ORIGINAL RESEARCH

Risk Factors Associated with Preterm Delivery in Singleton Pregnancy in a Tertiary Care Hospital in South India: A Case Control Study

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Background: Preterm delivery is a major obstetric complication and a leading cause of neonatal mortality and morbidity. It is also associated with significant costs in terms of psychological and financial hardship, to the families.

Objective: The primary objective of this study was to determine the risk factors associated with all preterm deliveries in singleton pregnancy in a tertiary care hospital and the secondary objective was to determine the fetal outcomes among women with preterm delivery.

Materials and Methods: A case control study was conducted between January 2019 and June 2019 in the Department of Obstetrics and Gynecology of a tertiary care center in Central Kerala, India. Women who delivered before 37 completed weeks of gestation were taken as cases and those who delivered at or after 37 weeks were considered as controls in a 1:1 ratio, approximately. Data regarding 191 cases and 200 controls were taken from delivery room records of the years 2016 to 2018 with the help of a predesigned checklist. Univariate and multivariate analysis were done to determine the magnitude of association between the exposure factors and preterm delivery.

Results: The mean age of study participants among the cases was 29.3 ± 5.1 years and controls was 28.1 ± 4.4. Pregnancy induced hypertension (aOR = 14.60; 95% CI 4.8, 44.1; p<0.001), abnormal amniotic fluid volume (aOR = 10.68; 95% CI 3.46, 32.98; p<0.001), premature rupture of membranes (PROM) (aOR = 10.27; 95% CI 4.82, 21.86; p<0.001), previous history of preterm delivery (aOR = 4.12; 95% CI 1.22, 13.85; p<0.002), history of urinary tract infection (UTI) during pregnancy (aOR = 3.67; 95% CI 1.39, 9.68; p<0.002), systemic diseases (aOR = 2.78; 95% CI 1.28, 6.39; p<0.001), anaemia (aOR = 2.54; 95% CI 1.28, 5.03; p<0.004) were found to be the independent risk factors for preterm delivery. On analyzing the fetal outcomes, the average birth weight of preterm babies was 2 ± 0.6 kg compared to 3.1kg among term babies.

Conclusion: Early detection and adequate treatment of various conditions like anaemia, pregnancy induced hypertension, UTI and systemic illness can help in reduction of the prevalence of preterm delivery.

Keywords: preterm birth, risk factors, case control study, singleton pregnancy

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Introduction

Preterm delivery is defined as any birth before 37 completed weeks of gestation, ie, 259 days since the first day of a woman's last menstrual period (LMP).[1] In India, the preterm deliveries constitute 23.6%[2] of the world's total. Preterm delivery is a major obstetric emergency and also a threat to population health. In developed

countries such as the UK, preterm birth occurs in 7% to 11% of pregnancies and is responsible for 85% of neonatal deaths in normally formed infants without any congenital abnormalities.[3]

Preterm birth complications are also the leading cause of death among children under 5 years of age, responsible for approximately 1 million deaths in 2015.[1] Compared to children born at term, preterm babies have increased risk of developing disabilities like neurodevelopmental impairment, cerebral palsy, learning disabilities, and respiratory illness.[4] The economic and social costs of preterm birth is high. Most cases require neonatal intensive care and other advanced treatments, which are resource intensive.[5] The consequences of preterm birth extend beyond the newborn period into infancy, adolescence and adulthood with enormous impact.[6] There is evidence that premature children have a higher risk of respiratory illnesses with lower achieved lung growth and increased risk of type 2 diabetes, hypertension, and other chronic diseases earlier in adulthood than those born at term.[7]

Preterm births can be classified as spontaneous (due to spontaneous preterm labour or preterm prelabour rupture of membranes) or provider-initiated (caesarean or labour induction, for a maternal or foetal indication).[6] Though the pathogenesis of preterm labour is not well understood, it probably represents early idiopathic activation of the normal labour process or the results of pathological insults. Preterm labour is now thought to be a syndrome initiated by multiple mechanisms, including infection or inflammation, uteroplacental ischaemia or haemorrhage, uterine overdistension, stress, and other immunologically mediated processes.[8]

