



## ASSOCIATION OF MATERNAL DYSLIPIDEMIA AND RISK OF PRETERM BIRTHS IN RURAL TERTIARY HEALTH CARE CENTRE: A PROSPECTIVE OBSERVATIONAL STUDY

**Dr. Rashmi Haswani\***

Junior Resident, Department of Obstetrics and Gynaecology, MGIMS and KHS Sewagram, Maharashtra\*Corresponding Author

**Dr. Poonam Varma Shivkumar**

Director Professor, Department of Obstetrics and Gynaecology, Medical Superintendent KHS Sewagram, Maharashtra

**Dr. Heena Kauser**

Junior Resident, Department of Obstetrics and Gynaecology, MGIMS and KHS Sewagram, Maharashtra

### ABSTRACT

**Background:** Maternal hyperlipidemia is common and consistent metabolic alteration in pregnancy. Associations between maternal lipid levels during pregnancy and risk for preterm birth have been found, although the lipid components and magnitude of associations have been inconsistent across studies. Therefore, the present study aim to evaluate the relationship of elevated triglycerides and cholesterol on the risk of preterm labor. **Material and Methods:** The present study was prospective observational study conducted during July 2021 to November 2022. A total sample size of 255 primigravida with Gestational age between 16-20 weeks confirmed by USG without any obstetrics complications were included. The study was conducted after obtaining clearance from the Ethical Committee of the institute. Any variation from normal lipid profile values was considered as dyslipidemia. Lipid profile of study subject was sent in 2nd trimester between 16 – 20 weeks. The maternal and fetal complications were recorded for these women. Data were double entered using Microsoft excel 2016 and analyzed using SPSS version 22. **Results:** the incidence of dyslipidemia at time of registration was 38.43% and 54.11% at the time of admission among patients. The statistically significant difference was seen in the women with altered lipid profile who delivered preterm (77.27%) compared to the women who delivered at term (46.03%) Patients with preterm delivery had more fetal complications and dyslipidemia as compared to term delivery with statistically significant difference. **Conclusion:** Dyslipidemia is a potential contributor to the pathogenesis of preterm delivery during pregnancy and may be used as a marker of elevated risk for preterm birth.

**KEYWORDS :** Maternal Dyslipidemia, Risk, Preterm, Rural

### INTRODUCTION:

According to the World Health Organization (WHO) Preterm delivery is defined as the delivery of an infant before the completion of 37 weeks (259 days) of gestation.<sup>1</sup> The important outcome of preterm delivery is a premature infant, which is the most common cause of infant mortality after the congenital abnormalities.<sup>2</sup> There are 3.6 millions per year neonatal deaths around the world, out of which 99% deaths are contributed by the developing countries.<sup>3</sup>

In recent time several research literatures is available for identifying beyond the accepted factors what are the reasons for having preterm birth. One of the factors identified is dyslipidaemia which includes changes in various lipoproteins.<sup>4</sup>

Associations between maternal lipid levels during pregnancy and risk for preterm birth have been found, although the lipid components and magnitude of associations have been inconsistent across studies.<sup>5,6</sup>

Maternal hyperlipidemia is common and consistent metabolic alteration in pregnancy. Plasma triglycerides and cholesterol may increase by 150% to 300% and 25% to 50% respectively.<sup>7-9</sup> Atherosclerosis of utero placental spiral arteries and the vital placental arteries combined with hypercoagulation may result in thrombosis and placental infarctions, which lead to placental insufficiency and hence fetal compromise.<sup>10</sup> This fetal compromise is in the form of preterm delivery.

In several studies, both high and low HDL, LDL, TG, and TC levels almost doubled the risk of spontaneous preterm delivery.<sup>11</sup> Some studies, on the other hand, have used maternal serum screening and rejected any relationship between the highest/lowest lipid levels and preterm labour.<sup>12</sup>

The influence of elevated maternal triglycerides and cholesterol has not been extensively studied. As elevated circulating levels of triglycerides and cholesterol are markers for increased risk of preterm labor in pregnant women. Therefore, the present study was conducted to evaluate the relationship of elevated triglycerides and cholesterol on the risk of preterm labor.

### OBJECTIVES:

- To study association of maternal dyslipidaemia and risk of preterm

births in rural tertiary health care centre.

