CHAPTER II
THEORY OVERVIEW

A. The Concept of Anemia in Pregnancy

1. Definition

Anemia is a condition where hemoglobin (Hb) levels in the blood are lower than the normal value of 11 g/dL, resulting in a decrease in the blood's capacity to transport oxygen to all tissues of the body (Ministry of Health, 2023). During pregnancy there is an increase in plasma volume that exceeds the increase in red blood cell mass, so that hemoglobin concentrations drop relatively in a phenomenon called physiological hemodilution. This decrease is a normal hematologic change in pregnancy and contributes to the decrease in Hb values often seen in pregnant women (Obianeli et al., 2024).

According to World Health Organization (WHO) standards, a pregnant woman is declared to have anemia if her hemoglobin level is below 11 g/dL (World Health Organization, 2021). This standard has been widely applied in Indonesia, including in Bengkulu Province, as a guideline in determining the diagnosis and treatment of anemia during pregnancy. Anemia in pregnant women remains an important health problem because it has the potential to increase the risk of various complications for both the mother and the fetus (Maulidyanti et al., 2025).

2. Etiology of Anemia in Pregnancy

The causes of anemia during pregnancy are complex and involve various factors, but the most dominant is a lack of nutrients that play an important role in the process of forming red blood cells or *erythropoiesis*. These causative factors include:

a. Intake (Nutrition)

Inadequate nutritional intake is one of the important causes of anemia in pregnant women. The need for iron, folic acid, and

other micronutrients increases during pregnancy to support blood production and fetal growth. Deficiencies in iron and folic acid intake through food can lead to deficiencies that then reduce hemoglobin production, thereby increasing the risk of anemia. A diet that is low in iron, lack of food variation, and low intake of micronutrients such as vitamin C that help iron absorption can worsen anemia conditions in pregnant women. Research shows that low iron intake and unbalanced diet are related to an increased incidence of iron deficiency anemia in pregnant women.

b. Iron Deficiency:

This is the cause of more than 90% of anemia cases in pregnancy, especially in developing countries such as Indonesia. This condition occurs due to the increased need for iron to support fetal growth, placental formation, and increased maternal blood volume during pregnancy. When intake from food is insufficient and adherence to iron supplement consumption is low, the risk of anemia increases significantly (Zhang et al., 2022).

c. Folic Acid and Vitamin B12 Deficiency:

Folic acid and vitamin B12 deficiency can cause megaloblastic anemia, which is a condition when the body produces large but abnormal and easily damaged red blood cells. During pregnancy, the need for these two vitamins increases to support DNA formation and cell maturation. Research in Indonesia shows that low folate intake is closely related to an increased risk of anemia in pregnant women (Annisa Mudrika et al., 2023).

d. Bleeding:

Bleeding, both acute and chronic, can cause a large amount of iron and red blood cell loss, thus contributing to the onset of anemia in pregnant women. Significant blood loss before or during pregnancy disrupts the body's iron balance and decreases the blood's capacity to transport oxygen (Ariyanti et al., 2022).

e. Chronic Diseases and Infections:

Chronic disease conditions and infections are important causes of anemia in pregnancy. Disorders such as chronic kidney disease, parasitic infections (e.g. malaria or worms), as well as prolonged inflammatory processes can inhibit erythropoiesis in the bone marrow through inflammatory mechanisms and iron redistribution for the immune response. As a result, red blood cell production decreases and hemoglobin levels also drop, so that pregnant women who suffer from chronic or infected diseases have a greater risk of anemia than those without the condition (Pasaribu et al., 2023).

f. Smoking:

Smoking, both as an active smoker and exposure to secondhand smoke, is an important risk factor that can contribute to the occurrence of anemia in pregnancy. Cigarette smoke contains carbon monoxide (CO) which binds to hemoglobin up to 200–250 times stronger than oxygen, thus forming carboxyhemoglobin and reducing the blood's ability to transport oxygen. This condition causes chronic tissue hypoxia which has an impact on decreasing functional hemoglobin in pregnant women (WHO, 2021).