The aetiology is multifactorial and therefore all preterm births have been taken into consideration. Studies show that education of the mother, age of 36 and above, history of preterm delivery, multiparity, maternal hypertension, diabetes, oligohydramnios, polyhydramnios, placenta previa, history of organic disorder (cardiac, renal, thyroid) and blood group A have significant correlation with recurrence of premature labour.[6,9] In addition, factors such as urinary tract infections (UTI), and diabetes were reported as risk factors.[10] Further, the poor mental health of mothers such as anxiety and depression has been associated with preterm birth consistently.[11–13]

The southern state of Kerala in India has shown a downward trend of neonatal mortality, infant mortality and maternal mortality rates, at 6 per 1000 live births, 7 per 1000 live births and 43 per 100,000 live births, respectively.[14] The decline of infant mortality rates has shifted the focus now to perinatal mortality rates which is a good indicator of the quality of care for both mother and child.

Though significant advances have been made in the management of preterm delivery and related complications, focus on preventable factors have been lacking.

Therefore, identifying the risk factors associated with preterm delivery is important as this can help in early and appropriate risk-specific management. Therefore, this study intends to determine the risk factors associated with preterm delivery in a tertiary care hospital in Kerala.

Materials and Methods

This case control study was done by reviewing labour room records of women who delivered within a period of 3 years from 2016–2018, in the Department of Obstetrics and Gynecology of Amrita Institute of Medical Sciences, a tertiary care centre in Kochi, Kerala, India. The study was done with the help of a predesigned checklist created on the basis of a literature review search and finalized after discussion with experts. The study was conducted over 6 months, between January to June of 2019. Cases were defined as all singleton pregnancies who delivered before 37 completed weeks of gestation in the period between January 2016 to December 2018 and controls were defined as all deliveries at or after 37 weeks of gestation in the same period. All preterm deliveries including those for medical indications were considered.

Cases of terminated pregnancies before 22 weeks of gestation (miscarriage), still birth after 22 weeks of gestation, multiple births and intrauterine death expulsion were excluded.

Permission was obtained from the hospital administration. The hospital administration provided data after removing all personal identifiers. Ethical approval for the study was obtained from the Institutional Research Ethics Committee (IRB-AIMS-2019-267 dated November 10, 2019) of the Amrita Institute of Medical Sciences and Research Centre. As it was a record based study the informed consent from persons was waived. The study was in compliance with the Declaration of Helsinki. Following are some definitions which have been applied in the diagnosis of exposure variables in this study.

Definitions:

1. Premature rupture of membranes, is the rupture of the fetal membranes before the onset of labour. In most cases, this occurs near term, but when membrane rupture occurs before 37 weeks' gestation, it is known as

preterm PROM. Spontaneous preterm rupture of the membranes (SPROM) is ROM after or with the onset of labour occurring prior to 37 weeks. It can lead to significant perinatal morbidity, including respiratory distress syndrome, neonatal sepsis, umbilical cord prolapses, placental abruption, and fetal death.[6]

2. Gestational diabetes mellitus is a type of diabetes that can develop during pregnancy in women who do not already have diabetes. It occurs when the body cannot make enough insulin during pregnancy. During pregnancy, a pregnant mother's body makes more hormones and goes through other changes, such as weight gain. These changes cause the body's cells to use insulin less effectively, a condition called insulin resistance.[9] A fasting blood glucose level of >92 mg/dl, one hour >180 mg/dl, two hours >153 mg/dl was diagnosed as gestational diabetes.

3. Chronic hypertension. Hypertension in an adult is defined as systolic pressure of 140 mm Hg or higher and diastolic pressure of 90 mm Hg or higher. Chronic hypertension is when a pregnant woman has pre-existing hypertension, or develops it before the 20th week of pregnancy.[15]

4. Pregnancy induced hypertension. It is defined as systolic blood pressure (SBP) >140 mmHg and diastolic blood pressure (DBP) >90 mmHg. It is classified as mild (SBP 140–149 and DBP 90–99 mmHg), moderate (SBP 150–159 and DBP 100–109 mmHg) and severe (SBP≥160 and DBP≥110 mmHg).[16]

5. Abnormal amniotic fluid volume is a standardized way to assess the sufficiency of amniotic fluid quantity in pregnancy. The amniotic fluid index is used in patients who are at least 24 weeks pregnant with a singleton gestation. The uterus is divided in four quadrants and each quadrant is examined in a systematic pattern. The deepest vertical pocket of fluid in each quadrant is identified and measured. Four measurements obtained in this way is added together to calculate the total amniotic fluid index. A value ranging from 5–25 cm is considered to be a normal amniotic fluid index. More than 25 cms denotes polyhydramnios and less than 5 cms denotes oligohydramnios.[17]

6. The perinatal period commences at 22 completed weeks (154 days) of gestation and ends seven completed days after birth.[18]

7. The neonatal period begins with birth and ends 28 complete days after birth. Neonatal deaths may be subdivided into early neonatal deaths, occurring during the first seven days of life (0–6 days), and late neonatal deaths, occurring after the seventh day but before the 28th day of life (7–27 days).

