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Determinants, Consequences, Sequelae, Treatment, and Prevention of Preterm or Premature Birth (Preemie): A Desktop Primer

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Abstract

Preterm birth (PTB) is a significant concern in obstetric care, affecting about 11% of all live births. It contributes significantly to perinatal morbidity, mortality, and long-term impairment (second to pneumonia). PTB can be prevented using a multimodal strategy, including public health initiatives, lifestyle changes, improved access to obstetric care, accurate prediction and diagnostic techniques, and efficient and focused therapies. Some areas have progressed, while others remain fraught with dispute and ambiguity. Primary prevention, involving patient education, smoking cessation, improvement in nutritional status, and avoidance of late preterm deliveries, has limitations. Secondary prevention concentrates on avoiding repeated PTBs, the most common risk factor.

A pessary or progesterone can prevent PTB in single or multiple pregnancies with a short cervix and no prior PTB. Cervical cerclage treats structural flaws or cervical weakness in high-risk women with a short cervix. Corticosteroids are the only antenatal intervention that improves post-delivery neonatal outcomes. They may also reduce newborn mortality, cerebral hemorrhage, and neonatal infection. Tocolytics, particularly calcium channel blockers and prostaglandin inhibitors, may provide the time required to deliver antenatal corticosteroids and, if necessary, transfer to a tertiary care institution. This study provides a holistic review of the history, consequences, differential diagnosis, sequelae, treatment, and prevention of PTB.

Keywords: *Congenital Disorders; Perinatal Morbidity; Pessary; Prostaglandin Inhibitor; Smoking Cessation*

Abbreviations

AP: Anterior-Posterior; BMI: Body Mass Index; CAM: Complementary and Alternative Medicine; CCB: Calcium Channel Blockers; CCI: Cervical Consistency Index; NICE: National Institute for Health and Care Excellence; NSAID: Non-Steroidal Anti-Inflammatory Drug; PTB: Preterm Birth; PTSD: Post-Traumatic Stress Disorder; RR: Relative Risk; TCM: Traditional Chinese Medicine

Introduction

Birth is the act of giving birth or the process of having children. Natural selection plays a role in the evolution of pregnancy and delivery. However, selective factors also highly influence reproductive processes, as emphasized by the fact that approximately one-third of implanted fetuses fail to survive birth [1]. Even in developed nations, where maternal and newborn mortality rates have been significantly reduced in recent decades, pregnancy and delivery remain comparably perilous because of the likelihood of particular challenges, such as preterm births (PTB) [1].

A PTB occurs earlier in a pregnancy when a baby is born before gestational week 37. In the 17th century, the average birth weight was 12 - 16 pounds. Between 1832 and 1935, Alexandre Gueniot defined PTB as a birth weight of fewer than 2300g. Infant mortality was very high in these years. Between 1777 and 1796, 96% of newborns died in Dublin, 85% in Paris, and 97% in America [2,3]. Excavations in Athens and Astypalaia uncovered the graves of premature newborns (in wells or pots) with gestational ages ranging from 24 to 37 weeks [4].

The words 'preterm' and 'premature' differed from what they now mean. Uncertainty persisted on whether these terms reflected immature development or a certain kind of hereditary taunt. These infants are believed to have low energy or vitality [5]. In the past, mothers, with the support of midwives, wet nurses, and wise grandparents, were considered the best people to care for newborns, especially preterm babies. With positive results, breastfeeding and whole-mother care were advocated for such babies in the late 1800s.

At that time, doctors in their specialties believed they were better equipped to deal with preterm problems. However, they could not deal with newborns' high mortality and morbidity or identify and treat these infants. No effort was spared to help the weak infant during the first few weeks of life. Newborns were cared for in foundling homes due to the inaccessibility of medical facilities. All these factors indicate that premature birth was not provided with the necessary attention at the time [3,5-7].

In 1866, Credé developed his double-walled Warme-Wänne in the Maternity of Leipzig; similar approaches were followed in Moscow and St. Petersburg. Tarnier incorporated an incubator, or couveuse, into the regular practice of the Maternité of Paris in 1880. The incubator set a three-way contest between mothers, obstetricians, and pediatricians about whom to care for the premature infant [5,6].

In the 1940s, nurses cared for preterm newborns, but mothers could not see or hold their babies. The care of the newborn included gagging, keeping them warm, and watching out for apnea. Parents and doctors were barred from handling the babies [8]. In the 1950s, significant medical advances, such as the introduction of exchange transfusions for jaundice, gastrostomies for feeding, new medicines, mist inhalations, and oxygen use for respiratory distress syndrome, were achieved, which drew attention to the importance of a physician's role of the physician [7].

Several 'miracle preemies' (those who beat great odds to live in the first place, considering the circumstances and knowledge at the time), including Isaac Newton, Charles Darwin, Winston Churchill, and Albert Einstein, have appeared throughout the history of humankind. They achieved remarkable feats in science and academics and became international leaders (Figure 1) [9].

