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**EFFECTS OF THE CONSUMPTION OF COMMERCIAL BREASTFEEDING
PRODUCTS (HEARTY LACTATION PRODUCTS) ON BREASTMILK OUTPUT AND
SERUM PROLACTIN LEVELS OF PRETERM LACTATING MOTHERS: A
RANDOMIZED DOUBLE-BLINDED CONTROL TRIAL.**

BY

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**THIS THESIS IS SUBMITTED TO THE UNIVERSITY OF GHANA, LEGON IN
PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF MPhil IN
MEDICAL BIOCHEMISTRY DEGREE.**

JUNE, 2024

DECLARATION

I, Isaac Noble Gyedu, hereby declare that this thesis titled “Effects of the Consumption of Commercial Breastfeeding Products (Hearty Lactation Products) on Breast milk Output and Serum Prolactin Levels of Preterm Lactating Mothers: A Randomized Double-Blinded Control Trial”, is originally my work and based on primary data I have gathered. To the best of my knowledge, it does not include any content that has been previously published by another individual or accepted for the conferral of any other degree from this university or elsewhere, unless appropriately acknowledged within the text.





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INTEGRI PROCEDAMUS

ABSTRACT

Breast milk is the preferred food for babies as it harbours essential macronutrients, amongst which are carbohydrates, proteins, and fats, along with micronutrients like iron, zinc, magnesium, vitamin A, C, D, K and B-complex, calcium, phosphorus and iron. It also contains protective elements like immunoglobulins (IgA), lactoferrin, lysozymes, hormones, growth factors and beneficial bacteria (bifidus) which aid in gut health and immunity. Worldwide, infant mortality is estimated to be 13%, as a result of inadequate breastfeeding. Galactogogues are compounds that can contribute to initiating, maintaining, or increasing breast milk production. For many years, diverse foods have been made from galactogogues including fenugreek, fennel, and oats. Even though the effect of galactogogues on breast milk production have been investigated in other geographical populations, little is known about their capacity to boost breast milk production in Ghanaian lactating mothers, whose diets vary significantly from the populations in other continents. The aim of the study was to investigate the effects of selected galactogogues-containing food products on serum prolactin levels and breast milk volume of lactating mothers, as well as weight of preterm babies for a 7-day duration. The study was conducted at the Neonatal Intensive Care Unit of the 37 Military Hospital. Participants were mothers who gave live birth on or before the 37th week of pregnancy. The study had 2 arms; a control group (granola placebo and chocolate drink placebo) and an intervention group (granola and chocolate drink). Each participant took a food product for 7 days consecutively. Breast milk volume and serum prolactin levels of the breastfeeding mothers and changes in the weight of the babies were recorded on the first and seventh days. By day 7, mothers who took the granola ($p < 0.0001$), chocolate drink ($p < 0.0001$), granola placebo ($p < 0.0001$), and chocolate drink placebo ($p = 0.0007$) had considerably higher mean breast milk volumes. There was no discernible difference between the preterm infants' weight and the mothers' serum prolactin levels on day 7 and day 1 values. On days 1 and 7, there was no discernible relationship between the intervention and placebo groups' breast milk volume and either serum prolactin levels

or newborn weight. In early postpartum mothers with lactation insufficiency, plant-based galactagogues had no effect on serum prolactin levels or the amount of breast milk produced. Further research is recommended to elucidate the molecular mechanisms regulating breast milk production and composition in lactating women.



I dedicate this work to my dear mother, Mary Adwoa Tokua, for her undying love and source of encouragement to me in all my endeavors.



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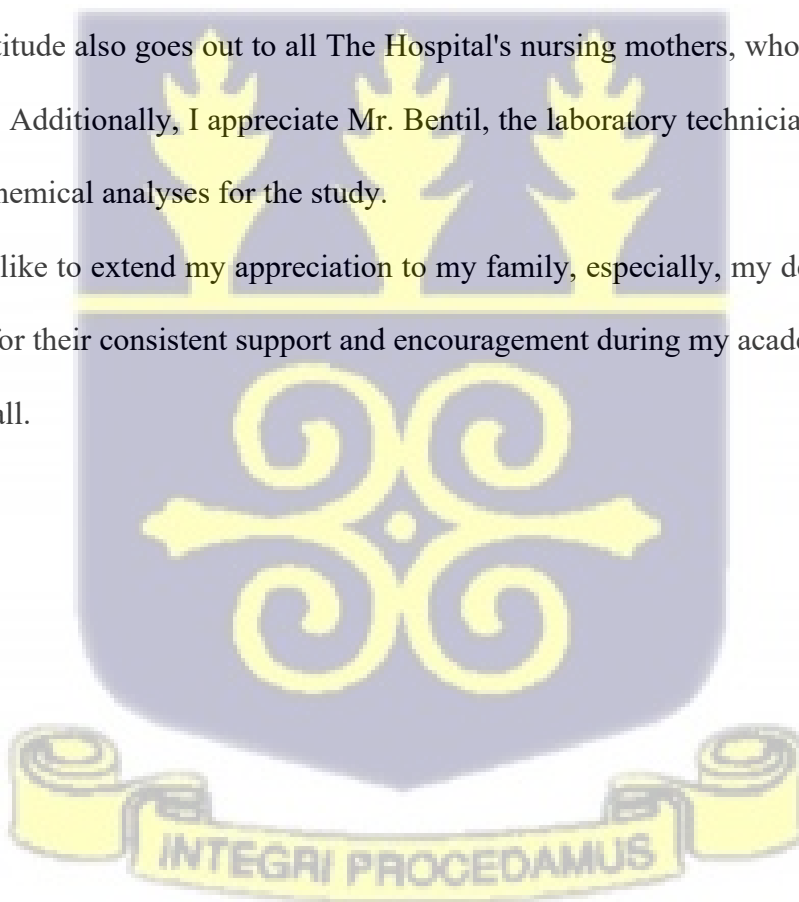


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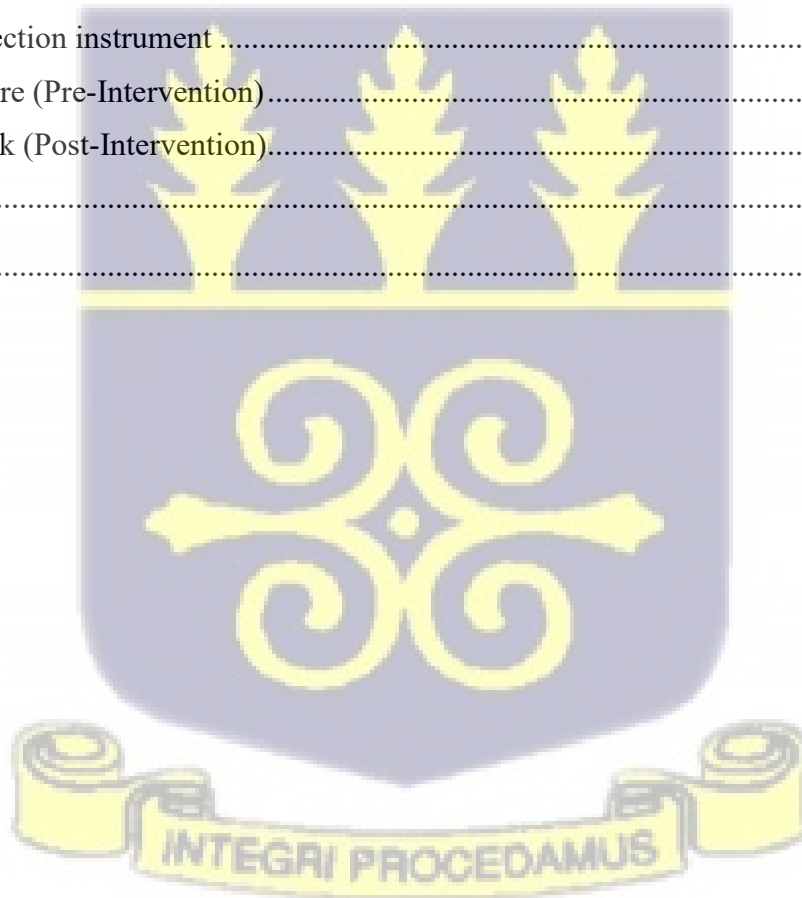


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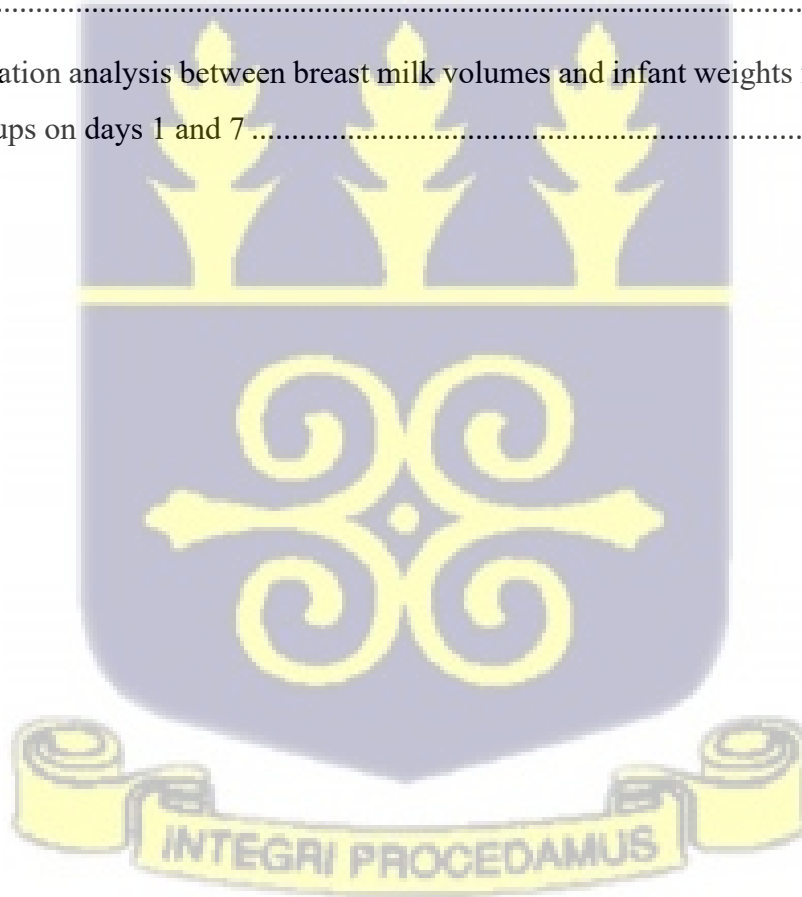
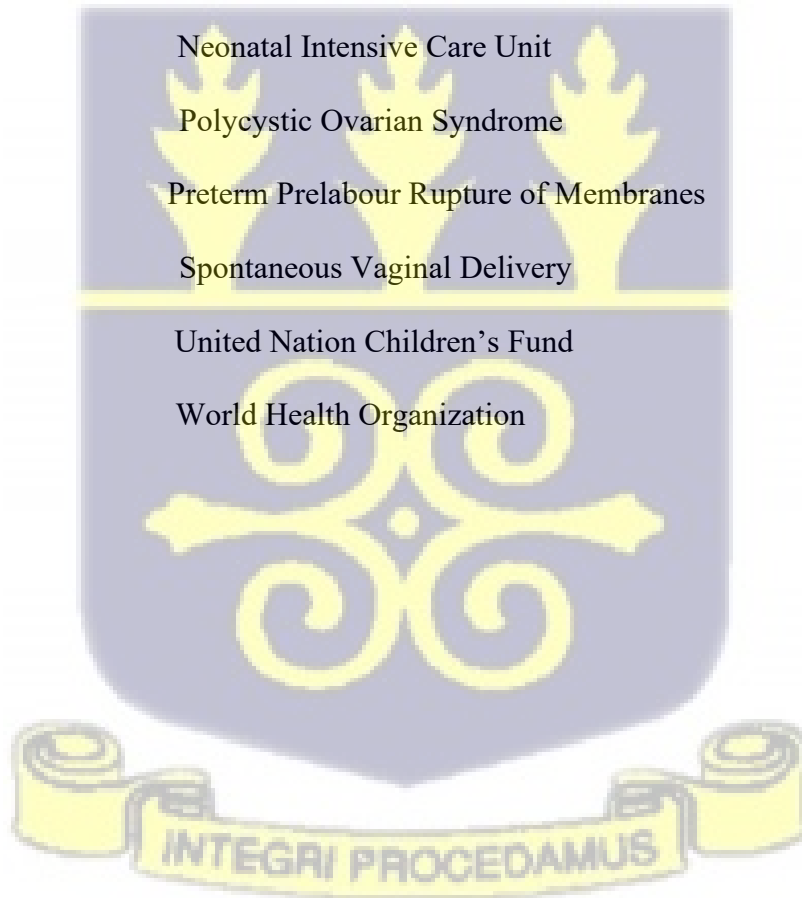


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CS	Caesarean Section
BFHI	Baby-Friendly Hospital Initiative
FDA	Food and Drugs Authority
FIL	Feedback Inhibition of Lactation
IEC	Information, Education and Communication
KMC	Kangaroo Mother Care
LBW	Low Birth Weight
LI	Legislative Instrument
LMIC	Low- And Middle-Income Countries
NICU	Neonatal Intensive Care Unit
PCOS	Polycystic Ovarian Syndrome
PPROM	Preterm Prelabour Rupture of Membranes
SVD	Spontaneous Vaginal Delivery
UNICEF	United Nation Children's Fund
WHO	World Health Organization



CHAPTER ONE

INTRODUCTION

1.1 Background

It is estimated that 13% of infant deaths globally are caused by inadequate breastfeeding either due to little or no milk production, poor feeding habits of the baby or little time on the part of the mother to exclusively breastfeed their babies for the six months period recommended by WHO (OMS-Unicef, 2018). In the year 2019 alone, preterm birth rates was recorded to rise globally from 9.8% to 10.6% (WHO, 2019). Sufficient nursing is essential for the survival of preterm babies. In Ghana, according to a research conducted by Kumador *et al.* (2025), 37.3% of births occurred before their due date. This is where the infants' nutrition and growth are greatly impacted by exclusive breastfeeding. It is believed that an infant's development and survival depends most heavily on the first 100 days of their existence (UNICEF, 2021).

Lactation is a complicated physiological process including hormonal, physical, and psychological elements. One of the main causes of the high percentage of unsatisfactory breastfeeding among nursing mothers is inadequate production of breast milk (Ali *et al.*, 2020). Galactogogues, another name for lactogogues, are compounds that can help initiate, maintain, or increase the rate at which breast milk is produced in lactating mothers (Turkyilmaz *et al.*, 2011). Similar evidence has also been shown based on the use of various pharmaceutical galactogogues, such as metoclopramide and domperidone (Grzeskowiak *et al.*, 2019). There have been foods and special herbs that act as galactogogues in our Ghanaian homes. Such galactogogues-containing herbs included in diets include dried baobab leaves (*Adansonia digitata*), tiger nuts (*Cyperus esculentus*), Nkontonmire/cocoyam leaves (*Colocasia esculenta*), Abemudro (a polyherbal formulation) Ali *et al.*, (2020) and Ayoyo/Jute leaves (*Corchorus olitorius*). Millet porridge, milk tea, saltpetre

porridge, and Tuo Zaafi (made with maize flour) are other examples of galactogogues-containing foods.

