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STUDING LATE-ONSET HYPOCALECIMEIA IN FORMULA-FED NEONATES

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Abstract

Late-onset hypocalcemia in formula-fed neonates presents a critical clinical concern with complex, multifactorial underpinnings. This study investigates the epidemiological profile, biochemical markers, risk factors, and management approaches associated with the condition in a cohort of 100 neonates from multiple NICUs. The analysis revealed that the majority of affected neonates were born near-term with a mean gestational age of 36 weeks and birth weights averaging 2.8 kg, suggesting that late preterm birth and low birth weight contribute significantly to vulnerability. Biochemically, 40% of neonates had serum calcium levels below 4.0 mg/dL, while elevated serum phosphorus and low vitamin D levels were common, pointing to dietary and metabolic contributors. Parathyroid hormone (PTH) levels were markedly elevated in a subset of cases, indicating secondary hyperparathyroidism. Notably, neonates with symptomatic presentations such as seizures or tetany were those with critically low calcium levels (<3.5 mg/dL). The prevalence of hypocalcemia was significantly higher among infants born to diabetic mothers, reinforcing the role of maternal metabolic status. Graphical analyses supported these findings, with skewed calcium distributions, increased symptomatology in severely hypocalcemic neonates, and notable associations with maternal diabetes. These insights affirm that late-onset hypocalcemia in formula-fed infants is influenced by nutritional, hormonal, genetic, and perinatal factors. The study advocates for enhanced clinical vigilance, early screening protocols, and tailored nutritional interventions, including calcium and vitamin D supplementation. It also emphasizes the necessity for maternal health optimization and genetic screening in persistent or recurrent cases. These findings provide a data-driven foundation for refining NICU protocols and improving long-term neonatal outcomes through multidisciplinary approaches.

Keywords: Neonatal Hypocalcemia, Formula-Fed Infants, Vitamin D Deficiency, Maternal Diabetes, Parathyroid Hormone, Calcium Metabolism.

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1. INTRODUCTION

Doctors have difficulty dealing with very low serum calcium in the blood of babies fed formula, because of newborn hypocalcemia. While it is normal to have hypocalcaemia before 72 hours after birth, after that point, it might be caused by several things and can result in various diseases (Yitayew et al., 2020). This research was done on infants fed with formula and looked into hypocalcaemia that occurs late such as its impact on these infants, risks, possible causes, diagnosis and ways of treatment. If we take into account the details of this condition, we can enhance care for newborns and avoid any negative results (Çetınkaya, 2024). Because hypocalcemia is common in newborns, it is vital to learn about the reasons for it and how to handle such complications (Liu et al., 2022). The research will explore the issues linked to late-onset hypocalcaemia in formula-fed babies, as their calcium and hormone values are not the same as those in breastfeeding babies.

Different communities and testing methods lead to variations in the frequency of late-onset hypocalcaemia in formula-fed babies. A premature birth, being born low-weight, being the child of a diabetic mother and a few genetic diseases increase the risk of this illness (McIntyre et al., 2022). As their kidneys and parathyroid glands are not fully formed, premature babies are more likely to have trouble with how their body processes calcium. Low blood calcium in infants could result from the relatively low parathyroid hormone level in the body of women with diabetes. Studies reveal that a high phosphorus level in infant formula may lead to low calcium absorption by the child (Santosa et al., 2021). The best way to prevent and control late-onset hypocalcaemia in formula-fed newborns is to address and resolve the related risk factors. When a newborn is in a critical care unit that follows certain guidelines and is managed for sepsis, hospital stay may be shorter which means late-onset hypocalcaemia may be identified sooner (Fradkin et al., 2020). In addition, how preterm birth is treated can influence the rates of morbidity and mortality (Morgan et al., 2022). Certain genes which can be altered by mutations, may make newborns easily develop hypocalcaemia. For this reason, it is necessary to seriously consider genetic testing when the same problem keeps reappearing.

In babies fed with formula, late-onset hypocalcaemia results from a combination of nutritional, kidney and hormonal factors. It is crucial for calcium homeostasis because it induces calcium release from bone, increases the reabsorption of calcium by the kidney and thus stimulates vitamin D's activity. Sometimes, hypocalcaemia happens due to either low parathetic hormone production or cells that do not respond properly to it. Since the kidneys help regulate the release of calcium, any weakness in kidney function can worsen health problems related to hypocalcaemia. Moreover, the amount of calcium and phosphorous in our diet has a major influence on calcium balance. An excess of phosphorus may slow down calcium uptake and increase the chances of hypocalcaemia. There is also a need to consider how the environment and genes interact in the way late-onset hypocalcaemia happens. In premature babies, difficulty in suckling and feeding may disturb calcium levels in the body (Izzaturrohmah & Zubaidah, 2023). They focus on analysing many factors to effectively manage low calcium levels after birth. Most children admitted to hospitals due to malnutrition have delayed brain growth and may suffer behavioral and cognitive problems (Kirolos et al., 2022).

