 (15.3%)	0	3 (2%)	1 (.6%)	6 (4%)

Table 5 shows the computed value of behavioural state of neonates during KMC. Increased deep quiet sleep state (80%) was found during KMC. The mean crying state was found to be less during KMC (4%) (Graph 7).

Table 6: Average Weight Gain in Different Groups During Hospital KMC Stay.

	Mean	STD. Deviation	Minimum	Maximum
Term	21.94	8.61	10.00	40.00
Late Pre Term	20.58	12.09	-17.50	92.50
Early Pre Term	18.76	10.33	-20.00	70.00
Total	19.93	11.33	-20.00	92.50

Table 6 shows average weight gain during KMC stay was 21.94 g/kg/day in term, 20.58 g/kg/day in late preterm and 18.76 g/kg/day in early preterm. The average day when neonates started gaining weight irrespective of groups was 8.5 days and average weight gain irrespective of groups is 19.9 g/kg/day.

Table 7: Morbidity of Neonates Enrolled in Our Study During Hospital KMC Stay.

	No.	%
Hyperbillirubinemia	4	-
Sepsis	5	-
Apnea	1	-
Hypothermia	0	-
Hypoglycemia	2	-

Table 7 shows morbidity of neonates observed during KMC ward stay were sepsis (5), apnea (1), hypoglycemia (2) and hyperbilirubinemia in (4).

Table 8: Morbidity of Neonates Enrolled in Our Study During Follow Up.

	No.	%
Severe Infection	1	-
Poor Weight Gain	2	-
Disability	0	-
Death	1	-

Table 8 shows morbidity of neonates observed during follow-up were poor weight gain was observed in 2, severe infection in 1, and death in 1.

Table 9: Perception of Mother Regarding Effect of KMC on Baby

Variables	Strongly agree	%	Agree	%	Undecided	%	total
KMC provides warmth	128	85.3	20	13.3	2	1.3	150
Baby feels secure	132	88	18	12	-	-	150
Reduces duration of hosp stay	122	81.3	18	12	10	6.6	150
Increases wt of baby	140	93.3	10	6.6	-	-	150
Duration of sleep is increased	142	94.6	8	5.3	-	-	150

Above table 9shows that (85.3%) mothers strongly agreed that KMC provides warmth to the

babies. 88% mothers feels that their baby is secure and majority of them feel that baby sleeps better and that it improves the weight of the baby.

Above data reveals that mothers are well aware about benefits of KMC for mothers.

Discussion

Kangaroo mother care has been proposed as an alternative method for caring low birth weight neonate. The method was first implemented by Roy and Martinez in 1979 at Maternal and Child Institute of Bogota, Colombia. It consists skin to skin contact, exclusive breast feeding and early discharge.

In India since its recommendation by WHO in 2003, its implementation is poor in spite of evidence favoring KMC as observed by Lawn et al. [8]. In Karnataka, many institutes have adopted this technique of care for low birth weight babies. One such institute is Basaweshwar and Sangameshwar Teaching and General hospital.

A hospital based observational study was performed on LBW neonate fulfilling inclusion criteria and shifted to ward, attached to level 3 NICU over a period of one- year and 6 months.

Our study group of 150 neonates included males more than females, SGA more than AGA, late preterm more than early preterm and term neonates.

In our study, neonates body temperature significantly increased after KMC. This is in accordance to study performed by Dandekar RH et al. [9] Ghavane et al. [10] Gathwala G. et al. [11] and many others. Baby is in contact with warm maternal skin and receives heat from mother's breast on each sideand from her chest in front and rise in skin temperature is as a result of conductance of heat from the mother to the infant.

Placement of the infant underneath a blouse improved insulation and prevents heat loss during the maternal kangaroo care. Higher temperature in the skin-to-skin contact in the present and the earlier studies provide evidence that maternal body is an efficient heat source for the baby. Thermal control is very important for LBW neonates because of their greater tendency towards hypothermia, and it thus contributes towards homeostasis.

A significant increase in respiratory rate, decrease in heart rate and increase in oxygen saturation was seen in neonates receiving KMC in our study. Acholet et al. [17] and Kadam et al. [14] found higher oxygen saturation and reduction in respiratory rates after KMC. Ventilation and perfusion are gravity dependent, so an upright position optimizes respiratory function. Also since the newborn is calm and comfortable in contact with its mother, this probably decreases the consumption of oxygen and thus causes an increase in saturation.

Decrease in heart rate may be associated with lower stress, calmer experiences in relation to the hospital routine and calm sleep. In our study though respiratory rate increased in contrast to Acholet et al. [17] and Kadam et al. [14] it was towards normal.

Present study recorded a higher proportion of neonates achieving transition from predominant expressed breast milk consumption (paladai or wati) to predominant direct breastfeeding during hospital kangaroo mother care. This was in accordance with Rao et al. (98%) [13] and Ramnathan et al (86%) [15]. Also all infants were on exclusive breast feeding at follow up and on were on regular supplements.

