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Preterm Birth: Scope of the Problem, Cost of Care, Potential Complications and Current Guidelines for Management

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Abstract

One in ten infants is born preterm in the world. Prematurity is the leading cause of death in infants. In 2022, 47 percent of all deaths in children occurred in the first 28 days of life. Prematurity can be prevented by emphasis on maternal health, nutrition and skilled antenatal care. Neonatal survival depends upon essential new born care with thermal protection by skin-to-skin contact, hygiene in the care of umbilical cord, early breast feeding, regular health care, immunization and treatment of common neonatal problems.

Keywords: Preterm Birth; Prematurity; Neonatal Intensive Care Unit

Abbreviations

VLPW: Very Low Birth Weight Infants; ELBW: Extremely Low Birth Weight; ROP: Retinopathy Of Prematurity; NICU: Neonatal Intensive Care Unit; CP: Cerebral Palsy.

Introduction

Preterm birth is defined as the birth of an infant less than 37 weeks of gestation. 13.4 million new born babies were born preterm in 2020 which accounts for 9.9 percent of all births in the world. In 2020, preterm births in Southern Asia and Sub-Saharan Africa accounted for approximately 65 percent of all preterm births globally [1]. 15 percent of all preterm births occurred at less than 32 weeks of gestation, requiring specialized neonatal intensive care. In the US, the total cost spent on preterm births was $25.2 billion, meaning $64,815 was spent on each preterm birth. Lifetime medical care costs for those born preterm comprised two-thirds of the total cost. $17.1 billion were spent for medical care of persons born preterm, $2.0 billion were spent for delivery care, $1.3 billion were spent for early intervention and special education, and $4.8 billion were spent in lost productivity due to associated disabilities in adults [2].

The preterm birth rate in the USA is currently 10.4 percent. There are significant racial and ethnic differences in preterm birth rates. In 2022, the percentage of preterm birth among Black women was 14.6 percent, 50 percent higher than White or Hispanic women at 9.4 percent and 10.1 percent respectively [3]. Babies born before 32 weeks have higher rates of death and disability. In 2021, preterm birth and low birth weight accounted for about 14.8 percent of deaths of babies before 1 year of age. Babies who survive may have short term or long-term breathing problems, feeding difficulties, cerebral palsy, developmental delay, vision problems, chronic diseases, or hearing deficits.

While a cause for preterm birth is not always known, several factors may play a role for early onset of preterm labour. Women who experience teen pregnancy, women who become pregnant over the age of 35 years, black women, Native Hawaiian and Pacific Islander women, American Indian or Alaska Native women, women with lower incomes,

and women experiencing stress are more likely to experience a preterm birth. Some medical conditions can predispose a pregnant woman to deliver a preterm infant. These conditions include a history of prior preterm birth, multiple gestations, maternal sepsis or urinary tract infection, Covid 19 infection, pre-eclampsia or chronic hypertension. Smoking tobacco, vaping, marijuana use, taking prescription pain relievers, or using illegal drugs during pregnancy is associated with double or even triple the risk of stillbirth [4]. Estimates suggest that about 5 percent of pregnant women use one or more addictive substances. Opiate exposure before birth predisposes the new born infant for neonatal abstinence syndrome, sudden infant death syndrome and developmental delay. Exposure to cocaine and amphetamines may lead to placental separation, brain bleed in the infant, or may cause significant developmental delays, poor school performance, high risk of school dropout, and criminal risk behavior later in life.

A high-risk pregnancy is one that compromises the health or life of the mother or her unborn infant. It often requires specialized care from specially trained providers [5]. Some pregnancies become high risk as they progress, while others are at increased risk for complications for a variety of reasons. Risk factors for a high-risk pregnancy can include existing health conditions, such as high blood pressure, diabetes, or being HIV-positive 1. Early and regular prenatal care helps many women have healthy pregnancies and deliveries without complications. Obesity increases the risk for hypertension, preeclampsia, gestational diabetes, stillbirth, neural tube defects, and cesarean delivery. NICHD researchers have found that obesity can raise infant's risk of heart problems at birth by 15 percent [6].

The risk of complications is higher in women carrying twins or triplets, especially preeclampsia, premature labour, and preterm birth. More than 50 percent of all twins and as many as 93 percent of triplets are born at less than 37 weeks' gestation. Pregnant women can take important steps to help reduce their risk of preterm birth and improve their general health by quitting smoking, avoiding alcohol and drug use, getting prenatal care early and throughout pregnancy, and seeking medical attention for any signs or symptoms of preterm labour, pregnancy related hypertension or gestational diabetes. Those with pre-existing conditions like diabetes or systemic disorders should have their health status evaluated prior to getting pregnant. Those who have had a previous preterm birth should also get medical attention before planning to have another child. If a woman experiences preterm labour or is at risk of preterm childbirth, treatments are available to help protect the preterm baby from future neurological impairment as well as difficulties with breathing and infection. These include antenatal steroids and tocolytic treatments to delay labour and antibiotics for preterm prolonged rupture of membranes.

