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CONSUMPTION OF FOLIC ACID IN PRECONCEPTION AND DURING PREGNANCY AND ITS ASSOCIATION WITH PRETERM BIRTH AMONG NEPALESE WOMEN: A CASE CONTROL STUDY

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BURAPHA UNIVERSITY
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This case-control study was aimed to determine the influence on consumption of folic acid supplement and dietary folate in preconception and during pregnancy on preterm birth among Nepalese postnatal women. A convenience sampling technique was conducted to recruit 84 postnatal mothers who delivered preterm and full-term babies from March to May 2018. Participants were asked to complete 5 self-reported questionnaires regarding demographic characteristics, consumption of folic acid supplement in preconception and during pregnancy and consumption of dietary folate in preconception and during pregnancy. Information about preterm births were obtained from medical records. Descriptive statistics, independent *t*-test, Pearson chi-square and binary logistic regression were computed for data analysis. Results of logistic regression showed that women who had high consumption of dietary folate consumption in preconception (OR = .60, 95 % CI = .42-.88) and during pregnancy (OR = .53, 95 % CI = .32-.92) were less likely to have preterm birth compared to women having less consumption. In this study women who consume folic acid supplement during pregnancy were (OR = .20, 95 % CI = .06-.67) less likely to have preterm birth but consumption of folic acid supplement in preconception does not found as a predictor (OR = .00, 95 % CI = .00-∞) to preterm birth.

The findings of the study suggest having high consumption of dietary folate in in preconception and during pregnancy and regular consumption of folic acid during pregnancy.

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CHAPTER 1
INTRODUCTION

Statement and significance of the problems

Healthy pregnancy and healthy birth outcome is the basic right of every pregnant women. Pregnancy is the period when women's body goes through many physical and psychological changes. Women need extra nutrition than regular time to adjust with the new changes and for the growing fetus. Every pregnancy needs enough care and proper nutrition to prevent from adverse outcomes. Knowledge about nutrition in pre and post conception is essential for all reproductive aged women because it has important benefits for the mother and child health. Despite having good knowledge about the importance of nutrition, there is still high prevalence of maternal and neonatal mortality.

Nutrition of women is directly associated with adverse effect of the maternal and fetal health. World is facing huge economic and social burden due to high prevalence of maternal and child mortality. Nutrition has lots of nutrients such as carbohydrate, protein, fat, vitamins that needs to be fulfilled during pregnancy. Folic acid is one of the major components of nutrition during pregnancy. Folic acid is water-soluble vitamin B, which has important role in carbon metabolism process, which is equally important for DNA synthesis, repair and methylation, and rapid growth and division of cell (Zheng et al., 2016). It helps to lower the risk of spinal bifida, encephalopathy and neural tube defects, miscarriage, recurrent miscarriage, preterm birth, preeclampsia, abruption placenta (Mantovani, Fillippini, Bortolus, & Franchi, 2014). The recommended dose is 400 mcg per day and ideal time to take folic acid is one month before pregnancy (Royal College of Obstetricians & Gynecologists [RCOG] 2014; World Health Organization [WHO], 2012).

There was widespread agreement and recommendations to prove that preconception and post conception nutrition plays vital role among reproductive aged women to have healthy birth outcomes. According to World Health Organization (WHO, 2012) reproductive age is considered from 15-49 years. In reproductive age, women need higher nutrition because of many physical and hormonal changes.

Adequate nutrition before reproductive age is to help the women for proper development and to ensure sufficient store of nutrition in later stage of life which can be helpful not only in pregnancy but in postmenopausal age (Dunneram & Jeewon, 2015). Evidence shows that despite of focusing on nutrition during pregnancy, if proper care is provided from adulthood period, preconception period will be helpful to reduce maternal and fetal mortality and morbidity. Women need to have enough knowledge about the balanced diet and its contents. Women who consume balanced diet in adequate amount were found to have low risk of maternal anemia, preterm birth and low birth weight (Zerfu, Umeta, & Baye, 2016).

Folate can be consumed from daily diet such as beans, lentils, and spinach. If women do not get sufficient folate during pregnancy then that can lead to numerous adverse results such as maternal anemia, preterm birth and small for gestational age. Consumptions of folate in preconception and early pregnancy is strongly associated with the decrease risk of preterm birth. It is recommended by WHO recommend that if 30-60 mg iron and 0.4 mg folic acid is taken daily as early as possible and continued throughout the pregnancy for all reproductive age then there will be noticeable change, i.e. it lowers the risk of preterm birth, maternal anemia and small gestational age (WHO, 2012; Liu et al., 2016 b). Consumption of folic acid in preconception period and higher maternal folate consumption during pregnancy are proven to increase the length of gestational week and helpful to reduce the risk of preterm birth among Asian women (Chen et al., 2014; Li et al., 2014).

From the review of the literatures many current evidences ratify that folic acid was one of the strong reason to reduce adverse pregnancy outcomes. Several health problems arise in the pregnancy and in postpartum period because of the less folic acid consumption such as preterm birth, maternal anemia, low birth weight and other long-term health effects associated with them. It is seen that women who had low intake of folic acid supplement and inadequate intake of folate diet were likely to give birth to the baby before complete gestational week. Many studies have proven that taking folic acid before and early trimester of pregnancy can reduce the risk of preterm birth effectively (Liu et al., 2016 b; Zheng et al., 2016; Nisar, Dibley, Mebrahtu, Paudyal, & Devkota, 2015).

Preterm birth is now coming up as a second leading cause of death after

pneumonia among under five years old children (Liu et al., 2016 a). It is estimated that 14.9 million babies were born preterm, 11.1 % of all live birth worldwide (Blencowe et al., 2012). United States invests more than $26 billion each year for different program to prevent and control preterm birth (Centers for Disease Control and Prevention [CDC], 2013). Preterm birth is the major cause of the death of the infant and it also influences many health problems such as learning disabilities, auditory and visual impairments in later stage of life (CDC, 2015). The rate of preterm birth is even more alarming in South East Asia as Bangladesh (0.24 million), India (0.330 million), Indonesia (0.028 million) and in Pakistan 23.6 % (0.102 million) (Liu et al., 2016 a). Preterm birth causes neonatal deaths and under five deaths globally (Nisar, Dibley, & Auguayo, 2016).

There are many factors found to have effect on preterm birth, commonly there were adverse maternal health condition such as hypertension, maternal anemia, gestational diabetes, history of preterm, stillbirth, small for gestational age, abortion and preeclampsia (Gwin et al., 2012; Kozuki et al., 2014; Muhihi et al., 2016; Murad et al., 2017). Some of the preterm is caused by the unhealthy behavior of mother such as smoking (Shrestha et al., 2013) and some of the preterm can happen due to lack of adequate and proper nutrition such as inadequate intake of balance diet, which contains good source of vitamin, protein, minerals and folate (Zhang, Zhou, Perkins, Wang, & Sun, 2017).

In spite of having universal access to health care utilization and high quality of prenatal care, the rate of maternal and infant mortality is high in many countries, every year six of 1000 newborn dies during their first year of life mainly due to preterm birth, birth defects and maternal complication during pregnancy (WHO, 2016). Women who took folic acid in preconception period can prevent risk of neural tube defect, spinal bifida, cleft lip and palate (CDC, 2015; Raut, Kharel, & Kela, 2017). In early pregnancy period folic acid intake substantially lowers the ratio of preterm birth and small for gestational age (Catov, Bondar, Olsen, & Nohr, 2011; Zheng et al., 2016). It was found that daily consumption of 5 mg of folic acid during early and mid-pregnancy could reduce 31 % chance of prematurity (Papadopoulou et al., 2013). Whereas it is found that folic acid might not be effective to minimize adverse outcome if taken in later stage of pregnancy (Liu et al., 2016 b). Effective

Intervention program regarding knowledge and practice of folic acid consumption before and during pregnancy is found to have effective on prevention of those complications and birth outcomes. (American College of Obstetrics and Gynecologists [ACOG], 2008; Liu et al., 2016 b).

Nepal is the country that follows many guidelines of World Health Organization protocols to improve health. Besides that, Nepal used to have high maternal mortality rate in the past that 548 per 100,000 live birth which is significantly reduced up to 258 per 100,000 in recent years (Bhusal, Bhattarai, & Bhaskar, 2015). High prevalence of anemia is also one of the major cause of maternal death in Nepal and to reduce this rate government started free distribution of iron supplement from the first antenatal visit (Shrestha, Poudel, Joshi, & Bhandari, 2015).