In our present study, behavioral state of the babies before and during KMC was studied using modified Braselton behavioral assessment scale. We found that there was increased deep quiet sleep state (80%) during KMC. The mean crying state was found to be less during KMC (4%). This finding was in comparison to the study done by Cattaneo A. Davanzo R, and Tamburlini G.

The study showed significant mean weight gain of 20 gm/day during hospital KMC and during follow up. This is in accordance with observation made by Cattaneo et al. (21.3 gm), [17] K. Ramanathan, et al. (15.9 gm), [15] Rao et al. (23.9 gm) [13] and Gathwala et al. (21.92 gm) [11]. We found that babies with KMC had better weekly length increment. This outcome was similar to study by Rao et al. [13] The increase in physical growth more rapidly may be due to exclusive breastfeeding, temperature maintenance, physiologic stability and decreasing morbidities. In our present study babies who had received KMC had better increment in weekly head circumference. This finding was similar to observations made by Rao et al. (0.75 cm) [13] and Gathwala et al. (0.59 cm) [11].

We could not confirm when the birth weight was regained as babies were discharged earlier and many did not turn up for initial follow up., but average duration needed when weight gain began after starting KMC was 8.5 days of chronological age in all groups.

Morbidity of neonates requiring NICU admissions apart from LBW in study were hyperbilirubinemia, sepsis, respiratory illness,

hypothermia, metabolic cause, central nervous system illness. In present study the babies receiving KMC had no hypothermia, This finding was similar to Kadam et al. [14] Rao et al. [15] Also, we hardly found any sepsis (5/150) which was in comparison to the findings of Rao et al. (4/103) [15] and Syed Ali et al. (4/58) [12]. The reason accounted for it might be due to early hospital discharge resulting in decreased chances of hospital acquired infection. The episodes of apnea in <32 weeks babies in KMC group was significantly less (1/300). This finding is similar to the finding of Rao et al. (4.3%) [15] and Syed Ali et al. (1.7%) [12]. Also 2 babies had hypoglycemia and 4 developed hyperbilirubinemia, which is common complication of preterm and it was managed as per protocol.

Most of neonates were observed on follow up at Newborn OPD. The rate of weight gain was satisfactory, with only 2 babies showing poor weight gain who were admitted and evaluated. Our study recorded a higher proportion of exclusive breastfeeding during follow up among KMC infants. Charpak et al. [16] reported that the proportions of KMC mothers who breastfed up to 3 months exclusively were significantly higher on statistical analysis. Higher breastfeeding rates were also observed by Ramnathan et al. [15] Morbidity in neonates observed during follow-up were severe infection in 2 requiring hospitalization. One baby with severe infection which was re-hospitalized expired, however these causes are not just directly related to KMC. Conde-AgudeloA et al. [7] found no evidence in difference in infant mortality in KMC as compared to conventional care after stabilization.

One of the strengths of our study is the high follow-up rate among KMC infants, comparable to other studies. The better follow-up rate in the KMC group could be due to the active involvement of the mother in the care of her LBW baby or the strong rapport between the KMC mother and the health personnel. Home visit was not possible in the present study. However, the higher follow-up by KMC mothers suggests that early discharge with regular follow-up of LBW infants is definitely feasible without compromising on the health of the baby.

In the present study, maternal acceptance of KMC was good and concurred with other studies. (85.3%) mothers in our study strongly agreed that KMC provides warmth to the babies. 88% mothers felt that their baby is secure and majority of them felt that baby sleeps better and that it improves the weight of the baby. All the mothers were able to practice KMC at home and no adverse events were reported. The response of the family and/ or the father was supportive. Few mothers during hospital KMC stay were confident enough to serve as advocates for KMC and they were an important source of support for the newly enrolled mothers. This study has demonstrated that KMC is feasible in the Indian household. However, KMC was initiated in the hospital under close supervision and guidance and only later continued at home. Further research should investigate the implementation of KMC after initiation in the community.

The limitations of our study are it's an observational study, sample being purposive and not a true representative of study population. As our study is confined to our hospital setting, the generalization to community cannot be made.

Conclusion

KMC promoted an improvement in body temperature, thereby contributing towards improvement of thermal control, decreased heart rate, increased peripheral oxygen saturation, improvement of tissue oxygenation and improved breathing rate, which brought greater respiratory comfort to the newborns. Thus, KMC promoted beneficial physiological changes for low-weight PTNBs and contributed significantly to their physiological control.

Kangaroo mother care accelerates growth pattern in LBW babies and reduces hospital stay. By promoting kangaroo mother care, exclusive breast feeding was ensured in LBW babies.

Kangaroo mother care had a protective effect on morbidities like hypothermia, sepsis and apnea. It is superior alternative to conventional method of care in institutions with limited resources.