In addition, other toxic substances in cigarette smoke such as lead and free radicals can inhibit heme synthesis, increase oxidative stress, and accelerate red blood cell damage (hemolysis). Exposure to cigarette smoke can also interfere with iron metabolism through increased inflammatory responses and hepcidine levels, so that the absorption and utilization of iron for hemoglobin formation is inhibited. As a result, pregnant women who are regularly exposed to cigarette smoke have a higher risk of anemia than pregnant women who are not exposed (Balali-Mood et al., 2021; Andarge et al., 2021).

3. Classification of Anemia in Pregnancy

Anemia in pregnant women is classified based on its severity into three categories, namely:

1) Mild anemia, which is when the level of hemoglobin (Hb) in pregnant women in the first trimester and third trimester is in the range of 10.0–10.9 g/dL, while in the second trimester it is in the range of 9.5–10.4 g/dL.
2) Moderate anemia, which is when the hemoglobin (Hb) level in pregnant women in the first trimester and third trimester is in the range of 7.0–9.9 g/dL, while in the second trimester it is in the range of 7.0–9.4 g/dL.
3) Severe anemia, which is when the hemoglobin (Hb) level in the entire trimester of pregnancy is <7.0 g/dL(World Health Organization, 2024).

Based on the cause or morphology, anemia is divided into (Suprapti et al., 2025):

a. Iron Deficiency Anemia:

   Due to a lack of iron supply, it is characterized by microcytic (smaller than normal) and hypochromic (paler) red blood cells.

b. Megaloblastic anemia:

   It is caused by a deficiency of folic acid or vitamin B12, characterized by macrocytic red blood cells (larger than normal).

c. Hemolytic Anemia:

It is caused by an increase in the destruction or breakdown of red blood cells (hemolysis) that is faster than their production.

d. Anemia:

It is caused by the failure of the bone marrow to produce sufficient amounts of red blood cells.

4. Pathophysiology of Anemia in Pregnancy

The most common pathophysiology of anemia during pregnancy is iron deficiency anemia, which develops gradually as the mother's and fetus' iron needs increase. This process begins when iron requirements exceed the available intake and reserves, so the body begins to experience a lack of iron supply to maintain optimal hemoglobin levels (Suprapti et al., 2025)

Its *pathophysiological stages include:*

a. Depletion of Iron Reserves:

The initial stage is characterized by a decrease in iron reserves in the form of ferritin stored in the liver, spleen, and bone marrow. In this phase, hemoglobin levels are generally still within normal limits, but ferritin levels decrease significantly as an early sign of reduced iron stores (Chibanda et al., 2023)

b. Erythropoiesis disorders:

As ferritin reserves become depleted, the supply of iron to the bone marrow is no longer sufficient to support the process of erythropoiesis (the formation of red blood cells). This condition causes a decrease in transferin saturation, which is an iron-transporting protein in plasma and has an impact on the disruption of hemoglobin synthesis. At this stage, hemoglobin levels may not have decreased too much, but signs of impaired erythrocyte formation begin to appear (Chibanda et al., 2023; Suprapti et al., 2025).

c. Iron Deficiency Anemia:

The final stage occurs when hemoglobin synthesis fails due to a sustained iron deficiency, so the bone marrow produces erythrocytes that are small in size (microcytic) and paler in color (hypochromic). This condition is accompanied by increased levels of hepcidin and pro-inflammatory cytokines, which worsen anemia by decreasing iron absorption in the intestines and inhibiting the release of iron from the body's reserves. As a result, the level of hemoglobin in the circulation drops below the normal limit and clinical symptoms of anemia begin to appear (Chibanda et al., 2023; Suprapti et al., 2025)

5. Clinical Manifestations

Anemia during pregnancy is a common condition and can cause a variety of symptoms, depending on its severity. In the early stages, the symptoms of anemia are often non-specific, making them difficult to recognize without a laboratory examination (Benson et al., 2021). One easy way to remember the symptoms of anemia in pregnant women is with the term 5L, namely Weak, Tired, Lethargic, Tired, and Lunglai, which indicates a decrease in energy due to a decrease in the blood's ability to carry oxygen (Benson et al., 2021).