### MATERIALS AND METHODOLOGY:

The present study was prospective observational study conducted at Outpatient department, maternity ward and Labour room of Maternal and Child health wing of rural tertiary health care centre. All Primigravida women willing to participate in the study fulfilling inclusion and exclusion criteria and who give consent to be a part of the study from July 2021 to November 2022 were the study subjects. The study was conducted after obtaining clearance from the Ethical Committee of the institute. A total sample size of 255 primigravida with Gestational age between 16-20 weeks confirmed by USG without any obstetrics complications were included.

Multigravida women, primigravida women with history of smoking, history of preterm births, medical complications like Cardiovascular disorder, Renal disorders; obstetrics complications like Gestational Diabetes Mellitus, Hypertensive disease of pregnancy, Cervical incompetence, Hydramnios, Multiple pregnancy and other causes for preterm births and patients who do not give consent were excluded from the study.

Any variation from normal lipid profile values was considered as dyslipidemia. (Serum cholesterol < 200mg/dl; Serum triglyceride: 10-150 mg/dl; Serum HDL: 40- 60 mg/dl; Serum IDL: 70- 130 mg/dl and Serum VLDL < 30 mg/dl)

The demographic factors were recorded, detailed history was taken and clinical examination- general, systemic and abdominal examination was done as per the departmental protocol. Routine blood investigations of the study subject were sent and sonography was done to know the exact gestational age. Lipid profile of study subject was sent in 2nd trimester between 16 – 20 weeks. The results of lipid profile of 5 parameters were studied and the subjects were grouped into normal lipid profile and abnormal lipid profile. The maternal and fetal complications were also recorded for these women of both the groups. Data were double entered using Microsoft excel 2016 and analyzed using SPSS version 22. Data was summarized in percentages and proportions. P value < 0.05 was considered statistically significant.

### RESULTS:

**Table 1) Distribution according to demographic variables:**

| Variables               |              | No. of Neonates (n=255) | Percentage |
|-------------------------|--------------|-------------------------|------------|
| Age                     | ≤20          | 04                      | 1.57       |
|                         | 21-25        | 124                     | 48.63      |
|                         | 26-30        | 94                      | 35.86      |
|                         | >30          | 33                      | 12.94      |
| Residence               | Rural        | 105                     | 41.18      |
|                         | Semi-urban   | 94                      | 36.86      |
|                         | Urban        | 56                      | 21.96      |
| Gestational age (weeks) | ≤13          | 34                      | 13.33      |
|                         | 14-16        | 89                      | 34.90      |
|                         | 17-20        | 132                     | 51.76      |
| Socio-economic status   | Upper        | 00                      | 00         |
|                         | Upper Middle | 29                      | 11.37      |
|                         | Lower middle | 156                     | 61.18      |
|                         | Upper lower  | 49                      | 19.22      |
|                         | Lower        | 21                      | 08.23      |

The table no. 1 describes demographic profile of the patients. The majority of patients were in age group 21-25 years (48.63%) and gestational age 17-20 weeks (51.76%). Most of the patients were in lower middle class. (61.18%)

**Table 2: Distribution according to dyslipidemia among patients:**

| Dyslipidemia | At time of registration |                | At the time of admission |                |
|--------------|-------------------------|----------------|--------------------------|----------------|
|              | Numbers                 | Percentage (%) | Numbers                  | Percentage (%) |
| Present      | 98                      | 38.43          | 138                      | 54.11          |
| Absent       | 157                     | 61.57          | 117                      | 45.89          |
| Total        | 255                     | 100            | 255                      | 100            |

The above table no. 2 shows, the incidence of dyslipidemia at time of registration was 38.43% and 54.11% at the time of admission among patients.

**Table 3: Distribution according to lipid profile among patients:**

| Lipid profile     | At time of registration (n=255) |              | At the time of admission (n=255) |            |
|-------------------|---------------------------------|--------------|----------------------------------|------------|
|                   | Normal (%)                      | Abnormal (%) | Normal                           | Abnormal   |
| Serum Cholesterol | 157(61.57)                      | 98(38.43%)   | 117(45.89)                       | 138(54.11) |
| Triglycerides     | 165(64.71%)                     | 90(35.29%)   | 125(49.02)                       | 130(50.98) |
| LDL               | 195(76.48)                      | 60(23.52%)   | 133(52.16)                       | 122(47.84) |
| HDL               | 211(82.75%)                     | 44(17.25%)   | 154(60.4)                        | 101(39.60) |
| VLDL              | 199(78.04%)                     | *56(21.96%)  | 169(66.28)                       | *86(33.72) |