LBW neonates mothers with the following antenatal risk factors (PROM, maternal anemia, PIH, twins, APH), medical disease (hypertension, diabetes, seizure disorder and infertility) needs immediate attention. Need of antenatal visits, home delivery risks, and contraceptive awareness needs to be spread. Strict hospital policy regarding antenatal screening for pregnancy related diseases, nutritional supplementation, indications for induction of labour, and awareness about care of newborn and KMC needs to be emphasized.

Recommendations

1. KMC is an effective intervention, which

can be safely included in the management of LBW neonates in kangaroo care ward and in NICU. KMC can be implemented as alternative method where NICU is over burdened with LBW neonates.

2. Education on KMC and its benefits should be organised for nurses and primary health care workers. Education and demonstration must be provided to each mother of LBWI and they should be encourage to practice KMC.
3. The LBW neonates should strictly be monitored before initiating KMC in hospital and after early discharge for any new complications.
4. Nurses and mothers must be encouraged to follow hygiene practices necessary to avoid infections.
5. Appropriate feeding method need to individualised to each LBW neonate and trained nurses need to support mother during hospital KMC stay.
6. Morbidity associated with LBW neonates should be followed up strictly in High Risk Clinic and early interventions are taken.
7. Once KMC is accepted by health facilities and medical professionals, it will be easier to extend the approach to the community, where KMC has the potential to reach numerous LBW babies.

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Review Article

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Risk factors of Neonatal Hyperbilirubinemia

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Abstract

Jaundice is the yellowish discoloration of the sclera and the skin due to increased bilirubin levels in blood. It is often a normal condition in the neonates, but when the levels of the bilirubin exceed a certain range, it requires intervention because it can have serious neurological sequelae and may even cause death in those who survive. There are some factors which can put the baby at an increased risk of developing hyperbilirubinemia. These risk factors may be maternal or neonatal. Maternal risk factors can include any history of drugs, other comorbid conditions, ABO and Rh incompatibility, ethnicity and others. Neonatal risk factors include gestational age, infections, trauma during birth, etc.

Keywords: Jaundice; Neonatal Hyperbilirubinemia; Bilirubin levels.

Introduction

Jaundice is the most common condition in neonates that requires medical attention and hospital readmission [1]. It is the yellowish discoloration of the sclera and the skin due to increased bilirubin levels in blood. It is often a normal condition in the neonates, but when the levels of the bilirubin exceed a certain range, it requires intervention because it can have serious neurological sequelae and may even cause death in those who survive. Therefore earlier recognition and appropriate intervention is required. It is classified as physiological when it appears in the first week of life, from day 2 to day 7 of life. About 60% of term infants develop jaundice in the first week. The incidence is much higher in preterm infants, about 85%. The jaundice is said to be pathological when it appears in the first 24 hours after birth or after the first week.

Hyperbilirubinemia can be due to increased levels of unconjugated bilirubin or due to increased levels of conjugated bilirubin levels. In neonates, most often, hyperbilirubinemia is due to increased levels of unconjugated bilirubin levels. In neonates, dermal icterus is first noticed in the face and proceeds downwards towards the rest of the body

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as the bilirubin levels increase [2-3]. There are some factors which can put the baby at an increased risk of developing hyperbilirubinemia. These risk factors may be maternal or neonatal. Maternal risk factors can include any history of drugs, other comorbid conditions, ABO and Rh incompatibility, ethnicity and others. Neonatal risk factors include gestational age, infections, trauma during birth, etc.

Maternal Risk factors for hyperbilirubinemia

a. ABO incompatibility

This is a type of immunogenic jaundice in which, the mother's antibodies are transferred to the fetus causing breakdown of the fetal RBC's, leading to hyperbilirubinemia. This occurs when the mother has blood group O. The antibodies in the blood of the mother may be transferred across the placenta and can cause lysis of the fetal RBC's This is less severe than Rh incompatibility because the ABO blood group antigens are expressed in many other tissues and this reduces the chances of the antibodies binding to the RBC's of the fetus. Also the fetus expresses fewer levels of the ABO group antigens [4-5].

b. Rh incompatibility

It is a major cause of hemolytic disease of the newborn. The risk is many times more when the mother is Rh D-negative caring an Rh D-positive child. Although other forms of Rh factor like c, C, e, E can also cause haemolysis, the incidence is less common. The direct Coombs test is used to identify those fetal RBC which are already bound by the anti D antibody, whereas the indirect Coombs test is used to detect the levels of anti-D antibody in the maternal serum [6]. This can be prevented from early recognition and administration of the anti D Ig and serial monitoring of the fetus until the Rh status of the fetus can be confirmed [5-6].

c. Drugs taken by the mother

Oxytocin, bupivacaine, antenatal dexamethasone have been associated with increased risk of jaundice. 10 -13% of neonatal hyperbilirubinemia may be due to oxytocin use. These drugs can cross placenta and enter the fetal circulation. Some of these drugs can cause the bilirubin to be displaced from the albumin and increase the levels of bilirubin in the blood [7-8].

