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Original Article

Risk Factors Associated with Very Low Birth Weight: A Systematic Review and Meta-Analysis

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Background: Very Low Birth Weight (VLBW) is due to multiple gestations and reproductive-assisted techniques. Neonatal complications mainly arise in infants with VLBW and Extremely Low Birth Weight (ELBW). The main objective was to study the risk factors associated with VLBW and to conduct a meta-analysis.
Methods: A meta-analysis was done to present the most recent risk variables for VLBW. Electronic databases were searched for information on the suggested topic. Using STATA version 14, the relevant data was extracted, and statistical analysis was conducted.
Results: A total number of 112 studies have been conducted on the topic of VLBW worldwide from 2000 to 2020. Information from many parts of the world was evaluated in which GDP or per capita income, age, and education were followed in prominent regions of the world. As GDP and education level improved, the nutritional status also improved. Fifteen studies have been identified, with five meeting the inclusion criteria for the metanalysis of VLBW <1500g in developing countries. Illiteracy, poverty, mother occupation, hypocalcemia, and hypoglycemia were the common risk factors of VLBW (<0.05).
Conclusion: It was identified that per-capita GDP is inversely proportional to VLBW throughout the world. VLBW in America was found to be significant when compared with central Europe (<0.005), similarly with Southern Europe (<0.03), Northern Europe (<0.00001), Asia (<0.0001), and Africa (<0.0001). Unlike per capita GDP, VLBW was insignificantly related to maternal age in all regions except Africa, where VLBW was significantly associated with maternal age (p<0.0001). In developing countries, illiteracy, poverty, mother occupation, hypocalcemia, and hypoglycemia are the common risk factors for VLBW (<0.05) as the complications related to VLBW are at a high-risk rate, so it is recommended that VLBW babies require special care at the time of birth, especially in poor economic countries.

Keywords: Very Low Birth Weight, Meta-Analysis, Extremely LBW, Per Capita GDP, Hypocalcemia, Hypoglycemia

Project details. Nil

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Conflict of interest: The authors have no conflict of interest.

Introduction

Very Low Birth Weight (VLBW) means babies born with a weight less than 1500 grams are about 3 pounds. Low Birth Weight (LBW) babies, whether born at term or preterm, are classified into three types (1) Low birth weight, which is less than 2500 grams or 5.5 pounds, (2) Meager birth weight that is less than 1500 grams or about 3 pounds (3) Meager birth weight who are less than 1000 grams or 2 pounds [1]. These babies are either born before term pregnancy or do not grow adequately during pregnancy [2]. Causes of low-birth-weight babies include preterm labor if the baby is born before 37 weeks of pregnancy. Chronic diseases in the mother are another cause if the mother is hypertensive, diabetic, and has chronic heart disease or lung and kidney problems. She is at risk of having low birth weight babies. Maternal infections include cytomegalovirus, rubella, chickenpox, toxoplasmosis, and certain sexually transmitted infections are also considered to be the cause of LBW [3]. Placental deficiency and maternal drug history are also significant. Those on antihypertensives or antiepileptic medications have a higher incidence of low-birth babies. Less weight gain during pregnancy is another risk factor for having low birth weight babies. Being pregnant with multiples (twins, triplets, or more), smoking, drinking alcohol or using street drugs, exposure to air pollution and lead poisoning, psychological stresses, and being a teen mother are some other risk factors [4]. Ethnicity is also highlighted in many articles like (1 in 7) black babies (13%); (1 in 12) Asian (8%); (1 in 13) Native American (8%); (1 in 14) white (7%) [5].