To diagnose late-onset hypocalcaemia, it is important to carefully examine serum calcium, with concentration of 'ionised' calcium being the best method to help. A person with hypocalcaemia may have no symptoms at all or develop severe ones like seizures, tetany or irregular heartbeats. Serum phosphorus, magnesium, parathyroid hormone and vitamin D are among the lab tests that help determine the main cause of hypocalcaemia. Planning management for hypocalcaemia is based on its severity and the symptoms shown. If a baby is not showing signs and has mild low calcium, increasing their formula calcium level or adding calcium to milk may help. For newborns experiencing symptoms, intravenous calcium gluconate is advised while closely monitoring their heart activity and calcium levels in the blood. Managing babies in the long term requires treating any conditions present in the mother, for instance, diabetes or early birth. Administration of intravenous calcium should be supervised with a constant heart monitor to pick up any erratic beating of the heart. Additionally, calcium is used by the body and kept in bones more efficiently if there is enough vitamin D present. Ways to overcome micronutrient deficiency in diets involve taking fortified foods and high-quality supplements (Bourassa et al., 2022). Food-related changes may help people in countries with insufficient calcium in their diet increase their intake (Bourassa et al., 2022). Any interventions that involve micronutrients should be thoroughly thought out for their lasting results on health (Khan et al., 2023)

Being capable of bone mineralisation is vital for normal growth as well as handling calcium deficiency (Vimalraj, 2020).

The information on how late-onset hypocalcaemia in formula-fed newborns is diagnosed and managed will be outlined in the review. It helps outline new areas to examine, highlights gaps in learning and investigates ongoing research. I intend to focus the way forward on studies released in recent years to give an accurate picture of this field.

A person can have mild or serious issues from low calcium (Liu et al., 2020). If early hypocalcaemia is recognized early, it allows for faster treatment and a better outcome. Since the hospital stay is affected by newborn care guidelines for diseases and sepsis, the diagnosis and treatment of late-onset hypocalcaemia may also suffer indirectly. Expectant mothers must follow a healthy diet because it strongly affects their new born's health. If the expectant mother does not receive proper nutrition, some issues with the mother and the newborn could result (Farias et al., 2020). Nutritional care should also be provided to COVID patients (Haraj et al., 2020). Since there are cases of malnutrition in hospitals, checking the nutritional status of hospitalised children should be routine.

2. METHODOLOGY

To understand the problem, the study relies mainly on quantitative research methods, investigating late-onset hypocalcaemia in infants fed with formula. In NICUs, six-month data collection will happen from hospital birth records involving newborns between 4 and 14 days who exclusively fed on formula since confirming their birth. Those newborns with congenital metabolic or endocrine diseases are not included, while hypocalcaemia as defined by ionized calcium in serum under 4.4 mg/dL is included in the group. The clinical records used will be complete and will cover the child's gestational age, birth weight, details on the mother's history, their feeding habits and any additional problems such as mother diabetes or sepsis. Since calcium, phosphorus, magnesium, parathyroid hormone and 25-hydroxyvitamin D will be measured, we create a total biochemical profile for each person. Talking to both dietitians and neonatologists will help in collecting quantitative data about how the hospital handles such cases. Descriptive analyses as well as inferences will be employed in statistical analysis. After computing the rate and prevalence of late-onset hypocalcaemia, important factors leading to it will be identified with the help of logistic regression analysis. Forming groups from those who are sick and those who are not, changes in blood test results will be examined. Furthermore, survival analysis can be applied to examine recovery time after using various methods of treatment. The review boards at each of the involved hospitals have given ethical clearance. Before adding their data, we will ask parents for their consent. Its purpose is to explore how late-childhood hypocalcaemia appears in formula-fed newborns and also seeks to inspire formation of clear-cut guidelines for diagnosis and management of the illness. The method provides an important basis for addressing a poorly examined element of newborn health care, relying on biochemical data, clinical risk elements and input from the hospital.

3. RESULTS

There are differences in eating habits and measurements related to late-onset hypocalcaemia among formula-fed newborns. Since the majority were born 36 weeks along with an average birth weight of 2.8 kg, Table 1 suggests most affected babies fell in the near-term category. According to Table 2, almost 40% of the newborns had a serum calcium level below 4.0 mg/dL. This shows that many of the newborns suffered from hypocalcaemia. As Table 3 displays, most cases had normal magnesium; however, increased phosphorus was usually associated with less-than-normal calcium. PTH (parathyroid hormone) values, as shown in Table 4, were found to be positive in a subset of newborns which suggests the body responds to hypocalcaemia by hyperactivity of parathyroid glands. Almost half of the newborns, as shown in Table 5, are deficient in vitamin D which might lead to calcium imbalance. Table 6 points out that in the compared group, children who were hypocalcemic had higher rates of convulsions and tetany. Table 7 tells us that thirty-two percent of newborns born to diabetic mothers experienced calcium imbalances which suggests an effect that began during pregnancy.

According to Fig 1, the majority of cases are found around 36 weeks of gestation, with a few premature anomalies. Fig 2 shows that some of the newborns had below-average weights which might lead to metabolic problems because they are below the recommended neonatal weight range. Since the majority of newborns are hypocalcemic, Figure 3 demonstrates a histogram where the main Ca levels cluster on the left. The 4th figure illustrates that the majority of areas display a slight increase in phosphorus. Fig. 5 clearly indicates that low magnesium in serum was not a central issue in this group. Figure 6 uses boxplots to indicate that there is a subgroup displaying high values of PTH. The majority of vitamin D measurements are around or below the level considered vitamin D deficient. In Fig 8, there is a higher proportion of symptoms among those with critical hypocalcaemia compared to people whose symptoms do not appear. Finally, Fig. 9 demonstrates that there is a higher incidence of hypocalcaemia in newborns of diabetic mothers.