Although WHO (2012), recommends that folic acid supplement should be taken from 12 weeks before conception, the awareness regarding the importance of preconception care was found very low among women in Nepal (Gautam & Dhakal, 2016). However, it has proven that preconception care has direct association with the health of baby and mother (CDC, 2013). In Nepal 81,000 babies are born preterm each year and 4,300 under five years children die due to direct preterm complications (KC et al., 2015). Although the consumption of folic acid supplement is increasing over the year from 23 % in 2001 to 79 % in 2011 (Nisar et al., 2016) in Nepal, but recent study shows only 69 % of women had consumption of folic acid supplement in their pregnancy (Raut et al., 2017).

The government has set the policy for free distribution of folic acid supplement which starts only from second trimester of pregnancy (Nepal Demographic Health Survey [NDHS], 2016). Many literatures prove that consuming folic acid can reduce the rate of adverse birth outcomes including preterm birth (Liu et al., 2016 b; Shaw, Carmichael, Yang, & Siega-Riz, 2011; Wang et al., 2015). In Nepal very, limited numbers of women have knowledge that taking folic acid is beneficial before pregnancy (Paudel, Wing, & Silpakar, 2012). Similarly, consumption of folic acid supplement during pregnancy is also found only 69.87 % in Nepal (Raut et al., 2017) and only 16.3 % of women in urban area know that folate affect the health of fetus (Paudel et al., 2012). Whereas, it was proven that periconceptional consumption and daily intake of 40 mcg of folic is found to reduce

preterm birth by 14 % (Li et al., 2014). Folic acid can be consumed from diet rich in folate.

Interestingly the diet which have high folate were easily accessible and common in daily meal such as dark green vegetables, beans, peas, organ meat, common vegetables and citrus fruits (Health Canada, 2008). Reproductive ages of women (15-49 years) were found to have underweight in Nepal (Bhandari, Sayami, Sayami, Kandel, & Banjara, 2014). To promote the safe motherhood government of Nepal has several intervention programs however there is lack of program which can promote dietary habit of women and educate women about the importance of consuming dietary folate and recognize the common foods which have high folate.

Evidence shows that consumption of folic acid either from diet or from supplement before conception and in different trimester can be effective to lower the risk of many birth complication such as low birth weight, preterm birth and intrauterine growth retardation (Nisar et al., 2015). Therefore, folate has been investigated substantially as a risk factor for preterm birth because of its increased demand during pregnancy and its proven potency in preventing neural tube defects and other congenital anomalies in babies, also this nutrient has been known for major role in one carbon metabolism and DNA methylation and synthesis (Chen et al., 2014; Scholl & Johnson, 2000).

To minimize the infant and maternal morbidity and mortality rate, government of Nepal is developing a maternal nutritional strategy and searching some effective intervention on focusing maternal nutrition which is highly required. However limited research has been conducted on maternal nutrition practices in focusing on preconception stage and during pregnancy.

The sustainable development goal ‘3’ set by WHO is to diminish the maternal and child mortality rates by 2025. Improving knowledge, attitude and practice of folic acid supplement among reproductive aged women and related potential health problem of mother and fetus should be taken as a long-term strategy. It will help to prevent the future risk of maternal and infant mortality rate. Health of the women should be taken as an essential component in order to have a healthy and uncomplicated pregnancy and healthy birth outcomes.

It is important to assess women’s health status on time to identify the

potential risk of pregnancy and provide appropriate management. There are several studies conducted in Nepal regarding folic acid supplement, anemia, preterm birth and small for gestational age. But as per researcher knowledge there has not been any study conducted to see the association of folic acid consumption and preterm birth among postnatal women in Paropakar Maternity Hospital, Kathmandu. Generating research evidence will not only create the awareness regarding the importance of consuming folic acid and its effect on child health. It also helps to develop strong strategies to provide proper awareness and motivate women to have high consumption of folic acid supplement and balanced diet to fulfill the need of folate. The finding of this study will help to understand the importance of taking folic acid prior to and during pregnancy to prevent the consequences of low and irregular intake of folic acid. Increasing awareness regarding sufficient nutrition prevents country from neonatal, infant and maternal mortality rates.

Research objectives

1. To determine the consumption of the folic acid and dietary folate in pre and post conception period among Nepalese postnatal mothers.
2. To examine the influence of folic acid supplement and dietary folate in preconception and during pregnancy on preterm birth among Nepalese postnatal women.

Research hypotheses

1. Consumption of folic acid supplement in preconception has influence on preterm birth.
2. Intake of dietary folate in preconception has influence on preterm birth.
3. Consumption of folic acid supplement during pregnancy on influence preterm birth.
4. Intake of dietary folate during pregnancy has influence on preterm birth.

Scope of the study

The aim of this study is to determine the association of consuming folic acid and dietary folate in preconception and during pregnancy and its association with

preterm birth among Nepalese women. The selected outcome is the baby with preterm birth. Participants of the study were all postnatal mothers who delivered preterm baby and women who delivered term baby. Study was carried out in Paropakar Maternity Hospital Kathmandu from March to May 2018.

Conceptual framework

Folate is the vitamin that can be consumed via different type of diets in our daily living and which are easily accessible, whereas folic acid is a supplement which is the synthetic form of the folic acid. Both are taken to overcome the lack of vitamin B9 and minerals in the body. Mostly women in reproductive age need high nutrition. The reason behind the high prevalence of anemia and preterm birth in developing regions is due to the low practice of consuming folic acid. Therefore, it is important to emphasize on the consumption of folic acid to minimize the risk of adverse birth outcomes. Consuming this multivitamin supplement and folic acid containing diet is even more important in low-income country like Nepal. Right dose of consuming folic acid not only prevents the deficiency of essential micronutrients from intrauterine life (WHO, 2012) but also helps to reduce the preterm birth other adverse fetal outcomes (Katz et al., 2014; Ogundipe et al., 2012; Sharif, Mohamedain, Ahmed, Nasr, & Adam, 2017). It is found that consuming diet containing folate and folic acid supplements in preconception and first trimester are more helpful for the baby to complete gestational age. WHO (2012), recommends that 30-60 mg folic acid should be given as early as possible before conception to prevent complication of birth.

Therefore, studies show that adequate intake of folate containing diet and folic acid before pregnancy is helpful to prevent preterm birth (Catov et al., 2011; KC et al., 2015; Zheng et al., 2016). The conceptual framework of this study is presented in figure 1.

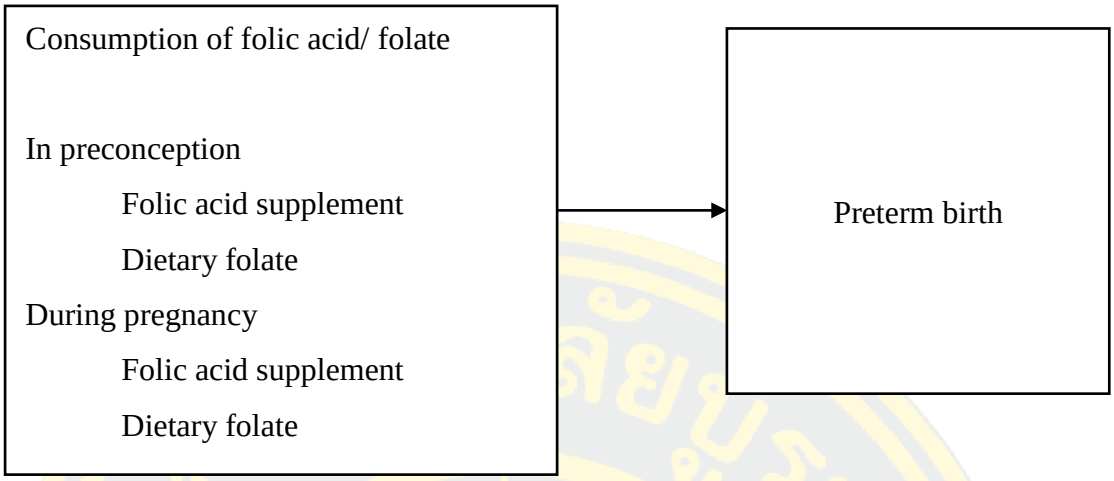

Figure 1 Conceptual framework

Definition of terms

Consumption of folic acid: Referred to the women consuming folic acid supplement and dietary folate in preconception and during pregnancy, was measured by 'Yes', 'No' questionnaire developed by the researcher based on WHO and CDC criteria of consumption of folic acid supplements during preconception and during pregnancy.

Dietary folate: It referred to the consumption of dietary folate from the food containing high folate in preconception (3 month before pregnancy) and during pregnancy. This section measured the level of consumption of dietary folate by women in preconception and during pregnancy based on the table of nutritional value set by the Health Canada (2008), and dose recommended by WHO (2012).

Consumption of folic acid supplement in preconception: Refers to the daily consumption of folic acid supplement by women before one month of pregnancy. Folic acid supplement is measured by "Yes", "No" questionnaire developed by the researcher. Women who took every day was considered to be used as recommendation of CDC (2017 a), and women who did not took or took some time was considered to be not used.