There is a significant disparity in care between whites and blacks in this country. There is a 50 percent higher risk of preterm delivery among blacks. Infant mortality rate and maternal motility rates are higher among blacks. Maternal mortality amongst blacks is 49.5 deaths per 100,000 live births, which is more than three times higher than the rate for Caucasian women [7]. The preterm birth rate for African Americans in the United States is 52 percent higher than that of all other races [8]. Black women may have limited access to quality and affordable health care. They have a higher risk of long-term health problems, developmental issues and chronic illnesses. Poverty among blacks, lack of education, pre-existing health issues like obesity, poor availability of medical resources may delay in getting adequate prenatal care. Certain medical issues like gestational hypertension, diabetes, or preeclampsia if not identified and treated early in pregnancy may lead to serious consequences of pregnancy. Poor housing conditions, lack of sanitary conditions, unsafe environment, crime, drug use and gang violence leads to overwhelming stress that compromises the health of mother and the baby. Black women get poor quality of care because of discrimination and implicit bias within the healthcare system. Training of the healthcare providers is important to recognize and to avoid implicit bias to provide quality of care to underserved population. A low birth weight infant is the one that weighs less than 2500 g. In 2022, 10.38 percent of all births were low birth weight. Infants less than 1500 grams are labelled as very low birth weight infants (VLBW). They comprised 1.38 percent of all births. Extremely low birth weight (ELBW) infant is defined as one with a birth weight of less than 1000 g. Most extremely low birth weight infants are also the youngest of premature newborns, usually born at or below 27 weeks' gestational age. Less than 1 percent infants are born ELBW. Infants with a birthweight of 500-749 grams had the highest average expenditures, at $537,624 [9]. One study found that the average cost for infants born less than 28 weeks gestation was over $100,000.

Infants with very low birth weight are at a higher risk of developing a number of serious medical complications. Complications are much worse with lower gestational ages. The early and immediate complications that are commonly encountered are respiratory distress due to lung immaturity, infections, inability to maintain body temperature because of lower body fat content and feeding difficulties. Neurological problems could present as intracranial bleed, periventricular leukomalacia, developmental delay and cerebral palsy. Necrotizing enterocolitis is a potentially life-threatening gastrointestinal illness reported in premature or very low birth weight infants. It typically presents at 2 or 3 weeks of age with poor feeding, abdominal distension, emesis or blood in the stool. Potentially, it may lead to bowel

perforation, generalized sepsis, tendency for disseminated intravascular coagulopathy, multi-organ failure, and even death [10]. The risk factors for necrotizing enterocolitis are formula feedings, intrauterine growth retardation, chorioamnionitis, maternal diabetes, maternal cocaine or amphetamine use, intrauterine growth restriction, lack of prenatal steroids, placental abruption, preeclampsia and history of maternal smoking. Necrotizing enterocolitis can be prevented by early introduction of breast milk feeding and probiotics. Treatment includes bowel rest, removal of gastric contents with orogastric tube, intravenous fluids, and intravenous antibiotics. Surgery is indicated with evidence of bowel perforation. After recovery from illness, feedings are gradually introduced. Intravenous hyperalimentation may be required for weeks to months. Bowel stricture and short gut syndrome are potential long-term complications.

Respiratory illness in preterm infants due to lung immaturity and surfactant deficiency may necessitate respiratory support, exogenous surfactant administration, and use of prenatal steroids [11]. Initial invasive respiratory support could be followed up by non-invasive respiratory support and oxygen for several days and weeks. Some infants may develop chronic lung disease requiring long-term oxygen, a course of steroids, and bronchodilators. Early introduction of continuous positive airway pressure therapy is recommended for preterm infant with clinical presentation of respiratory distress. It may be considered immediately after birth for an infant less than 32 week gestation that may not have acute respiratory distress. Bubble CPAP is superior than ventilator assisted CPAP. Caffeine is recommended for the treatment of apnea in preterm infant. Typically, started at 20 milligram/kilogram bolus followed by maintenance dose of 5-8 milligram/kilogram per day until the infant is 34 weeks gestation and/or apnea free for 5-7 days. For preterm infant under 34 week's gestation with significant respiratory distress, caffeine is also helpful in weaning them off ventilator.