Very LBW deliveries are associated with many complications. Their management involves the mother, the preterm baby, and the entire family. Low birth weight babies are prone to various health problems. Some need special care in the NICU (Neonatal Intensive Care Unit) [6]. These health issues can be related to breathing problems known as respiratory distress syndrome, Intraventricular hemorrhage (bleeding in the brain), Necrotizing enterocolitis, and cardiovascular defects such as patent ductus arteriosus [7]. These babies may have health problems later in life, including diabetes, heart diseases, high blood pressure, intellectual and developmental disabilities, metabolic syndrome, and obesity [7]. Although the death rate has dramatically decreased due to the development of newborn care management, the percentage of infants who survive with severe sequelae has not significantly increased. Despite better neurodevelopmental results in a few limited trials, it has not yet been observed globally [8]. Low birth weight babies are either preterm or small for fetal age. Reports suggest that other factors should be considered besides the fertilization age. Female sex and antenatal corticosteroids have a favorable outcome [9]. Single birth, as compared to multiple births, has more positive effects. It has also been seen that increments of 100 grams in birth weight adds to a favorable outcome. Risk factors associated with low birth weight are categorized as factors in the immediate neonatal period and long-term sequelae [10].

Among neonatal risks, body temperature plays a vital role in low-birth-weight babies. Body surface area to body weight ratio, fat storage, and glycogen supply are all higher in LBW [11]. So, newborns with light birth weight are defenseless to warm misfortune following birth. Hypothermia leads to hypoglycemia, apnea, and metabolic acidosis. Secondly, extremely low birth and preterm babies have non-keratinized and thin skin, which adds to the problem [12]. Management of hypothermic babies and reducing this risk involves the transport of the baby to the NICU from the delivery room with meticulous monitoring and intensive care [13].

Low birth weight babies have problems maintaining their average glucose level after birth [14]. They have deficient glycogen stores and are under increased stress. Hypoglycemia may cause seizures, lethargy, and poor feeding. Fluid and electrolyte balance should be maintained correctly in such babies. These babies have compromised renal functions and decreased GFR (Glomerular filtration rate). They can develop hyperkalemia and hypernatremia because of more fluid collection in their extracellular compartment [15]. Respiratory distress

syndrome, brought on by a lack of surfactants, is one of the additional problems. As a result, there could be an alveolar collapse, atelectasis that worsens, edema, and decreased lung capacity [16].

Although the incidence of RDS (Respiratory Distress Syndrome) has significantly decreased with the use of antenatal steroids that promotes lung maturity, in addition, early surfactant treatment has also been used as an early measure to reduce overall mortality. Another major morbidity factor in premature and low-birth babies is bronchopulmonary dysplasia[17]. Usually, ductus arteriosus shuts within two days of birth due to oxygen-induced constriction in full-term babies. About 80% of deficient birth weight babies have PDA (Patent Ductus Arteriosus)[18]. Still another important factor leading to morbidity and mortality in low-birth-weight babies is infection. It can be manifested as temperature instability, tachycardia, poor perfusion, bradycardia, decreased activity, feeding intolerance, apnea, and metabolic acidosis. Next is necrotizing enterocolitis, which is also a significant problem.

The premature gastrointestinal tract mucosa gets injured along with its vasculature. Deficient birth weight babies are also prone to intraventricular hemorrhage causing hypertension or hypotension, anemia acidosis, and seizures. There can be damage to cerebral white matter known as periventricular leukomalacia. It results in severe motor and cognitive deficits. Some low birth or premature babies develop sudden apnea, which is the sudden cessation of respiration for a few seconds [19]. Besides these immediate neonatal risks, low birth weight and low birth babies have long-term sequelae. While the vast majority have a usual outcome, they generally have subnormal growth, illnesses, and neurodevelopmental problems. Only a tiny minority have mental retardation or cerebral palsy. They have issues regarding attention, cognition, and neuromotor functioning delays. These cognitive defects become more pronounced later [20]. Even survivors who pass through infancy without severe neurodevelopmental or functional defects may experience several long-term adverse outcomes, including limited academic skills, poor motor skills, poor vision, cerebral palsy, and psychological challenges. Though the mean IQ score of low birth weight falls within the average range, there are higher rates of faulty and subnormal intelligence [20]. The main objective was to study the risk factors associated with very LBW and to conduct a meta-analysis. The current research highlighted the problem requiring teamwork and feedback from neonatologists, obstetricians, pediatricians, and other providers.