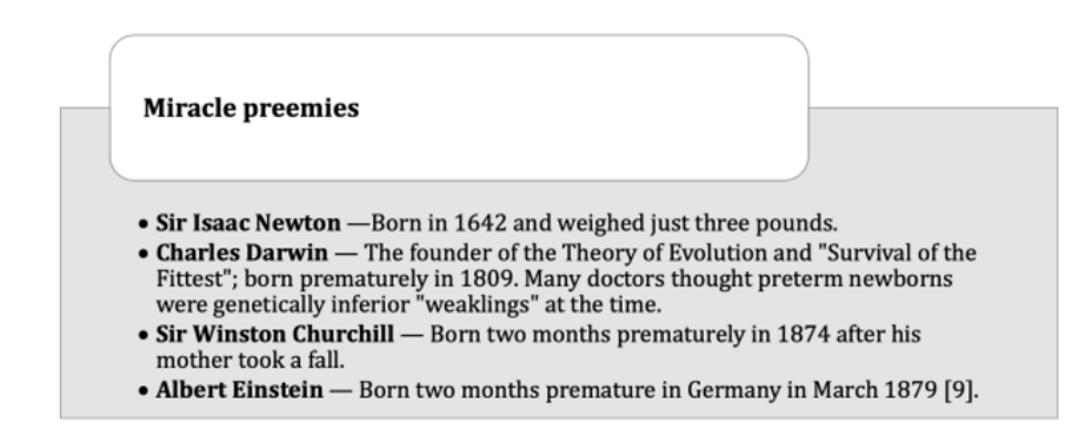

Figure 1

Discussion

Preterm or premature birth

PTB is a condition characterized by time and is not a clinical phenotype [10]. The WHO defines PTB as any birth that occurs before 37 weeks of gestation or within 259 days after the start date of the last menstrual period of a woman [11]. Premature newborns are classified according to the time they are born (such as early preterm, late preterm, moderate preterm, very preterm, extreme preterm, and full-term) (Figure 2) [12-15].

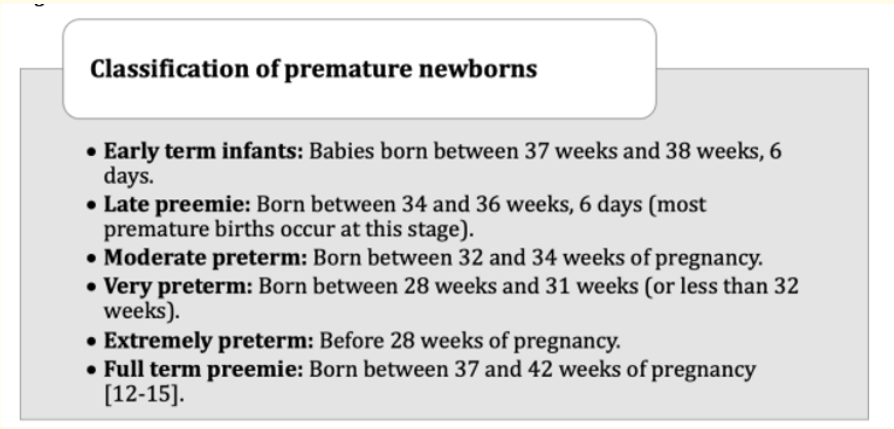

Figure 2

PTB is classified primarily into two categories: (1) spontaneous PTB (sPTB) and (2) provider-initiated PTB (defined as the induction of labor or elective cesarean section before 37 weeks of gestation for maternal or fetal causes or other nonmedical reasons, previously

referred to as "iatrogenic") [15,16]. Approximately 70 - 80% of PTBs are spontaneous, occurring due to preterm labor (40 - 50%) or premature preterm rupture of the membranes (PPROMs) (20 - 30%). In rare cases, cervical insufficiency causes PTB. A healthcare professional initiates the remaining 20 - 30% of PTBs due to maternal or fetal concerns that endanger the health of the mother or fetus (e.g., pre-eclampsia, placenta previa, abruptio placentae, fetal growth restriction, and multiple gestations). Additionally, pregnancy complications can result in spontaneous or provider-initiated PTB [17]. The causes of PPROM are explained in the following graphic (Figure 3) [18,19].

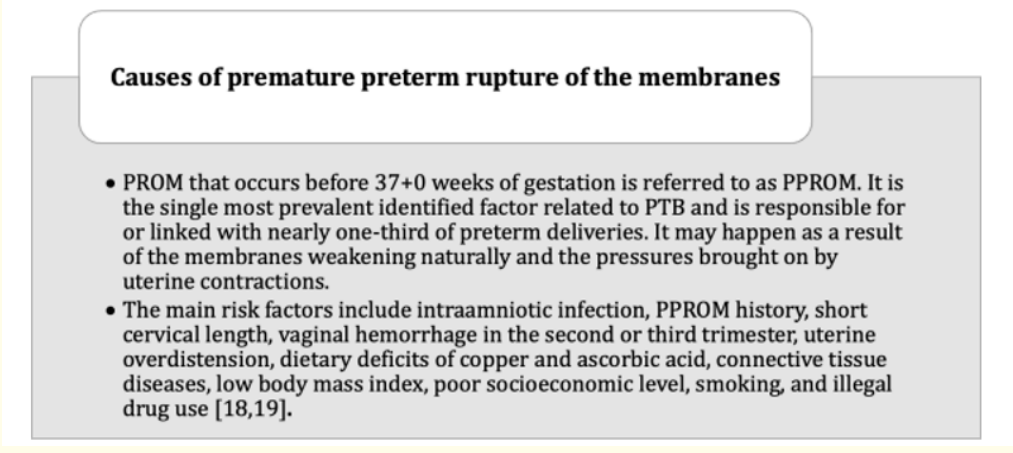

Figure 3

Several families and genome-wide association studies have obtained preliminary data demonstrating a genetic effect on gestational duration [20]. Studies of monozygotic twin pairs have revealed that up to 40% of the heredity factors involved in PTB are single nucleotide polymorphisms, which have been repeatedly shown to have a relationship with the disease [21]. The risk of PTB is also higher in women who were born prematurely, have a sibling who was born prematurely, or have a sister who had a PTB [20,22-26]. PTB occurs in approximately 60% of twin, triplet, and other multiple deliveries [27].

Etiology and risk factors for PTB

Several underlying conditions may lead to preterm labor. The four primary pathways are shown in Figure 4.