In addition to the 5L symptoms, pregnant women with anemia may experience dizziness, headaches, blurred or flickering vision, shortness of breath, and heart palpitations, especially when doing physical activity. This is the body's response to the lack of oxygen in the tissues (Benson et al., 2021). A physical examination usually shows paleness of the conjunctiva of the eyes, lips, and base of the nails, which is a typical sign of anemia. In more severe cases, tachycardia or rapid heartbeat can appear as the body attempts to maintain the oxygen supply (Benson et al., 2021). By recognizing these physical symptoms and signs, early detection of anemia in pregnant women becomes easier, so

that prevention and management measures can be carried out more precisely and effectively.

6. Risk factors

The incidence of anemia in pregnant women is influenced by various interrelated factors, including demographic, socioeconomic, and nutritional factors. These factors can theoretically be explained through Blum's Health Determinant Model (1974) which states that the degree of health is influenced by four main factors, namely human biology, behavior, environment, and health services. In the context of this study, exposure to cigarette smoke is positioned as an environmental factor that has the potential to affect the health of pregnant women, especially the incidence of anemia.(Yanti & Arianti, 2024)

a. Human *Biology*

Human biological factors are factors that come from the physical and physiological conditions of individuals. These factors include maternal age, gestational age, parity, health status, and folic acid and vitamin B12 deficiency.

Pregnant women with the age of <20 years or >35 years have a higher risk of developing anemia due to an imbalance between iron needs and reserves (Norfitri, 2023).

High parity and close pregnancy distance can deplete the mother's iron reserves, while in the second and third trimesters iron needs increase due to hemodilution and fetal growth (Norfitri, 2023).

In addition, certain health conditions as well as micronutrient deficiencies such as folic acid and vitamin B12 can interfere with the erythropoiesis process, thereby increasing the risk of anemia in pregnant women (Norfitri, 2023).

b. Behavioral Factors (*Lifestyle / Behavior*)

Behavioral factors are related to the habits and actions of pregnant women that affect their health status. These factors include iron intake and the mother's level of knowledge about anemia and

nutritional needs during pregnancy. Low iron intake, both from food and supplements, is the main cause of anemia in pregnant women.

Low knowledge can lead to suboptimal health behaviors, such as not paying attention to a nutritious diet and not complying with taking blood supplement tablets (TTD), thus increasing the risk of anemia (Khairunnisa et al., 2023).

c. Environmental Factors

Environmental factors include the social and cultural conditions surrounding pregnant women. These factors include education, socioeconomic status, culture, and husband support. Education and low socioeconomic status limit access to health information, nutritious food, and health services.

Cultural practices in the form of food abstinence during pregnancy can lead to low protein and iron intake (Dewi, 2024).

In addition, lack of husband's support, both emotionally, morally, and financially, can reduce the motivation of mothers to maintain a healthy diet, consume TTD, and make ANC visits, thereby increasing the risk of anemia (Rahmi et al., 2022)

d. Health Care Services

Health service factors related to access and utilization of health services, especially visits *antenatal care* (ANC). ANC plays an important role in early detection of anemia, monitoring nutritional status, administering blood supplemental tablets, and health education for pregnant women. Pregnant women who do not regularly or rarely make ANC visits have a higher risk of developing anemia than mothers who make optimal use of ANC services (Nurvinanda et al., 2023).

7. Complications

Anemia during pregnancy if not treated properly can cause serious complications for both mother and fetus.

a. Maternal (Maternal) Complications:

Anemia in pregnant women can increase the risk of bleeding both before and after childbirth due to suboptimal uterine contractions. In addition, mothers with anemia tend to be more susceptible to infections, preeclampsia, and preterm labor. In the case of severe anemia, this condition can overload the heart so that it has the potential to cause heart failure. Recent studies have also shown that severe anemia is associated with a significant increase in maternal morbidity, including the need for large amounts of blood transfusions as well as intensive care after childbirth (Alfiana et al., 2024)

b. Fetal and Neonatal (Fetute/Infant) Complications:

Anemia in the mother can cause stunted fetal growth in the womb (*Intrauterine Growth Restriction*), which leads to Low Birth Weight (BBLR). The risk of fetal death, premature birth, and asphyxia at birth also increases. Babies born to anemic mothers are at higher risk of developing anemia in early life and can have an impact on impaired cognitive and motor development later in life (Mardiaturrahmah & Anjarwati, 2020).