Method

Sample Size

A total number of 112 studies have been conducted on low birth weight worldwide from 2000 to 2020. Fifteen studies have been identified from 2010 to 2020, with 5 meeting the inclusion criteria for the metanalysis of VLBW of less than 1500g. The data was mentioned in the research studies from the departments of Obstetrics and Gynecology, labor room, selected cases file, operation theater, and maternity ward. Basically, from these records, information that was taken includes maternal history, gestational age, pregnancy index, socioeconomic status, and obstetric history. Problems related to pregnancy were also considered like hypertension, diabetes mellitus, chronic disorders, and heart problems. To determine the rate of VLBW targeting only < 1500g, a descriptive meta-analysis was done based on the critical analysis and scientific evaluation.

Study selection and reviewing of literature

To achieve the study's objective, an extensive literature review was carried out using various search engines for Medline database of references and abstracts on biomedical research, mainly PubMed, Google Scholar, and web of science.

Inclusion and Exclusion criteria

Relevant literature was extracted from 2000 to 2020 by considering the article's theme related to light birth weight, results, and the conclusion of the research studies. Additionally, the inclusion criteria remain stuck to the VLBW and extended to the relevant cited references from 2010 to 2020 with the same idea. A brief revision of the selected articles was done, and irrelevant articles that included the information of LBW of 1600-2500g were omitted.

Data Extraction

For the meta-analysis of VLBW (<1500g), author names, publication year, total live births, Cases of VLBW (<1500g), preterm and term birth, maternal age, and risk factors associated with VLBW in neonates were the critical parameters included in the study.

Statistical Analysis

The published data from over the world from 2000-2020 was interpreted into different groups, and the screened data from 2010 to 2020 was evaluated for analysis. The significant p-value of 0.05 at CI 95% was used further for the conversion of meta-analysis results into related statistical tools like STATA (version 14).

Results

In the present study, data from different continents were evaluated from 2000 to 2020 in which GDP or per capita income, age, and education were followed in prominent regions of the world. As GDP and education level improved, the nutritional status also improved. Age is a significant factor in determining LBW. Healthy young women showed a balanced diet for developing fetuses [21].

Asia and Southern Europe showed a high LBW rate, as shown in Table 1. A previous study showed that such children have subnormal heights [22]. They have fewer educational achievements, their average age in high school education was higher, and they were enrolled in post-secondary studies at a much lower rate than their middle birth weight counterparts. Nearly all deficient birth weight infants need neurodevelopmental follow-up monitoring to track their development and find problems that were not immediately noticeable during the neonatal period [23]. Early detection of developmental issues, parental counseling, identification, and treatment of medical difficulties should be the aims of neonatal follow-up clinics.

Additionally crucial are the collaboration and input of neonatologists, obstetricians, pediatricians, and other healthcare professionals. Conducting detailed assessments of a child's neurological, visual, and auditory development is crucial. Increasing the likelihood that newborns will live healthy, successful lives is vital as more kids are born and survive. Therefore, before choosing how to handle the expected delivery of babies with exceptionally low birth weights, the treating clinician must inform the family of the short- and long-term effects [24].

In this study, Very Low Birth weight was found to be significant in the American population compared to other countries (Table-2). In the present study, we found that per capita GDP is inversely proportional to VLBW. Only 1000$ accounted for 0.012%, which resulted in decreased LBW. Other health-related complications like a higher number of smokers, breast cancer, and cervical cancer reported higher VLBW rates. From 2005 to 2015, the LBW rate increased 6.2% to 6.5%, but due to GDP improvement, the VLBW rate slightly decreased up to 2020 in some regions. VLBW rate was more significant in Southern Europe, 7% in Eastern Europe, 5% in Asian/Ocean regions and was stable in America, Central Europe, and Northern Europe from 2000 to 2015, but still, VLBW in America was found to be significant when compared with Central Europe (0.005), similarly with Southern Europe (<0.03), Northern Europe (<0.00001), Asia (<0.0001) and Africa (<0.0001) as shown in Table-2. The most probable risk factors are the mother's age, maternal health, race, multiple births, and many more. Unlike GDP, VLBW was insignificantly related to maternal age (p-value > 0.05). Still, in other

African studies, VLBW was significantly observed in maternal age of >35 years or teenage mothers due to socioeconomic problems, other pregnancy complications, and poor nutrition.