Consumption of dietary folate in preconception: Refers to frequency and portion of daily consumption of diet containing folate before three months of pregnancy. The questionnaire developed by the researcher measured the frequency

and portion of food items based on the table of nutritional value set by the Health Canada (2008), and dose recommended by WHO (2012), in preconception. High consumption is considered as consuming folate according to recommendation of WHO in preconception.

Consumption of folic acid supplement during pregnancy: Referred to the daily consumption folic acid supplement by women from the period of conception to throughout the pregnancy. Consumption of folic acid supplement during pregnancy is measured by questionnaire developed by the researcher based on the recommendation of WHO (2012).

Consumption of dietary folate during pregnancy: Refers to the frequency and portion of daily consumption of diet containing folate after conception to throughout the pregnancy. The questionnaires developed by the researcher was used to measure the frequency and portion of food items based on the table of nutritional value set by the Health Canada (2008), and dose recommended by WHO (2012).

Preterm birth: Refers to live birth of baby < 37 completed gestational weeks. The information was retrieved from medical record. This section gave information about the level of preterm birth and full-term birth of baby.

CHAPTER 2
LITERATURE REVIEWS

The purpose of this study was to determine the consumption of folic acid before and during pregnancy among postnatal mother and to examine the influence of consuming folic acid supplement and dietary folate in preconception and during pregnancy among postnatal mothers. In this chapter, the researcher reviewed articles related to folic acid consumption, folate containing diet, its importance and recommendation prior and during pregnancy. This chapter also focused on consistency of consuming folic acid related to preterm birth. The literature review was presented as

1. Importance of folic acid in preconception and during pregnancy
2. Association of common factors with preterm birth
3. Association of folic acid consumption with preterm birth
4. Summary

Importance of folic acid in preconception and during pregnancy

Healthy mother and healthy baby is the wish and demand of every society and community. In spite of focusing on the women's health during pregnancy, evidence shows that if proper care is provided at infancy, adulthood, preconception period, during pregnancy and in lactating phase then it will be helpful to reduce maternal and infant mortality and morbidity. Evidence shows that women who consume inadequate nutrition during pregnancy have 2-fold higher risk of being anemic along with 4.7-fold higher risk of preterm birth (Zerfu et al., 2016).

According to WHO 41 % of pregnant women are anemic worldwide and half of them are thought to be anemic because of iron deficiency (WHO, 2012). Similarly, 46 % of deaths among under five newborns was because of adverse birth outcomes (WHO, 2017). Complication of neonatal health is associated with maternal health. Most of the cause related to nutrition and pregnancy complication were found in low-income countries. Sierra Leone has 1,360 maternal death/ 100,000 live birth (WHO, 2016). In India, there were 45,000 maternal death/ 100,000 live birth in 2015

(WHO, 2015 b). A cross sectional study set to determine nutritional status among pregnant mother in Bangladesh found that 20 % of pregnant women were severely malnourished, 54 % of women were moderately malnourished and only 21 % women were found to be well nourished (Hossain, Sarwar, Reja, & Akter, 2013), In this era almost every educated and adolescents believes that women need extra nutrition to have better outcome of the pregnancy. Nutrition level of the mother can be changed according to the diet plans. Dietary habit plays a vital role in changing the nutritional status of the women during pregnancy.

Maintaining a healthy balanced diet is very essential to achieve optimum level of health throughout life. Importance of nutrition is not only limited during the pregnancy stages, but also equally important before conceiving the child. Maternal diet from preconception throughout the pregnancy is helpful to reduce maternal and fetal morbidities. Good nutrition prior to conception depends upon the availability of nutrients such as calcium and iron. Deposition of such nutrients can help women to maintain good nutrition during pregnancy and ensure the adequate nutrition for development of fetus.

The term folate is derived from the Latin word “folium” which means leaf. The folate can be achieved from regular balanced diet. Folate is particularly present in dark leafy green vegetables, whole grains, beans and peas and organ meats. Folic acid is type of vitamin B, which has important role in synthesizing DNA, repair and methylation (Liu et al., 2016 b). Whereas folic acid is the synthetic form of folate that is found in the form of supplement and it can also be added to fortified foods (Greenberg, Bell, Guan, & Yu, 2017). Requirement of folic acid is five to ten folds higher in pregnant women in comparison to non-pregnant women, Folic acid helps in the growth and division of cells and tissues and increases the maternal blood volume. It is important for women to consume folic acid containing diet or supplement before conception and during pregnancy because it is directly related to the growth and division of the cell in fetus. Consumption of 400 mcg folic acid everyday three month before conception can reduce the risk of maternal and fetal mortality and morbidity because maternal undernutrition and iron deficiency has accounted for at least 20 % of maternal mortality worldwide (Sebatian, Yadav, Jeyaeelan, Vijayasekvi, & Jose, 2015; WHO, 2012).

If women have enough consumption of folic acid in her body at least one month before pregnancy then it can be helpful to prevent many congenital anomalies of the baby (CDC, 2017 a). The common folate containing food are Dark green leafy vegetables, peas, asparagus, lentils, pulses, whole wheat, liver and kidneys, and they are practiced commonly worldwide. The dietitian of Canada states that the great sources of folates are vegetables, fruits, whole grains, meat and beans (Health Canada, 2008). Women in developing countries can change their diet pattern and increase the level of folic acid by consuming easily accessible foods. The study showed that in developed country also women follow unhealthy dietary patterns in every trimester of pregnancy (Sengpiel et al., 2014). In Nepal, the dietary habit of women also varies because of the geographical regions. Women in mountains usually do not consume dark green leafy and other vegetables whereas it is quite easily to access for women from hills and plain area. However low intake of these food was found in women from hills and plain area due to lack of awareness about consuming diet which is high in folate (Bhandari et al., 2016). In Nepal women in urban area are more attracted towards junk foods like instant noodles, white breads and other bakery items made by flour, instead of homemade and organic foods. The study conducted in Norway regarding dietary patterns showed that modified and healthy dietary patterns consumed from beginning of pregnancy lowered the risk of preterm birth from 12 % to 9 % (Ogundipe et al., 2012). If women become conscious and opt for healthy lifestyle and follow the particular dietary habit before and during pregnancy, it will help to achieve good health outcomes.

Similarly, the folic acid fortified foods and folic acid supplement in the form of multivitamins are common and easily accessible in developed countries. But it was found from the evidence that majority of women in preconception and during conception do not take sufficient nutrition to full fill the daily requirement of folic acid intake (Greenberg et al., 2017). Although there is a strong recommendation from many organizations regarding the consumption of folic acid before and during pregnancy but most of the countries who come under the poverty line still have high maternal and infant mortality and morbidity rate (Lee et al., 2013; Liu et al., 2016 a; Say et al., 2014). The main reason found behind that fact was a lack of awareness of consuming folic acid and its importance of consuming it before and after conception.

Therefore, it was necessary to run the proper and more effective awareness and encouragement program to promote the dietary habit of women at least before three month of pregnancy and throughout the pregnancy. Previous evidences have proved that diet containing sufficient amount of folic acid is beneficial to minimize the adverse effect of the pregnancy (Chitayat et al., 2016; Liu et al., 2016 b). Therefore, folic acid is found as one of the important components of nutrition among reproductive aged women.

Importance of folic acid in preconception

Preconception care among reproductive age women is found highly important for healthy birth outcomes (Api, Breyam, Centiner, Demir, & Ecder, 2015; CDC 2013; WHO, 2012). The definition of preconception care is "the provision of biomedical, behavioral and social health interventions to women and couples before conception occurs, aimed at improving their health status, and reducing behaviors and individual and environmental factors that could contribute to poor maternal and child health outcomes. Its ultimate aim is to improve maternal and child health outcomes, in both short and long term" (CDC, 2013).

Folate is believed as natural vitamin that is essential for reproductive aged women. Its deficiency can be caused by inadequate nutrition, genetic factors and environment. It is found that without adequate consumption of folic acid women can be anemic and this can cause her baby being born as a preterm (Api et al., 2015; Mei et al., 2014). Folate can be consumed from commonly available foods such as beans & peas, lentils, fruits and vegetables (Zheng et al., 2016).

Consumption of 400 mcg folic acid every day in preconception period is found to minimize the incidence of many maternal complication and infant birth defect such as maternal anemia, preterm birth, small for gestational age and other health problem such as cardiac problems, spinal bifida, anencephaly and neural tube defects (Api et al., 2015; Bortolus et al., 2014; CDC, 2010). Consumption of folic acid in preconception is also found to have strongly associated with reduction of cleft lip palate and neural tube defect (Bortolus et al., 2014; Kelly, O'Dowd, & Reulbach, 2012). Many studies have concluded that consumption of folic acid in preconception period can be helpful in minimizing the risk of adverse birth outcome.