8. Governance

The management of anemia in pregnancy focuses on *promotive, preventive, and curative* efforts, which are adjusted to national policies.

a. Prevention (*Preventive*):

Efforts to prevent anemia during pregnancy are one of the main focuses in national health policy. The government through the Ministry of Health of the Republic of Indonesia runs an iron supplementation program for pregnant women in the form of giving Blood Supplement Tablets (TTD) containing 60 mg of elemental iron and 400 µg of folic acid. Pregnant women are recommended to take at least 90 tablets during pregnancy to prevent iron deficiency. In addition to supplementation, promotive strategies are carried out

through education and nutritional counseling regarding the importance of consuming iron-source foods such as red meat, liver, eggs and green vegetables, accompanied by the intake of foods high in vitamin C so that iron absorption is more optimal (Ministry of Health, 2023; Khairunnisa et al., 2023)

b. Treatment (*Curative*):

The management of anemia in pregnant women is carried out by monitoring hemoglobin levels from the first antenatal visit to before delivery. If hemoglobin levels show mild to moderate anemia, then the dose of Blood Supplement Tablets (TTD) is increased and evaluated periodically. In cases of severe anemia (Hb < 7g/dL) or if clinical symptoms are found that indicate complications, follow-up interventions are needed, such as intravenous iron preparations or blood transfusions, especially in referral health facilities. This step is in line with the guidelines of the Ministry of Health and the recommendations of the Obstetric Organization, the International Federation of Gynaecology and Obstetrics (FIGO), which affirms that severe anemia in pregnancy requires immediate treatment to prevent risks to the mother and fetus (Ministry of Health, 2023; O'Toole et al., 2024; Ubom et al., 2025).

B. Exposure to Cigarette Smoke in the Household

1. Definition of Cigarette Smoke Exposure

Exposure to secondhand smoke in households, often referred to as exposure to secondhand smoke (*Exposure to Cigarette Smoke*), occurs when a non-smoking person inhales tobacco smoke from the surrounding environment. The smoke consists of two main components, namely sidestream smoke (*Side Smoke*) from the tip of the lit cigarette and the main stream smoke (*Mainstream Smoke*) exhaled by an active smoker. Both types of smoke contain various toxic substances such as carbon monoxide and nicotine, which can lower hemoglobin levels by

inhibiting the oxygen bonds in the blood. As a result, pregnant women who are regularly exposed are at risk of hypoxia and anemia, especially if exposure occurs in an enclosed space (Hermaliana et al., 2025).

2. Toxic Content in Cigarette Smoke

Cigarette smoke contains more than 7,000 chemical compounds, of which hundreds are toxic and about 70 are carcinogenic (Ministry of Health, 2022). Some of the most relevant toxic substances for hematological disorders and anemia include:

a. Carbon Monoxide (CO):

This colorless, odorless toxic gas binds to hemoglobin much more strongly than oxygen (about 200–250 times), reducing the blood's ability to transport oxygen to the body's tissues (Ministry of Health, 2022).

b. Lead (Pb):

It is a toxic heavy metal that can accumulate in body tissues, especially bones and blood. Long-term exposure can inhibit the formation of red blood cells (erythrocytes) as well as cause disorders in the nervous system and kidneys (Ministry of Health, 2022).

c. Free Radicals (Oxidants):

Although reactive, the results of tobacco burning trigger oxidative stress that damages cell and tissue structures, thereby contributing to cellular damage and impaired biological function (Ministry of Health, 2022).

d. Cyanide:

These toxic substances inhibit the ability of cells to utilize oxygen normally, thereby degrading cellular respiration efficiency and risking damaging organ function (Ministry of Health, 2022).

3. Mechanism of Impact of Cigarette Smoke on Blood

Exposure to toxic substances from cigarette smoke can theoretically trigger anemia through several interconnected pathophysiological pathways:

a. Formation of Carboxyhemoglobin (COHb):

When carbon monoxide (CO) in cigarette smoke is inhaled, it will compete with oxygen to bind to hemoglobin, and because its affinity is much higher, CO forms a stable complex (carboxyhemoglobin/COHb) that reduces the amount of functional hemoglobin. As a result, the blood's capacity to transport oxygen decreases, resulting in chronic hypoxia, a mechanism that may explain the decrease in Hb in pregnant women exposed to secondhand smoke (Bizoń et al., 2021).

b. Inhibitions of Heme Synthesis:

Lead (Pb) can inhibit an important enzyme in heme biosynthesis, namely *δaminolevulinic acid dehydratase* (ALAD) and ferrochelatase. This inhibition leads to the accumulation of heme precursors such as ALA and *protoporphyrinogen*, so heme production is disrupted. Since heme is a non-protein component of hemoglobin, this disorder has the potential to decrease hemoglobin synthesis and increase the risk of anemia. This mechanism is relevant for exposure to lead through cigarette smoke, which can be a source of heavy metals for the body (Balali-Mood et al., 2021).

c. Oxidative Stress and Hemolysis:

Free radicals from cigarette smoke increase oxidative stress by damaging the lipid membranes of red blood cells, making them stiff, brittle, and easily broken down (*Hemolysis*). This increase in hemolysis shortens the life of erythrocytes and potentially lowers hemoglobin levels. Research shows that smokers have high levels of *malondialdehyde* (MDA) and lower antioxidant activity (SOD) than non-smokers, supporting the oxidative stress mechanism caused by cigarette smoke (Khudhur et al., 2025).

C. Exposure to Cigarette Smoke in the Social Environment

Exposure to cigarette smoke in the social environment occurs when pregnant women inhale cigarette smoke outside the home, such as at work, public spaces, or when participating in community activities. This condition is often because pregnant women cannot fully control the surrounding environment, especially in workplaces or public areas that have not strictly implemented no-smoking area rules. Exposure can last a long time, for example 6–9 hours during work, so the amount of cigarette smoke that enters the body becomes larger. Some studies have shown that rooms where many people smoke, such as restaurants, cafes, markets, or workplaces, can have very poor air quality, with fine particulate matter (PM2.5) levels reaching 200–600 μg/m³, well above the WHO safe limit (World Health Organization, 2023). This makes pregnant women more susceptible to exposure to chemicals from cigarette smoke even though they do not participate in smoking.

Exposure in a social environment is dangerous because sidestream smoke (smoke from the burning tip of a cigarette) contains more toxic substances than smoke exhaled by smokers. When pregnant women inhale the smoke, various chemicals such as carbon monoxide (CO), benzene, cadmium, nicotine, and fine particles will enter the lungs. CO then diffuses into the blood through the alveoli and binds to hemoglobin (Hb) much more strongly than oxygen. The bond of CO with Hb forms carboxyhemoglobin (COHb), so that Hb that is supposed to carry oxygen becomes unable to function. As a result, the body experiences conditions such as "functional anemia", where Hb is still present but unable to work optimally. In some pregnant women, COHb levels can increase by up to 1.8–3% simply due to exposure to smoke in a social environment (Balali-Mood et al., 2021; Kinoshita et al., 2020).

In addition to CO, very small PM2.5 particles can enter blood vessels and trigger oxidative stress. This condition damages the red blood cell membrane so that the cell breaks down faster (hemolysis) and the erythrocyte life becomes shorter. The reduced number of red blood cells certainly has an

impact on the decrease in hemoglobin. Other chemicals such as benzene and cadmium can also inhibit the absorption of iron in the intestines, making it difficult for the body to produce new Hb. In fact, some of the toxic substances in cigarette smoke can interfere with the function of the bone marrow, where the formation of red blood cells takes place (Balali-Mood et al., 2021).

Not only that, exposure to cigarette smoke can also trigger inflammatory reactions in the body. This inflammation increases levels of the hormone hepcidin, which is a hormone that inhibits the absorption of iron. When hepcidin increases, it becomes more difficult for the body to absorb and utilize iron to form hemoglobin, a process often referred to as anemia due to inflammation. Research shows that pregnant women who are frequently exposed to cigarette smoke at work or in public spaces have up to three times higher risk of anemia than those who are not exposed (Benson et al., 2021; Chibanda et al., 2023).

In summary, exposure to cigarette smoke in the social environment both at work and public activities can reduce pregnant women's Hb levels in several ways: reducing the ability of Hb to carry oxygen, accelerating red blood cell damage, inhibiting iron absorption, and interfering with the process of red blood cell formation. Because this exposure occurs repeatedly and over a long period of time, the risk of anemia in pregnant women increases significantly.