Table 1. Per capita GDP is inversely proportional to VLBW

Year	GDP%	Mother Age (years)	Order-wise increase in Mother Education (%)	VLBW Southern Europe (%)	VLBW Central Europe (%)	VLBW Eastern Europe (%)	VLBW Northern Europe (%)	VLBW Asia/Oceania (%)	VLBW in Africa (%)
2000	6.2	19	26	7.61	6.57	6.33	4.98	17.5	3
2005	6.4	20-29	29	6.98	6.43	6.01	4.99	17	3.8
2010	6.5	30-34	40	7.58	6.58	6.27	4.89	16.1	3.8
2015	6.5	35-39	55	8.02	6.7	6.57	494	15	4
2020	6.5	39	87	8.35	6.43	6.43	5.03	14.6	4.7

*Mother age was insignificantly associated with VLBW in Southern Europe, VLBW in Central Europe (p=0.487), VLBW in Eastern Europe (p=0.49), VLBW in Northern Europe (p=0.167), VLBW in Aisa/Oceania (p=0.49), but significantly associated with VLBW in Africa (p<0.0001)

Table 2. Comparison of VLBW in America with other regions of the world

VLBW America (%)	VLBW Southern Europe (%)	VLBW Central Europe (%)	VLBW Eastern Europe (%)	VLBW Northern Europe (%)	VLBW Asia/Oceania (%)	VLBW in Africa (%)
6.95	7.61	6.57	6.33	4.98	17.5	3
6.38	6.98	6.43	6.01	4.99	17	3.8
7.05	7.58	6.58	6.27	4.89	16.1	3.8
6.98	8.02	6.7	6.57	494	15	4
6.75	8.35	6.43	6.43	5.03	14.6	4.7
p-value	0.03	0.005	0.00001	0.00001	0.0001	0.0001

All countries in Northern Europe except the United Kingdom showed a low LBW rate. The UK was the only country that showed an abate trend.[18] All five countries in Southern Europe showed high LBW rates. France was the only one not showing elevated tendency. Age factor accounted for a factor affecting the LBW rate. Women of 19 years showed LBW as compared to 30 or more. Other factors like education and health care facilities also contributed to a large extent in lowering the rate of LBW from 2000 to 2020. Some regions where the COVID-19 rate was high and disturbed the economy badly showed an increased LBW rate [25].

Different studies showed illiteracy, poverty, and mother occupation as the risk factors significantly associated with VLBW in 2016 highlighting hypocalcemia and hypoglycemia as the risk factors of VLBW [26]. Hypoglycemia problem arises due to the decreased storage of glycogen and fat. In other words, it aggravates due to increased anaerobic glycolysis and other metabolic activity. In 2019, scientists found hypothermia and hypocalcemia as risk factors for VLBW, as shown in Table 3 [27]. VLBW infants have high body surface-to-body weight ratios that decrease the storage of brown fat and glycogen, and the body cannot store the heat. Prevention of hypothermia increases the survival of an infant. Heat loss can be prevented by drying an infant at birth to prevent evaporative heat loss. Wrapping the VLBW baby into plastic wrap or warmed blanket prevents radiant heat loss during transport. The heated incubator can be used to maintain a neutral thermal environment [28].