Healthy dietary habit of women before pregnancy can help women to prevent from many maternal and fetal complication such as a preterm birth. As folate can be consumed from common food and the requirement of folate before pregnancy is to meet the need of providing extra nutrition for the baby. Studies shows that dietary intake of women before pregnancy also varies in developed and developing countries (McGowan & McAuliffe, 2013; Zhang et al., 2017). Women in developed countries were found to have proper nutrition before pregnancy in comparison to women in developing countries. In Nepal 18 % of reproductive aged women were suffering from malnutrition (Bhandari et al., 2014).

Although consumption of folic acid prior to pregnancy has lots of advantage however, its prevalence varies between developing and developed countries. From the evidence it seems that knowledge of taking folic acid in preconception period is high in European countries than in South East Asia. Evidences shows that low income countries have less awareness about concept of preconception care along with the importance of consuming folic acid in preconception period. The study conducted in Netherland found that consuming folic acid during preconception period had 68 grams higher birth weight and 13-gram higher placental weight (Timmermans, Jaddoe, Hofman, Steegers-Theunissen, & Steegers, 2009). Whereas the study conducted in Italy shows that only (23.5 %) women had taken folic acid before pregnancy (Nilsen et al., 2016). The large prospective cohort study conducted in China concluded that consumption of folic acid in preconception period can help to lower the risk of preterm birth to 8 % (Zheng et al., 2016).

A cross sectional study conducted in Netherland showed that despite of having educational intervention about importance of folic acid consumption, the intention seeking preconception was found insufficient and knowledge of taking folic acid in preconception period was directly related to intention of preconception care, low socio-economic status and level of education (Temel et al., 2015). The study conducted in urban area of Nepal to assess the knowledge of preconception care among reproductive aged women concluded that although there was high prevalence (79 %) of women agreed about benefits of folic acid consumption but only (11.46 %) were aware of taking folic acid before 3 months of conception (Gautam & Dahal, 2016). The knowledge of consuming folic acid either from supplement or diet in

preconception and its importance is highly needed to investigate in improving the reproductive health of women and children.

From above evidence it is concluded that consumption of folic acid from preconception period is essential to have better maternal and fetal outcomes and help to reduce the infant mortality and morbidity rates. As a result, evidences show that there is need to have effective intervention program to increase the awareness of proper dietary habit and nutrition for reproductive age women prior to conception such as change in lifestyle and focus on healthy diet.

Importance of folic acid during pregnancy

Worldwide 830 women and 1.2 billion children having age less than five years die every day because of preventable cause (Blencowe et al., 2012; WHO, 2016). This statistic indicates the huge financial, social and national burden. Death of mother and child is directly associated with the future of the nation and world. Interestingly, it is found that most of the maternal and child mortality can be prevented by little effort like increasing knowledge regarding the importance of proper nutrition intake during pregnancy. Women who have poor nutrition are more prone to increase the high risk of maternal and fetal mortality and morbidity. Dietary habit of women should be improved during pregnancy to fulfill the need of nutrition of two people, as fetus gets all the nutrition for his growth and development through placenta from mother. However nutritional status of the women depends upon the availability of food and dietary habit.

Healthy dietary habit during pregnancy can help to fulfill the need of folic acid. Society of Obstetricians and Gynecologists of Canada recommends women to intake folate containing diet because unlike other nutrients it is mostly needed for the production of red blood cells and it prevents other fetal complication (Wilson et al., 2015).

There are some easily available food and fruits which are very good sources of folate in natural way. Several studies have proved that consuming folic acid in early stage of pregnancy can reduce the maternal and neonatal mortality and morbidity rates (Liu et al., 2016 b; Zhang et al., 2017). Although satisfactory level of understanding about the folic acid is found among women, but high prevalence of maternal and neonatal mortality and morbidity rates indicates that more focus is

needed to raise awareness about the importance of folic acid consumption. Folic acid deficiency is strongly related with maternal anemia which comes as a major health problem in pregnancy and leads to poor neonatal birth outcomes such as preterm birth and small for gestational age (ACOG, 2008; Api et al., 2015).

The case control study was conducted in China to evaluate dietary nutrient intake among Chinese pregnant women. The main objective of the study was to explore the association between dietary nutrients and preterm birth. It was found that women who had preterm delivery were less likely to consume food containing folic acid and vitamin supplements at the time of conception whereas the women who had appropriate gestational age were more likely to had folate containing food with supplements and other nutrients in early stage of pregnancy (Zhang et al., 2017). According to web based cross sectional study conducted throughout UK to explore the diet and supplement practice before, during and after pregnancy showed that majority (93.2 %) young women agreed to consume folic acid to some extent but only (54.6 %) were found to take folic acid regularly as per the recommendation of World Health Organization (Soltani, Douxbury, Rundle, & Marvin-Dowle 2017).

Many current evidences have proved that all these problems are positively correlated with consumptions of folic acid supplement in the different trimester of pregnancy (Api et al., 2015; Liu et al., 2016 b; Zheng et al., 2016). A cross sectional study conducted in India showed that (53.25 %) of women were aware of taking folic acid in first three month of pregnancy and (51.25 %) had received folic acid supplements (Hisam, Rahman, & Mashhadi, 2014). Another study from India among rural pregnant women regarding knowledge of periconceptional intake of folic acid showed that only (36.6 %) women have heard about the folic acid and (33.3 %) of women agreed that folic acid have some effects in the pregnancy (Deepti, Anila, Arup, & Vinohar, 2013). Similarly, in China only (34.1 %) of all respondents were aware of the need of folic acid (Li et al., 2014).

Requirement of folate during pregnancy is to meet the need of extra blood for both mother and baby. A cross sectional study conducted in Nepal to examine the relationship between maternal nutritional status, food intake and pregnancy weight gain was found to have average intake of folate among Nepalese women from diet that is 978.74 microgram and the type of food consumed by women were 64 % cereal-

based products, 8 % pulses, 7 % vegetables, 4 % meat, 3 % fruits, 4 % oil and 5 % miscellaneous (Acharya et al., 2016) The amount of folate in different food is set by the government of Canada. According to these values if women consume whole grains, dark green vegetables, fruits and specific meat then they will not suffer from deficiency of folic acid. These types of food are common all over the world including Nepal (Health Canada, 2008; NDHS, 2016). In most of the countries women practice poor dietary habit with intake of low folate containing food. Women need to have multivitamin supplements in pregnancy that is about 1600 mg and six times greater in the third trimester and folic acid supplement should meet this criterion to prevent women from complications (Li et al., 2014).

Recent case control study was conducted in Sudan among postnatal mother to assess the serum level of folic acid in preterm birth. It was found that there was low intake of folic acid in women who delivered preterm birth and found positive correlation between duration of gestational age and folic acid level (Sharif et al., 2017). Similarly, the recent cross-sectional study carried out in Nepal found consumption of folic acid during pregnancy is significantly correlated with birth weight of the baby (Raut et al., 2017).

Majority of evidences suggests that study of consumption of folic acid during pregnancy is important. Even though there is satisfactory level of knowledge found in the state of pregnancy regarding consumption of folic acid however it is not found in practice and world is bearing a huge loss from it.

Target population of the folic acid

To improve the health of the adolescents, pregnant women and to minimize risk of neonatal mortality and morbidity, distribution and consumption of the folic acid should be compulsory from preconception period throughout pregnancy. Many evidences resulted that consuming folic acid before pregnancy and in first trimester were less likely to have preterm birth and low birth weight babies.

Most of low income countries are more prone to develop maternal and infant mortality rate which is directly associated with dietary habit of mother. In developing countries due to lack of knowledge and resources, women were unable to consume sufficient amount of folic acid from diet. Although the knowledge of nutrition and folic acid consumption is important before and during pregnancy for all reproductive

aged women, there are lot of reasons behind that to affect the awareness of consuming proper nutrition among pregnant women. In the context of Nepal, mainly education, socio economic status, culture and geographical variation were common (Bhandari et al., 2016).

Women of reproductive age group are more likely to develop the reproductive risk and have lower level of folate that results in the deficiency of it. Since many complications of mother and baby is related with consumption of the folic acid it is important to implement the effective intervention program to promote healthy diet among reproductive aged women. Literature also supports this fact that women consuming folic acid about 0.36 mg to 4.0 mg daily from preconception to first trimester are more likely to reduce the risk of neural tube defects than non-user (De-Regil, Fernández-Gaxiola, Dowswell, & Peña-Rosas, 2009). WHO and CDC recommends that women who are diagnosed maternal anemia during pregnancy need 60 mg daily intake of folic acid (CDC, 2013; WHO, 2015 a). To fulfill this requirement, there is a need of high awareness regarding importance of folic acid in preconception and during pregnancy.