Galactogogues-containing foods related to groundnuts and peanuts include mashed kenkey mixed with groundnut paste, maize porridge mixed with groundnut paste, groundnut-prepared Aleefu (Amaranth sp.), groundnut-infused soup made with Bra leaves (*Hibiscus sabdariffa*), soup made with Werewere (*Citrulus colocynthis*) and soup made solely of groundnuts (Ali *et al.*, 2020).

1.2 Problem Statement

Inadequate breast milk has been cited as one of the key reasons why most mothers are unable to complete the six months of exclusive breastfeeding (Agyekum *et al.*, 2022). Early introduction of infants to solids before six months has also been linked to increased morbidity and mortality (Wilson *et al.*, 1998). Breastfeeding remains a crucial aspect of infant nutrition, particularly for preterm infants who require specialized care due to their vulnerable health status. In many regions of the world, including sub-Saharan Africa, breastfeeding challenges are prevalent, hindering optimal infant care and nutrition. One significant area of interest is the use of herbal galactogogues, which are natural substances claimed to enhance breast milk production, as a potential solution to address breastfeeding difficulties in preterm infants.

Despite traditional beliefs and anecdotal evidence surrounding the efficacy of herbal galactogogues, limited scientific research has been conducted to establish their safety and effectiveness. Moreover, the influence of these herbal remedies on breast milk production and residual breast milk volume in lactating mothers is essential to develop evidence-based intervention practices in small infant care, especially in the context of challenges faced in sub-Saharan Africa.

The rate of preterm births has increased globally, but there is a dearth of statistics from resource-limited nations like Ghana. The scanty data that is available indicate that preterm birth rates have increased throughout the last 20 years in most nations, especially those from low- and middle-incomes (Unar-Munguía *et al.*, 2018). The Sustainable Development Goal 3 aim of bringing the neonatal mortality rate down to 12 per 1,000 live births by 2030 may, thus, be partially met by comprehending and putting into practice a solution that can offer preterm birth optimal health. If breast milk levels are adequate, mothers are likely to complete the six months exclusive breastfeeding regime. This will reduce Ghana's under-5-year-old children's risk of morbidity and death.

Herbal products like fennel, fenugreek, moringa and other galactagogues (oats, chia seeds and flax seeds) have been shown to improve breastmilk outcomes in breastfeeding mothers in other parts of the world (Vakili & Mobini, 2023). However, no study has been done to ascertain their galactogenic activity in lactating mothers of preterm babies. Also, the geographical location of Ghana may imply the metabolism of Ghanaians could differ from the populations in other parts of the world, as different food products are consumed by Ghanaians. Therefore, data generated from this study could provide evidence for the suitability and ability of these galactogous to enhance breast milk production in Ghanaian lactating mothers.

1.3 Justification

Breastfeeding is a crucial aspect of maternal and infant health, especially for preterm infants who are more vulnerable to various health challenges. Breast milk provides essential nutrients, antibodies, and growth factors that promote optimal growth and development in infants (Ballard

& Morrow, 2013). However, some lactating mothers may experience challenges with low breast milk production, which can negatively impact their ability to exclusively breastfeed their infants. Galactagogue is a common remedy used by nursing mothers to increase the amount of breast milk they produce. Data from this study provide evidence-based insights that healthcare professionals and lactating consultants can utilize to offer informed guidance and support to lactating mothers of preterm babies.

Breastfeeding is essential for preterm newborns, who experience special obstacles throughout the neonatal period, to maintain their growth and immune system development. Understanding the influence of herbal galactogogues on the production of breast milk in lactating mothers has the potential to lead to interventions that could enhance the nursing experience of preterm infants, hence augmenting their general health and welfare.

Pharmacological interventions for lactation support may have potential side effects and interactions with other medications. If herbal galactogogues are found to be effective, they could offer a natural and safer alternative to pharmacological interventions, reducing potential risks for both the mothers and their preterm infants.

Improved breast milk production can lessen the need for costly formula feeding or parental nutrition in the neonatal intensive care unit (NICU). Through the clarification of the impacts of galactagogue consumption, this study has the potential to improve infant care and lower costs in medical institutions.

Hence, this study holds significant importance in enhancing breastfeeding support for preterm infants and their mothers. The results obtained from this study can be instrumental in informing evidence-based lactation practices, contributing to improved neonatal care, and advancing

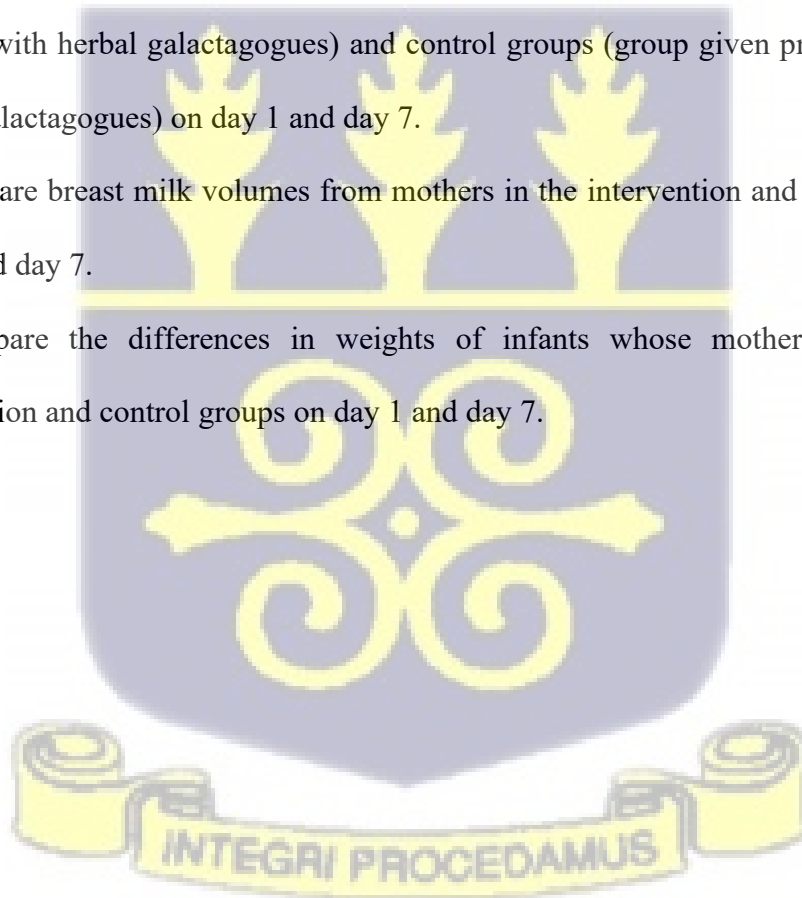
knowledge in the fields of herbal medicine and lactation physiology. Ultimately, the research aims to make a positive impact on maternal and infant health outcomes, supporting the well-being of families and the broader community.

1.4 Main Objective

To assess the effects of herbal galactagogues-containing lactation products on breast milk production, serum prolactin levels in preterm lactating mothers and infant weight.

1.5 Specific Objectives

- To compare the serum prolactin levels of mothers in the intervention group (group given product with herbal galactagogues) and control groups (group given product without the herbal galactagogues) on day 1 and day 7.
- To compare breast milk volumes from mothers in the intervention and control groups on day 1 and day 7.
- To compare the differences in weights of infants whose mothers constituted the intervention and control groups on day 1 and day 7.



CHAPTER TWO

LITERATURE REVIEW

2.1 Breast milk production

Women's mammary glands secrete a fluid known as breast milk. It is made up of water, carbohydrates, protein, fat, minerals, vitamins, enzymes and antibodies. The main primary and healthiest natural food for infants is breast milk, which is also crucial to their survival (Shah *et al.*, 2022). Inadequate breastfeeding is thought to be responsible for 13% of infant mortality worldwide (Abdulla *et al.*, 2022). According to Sharma (1996), the most common reason for breastfeeding failure, or hypogalactia, is a reduced supply of breast milk. This reduction can occur due to factors such as preterm birth, illnesses affecting either the baby or the mother, separation of mother and baby, efforts to re-lactate after a lengthy suspension, indirect lactation (through breast pumps or hand expression of milk), or periods of anxiety, exhaustion, and emotional stress (Sharma, 1996). Human milk's composition varies dynamically throughout the course of a baby's development (Chiurazzi *et al.*, 2021). Colostrum, mature milk and transitional milk are the three categories of human milk (Rio-Aige *et al.*, 2023). The term "colostrum" describes the first milk that is produced, and has a high whey protein content in the absence of casein (Rio-Aige *et al.*, 2023). Mature milk is produced 15 days after giving birth, while transitional milk is produced by nursing mothers between 5 and 15 days after giving birth (Sala-Vila *et al.*, 2005). To ensure that breastfeeding is successful, it is imperative to follow certain feeding practices, including placing and attaching the baby correctly and nursing whenever needed throughout the day (Degefa *et al.*, 2019). A thriving infant has been observed to consume between 478 and 1356 milliliters per day, while exclusively breastfed infants typically take between 750 and 900 milliliters per day (Kent, 2007). When secretory activation occurs, milk supply often increases quickly; by two weeks after giving birth,

92% of women of full-term infants are producing at least 440 mL of milk per day (Kent, 2007). Most successfully breastfed babies will regain their birth weight by the time they are seven days old (Kellams *et al.*, 2017). Breastfeeding is a vital form of nutrition even after the neonatal stage because of its ongoing benefits, which includes decreased rates of infection, diabetes, polycystic ovarian syndrome, obesity, cardiorespiratory disorders and allergy diseases (Masi & Stewart, 2024). According to Joosten & Vermeulen (2024), the importance of feeding premature newborns with human milk is increasing since necrotizing enterocolitis is more likely in young babies who are fed with formula milk. However, producing enough milk might be challenging for mothers of premature infants (Madiba & Sengane, 2021). Separating babies from their mothers, feeding them through an orogastric tube, worrying about having a preterm infant, having a good breast attachment, feeding frequently, resting the mother, confidence, support from family and peers, pain (including painful nipples), additional bottle feedings, and not encouraging suckling are just a few of the factors listed by Amir (2006) that may prevent a mother from producing enough milk. Consequently, the majority of premature infants are denied access to breast milk (Chen *et al.*, 2025). The health of the premature newborn in this case depends on all efforts being made to assist mothers in establishing adequate breastfeeding.

Disruptions in lactation hormones can impact milk production. These disorders include hyperandrogenism (Betzold, 2004), obesity, thyroid disease, polycystic ovarian syndrome (PCOS), and postpartum hemorrhage or hypopituitarism. Research indicates that a third of mothers with gestational diabetes experienced delayed lactation onset (Matias *et al.*, 2013). Another study suggested that reduced insulin responsiveness might cause an overexpression of a gene regulating an insulin signaling pathway, thus lowering milk production, a finding supported by recent research (Nommsen-Rivers, 2016). Hormonal contraceptives are among the medications that can

suppress lactation because they interfere with the hormonal processes that cause lactation. As milk production relies on both the amount of milk removed and the efficacy of the suckling stimulus, a baby who does not efficiently suck enough milk from the mother, could lead to insufficient milk production (Geddes, 2008; Zhang, 2016). Neonatal causes like hypotonia, oromotor dysfunction, and anomalies of the oral cavity - such as clefts of the hard or soft palate or a tight lingual frenulum are a few examples (Amir, 2006; Kent *et al.*, 2012). Often, identifying a single cause for decreased milk production is challenging; instead, the underlying reason is usually multifaceted (Foong *et al.*, 2020).

2.1.1 Exclusive Breastfeeding

According to Kramer & Kakuma (2012), exclusive breastfeeding refers to breast milk provided solely to newborns, without any other food or drink between the ages of one and six months; other foods or beverages are not added to or substituted for it. Additionally, children who are nursed exclusively have been shown to have superior cognitive capacities, have a lower chance of becoming fat or overweight adults and to be prone to non-communicable diseases as well. In addition to that, mothers benefit from exclusive nursing since it lowers their chances of developing uterine and breast cancer (Anstey *et al.*, 2017). However, there are still a lot of careless advertisements for formula milk and other breast milk substitutes, which makes exclusive breastfeeding difficult to achieve (Brady, 2012). One strategy to enhance a child's nutritional health throughout the first 100 days of life is exclusive breastfeeding (Kramer & Kakuma, 2012).

The World Health Organisation (WHO) and the United Nations Children's Fund (UNICEF) established the exclusive breastfeeding practice, which entails mothers giving their newborns solely breast milk throughout the first six months of life. The United Nations Children's Fund lists Côte d'Ivoire (4%), Chad (2%), Sierra Leone (8%) and Gabon (6%) as among the nations having

low rates of exclusive breastfeeding. Rwanda (85%) and Benin (70%) are two other nations in the region that have attained higher rates of exclusive breastfeeding as compared to the others (United Nations Children's Fund, 2011). About 63% of Ghanaians exclusively breastfeed their children (Mensah *et al.*, 2017). The sub-region exclusive breastfeeding rates have improved (Tampah-Naah & Kumi-Kyereme, 2013), however, this implies that these rates could be impacted by social and environmental factors. These have put pressure on a few sub-regional governments to adopt, develop, and put into action, plans to encourage mothers to breastfeed their babies exclusively (Mensah *et al.*, 2017). In Ghana, various initiatives have been launched to ensure exclusive breastfeeding for babies. Two notable factors measures the adoption of the 1991 Baby-Friendly Hospital Initiative (BFHI) and the establishment of the BFHI Authority (OMS-Unicef, 2018). The BFHI Authority was responsible for overseeing the initiative's execution, developing a breastfeeding policy, and creating implementation strategies (Mustafa, 2018). The BFHI Authority was also tasked with making sure that all hospitals across the nation have master trainers trained in lactation management (Mustafa, 2018). According to Mustafa (2018), the employment of healthcare professionals gave mothers early encouragement to exclusively breastfeed their babies. The Ghana Breastfeeding Promotion Regulation 2000, referred to as Legislative Instrument [LI] 1667, is another intervention. The LI 1667's primary goal was to discourage the aggressive promotion of breast milk substitutes and to support breastfeeding as a national health practice (Tampah-Naah & Kumi-Kyereme, 2013). The Food and Drugs Authority of Ghana claims that the country's failed attempt to encourage exclusive breastfeeding is because the Breastfeeding Promotion Regulation 2000, which prohibits the marketing of breast milk substitutes, was broken. Alternative approaches, such as materials for advocacy and information, education, and communication (IEC), are intended for use by the general public as well as by health professionals.

According to Kramer & Kakuma (2012), to promote exclusive breastfeeding, breastfeeding interventions must be developed and put into practice. Patel *et al.* (2015) stated that mother and child variables, however, are quite important, as the practice helps the mother, both financially (because breast milk is given for free) and emotionally. It also helps the infant develop a stronger bond with its care by providing it with the calories and nutrients it needs in its early stages of life (Patel *et al.*, 2015).