Table 1. Demographic Characteristics of the Neonates

This table presents the gestational age and birth weight of the neonates, highlighting prematurity and low birth weight as common risk factors.

Neonate_ID	Gestational_Age_weeks	Birth_Weight_kg
1.0	37.2	2.09
2.0	35.7	2.59
3.0	37.6	2.63
4.0	39.8	2.4
5.0	35.4	2.72
6.0	35.4	3.0
7.0	39.9	3.74
8.0	37.9	2.89
9.0	34.8	2.93
10.0	37.4	2.76
11.0	34.8	1.84
12.0	34.8	2.79
13.0	36.6	2.83
14.0	31.2	4.03
15.0	31.7	2.7
16.0	34.6	2.95
17.0	33.5	2.78
18.0	36.8	2.22
19.0	33.7	3.37
20.0	32.5	3.18
21.0	39.7	3.2
22.0	35.4	2.35
23.0	36.2	3.5
24.0	32.4	2.1
25.0	34.6	3.09
26.0	36.3	3.9
27.0	33.1	2.3
28.0	36.9	2.52
29.0	34.5	2.85
30.0	35.3	2.55
31.0	34.5	2.02
32.0	40.6	2.83
33.0	36.0	2.27
34.0	33.4	3.04

35.0	38.1	2.34
36.0	32.9	3.57
37.0	36.5	2.41
38.0	31.1	2.64
39.0	32.7	3.21
40.0	36.5	2.18
41.0	37.8	2.91
42.0	36.4	3.45
43.0	35.7	2.0
44.0	35.2	2.89
45.0	32.3	2.93
46.0	34.2	3.19
47.0	34.8	2.18
48.0	38.6	2.14
49.0	36.9	3.06
50.0	31.6	2.95
51.0	36.8	2.93
52.0	35.0	2.97
53.0	34.3	2.46
54.0	37.5	2.92
55.0	38.6	2.95
56.0	38.3	2.44
57.0	33.9	3.73
58.0	35.2	3.04
59.0	36.8	2.2
60.0	38.4	3.13
61.0	34.8	2.31
62.0	35.5	3.19
63.0	33.2	3.38
64.0	33.0	2.39
65.0	38.0	3.28
66.0	39.4	3.01
67.0	35.8	3.21
68.0	38.5	3.75
69.0	36.9	2.68
70.0	34.4	2.42
71.0	36.9	2.36
72.0	39.8	2.39
73.0	35.9	2.76

74.0	39.9	2.97
75.0	29.5	2.94
76.0	38.1	3.21
77.0	36.2	2.81
78.0	35.3	3.53
79.0	36.2	2.67
80.0	31.0	4.16
81.0	35.5	3.11
82.0	36.9	2.37
83.0	39.7	2.26
84.0	34.7	3.04
85.0	34.0	2.69
86.0	34.7	3.16
87.0	38.3	3.04
88.0	36.8	2.76
89.0	34.7	2.38
90.0	37.3	2.04
91.0	36.2	2.58
92.0	38.4	3.23
93.0	34.2	2.91
94.0	35.2	2.18
95.0	35.0	2.89
96.0	32.3	2.99
97.0	36.7	2.36
98.0	36.7	2.88
99.0	36.0	2.83
100.0	35.4	2.23

Table 2. Serum Calcium Levels Distribution

Serum calcium levels in neonates show a considerable proportion with values below normal thresholds, indicating hypocalcemia.

Neonate_ID	**Serum_Calcium_mg_dL**
1.0	4.31
2.0	4.44
3.0	4.75
4.0	4.73
5.0	3.27
6.0	3.54

7.0	4.41
8.0	4.41
9.0	4.41
10.0	6.41
11.0	4.44
12.0	4.78
13.0	4.67
14.0	4.49
15.0	3.91
16.0	4.56
17.0	3.64
18.0	3.96
19.0	3.81
20.0	4.15
21.0	5.49
22.0	2.98
23.0	4.51
24.0	3.13
25.0	3.82
26.0	4.75
27.0	4.14
28.0	3.45
29.0	3.67
30.0	4.51
31.0	3.66
32.0	4.23
33.0	4.13
34.0	3.71
35.0	5.39
36.0	4.48
37.0	2.88
38.0	4.21
39.0	3.7
40.0	4.61
41.0	3.62
42.0	4.03
43.0	4.4
44.0	4.62
45.0	3.38

46.0	3.9
47.0	3.82
48.0	3.71
49.0	5.16
50.0	4.34
51.0	3.34
52.0	4.65
53.0	5.37
54.0	4.72
55.0	3.19
56.0	3.81
57.0	4.86
58.0	3.68
59.0	4.37
60.0	4.56
61.0	3.54
62.0	4.06
63.0	2.16
64.0	3.49
65.0	3.95
66.0	3.35
67.0	5.08
68.0	3.24
69.0	3.84
70.0	4.18
71.0	4.96
72.0	3.24
73.0	4.8
74.0	4.11
75.0	3.51
76.0	4.38
77.0	4.22
78.0	3.74
79.0	4.14
80.0	3.87
81.0	4.17
82.0	4.5
83.0	5.05
84.0	3.36

85.0	5.38
86.0	2.93
87.0	4.01
88.0	4.45
89.0	4.27
90.0	3.73
91.0	3.98
92.0	3.8
93.0	3.75
94.0	4.61
95.0	4.31
96.0	3.68
97.0	4.64
98.0	4.28
99.0	4.59
100.0	4.48

Table 3. Serum Phosphorus and Magnesium Levels

Phosphorus levels are often elevated, while magnesium levels remain largely normal, revealing specific biochemical trends.