Basically, low-income countries in South East Asia and Africa have high prevalence of insufficient folic acid intake. Study conducted in Malaysia among reproductive women shows that whether (88.3 %) of women have heard about folate, only (8 %) have good knowledge about consumption of folate and only (12 %) were assessed to have good intake (Keshavarzi, Ting, Yi, & Yusoff, 2016; Englund-Ögge et. al., 2014). The study conducted in China to assess the knowledge, attitude and practice of folic acid intake for prevention of birth defects in Chinese women of childbearing age shows that (49.7 %) women have awareness of the benefits of folic acid and (34 %) of women knows the correct time of intake of folic acid (Wang et al., 2015). Similarly, the study conducted in Africa shows that (55 %) of pregnant women have knowledge about folate but only (12.5 %) have good understanding about the benefits of consuming it (Mbhenyane & Cherane, 2017).

Based on the literature reviewed, it is found that adolescent girl and pregnant women are most vulnerable population for risk of maternal and neonatal mortality and morbidity. Prevalence of anemia and adverse birth outcome was found high in low and middle-income setting population. To improve maternal and child health, it is

important to focus on folic acid containing diet and regular use of supplements. Therefore, healthy diet, lifestyle and sufficient awareness will help to diminish the fatality of maternal and child health.

Most of the countries in the world including Nepal follow the World Health Organization recommendation of folic acid to promote the health of reproductive aged women. But the time of administering folic acid in reproductive aged women may vary, for examples, in United States folic acid is recommended before conception but in Nepal, it is administered early from second trimester of pregnancy (CDC, 2017 a; NDHS, 2012; Sexual and Reproductive Health of Adolescents and Youth in Nepal [SRHAYN], 2013).

Distribution and consumption of folic acid in Nepal

Nepal is a developing country located in Southeast Asia and in Himalaya region. Nepal has population of approximately 30 million and median age is 21.6 years. The constitution of Nepal provides free basic public health care policy for advanced and traditional medicine. People can access free health care from government health facilities. The aim of the healthcare system is to provide optimum health to all the population and to achieve universal coverage. Along with many developing and developed countries Nepal has accepted the millennium development goal and made noticeable reduction in maternal and neonatal mortality rate from 2001 to 2011. There are many health policies and strategies to promote maternal and child health. Improving maternal and child health is the major concern of the Ministry of Health of Nepal. Currently many health intervention programs are running, and Nepal is just about to finish second long-term in-house goal, which is 1997-2017 (NDHS, 2016). Nepal is now committed to meet the target set by sustainable development goal that is reducing newborn mortality rate up to 11 or less in per 1000 live birth by 2035.

The nutritional status of reproductive age women is not satisfactory. The prevalence of short stature is (11 %), women who are having BMI less than (18.5 %) are (17 %) followed by (22 %) of women are considered obese (BMI > 25.0), along with that Nepal have high prevalence of (42 %) maternal anemia (KC et al., 2015; NDHS, 2016). Although the unsatisfactory situation of maternal health status is prevalent among reproductive age women, there is variation of consuming nutritional diet and adopting nutritional dietary habit. Because of many cultural diversities also

women do not consume proper nutrition such as women from some specific cast do not consume meat and some kind of beans. The study conducted in Nepal to assess the dietary intake patterns and nutritional status of women of reproductive age reported poor health status and irregular pattern of dietary intake, the pattern of diet intake is varying from geographical area and also depends on the culture (Acharya et al., 2016; Bhandari et al., 2016). Whereas majority of women from mountains consume pulses and legumes thrice a week and less consumption of vegetables and in plain region intake of dark green vegetables and lentils, beans and peas are high but there is a less consumption of meat and fruits (Bhandari et al., 2016).

This fact is also supported by the study of Saudi Arabia which shows the significant positive relationship between dietary intake and pregnancy outcome for pregnant women and it is found that women were 2.8 % and 4.4 % were seen undernourished and lower dietary intake shows higher risk of preterm birth (Shaw et al., 2011). Even though, there are availability of food having high folate in Nepal, but the practice of consuming is low in all over the country. The main reason behind this is low educational status and lack of sufficient knowledge among reproductive age women regarding the importance of consuming folate along with lack of recognition of food that have high folate, gender inequality, low economic status of the people.

So far about the supplementation of folic acid, government of Nepal has launched the first phase of iron supplementation program in 2003, the program first ran in five districts and later on it was expanded to all over the country by 2011 (NDHS, 2012). By 2011 it was found that 80 % of women were taking folic acid supplementation during pregnancy. Earlier Nepal had a very high (75 %) prevalence maternal anemia and consumption rate of iron was only 23 % among pregnant women. The rate of iron folic acid (Government of Nepal has distributed the combination form of iron and folic acid tablets) has been increased after years up to (80 %) and rate of anemia was decreased at (48 %) in 2011 (NDHS, 2016).

Eventually, Nepal has high infant mortality rate which is 32 deaths per 1000 live birth (NDHS, 2016). Nepal has 14 % preterm birth of 1000 live birth, which means, 81,000 babies are born before completion of gestational age (NDHS, 2016). From the evidence it was found that preterm birth is highly associated with the

maternal nutrition and folic acid supplementation (KC et al., 2015; Liu et al., 2016 b; NDHS, 2012; Zheng et al., 2016). However, the government of Nepal has policy to administer iron folic acid from second trimester of pregnancy (NDHS, 2012).

Association of common factors with preterm birth

Every child has right to survive, the baby born before completion of total gestational week or whole pregnancy period is called preterm birth. Preterm birth is defined as a "baby born after 28 weeks and before 37 weeks of gestation whereas full term considers 40-42 weeks of gestation" (CDC, 2017 b; WHO, 2012). Before conception to throughout the pregnancy mother need to take care of her health and fetus. The time of pregnancy demands 12-fold higher nutrition compared to other time (Zheng et al., 2016). From the first to second trimester fetus need to go through some important transition of formation, development and maturation of main organs like brain, lungs, liver which needs time to develop fully by the last trimester of pregnancy (CDC, 2013). Baby born before 32 weeks of gestation have high chance of death and disability, which may have breathing/ feeding difficulties, cerebral palsy, delay development and vision/ hearing problems (CDC, 2013; Wilson et al., 2015). Over 1 million children die each year due to complications of preterm birth and visual, learning and hearing disability rate is high among them (WHO, 2012). In Nepal, 81,000 babies are born preterm each year that is 14 % per 1000 live birth and 4,300 children of age below five years die due to direct preterm complications (KC et al., 2015).

There are many different factors like socio-demographic, maternal, fetal and environment which can affect preterm birth. Among them maternal age, education level, occupation, history of previous pregnancies, psychological stress, habit of using substance, presence of medical illness, nutrition, exercise during pregnancy, infection during pregnancy, consumption of folic acid and frequency of antenatal visit are important (Araz-Ersan et al., 2013; CDC, 2015; Liu et al., 2016 b; WHO, 2012). There is a widespread agreement that a continuum of care approach is necessary to further reduce maternal, newborn and child deaths (Dean et al., 2013). The increasing incidence of preterm birth worldwide indicates many modifiable factors which affect in preterm birth has not been sufficiently investigated. Strong determination is needed

to minimize preterm birth and its complication. The action should be focused on reducing adolescent birth, preconception care, enough antenatal visit, care during pregnancy and safe and effective management of labor and delivery and efficient management of postpartum care.

There are 184 countries in the world having the problem of preterm birth and the rate is 5 % to 18 % (WHO, 2016). Even-though preterm birth varies from region to region but the factors affecting the preterm births were found similar. In developed country the factor that mostly affected preterm birth is less gestational age, educational status, pregnancy induced hypertension, gestational diabetes, infection using alcohol during pregnancy, anemia, marital status, previous history of abortion and obesity (Ghimire & Pandey, 2013; Gwin et al., 2012; Masho, Munn, & Archer, 2014). Similarly, in developing country the most common factors associated with preterm birth are early marriage, minimum interval of pregnancy, history of unsafe and numbers of abortion, multi parity and gravida, intake of insufficient nutrition, less antenatal visit, smoking and use of alcohol, several different medical conditions and lack of education (Alijahan, Hazarati, Mirzarahimi, Pourfarzi, & Hadi, 2014; Katz et al., 2014; Kumar, Asha, Murthy, Sujatha, & Manjunath, 2013; Muhihi et al., 2016; Murad et al., 2017).

Among many factors of preterm birth maternal age is considered as a one of the factor that affects preterm birth which is found in women who deliver baby below 18 years and in advanced age that is > 35 years. Being pregnant in early age can cause many maternal and child health complications because there could be biological as well as emotional immaturity regarding care of pregnancy. In 2015 there was one birth to every 10 girls aged 15-19 years in the African region (WHO, 2016). Women who gets pregnant in adolescent age < 18 and advanced age > 35 has higher chance of preterm birth (Araya, Díaz, Paredes, & Ortiz, 2017; Beeckman, Loucks, Downe, & Putman 2012). In Nepal median age of women to get married is 17.5 years, most of them got pregnant within the first year of married life (NDHS, 2012). This is supported by another study conducted in Nepal which shows maternal age < 19 years and was found significant to preterm birth (Ojha, 2015). Similarly, advanced maternal ages of women were also found as a risk factor for preterm birth. The study conducted

in Brazil showed that women who got pregnant in advanced age had more risk to deliver preterm baby (Leal et al., 2016).