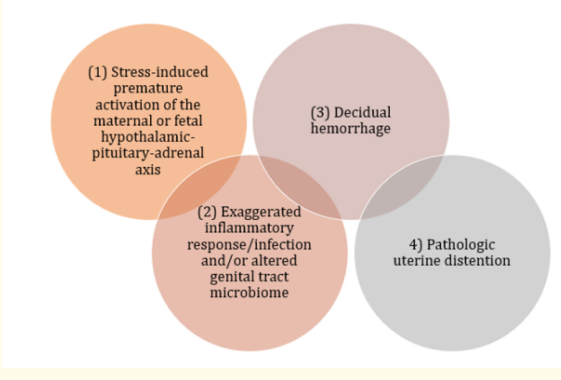

Figure 4: *Etiology of preterm births [28,29]*

PTB is associated with a wide range of risk factors, with multifetal gestation being the most severe. A prior PTB increases the risk of PTB in each subsequent pregnancy [28,29]. PTB is positively affected by socioeconomic status, nutritional status, educational attainment, and the mother's occupation. It is influenced by chronic diseases (including diabetes, hypertension, and vascular diseases), anemia, infections (such as urinary tract infections, bacterial vaginosis, and intraamniotic infections), periodontal disease, genetic susceptibility, and gynecological and familial histories.

Pregnancy complications, such as gestational diabetes, hypertension, and preeclampsia, are more likely to develop in overweight and obese women, increasing the probability of preterm labor. Other risk factors are listed in Figure 5 [30-37].

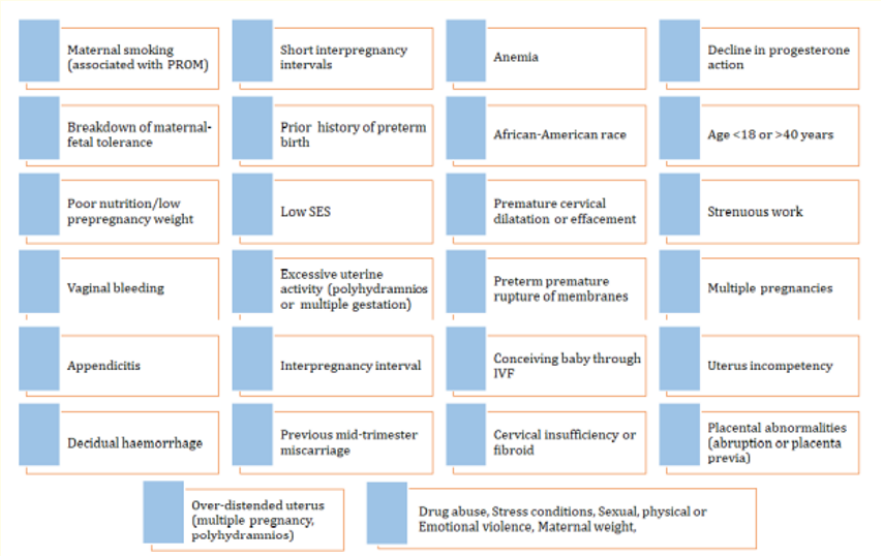

Figure 5: *Precipitating factors or events leading to preterm births [30-37]*

Characteristics and diagnostic findings of PTB

Preterm labor is identified primarily by clinical history, signs, and medical examination. Also, a pertinent account of previous and present obstetrical difficulties may be helpful. Fetal biometry should be performed if an early gestational age ultrasound is inaccessible. When evaluating the patient in labor, it is crucial to consider the mother's vital signs, the fetus's heart rate, and the frequency, length, and strength of contractions [14].

A physical examination helps determine firmness, abdominal pain, fetal growth, and position. Cervical examination can help detect asymptomatic dilation and effacement. The cervical consistency index (CCI) predicts preterm delivery more accurately than cervical length. The CCI measures the anteroposterior (AP) cervical diameter before and after (AP1) and is calculated as (AP1/AP) × 100.

Consistent contractions before maturing gestational age are associated with specific preterm labor symptoms such as cervical change, pelvic discomfort, menstrual-like pains, watery vaginal secretions, abdominal discomfort with and without diarrhea, and lower spine discomfort. Additionally, if the cervical dilation is > 2 or 3 cm at fewer than 34 weeks, the patient is more likely to deliver prematurely. A short cervix, determined by transvaginal ultrasound, is another sign [14,38].

If PPROM is suspected, a speculum examination visualizes amniotic fluid that flows from the cervical canal and accumulates in the vagina. A membrane rupture may be detected by fern and pH testing of the collected vaginal secretions. The amniotic fluid has a pH of 7.1 - 7.3. Alkaline vaginal PH, likely caused by bacterial vaginosis, may predict premature delivery. A vaginal PH level of > 5 may triple the risk of premature delivery. Furthermore, alkaline vaginal PH is more reliable in predicting late preterm delivery (34 - 37 weeks) than early PTB (34 weeks) [14].

Another indication of early labor is the release of fetal fibronectin due to the breakdown of the cervical extracellular matrix. Although this test is specific, it needs to be more accurate. Positive results do not always signal that membranes have burst prematurely. However, a negative result confirms the integrity of the membrane [14].

Biochemical markers for predicting PTB

Biochemical markers can also predict PTB. PPROM or labor can be predicted quickly on the bedside using readily available biological fluids such as whole blood/serum/plasma, urine, saliva, amniotic fluid, and cervical fluid. These bodily fluids are abundant in proteins and metabolites, whose concentrations change in response to pregnancy and adverse pregnancy conditions [39].