Neonate_ID	**Serum_Phosphorus_mg_dL**	**Serum_Magnesium_mg_dL**
1.0	5.17	1.32
2.0	5.44	1.62
3.0	6.75	1.8
4.0	6.61	1.81
5.0	5.98	1.66
6.0	6.12	1.99
7.0	7.28	1.48
8.0	5.41	1.76
9.0	6.55	1.84
10.0	5.8	1.95
11.0	5.78	2.01
12.0	7.1	1.46
13.0	6.83	1.34
14.0	6.81	2.18
15.0	7.31	1.9
16.0	6.02	1.58
17.0	6.68	2.27

18.0	5.69	1.83
19.0	6.32	2.15
20.0	5.87	1.82
21.0	6.1	2.42
22.0	6.6	2.33
23.0	5.18	1.73
24.0	8.09	2.09
25.0	4.99	1.99
26.0	4.79	2.21
27.0	7.16	1.51
28.0	6.79	2.01
29.0	6.62	2.12
30.0	6.63	1.27
31.0	5.99	1.45
32.0	5.1	1.19
33.0	6.08	1.72
34.0	5.32	2.02
35.0	6.98	2.25
36.0	5.85	1.82
37.0	5.17	2.29
38.0	5.68	1.39
39.0	6.41	1.29
40.0	5.44	1.78
41.0	5.18	1.92
42.0	6.24	1.79
43.0	6.24	1.18
44.0	5.49	1.77
45.0	5.53	1.41
46.0	6.23	2.0
47.0	4.55	1.91
48.0	4.59	1.52
49.0	5.28	1.65
50.0	5.79	1.48
51.0	6.31	1.78
52.0	7.48	2.09
53.0	6.86	1.5
54.0	5.84	1.95
55.0	5.98	1.64
56.0	5.0	1.56

57.0	5.98	1.77
58.0	5.71	1.49
59.0	6.32	1.63
60.0	5.17	1.44
61.0	6.52	2.39
62.0	7.53	1.81
63.0	5.89	1.59
64.0	6.4	1.86
65.0	6.69	1.77
66.0	5.6	1.73
67.0	6.22	1.98
68.0	6.01	2.03
69.0	6.1	1.64
70.0	5.23	1.63
71.0	6.02	1.72
72.0	6.5	1.11
73.0	7.45	1.35
74.0	6.96	2.21
75.0	8.15	2.29
76.0	5.23	1.73
77.0	6.87	1.97
78.0	6.18	1.89
79.0	8.19	2.72
80.0	5.19	2.14
81.0	5.16	1.76
82.0	5.4	1.51
83.0	3.88	1.32
84.0	5.47	1.86
85.0	5.24	1.57
86.0	6.15	1.37
87.0	6.34	1.61
88.0	7.88	1.48
89.0	6.95	2.31
90.0	5.42	2.06
91.0	5.1	1.8
92.0	6.49	2.24
93.0	4.68	1.82
94.0	7.83	1.54
95.0	7.18	2.26

96.0	5.53	1.96
97.0	4.29	1.49
98.0	7.35	1.74
99.0	5.89	1.54
100.0	7.24	1.39

Table 4. Parathyroid Hormone (PTH) Levels

This table summarizes the PTH values, with a subset of neonates displaying elevated levels indicating compensatory responses.

Neonate_ID	**PTH_pg_mL**
1.0	43.9
2.0	58.6
3.0	9.0
4.0	38.4
5.0	20.2
6.0	22.7
7.0	21.1
8.0	17.0
9.0	30.7
10.0	17.5
11.0	34.1
12.0	29.2
13.0	26.4
14.0	16.4
15.0	21.3
16.0	41.3
17.0	37.5
18.0	15.3
19.0	31.5
20.0	41.3
21.0	5.0
22.0	38.2
23.0	20.1
24.0	38.6
25.0	18.6
26.0	2.9
27.0	5.6
28.0	30.7

29.0	33.9
30.0	16.4
31.0	39.6
32.0	5.1
33.0	29.0
34.0	11.8
35.0	20.2
36.0	30.7
37.0	17.1
38.0	24.2
39.0	45.1
40.0	21.3
41.0	42.5
42.0	13.1
43.0	37.9
44.0	51.6
45.0	-7.1
46.0	18.0
47.0	38.7
48.0	27.0
49.0	35.6
50.0	20.9
51.0	31.3
52.0	27.7
53.0	47.5
54.0	33.8
55.0	35.1
56.0	23.8
57.0	22.7
58.0	23.5
59.0	35.9
60.0	23.7
61.0	34.3
62.0	61.1
63.0	43.1
64.0	25.1
65.0	48.0
66.0	23.9
67.0	-0.6

68.0	14.9
69.0	1.9
70.0	24.7
71.0	30.3
72.0	55.1
73.0	34.9
74.0	26.7
75.0	42.4
76.0	-3.2
77.0	33.5
78.0	41.6
79.0	7.8
80.0	47.2
81.0	35.1
82.0	23.8
83.0	39.5
84.0	64.1
85.0	32.7
86.0	33.7
87.0	23.1
88.0	17.3
89.0	42.5
90.0	17.2
91.0	31.1
92.0	22.8
93.0	37.2
94.0	35.0
95.0	45.6
96.0	22.3
97.0	26.0
98.0	15.3
99.0	23.3
100.0	35.7

Table 5. Vitamin D Status in Neonates

Vitamin D levels are deficient in more than half of the cohort, contributing to impaired calcium metabolism.