Similarly, parity also has been found to increase the risk of adverse neonatal outcomes, such as an intrauterine growth retardation and prematurity. Although it was found that high parity is related to increase risk of hypertension, uterine rupture and other complication that can cause preterm birth. The study conducted in Vancouver showed that older primiparous were at higher risk of preterm birth then older multiparous (Lisonkova, Janssen, Sheps, Lee, & Dahlgren, 2010). Another study also has found nulliparous < 18 years have the high odds of adverse neonatal outcomes compared to women who were multi parity (Katz et al., 2013).

In today's world smoking have become an integral part of the daily life of most men and women, who use/ misuse without knowledge of its detrimental effects. Smoking during pregnancy and postnatal period has several short and long-term health risks associated with children like preterm birth, fetal growth restriction, low birth weight, sudden infant death syndrome, neurodevelopmental and behavioral problems, obesity, hypertension, type 2 diabetes, impaired lung function, asthma and wheezing (Leal et al., 2016). Smoking causes obstetric risk in child bearing mother (Christian et al, 2004). A Study showed that women who smoked during pregnancy had (11.3 %) increased risk of preterm birth compared to non-users (Marufu, Ahankari, Coleman, & Lewis, 2015; Meghea et al., 2014). Nepal has the high rate of tobacco use in South Asia with 30 % men and 9 % women smoking cigarettes and 38 % men and 6 % women using other forms of tobacco (Shrestha et al., 2013). The study conducted to assess the consumption of tobacco during pregnancy among pregnant women found that (19.2 %) women use tobacco during pregnancy in Nepal (Shrestha et al., 2013).

There are several preterm birth prevention programs conducted by many organization which targets to reduce infant mortality rates in Nepal. Sustainable development goal number 3 is all about including the child health with other health programs. However, it is well understood that there are many predisposing factors that can be modifiable in cost effective way. Many studies from various countries showed that preterm birth can be prevented because most of the factors were related to

intrauterine life of the fetus which begins with mother such as maternal age, maternal health behavior and pregnancy period.

Association of folic acid consumption with preterm birth

In the world scenario preterm birth has highest prevalence and considered as a second leading cause of death of neonatal mortality and morbidity. Preterm birth can develop short or long-term health hazards such as respiratory problems, learning disability and hearing and vision impairment in later stage of life (CDC, 2013). According to WHO, South East Asia and Sub Saharan Africa accounts for 60 % of preterm birth of world (Blencowe et al., 2012). Preterm birth is common among developed countries as well. In United States each year 500,000 preterm birth occurs which is almost 1 in every 10-birth followed by many complications (CDC, 2015). To prevent and control preterm birth complication U.S. invest more than $26 billion each year (CDC, 2013). There are many factors, which are claiming to be the reason to cause preterm birth, but the exact cause of preterm is still idiopathic. During searching the literature many factors were found to have association with preterm birth among them socio demographic characteristics, maternal nutrition before and after pregnancy, medical and obstetric history were significantly found higher (Gwin et al., 2012; Hashim, Farooqi, Naqvi, & Jaffery 2014; Muhihi et al., 2016; Shaikh et al., 2011).

Among aforementioned causes, the maternal nutrition is the most common cause of preterm birth because health of mother is directly associated with health of baby. Baby gets all nutrients for its development through placenta of mother. Whereas from the evidence it was found that most of the preterm birth is related to maternal nutrition. Women need 5 to 10-fold high nutrition during pregnancy to lower the risk of preterm birth (Zheng et al., 2016). Consuming high folate diet and regular consumption of folic acid from preconception periods were found to reduce the risk of preterm birth (Li et al., 2014; Liu et al., 2016 b) because folate or folic acid is essential for cell division and increase maternal blood flow which is essential for development of fetus. Additionally, it was found that anemic mother was found to have high risk of delivering baby before completion of total gestational weeks (Vural et al., 2016). The prevalence of maternal anemia in Nepal is 35 % (KC et al., 2015).

Cohort study conducted in Denmark also showed that regular intake of folic acid from preconception to throughout the pregnancy can be helpful to increase basal metabolic rate of women and reduce the risk of preterm birth (Catov et al., 2011). The study conducted in Pakistan showed that intake of folic acid from the first trimester of pregnancy can reduce the risk of neonatal and under five mortality rates (Nisar et al., 2015). In association to this fact, there are many studies that shows consumption of folic acid supplements and dietary folate from pre-conception period and throughout the pregnancy is helpful in lowering the risk of preterm birth (Li et al., 2014; Liu et al., 2016; Murad et al., 2017; Zhang et al., 2017; Zheng et al., 2016).

Large cohort study conducted in China revealed that intake of folic acid from preconception and post conception is helpful in reducing the risk of preterm birth and 10 mcg intake of dietary folate throughout the pregnancy helps to lower the risk of preterm birth (Liu et al., 2016 b). This was supported by the evidence that preterm birth is (5.28 %) among women using folic acid and (6.10 %) among non-users, this study also emphasized that consuming 400 mcg folic acid throughout the pregnancy can reduce the risk of spontaneous preterm birth (Li et al., 2014). The similar evidence with aim to evaluate the prevalence and risk factors for preterm birth and small for gestational age carried out among rural Chinese population revealed that if women take folic acid three month before conception then it is considered as protective factors for adverse birth outcomes (Chen et al., 2017).

From the literature it is proved that consuming folic acid from pre-conception period and including folate in regular diet will be helpful to increase maternal and child health and helps to reduce preterm birth. Unfortunately, despite of easy access of folate containing diet and folic acid supplements, preterm birth is a major problem, which is directly related to death and many complications of the child. Insufficient knowledge was found in women and family members in Nepal regarding use and pattern of taking folic acid supplements. Number of studies shows that despite accessibility of folic acid, women have less practice of folic acid intake throughout the pregnancy. Recent study conducted to identify the relationship between mother's health behavior during stages of pregnancy and preterm delivery have found that consuming folic acid in pre-pregnancy can reduce the risk of preterm birth (Sutan, Mohamed, Tamil, & Yusof, 2016). From the literature it was found that practice of

folic acid intake was found lower in comparison to its awareness. The study conducted in South India illustrated that only 31.1 % of respondents were aware that folic acid should be consumed for 100 days whereas 25.9 % consumed at least above 90 days and only 5.9 % consumed folic acid tablets more than 100 days (Kumar, Kar, Sarkar, & Kumar, 2014).

Even-though there is high recommendation by WHO (2015 a), that 400 mcg intake of folic acid is beneficial for all age group women. It is proved that deficiency of folic acid at the conception and in early pregnancy is associated with many risks. In Nepal, government has the policy to supply folic acid supplements right from the second trimester. Government of Nepal is distributing folic acid for free to pregnant women via health care centers. Although the statistics of government shows high rate of consuming folic acid among pregnant women however one of the study conducted in Nepal shows that awareness regarding importance of folic acid consumption was found very low (Paudel et al., 2012). Consumption of folic acid is directly related to birth and health of the baby. It is important to determine the consumption of folic acid before and during pregnancy and its association with preterm birth among Nepalese women.

Summary

The chapter, literature review provided the insights of existing evidences on the consumption of folic acid from diet and supplements along with its importance and benefits regarding time and dose. From the evidence it was felt that the need of proper nutrition for women from initial phase of reproductive age can help to improve healthy birth outcomes. There are many factors that come into the researcher knowledge, among them adequate consumption of folic acid either from supplement or diet before and during pregnancy periods has a strong association with preterm birth. Consumption of folic acid was found to be important and helpful to decrease the risk of maternal child mortality and morbidity. The need of awareness was mostly felt in low and middle-income countries and rural communities because these countries were found to have lower consumption of folic acid and high rate of preterm birth. There are number of studies regarding factors affecting preterm birth in Nepal (KC et al., 2015; Ojha, 2015; Shrestha, & Shrestha, 2013; Tuladhar & Dhakal, 2012).

Nepal government statistics shows a high rate of distribution of folic acid supplements, but the prevalence of preterm birth, infant mortality and morbidity accounted higher in Nepal along with South East Asia. Based on the literature, lack of awareness and practice of adequate intake of folate diet and folic acid supplements was found before and during pregnancy. The reason behind it could suspect the less and inadequate practice and lack of awareness about importance of folic acid consumption in preconception and during pregnancy. Despite of all these facts there was not any study found in Nepal as per researcher knowledge regarding consumption of folic acid in preconception and during pregnancy and its association with preterm birth.