d. Ethnicity

A study conducted by Setia S et al. [9], showed that babies born to asian parents were found to have higher risk of developing jaundice when compared to their white, age and risk factors matched individuals. Asian babies were all found to have recognized gene mutations relating to hyperbilirubinemia.

e. Previous sibling with hyperbilirubinemia

A study by Khoury MJ et al. [10] mentioned that the increased risk of hyperbilirubinemia in infants with a sibling treated for the same, has a familial factor and no role of environmental factors.

f. Mode of delivery

Babies born by oxytocin induced vaginal delivery have higher bilirubin levels than those born by LSCS. Vacuum extraction is also associated with increased incidence of jaundice [7-8].

g. Maternal age

A study conducted by Srivastav et al. [11] showed that the incidence of neonatal hyperbilirubinemia was greater in younger mothers. Another study by Zhang B et al. [12] showed that the relative incidence of neonatal hyperbilirubinemia is associated with maternal age, with a peak in incidence at 26 years of age.

h. Infants of diabetic mother (IDM)

Macrosomia, commonly found in IDM, can cause increased risks of trauma during delivery and have higher rates of induced labor and Caesarean sections, these babies are also more prone to have polycythemia. These factors, by themselves, also contribute to the increased bilirubin levels. A study conducted by Peevy KJ et al. [13] showed that Large for gestational age babies born to diabetic mother were associated with higher levels of Hyperbilirubinemia when compared to appropriate for age (AGA) infants of diabetic mother and infants born to normal mothers. This was attributed by the study to an increased heme -turnover, measured by carboxyhemoglobin levels.

i. Breast feeding jaundice

Breast feeding jaundice is a preventable form of jaundice, which occurs due to caloric deficiency and or due to insufficient feeding of the neonate. It may be because the baby does not get adequate milk, does not have a good latch or is not fed frequently enough. It can also be because the breast milk has been replaced by some other substitute

or if the mother has an improper diet leading to decreased secretion. When the baby is not well fed the baby may go into dehydration and there is decreased excretion of unconjugated bilirubin from the blood, an increased eneterohepatic re-uptake of bilirubin leading to hyperbilirubinemia. Breast milk increases the movements of the bowel, helping to secrete the accumulating bilirubin, thus decreasing the incidence of jaundice. A weight loss of about 7-10%, by day 3 is an indication of inadequate breast feeding. Therefore daily weight monitoring and adequate and proper breastfeeding can reduce the incidence of breastfeeding Jaundice [5-9].

Perinatal Risk Factors for hyperbilirubinemia

a. Infections

Sepsis results in jaundice, early in the first week of life but is also accompanied by other signs of sepsis. The most common cause is Group B streptococcous, followed by E.coli and then other organisms. The underlying mechanism has been attributed to several factors including cholestasis, acidosis and increased hemolysis of RBCs. Urinary tract infections is the one of the causes of infection associated with neonatal jaundice. It presents with jaundice after the first week of life, is moderate, resembles physiological jaundice and may not require any treatment. The causative organisms can be Klebsiella, E. coli, Staphylococcus epidermidis, Staphylococcus aureus and Acineobacter. The hyperbilirubinemia is probably due to hemolysis caused by gram negative organisms [13-15].

b. Birth Trauma

Blood sequestration like haematoma, those caused due to bruising during delivery and intracranial haemorrhage can cause increase in the load of bilirubin levels in the neonate, taxing the immature liver conjugation enzymes, leading to hyperbilirubinemia.

i. Hematoma: This usually refers to extra cranial injuries that result in oedema or bleed in different regions of the scalp or skull and other regions as a result of injury received during delivery. They made be cephalohematoma, subgaelel hematoma, bruising during delivery. These injuries could be due to instrumental delivery, Cephalo-pelvic disproportion, large for gestational age (LGA) babies and breech deliveries.

ii. Intracranial haemorrhage: Subdural (SDH) and intra-parenchymal haemorrhage are more common in term infants whereas primary Subarachnoidal (SAH), intra ventricular haemorrhage (IVH) and cerebral haemorrhage are more common in preterrm infants. The risk of intracranial haemorrhage increases in neonates born from protracted or precipitous labor, instrumental delivery such as forceps, ventouse extraction, vaginal breech delivery, in primiparity [15-18].