8. Pregnant women with a haemoglobin level of <11 g/dL were considered anaemic.[19]

Based on the study conducted by Rao[19] et al titled "A case control study on risk factors of preterm deliveries in a secondary care hospital, South India" the prevalence of cases exposed to gestational hypertension was found to be 21.4% and controls 7.8%; OR = 3.23; with 80% power at 95% confidence. Considering the common risk factors of gestational hypertension and PROM the minimum sample size varied from 106–130 in each arm. We rounded it to 200 controls and 191 cases in a ratio of approximately 1:1.

Data Collection and Variable Definition

Data for the same was obtained from labour room records and details regarding the probable risk factors of the participants who had a preterm delivery from the years 2016–2018 such as maternal age, belonging to an urban or rural area, parity index, infertility, history of abortion, pregnancy induced hypertension, gestational diabetes mellitus, hypothyroidism, anaemia, history of preterm delivery, location of placenta, premature rupture of membranes, amniotic fluid volume, history of UTI during pregnancy, history of any other infections during pregnancy and history of other medical conditions were abstracted from the records with the aid of the pre-designed checklist. Categorization to urban/rural area was based on local address of study participants belonging to Panchayats and Municipalities/Corporations. Other details regarding the fetal birth weight, fetal presentation, NICU admission and other comorbidities of the fetus were also collected from the records. From the identified cases and controls 20 in the cases and 15 in the controls were rejected due to incomplete data such as the absence of address, incorrect hospital number, etc.

Statistical Analysis

Data was entered into MS Excel software and statistical analysis was carried out with the help of SPSS software, version 20. Using the Chi-square test the distribution of socio-demographic, maternal, medical and reproductive histories according to preterm delivery status were examined. Frequencies, means, and proportions of variables were computed. Stepwise multivariate logistic regression analysis was used to predict the independent risk factors of premature birth. Predictors at a p value <0.2 in a bivariate

analysis were included in the multivariate logistic regression model. The Nagaelker R2 was 0.453. The fit was checked with the Hosmer Lemeshow test. A P value of 0.794 shows that the given model fits the data well. Multicollinearity was checked by collinearity statistics such as tolerance and variance inflation factor. Quantitative variables such as age were compared with independent sample *t* test.

Results

The mean age of cases 29.27 ± 5.08 was significantly higher than that of the controls at 28.05 ± 4.38, (not in table). Among all the cases, 114 (59.7%) were multiparous compared to 111 (55.5%) among the controls and this difference was not significant.

Among the 191 cases, univariate analysis showed factors like pregnancy induced hypertension (PIH) (OR = 11.77; p<0.001), abnormal amniotic fluid volume (OR = 10.99; p<0.001), premature rupture of membranes (OR = 5.76; p<0.001), previous history of preterm labour (OR = 4.78; p = 0.003), presence of other systemic diseases such as bronchial asthma, chronic hypertension, cardiac abnormality and overt diabetes (OR = 4.41; p<0.001,) urinary tract infection (UTI) (OR = 3.77; p = 0.002), anaemia (OR = 2.30; p = 0.004), and gestational diabetes mellitus (OR = 1.88; p = 0.039) to be significantly associated risk factors. Factors like place of residence, parity index, history of infertility, abortion, hypothyroidism, position of placenta, vaginal infections and any other infections during pregnancy were statistically non-significant (Table 1).

After multivariate regression analysis PIH, amniotic fluid volume, premature rupture of membranes, history of previous preterm delivery, UTI, anaemia, other systemic illness such as bronchial asthma, cardiac abnormalities, gestational diabetes mellites, chronic hypertension were found to be independently associated with premature labour (Table 2).