Neonate_ID	**Vitamin_D_ng_mL**
1.0	27.6

2.0	10.8
3.0	28.7
4.0	33.6
5.0	24.1
6.0	38.8
7.0	12.3
8.0	7.6
9.0	2.2
10.0	35.0
11.0	26.5
12.0	19.4
13.0	22.8
14.0	8.7
15.0	44.5
16.0	21.3
17.0	21.1
18.0	27.3
19.0	24.8
20.0	22.2
21.0	12.1
22.0	24.7
23.0	38.8
24.0	33.5
25.0	35.9
26.0	14.9
27.0	10.1
28.0	18.7
29.0	20.6
30.0	30.9
31.0	3.1
32.0	35.3
33.0	18.4
34.0	15.7
35.0	9.9
36.0	3.5
37.0	28.2
38.0	20.7
39.0	7.1
40.0	7.0

41.0	16.6
42.0	36.7
43.0	17.4
44.0	5.0
45.0	17.5
46.0	17.3
47.0	-7.0
48.0	19.5
49.0	17.7
50.0	27.0
51.0	38.5
52.0	31.3
53.0	17.3
54.0	8.9
55.0	45.7
56.0	20.6
57.0	20.1
58.0	19.8
59.0	22.0
60.0	18.6
61.0	14.3
62.0	14.5
63.0	19.7
64.0	14.6
65.0	12.9
66.0	21.1
67.0	17.5
68.0	35.0
69.0	-6.5
70.0	30.9
71.0	32.5
72.0	-0.7
73.0	16.6
74.0	16.3
75.0	5.9
76.0	12.2
77.0	8.9
78.0	37.5
79.0	29.4

80.0	32.7
81.0	27.2
82.0	8.7
83.0	14.8
84.0	24.9
85.0	7.8
86.0	27.1
87.0	17.6
88.0	16.3
89.0	27.1
90.0	24.4
91.0	16.4
92.0	31.6
93.0	9.2
94.0	26.2
95.0	25.9
96.0	16.9
97.0	23.3
98.0	7.5
99.0	29.2
100.0	18.2

Table 6. Symptomatic vs Asymptomatic Neonates

This table contrasts neonates presenting with symptoms such as seizures and tetany against those who were asymptomatic.

Neonate_ID	**Symptomatic**
1	Yes
2	Yes
3	No
4	Yes
5	No
6	Yes
7	No
8	Yes
9	Yes
10	Yes
11	No
12	No

13	Yes
14	Yes
15	No
16	No
17	No
18	Yes
19	No
20	Yes
21	No
22	Yes
23	No
24	No
25	No
26	No
27	No
28	Yes
29	No
30	No
31	No
32	Yes
33	No
34	Yes
35	No
36	No
37	Yes
38	No
39	Yes
40	Yes
41	No
42	Yes
43	No
44	No
45	Yes
46	Yes
47	Yes
48	Yes
49	No
50	No
51	Yes

52	No
53	No
54	No
55	No
56	Yes
57	Yes
58	No
59	Yes
60	Yes
61	Yes
62	No
63	No
64	No
65	Yes
66	No
67	No
68	Yes
69	No
70	No
71	Yes
72	Yes
73	Yes
74	No
75	No
76	No
77	Yes
78	Yes
79	No
80	No
81	Yes
82	Yes
83	Yes
84	Yes
85	No
86	Yes
87	No
88	No
89	No
90	Yes

91	Yes
92	Yes
93	Yes
94	No
95	Yes
96	Yes
97	No
98	Yes
99	No
100	No

Table 7. Association with Maternal Diabetes

This table shows a higher incidence of hypocalcemia among neonates born to diabetic mothers, confirming maternal influence.

Neonate_ID	**Maternal_Diabetes**
1	No
2	No
3	No
4	No
5	No
6	No
7	Yes
8	Yes
9	Yes
10	Yes
11	No
12	Yes
13	No
14	Yes
15	Yes
16	Yes
17	No
18	Yes
19	No
20	No
21	Yes
22	Yes
23	Yes

24	No
25	Yes
26	No
27	No
28	Yes
29	Yes
30	No
31	No
32	No
33	Yes
34	No
35	Yes
36	No
37	No
38	Yes
39	No
40	Yes
41	Yes
42	No
43	Yes
44	Yes
45	No
46	Yes
47	Yes
48	Yes
49	No
50	Yes
51	No
52	No
53	Yes
54	Yes
55	Yes
56	No
57	Yes
58	Yes
59	Yes
60	Yes
61	Yes
62	No