Therefore, this study was important to carry out to fulfill the gap of knowledge among Nepalese women regarding consumption of dietary folate and folic acid supplements in preconception and during pregnancy and its association with preterm birth. So, on the basis of literature review, consumption of folic acid among Nepalese women was assessed in postnatal ward of tertiary maternity hospital to determine the association and examine the influence on consumption of dietary folate and folic acid supplement for their pregnancy with preterm birth.

CHAPTER 3
RESEARCH METHODOLOGY

This chapter was describing research design, setting, population and sample, sample size, sampling, research instruments, protection of human subjects, data collection procedures and data analysis.

Research design

A hospital-based case control design was used for this study.

Study setting

This study was conducted in Paropakar maternity hospital in Kathmandu Nepal. It is one have the territory level and national referral hospital for maternity and first birthing center of Nepal that provides maternity and gynecological services to women. It was under control of the government of Nepal. It is 415 bed hospital, where as 336 beds are allocating for inpatient admission, 241 beds are for Obstetric cases, 61 for gynecological cases, 34 for newborn and 79 beds are allocated as a services bed, 54 doctors, 172 nurses and 40 paramedical provide health care services in the facility. The hospital provides free antenatal clinic and advanced surgeries facility and emergency services regarding obstetrics and gynecology. Antenatal clinic provides services 6 days a week excluding Saturday. OPD of hospital receive approx. 300 registration each day among them ANC visit is 150-200 each day (KC et al., 2015). The hospital distributes folic acid and iron supplement free of cost for pregnant women from second trimester of pregnancy to 6 weeks of postpartum period. The hospital has three delivery units and Kangaroo mother care unit along with special newborn care unit and neonatal intensive care unit to provide care for small babies. The hospital has record of 22,000 deliveries annually.

Population and sample

Target population for this study was the postnatal women who delivered singleton baby in Paropakar Maternity Hospital Kathmandu, Nepal. Inclusion criteria was set to target population are following:

1. Age ≥ 18.
2. Nepali national
3. Singleton delivery
4. Able to read and write Nepali language
5. Has no any serious medical condition or disease which contribute to preterm birth

Sample size

Sample size in this study was calculated by using the formula of Tabachnick and Fidell (2007) with multiple independent variables. Formulation of Tabachnick and Fidell:

n = 50 + 8 m

Explanation:

n = desired sample size

m = the number of independent variables

There were 4 independent variables that were used as

n = 50 + 8 m

n = 50 + 8 (4)

n = 82

This study, the sample size was 82, and 2 respondents were included in study as a missing population. Therefore, sample size in this study was 84 participants. Since this study based on case control design and follow 1:1 ratio, so 84/ 2 = 42 as a case group (mother delivered preterm birth) and 42 as control group (mother delivered full term birth) were obtained.

Sampling technique

The samples were recruited by using non-probability convenience sampling method. A 1:1 ratio of case control design was using for the study. 42, mother who had birth < 37 weeks of gestation was taken as a case and 42 mothers who delivered full term birth > 37 to < 42 weeks taken as a control group. All cases and control

group were selected without congenital anomalies and neurological impairment. Data was collected from 10.00 am to 4.00 pm and every day at postnatal ward Paropakar Maternity and Women's hospital Kathmandu.

Research Instruments

This study used six types of questionnaires which includes demographic characteristic, four questionnaires on consumption of folic acid supplement and dietary folate in preconception and during pregnancy and the reviewed medical record for the status of the preterm birth of the baby.

1. Demographic information

The general information of the postnatal mother was obtained for this section. This includes information of age, education, occupation, gravida, Para, previous obstetric history, habit of smoking, presence of birth defects such as cleft lip, neural tube defect, previous birth experience about premature and low birth weight. This all information was measured by "Yes" "No" questions.

2. Information from medical records

Information was retrieved from medical record about the status of preterm birth and full-term birth based on criteria set by World Health Organization and birth weight of the baby during birth.

3. Questionnaire on consumptions of folic acid supplements in preconception [CFASP]

The CFASP questionnaire was developed by the researcher based on literature review (Alfonso, Ehrenstein, Bandoli, & Ritz, 2016; Gebreamlak, Dadi, & Atnafu, 2017; Zheng et al., 2016). There were 2 items to collect the information of consumption (4 mg) of folic acid supplement by women one month before conception. Question no 1 was responsible for consumption of folic acid supplement in preconception and it has option "Yes" and "No". Score from question no. 1 and question no. 2 was using to collect information about the frequency of consumption of folic acid supplement, response from question no 1 and 2 categorized as used and not used. "Used" was evaluated women consuming folic acid as per the recommendation of WHO.

4. Questionnaire on consumptions of folic acid supplements during pregnancy [CFASDP]

The CFASDP questionnaire was developed by the researcher based on literature review (Alfonso et al., 2016; Gebreamlak et al., 2017; Zheng et al., 2016). There were 3 items which used to collect the information about the continuity and frequency of the consumption of folic acid supplements during whole three trimesters of pregnancy. The options were measured as not taken = 0, once a week = 1, 3 days a week = 2 and everyday = 3. Total score ranged from 0-9 and higher score considered that women took folic acid supplement during pregnancy according to recommendation of WHO.

5. Questionnaire on consumption of dietary folate in preconception [CDFP]

The CDFP questionnaire was developed by the researcher to collect the information of women's habit of consuming dietary folate before pregnancy. Based upon the design, use and interpretation of food frequency questionnaire by Norwegian institute of public health and report published by the government of Canada on different food items containing folate (Health Canada, 2008) which were similar to Nepali food. This section has seven types of food which contain high folate. Researcher calculated requirement of daily dose of folate from each food in preconception for women, as per recommendation of WHO. Consumption of dietary pattern was differentiated intro four parts. Whereas never intake = 0, less than ½ cup/ day = 1, ½ cup/ day = 2, 1 cup/ day = 3 and 2-5 cup/ day = 4. This suggest 2 to 5 cup as high intake of folate. Total score ranged from 0 to 28, where highest score considered to be high consumption of dietary folate in preconception. (Amount of food was measure by a cup that contains 125 ml water).

6. Questionnaire on consumption of dietary folate during pregnancy [CDFDP]

The questionnaires on CDFDP was developed by the researcher based upon the design, use and interpretation of food frequency questionnaire by Norwegian institute of public health by and report published by the government of Canada on different food items containing folic acid (Health Canada, 2008). This section was about the information of women's dietary habit and consumption of diet which

contain folate throughout the pregnancy period. This section has seven types of food. Researcher calculated daily requirement of folate from each food women need during pregnancy as per recommendation of WHO. Consumption of dietary pattern was categorized as never intake = 0, intake less than ½ cup/ day = 1, ½ cup/ day, a cup/ day = 2, 1 cup/ day = 3 and 2-5 cup/ day = 4. This category was based on food guide published by government of Canada (Health Canada, 2008). This suggest 2 to 5 cup as high intake of daily folate. Total score ranged from 0-28, where highest score was considered to be high consumption of dietary folate during pregnancy (Amount of food measured by a cup that contains 125 ml water).

Translation process

The original questionnaires and informed consent were in English and translated to Nepali language by Back-translation technique (Cha, Kim, & Erlen, 2007). The backward translation procedure was performed by three experts who were bilingual fluent translators, in English and Nepali as well as familiar with domain of maternal and child health. This translational model had a cycle of steps as follows.

1. Two translators translated the original questionnaires independently from English to Nepali.
2. The researcher and two translators discussed and combined the Nepali version to be the one upon agreement.
3. Another translator translated the final Nepali version to converse to English.
4. Finally, the researcher and researcher's major advisor checked the back translated English version for language accuracy and comparability of the contents, culture and meanings between the English back-translated and the English version.

Local supervisor

Nurse in charge of postnatal ward of Paropakar maternity and women's hospital was appointed as a local supervisor for researcher during data collection period from March to May 2018.

Psychometric properties of instruments

Test of validity

The instrument of consumption of folic acid supplementation is before and during pregnancy and behavior of women regarding dietary intake of folic acid in preconception and during pregnancy was developed by the researcher. Content validity for the newly developed questionnaires was evaluated by the panel of 5 experts with the background of folic acid, maternal and child health and nursing research. Three experts were from faculty of nursing of Biratnagar Nursing campus, Nepal. Two experts were MBBS/ MD, from the Paropakar maternity and women's hospital. The content validity index was (1.0) calculated for newly developed instruments.

Test of reliability

A pilot study was carried out with 20 respondents meeting inclusion criteria to test the internal consistency of the instruments. Questionnaire of consumption of dietary folate in preconception [CDFP] and during pregnancy [CDFDP] and folic acid supplement during pregnancy [CFASDP] were tested for reliability with 20 respondents who had similar characteristics with the sample of the study and meet inclusion criteria. In this study Cronbach alpha coefficient of these questionnaires were 0.83, 0.82 for CFASDP, CDFP and 0.77 for CDFDP respectively.