About a fifth (19.4%) of the cases had PIH compared to 2% among the controls. After multivariate regression, women suffering from PIH, had 14.6 times higher risk of having preterm delivery than women who did not have PIH (aOR = 14.61; 95% CI 4.8, 44.1; p<0.001) which is why it is also a medical indication for intervention.

Women with extremes of amniotic fluid volume, oligo and polyhydramnios were found to have 11 times more risk of preterm delivery than women with normal amniotic fluid volume (aOR = 10.99; 95% CI 3.45, 32.97; p<0.001). The crude odds of women with premature rupture of

membrane having a preterm delivery was 5.76 which doubled to 10.26 (95% CI 4.82, 21.85; p<0.001) after multivariate regression. It was found that in women with a previous history of preterm delivery there is 4 times more risk of having preterm delivery than women who did not have previous history (aOR = 4.11; 95% CI 1.22, 13.85; p=0.002). The proportion of UTI among cases was four times more among cases at 12% compared to 3.5% in controls. After regression the adjusted odds was 3.67 (95% CI 1.39, 9.68; p=0.002).

Systemic diseases such as overt diabetes mellitus, chronic hypertension, bronchial asthma and cardiac abnormalities were documented in the records of 18.8% of cases compared to 5% of controls with a crude odds of 4.4 (p<0.001). After regression, systemic diseases continued to be an independent risk factor albeit with a reduced odds of 2.78 (95% CI 1.28, 6.39; p<0.001). A very treatable and preventable condition such as anaemia was also found to be an independent predictor increasing the risk of preterm deliveries by 2.5 times (OR = 2.54; 95% CI 1.28, 5.02; p=0.004) (Table 2). Among all the independent risk factors, PIH and other systemic diseases are medically manageable by adequate treatment at the proper time. Anaemia is eminently preventable and so is UTI by adequate intake of iron supplements, iron rich food and fluid respectively during the antenatal period.

The fit was checked using the Hosmer Lemeshow test. A p value of 0.794 shows that the given model fits the data well. Multicollinearity was also checked with collinearity statistics. All the predictors tolerance value were close to 1 and VIF<2.5 shows the absence of collinearity (Table 3).

Fetal Outcomes

The average birth weight of preterm babies was significantly lower at 2.1kg ± 0.6, compared to 3kg ± 0.4 (p<0.01) among the term babies. The fetal outcomes were also poor in the preterm group with 4 (2.1%) deaths compared to none in the control group. Among 191 preterm babies, 30 (15.7%) were in breech position, while among the 200 term babies only 4 (2%) babies were breech deliveries. More than a half (51.8%) of the preterm babies required neonatal intensive care unit (NICU) admission, while only 14 (7%) of term babies had NICU admission. About 9 (4.7%) preterm babies had intrauterine growth retardation (IUGR), whereas only 6 (3%) term babies had IUGR. Among the preterm babies, 13 (6.8%) had a cardiac abnormality, 5 (2.5%) had renal abnormalities and 5 (2.5%) had respiratory distress.

Table 1 Association of Risk Factors of Preterm Birth

Risk Factor	Group	Case		Control		OR	P- value
		Number	Percentage	Number	Percentage		
Pregnancy induced hypertension	YES NO	37 154	19.4 80	4 196	2 98	11.77	<0.001
Amniotic fluid volume	NORMAL ABNORMAL	156 35	81.7 18.3	196 4	98 2	10.99	<0.001
Premature rupture of membranes	YES NO	48 143	25.1 74.9	11 189	5.5 94.5	5.76	<0.001
History of previous preterm delivery	YES NO	17 174	8.9 91.1	4 196	2 98	4.78	0.003
Other systemic diseases	YES NO	36 155	18.8 81.2	10 190	5 95	4.41	<0.001
Urinary tract infection	YES NO	23 168	12 88	7 193	3.5 96.5	3.77	0.002
Anaemia	YES NO	39 152	20.4 96.6	20 180	10 90	2.31	0.004
Gestational diabetes mellitus	YES NO	33 158	17.3 82.7	20 180	10 90	1.88	0.039
Area of residence	Rural Urban	62 129	32.5 67.5	54 146	27 73	0.77	0.268
Parity	PRIMI MULTI	77 114	40.3 59.7	89 111	44.5 55.5	1.18	0.415
Infertility	YES NO	23 168	12.0 88	23 177	11.5 88.5	1.05	0.877
History of abortion	YES NO	47 144	24.6 75.4	35 165	17.5 82.5	1.54	0.106
Hypothyroid	YES NO	33 158	17.3 82.7	21 179	10.5 89.5	1.78	0.057
Placenta	NORMAL ABNORMAL	186 5	97.4 2.6	199 1	99.5 0.5	5.35	0.197
Vaginal infection	YES NO	7 184	3.7 96.3	4 196	2 98	1.86	0.371
Other infection	YES NO	15 176	7.9 92.1	11 189	5.5 94.5	1.46	0.419