Mechanistic biomarkers for PTB include extracellular matrix breakdown, prenatal stress, fetal abnormalities, intrauterine infection and inflammation, and pathways for estrogen metabolism (Figure 6) [40-47].

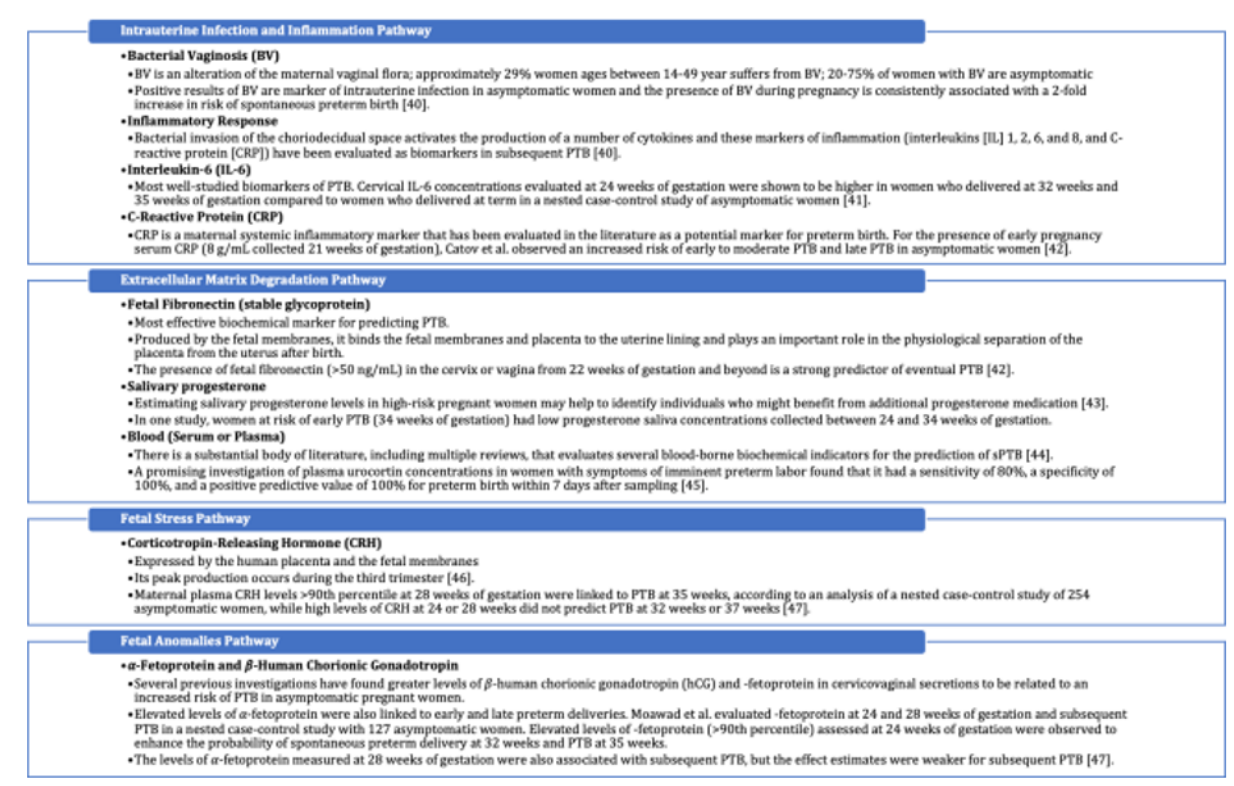

Figure 6: *Biochemical markers for preterm births [40-47]*

Adverse effects and sequelae of PTB

Preterm delivery is significant due to the challenges the newborn experiences due to its prematurity and how these complications affect the survival and future development of the infant. Moreover, complications can occur due to underdeveloped body organs that are not yet ready to maintain a life outside the uterus [48]. The sequelae of PTB sequelae are a significant public health hazard, accounting globally for 35% of newborn mortality and 50% of all deaths in the first 28 days of life [12].

A PTB baby also has an increased risk of health complications, such as respiratory problems, cardiovascular disorders, moderate/severe cognitive impairment, motor impairment, infections, cerebral palsy, bronchopulmonary, sepsis, periventricular leukomalacia, seizures, intraventricular hemorrhage, infections, dysplasia, feeding difficulties, and hypoxic ischemia (Figure 4). They are also more likely to develop late-onset illnesses such as metabolic disease, high blood pressure, and type II diabetes [11,49,50]. There is an increased likelihood that they may experience hospital readmissions or mortality following their release, indicating a higher level of risk.

PTB is also associated with increased healthcare costs, and families with a newborn with PTB often face severe psychological and financial difficulties. A family's hardship of a family with a premature baby (immaturity of the brain, lungs, immune system, kidneys, skin, eyes, and gastrointestinal system) extends far beyond financial expenditures. The long-term disability of a new family member can significantly affect the lives of parents, siblings, and extended relatives. Family members can experience stress because of the preterm infant's physical health and neurological prognosis, which can cause anxiety, postpartum depression, post-traumatic stress disorder (PTSD), fatigue, flashbacks, and parental and family disputes (Figure 7). Furthermore, women with a preterm baby are more likely to have an illness and unpleasant thoughts toward their baby in the months following delivery [11,48,50-52].