D. The Relationship between Cigarette Smoke Exposure and the Incidence of Anemia in Pregnant Women

Exposure to secondhand smoke in pregnant women, both at home and at work, has been shown to be associated with decreased hemoglobin (Hb) levels and an increased risk of anemia. Cigarette smoke contains carbon monoxide (CO) which easily binds to hemoglobin, even 200–250 times stronger than oxygen. This bond forms carboxyhemoglobin and decreases the blood's ability to transport oxygen. The condition of lack of oxygen can affect the tissues of the mother and fetus, thus triggering anemia during pregnancy (Alfiana et al., 2024). In addition to CO, other harmful substances such as

nicotine, benzene, and fine particulate matter (PM2.5) can interfere with iron absorption and inhibit the formation of red blood cells. Pregnant women who are exposed to secondhand smoke every day from family members at home and co-workers generally have lower Hb levels than those who are not exposed (Hermaliana et al., 2025).

Several studies have stated that pregnant women who become passive smokers have a 2-3 times greater risk of developing anemia. Exposure to cigarette smoke for one hour or more per day is associated with a decrease in hemoglobin levels of about 0.5–1.2 g/dL and the appearance of complaints such as dizziness, weakness, and decreased hematocrit values. This condition can affect the welfare of the mother and the growth and development of the fetus (Choirunnisa et al., 2022; Suprapti et al., 2025).

Other studies have also found that pregnant women who live or work in environments with active smokers are more prone to moderate to severe anemia. Cigarette smoke accumulated in the room can degrade air quality and increase exposure to CO and free radicals that interfere with oxygen and iron metabolism. The impact can be in the form of continuous fatigue, a decreased immune system, and impaired fetal growth (Deng et al., 2024).

The findings are corroborated by an international study from *Ethiopia* which suggests that exposure to indoor air pollution, including cigarette smoke, has a meaningful relationship with an increased risk of anemia in pregnant women. Exposure to cigarette smoke at home and work causes increased levels of CO and fine particulates which has an impact on lowering Hb levels and disrupting the formation of red blood cells This confirms that exposure to cigarette smoke is one of the important environmental factors in influencing the incidence of anemia in non-smoking pregnant women (Andarge et al., 2021).

E. Theoretical Framework

This theoretical framework visually explains how various factors interact in causing anemia in pregnant women, based on the Blum Health Determinants Model (Blum, 1974) which states that the degree of health is

influenced by environmental factors, behavior, health services, and human biology, with a focus on exposure to cigarette smoke positioned as environmental factors (main independent variables) that contribute to the occurrence of anemia, while age, education, parity, and nutritional status are biological and behavioral factors that can affect the incidence of anemia in pregnant women in the context of the study *Case control*.

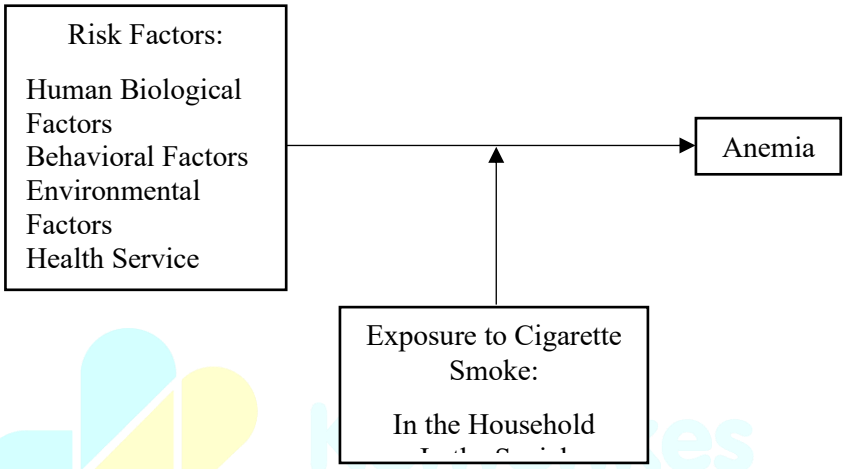

Chart 1 Theoretical Framework

Sources: (Annisa Mudrika et al., 2023; Blum, 1974; Ministry of Health of the Republic of Indonesia, 2023; Pasaribu et al., 2023; Yanti & Arianti, 2024; Zhang et al., 2022).