Discussion

Our study was done with the purpose of finding out the risk factors associated with preterm labour in a state with low neonatal mortality rate and good indices of maternal and child health care. The current study shows that pregnancy induced hypertension (PIH), abnormal amniotic fluid volume, premature rupture of membranes, a history of previous preterm delivery, a history of urinary tract infections during pregnancy, systemic illness like bronchial asthma, cardiac abnormalities, anaemia, overt diabetes mellitus and chronic hypertension are independent risk factors for preterm labour. Though the precise mechanism of preterm birth is not known in many cases, the factors associated with preterm birth but not in the causal pathway can be used to explain preterm birth.[5]

Table 2 Independent Risk Factors of Preterm Birth

Risk Factors	Multivariate OR	95% CI	P value
Pregnancy induced hypertension	14.61	4.838–44.105	<0.001
Amniotic fluid volume	10.67	3.458–32.979	<0.001
Premature rupture of membrane	10.27	4.824–21.859	<0.001
History of previous preterm delivery	4.12	1.224–13.853	0.002
Urinary tract infection	3.67	1.390–9.682	0.002
Other systemic diseases	2.78	1.28–6.395	<0.001
Anaemia	2.54	1.281–5.026	0.004

Table 3 Collinearity Statistics

Model	Collinearity Statistics	
	Tolerance	VIF
AGE	0.866	1.154
PREMAT RUP	0.965	1.037
H/O ABORTION	0.939	1.065
PIH	0.907	1.102
GDM	0.902	1.108
HYPT	0.965	1.036
ANAEMIA	0.981	1.019
H/O PRETM	0.932	1.072
AF VOL	0.944	1.059
UTI	0.965	1.036
Other disease	0.914	1.094
MODE OF DELIVERY	0.881	1.135

In the present study the mean maternal age is 29±5.08 yrs which is comparable with a study in central Kerala[20] where 42.6% of the women with preterm delivery were in the 26 to 30 years age group and in the north Indian state of Punjab where the mean age was 24.67±4.08 years.[21]

About 12% (aOR: 3.67; 95% CI 1.3, 9.6) of the women with preterm delivery had UTI, which was comparable to that in the northern Indian state of Punjab at 13%.[22] However, some studies in Kerala and Haryana have reported UTI at double the proportion at 30% to 34%.[20,23] The spontaneous preterm births are largely due to PPROM and in a hospital-based study in Uttar Pradesh[24] 39% of the patients with PPROM were found to have a UTI infection. UTI when diagnosed early and treated adequately can prevent preterm delivery. Preventive habits such as adequate fluid intake and maintaining personal hygiene should also be an essential part of the antenatal advice.

Premature rupture of membranes is a common risk factor for preterm delivery. In our study 25.1% of the cases had premature membrane rupture, which is comparable with the other studies where it varied between a fourth to a fifth.[22,25] Special attention and conservative management of women with risk factors of premature rupture of membranes like history of abortion, previous PROM can also be beneficial.

PIH was the commonest obstetric risk factor in the study in Karnataka[19] with more than a fifth, 21.4% of the women with preterm delivery having PIH. In our study also PIH occurred among a fifth of the women (19.4%) with preterm labour, in concordance with the previous studies.[19,24] In a study from Bangalore hypertensive disorders were the commonest risk factor at 32.9% whereas in Uttar Pradesh it was much lower at (18.6%) corresponding to the lower levels of hypertension in the community.[23,24] Early detection and adequate treatment of pregnancy induced hypertension is critical as those with PIH are 15 times (95% CI: 4.8–44.1) more likely to have premature delivery resulting in poor outcomes. Uncontrolled PIH can also be an indication for early intervention.