It was observed that at time of registration majority of patients have dyslipidemia in the form of abnormal serum cholesterol (38.43%), abnormal TGS (35.29%), abnormal LDL (23.52%) and abnormal HDL. (17.25%) While at the time of admission patients had dyslipidemia as a form of abnormal serum cholesterol (54.11%), abnormal TGS (50.98%), abnormal LDL (47.84%) and abnormal HDL. (39.60%) which was more as compared to the lipid profile at registration with statistical significance. (P<0.05)

**Table 4: Association of Dyslipidemia, Gestation and Term Of Delivery**

| Type of delivery      | Age of Gestation |             | Total         | Dyslipidemia |             | P VALUE (<0.001 S) |
|-----------------------|------------------|-------------|---------------|--------------|-------------|--------------------|
|                       |                  |             |               | Present      | Absent      |                    |
| Vaginal               | Preterm          | 60 (25.64)  | 234 (91.76 %) | 45 (75%)     | 15 (25%)    |                    |
|                       | Term             | 174 (74.36) |               | 85(48.85 %)  | 89(51.15 %) |                    |
| Instrumental delivery | Preterm          | 1(25%)      | 5 (1.96%)     | 1(100%)      | 0           |                    |
|                       | Term             | 4(75%)      |               | 0            | 4(100%)     |                    |
| LSCS                  | Preterm          | 5(31.25%)   | 16 (6.66%)    | 5(100%)      | 0           |                    |
|                       | Term             | 11(68.75 %) |               | 2(18.18 %)   | 9(81.81 %)  |                    |

|       |         |            |  |             |              |  |
|-------|---------|------------|--|-------------|--------------|--|
| Total | Preterm | 66(25.88)  |  | 51(77.27 %) | 15(22.73 %)  |  |
|       | Term    | 189(74.12) |  | 87(46.03 %) | 102(53.97 %) |  |

The above table shows association of type of delivery and dyslipidemia. It was observed that majority of patients with Vaginal delivery had dyslipidemia (55.55%) as compared to normal lipid levels (44.45%) with statistically significant difference by chi square test. (P<0.001). The statistically significant difference was seen in the women with altered lipid profile who delivered preterm (77.27%) compared to the women who delivered at term (46.03%)

**Table 5: Association of dyslipidemia and NICU admission:**

| NICU admission | Dyslipidemia |        | P value    |
|----------------|--------------|--------|------------|
|                | Present      | Absent |            |
| Required       | 26           | 07     | <0.001 (S) |
| Not-required   | 112          | 110    |            |
| Total          | 138          | 117    |            |

It was observed that majority of patients were with NICU admissions had dyslipidemia (78.78%) as compared to normal lipid levels (21.22%) with statistically significant difference by chi square test. (P<0.001)

**Table 6: Association of dyslipidemia, vaginal mode of delivery and neonatal complications:**

|                | Neonatal complications | Dyslipidemia |        | P value |
|----------------|------------------------|--------------|--------|---------|
|                |                        | Present      | Absent |         |
| Preterm (n=66) | Hypoglycemia           | 10           | 02     | <0.001  |
|                | Hyperbilirubinemia     | 20           | 02     |         |
|                | Severe birth asphyxia  | 11           | 02     |         |
|                | Meconium aspiration    | 10           | 01     |         |
|                | Total                  | 51(77.27%)   | 7      |         |
| Term (n=189)   | Hypoglycemia           | 02           | 06     |         |
|                | Hyperbilirubinemia     | 01           | 08     |         |
|                | Severe birth asphyxia  | 03           | 08     |         |
|                | Meconium aspiration    | 03           | 10     |         |

The above table shows association of dyslipidemia, and neonatal complications. It was observed that 77.27% of patients with preterm delivery with fetal complications had dyslipidemia as compared to term with statistically significant difference by chi square test. (P<0.01)

## DISCUSSION:

A gestational rise in blood TGL and cholesterol during a pregnancy causes a significant physiological hypertriglyceridemia. It is believed that enhanced maternal fat deposition during the first half of a typical pregnancy (a relative anabolic condition) is essential for the following hypertriglyceridemia that typically develops in later gestation (relative catabolic state). As seen by pronounced increases in blood TGL and cholesterol, circulating concentrations of VLDL and LDL typically rise with gestation. Instead of decreased clearance, the increased entry of triglyceride-rich lipoproteins, especially VLDL, into the circulation is what causes the hypertriglyceridemia. The present study was carried out with the aim to assess the association of levels of serum triglycerides and cholesterol with probability of preterm delivery.