Neonatal Risk factors for hyperbilirubinemia

a. Birth weight and gestational age

Low birth weight babies and small for gestational age babies are at high risk neonatal hyperbilirubinemia. 36-38 weeks babies are at 7-8 times high risk; babies <36 weeks are 13 times more risk for hyperbilirubinemia [16-19].

b. Gender

Male gender is a known risk factor for hyperbilirubinemia. Higher incidence of hyperbilirubinemia was found in male babies as compared to female babies which was reported by Tioseco JA et al. (17).

c. Glucose-6-phosphate dehydrogenase (G6PD) deficiency

It is an X-linked recessive disorder. The G6PD is required for the production of Nicotinamide adenine dinucleotide phosphate (NADPH) in the body. It is found in abundance in RBC and helps to combat oxidative stress. It is the only source of NADPH in the RBC's, where oxidative stress in maximum, due to their role as oxygen carriers. Therefore deficiency of this enzyme less to hemolysis of RBC's which increase during periods of oxidative stress. Neonatal jaundice is one of the earliest presentation of this disease, with a peak in jaundice during the second or the third day of life [20].

d. Pyruvate kinase deficiency

It is an autosomal recessively inherited enzyme defect. The enzyme is a part of the glycolytic pathway. This enzyme plays an important role in RBC as they produce Adenosine Triphosphate (ATP) only through anaerobic glycolysis. The deficiency of this enzymes thus leads to increased breakdown of RBC and increases the risk of hyperbilirubinemia in neonates. Few studies have been done to analyse the prevalence of pyruvate kinase deficiency in India. Kedar et al. [21] reported that the prevalence of PK deficiency in Indian neonatal jaundice cases is 3.21%, which is relatively high. All of the neonates with this deficiency presented with unconjugated

hyperbilirubinemia and reticulocytosis in the first 2 weeks.

e. Hereditary spherocytosis

It is inherited in an autosomal dominant or recessive pattern, with severity being more in the recessive pattern. In neonates with hyperbilirubinemia, an mean corpuscular hemoglobin concentration (MCHC) of 32 or greater, Mean corpuscular volume (MCV) is usually in normal range, and spherocytes on peripheral smear, should arouse a suspicion of hereditary spherocytosis. A direct Coombs test (DCT) can rule out auto-immune hemolytic anaemia and ABO incompatibility as a cause of spherocytosis. Osmotic fragility test can be done in neonates, but the RBC in neonatal period are more resistant to hemolysis, so neonatal control should be used. The definitive treatment is splenectomy [22-23].

f. Elliptocytosis

It is usually diagnosed based on the presence of oval or elliptical RBC on peripheral smear. It is usually goes undetected as it is either asymptomatic or causes moderate hyperbilirubinemia in the neonatal period, unless it is inherited with other disorders of RBC [24].

g. Conditions which decreased hepatic uptake and conjugation

i. Gilbert syndrome

It is a benign condition of the liver, in which the liver cannot properly conjugate the bilirubin due to an insufficiency of a liver enzyme known as uridine disphosphate-glucuronosyl transferase-1A1 (UGT1A1) that is coded by UGT1A1 gene, due to promoter defects that results in mis-sense mutations. This disease is usually diagnosed in adolescent, due to yellowish discoloration of the eyes and skin. It is inherited as an autosomal recessive pattern. A study conducted by Forough Sakai et al showed that the Gilbert syndrome does not in itself cause severe hyperbilirubinemia but associated with other risk factors may contribute to increased levels of bilirubin [25-26].

ii. Crigler Najjar syndrome

This is of two types, both of which are inherited in an autosomal recessive pattern. Type 1 is more predominant in infancy and can result in increased levels of bilirubin during neonatal period. It is associated with the complete deficiency of UGT1A1 activity. This reduces the UDP glucoronyl transferase activity and increases the levels of unconjugated bilirubin levels in blood. Early liver transplantation is the best treatment to prevent death and ongoing brain damage [27]. CN type 11, has reduced activity of enzymes UDP glucosenyltransferase. It may present in infancy or in adults.

iii. Pyloric stenosis

The exact mechanism of hyperbilirubinemia in hypertrophic pyloric stenosis is not known but it has been attributed to decrease in activity of hepatic glucoronyl transferase or increased activity of intestinal glucuronidase, which converts the conjugated bilirubin to the unconjugated form and increases the reuptake of bilirubin through the enterohepatic system [28].

iv. Hypothyroidism

Congenital hypothyroidism is well known cause of prolonged neonatal jaundice. The exact cause of hyperbilirubinemia in congenital hypothyroidism is not known but it has been implicated with the delayed maturation of the liver enzymes, like uridine glucoronyl transferase, cholestasis and decreased metabolism of bilirubin. It is one the causes of preventable intellectual disability [29].

h. Conditioned which increased enterohepatic reabsorption

i. Bowel obstruction

Bowel obstruction in the neonates like duodenal atresia, jejunal atresia, malrotation, iliac atresia, meconium plug, can cause biliary cholestasis and increased hepatic reuptake of bilirubin by the enterohepatic circulation. This is a type of pathological jaundice that requires surgical repair.