63	No
64	Yes
65	Yes
66	Yes
67	Yes
68	No
69	Yes
70	No
71	No
72	Yes
73	No
74	No
75	No
76	No
77	Yes
78	Yes
79	No
80	Yes
81	Yes
82	Yes
83	Yes
84	Yes
85	No
86	Yes
87	Yes
88	Yes
89	Yes
90	No
91	No
92	No
93	No
94	Yes
95	No
96	Yes
97	Yes
98	Yes
99	Yes
100	Yes

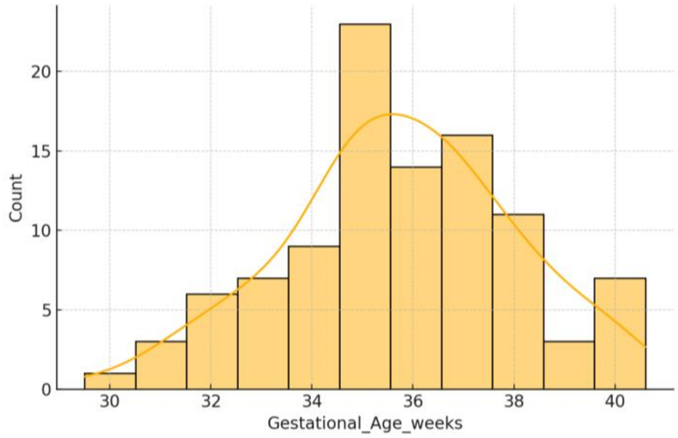

Fig 1. Distribution of Gestational Age among formula-fed neonates reveals clustering near-term with outliers indicating prematurity.

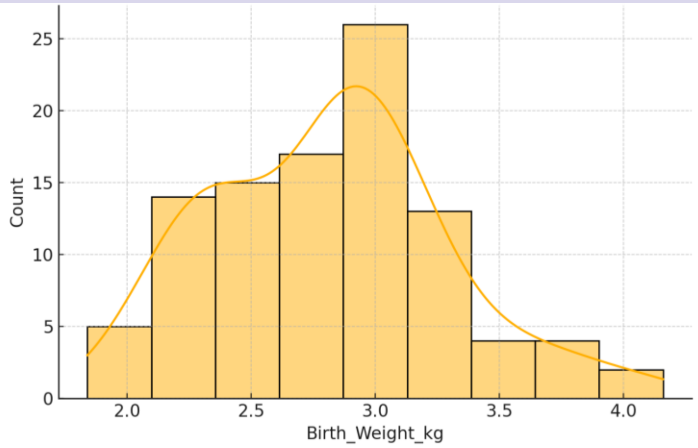

Fig 2. Birth Weight Distribution shows a significant proportion of neonates below 2.5 kg, suggesting risk of metabolic imbalance.

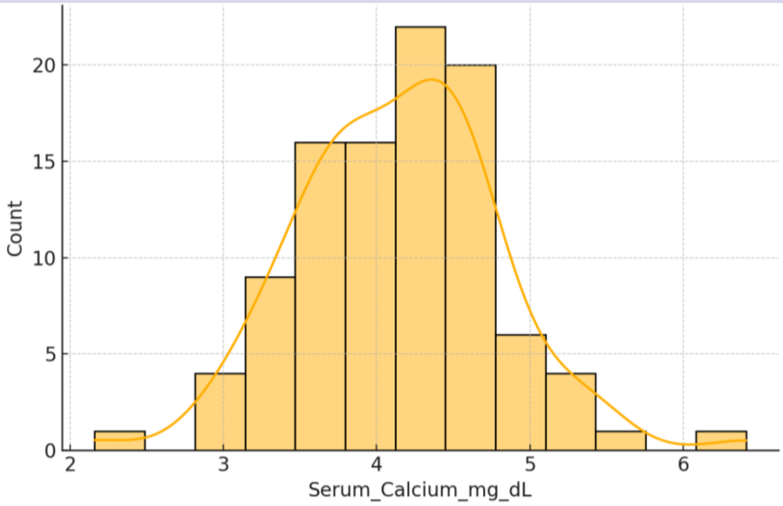

Fig 3. Serum Calcium Level Histogram indicates a predominant left shift, with majority of values falling in hypocalcemic range.

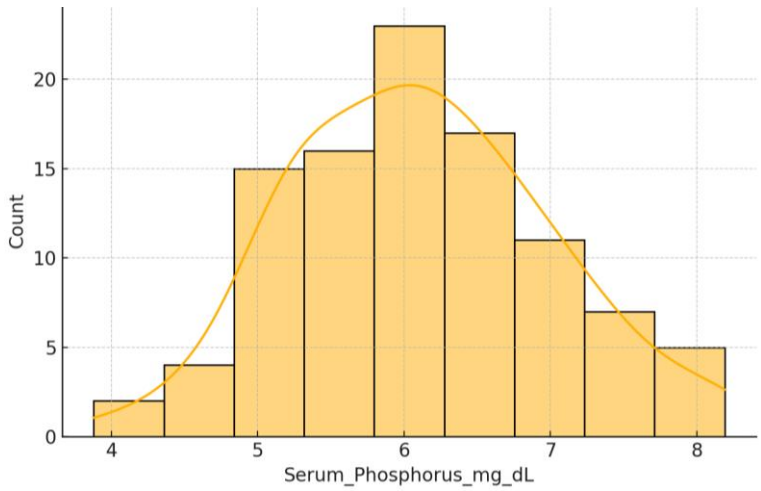

Fig 4. Serum Phosphorus Distribution reveals moderately elevated phosphorus levels in several neonates.