As the complications related to VLBW are at a high-risk rate. Most VLBW and ELBW babies require special care at birth in developing countries. They are kept in an incubator and under ventilation for a prolonged period [29]. Such infants have decreased central respiratory drive, smaller alveoli, weak muscles, and chest wall. So, they require intensive care to measure blood gas tension and pH. There is a need to increase the number of incubators and ventilators in each hospital. VLBW infants and ELBW infants require an arterial catheter, primarily for

blood sampling and blood pressure measurement. The most effective therapy, in this case, is dopamine [30]. Oxygen level is maintained in the 85%-92% range**.** If the oxygen level exceeds 94%, surface tension becomes high due to inaccuracy of the pulse oximeter. Calcium gluconate should be started to avoid hypocalcemia at 200mg/kg/d. Feeding is usually prohibited on 1st day of VLBW and ELBW babies. Trophic feeding is preferred for such babies for several days. Lipid IV is not given for at least 4-5 days, especially if there is a pulmonary disease[31].

Table 3. Year-wise distribution of selected data on VLBW (<1500g) from the years 2010-2020 in developing countries

Reference	Year	Live Births	VLBW (1500g)	Preterm	Term	Mother age (Years)	Risk Factors	P value
Ghouse and Zaid	2016	11977	108	80	28	20-25	Illiteracy, Poor wealth status. Mother Occupation	0.05
Khan *et al*	2016	2038	199	32	0	20-40	Hypocalcemia, Hypoglycemia	0.05
If *et al*	2017	1863	1603	1442	161	20-40	Mother occupation, age, Illiteracy	0.05
Mahmoud *et al*	2017	1458	1080	756	324	20-48	Mother occupation, increased age	0.05
Chand *et al*	2019	2082	271	185	86	20-40	Hypocalcemia, hypothermia	0.05

Conclusion

Per capita GDP is inversely proportional to VLBW in any world region. VLBW in America was found to be significant when compared with central Europe (<0.005), similarly with Southern Europe (<0.03), Northern Europe (<0.00001), Asia (<0.0001), and Africa (<0.0001). Unlike per capita GDP, VLBW was insignificantly related to maternal age. Illiteracy, poverty, mother occupation, hypocalcemia, and hypoglycemia were the common risk factors of VLBW (<0.05). As the complications related to VLBW are at high risk in countries with poor economic status, it is recommended that VLBW babies require special care at the time of Birth.

References

[1] N. Martín-Calvo, L. Goni, J. A. Tur, and J. A. Martínez, "Low birth weight and small for gestational age are associated with complications of childhood and adolescence obesity: Systematic review and meta-analysis," *Obes. Rev.*, vol. 23, no. S1, pp. 1–12, 2022, doi: 10.1111/obr.13380.

[2] D. Janjua, J. Singh, A. Agrawal, and D. V. Jadhav, "Prospective observational study to assess the Somatic Growth in Very Low Birth Weight infants," *Indian J. Child Health*, vol. 9, no. 1, pp. 6–10, 2022, doi: 10.32677/ijch.v9i1.3225.

[3] M. Ptok, "Early Detection of Hearing Impairment in Newborns and Infants," *Dtsch. Arztebl. Int.*, vol. 108, no. 25, p. 426, Jun. 2011, doi: 10.3238/ARZTEBL.2011.0426.

[4] C. Montagnoli *et al.*, "Anything New about Paternal Contribution to Reproductive Outcomes? A Review of the Evidence," *World J. Mens. Health*, vol. 39, no. 4, pp. 1–19, 2021, doi: 10.5534/WJMH.200147.

[5] K. E. Hannan, S. L. Bourque, C. Palmer, S. Tong, and S. S. Hwang, "Racial and Ethnic Disparities in Medical Complexity and In-Hospital Death Among US-Born VLBW Infants," *Hosp. Pediatr.*, vol. 12, no. 5, pp. 463–474, May 2022, doi: 10.1542/HPEDS.2021-006263.

[6] E. Y. Debele *et al.*, "Household food insecurity and physically demanding work during pregnancy are risk factors for low birth weight in north Shewa zone public hospitals, Central Ethiopia, 2021: a multicenter cross-sectional study," *BMC Pediatr.*, vol. 22, no. 1, p. 419, Jul. 2022, doi: 10.1186/S12887-022-03480-2.