The conjugated form of bilirubin is converted to unconjugated forms which can be taken up into the enterohepatic circulation. The jaundice usually evolves after the defect is repaired [30].

ii. No enteric feeding

It has been found that fasting increases the levels of enterohepatic circulation by decreasing gut motility in infants. Total parental nutrition in the neonates can be a cause of cholestasis, due to decreased motility in neonates, resulting in

neonatal hyperbilirubinemia. A positive correlation has been found with the early initiation of feeding that is feeding within the first hour of life and the levels of bilirubin in blood after 24 hours [31-32].

iii. Delayed meconium passing

The delayed passage or decreased frequency of meconium makes bilirubin in meconium available for enterohepatic circulation and may increase the possibility of hyperbilirubinemia [33]. Although studies conducted to evaluate the effect of early passage of mecum on serum bilirubin levels were inconclusive.

Other factors

a. Early discharge from the hospital

Discharge from the hospital at or before 48 hours postpartum increases risk of hyperbilirubinemia development because neonates are home, not under direct medical supervision at age 3 to 5 days when bilirubin levels are most likely to peak [34-35].

b. Influence of season on bilirubin levels

In a study conducted by Bala J et al. [36], it was found that the risk of neonatal hyperbilirubinemia is more in infants born in the summer than those born in the winter. This can be associated with an increase in the ambient temperature and an increased frequency of breast feeding which can inhibit the liver enzymes and reducing the conjugation of the bilirubin in the blood.

Conclusion

Hyperbilirubinemia is one of the most common causes of hospital readmission in the neonatal age group. It has been associated with various risk factors. Severe hyperbilirubinemia can result in significant neuro-developmental damage. Early recognition of infants at risk, proper examination and follow up with timely intervention, can reduce the morbidity and mortality of hyperbilirubinemia.

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Case Report

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Epidemic Dropsy in a Single Joint Family in Uttar Pradesh: A Case Report

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Abstract

Dropsy is due to consumption of mustard oil contaminated with argemone oil. It usually occurs in epidemic outbreaks with acute manifestation of bilateral pitting edema, erythema, and local tenderness along with cardiac and respiratory problems in severe cases leading to death. We report an outbreak in a single joint family with major manifestation of bilateral pitting edema, erythema, and local tenderness in seven family members. Reported case was having serious clinical manifestation involving cardiac and respiratory systems. The diagnosis of epidemic dropsy should be strongly suspected if there is repeated clustering of bilateral pedal edema cases within a single family, especially in an area consuming mustard oil.

Keywords: Epidemic dropy; Argemone oil; Bilateral Pedal Edema; Mustard oil.

Introduction

Epidemic dropsy results from ingestion of edible oil (mustard oil) adulterated with Argemone oil [1]. It is an acute non-infectious disease characterized by pitting edema of the extremities, especially of the lower limbs; cutaneous erythema; local tenderness, vomiting, watery diarrhea, and glaucoma [2,3,4]. Dihydrosanguinarine (87%) & Sanguinarine (5%), are responsible for symptoms, Sanguinarine has been shown to produce widespread capillary dilatation coupled with increased capillary permeability, leading to edema and high cardiac output failure [1]. Diagnosis must be considered during an outbreak of bilaterally symmetric edema in more than one member of a family or community consuming mustard oil, hypoalbuminemia with normal urinalysis, raised plasma pyruvate levels [1]. Withdrawal of the contaminated cooking oil is the most important initial step in treatment, Bed rest with leg elevation and a protein-rich diet and supplementation of calcium, antioxidants (vitamin C and E) and thiamine and other vitamin B complex are commonly used. We report a sporadic case of dropsy in single Family, presenting with high output cardiac failure.

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Case Report

Eleven (11) years male child presented with swelling of whole body (starting from feet) from last 12 days, cough and fever for last 3 days and breathlessness for one day. On physical examination, child had bounding pulse, tachypnea, tachycardia, severe pallor, sub-conjunctival hemorrhage, bilateral pitting edema, cutaneous telangiectasia with red erythematous macules. Juglar Venous Pressure was raised, with pistol shot sounds over femoral &brachial artery and hepatomegaly (5 cm) and cardiac failure. Child clinical condition was progressively deteriorated and involves multi organ dysfunction syndrome (MODS). Laboratory reports showed pancytopenia, acute kidney injury and metabolic acidosis. Seven members of the family were bilateral pitting swelling over legs. All family members consumed mustard oil from a common source, mustard seeds were brought and grinded outside. We managed the child conservatively with frusomide, multivitamin, antioxidant, mechanical ventilation and vasopressors, but child expired at Day seven of admission. One of the sibling had sub-conjuctival hemorrhage (Fig. 1) and bilateral pitting pedal edema, which gradually resolved on discontinuation of mustard oil consumption. Rest of the involved family members had bilateral pitting pedal edema (Fig. 2) which gradually subsided with time. Nitric acid test was done in mustard oil sample, but it was negative (new sample was used and this test is sensitive to a concentration of >0.25%).