2.2 Lactation

Childbirth is a demanding experience and brings about substantial changes in the hormonal profile, particularly with regard to stress-related hormones. According to del Castillo-Hegyí *et al.* (2022), there are several risk factors for delayed lactogenesis, including primiparity, prolonged labor, stress during labor and delivery, and elevated cord glucose levels. Around the middle of pregnancy, a process known as lactogenesis (milk synthesis) begins. It has been divided into two stages, lactogenesis I and II, and is influenced by several hormones, including cortisol, oestrogen, insulin, progesterone, prolactin, and human placental lactogen (Truchet & Honvo-Houéto, 2017). The initial phase of secretory differentiation, called lactogenesis I, occurs when mammary epithelial cells transform into secretory mammary epithelial cells capable of synthesizing lactose, proteins, and immunoglobulins - all essential components of milk. Physiological hurdles to the development of lactation can be caused by delayed childbearing, high rates of caesarean sections, intense labour lasting more than an hour, and obesity. The fast drop in maternal serum progesterone following placenta expulsion initiates the secretory phase of lactogenesis, also known as lactogenesis II. This also causes a drop in oestrogen levels, but prolactin, insulin, and cortisol levels remain elevated (Truchet & Honvo-Houéto, 2017). In term pregnancies, the lactogenesis II stage takes place. The first four days after giving birth are spent producing colostrum, and the next ten days are spent

producing transitional milk secretion before mature milk is generated. After the first 24 hours postpartum, milk supply grows quickly and stabilizes at 750–800 mL/24 hours on average for a term infant after one month (Kent, 2007). Efficient and prompt milk removal increases milk supply; sufficient milk removal by the third postpartum day is essential for the development of continued effective breastfeeding (Kent *et al.*, 2012). Prolactin and oxytocin, two endocrine hormones, as well as sufficient and consistent milk removal, control milk production. While myoepithelial cells surrounding mammary alveoli contract in response to oxytocin, generating milk ejection, or "milk let-down," prolactin is required to sustain milk production (Truchet & Honvo-Houéto, 2017). Hormone levels are kept at a minimum once milk secretion is initiated, and continued production is controlled by regular and consistent milk removal. The way the breast is emptied during feedings, which is influenced by the newborn's hunger, determines the amount of milk produced in a term infant (Kent *et al.*, 2012). The low molecular weight hormone known as Inhibition of Lactation (FIL) is the cause of the milk-stimulating impact of the milk removal process (Abascal & Yarnell, 2008). As FIL builds up in the breast alveoli, prolactin production is gradually inhibited. Because repeated withdrawal of breast milk reduces the FIL action to sustain milk supply, this barrier ends when lactogenesis III occurs Anderson & Valdés (2007) and insulin plays a role in this.

2.2.1 Preterm and Lactation

Lactogenesis may not proceed according to plan in cases of preterm delivery. Successful lactation may be negatively impacted by a delay in secretory activation (Chapman & Pérez-Escamilla, 1999). Mothers with preterm infants may have some complications at this point as an indicator of preterm delivery, prenatal corticosteroids, maternal illness, and surgical delivery (Gyamfi-Bannerman *et al.*, 2016). Because the very preterm infant's typical mechanism of nursing is

limited, mothers of these infants have to use mechanical expression to determine their milk supply (Kent *et al.*, 2012). A research conducted by Cerasani *et al.*, (2020) highlighted how crucial it is for mothers of preterm infants to develop adequate breast milk production in the early postpartum phase. Research indicates that mothers who produce less than 140 millilitres per day on the fourth postpartum day are 9.5 times more likely to have low or insufficient milk supply by the sixth week of the postpartum period (Case-Smith *et al.*, 1989).

Many mothers find it challenging to sustain a milk volume adequate to satisfy the nutritional needs of their extremely preterm infants (Hill *et al.*, 2005). Research indicates that a mother of a preterm newborn should suction at least 500 mL/day or 3500 mL/week to meet her infant's demands upon discharge. This means that a mother should pump 80–100 mL each time, six times a day (Hill *et al.*, 2005). A report generated by American Academy of Pediatrics (2021) reveals it can be anticipated that a mother who is making more than 3,500 millilitres by week two will continue to produce this sufficient amount in weeks four and five. The report also stated that a mother has roughly a 50% probability of attaining the minimum of 3500 mL/week by week 5 postpartum if she is producing ≥ 1700 mL/week but < 3500 mL by week 2. The report goes ahead to show that the outlook is severe for a mother producing less than 1700 mL per week. (less than 40 mL every pumping), as 100% of them will not meet the 500 mL per day target by weeks 4-5 after giving birth. The insufficient amount of milk and its subsequent decrease in production throughout the next few weeks present difficulties for the mother who is anxious to nurse her child (Gatti, 2008). According to Piccolo *et al.*, (2022), mothers who exhibit a decrease in breast milk production and are likely to cease expressing breast milk for their child, other strategies might need to be investigated.

2.3 Galactogogues

Galactogogues are chemicals that are believed to help initiate, continue, or increase the production of breast milk Foong *et al.*, (2020). They consist of natural supplements and pharmaceuticals. Exogenous hormone therapy (thyroid and growth hormone) and legal medications having a galactagogue effect (metoclopramid, sulfuride, domperidon, and chlorpromazine) are often utilized in Europe and the USA (Asztalos *et al.*, 2012). According to Sim *et al.* (2014), people utilized herbal treatments, which are said to be the safest galactagogues now on the market, as an alternate method of resolving the problem due to the negative effects caused by pharmaceutical galactagogues. There is a long history of using herbs and products made from them to boost milk production. Herbal medicinal plants are used by traditional medicine practitioners and others to boost milk secretion in breastfeeding women in various regions of the world, especially in underdeveloped countries with a folklore legacy. In certain regions of the world, numerous other plants are also said to have galactagogue qualities.

2.3.1 Galactagogue foods in Ghana and Africa

Among Ghanaians, major lactogogues include herbs and a few native crops. A research conducted by (Ali *et al.*, 2020), in the Brong-Ahafo area, a polyherbal compound called abemudro is commonly used to enhance lactation; a previous study in Ghana's eastern region also documented its use. Although the use of lactogogues during pregnancy in Ghana is low, it is thought to prepare the breast for increased milk production after birth (Ali *et al.*, 2020). Dried fish and *Mangifera indica* L. (mango) were also mentioned in another study by Ullah *et al.*, (2024) to be avoided as natural foods that affect breast milk quality and quantity in Angola. Throughout the conversation, it was explained how watery milk and diarrhoea in children can be caused by dried fish and mango. Numerous investigations revealed that phytochemicals can affect an infant's health when they are

passed from a mother to her child through breast milk (Song *et al.*, 2013). The Angolan people often utilise *Monodora myristica*, or calabash nutmeg, as a treatment for decreased breast milk production. *Salacia erecta*, *Saccharum officinarum* (sugar cane), and *Abrus precatorius* L. (Jequirity bean) are further common treatments (Jendras *et al.*, 2020). Herbal galactagogues also include milk thistle, fenugreek, lemon grass, fennel, and moringa. Galactagogue ingestion is still prevalent under traditional postpartum practices.

2.3.2 Fenugreek

Fenugreek (*Trigonella foenum-graecum*), of the pea family, originates from Europe (Basch *et al.*, 2011). This Greek hayseed has been used as a natural galactagogue since ancient times. Native to the Mediterranean, Southern Europe, and Western Asia, fenugreek contains 26.2 g of protein, 5.8g of fat, 44.1g of carbohydrates, and 333 kcal per 100 grams. Its seeds are composed of 50% fiber, with 30% being soluble fiber and 20% insoluble fiber. Natural sources of iron, silicon, salt, and thiamine include fenugreek (Wahab Gbolahan Ayoade *et al.*, 2023). (Sim *et al.*, 2014) suggest that fenugreek may also boost milk production because it serves as a sweat production stimulant, and the breasts are modified sweat glands. According to Mohanty *et al.*, (2014), a variety of phytochemicals, such as alkaloids, isoflavones, polyphenols, tannins, and saponins, have an impact on milk production. They have been shown to increase lactation by raising prolactin levels, accelerate let-down, and help increase the percentage levels of milk proteins. According to Turkyilmaz *et al.* (2011) and Gupta & Shaw (2011), a galactagogue might boost milk volume by exerting an estrogen-like effect. It has also been proposed that fenugreek might exhibit estrogen-like activity (Gabay, 2002).

Studies have demonstrated two effective strategies for enhancing milk production using galactagogues (Tabares *et al.*, 2014). First, phytoestrogens in galactagogues get attached to receptors in the mammary glands, promoting the proliferation of alveolar cells. These phytoestrogens then interact with the β -estradiol receptor with the bombardment of the α -isoform of the membrane-associated estrogen, potentially triggering the production of the prostate gene. Additionally, according to Tabares *et al.* (2014), phytoestrogens function as dopamine antagonists, by blocking the pathway activated by dopamine receptors, which increases prolactin secretion and stimulates milk production. Fenugreek seeds contain chemicals that resemble estrogen and have been shown in one study to increase the production of pS2 in MCF-7 cell lines through in vitro experiments; a common marker for determining a compound's estrogenicity is the pS (Sreeja, 2010). Although the precise mode of action is yet unknown, the phytoestrogens and diosgenin (a kind of steroidal sapogenin) content of fenugreek seem to be responsible for the rise in milk flow reported from its usage (Sreeja, 2010). Phytoestrogens can be bombarded to both α and β estrogen receptors and have a chemical structure similar to natural estrogen. Consequently, they may act as estrogen agonists, potentially altering the structure or function of the endocrine system (Patisaul & Jefferson, 2010). Consistent with these findings, Turkyilmaz *et al.* (2011) observed that the fenugreek group had nearly two times the volume of colostrum expressed milk compared to the placebo group.

Individuals allergic to chickpeas or other members of the Fabaceae family, such as soybeans or peanuts, should avoid consuming fenugreek. While fenugreek influences lactogenesis and prolactin levels during the initial stages of lactation, it does not influence the established volume of breast milk or alter prolactin levels later on. While incidences of asthma, rhinitis, fainting, and facial edema have also been described, adverse effects may include nausea, diarrhea, and flatulence

(Yacobucci, 2016). Fenugreek has also been suggested to possess estrogenic properties. Fenugreek seeds contain chemicals that resemble estrogen and have been shown in one study to increase the production of pS2 in MCF-7 cell lines using in vitro experiments (Betzold, 2004). A common measure for determining a compound's estrogenicity is pS2. The increase in milk flow reported from fenugreek use appears to be explained by its phytoestrogens and diosgenin content (a form of steroidal sapogenin), while the precise mechanism of action is still unknown. Phytoestrogens can bind to both alpha and beta estrogen receptors and share a molecular structure similar to that of endogenous estrogen. As a result, they may behave as estrogen agonists or antagonists, which may change how the endocrine system is structured or functions (Betzold, 2004).

2.3.3 Fennel

Foeniculum vulgare, commonly known as fennel, is a licorice-flavored herb native to the Mediterranean region. It is most renowned for treating colic and dyspeptic disorders in infants (Badgujar *et al.*, 2014). Although, traditionally used to stimulate milk production, fennel has estrogenic properties that could theoretically suppress lactation (Conover & Buehler, 2004). No contraindications for using fennel during lactation have been recognized, though other sources predict limiting its usage to short periods (Yacobucci, 2016). Potential detrimental effects include atopic dermatitis and photosensitivity, and individuals allergic to celery or carrot may also have cross-sensitivity to fennel. Fennel seeds can enhance gastrointestinal motility. Because of its elevated levels of calcium, magnesium and iron, fennel bombards ciprofloxacin and other fluoroquinolones, reducing their bioavailability; therefore, concurrent use should be approached with caution (Yacobucci, 2016).

2.3.4 Moringa

Found throughout most of Ghana, *Moringa oleifera* is a member of the monogenetic Moringaceae family (order Brassicales). This plant serves both medical and non-medicinal purposes. Due to its great nutritional content and wide range of medical applications, the plant is being grown for a variety of reasons (Zhao, 2020). *M. oleifera* Lam is a deciduous tree with thin leaves that looks like a leguminous species from a distance. It is very graceful when in blossom but is easily recognised when in fruit. The tree grows to a height averagely 10-12 m high (Oladeji *et al.*, 2020). *M. oleifera* can be classified into seven categories. These are medicine, food, firewood, fodder, fencing, gum, and coagulant (Gandji *et al.*, 2018).

According to Nurmiaty *et al.* (2016), Moringa leaves are often consumed as a vegetable due to their rich nutritional profile. In 100 grams of fresh Moringa leaves, you will find 92 calories, 6.8 grams of protein, 1.7 grams of fat, 12.5 grams of carbohydrates, and 0.9 grams of fiber. These leaves are as well a significant source of essential vitamins, including 6.78 mg of carotene (vitamin A), 0.06 mg of thiamine (vitamin B1), 0.05 mg of riboflavin (vitamin B2), 0.8 mg of niacin (vitamin B3), and 220 mg of vitamin C. Additionally, fresh Moringa leaves are packed with minerals: 440 mg of calcium, 0.07 mg of copper, 0.85 mg of iron, 42 mg of magnesium, 70 mg of phosphorus, 259 mg of potassium, and 0.16 mg of zinc (Nurmiaty *et al.*, 2016).

Moringa leaves have been shown to enhance lactation, evidenced by an improvement in maternal serum prolactin levels. Education about lactation can enhance mothers' understanding, attitudes, and practices towards breastfeeding for up to six months (Nurmiaty *et al.*, 2016). Prolactin is the primary hormone in the commencement of lactation. Moringa leaf powder is a potent galactagogue that increases the volume and facilitates the production of breast milk (Muslimin *et al.*, 2023).

Research proves that *Moringa oleifera* is a rich source of essential nutrients that help prevent diseases.

Moringa oleifera is globally recognized for its nutritional and therapeutic benefits. The nutrients in Moringa, such as proteins, minerals, and vitamins, help maintain osmotic balance and activate enzymes essential for physiological functions (Anjorin *et al.*, 2010). Moringa is widely ready to use throughout the country, and its leaves comprises only trace amounts of anti-nutritional factors like tannins and saponins (Deepa, 2019; Moyo *et al.*, 2009). The iron content in Moringa leaves is particularly high, being 25 times greater than that of spinach and three times more than almonds. Moreover, the leaves are rich in vitamin C, containing 220 mg per 100 grams, which is seven times more than oranges and ten times more than grapes (Susilowati *et al.*, 2022). This vitamin C enhances iron absorption by acting as a reducing agent that converts ferric iron into ferrous iron, maintaining intestinal pH, and preventing iron precipitation. It can also act as a chelator, forming iron ascorbate to facilitate easier absorption (Tirtawati *et al.*, 2021). Additionally, herbal galactagogues mixtures such as shatavari, fenugreek, and jivanti (*Letptadenia*) possess similar properties and are available in herbal shops.

In the study carried out by (Fungtammasan & Phupong, 2022), *Moringa oleifera* leaves were recognized as a herbal galactagogue intended to improve breast milk volume. Although a daily dose of 900 mg of Moringa leaves did not lead to a significant elevation in breast milk volume among early postpartum mothers, the Moringa group yielded 47% more breast milk compared to the control group. Moreover, the proportion of exclusive breastfeeding at six months for the Moringa *oleifera* group achieved the WHO targets. Consequently, according to Ali *et al.* (2020), a galactagogue formulation that includes *Moringa oleifera* leaves can effectively enhance breast milk production. Ali *et al.* (2020) investigated the effects of Moringa leaf extract and Moringa leaf

flour on both the quality and volume of breast milk in mothers with infants aged 0-6 months. Their results showed no notable differences in the composition of breast milk (such as iron, vitamin C, and vitamin E) between the groups. Nonetheless, the group that consumed Moringa leaf extract exhibited a more significant increase in breast milk volume.

2.3.5 Galactagogue Suppressers

Certain herbal products could have the opposite effect and reduce breast milk production (Finny *et al.*, 2015). Thus, women who want to increase their milk production should refrain from using these substances. When administered to the breasts, jasmine petals have been shown to dramatically reduce milk production, breast engorgement, and prolactin levels (Finny *et al.*, 2015). Depending on their potency, these results may conceivably be extended to jasmine essential oils and perhaps even fragrances. Additionally, pyridoxine, a vitamin B6 that is consumed in excess, may be linked to milk suppression. Sage, camphor, and bilberry have perhaps possibly been used as breast milk production suppressants (Finny *et al.*, 2015). In western countries, during weaning, common herbs used to reduce lactation include parsley, sage, and peppermint (Sim *et al.*, 2013). Some research have shown that lowering an animal's energy supply causes it to produce less milk (Martens, 2023); nevertheless, since lactating mothers' energy consumption is still being understudied, judgements regarding this cannot yet be drawn.