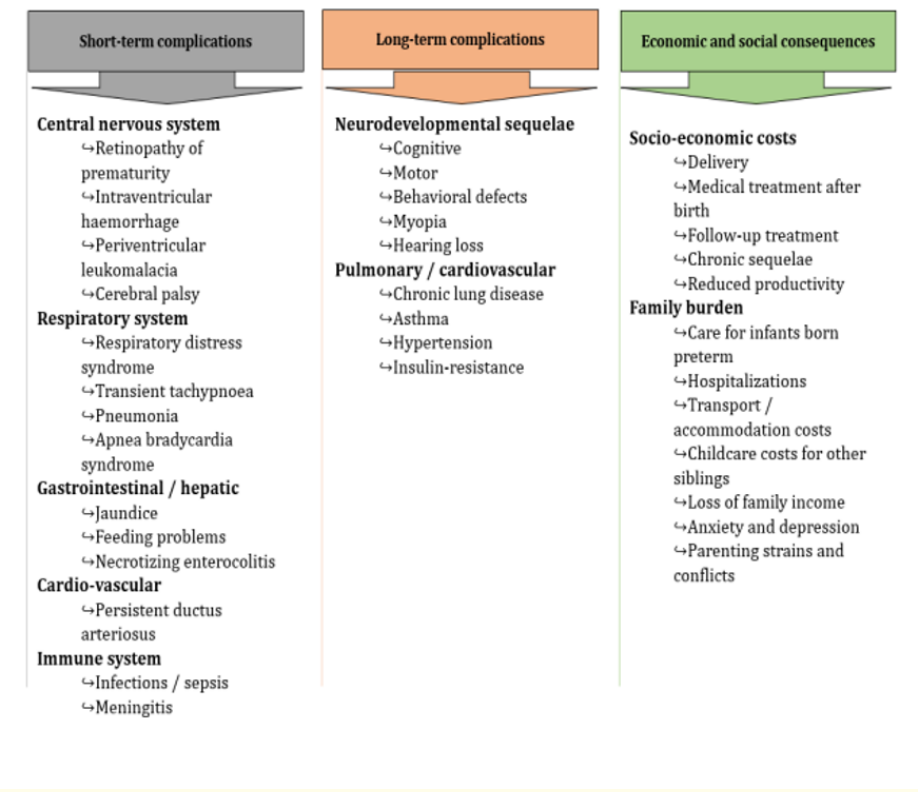

Figure 7: *Complications of preterm birth [50]*

Epidemiology of PTB

PTB rates have increased in most countries in recent years. Globally, PTB ranks as the second leading direct cause of mortality in children younger than five years of age (after pneumonia) [53]. PTB is prevalent in 184 nations, ranging from 5% to 18%. It affects approximately 15 million of the 130 million newborns born yearly (1 in every ten preterm newborns). About 1 million children die from complications related to PTB each year, placing a substantial strain on parents, caregivers, and healthcare systems. In middle-income countries, the inefficient use of technology has increased the impairment burden among preterm newborns that survive the neonatal period [16,54-56].

The top 10 nations with higher PTB rates are India, China, Nigeria, Pakistan, Indonesia, the United States, Bangladesh, the Philippines, the Democratic Republic of the Congo, and Brazil [16,56]. According to studies, Malawi has the highest PTB rate (18.1%), followed by Comoros (16.8%), Congo (16.7%), and Zimbabwe (16.6%) [2].

A PTB is more likely to occur in women younger than 18. Women over 35 are also more likely to have preterm infants due to the increased probability of illnesses requiring premature delivery [57]. However, racial and ethnic differences in PTB rates continue to exist. African-American/Black and Afro-Caribbean women are 1.5 - 1.6 times more likely to have PTB than other racial or ethnic groups (particularly Whites) [32]. In the United States and the United Kingdom, PTB rates ranged from 16% to 18% among Black women compared to 5 - 9% among white women. Women who identify as Black, African-American, or Afro-Caribbean are usually at increased risk of giving birth to preterm babies [38,58].

Furthermore, studies have indicated that PTB is more prevalent in males than in female babies, accounting for approximately 55% of all PTBs. It is also associated with a higher risk of fetal and neonatal deaths and long-term abnormalities in men than in women born at the corresponding gestation [15].

Prenatal and perinatal interventions for PTB

Progesterone therapy: Progesterone therapy helps women conceive and maintains uterine quiescence (effective in women from 16 to 24 weeks of pregnancy and extending up to 34 weeks of gestation) [34,59]. Antenatal progesterone medication is the most effective treatment for reducing the risk of recurrence of PTB in women with single-gestation pregnancies and a history of PTB. In a meta-analysis of RCTs in women with a history of PTB, progesterone significantly reduced the risk of PTB at < 34 weeks (RR = 0.3; 95% CI: 0.14 - 0.69), PTB at < 37 weeks (0.55; 0.42 - 0.74), perinatal death (0.50; 0.33 - 0.75), and admission to neonatal intensive care (0.24; 0.14 - 0.40) [60].

Moreover, evidence suggests that women with a cervical length of ≤20 mm before 24 weeks of pregnancy and no history of sPTB can be prescribed vaginal progesterone. Treatment with 200 µg of vaginal micronized progesterone daily decreased sPTB by 44% in asymptomatic women with a cervical length of ≤15 mm at 20-25 weeks of gestation (RR = 0.567; 95% CI: 0.367 - 0.864) [61]. However, current research indicates that progesterone treatment is ineffective in preventing premature delivery in subsequent pregnancies, preterm labor, or preterm prelabor membrane rupture [53].

Cervical cerclage: The cervix is wrapped with sutures before or during labor. Cervical cerclage is recommended to address structural flaws or cervical weakness in high-risk women with a short cervix. For women who have previously experienced preterm delivery and have a cervical length of ≤ 25 mm or less, the implementation of cervical cerclage has been shown to lower the incidence of preterm birth and perinatal mortality. A meta-analysis by Alfirevic., *et al*. (2017) demonstrated that cervical cerclage significantly decreased PTB by 20% and lowered perinatal fatalities compared with no therapy [62]. However, cerclage is associated with substantially more C-section deliveries and higher rates of fever, vaginal secretions, and bleeding. It is also not recommended for pregnancies with multiple gestations and is associated with a twice greater risk of premature birth in twin pregnancies (RR = 2.1; 95% CI 1.3 - 4) [63].