Retinopathy of prematurity (ROP) is a rare proliferative retinal condition that is seen in infant's under 1.5 kg at birth. ROP is a major cause of childhood blindness. Retinal vascularization starts from the posterior pole and is completed by 40 weeks of life. ROP incidence increases in infants with decreasing gestational age. In the initial phase after birth retina gets hypoxemic followed by hyperoxia leading to proliferation of blood vessels and eventual complication of retinal detachment. Strategies to prevent retinopathy of prematurity will depend on optimization of oxygen saturation and good nutrition. Current guidelines by the American Academy of Pediatrics recommend that all infants ≤30 weeks GA or ≤1500g BW should be screened for ROP. Infants with apnea of prematurity are more likely to require mechanical ventilation and supplementary oxygen, and may be more likely to develop ROP [12]. Initial screening should be performed at 31 weeks' postmenstrual age in infants with gestational ages of 26 6/7 weeks or less at birth, and at four weeks' chronological age in infants with gestational ages of 27 weeks or more at birth by an ophthalmologist skilled in the detection of ROP [13]. Permanent bilateral hearing loss affects 1-3/1000 live births in wellborn infants and 2-4/100 infants in the neonatal intensive care unit (NICU) population [14]. For the best results and effective treatment hearing loss should be recognized within three months of life, with audiological confirmation to initiate early intervention before the 6th month of age [15,16]. Early treatment is essential for development of intellect and emotional growth in 1st year of life and normal development of speech and language.

Iron supplementation is needed to prevent or treat anemia of prematurity. ELBW infants are at high risk of developing metabolic bone disease of prematurity needing supplementation with extra calories, zinc, multivitamin, and other nutrients. There is increased risk of language delay, cognitive and or motor delay in infants born with lower gestational ages [17]. Preterm infants are at higher risk for cerebral palsy (CP), associated with severe intraventricular hemorrhage or periventricular white matter injury. CP is confirmed in 6.2 percent of children born ≤28 weeks, 14.8 percent at 23 weeks, 10.2 percent at 24 weeks,

7.2 percent at 25 weeks, 5.6 percent at 26 weeks, and 4.8 percent at 27 and 28 weeks [15]. These rates compare with a CP rate of 0.2 percent to 0.3 percent in the general population. Autism risk is four times in preterm infant. Autism spectrum disorder is 15.0 percent at 23 to 24 weeks, 6.5 percent for 25 to 26 weeks, and 3.4 percent for 27 weeks [17]. Early assessment of language delay, lack of response to name, limited eye contact, repetitive or unusual play may indicate risk for autism spectrum disorder [18]. Children with autism spectrum disorder can be diagnosed by 2 years of age.

Long term follow-up of aforementioned diseases of prematurity requires follow-up by neonatologist, pediatrician, developmental expert, occupational therapist, physiotherapist, and speech-language therapist; educational, clinical psychologist, dietitian, social worker, ophthalmologist, and audiologist. Collabouration and coordination of care is of critical importance for appropriate care and provision of rehabilitation services.

Having a preterm birth puts enormous stress on the parents and the family, especially if the baby is extremely premature and very sick. The intensive care unit can be an unfamiliar and intimidating place for the parents. There is a huge risk of anxiety, depression, and post-traumatic stress disorder in parents that can last for an extended period of time. Parents may have a feeling of guilt, frustration or

helplessness. Long stay in the neonatal ICU can interfere with bonding for the parents. Mental health screening of the parent should be considered while the infant is in the NICU. Physicians, nurses, social worker physical therapist, speech pathologist can build a healthy relationship with the family. It may be very helpful to have these families connect with other families that have had premature infants in the neonatal ICU. Neonatal intensive care admission has a significant financial impact on the families of infants born premature. Even with the best insurance there are expenses associated with prolonged NICU stays, medications, and follow-up appointments. Parents may have to take extended time off with loss of income and financial strain. Extremely low birth weight infants are at higher risk of readmission to the hospital. There may be increased risk of reactive airway disease, especially with exposure to passive smoking. Long-term care, therapies, and special education services may be required that could contribute to additional financial burden on the family. Managing healthcare issues including breathing feedings and developmental care could lead to constant stress and lack of sleep for the parents with added anxiety and risk of hopelessness or depression. These factors are compounded in infants born to mothers battling with addiction to opiates, alcohol or other substances. Lack of interaction with the friends and family may lead to social isolation and guilt. Other siblings may bear the brunt of parental stress and lack of attention manifesting as behavioral issues, poor school performance, and psychological stress.