2.4 Preterm Infants

According to the WHO, infants with low birth weight (LBW) have a birth weight of under 2.5 kg, while preterm infants have a gestational age of less than 37 weeks. Newborns account for over 45% of all deaths in children under five, and 60–80% of newborn deaths are caused by premature birth or small size for gestational age. The WHO study from 2021 states that the prevalence of

preterm births is 12.5%. Anto *et al.* (2022) reports that the prevalence is 37.3% in Ghana. Infants born with low birth weight (LBW) are at a 2- to 10-fold higher risk of death in comparison to infants born at term and with a normal birth weight.

Blencowe *et al.* (2012) describe preterm birth as a worldwide crisis as well as a major cause of newborn deaths and long-term health issues. A baby is classified as preterm if born before 37 weeks of gestation. Although the precise cause of preterm birth is not fully understood, it is generally divided into two categories: provider-initiated preterm birth (such as labor initiation or prelabor elective cesarean for maternal or fetal reasons) and unexpected preterm delivery (such as the natural onset of labor or preterm premature rupture of membranes) (Goldenberg *et al.*, 2012).

The varied causes, encompassing both individual and environmental factors, make it challenging to predict and prevent preterm birth in antenatal care (Blencowe *et al.*, 2012). A multi-country study in low- and middle-income countries (LMICs) found that unexpected preterm births are prevalent, and preterm infants face a higher risk of mortality (Gurung *et al.*, 2020). Preterm neonates are more vulnerable compared to full-term newborns to issues such as malnutrition, chronic illnesses, early death, neurocognitive and motor impairments (Christian *et al.*, 2014).

A study by Goldenberg *et al.*, (2012) highlight that the probability of neonatal mortality due to preterm birth complications in Africa is over nine times higher than in Europe. Preterm birth rates vary globally, ranging from 5% to 18% across 184 count (Alamneh *et al.*, 2021). Out of the 130 million babies born annually worldwide, 15 million are preterm. Sub-Saharan Africa and Asia, which collectively represent half of all global births, exhibit the highest preterm birth rates (Alamneh *et al.*, 2021)

2.4.1 Preterm Dangers

Due to concerns about survival and quality of life, preterm births (births occurring before 37 weeks) have gained increased attention in the public health field (Soltani *et al.*, 2019). Around 81% of preterm births worldwide roughly 15 million preterm births yearly, or 1 in 10 deliveries occur in South Asia and Sub-Saharan Africa.

According to the World Health Organisation, prematurity is the primary cause of low birth weight and the first of the six main causes of mortality for children under five, accounting for around one million fatalities annually worldwide. Preterm births are associated with numerous complications, including respiratory distress syndrome, bronchopulmonary dysplasia, intraventricular hemorrhage and many others. These complications create significant financial, psychological, and physical strains on affected families. In high-income nations, the primary causes of preterm delivery include the increased use of assisted reproductive technologies, which often result in multiple gestations, and conception at an older maternal age, which leads to more complex pregnancies. In contrast, in low-income countries, preterm births are strongly associated with diseases such as malaria and HIV, as well as teenage pregnancies.

Preterm survival has improved in higher levels in higher income as compared to middle- and lower-income countries due to numerous effective interventions, such as the use of antenatal corticosteroids, the administration of maternal antenatal magnesium sulphate, the use of surfactants, antibiotics for preterm prelabour rupture of membranes (PPROM), and more (Cousens *et al.*, 2010).

In addition to organ maturity, which depends on birth weight and gestational age, the survival of preterm infants is supported by effective health systems. Research indicates that establishing

specialized neonatal care units in district hospitals, providing early respiratory support, ensuring adequate prenatal care, using low-dose aspirin and first trimester biomarkers to reduce the risk of pre-eclampsia, administering progesterone, and performing procedures such as cerclage for cervical insufficiency all significantly extend pregnancy duration and enhance survival rates (Ndelema *et al.*, 2016).

2.4.2 Interventions for Preterm

A global assessment published by Africa's Newborns identified eleven interventions, including hospital-based Kangaroo Mother Care (KMC), that were found to enhance the survival of preterm and low birth weight (LBW) newborns. There's a good chance that identifying small newborns and giving them extra assistance with eating will lower the likelihood of neonatal mortality.

KMC is an intervention used to care for preterm infants and enhance their outcomes. In order to address issues with mother-child separation, hospital overcrowding, and incubator shortages for low birth weight babies, KMC was founded in Colombia in 1978 (Conde-Agudelo & Díaz-Rossello, 2016). KMC is the term for skin-to-skin contact, which keeps a baby warm, encourages exclusive breastfeeding, and makes it easier for a patient to leave the hospital early. For low birth weight (LBW) newborns, it has been suggested as an alternative to incubator care (Conde-Agudelo & Díaz-Rossello, 2016). In order to avoid interfering with the breastfeeding schedule, carers can grant KMC access to other family members, such as the babies' fathers and grandmothers. KMC often begins in the hospital and continues at home following discharge with planned follow-up visits to weigh the infant, provide feeding advice, and look for any warning indications (Nguah *et al.*, 2011a). Evidence supports KMC's safety and efficacy in stable preterm infants. KMC is at least as safe and effective as incubator care for low birth weight (LBW) children weighing 2000 g or less who are unable to control their body temperature (Charpak *et al.*, 2005).

A recent systematic study by Katz *et al.*, (2013) revealed that KMC significantly lowers infant mortality and morbidity, primarily due to infections, among preterm neonates weighing ≤ 2000 g in hospitals. A Cochrane review from 2003 found no mortality advantage with KMC. KMC was originally implemented in Ghana in 2007 and is presently used in six of the country's sixteen regions (Nguah *et al.*, 2011). Mothers are frequently encouraged to continue at home after starting the practice in the hospital. However, a lot relies on the specific conditions in the neighbourhood and at home. While there seems to be some success in getting parents to start KMC at the facility, there isn't much data to back up KMC follow-up at community health centres after the woman and child are released.

2.4.3 Preterm in Ghana

Background Prematurity (gestational age < 37 completed weeks) accounts for the majority of neonatal deaths worldwide and most of these occur in the low-resource countries, such as Ghana (Agbeno *et al.*, 2021). A research conducted by Agbeno *et al.* (2021) at Cape Coast Teaching Hospital (CCTH) had a total of 27,320 preterm deliveries from 2010 to 2019. Of these, 1,282 were live preterm births, giving a prevalence of live preterm babies over the ten-year period of 4.7% (1,282/27,320). According to Agbeno *et al.* (2021) an increasing trend in prevalence was observed with 2019 recording the highest at 9% (271/3027). Each year in Ghana, approximately 128,000 preterm births occur, with 8,400 of these newborns dying before the age of five due to their prematurity (Roberge *et al.*, 2017). An increase in preterm birth rates at Ghana's leading referral hospital, Korle Bu Teaching Hospital, from 9.3% to 18.9% over the past fifteen years (2003 to 2019). This trend has raised public health concerns, as preterm births have been associated with factors such as advanced maternal age (> 35 years), inadequate antenatal care, preeclampsia, antepartum hemorrhage, and preterm premature rupture of membranes (PPROM).

According to a research conducted by Adom-Miah *et al.* (2025) at the Greater Accra Regional Hospital in Accra, Ghana, preterm birth remains a pressing concern. Although existing studies have largely focused on obstetric determinants, there is limited data on the broader range of factors contributing to preterm birth in Ghanaian contexts (Adom-Miah *et al.*, 2025). The Greater Accra Regional Hospital (GARH), a key secondary referral facility, reports a high frequency of preterm cases, often associated with conditions such as premature rupture of membranes (PROM) and pre-eclampsia (Adom-Miah *et al.*, 2025). A recent report from the 2024 Paediatric Society of Ghana's Prematurity Awareness Month launch highlights that Ghana's preterm birth rate has risen to 14.5 %, surpassing the global average of 10 % (Adom-Miah *et al.*, 2025).

2.5 Prolactin

Prolactin (PRL) is a peptide hormone mainly produced and released by the adenohypophysis. Its release into the bloodstream is stimulated by the suckling reflex at the maternal nipple (Zuppa *et al.*, 2010). Many current galactagogues work to enhance lactation by enhancing the vast production and release of PRL from the anterior pituitary gland. These medications function through various mechanisms, such as directly stimulating the adenohypophysis, inhibiting the hypothalamic secretion of PRL inhibitory factor (PIF), and promoting the hypothalamus to release PRL-releasing hormone.

2.5.1 Structure of Prolactin

The polypeptide hormone prolactin plays a pivotal role in maintaining homeostasis, overseeing numerous processes essential for breast growth and lactation (Li *et al.*, 2019). Structurally, prolactin is similar to placental lactogen hormone and growth hormone, belonging to the

prolactin/growth hormone/placental lactogen family characterized by a conserved helix bundle derived from a common ancestral gene.

Upon proteolytic cleavage of the signal peptide from the prolactin prohormone (pre-prolactin) and subsequent post-translational modifications, prolactin consists of 199 amino acids (Jin & Fan, 2019). While primarily synthesized and secreted by the anterior pituitary under hypothalamic control mediated by dopamine, prolactin can also be produced by other tissues such as the uterus, immune system, central nervous system, and mammary glands (Li *et al.*, 2019). Synthesis of prolactin in these tissues can be triggered by various stimuli including light exposure, olfactory cues, stress, and breast stimulation (Bernard *et al.*, 2019).

Dopamine antagonists, thyrotropin-releasing hormone (TRH), and oestrogen (during pregnancy) are additional variables that enhance prolactin production. Less than 20 ng/ml is the typical low level of prolactin in males (Freeman *et al.*, 2000). A possible underlying medical process, such as a pituitary adenoma or a pharmaceutical side effect, may be indicated by an abnormal rise in males, which calls for more assessment. Males and non-lactating, non-pregnant females have low levels of prolactin, less than 25 ng/ml (Vilar *et al.*, 2019).

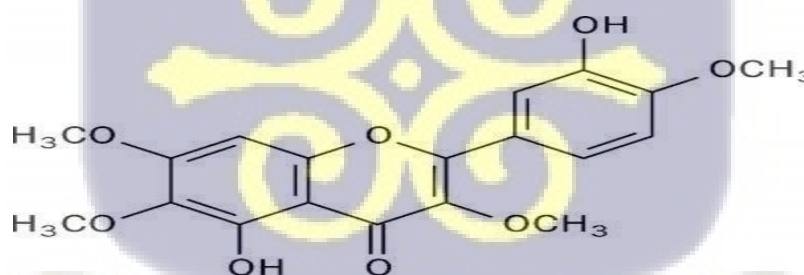


Fig 2.1: Molecular structure of prolactin.

2.5.2 Prolactin levels in Women

Prolactin (PRL) levels increase significantly during pregnancy, rising from approximately 10 ng/ml in the nonpregnant state to about 200–400 ng/ml at full term. Following childbirth, baseline PRL levels in lactating women do not return to pre-pregnancy values but average around 100 ng/ml

at three months and 50 ng/ml at six months postpartum (Cregan *et al.*, 2002). This sustained elevation is influenced by frequent breastfeeding sessions, which trigger peaks in PRL concentration, with the highest levels occurring during nighttime and early morning hours.

2.5.3 Prolactin Roles

Particularly in women, prolactin plays a vital function in the physiology of the breast. Clinically relevant pathologic disorders arise from either excessive or insufficient secretion of prolactin (Müezzinoğlu *et al.*, 2007). Normal lactation capacity is correlated with prolactin hormone levels. Prolactin level imbalances may impair this capacity. A mother cannot produce milk if the levels are too low, while galactorrhea in non-breastfeeding males or females might result from overly raised levels of prolactin (Auriemma *et al.*, 2019). Additionally, the menstrual cycle may be significantly impacted by a prolactin imbalance. Because prolactin inhibits the release of GnRH in females, it causes amenorrhoea, or the absence of menstruation (Auriemma *et al.*, 2019). However, the clinical implications of abnormalities in prolactin levels differ in men. Males who have elevated levels of prolactin may experience headaches and reduced libido. The rise in prolactin impacts the hypothalamus-pituitary reproductive axis, leading to a decrease in libido which is associated with reduced spermatogenesis (Müezzinoğlu *et al.*, 2007).

The infundibular stalk connects the pituitary gland, which is housed in a protective bone structure just behind the nasal bridge, to the brain. The pituitary gland's synthesis and secretion of several hormones, including prolactin, are primarily controlled by the hypothalamus (Müezzinoğlu *et al.*, 2007). The anterior and posterior parts of the pituitary gland are structurally distinct. In contrast to the posterior pituitary, which mainly serves as a pathway for hormones synthesized by the hypothalamus, the anterior pituitary is capable of producing and secreting its own hormones. Lactotrophs in the anterior pituitary gland produce prolactin (Li *et al.*, 2019). Pregnancy causes an

increase in lactotrophs due to the body's natural requirement to produce breast tissue and make preparations. Elevated levels of progesterone and oestrogen are present throughout pregnancy and serve to encourage the growth of breast tissue. Prolactin secretion and synthesis are not substantially affected by oestrogen (Gosi & Garla, 2023). Surprisingly, nipple stimulation or nursing is the most powerful inducer of prolactin production (Raut *et al.*, 2019). This mechanical process activates the nipple's sensory nerves, which then send a signal to the arcuate nucleus in the spinal cord. This nucleus then blocks the production of dopamine, eliminating the dopamine's inhibitory effect on prolactin.

Concurrently, the nipple's afferent signal stimulates the paraventricular and supraoptic nuclei, increasing oxytocin synthesis and permitting "let-down" of milk (Sousa, 2022). Vasoactive intestinal peptide (VIP) and oxytocin both encourage dopamine inhibition, which permits prolactin synthesis (Kumar, 2019). Since the two main hormones that control menstruation are luteinizing hormone (LH) and follicular stimulating hormone (FSH), breastfeeding women will suffer a brief amenorrhoea period until they quit nursing (Raut *et al.*, 2019). In addition to acting as a natural contraceptive, this process might influence how far apart pregnancies occur (Sousa, 2022).

2.5.4 Prolactin Role during Pregnancy and Lactation

While prolactin plays a role in various physiological processes, its main functions include stimulating milk production and the development of mammary glands within breast tissue. Prolactin stimulates the proliferation of mammary alveoli, which are the structures responsible for producing milk (Freeman *et al.*, 2000). The breast alveolar epithelial cells synthesize key components of milk such as lactose (the carbohydrate), casein (the protein), and lipids in response

to prolactin (Gosi & Garla, 2023). During periods of high progesterone levels, such as during pregnancy, prolactin receptors on the glandular tissue of the breast are down-regulated.

Lactogenesis is made possible by the downregulation of prolactin receptors on mammary alveolar cells during the postpartum period, which is caused by a decline in circulating progesterone levels. After childbirth, prolactin levels do not remain constantly elevated. Instead, they increase when the nipples are stimulated, allowing control over milk production. Prolactin levels remain elevated as long as breastfeeding continues. Milk production by the mammary glands decreases when breastfeeding ceases, leading to a drop in prolactin levels to a baseline level. If a mother decides not to breastfeed her child, prolactin levels return to non-pregnant levels within one to two weeks (Freeman *et al.*, 2000).