Pessary: The cervical pessary is made of soft, flexible silicone. It is folded and placed around the cervix through a painless vaginal examination [64]. The pessary prevents the membranes from rupturing and the cervix from dilating too early. It may also strengthen the immunological barrier that protects the vaginal microbiological flora from the chorion and helps prevent PTB [65]. A study on cervical pessaries demonstrated that the birth rate before 34 weeks was considerably lower in women who used cervical pessaries versus those who did not (6% vs. 278%; OR = 0.189; 95% CI: 0.08 - 0.36) [66].

Management of preterm labor

Antibiotics: The National Institute for Health and Care Excellence (NICE) and the Royal College of Obstetricians and Gynecologists (RCOG) guidelines recommend considering prophylactic antibiotics in women with PPROM. Erythromycin, 250 mg, should be administered four times daily for ten days or until labor begins, whichever comes first. In women who cannot use erythromycin, oral penicillin can be prescribed for 10 days or until established labor, whichever occurs first. If PPROM findings for amniotic fluid on a speculum, insulin-like growth factor binding protein-1, or placental alfa-microglobulin-1 are negative, antibiotics are not recommended. The NICE guidelines do not recommend regular antibiotic administration to women with PTB with intact membranes [67,68].

Corticosteroid therapy: Once PTB is confirmed, a session of corticosteroids is the only treatment that will improve infant outcomes. Betamethasone (two 12-mg intramuscular doses administered 24h apart) or dexamethasone (four 6-mg intramuscular doses administered every 12h) is suggested between 24 and 34 weeks of gestation. However, it may be administered as early as 23 weeks of pregnancy in women who may deliver within seven days, regardless of the membrane condition.

This use reduces newborn morbidity and mortality. Compared with infants whose mothers did not receive prenatal corticosteroids, those who received them were less likely to experience breathing difficulties, intraventricular hemorrhage, and necrotizing enterocolitis.

Recent research indicated that a second course of prenatal corticosteroid rescue might be considered if the initial dose was administered more than seven days ago and the risk of premature birth continues before 34 weeks of gestation [34,69]. The results of a randomized controlled study on dexamethasone and betamethasone are pending [59].

Tocolytic agents: These agents delay birth so that antenatal corticosteroids and magnesium sulfate can be administered, and the woman can be transported to a tertiary care center with a newborn critical care unit. Four primary groups of tocolytic are used, each of which has a different level of safety and efficacy: β-adrenergic agonists (such as terbutaline), magnesium sulfate, calcium channel blockers (CCBs)—nifedipine, nicardipine—and non-steroidal anti-inflammatory drugs (NSAIDs)—prostaglandin inhibitors (e.g., indomethacin, ketorolac) [34,70]. According to a systematic review and network meta-analysis, prostaglandin inhibitors and CCBs are the best tocolytics for four outcomes: 48-h delay, newborn death, neonatal respiratory distress syndrome, and maternal side effects (all causes) [71]. Furthermore, studies have revealed that indomethacin, in combination with magnesium sulfate, is a feasible alternative for treatment before 32 weeks of gestation [69]. Figure 8 summarizes common tocolytic and their dosage, administration, and side effects [28,34,68,70].

Tocolytic, despite their widespread use, lacks strong evidence to prevent PTB. Figure 9 details the general contraindications of tocolytic [34,70].

Magnesium sulfate: Magnesium sulfate has been demonstrated to preserve the fetus's nervous system, lowering prenatal cerebral palsy and motor dysfunction. Therefore, the NICE and RCOG guidelines recommend magnesium sulfate treatment during established preterm labor and scheduled premature delivery within 24h [68]. According to a 2009 Cochrane analysis, prenatal magnesium sulfate treatment in mothers at risk of PTB significantly decreased the incidence of cerebral palsy in their babies (RR = 0.70; 95% CI 0.53 - 0.88).

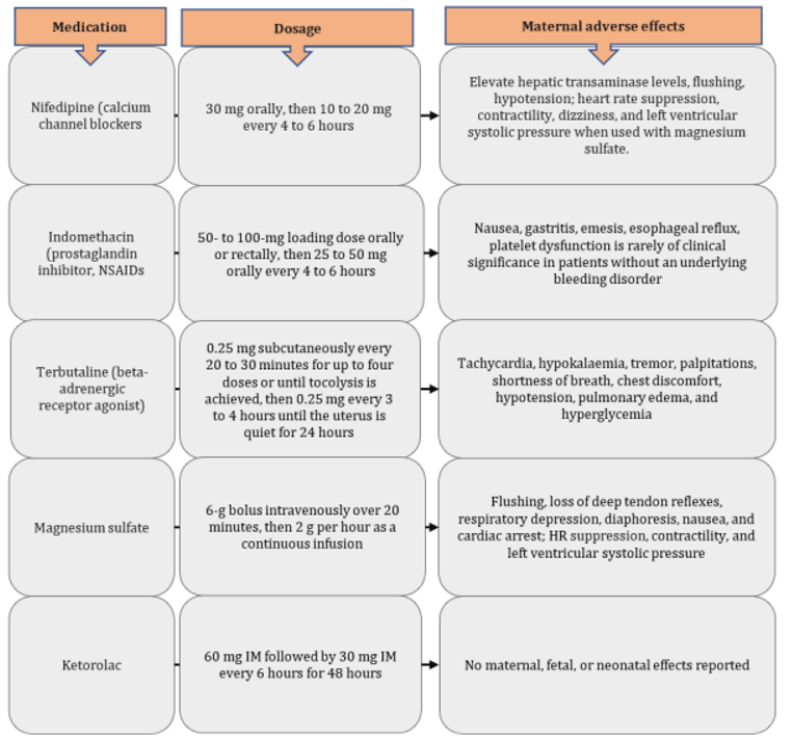

Figure 8: *Summary of the recommended tocolytic for managing preterm labor [28,34,68,70]*