In the present study, 48.63% cases were between the age group 21 to 25 years due to early marriages in rural areas. The studies done by Ottun et al.<sup>13</sup> (2022), Meng-Yi Dai et al.<sup>14</sup> (2020) and KK Ryckman et al.<sup>15</sup> (2018) on maternal dyslipidemia found majority of pregnant women of age group 20-35 years.

The incidence of dyslipidemia at time of registration was 38.43% and 54.11% at the time of admission among patients. The lipid profile at admission was more as compared to the lipid profile at registration with statistical significance. (P<0.05) (Table 2 & 3)

Pusukuru R et al.<sup>16</sup> (2016) stated that total Cholesterol, Triglycerides, LDL Cholesterol, VLDL-Cholesterol increased in both second and third trimester.

Ghodke B et al.<sup>17</sup> (2017) studied the association of serum lipid levels

during the second and third trimesters mean cholesterol levels in patients with preterm in second and third trimesters were 213.33 mg/dl and 243.66 mg/dl, respectively.

Maymunah AO et al.<sup>18</sup> (2014) and above studies found that dyslipidemia was found in second and third trimesters which is consistent with our findings.

It was observed that majority of patients with Vaginal delivery had dyslipidemia (55.55%) as compared to normal lipid levels (44.45%) with statistically significant difference by chi square test. ( $P < 0.001$ ). The statistically significant difference was seen in the women with altered lipid profile who delivered preterm (77.27%) compared to the women who delivered at term (46.03%) (Table 4)

Catov et al.<sup>19</sup> (2007) and co-workers showed that an elevation in maternal cholesterol level early in gestation was associated with an increased risk of preterm delivery. This was corroborated by the finding from this present cohort study where we reported an elevated risk for preterm birth among mothers with high maternal cholesterol. Mudd et al.<sup>20</sup> (2012) stated a correlation between lipid levels and the likelihood of morbidity from premature. Low levels of TC, LDL-c, and HDL-c are associated to a slightly increased risk of preterm births that are medically necessary, while high levels of TC, LDL-c, and triglycerides are linked to spontaneous preterm births, according to the authors.

It was observed that majority of patients were with NICU admissions had dyslipidemia (78.78%) as compared to normal lipid levels (21.22%) with statistically significant difference by chi square test. ( $P < 0.001$ ) (Table 5) Patients with preterm delivery had more fetal complications had dyslipidemia as compared to term with statistically significant difference (table 6)

Jelliffe-Pawlowski LL et al.<sup>21</sup> (2014) determined the presence of dyslipidemia in female results spontaneous preterm births and increased NICU admissions and neonatal complications. Pregnancies resulting in early preterm birth (PTB) were more likely than term pregnancies to have elevated midpregnancy TNF- $\alpha$  levels in combination with lipid patterns suggestive of hyperlipidemia.<sup>21</sup>

There are several limitations to this study. Their demographic, socioeconomic or medical characteristics could be small. Our results from the specific ethnic groups may not be generalizable to other population. Socioeconomic factor such as dietary intake may affect triglycerides and cholesterol concentration and risk. Finally, elevated maternal cholesterol levels may play a role in the mechanism of under lying preterm delivery or may simply be a marker for risk of preterm delivery.<sup>9-11</sup>

As preterm births is the leading cause of adverse neonatal outcome, it becomes important to find out the cause of preterm birth and provide treatment for the same. This current evidence may motivate the further study on the potential benefits of treatment of hyperlipidemia in pregnancy and its effects on maternal-fetal outcomes. It can be considered as a risk factor for preterm births so it is to be assessed in all trimesters and preventive measures should be planned accordingly.

## CONCLUSION:

The study concludes that dyslipidemia is a potential contributor to the pathogenesis of preterm delivery and may be used as a marker of elevated risk for preterm birth.

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