2.5.6 Prolactin in Men

Serum prolactin levels typically range from 2 to 18 ng/ml in men, 2 to 30 ng/ml in women, and increase significantly to 10 to 210 ng/ml during the final trimester of pregnancy. In cases of prolactinomas, which are tumors that secrete prolactin, serum prolactin levels are usually higher than 200 ng/mL (Gosi & Garla, 2023). Magnetic resonance imaging (MRI) is the preferred imaging technique for diagnosing pituitary adenomas, including prolactinomas.

2.5.7 Pathophysiology of Prolactin

Prolactin's pathophysiology can involve either excessive or insufficient production. Insufficient prolactin production can lead to lactation failure, whereas excessive prolactin production can cause symptoms such as galactorrhea (inappropriate milk production) and infertility (Jin & Fan, 2019).

Inadequate prolactin levels may result from destruction of the anterior pituitary gland. Conversely, causes of excessive prolactin include disruption of the hypothalamus-hypophyseal tract or reduced dopamine inhibition, often due to antipsychotic medications (Al-Chalabi *et al.*, 2023). Additionally, prolactinomas tumors that secrete prolactin are a common cause of prolactin excess (Al-Chalabi *et al.*, 2023). Whatever the reason for the excess prolactin, it inhibits GnRH, which causes infertility in both sexes and causes both men and women to produce breast milk inappropriately (galactorrhea) (Al-Chalabi *et al.*, 2023). Regardless of the cause, prolactin excess can be treated with dopamine agonist drugs such as cabergoline and bromocriptine (Bernard *et al.*, 2019). It's crucial to understand that galactorrhea is a possible symptom of hypothyroidism. Either prolactin excess or deficiency is linked to prolactin-related diseases (Bernard *et al.*, 2019).

2.5.7.1 Prolactinoma

The most prevalent secreting pituitary adenoma is called a prolactinoma. The anterior pituitary gland's pituitary lactotrophic cell growth is what defines it. According to (Li *et al.*, 2019), 90% of prolactinomas are micro adenomas, or smaller than 1 cm in diameter, and they do not cause any symptoms. The typical prolactinoma presentation is a young woman experiencing infertility, galactorrhea, and irregular menstruation. Men who experience hypogonadism due to decreased LH and FSH secretion may report decreased libido and erectile dysfunction (Müezzinoğlu *et al.*, 2007).

When a patient has a big prolactinoma (macro adenoma larger than 1 cm), the tumour compresses the optic chiasma, resulting in compressive symptoms such as bi-temporal hemianopsia. In situations of prolactinoma, dopamine agonists such as cabergoline and bromocriptine are recommended as first-line treatments (Sousa, 2022). Because it has a longer half-life and fewer adverse effects than bromocriptine, cabergoline is the better option. On the other hand, cabergoline

lowers tumour size by roughly 90%, normalises prolactin in up to 95% of patients, and manages symptoms in the majority of patients.

Due to their dopamine blocking, first-generation antipsychotics including haloperidol and fluphenazine might result in prolactin excess symptoms like galactorrhea and gynecomastia (Auriemma *et al.*, 2019). In several dopaminergic routes, including the tuberoinfundibular tract, where dopamine tonically prevents prolactin and then disinhibits prolactin release, the specific process entails non-selective D2 dopamine-receptor inhibition. Constitutively active lactotrophic cells are made possible by the lack of dopamine-mediated disinhibition (Vilar *et al.*, 2019).

2.5.7.2 Sheehan Syndrome

The hallmark of Sheehan syndrome is anterior pituitary infarction, which frequently happens during childbirth but does not show symptoms until the postpartum phase with a variety of endocrinopathies. Significant blood loss after childbirth is part of the pathophysiology of Sheehan syndrome, as it affects the blood flow to the enlarged anterior pituitary gland. Pituitary ischemic necrosis is the result of prolonged ischemia (Bernard *et al.*, 2019).

In cases of anterior pituitary gland injury, which can involve cells including lactotrophs responsible for prolactin secretion, hormone production may cease. Screening postpartum mothers who present with new-onset endocrinopathies or an inability to lactate requires a heightened clinical suspicion, as symptoms may not appear until several months later after the infarction episode (Kumar, 2019).

Agalactorrhea, the inability to lactate, is a prominent initial symptom of Sheehan syndrome, a condition where the anterior pituitary gland undergoes pathological damage (Vasconcelos *et al.*, 2024). Other symptoms associated with hormones produced by the anterior pituitary gland include

amenorrhea, reduced libido, or signs of thyroid insufficiency. Sheehan syndrome exemplifies a pathological scenario where prolactin insufficiency is evident (Vasconcelos *et al.*, 2024).

A lack of prolactin may be secondary to other causes that mainly impact the anterior pituitary. Infections like histoplasmosis and TB, as well as mass effects like craniopharyngiomas, can impede the anterior pituitary's ability to release hormones. Hyperprolactinemic etiologies also include infiltrative disease processes such as hemochromatosis and sarcoidosis. Finally, autoimmune diseases that affect the synthesis of prolactin include SLE, antiphospholipid syndrome, rheumatoid arthritis and many others (Gosi & Garla, 2023).



CHAPTER THREE

METHODOLOGY

3.1 Study Design

The research was a double-blinded, randomized controlled trial. Participants were recruited over a period of 6 months as they reported to the neonatal intensive care unit (NICU) of the 37 Military Hospital. The study had 2 arms; an intervention group and a control group. The study's main goal was to measure the mothers' serum prolactin levels and breast milk output in all groups twice: once at baseline (day 1) and once after the intervention (day 7).

Participants were randomly allocated to the intervention and placebo groups via a secret ballot procedure. The intervention groups were given a product, and guidance on how to use the product within a one week period, and had to physically pump breast milk four times a day. The control groups were given products which did not contain galactagogues, and were also subjected to same procedure as those in the intervention group. Every participant in the study had their breast milk volume and newborn weight measured every day for seven days. Nonetheless, only measurements (breast milk volume and newborn weight) obtained at baseline (Day 1) and at the end of the intervention (Day 7) were used for data analysis. Fenugreek, fennel, and moringa are examples of galactagogues that are present in the products.

3.2 Study Site

Ghana's capital, Accra, also serves as the hub of the country's most populous region, the Greater Accra Region. The largest city in Ghana, Accra, has a population of over two million and is representative of an urban African city. Originally founded and put into service on July 4, 1941, the 37 Military Hospital is in the center of Accra and was designed to treat soldiers injured during World War II. Since it was the 37th hospital constructed by the British Empire, it was given the

name 37. The military of Ghana oversees this facility, which is known for its high standards of security and medical care.

The preterm newborns at 37 Military Hospital are admitted to the NICU, which served as the study site. This unit, which falls under the hospital's pediatric unit, is staffed by military officers who are also medical experts known as the Officer in Charge. Preterm infants administered here are kept in incubators to enable them to grow adequately to survive in the outside world. Instead of being nursed, the newborns admitted to the NICU are administered extracted milk through a nasogastric tube or a spoon. The Unit provides inpatient care around the clock. Referrals are received from maternity homes, private and district hospitals, and home births from the Accra metropolitan area. In addition to functional incubators and overhead radiant heaters, the unit offers a dedicated area where mothers can change into hospital scrubs and shoes before going into the inner room to meet their kids and express their breast milk. The incubators, paediatricians, staff nurses on shift rotation, a waiting space with a nurse answering questions, and a refrigerator for storing breast milk are all located in the inner room.

3.3 Study Population

Mothers of pre-term babies (37 weeks and below) reporting to the NICU at the 37 Military Hospital. The department receives an average of 20 to 30 preterm cases per month. The gestational age for preterm birth is 37 weeks or below. The study population constituted mothers of these preterm infants, who fall within the inclusion criteria, and were willing to be part of the study.

3.3.1 Criteria

Ages Eligible for Study: 18 - 45 Years (Adult)

Sexes Eligible for Study: Female

3.3.1.1 Inclusion Criteria

- Lactating mothers with babies born on or before 37th week of gestation
- Mothers 1-10 days postpartum
- Mothers with breast milk volume below 200ml per day
- Mechanically pumping breastmilk throughout the four to seven days before admission, at least four times per day on average.

3.3.1.2 Exclusion Criteria

- Pregnant mothers
- Lactating mothers with full term babies
- Mothers with breast engorgement
- Mothers on Reglan, Domperidone, or other medications/herbals for inducing milk production
- Mothers who were ill, hospitalized, or taking the following medications:
 1. Diuretics
 2. Pseudoephedrine
 3. Anticholinergics
 4. Warfarin or any anticoagulant
 5. An estrogen-containing birth control pill
- Mothers who had undergone breast surgery that could affect milk synthesis or production
- Mothers diagnosed with Polycystic Ovary Syndrome (PCOS)
- Mothers diagnosed with asthma or atopic diseases
- Mothers allergic to peanuts or soybeans
- Mothers whose milk supply exceeded 600 mL per 24 hours

- Infants with congenital anomalies or acute conditions such as pneumonia, sepsis, or necrotizing enterocolitis
- Mothers with obstetrical evaluations recommending exclusion

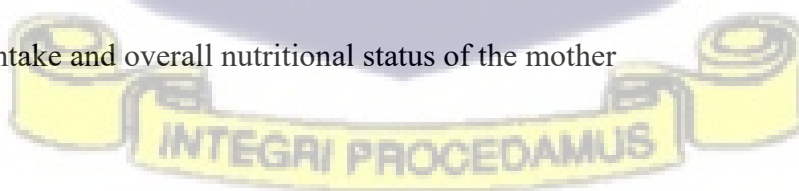
3.3.2 Variables: Dependent & Independent

- Breast milk production: Breast milk pumped out by mothers were measured quantitatively (millilitres) over the first 7 days. Babies in the NICU are fed pumped breastmilk by spoon or cup because of their inability to suck effectively.
- Serum prolactin level: This represents the concentration of prolactin hormone in the blood serum of lactating mothers. It was measured in nanograms/millilitre (ng/ml) on the first and seventh day of the study.

3.3.3 Control Variables

In order to ensure the validity of the study and control for potential confounding factors, the following control variables were considered in this study:

- Maternal age and demographics
- Preterm infant data (gestational age and birth weight)
- NICU practices and treatments
- Pre-existing medical history of mothers
- Dietary intake and overall nutritional status of the mother



3.4 Materials and Method

3.4.1 Sampling

The study was a double-blinded, randomized controlled trial. The study's primary outcome was assessed twice, at baseline (day 1) and post-intervention (day 7), for the serum prolactin levels, breast milk volumes of mothers and infants' weight in both groups; intervention and control. The 2 intervention groups of the study were those who either took chocolate with herbal galactagogue or granola with herbal galactagogue, and received lactation advice on how to improve breast milk production for one week. The 2 control groups received either a chocolate drink or granola without the herbal galactagogue and also received lactation advice on how to improve breast milk production for one week.

3.4.2 Products

The products have more than one galactagogue present: fenugreek, fennel and moringa. These are lactation products produced by Hearty Nutrition Enterprise in Ghana. These are their composition;

- Chocolate drink (FDA/dk 21-1461): cocoa powder, chia seeds, flax seeds, fenugreek, fennel, cinnamon, brewers' yeast.
- Placebo chocolate drink: cocoa powder, cinnamon and brewers' yeast.
- Granola (FDA/Ce 21-1047): rolled oats, raisins, brewer's yeasts, almonds, honey, pumpkin seeds, flax seeds, chia seeds, fennel, moringa and fenugreek.
- Placebo Granola (FDA/Dk 21-1461): rolled oats, raisins, brewers' yeasts, almonds, honey, and pumpkin seeds.

3.5 Sample Size Calculation

Sample size formular (n) = $2[2(a+b)^2 \times SD^2 \div (d)^2]$ at 95% confidence level.

Where:

SD = standard deviation

d = mean difference between treatment group and control group according to Bumrungpert *et al.* (2018).

n = sample size

a = conventional multiplier of alpha, when alpha is 0.05

b = conventional multiplier for power (0.80) when beta is 0.20 where $\beta = 1 - p = 0.20$

SD = 312

d = 503 ml

Significant level ($\alpha = 0.05$)

b = 0.842

a = 1.96

This formular is the ideal formula for a randomized controlled study, and the value of standard deviation and mean difference were obtained from a prior similar study that investigated mixed galactogogues.

$$n = 2[2(1.96 + 0.842)^2 \times (312)^2 \div (503)^2]$$

$$n = 2[6.04]$$

$n = 12$

Hence 12 participants were recruited for each group (intervention groups and control groups).

Participants who were recruited but could not complete the study for reasons such as adverse effects of the product, death of their infants or personal decision to opt out were not included in the data analysis. Due to the small sample size, attrition was included to accommodate for participants that could not complete the study.

Attrition rate of 25% of the sample size was employed, which helped with the participants that left the study. Since the number has to be evenly distributed among the 4 groups, an attrition value of 8 was used.

Therefore, $8 + 24 = 32$ participants.

Hence, the new sample size was 32.

3.7 Method

Mothers who met the inclusion criteria were approached by the investigator after the nurse in charge of the ward informed the investigator of infants on admission that met the criteria immediately after they were admitted. The mothers were educated about the purpose of the study, and they were provided a brief background about the importance of the study, possible side effects, what mothers were expected to provide to the investigator: allowing for her blood to be taken and information about the mother and the infant. Mothers that accepted were given a copy of a consent form to sign, and a copy was given back to the mother, and the original copy was kept with the investigator. The study on the milk volume was conducted for 7 days because according to Izaddoost *et al.*, (2023), breast milk volume increases from day 1 to day 3 of postpartum and either

decreases or remains constant from the 4th day, and that can also relate with the prolactin levels in the body.

The unit has a military person or nurse who offers education to mothers early in the morning in both English and the local dialects, and she first introduced the researcher to the mothers. After the questionnaire was filled, participants were randomly allocated to the intervention and placebo groups via a secret ballot procedure. The investigator, with the help of nutritional consultants in the hospital, explained how to take the products within the one week study period to the participants. The phlebotomist was then asked to take 2ml of blood from the participant into the serum container which was subsequently sent to the laboratory for the baseline test of the serum prolactin level. The baseline breast milk volume for the day were also recorded, where the participants were given a manual breast pump and two storage containers for them to express breast milk four times in a day. The investigator verified the volume from each pump before it was transported to the refrigerator to be kept safe for feeding the baby. The nurse taught the mothers how to sterilize the containers before use, to prevent contamination. The mean volume of breastmilk before the intervention was expected to be below 200 ml, and the post-intervention mean volume was greater than 400 ml. The weights of the infants were measured on the weighing scale by the nurse of the ward, and at the public health department (if the infant was discharged before the 30th day), and the volume of breastmilk was measured using the storage containers, which were calibrated for readings.

Mothers were recruited immediately after their infants were admitted to the ward until the sample size was obtained. Four mothers dropped out, three lost their infants before the study ended, and one did not like the taste and smell of the product.

The infants admitted to the NICU were not breastfed directly, but breast milk was expressed to feed them via a spoon or nasogastric (NG) tube. Mothers were given a room by the ward with beds for them to rest when they arrived, change into hospital scrubs and express milk in private. The total volume expressed on the recruiting day was recorded as the baseline volume of breast milk.

After this the breast milk volume for the day was taken and blood was withdrawn. The participants took the product in the morning before expressing the breast milk, and at the end of each day, the volume of each pump was recorded in the record book. On the 7th day, the blood was taken between 8 am and 10 am for the post-intervention serum prolactin level analysis. The weight of the infant on the 7th day was also recorded. The protocol of the study included no sharing of any items by all participants. The daily dietary records of each participant were also taken.