Extremes in amniotic fluid – oligohydramnios and polyhydramnios were found to be associated with preterm delivery.[5] In this study too we found that 18.3% of the women with preterm delivery had abnormal amniotic fluid volume, though the study conducted by Chythra et al[19] in

the neighbouring state did not find any association. In another study in Bangalore only 9.7% with extremes of amniotic fluid had preterm birth.[25]

In a study by Kusum et al[22] about a half (48%) of subjects were found to be anaemic compared to about a fifth in this study. We also found that anaemic women were three times more prone to have preterm delivery. The lower levels of anaemic patients may be due to the better antenatal care and higher awareness in the state. Other studies across the world have also shown that low nutritional status as indicated by low BMI[26–28] and low levels of folate[27] can lead to preterm birth. Low concentrations of minerals such as iron are associated with decreased blood flow and increased maternal infections.[28,29] In fact, eating disorders during pregnancy have been associated with preterm birth in 36% of studies in a review article.[30] Anaemia can be prevented by adequate maternal nourishment during the period of gestation and by the provision of prophylactic iron doses for 100 days through the iron deficiency anaemia prevention program of the Govt of India.[31] The importance of adherence to intake of iron and folic should also be stressed to the antenatal women.

The average birth weight of preterm babies is 2.1 ± 0.6 kg, while that of term babies are 3±0.4 kg. Out of the 191 preterm babies, 4 (2.1%) died and 51.8% required NICU admissions. Among the preterm babies, 13 (6.8%) had a cardiac abnormality, 5 (2.6%) babies had renal abnormalities, 5 (2.5%) had respiratory distress and 9 (4.7%) had IUGR. In a similar study in Bangalore, the neonatal mortality was 6.9% and the NICU admissions was 66.5%.[25] The NICU admissions were either for observation for prematurity and various other complications like perinatal asphyxia, respiratory distress syndrome and sepsis. Thus, identifying women at risk of preterm labour and their proper treatment and care can reduce poor outcomes.

Strengths of the study include the fact that factors like confounding were addressed by doing a multivariate analysis and strong association was found with risk factors like PIH (14.608), AF volume (10.679) and PROM (10.269), followed by a history of previous preterm delivery (4.118), UTI (3.669) and anaemia (2.537). Collinearity has also been ruled out among the independent variables. High p values rule out the possibility of it being due to chance.

Some of the limitations of the study include the possibility of selection bias. The study was conducted in a hospital setting and may not be representative of the entire population of women with preterm delivery in Kerala. However, as the study is done in the state of Kerala where 99% of the deliveries are institutional the study can be considered to be representative of the population.[32] About 9.09% and 13.5% of records each of cases and controls was discarded as these records did not have the correct hospital registration number or address of the patients mentioned. Since it was a record-based study, the information on BMI, maternal education, and economic background were not available. Hence these variables were not included in the study. Non-obstetrical risk factors like maternal malnutrition, SES, trauma, alcohol use, exposure to second hand smoking, physical activity, and depression were not looked into as the data was obtained from hospital records. Another limitation is that, though there are studies in other parts of the world where air pollution such as the presence of sulfur dioxide is associated with adverse birth outcomes,[33] it could not be considered due to lack of data. Measurement of exposure variables such as anaemia was made based on the Hb values recorded in the first trimester which may have improved, thus overestimating effect.

Conclusion

Addressing the burden of preterm birth is crucial to achieving Sustainable Development Goal 3 and for reducing preterm-related neonatal and child mortality.[34] Most efforts so far have been focussed on tertiary interventions. These measures have reduced perinatal morbidity and mortality, but the incidence of preterm birth is increasing. The clinical implications for this are that advances in primary and secondary care are necessary such as preventing anaemia, UTI and controlling blood pressure through adequate medication.[35] Women with systemic diseases require additional care to prevent the risk of preterm birth.

Acknowledgment

Author Contributions

1. Raveena PS – Concept, Data Collection, and Implementation of the study.
2. Parvathy A – Concept, Data Collection, and Implementation of the study.
3. Neelanjana A – Concept, Data Collection, and Implementation of the study.
4. Sudha S – Guidance in Concept, Data Collection, and Implementation of the study.

5. Steffi Ann Varughese – Editing and analysis of the draft manuscript.
6. *Aswathy Sreedevi – Concept development, Analysis and Editing the draft manuscript.
7. Sheejamol S – Analysis and Statistical guidance.

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that there are no conflicts of interests in relation to this work.

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