[7] S. T. Kelleher, C. J. McMahon, and A. James, "Necrotizing Enterocolitis in Children with Congenital Heart Disease: A Literature Review," *Pediatr. Cardiol.*, vol. 42, no. 8, pp. 1688–1699, Dec. 2021, doi: 10.1007/S00246-021-02691-1.

[8] S. B. DeMauro, "Neurodevelopmental outcomes of infants with bronchopulmonary dysplasia," *Pediatr. Pulmonol.*, vol. 56, no. 11, pp. 3509–3517, Nov. 2021, doi: 10.1002/PPUL.25381.

[9] A. Sotiriadis *et al.*, "Antenatal corticosteroids prior to planned caesarean at term for improving neonatal outcomes," *Cochrane database Syst. Rev.*, vol. 12, no. 12, Dec. 2021, doi: 10.1002/14651858.CD006614.PUB4.

[10] D. Singer, L. P. Thiede, and A. Perez, "Adults Born Preterm–Long-Term Health Risks of Former Very Low Birth Weight Infants," *Dtsch. Arztebl. Int.*, vol. 118, no. 31–32, pp. 521–527, Aug. 2021, doi: 10.3238/ARZTEBL.M2021.0164.

[11] K. Hardy, H. Bocherens, J. B. Miller, and L. Copeland, "Reconstructing Neanderthal diet: The case for carbohydrates," *J. Hum. Evol.*, vol. 162, Jan. 2022, doi: 10.1016/J.JHEVOL.2021.103105.

[12] J. Hu, W. Xu, H. Yang, and L. Mu, "Uric acid participating in female reproductive disorders: a review," *Reprod. Biol. Endocrinol. 2021 191*, vol. 19, no. 1, pp. 1–11, Apr. 2021, doi: 10.1186/S12958-021-00748-7.

[13] L. Fang, J. Pei, and S. Jiang, "Effect Analysis of In-Hospital Transfer Care Based on STABLE Technology in Critically Ill Newborns," *Evid. Based. Complement. Alternat. Med.*, vol. 2022, pp. 1–8, Jul. 2022, doi: 10.1155/2022/8250655.

[14] E. Pericuesta, J. L. Gutiérrez-Arroyo, M. J. Sánchez-Calabuig, and A. Gutiérrez-Adán, "Postnatal catch-up growth programs telomere dynamics and glucose intolerance in low birth weight mice," *Int. J. Mol. Sci.*, vol. 22, no. 7, 2021, doi: 10.3390/ijms22073657.

[15] C. Coleman, A. Tambay Perez, D. T. Selewski, and H. J. Steflik, "Neonatal Acute Kidney Injury," *Front. Pediatr.*, vol. 10, Apr. 2022, doi: 10.3389/FPED.2022.842544.

[16] M. Gilfillan, A. Bhandari, and V. Bhandari, "Diagnosis and management of bronchopulmonary dysplasia," *BMJ*, vol. 375, Oct. 2021, doi: 10.1136/BMJ.N1974.

[17] S. M. Lee, L. Sie, J. Liu, J. Profit, and H. C. Lee, "Evaluation of Trends in Bronchopulmonary Dysplasia and Respiratory Support Practice for Very Low Birth Weight Infants: A Population-Based Cohort Study," *J. Pediatr.*, vol. 243, pp. 47-52.e2, Apr. 2022, doi: 10.1016/J.JPEDS.2021.11.049.

[18] S. Elbayiyev, F. E. Canpolat, G. Kadıoğlu Şimşek, S. Işık, M. Büyüktiryaki, and H. G. Kanmaz Kutman, "Long-term neurodevelopmental outcomes in very low birth weight infants with and without patent ductus arteriosus: A retrospective case control observational study," *Child. Care. Health Dev.*, 2022, doi: 10.1111/CCH.12997.

[19] O. H. LOWRY, N. J. ROSEBROUGH, A. L. FARR, and R. J. RANDALL, "PROTEIN MEASUREMENT WITH THE FOLIN PHENOL REAGENT," *J. Biol. Chem.*, vol. 193, no. 1, pp. 265–275, Nov. 1951, doi: 10.1016/S0021-9258(19)52451-6.