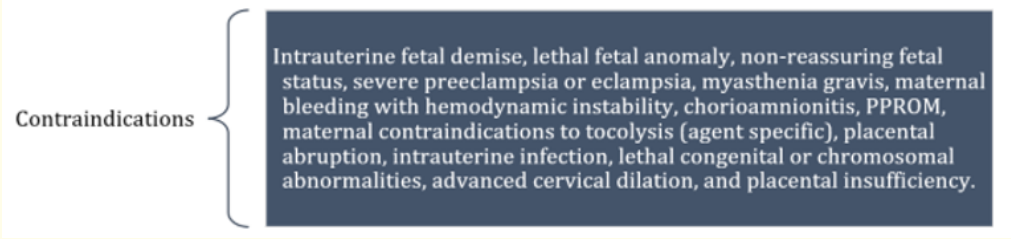

Figure 9: *Contraindications to tocolytics [34,70]*

However, considering that magnesium sulfate may cause respiratory depression and cardiac arrest in expectant mothers, institutional standards for evaluating its proper use must be followed [72].

Complementary and alternative medicine (CAM) treatment methods to prevent PTB

Complementary and alternative medicine (CAM) is a broad category of healthcare care treatments and therapies created outside traditional allopathic medicine, focusing on modifying health behavior [73,74].

NICE guidelines classify CAM into three categories-natural products, which include herbs, minerals, vitamins, and probiotics. Mind and Body practices include chiropractic treatment, yoga, meditation, spinal manipulation, osteopathic manipulation, and traditional healing methods. Additional Alternative Medical Modalities include traditional healing, Traditional Chinese Medicine (TCM), homeopathy, Ayurvedic medicine, and naturopathy [74].

According to recent reports, CAM procedures are used by 69% of women in the United States, 57% in England, 52% in Australia, 51% in Germany, and 70% in Bangladesh [75-79]. However, compared with obstetricians and gynecologists, experts in maternal-fetal medicine are more likely to argue against using CAM therapies to lower the risk of PTB [80].

Per several Cochrane investigations, some evidence favors using acupuncture and acupressure to manage nausea and vomiting during pregnancy, manage labor pain, and induce labor. Chamomile, ginger, mint, and lemon oil can also help reduce nausea and vomiting in the first trimester of pregnancy.

Moreover, several randomized trials involving yoga and relaxation practices showed reduced rates of intrauterine development retardation, PTB, low birth weight babies, pregnancy discomfort, and reported sleep disturbances [80,81]. Despite the increased use of CAM therapies, speculation on their safety and efficacy on the health of the mother and newborn during pregnancy is due to the scarcity of data.

Nutritional interventions

It is essential to evaluate a woman's nutritional state and body mass index (BMI) because these factors influence the risk of PTB. Prenatal vitamins, including iron, folic acid, and calcium, are generally recommended and may also help reduce the incidence of PTB (in some circumstances). Pregnant women in undernourished areas are advised to supplement their diet with a balanced amount of protein and energy and receive nutrition instructions to improve the overall health of their pregnancies. Similarly, supplementation may be advised for people at risk of low vitamin D levels to improve the outcomes of all pregnancies [82].

A Danish cohort study by Mikkelsen., *et al*. (2008) revealed that eating a Mediterranean diet in the middle of pregnancy, which includes eating fish at least twice a week and using olive or grape seed oil, as well as > 5 pieces of fruits and vegetables each day and no more than 2 cups of coffee, was associated with a 72% lower risk of PTB [83].

Also, a meta-analysis by Chia., *et al*. (2019) revealed that following a "healthy" diet that includes enough fruits, vegetables, whole grains, low-fat dairy, and lean protein meals reduces the incidence of PTB (0.78; 95% CI: 0.69 - 0.90) [84].

According to limited research, supplementation with both vitamin D and zinc (5 - 44 mg/day each) may be a useful preventative measure for PTB [85]. A Cochrane analysis found evidence of a small but substantial 14% reduction in PTB with prenatal zinc supplementation (alone or in conjunction with other micronutrients) compared with a placebo [86].

Fish supplements containing omega-3 fatty acids can improve pregnancy outcomes by reducing preeclampsia, preventing PTB, and increasing birth weight. Consensus standards recommend that pregnant women ingest at least 200 mg of docosahexaenoic acid daily to improve the quality of their pregnancies and the health of their fetuses [87,88]. However, only a minor positive impact was discovered in premature birth investigations.

In one study, the average gestation period for women who used omega-3 fatty acids during high-risk singleton pregnancies was 8.5 days longer than that for women in the control group [89-91]. Generally, the data were deemed insufficient to suggest regular use of omega-3 fatty acids to prevent PTB.

Prevention strategies for PTB

A summary of recommendations and strategies for preventing PTB is detailed in Figure 10 [50,92-95].