3.7.1 Blood Sampling & Prolactin Testing

At 2 time points during (Day 1 and Day 7) of the study, 2 ml of venous blood was taken from participants (mothers) to determine the levels of prolactin via automated immunoassay. The blood samples were centrifuged and kept in -80 °C for chemical analysis. Prolactin levels were measured using the Advia Centaur XP model analysis (Siemens) and the chemi-luminometric method, and were reported in terms of nanogram per millilitre. The blood taken from the mothers was discarded by incineration at the hospital after analysis was done.

3.8 Quality Control

The participants' credentials and records were protected under lock and key. Any record or information given before the study, obtained during or after the study, was treated as confidential and was not, under any circumstances, revealed to third parties without appropriate consent.

Personal information was treated as such, and in cases of data interpretation, participants' names were not attached for traceability unless with appropriate consent and urgent necessity.

3.9 Data Analysis Plan

All groups' demographic characteristics (age, parity, ethnicity, marital status, gravidity, parity) were analysed. The mean, standard deviation and ranges for serum prolactin, breast milk volume and infant weight were reported. All data were entered using Microsoft Excel 2013 version, and the statistical analysis was done using SPSS version 25 software. Paired T-test was used for analysis of differences in serum prolactin, breast milk volume and infant weight between the same groups before and after the study. The hypothesis was that both groups had no significant difference in mean. A p-value of less than 0.05 was considered significant.

3.10 Ethical Consideration

Ethical approval was sought from the Ethical and Protocol Review Committee of the University of Ghana Medical School at Korle-Bu, with the Protocol Identification Number: **CHS-Et/M.1 – P 5.10 /2023-2024**, and also from the 37 military Hospital Institutional Review Board (IRB) and the authorities of the NICU where the study took place. Consents were obtained from the participants before the study began.

3.11. Monitoring & Compliance to Study Protocol by Participants

Mothers who were on admission for up to a week are the ones who were recruited. Two pediatric nurses in the ward were assigned to administer the products to the mothers and assisted also with recording, blood withdrawals and infant weighing.

CHAPTER FOUR

RESULTS AND DISCUSSIONS

4.1. Demographic data of the study participants

Thirty-two mothers were recruited for this study at the onset, and 8 mothers were excluded by the end of the study (Table 4.1). The eight mothers consisted of 3 mothers that lost their babies, 3 mothers who opted out of the study for personal reasons, and 2 mothers who did not show up. Hence, the total sample size used in this study was 24.

The granola intervention group, chocolate drink group, placebo granola group and placebo chocolate drink group had 6 participants for each group (Table 4.1). Two mothers were between 40 – 49 years old, eleven mothers were in the age range of 20 – 29 years, which was the highest frequency of participants, and was followed by the 30 – 39 years age range, which had 10 participants. More than half of the mothers (14 participants) were married, and the remaining 10 mothers were single. For education background, tertiary level of education had 10 mothers, and was followed by 8 mothers with only senior high school education and 5 mothers with only junior high school education.

Mothers who delivered their preterm infant through Spontaneous Vaginal Delivery (SVD), which is a normal birth through the vagina and requires no surgical procedure, were 11 participants, and the mothers that delivered through a Caesarean Section (CS) were 13 participants. Analysis of the gestational age of the infants showed that most infants were in the late preterm range (35 – 37 weeks; 14 infants), and was followed by the moderate preterm range (33 – 34 weeks; 6 infants), very preterm (28 – 32 weeks; 3 infants), and extreme preterm (< 28 weeks; 1 infant). The number of pregnancies (gravidity) had 4 categories; mothers that underwent the first pregnancy had 8

Table 4.1: Demographic features of mother and babies of the study population

	Granola (n = 6)	Chocolate drink (n = 6)	Granola Placebo (n =6)	Chocolate drink Placebo (n =6)
Age				
10 – 19 years	-	-	-	1
20 – 29 years	2	3	4	2
30 – 39 years	4	2	1	3
40 – 49 years	-	1	1	0
Marital status				
Single	2	2	4	2
Married	4	4	2	4
Educational level				
No level	-	-	-	1
Junior High	1	3	-	1
Senior High	2	1	2	3
Tertiary	3	2	4	1
Mode of Delivery				
Vaginal	2	3	4	2
C.S.	4	3	2	4
Employment				
Employed	6	4	3	5
Unemployed	-	2	3	1
Gravidity				
1 st pregnancy	1	1	3	3
2 nd pregnancy	4	2	2	1
3 rd pregnancy	-	2	-	-
4 th pregnancy/more	1	1	1	2
Parity				
Primiparous	1	1	5	4
Multiparous	5	5	1	2
Gestational Age				
Extreme (< 28 weeks)	-	-	-	1
Very Preterm (28–32 weeks)	1	-	-	2
Moderate (33–34 weeks)	1	-	4	1
Late preterm (35–37 weeks)	4	6	2	2

4.2. Comparative analysis of intervention and placebo products on breast milk volume, serum prolactin and infant weight

Breast milk volume, serum prolactin levels and infant weight were measured on day 1 (baseline) and on day 7 to ascertain the effect of the intervention and placebo products on these parameters. The values from the 6 participants were used to calculate each group's mean and standard deviation. Prior to administering the lactation products on day 1 (baseline), the breast milk volumes collected from the participants in the intervention (granola and chocolate drink) groups were not significantly different from those in the corresponding placebo groups (Table 4.2). A four-fold increase in the mean breast milk volume was recorded for the participants on granola treatment on the seventh day compared to the baseline, whereas a 3.63-fold increase was obtained for the participants on granola placebo (Fig. 4.1A). Moreover, a 3.88-fold increase in mean breast milk volume was obtained on day seven compared to the baseline for the participants on chocolate drink and a 2.87-fold increase was obtained for participants on chocolate drink placebo. The highest difference in mean breast milk volume from day 1 to day 7 was obtained for participants on the granola treatment. It was followed by participants on the granola placebo and the chocolate drink. Participants on the chocolate drink placebo recorded the lowest difference in mean breast milk volume. The mothers given the granola or chocolate drink products containing galactagogues produced significantly higher mean breast milk volume on day seven compared to the mean volume reported on day 1 ($p < 0.0001$ for granola and $p < 0.0001$ for chocolate drink). The mean breast milk volumes of the mothers on placebo products were also significantly different on days 1 and 7 ($p < 0.0001$ for granola placebo and $p = 0.0007$ for chocolate drink placebo). Collectively, these data demonstrate that the placebo products caused statistically significant improvement in breast milk production in the early postpartum mothers of preterm infants within the 7 day study

duration. The inclusion of the natural galactagogues in granola and chocolate drink also caused an additional modest increase in breast milk volume on day 7 relative to the corresponding placebo products, even though the difference in breast milk volumes was not statistically significant (Table 4.2). The mothers on granola placebo and chocolate drink placebo recorded modest increases in mean prolactin levels on day 7 compared to day 1 (14.5 ug/ml and 13.8 ng/ml, respectively, Figure 4.1B). The inclusion of galactagogues in the granola and chocolate drink did not cause statistically significant increase in the mean prolactin levels on the 7th day compared to day 1 ($p = 0.2422$ for granola and $p = 0.0993$ for chocolate drink). The data also indicated that the mean prolactin level for the participants in the chocolate drink group was significantly lower relative to the chocolate drink placebo group on both day 1 and day 7 (Table 4.3). It can be inferred that the relatively low mean prolactin levels in the chocolate drink group is not dependent on the effect of the lactation product and might reflect the physiological states of the participants on day 1. Further analysis demonstrated there was no statistically significant correlation between breast milk volume and serum prolactin levels on days 1 and 7 for each treatment group (Table 4.4).

The preterm infants of the 24 mothers were weighed on day 1 (baseline) and day 7 to ascertain the effect of the lactation products consumed by their mothers on the weight of the infants. The difference in mean weight of the infants whose mothers consumed the granola product was equivalent to the infants whose mothers consumed the granola placebo product, indicating that consumption of these products by the mothers had no detectable effect on the weight of their infants on day 7 (Figure 4.1C). Moreover, the difference in the mean weight of the infants whose mothers consumed the chocolate drink was similar to the infants whose mothers consumed the placebo chocolate drink. Statistical analysis also indicated no significant difference in the mean infant weight reported on day 7 compared to the baseline weight for all four groups in the study.

Moreover, the low infant weights recorded by the chocolate drink placebo group relative to the chocolate drink group on days 1 and 7 were not statistically significant (Table 4.6). Furthermore, no statistically significant correlation was obtained between breast milk volume and infant weight on days 1 and 7 for each treatment group (Table 4.7). Hence, it can be inferred that the consumption of products containing galactagogues by the mothers did not lead to a significant increase in the weight of the infants on the seventh day of the study.

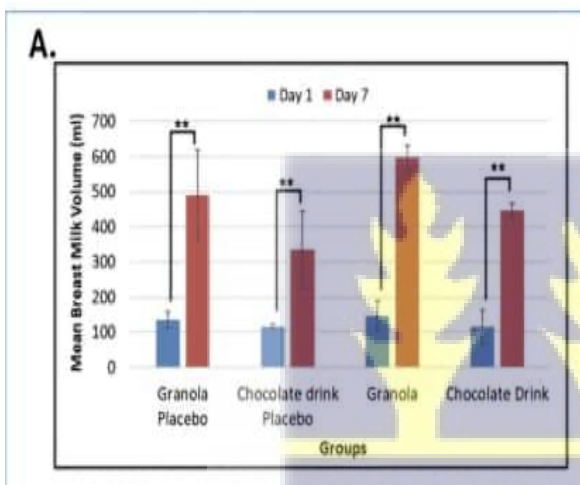


Table 4.2: Statistical analysis of breast milk volumes for the control and intervention groups on days 1 and 7

Comparison of control and p-value intervention groups.

Day 1

Granola placebo vs granola 0.5608

Chocolate drink placebo vs 0.9355
Chocolate drink

Day 7

Granola placebo vs granola 0.0780

Chocolate drink placebo vs 0.0351
Chocolate drink

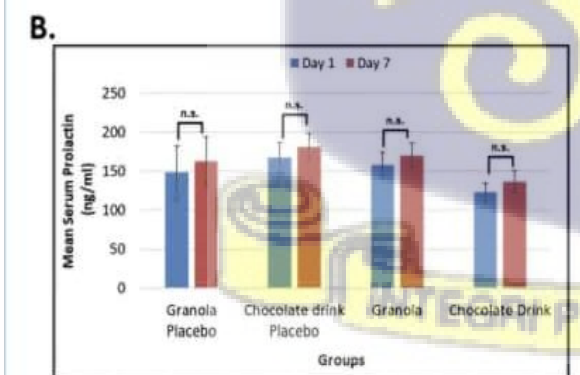


Table 4.3: Statistical analysis of serum prolactin levels for the control and intervention groups on days 1 and 7

Comparison of control and p-value intervention groups.

Day 1

Granola placebo vs granola 0.5270

Chocolate drink placebo vs 0.0008
Chocolate drink

Day 7

Granola placebo vs granola 0.6199
 Chocolate drink placebo vs 0.0007
 Chocolate drink

C.

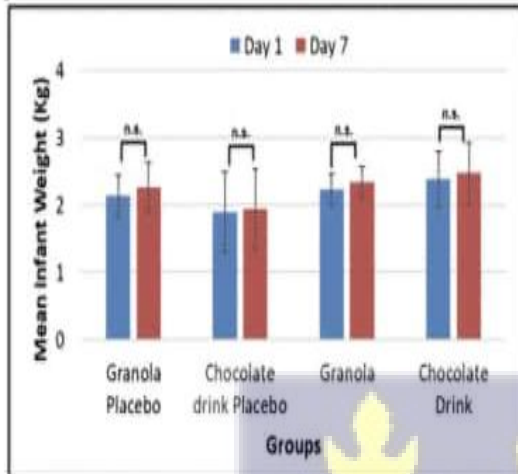


Table 4.4: Correlation analysis between breastmilk volumes and serum prolactin levels for the control and intervention groups on days 1 and 7

Groups	Pearson correlation coefficient	p-value
Granola placebo		
Day 1	-0.3846	0.451
Day 7	0.8122	0.050
Chocolate drink placebo		
Day 1	-0.2454	0.639
Day 7	0.1504	0.776
Granola		
Day 1	-0.001	0.99
Day 7	-0.094	0.859
Chocolate drink		
Day 1	0.6467	0.165
Day 7	0.4992	0.313

Figure 4.1: effects of lactation products on breast milk production, serum prolactin levels and infant weight.

4.3. Local diets consumed by the participants believed to boost breast milk production

Lactating mothers in Ghana are usually encouraged to consume local diets believed to boost breast milk production. The participants were interviewed daily to obtain information on diets they consumed, from which deductions were made, and used as confounding factors during the analysis of the data, in case participants consumed diets which have galactogenic properties.

Six (6) of the twelve (12) participants in the placebo groups indicated they consumed millet porridge whereas four (4) participants from the intervention (granola & chocolate drink) groups consumed other foods with galactagogue properties. Three (3) participants from the intervention and placebo groups consumed groundnut-containing galactagogues while one (1) participant each from the placebo and intervention groups consumed soup containing ayoyo leaves, which is believed to boost breast milk production in lactating mothers. It can be inferred that these indigenous diets are potential confounding factors that could have affected the outcomes of the study objectives.

Table 4.5: Number of participants that consumed local diets believed to boost breast milk production in lactating mothers.

Galactagogues-containing diets	Intervention groups (n = 12)	Placebo groups (n = 12)
<i>Herbs-related galactagogues</i>	1 participant (soup containing ayoyo leaves)	1 participant (soup containing ayoyo leaves)
<i>Hot galactagogues</i>	4 participants (millet porridge, corn porridge)	6 participants (millet porridge)
<i>galactagogues from groundnuts</i>	3 participants (groundnuts & maize, groundnut soup, mashed kenkey & groundnuts)	3 participants (mashed kenkey & groundnuts)
<i>Non-galactogenic foods</i>	4 participants (apples, watermelon, rice)	2 participants (coconut, tom brown porridge)

Table 4.6: Statistical analysis of infant weights from the control and intervention groups on days 1 and 7

Comparison of control and intervention groups	p-value
Day 1	
Granola Placebo vs Granola	0.5844
Chocolate drink placebo vs Chocolate drink	0.1270
Day 7	
Granola Placebo vs Granola	0.6727
Chocolate drink placebo vs Chocolate drink	0.1153
p-value < 0.01 was considered statistically significant	

Table 4.7: correlation analysis between breast milk volumes and infant weights for the control and intervention groups on days 1 and 7

Groups	Pearson correlation coefficient	p-value
Granola placebo		
Day 1	0.3312	0.521
Day 7	-0.2705	0.604
Chocolate drink placebo		
Day 1	0.5743	0.233
Day 7	-0.6167	0.192
Granola		
Day 1	-0.6104	0.198
Day 7	0.5399	0.269
Chocolate drink		
Day 1	0.08204	0.877

Day 7	0.5254	0.284
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p-value < 0.01 was considered statistically significant



4.4 Discussion

4.4.1: Galactagogue Consumption Versus Prolactin levels, Breast milk Volume and Infant Weight

The present study assessed the effect of two food products containing plant-derived galactagogues on breast milk production and serum prolactin levels in early postpartum mothers of preterm infants. We also evaluated the impact of the mothers' consumption of these galactagogues containing food products on the weight of preterm infants. The intervention and placebo products investigated by this study caused a significant increase in mean breast milk volume in the early postpartum mothers by day 7. However, mean serum prolactin levels of the mothers and mean infant weight were not significantly different on days 1 and 7.