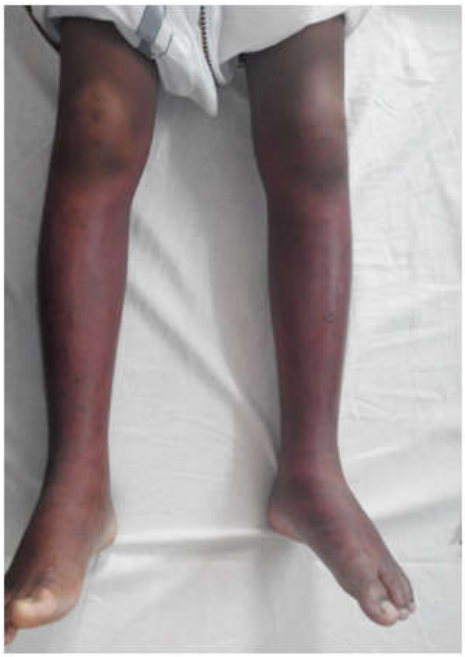

Fig. 1: Cutaneous telangiectasia with red erythematous macules in admitted child.

Fig. 2: Conjuctival hemorrhage in sister

Fig. 3: Family members with pitting pedal odema

Fig. 4: Family members with pitting pedal odema

Discussion

Epidemic dropsy is reported from time to time from states of West Bengal, Bihar, Orissa, Madhya Pradesh, Uttar Pradesh, Gujarat, Maharashtra and Delhi, generally sparing South Indian States where the predominant cooking fat is coconut oil [4,5]. The condition was first reported by Lyon in 1877 from Calcutta [6]. Dropsy is a disease that occurs in epidemics, review of scientific literature could yield only three case studies reporting outbreaks restricted to a single family, although the rest of the outbreaks affected more than one family [7,8]. In this outbreak only clustering of pedal edema was present in all the family members, one child has progressive disease due to multi system involvement and secondary infection, but major problem lies in high output cardiac failure, which was not responded to treatment. The suspicion of

dropsy in index case rests upon identification of clustering of pedal edema within family, which cannot be confirmed by detection of argemone oil in mustard oil used for cooking. Public awareness and education to farmer about argemone maxicana are key intervention to prevent dropy. Hence, the diagnosis of epidemic dropsy should be strongly suspected if there is repeated clustering of bilateral pedal edema cases within a single family, especially in an area consuming mustard oil.

Conclusion

The diagnosis of epidemic dropsy should be strongly suspected if there is repeated clustering of bilateral pedal edema cases within a single family, especially in an area consuming mustard oil. Public awareness about food adulteration act and education to farmer about argemone maxicana are key intervention to prevent dropy.

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Case Report

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Hypercalcemic Crisis, Can be Iatrogenic

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Abstract

The recommended upper limits for long term vitamin D intake are 1000 IU for children <1 year old and 2000 IU for older children and adults. Vitamin D intoxication can occur with long term high intake or with a substantial acute ingestion. Excess 25 (OH) D causes bone resorption and intestinal absorption of calcium leading to hypercalcemia. Hypercalcemia is defined as a serum calcium concentration that is greater than two standard deviations above the normal mean. Hypercalcemia is generally considered to be mild, moderate, and severe for total serum calcium concentrations <12 mg/dL (3.00 mmol/L), between 12 and 14 mg/dL (3.00 to 3.50 mmol/L), and >14 mg/dL (3.50 mmol/L), respectively. Children with vitamin D intoxication present with symptoms of hypercalcemia, such as poor appetite, weight loss, abdominal pain, vomiting, constipation, polyuria, and polydipsia, and in severe cases, life-threatening dehydration. We report a case of hypercalcemic crisis presenting in emergency department.

Keywords: Hypercalcemia; Intoxication; Vitamin-D.

Introduction

Vitamin D intoxication is a rare event, however, the exact incidence is unclear because there are no systematic studies that have addressed this question. Vitamin D intoxication from dietary sources has been reported from United Kingdom due to excessive milk fortification [1]. Excess 25 (OH) D causes bone resorption and intestinal absorption of calcium leading to hypercalcemia. Hypercalcemia is defined as a serum calcium concentration that is greater than two standard deviations above the normal mean. Hypercalcemia is generally considered to be mild, moderate, and severe for total serum calcium concentrations <12 mg/dL (3.00 mmol/L), between 12 and 14 mg/dL (3.00 to 3.50 mmol/L), and >14 mg/dL (3.50 mmol/L), respectively [2]. Children with vitamin D intoxication present with symptoms of hypercalcemia, such as poor appetite, weight loss, abdominal pain, vomiting, constipation, polyuria, and polydipsia, and in severe cases, life-threatening dehydration [3,4]. We report a case of hypercalcemic crisis presenting in emergency department.