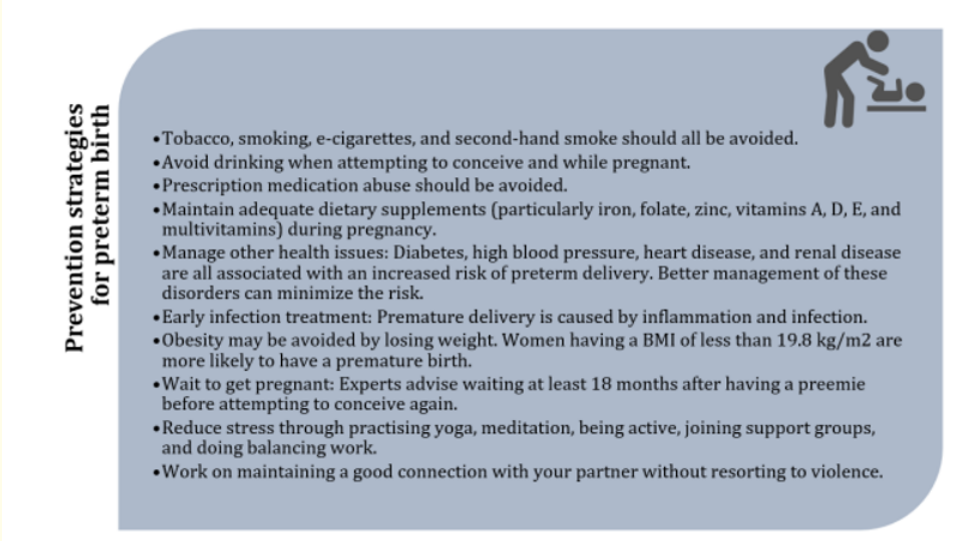

Figure 10: *Strategies and recommendations for preventing preterm births [50,92-95]*

Future of premature birth research, treatments, and prevention

Research is an area of the healthcare sector in which patients and the general public are not involved at all levels [96]. Gaining a deeper understanding of what is known and identifying knowledge gaps will help create the best care for pregnant women and their newborns [64]. Therefore, adopting a hypothesis-free methodology is vital in future research on the physiology of preterm delivery. This method involves changing away from analyzing specific inflammatory genes or pathways and toward a systems biology approach using next-generation sequencing in conjunction with proteome studies on patient or control samples [50].

Currently, biochemical signs cannot be used to predict frequent late-pregnancy complications, including preterm labor, with adequate precision. The creation of multivariate classification models and the simultaneous measurement of various biomarkers, such as cervical length, biochemical marker(s), and demographic/risk factor(s), constitute a viable strategy to enhance diagnostic effectiveness [39]. Regarding the prediction of term labor, the combined predictive power of the oxidative stress biomarker SOD1 and the total oxidant capacity was greater than that of either biomarker alone [97].

The development of new medications and medicinal herbs, and probiotics for treating and preventing premature delivery are areas of increasing interest (Figure 11) due to their potential therapeutic advantages in gynecology and obstetrics [64,98-102].

Conclusion

The primary objective of obstetric care is the prevention of PTB. Advancements in newborn care have helped improve outcomes for several premature babies, although these improvements do not match an equal improvement in the capacity to avoid preterm delivery. More studies are needed regarding the causes of PTB, as well as better techniques to assess PTB and innovative therapies to prevent and

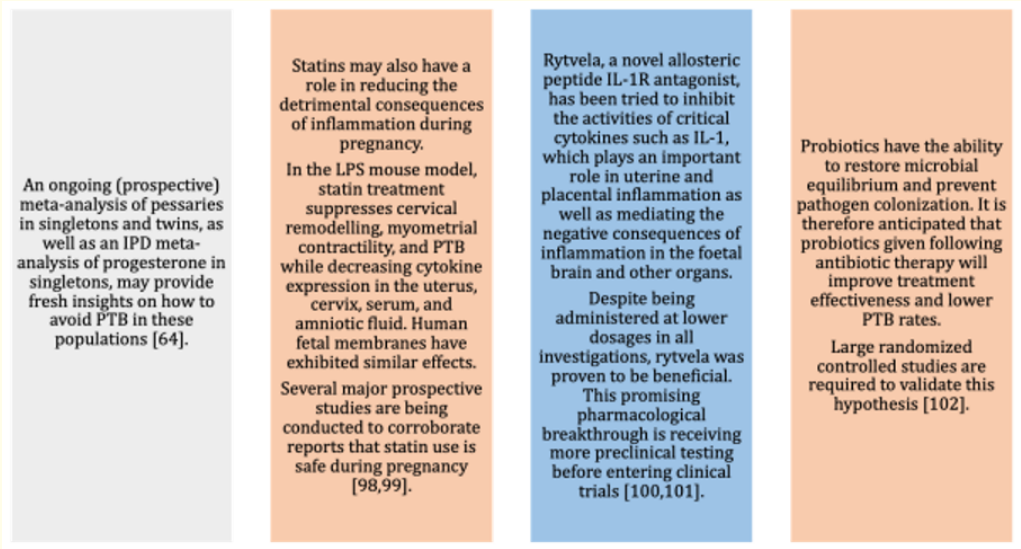

Figure 11: *Future treatments and prevention strategies for premature births [64,98-102]*

manage the effects of PTB, especially in low-resource settings. Enhancing the standard of maternal and infant care on a larger scale is necessary for better identification, prevention, and treatment of PTB.

Evidence shows that various therapies can significantly and effectively prevent premature births. Translational activities are beginning to influence PTB rates, and research on causative pathways and new diagnostic and therapeutic methods is now showing results. For example, progesterone with cerclage may prevent recurrence in women with prior TBP. Ongoing research focuses on how a pessary affects these high-risk women. Significant collaboration between physicians, patient organizations, pharmaceutical companies, and (worldwide) governments is warranted to minimize morbidity and mortality from PTB.

Conflict of Interest Statement

The authors declare that this paper was written without any commercial or financial relationship that could be construed as a potential conflict of interest.

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