Moreover, the study identified no correlation between breast milk volume and either serum prolactin or infant weight. Fennel and fenugreek are derived from the seeds of *Foeniculum volgare* and *Trigonella foenumgraecum*, respectively, and are notable for enhancing breast milk production in lactating mothers. Previous studies by Ghasemi *et al.* (2015) and Turkyilmaz *et al.* (2011)

have both reported that consumption of herbal tea containing fenugreek led to a significant increase in breast milk volumes in the first few days after childbirth. *Moringa oleifera* also boosts breast milk production in early postpartum mothers of preterm infants. Our data demonstrate that both the intervention and placebo food products used in this study caused a significant improvement in breast milk production in lactating mothers of preterm infants. The data also highlight the crucial role of these lactation products in minimising undernutrition in preterm infants caused by insufficient breast milk production. We also demonstrated that the increase in breast milk production was not due to increased serum prolactin levels after administering the food products containing galactagogues. Even though higher levels of serum prolactin in lactating mothers have

been associated with increased breast milk production, our data indicate that the basal threshold of prolactin necessary for stimulating the production of breast milk is sufficient to attain breast fullness in mothers of preterm infants consuming food products containing galactagogues. The events leading to childbirth can be stressful and may result in a concomitant delay in breast fullness and a reduction in lactose concentration in breast milk. Breastmilk is predominantly carbohydrates, fats, proteins, and water; hence, lactating mothers are usually advised to eat well and consume foods containing agents known to boost breast milk production, especially when the volume of milk produced daily is insufficient for the nutritional needs of the neonate. The fulfilment of the dietary needs of preterm infants is vital for facilitating their survival and proper growth and development during the first weeks after birth.

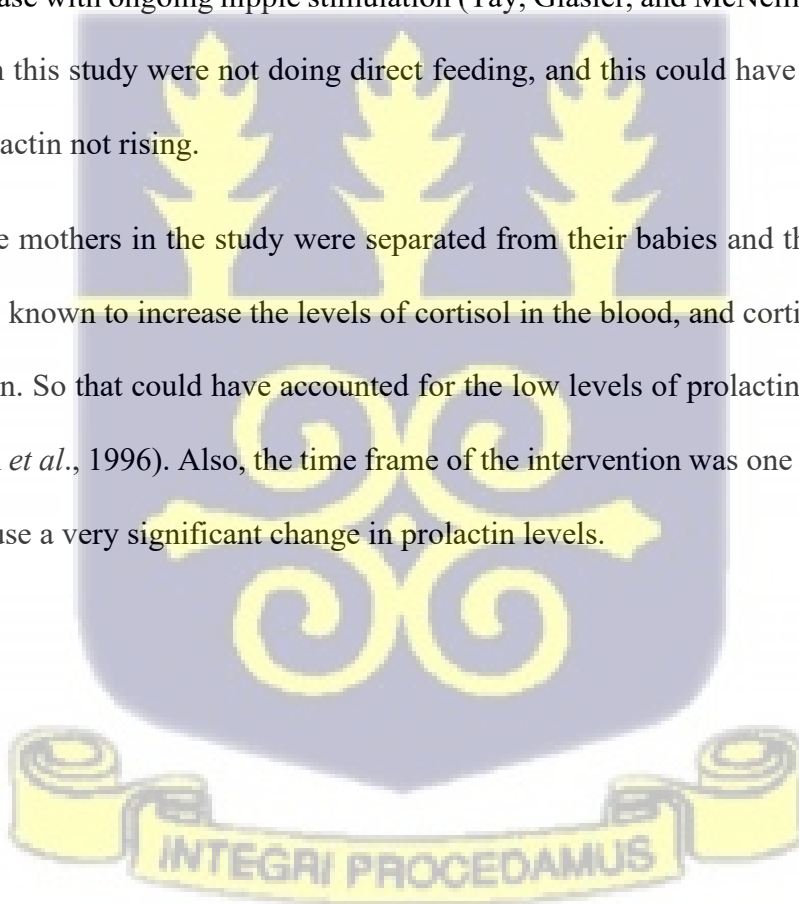
Breastfeeding also enhances the immunity of neonates against infectious diseases, highlighting the vital role of breast milk in ensuring well-being and good health in infants. Preterm infants typically have birth weight below 2.5kg, necessitating adequate nutrition using breast milk to facilitate holistic growth and development. Continuous monitoring of the weight of preterm infants after birth also enables pediatric healthcare professionals to evaluate the health status and well-being of the infant. We demonstrated that there was no difference in the weights of preterm infants who received galactagogues containing food products during the 7-day study period and those who received the placebo. This observation may be attributed to the study's short duration. A longer duration for monitoring the weight of preterm infants whose mothers are continuously receiving galactagogues-containing food products would provide comprehensive insight into the plant-derived galactagogues' effect on the infant weight. Assessment of the effect of the plant-derived galactagogues on lactose concentration and other nutrients in breast milk would also provide useful data for an in-depth evaluation of the nutritional benefits of galactagogues-stimulated breast milk

for preterm infants. Psychological well-being, stress, diet, and the environment of lactating mothers are potential confounding factors that may affect breast milk production in the study participants. Hence, a potential limitation of this study is the absence of the measurement of cortisol levels in the study participants who received either the intervention or placebo lactation products.

4.4.2 The effect of nipple stimulation on prolactin levels

When a baby nurses, the prolactin level in the mother's blood increases, which triggers milk production by the mammary alveoli. Prolactin levels peak around 30 minutes after birth, and continue to increase with ongoing nipple stimulation (Tay, Glasier, and McNeilly, 1996). So, most of the mothers in this study were not doing direct feeding, and this could have been attributed to the levels of prolactin not rising.

Also, most of the mothers in the study were separated from their babies and that caused a lot of anxiety. Stress is known to increase the levels of cortisol in the blood, and cortisol suppresses the levels of prolactin. So that could have accounted for the low levels of prolactin remaining almost the same (Nissen *et al.*, 1996). Also, the time frame of the intervention was one week and this was quite short to cause a very significant change in prolactin levels.



CHAPTER FIVE

CONCLUSION, RECOMMENDATION, STRENGTH AND LIMITATIONS

5.1: Conclusion

Plant-based galactagogues had no effect on serum prolactin levels and little effect on boosting the volume of breast milk produced in early postpartum mothers. Prolactin levels were not significantly affected because most of the mothers were not doing direct breastfeeding and were stressed. These factors affect prolactin secretion. However, since there was still improvement in the levels of breastmilk production, the mechanism of the breastfeeding products may be attributed to the influx of flavonoids acting on other targets. The molecular processes that control the bioavailability of prolactin, composition and production of breast milk in nursing mothers require further investigation.

5.2 Recommendations

It would have been interesting to know how the products affect all the hormones involved in lactogenesis, not just prolactin. It is therefore recommended that a subsequent study be carried out to ascertain the effects of the food products on all the hormones involved in lactogenesis.

It is also recommended that a subsequent study be carried out with a larger sample size with longer period for taking the products for a more resounding conclusion about the effectiveness of the products to be drawn.

Again, it is recommended that a subsequent study be carried out, involving different health centers in different parts of the country, to ascertain how the ingredients would augment breast milk production and affect serum prolactin levels in lactating mothers from different cultural backgrounds across the country. This is vital because [people of different cultural backgrounds](#)

[prefer to consume certain kinds of food products which would have an effect on their breast milk production.](#)

5.3 Strengths and Limitations

The number of preterm mothers who stayed in the facility for a week was limited, which affected the sample size of the present study. Moreover, the number of preterm infants reporting to the facility were very few during the 6-month study period, and several mothers did not consent to participate in the study. These reasons accounted for the low sample size, which was a limitation of the study. There was a high fall out rate because of how sensitive the subject of breastfeeding is to the mothers and compliance to the study protocols.

The absence of tests for milk content and oxytocin levels also prevents a more conclusive response on the lactagogue mix's effects. Since all three of the main galactagogues have been shown in the literature to have a galactogenic impact but no effect on prolactin change, the combination of herbs utilized in the foods, not only demonstrated originality but also made it impossible to determine which galactagogue was influencing the outcomes, especially, prolactin change.

The one week study period did not provide enough time for the time for the products to fully take effects in the participant to enable a more valid conclusion to be drawn from the study.

Not all participants allowed themselves to be controlled with respect to what they were eating during the study period. This affected the outcome of the research as it is anticipated that some of the personal food eaten by some participants also had galactogogenic properties, which might have confounded the research.

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APPENDIX I

Information sheet (consent form, Assent Form and Parental Consent Form)

Consent form

Title: **EFFECTS OF THE CONSUMPTION OF COMMERCIAL BREASTFEEDING PRODUCTS (HEARTY LACTATION PRODUCTS) ON BREASTMILK OUTPUT AND SERUM PROLACTIN LEVELS OF PRETERM LACTATING MOTHERS: A RANDOMIZED DOUBLE-BLINDED CONTROL TRIAL.**

Principal Investigator: Isaac Noble Gyedu

Address: University of Ghana, Department of Medical Biochemistry, Accra - Ghana]

General Information about the Research

Fennel, fenugreek, and moringa are herbs that have been shown to have several health benefits, such as improving gut health and overall health. It has also been used over the years to promote breast milk production in traditional medicine in different parts of the world. In Ghana its use is limited and a lot of people do not know about the herb because it is not indigenous to us. However, some commercial breastmilk-enhancing products have fennel and fenugreek as a component; an example is Mother's Milk product by Traditional Medicinals USA. There is however no study in Ghana evaluating the galactogenic ability of these in breastfeeding mothers.

The objective of the study is to provide commercially made galactogenic products to lactating mothers with preterm babies from 0-37 weeks while monitoring their effect on the mother's serum

prolactin level, breast milk production, and baby weight. Participants will be required to offer venous blood samples for monitoring prolactin levels. The baby's weight may be taken regularly as part of monitoring.

These are lactation products produced by Hearty Nutrition Enterprise in Ghana. The products are all FDA-approved. These are their composition

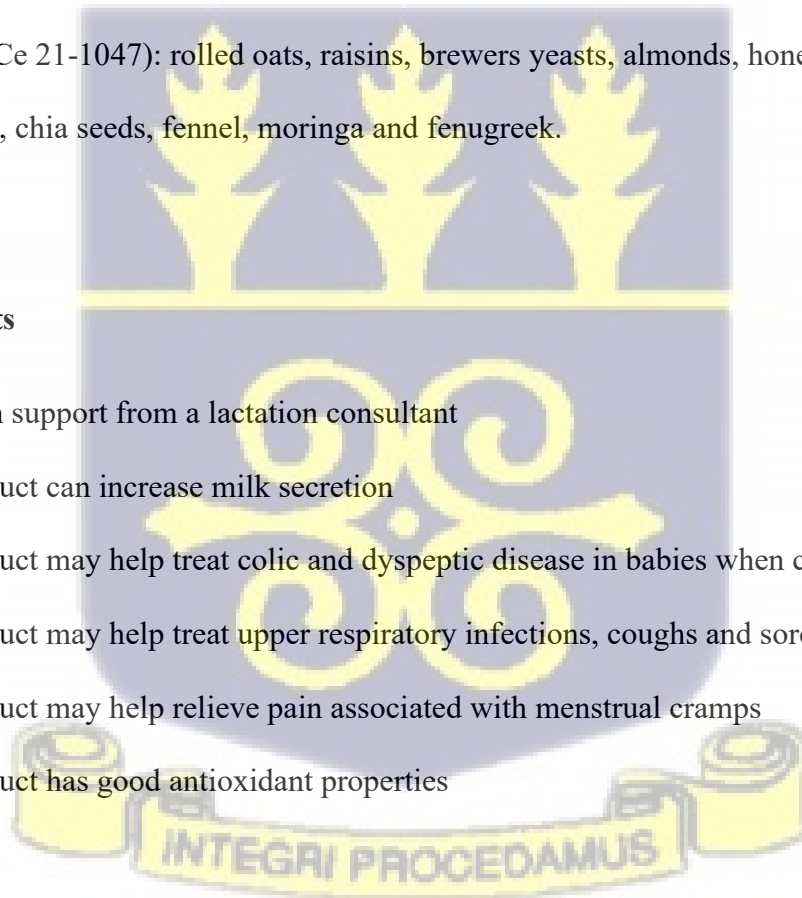
Products

Chocolate drink (FDA/dk 21-1461): cocoa powder, chia seeds, flax seeds, fenugreek, fennel, cinnamon, brewers' yeast.

Granola (FDA/Ce 21-1047): rolled oats, raisins, brewers yeasts, almonds, honey, pumpkin seeds, flax seeds, chia seeds, fennel, moringa and fenugreek.

Possible Benefits

- Lactation support from a lactation consultant
- The product can increase milk secretion
- The product may help treat colic and dyspeptic disease in babies when consumed by mothers
- The product may help treat upper respiratory infections, coughs and sore throat
- The product may help relieve pain associated with menstrual cramps
- The product has good antioxidant properties



Overall Benefits of the Project

If the objectives are achieved, the project will help increase the six-month exclusive breastfeeding rates in Ghana since low breastmilk production has been cited as one of the key reasons why most mothers are unable to complete the six-month exclusive breastfeeding for their babies.

Also, since exclusive breastfeeding has been associated with lower levels of morbidity and mortality in babies, we believe that if mothers are getting enough breastmilk for their babies there will be lower morbidity and mortality rates in those babies whose mothers are in the intervention group.

Possible Risks and Discomforts

Moringa, Fennel and fenugreek consumption may be associated with discomfort in some people. The common adverse reaction to fennel includes:

- Nausea
- Vomiting

All participants are entreated to consider the warnings below and give reliable information pertaining to their allergens and medications if any. People who have been given these precautions

- Avoid use if there is hypersensitivity to carrots, celery, or mugwort.
- Do not use when using antibiotics.
- Do not use when you have record of epilepsy or seizure disorder

- This product contains moringa, fennel and fenugreek. Don't take if you are allergic to moringa or any ingredients contained in this product

Ways of controlling adverse effects

- A doctor, whose number will be given to all participants will be on call during the intervention phase of the project to handle any challenges with any discomfort that any participants will experience.

Sample Collection

At 2 time points during (Day 1 and Day 7) of the study 2 ml of venous blood will be taken from participants to determine the levels of prolactin automated immunoassay. The blood will be taken between 8-10am by the hospital's phlebotomist in the laboratory as the recruits will be present in the laboratory for blood collection before the sample is given. The blood will be analyzed for prolactin levels.

Participants will be given a notebook to write the volume of milk expressed each. The number of expressions per day by the pump will be used to measure the mean volume before and after the intervention, where the pre-intervention mean volume will be below 200ml and the post-intervention mean volume will be 400ml or greater.

Alternatives to Participation

Not applicable in this study.

Confidentiality

The participants' credentials and records will be protected to the best of our capabilities. Any record or information given prior to the study and obtained during or after the study will be treated as confidential and will not under any circumstances be revealed to third parties without appropriate consent. Personal information will be treated as such and in cases of data interpretation, participants name will not be attached for traceability unless with appropriate consent and urgent necessity.