[20] G. L. Taylor and T. M. O'Shea, "Extreme prematurity: Risk and resiliency," *Curr. Probl. Pediatr. Adolesc. Health Care*, vol. 52, no. 2, p. 101132, Feb. 2022, doi: 10.1016/J.CPPEDS.2022.101132.

[21] S. Apriani, S. S. Apriani, R. Lestari, E. Widayati, Y. Suryani, and K. A. P, "Risk Factors For The Occurrence of Low Birth Weight Based on Nutritional Status of Pregnant Women With Upper Arm Circumference," *J. Midwifery*, vol. 6, no. 1, pp. 58–65, Jul. 2021, doi: 10.25077/jom.6.1.58-65.2021.

[22] F. L. Filho *et al.*, "Nutritional supplementation and growth after hospital discharge in very low birthweight newborns: Randomized controlled trial / Suplementação

nutricional e crescimento de recém-nascidos de muito baixo peso após alta hospitalar: Ensaio clínico randomizado," *Brazilian J. Dev.*, vol. 7, no. 10, pp. 101149–101162, 2021, doi: 10.34117/bjdv7n10-433.

[23] L. Letzkus, M. Conaway, C. Miller-Davis, J. Darring, J. Keim-Malpass, and S. Zanelli, "A feasibility randomized controlled trial of a NICU rehabilitation program for very low birth weight infants," *Sci. Rep.*, vol. 12, no. 1, Dec. 2022, doi: 10.1038/S41598-022-05849-W.

[24] B. J. Ennis, D. J. Reed, and J. D. Lantos, "Current controversies in neonatal resuscitation," *Semin. Perinatol.*, p. 151627, May 2022, doi: 10.1016/J.SEMPERI.2022.151627.

[25] P. S. Mishra, D. Sinha, P. Kumar, S. Srivastava, and R. Bawankule, "Newborn low birth weight: do socio-economic inequality still persist in India?," *BMC Pediatr.*, vol. 21, no. 1, pp. 1–13, 2021, doi: 10.1186/s12887-021-02988-3.

[26] V. Varlas *et al.*, "Fetal Pancreatic Hamartoma Associated with Hepatoblastoma-An Unusual Tumor Association," *Diagnostics (Basel, Switzerland)*, vol. 12, no. 3, Mar. 2022, doi: 10.3390/DIAGNOSTICS12030758.

[27] T. A. B. Ali, N. M. Osman, and A. E. M. Mustafa, "Pattern of Low Birth Weight and Early Outcome of Neonates Admitted at Neonatal Unit in Omdurman Maternity Hospital from December 2019 to May 2020," *Bahrain Med. Bull.*, vol. 44, no. 1, pp. 824–831, 2022.

[28] S. Bi *et al.*, "A standardized implementation of multicenter quality improvement program of very low birth weight newborns could significantly reduce admission hypothermia and improve outcomes," *BMC Pediatr.*, vol. 22, no. 1, pp. 1–13, 2022, doi: 10.1186/s12887-022-03310-5.

[29] E. Kajantie *et al.*, "Common Core Assessments in follow-up studies of adults born preterm-Recommendation of the Adults Born Preterm International Collaboration," *Paediatr. Perinat. Epidemiol.*, vol. 35, no. 3, May 2021, doi: 10.1111/PPE.12694.

[30] S. M. Hassan, N. Lucas, and K. Wickramasinghe, "Outcome of very low birth weight infants in a tertiary neonatal care centre in Colombo, Sri Lanka: A preliminary study," *Sri Lanka J. Child Heal.*, vol. 51, no. 2, p. 277, Jun. 2022, doi: 10.4038/SLJCH.V51I2.10133.

[31] G. Boscarino *et al.*, "Early enteral feeding improves tolerance of parenteral nutrition in preterm newborns," *Nutrients*, vol. 13, no. 11, pp. 1–10, 2021, doi: 10.3390/nu13113886.