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Case Details

A 6 yr old boy presented with fever for 2 months, vomiting and pain in abdomen for 1 month, and generalised body pain for 15 days. Child had taken treatment outside and received intramuscular injection weekly for 6 weeks. History of polyuria, polydipsia, constipation, was present and child was completely immunised. Family history of neurofibromatosis was present in mother (Fig. 1). On examination child was conscious, irritable, with cold extremities, feeble pulses, tachycardia (130/min), tachypnoea (40/min), with a BP of 80/60 mm Hg with a urine output of 6 ml/kg/hr. Head to toe examination was positive for cachexia, sunken eyes, pallor, bitots spots in bilateral eyes, angular cheilosis, multiple café-au-lait spots (>6) (Fig. 1), and bilateral lisch nodules in slit lamp examination. Anthropometry was suggestive of severe undernutrition. Systemic examination was normal except flat abdomen with dilated loops, visible peristalsis. Lab investigation reveals raised ionic calcium (2.45 mmol/l), hypercalcemia (14.9 mg/dl), hypokalemia, hypercalciuria decreased serum i PTH (2.8 pg/ml) and increased 25-OH vitamin D (374 ng/l). USG KUB was suggestive of early medullary nephrocalcinosis (Fig. 2). Bone marrow examination and X-ray chest, max, CECT abdomen were normal. Child was managed for shock and other life-threatening complications. Hypercalcemia was managed by giving 1.5 times of normal maintenance fluid 5% DNS, furosemide at 1 mg/kg/day (after normal potassium), and prednisolone at 1 mg/kg/day for 2 weeks followed by tapering over next 2 weeks. Infollow, up at 2 months child showed weight gain, and decreased 25-OH vitamin D (110 ng/l) and serum calcium (11 mg/dl).

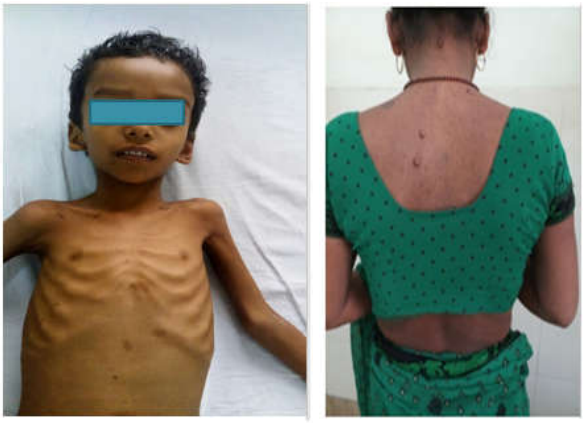

Fig. 1: Pictures of child (multiple café-au-lait spots>6) and mother (neurofibroma) with neurofibromatosis type 1.

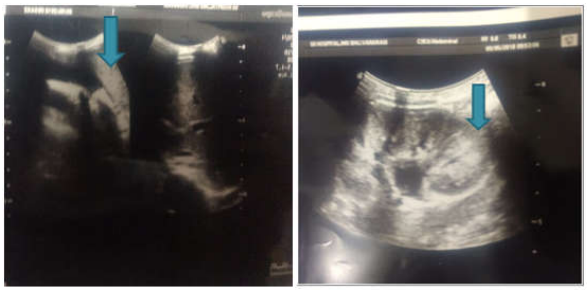

Fig. 2: Pictures of Ultrasound KUB showing features of Early Medullary Nephrocalcinosis.

Discussion

Hypervitaminosis D can occur with long term high intake or with a substantial acute ingestion. The recommended upper limits for long term vitamin D intake are 1000 IU for children <1 year old and 2000 IU for older children and adults. The diagnosis of vitamin D intoxication is based on elevated serum 25OHD concentrations, which are associated with hypercalcemia or hypercalciuria, and PTH is suppressed with evidence of nephrocalcinosis. Vitamin-D intoxication can occurs after use of over fortified formula feeds [5], or dosing errors because of parent misinterpretation of the prescribed doses [6,7]. Clinical features of intoxication manifest at or more serum levels of vitamin D (25OHD) 150 ng/dl and it because of hypercalcemia. Treatment required in case of symptomatic hypercalcemia and start with removal of source of vitamin and management of hypercalcemic crisis. The first line of therapy of hypercalcemia used in this case was hydration with normal saline at 1.5–2.5 maintenance to increase the glomerular filtration rate and calcium excretion with furosemide at 1–2 mg/kg/d, as divided doses every 4–6 hours, Thiazides should be avoided as it increases calcium reabsorption. Despite this hypercalcemia persists, we use Prednisone at 1 mg/kg/d, given as divided doses every 4 hours up to 2 weeks, then tapered over in next two weeks [8]. The response to therapy seen after 72 hours of steroid.

Conclusion

Clinical features of vitamin D intoxication manifest at or more serum levels of vitamin D (25OHD) 150 ng/dl and it because of hypercalcemia. Hypercalcemia, clinically manifests as poor appetite, weight loss, abdominal pain, vomiting, constipation, polyuria, and polydipsia, and in severe cases, life-threatening dehydration and hypovolumic shock. Hydration, and steroid were treatment options.

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