Compensation

Participants in this study will be given

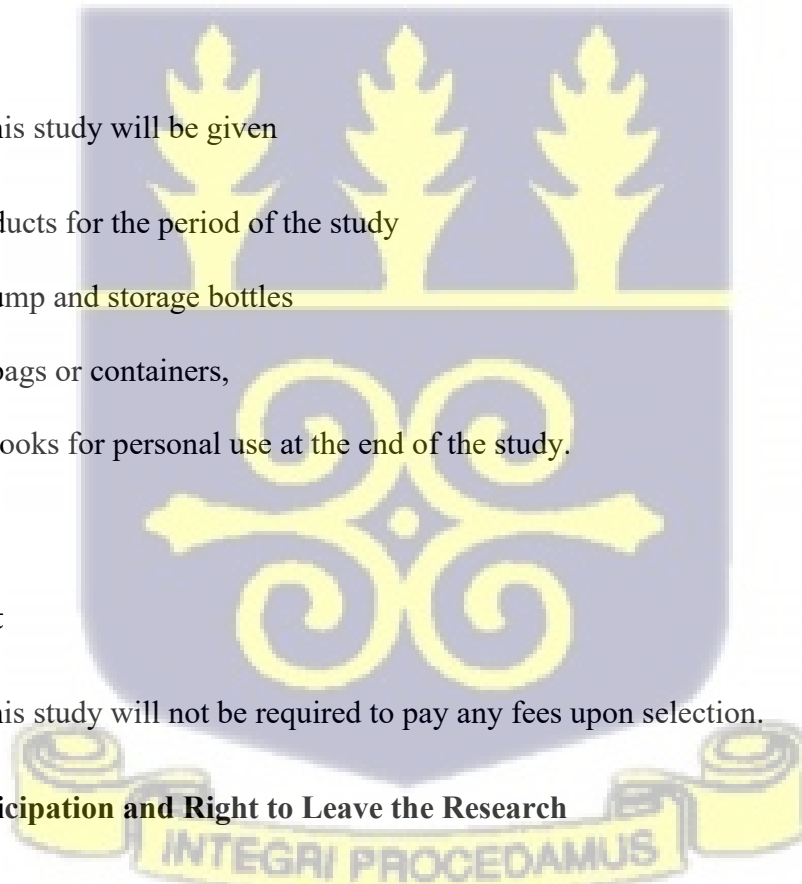
- Free products for the period of the study
- Breast pump and storage bottles
- Storage bags or containers,
- Record books for personal use at the end of the study.

Additional Cost

Participants in this study will not be required to pay any fees upon selection.

Voluntary Participation and Right to Leave the Research

The study to be conducted is a voluntary one and participants will be allowed to leave with reasons concerning their comfort and other personal reasons without consequences.



Termination of Participation by the Researcher

Researcher can terminate the participants' participation in the study when the participant fails to meet inclusion criteria for the study or falsified information are found pertaining to the participant.

Notification of Significant New Findings

Participants will be updated on any new observation found that may determine whether or not the participant should continue with the study.

Contacts for Additional Information

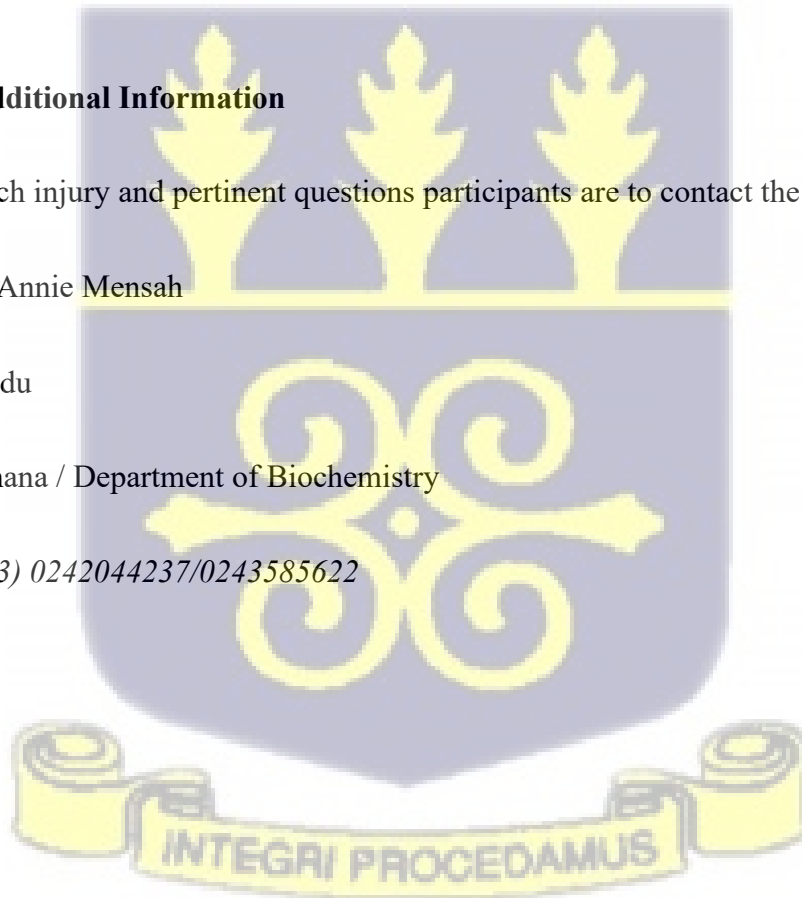
In case of research injury and pertinent questions participants are to contact the persons below.

Dr. Wilhelmina Annie Mensah

Isaac Noble Gyedu

University of Ghana / Department of Biochemistry

Telephone: (+233) 0242044237/0243585622



Volunteer Agreement

The above document describing the benefits, risks and procedures for the research title:

EFFECTS OF THE CONSUMPTION OF COMMERCIAL BREASTFEEDING PRODUCTS (HEARTY LACTATION PRODUCTS) ON BREASTMILK OUTPUT AND SERUM PROLACTIN LEVELS OF PRETERM LACTATING MOTHERS: A RANDOMIZED DOUBLE BLINDED CONTROL TRIAL has been read and explained to me. I have been given an opportunity to have any questions about the research answered to my satisfaction. I agree to participate as a volunteer.

Date

Name and signature of volunteer

If volunteers cannot read the form themselves, a witness must sign here:

I was present while the benefits, risks and procedures were read to the volunteer. All questions were answered and the volunteer has agreed to take part in the research.

Date

Name and signature of witness

I certify that the nature and purpose, the potential benefits, and possible risks associated with participating in this research have been explained to the above individual.

Date

Name signature of person who obtained consent

APPENDIX II

All Data Collection instrument

Questionnaire (Pre-Intervention)

Client Name _____

Client Child's name _____

Mother's Age _____ Place of Residence _____

Hometown _____ Educational background _____

Occupation _____ Marital Status _____

Number of successful deliveries _____

Number of Pregnancies _____

History of Smoking _____

Mode of delivery _____

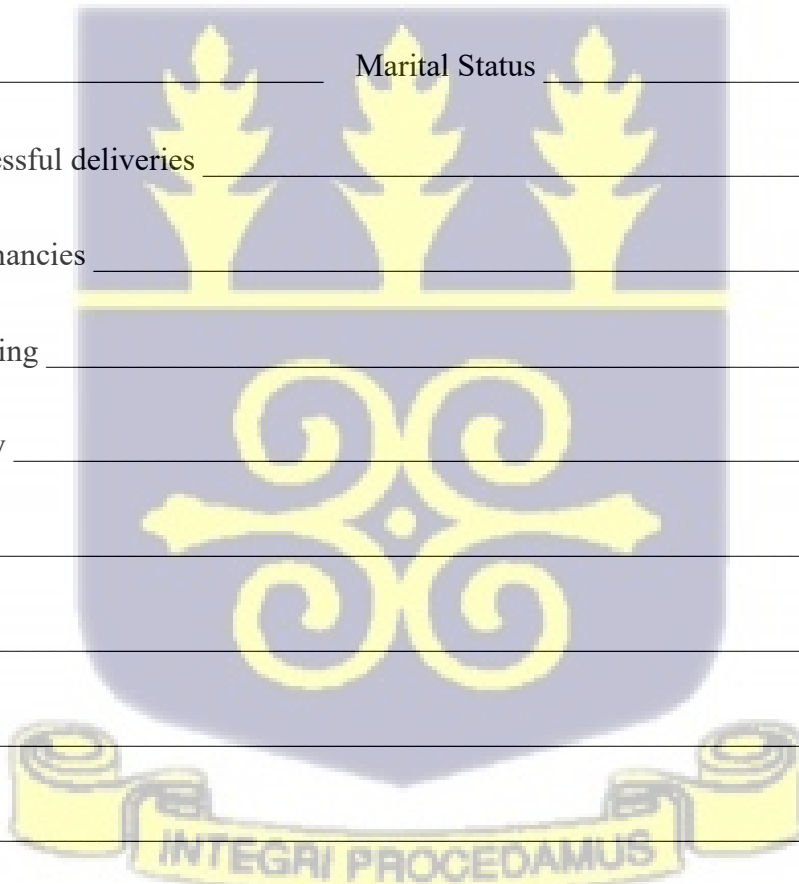
Gestational age _____

Postnatal age _____

Birth weight _____

Current weight _____

Do you have any known allergies or food intolerance?



Are you aware of special foods or herbs that can make you produce more breastmilk?

Have you been recently diagnosed of Type 2 Diabetes, Asthma, Polycystic Ovary Syndrome (PCOS), Hypertension (High Blood Pressure), HIV or any medical condition?

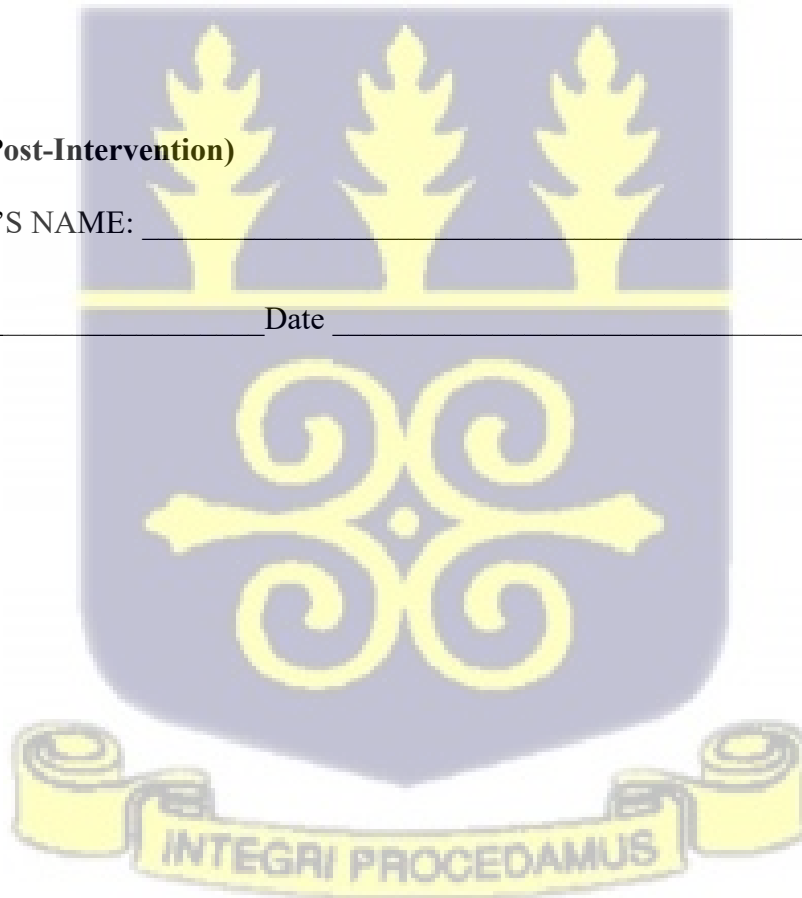
Have you had a breast surgery before? Yes or No

Is your infant been diagnosed of any congenital anomaly or acute problems (pneumonia, sepsis, necrotizing enterocolitis) _____

Record Book (Post-Intervention)

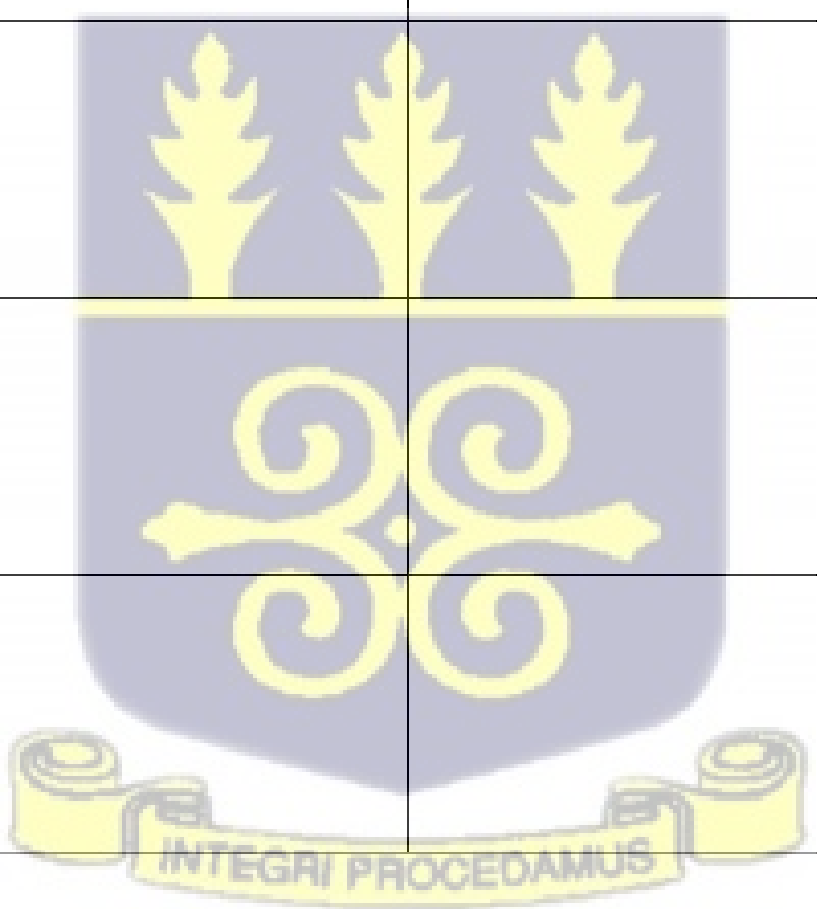
PARTICIPANT'S NAME: _____

Day _____ Date _____



DIET HISTORY

Time	Meal taken



The watermark is the official crest of the University of Ghana. It features a shield with a blue background. The top section of the shield contains three golden pine trees. The bottom section contains a golden stylized knot or fleur-de-lis-like symbol. Below the shield is a golden ribbon banner with the Latin motto 'INTEGRI PROCEDAMUS' written in blue capital letters.

After taking the sample, are you experiencing any adverse effects like gastrointestinal discomfort, shortness of breath, allergic reactions, urticaria, pruritus, edema or decreased urine volume? _____

Current birth weight _____

Number of times per day you took the sample product

BREASTMILK VOLUME AFTER EVERY PUMP

Time	Volume(ml)



APPENDIX III

Personnel

- The personnel involved in the study include the investigator, who will run the study, conduct the interviews, and provide counselling.
- The supervisor who will supervise the investigator.
- Two NICU nurses on duty who will assist mothers on how to use the pumps, sterilize the containers before use, take daily weight of infants and assist in the blood taking.
- The phlebotomist or nurse who will draw blood from the mothers for prolactin analysis.
- The head of the department and the nurse in charge are also included in the study to supervise the study and provide immediate medical assistance to mothers who made experience adverse effects from the product.