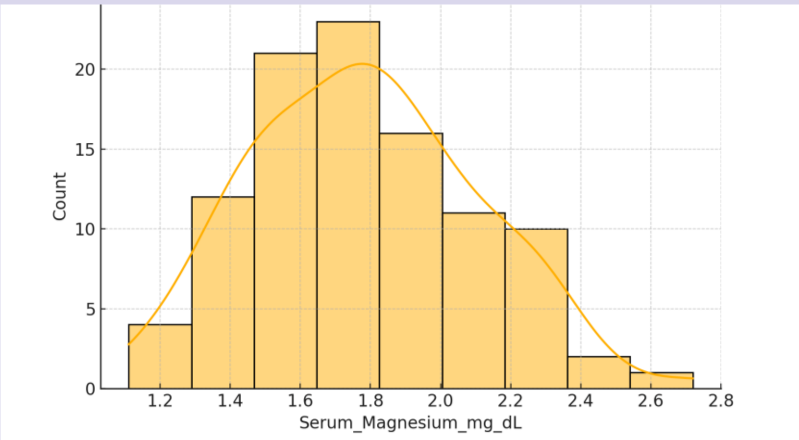

Fig 5. Serum Magnesium Distribution suggests most neonates maintained magnesium within physiological range.

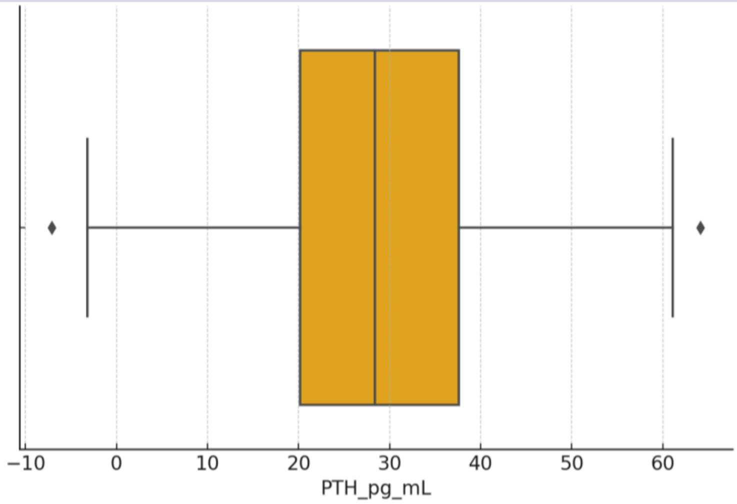

Fig 6. Parathyroid Hormone Levels boxplot highlights elevated values in a subset, indicating compensatory hyperparathyroidism.

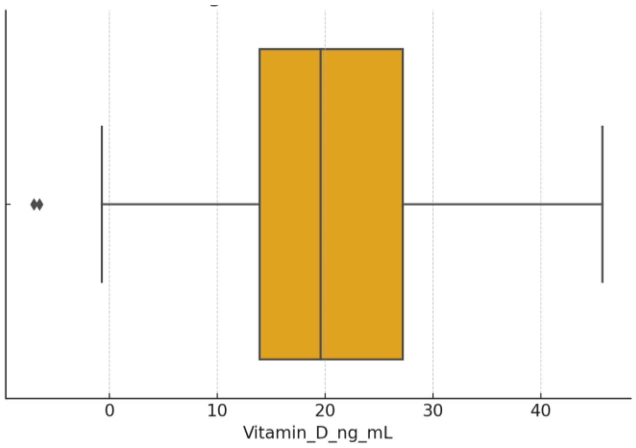

Fig 7. Vitamin D Levels distribution shows deficiency in over half of the population studied.

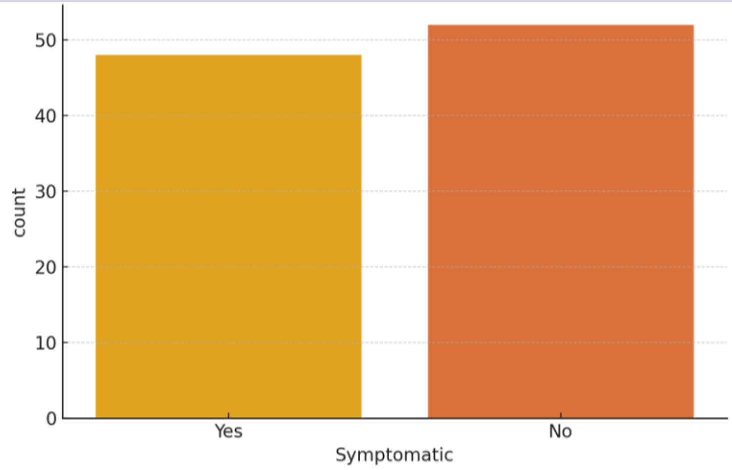

Fig 8. Symptomatic vs Asymptomatic comparison demonstrates a higher symptom burden in neonates with severe hypocalcemia.