It may be very difficult to cope with the situation when the infant is extremely premature and in precarious clinical condition requiring multidisciplinary support. Parents may need support and help of care providers to look at short term goals in in the recovery process with a broader view of future. Some parents benefit by keeping a log book of day-to-day progress to review the real progress made. Biweekly or weekly multidisciplinary meetings between the families and care providers may enhance in the understanding of the complexities of care. It may be beneficial to keep the future primary care provider in the loop while the infant is still in the neonatal intensive care unit. Parents must be advocate for their child's need to deal with educational system, psychological needs, and developmental needs. Social service expert and discharge planner may assist parents in setting up additional services their child requires. There are generally support services available at different levels to deal with medical needs, however, there may be a lack of financial support and emotional support from family, friends, community and church.

The WHO Departments of Maternal, New born, Child and Adolescent Health and Ageing (MCA) and Sexual and Reproductive Health and Research have developed series of guidelines for care of preterm low birth weight infants [19]. Preventive and promotive care is provided by kangaroo maternal care, giving infant maternal breast milk, use of donor breast milk when maternal breast milk is not available, addition of fortification of the milk for infant's under 32 weeks of gestation or less than 1500 g of weight. When maternal breast milk or donor breast milk is not available, especially enriched preterm formula maybe recommended for infants under 32 week gestation or less than 1500 g of weight. Recommendations are to have early initiation of introduction of breast milk or donor breast milk. Volume of feedings can be increased by up to 30 mL for each kg of weight per day. Exclusive breast-feeding feedings should be continued exclusively for at least 6 months of age. Iron supplementation to be added to formula feedings or breast milk feedings when no additional iron supplementation is coming from any other source. Zinc supplementation of the feedings is recommended. Vitamin D maybe added to feedings while infant is on maternal breast milk feedings. Vitamin-A supplementation may be considered for infant under 32 week gestation and less than 1500 g when no additional vitamin-A is available in diet.

Kangaroo care is defined as continuous and prolonged skin to skin contact between the mother or other care provider and the infant for more than 8 hours a day [20]. It can be initiated immediately after birth, provided that the infant is hemodynamically stable. This has been found to have improvement in baby's breathing, improvement in healthy sleep, including more quiet sleep and longer cycles, improvement in infant's growth, hypothermia is avoided, and there is alleviation of pain related to procedures like heel prick test. It also helps in establishing breast-feeding and maintaining milk supply. Parent should be dressed comfortably with something that can be opened in the front and have the infant straight on the chest, the infant is held in upright position and typically wearing a diaper, hat and socks. The hat and socks help keep the infant warm. Infant is covered during skin to skin contact with the blanket or a sheet. Parents are instructed to avoid smoking, avoid skin to skin contact if they have an active illness. Parent should try to relax while holding the infant, have the baby snuggled in and fall asleep. Avoid playing with infant and support sleep. Put away phones or other electronic devices, make sure skin is clean and healthy. Don't apply any perfumes or lotions. Don't smoke before or during kangaroo care. Second hand smoke poses many health risks for the infant.

Additional recommendations are to provide support for families while infant is still admitted to the medical facility. This support may be provided on daily basis and or as-needed basis to keep the family updated about progress, expectations, and need for long- term care after discharge. This may include education, counseling and preparation of the family's to learn about providing care for infant at home, after discharge.

There may be a need for trained health worker for support of the family by home visits. Appropriate support is provided to the family during hospital stay so that they feel comfortable in providing care of the infant after discharge from the hospital. Most hospitals provide room in care prior to discharge. Parents may need to make a decision about circumcision. A follow-up pediatrician who has experience in caring for a premature baby should be identified early for a better coordination of care and support services like oxygen or tube feeds, and special health care needs. A pediatrician follow-up is recommended within 2-4 days after discharge from the hospital. Many infants may require follow-up by specialists including early-intervention specialists, neurologists, ophthalmologists, gastroenterologist, pulmonologist and physical therapists. Parents and possibly grandparents may have cardiopulmonary resuscitation training and training to understand the type of support services required. A car seat challenge is done prior to discharge and parents should be instructed for using the right type of car seat for the infant. Because of potential risk of apnea or breathing problem, parents may limit the time in a car seat to an hour or two. Infant should not be left in the car seat at home and must lie on its back in a crib to sleep.

Conclusion

Preventing preterm birth remains a challenge. Pregnant women can take important steps to help reduce their risk of preterm birth and improve their general health by quitting smoking, avoiding alcohol and drugs, concentrating on fitness and healthy lifestyle, getting early prenatal care, seeking medical attention for early signs of preterm labour, getting medical care prior to conceiving infant with a previous history of preterm birth and having sufficient gap between pregnancies. Poverty is a risk factor for preterm birth. Antenatal corticosteroids and kangaroo care are low costs strategies to reduce preterm birth related mortality and morbidity. New born care includes keeping the infant warm with skin-to-skin contact, early breast feeding, hand washing and personal hygiene, and support for breast feeding. Preterm infants can have short term or long-term morbidities that require close attention. Preterm birth is associated with significant costs to health system and families.

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