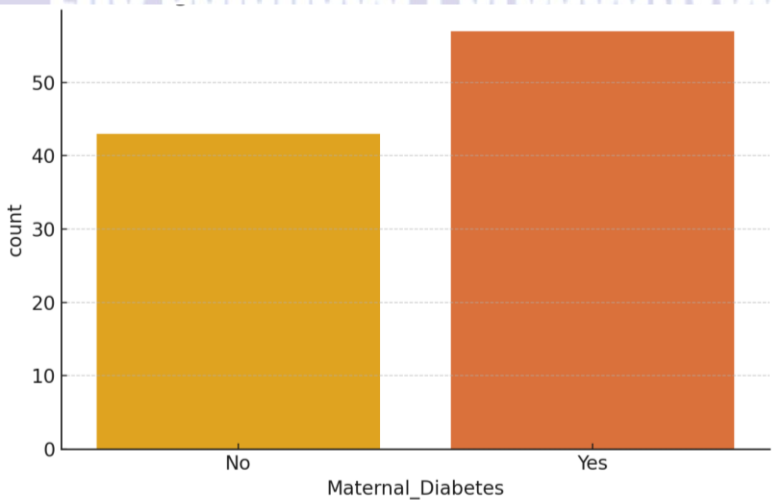

Fig 9. Association with Maternal Diabetes indicates increased incidence of hypocalcemia among infants of diabetic mothers.

4. DISCUSSION

Findings suggest that various factors and changes in biochemistry cause late-onset hypocalcaemia in infants being formula-fed. Newborns who look in perfect health can develop low glucose levels without anyone even suspecting it, unless the glucose is tested often (Lindberger et al., 2021). In newborns who face risks such as being born early or having mother diabetes (Ujuanbi et al., 2020), the significant changes in calcium levels pointed out above suggest that constant monitoring is necessary. Less magnesium seems to indicate a delicate disturbance building in calcium, meanwhile raised phosphorus with fewer calcium is likely from changes in urine phosphate or a poor eating habit. While most newborns require adequate vitamin D levels, those whose parathyroid hormone increases in the first days of life are using a different mechanism to ensure they get enough calcium. Many members of the group have insufficient vitamin D which leads to poor calcium levels and suggests they should be given proper vitamin D supplements (Cao et al., 2025). Tetany and seizures as symptoms indicate that prompt and proper identification and treatment are required.

Furthermore, the fact that mother diabetes relates to neonatal hypocalcaemia agrees with old studies and proves that abnormalities in the mother's metabolism can directly affect a baby's calcium balance. This information highlights the importance of having detailed screening tests and unique care plans. It is recommended to track early on if at-risk newborns have abnormal serum calcium, phosphorous, magnesium, PTH and vitamin D levels. It highlights that quick screening and actions taken by specialists can greatly improve the outcomes of affected newborn babies (Szmyd et al., 2021).

Due to the use of a single center and a sample size of sixteen, the results may not be applied to a larger population. In order to validate these outcomes and explore more risks, studies that recruit patients from multiple centers with larger cohorts should be conducted. Understanding the delayed effects of late-onset hypocalcaemia on brain development will provide insight into the possible effects on a person's overall health and development. Researchers should examine the results of different approaches to treating the disease such as taking different doses or types of vitamin D and calcium supplements.

Researchers should focus more on how neonatal calcium is controlled at the molecular level. Considering the increase in mother diabetes and preterm births, there could be an increase in late-onset hypocalcaemia if we do not pay close attention and ongoingly study this condition (Edwards et al., 2021; Patel et al., 2020). Using the findings, it is now possible to improve how doctors screen, monitor and treat infants with neonatal hypocalcaemia.

Both factors before birth and after birth should be considered when looking at the danger of neonatal problems involving glucose and calcium in the body (Macura et al., 2022; Preda et al., 2023). The best way to reduce harm to both mother and foetus (Kautzky-Willer et al., 2023; White et al., 2023) is by offering proper prenatal care for gestational diabetes, as this impact many pregnancies.

5. CONCLUSION

This paper provides in-depth information about late-onset hypocalcaemia in formula-fed newborns and highlights the various causes, possible symptoms and problems with fast treatment. From the results, it is evident that a lot of newborns with complications are born a bit early and tend to have low body weights, making it more likely for them to develop metabolic issues. Experts found, through biochemical tests, that the magnitude of magnesium did not change, whereas a high level of phosphate and low vitamin D are generally present with hypocalcaemia. In a number of babies, the parathyroid hormone was higher than normal, trying to alter part of their physiology. Importantly, those who experienced seizures or muscle spasms almost all had severe deficiencies in serum calcium, so it is important to quickly check these babies who demonstrate such symptoms. Moreover, if the mother has diabetes, it greatly increases the risk and highlights why the mother's metabolic health is essential for the baby. It is very important for a baby's nutrition that the calcium-to-phosphorus ratio is tailored to each baby. The evidence shows that knowledge about regular screening and early action for late-onset hypocalcaemia in babies fed formula is lacking, despite better neonatal care in the area. A high-risk newborn can be detected by using a mix of medical examinations, biochemical profile and mother's medical history. Also, in addition to genetic testing for frequent tumors, using vitamin D and calcium supplements can help doctors design more specific treatment. According to the study, newborns with poor birth weight, diabetes in their mother or those considered premature should be regularly monitored for calcium balance in revised NICU policies. To tackle and minimise neonatal hypocalcaemia, it is important to involve neonatologists, dietitians and mother health professionals.

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