Protection of human subjects

The researcher was aware of research ethics in conducting research. The researcher introduced and described the study aims and confidential information, benefits methods and rights of subject. In order to maintain anonymity, identification code was used on questionnaire sheet of each participants and participants name was not asked.

Data collection was maintained under strictly confidentiality and is accessible to only researcher and accessible to principal advisor or the thesis committee if need be in the future. Participant comfort measure such as privacy, a warm room, and a comfortable bed was provided during interview. Data collection procedure did not affect the any regular routine care in the postnatal ward and mothers. The participants meeting inclusion criteria were well explained about the

research purpose. Informed consents were obtained from the participants who were willing to be in study. Participation in this study was completely voluntary and participants were explained about their right to withdraw their participation at any time before and during the process of collection of data. All data were stored in safe place and only utilized for the purpose of this research, and the results were reported as group of data.

Ethical consideration

Research proposal as reviewed and approval was obtained from Institutional Review Board (IRB) faculty of nursing, Burapha University. The proposal was submitted to Nepal Health Research Council and Paropakar Maternity and Women's Hospital and approval was taken. The purpose, procedures, benefits and safety related to the risk of the study to participants was well explained. Informed consent was taken from participant before starting the data collection procedure.

Data collection

Data in the study collected by the researcher.

1. After the proposal was approved by the Institutional Review Board, the letter from the Dean of Faculty of Nursing, Burapha University was submitted to the Paropakar maternity and women's hospital, Kathmandu, Nepal for seeking their approval for data collection.
2. After getting the permission from Nepal health research council, the researcher applied to the Paropakar maternity and women's Hospital to get the permission for data collection.
3. After receiving permission from the medical superintendent of Paropakar Maternity and Women's Hospital researcher met the nursing in-charge of the postnatal ward of hospital, introduce herself and explain about the purposes and method of study. Get permission to review medical record of the mother.
4. Self-reported questionnaires were administered, and medical record were reviewed to collect the data.
5. The researcher invited mother at a time into private room for data collection, then asked and help women to settle comfortably.

6. Researcher politely introduced herself and talked with mother for about 5 min to build rapport and marked mother comfortable with researcher. Then explained brief about the data collection procedure and informed the process would take only 10 to 15 min to complete the questionnaire and informed consent was obtained.

7. Researcher also assisted postnatal mother by further explaining the questionnaire whenever they needed but no leading questions were asked.

8. After having all the necessary information, the researcher checked the entire questionnaire for completeness from the participation.

9. Thanks, was given to participants mothers to get participate in the study. The researcher helped her to go back to her bed and make herself comfortable.

Data analysis

All data were analyzed by using statistical software: the alpha level of significance was set for < 0.05.

1. Descriptive statistics: Demographic and obstetric information were described using frequency and percentage for categorical data and mean and standard deviation for continuous data.

2. Inferential statistics: Pearson chi-square, Independent *t*-test and Fisher exact test were used to determine the consumption of folic acid supplements and consumption of dietary folate in preconception and during pregnancy with preterm birth. Binary logistic regression was used to determine the predictors that influence the consumption of folic acid supplements and dietary folate in preconception and during pregnancy on preterm birth. The inferential statistical analysis was measured at 95 % confidence level.

CHAPTER 4
RESULTS

This chapter deals with the analysis and interpretation of the data collected from 84 postnatal mothers who delivered preterm and full-term, Paropakar Maternity hospital Kathmandu. First objective of this study was to determine the consumption of folic acid supplements and dietary folate in preconception and during pregnancy among Nepalese postnatal women. Secondly to examine the influence of consumption of folic acid supplement and dietary folate in preconception and during pregnancy with preterm birth among Nepalese postnatal women. Result from data were analyzed using Independent t test, Pearson's chi square test, Fisher exact test and logistic regression was used to assess the association and influence of folic acid supplements and dietary folate in preconception and during pregnancy. This chapter presents the demographic and obstetric characteristics of the study sample, followed by description of the study variables.

Part1: Demographic and obstetric characteristics of respondents

Part2: Consumption of folic acid supplement and dietary folate in preconception and during pregnancy

Part3: Factors predicting preterm birth

Part 1 Demographic and obstetric characteristics of respondents

1. Demographic characteristics of respondents

There were 84 women participating in this study composing and equal number of preterm and full-term births. Independent *t*-test resulted that women with preterm birth have low mean score (M = 29.71, SD = 6.59) to compare with full term mothers. Result of independent *t*-test showed that women with preterm birth have significantly high number of pregnancy (M = 2.14, SD = .65) compared with women having full term birth. Whereas, in regard to parity mother delivered preterm birth have similar mean score (M = 2.14, SD = .65) and (M = 1.83, SD = .62) among both groups.

Table 1 Demographic and obstetric characteristics of respondents (N = 84)

Demographic/ obstetric characteristics	**Preterm (*n* = 42)**		**Full term (*n* = 42)**		***t***	***p*-value**
	M	***SD***	***M***	***SD***		
Age	29.71 (range 18-34)	6.59	25.1 (range 18-34)	4.17	-3.84	.00
Gravida	2.14 (range 1-3)	.65	1.83 (range 1-3)	.70	81.58	.04
Parity	1.83 (range 1-3)	.62	1.67 (range 1-3)	.82	75.65	.30

2. Demographic and Obstetric characteristic of respondents

Results of Pearson chi-square shows women who had preterm birth were significantly low education level compared with full term birth, ($\chi 2$ = 8.15) and (p-value = .02). All women were married in both group. There was not much variation found in terms of occupation whereas, 10 women with preterm birth and 12 women with full term birth worked outside of home (p-value = .25). From the result of Fisher exact found that was out of 42 women 12 women who delivered preterm birth had history of miscarriage, which is higher to compare to women delivered full term birth (p-value = .05). History of previous preterm birth were not found much differences among women having preterm birth compared to women having full term birth which was (p-value = .36) and similarly, history of abortion due to fetal anomalies was also found not any significant difference between women (p-value = 1.00) delivered preterm and full-term birth.

Result of Pearson chi-square found habit of smoking before pregnancy was higher among preterm mother to compare to full-term mothers ($\chi 2$ = 7.24) and (p-value = .01). Experiencing anemia before pregnancy was found higher among women who delivered preterm baby, that ($\chi 2$ = 17.36), (p-value = .00) to compare with women who delivered full baby. History of previous stillbirth of baby was found low in both group (p-value = .23). Similarly, the result of previous history of low birth weight was also found similar with preterm birth (p-value = .27) and full-term

birth women. Likewise, women who have previous history of congenital anomalies i.e. cleft lip or palate and neural tube defect were also found similar on both group (*p*-value = .12).

Table 2 Demographic and obstetric characteristics of women (*N* = 84)

Demographic/ obstetric characteristics	**Preterm (*n* = 42)**		**Full term (*n* = 42)**		***χ2***	***p*-value**
	n	**%**	***n***	**%**		
Education						
Up to primary	5	71.4	6	28.6	8.15	.02[a]
Secondary	18	52.9	16	47.1		
University level	9	31	20	69		
Marital status						
Married	34	47.22	38	52.8		.35[b]
Widowed/ divorced	8	66.67	4	33.33		
Occupation						
Housewife	32	51.61	30	48.39		.25 [b]
Jobholder	10	45.45	12	54.55		
Miscarriage						
No	30	44.1	38	55.9		.05 [b]
Yes	12	75	4	25		
History of premature birth						
No	38	48.1	41	51.9		.05 [b]
Yes	4	80	1	20		
History of abortion						
No	41	50.6	40	49.4		1.00 [b]
Yes	1	33.3	1	66.7		

Table 2 (Cont.)

Demographic/ obstetric characteristics	Preterm (*n* = 42)		Fullterm (*n* = 42)		*χ2*	*p*-value
	n	%	*n*	%		
Smoking						
No	41	50.6	40	49.4	7.24	.01[a]
Yes	17	73.91	6	26.1		
History of anemia						
No	19	33.9	37	66.1	17.36	.00 [a]
Yes	23	82.1	5	17.9		
History of still birth						
No	33	46.5	38	53.5		.23 [b]
Yes	9	69.2	4	30.8		
Low birth weight						
No	36	47.4	40	52.6		.27 [b]
Yes	6	69.2	2	25		
Congenital anomalies						
No	38	47.5	42	52.5		.12 [b]
Yes	4	100	0	0		

[a] Pearson chi square test, [b] Fisher exact test

3. Status of preterm birth infant

Table 3 shows that half of baby born preterm were comes under the criteria of very preterm birth (50.0 %) (i.e. fall under the 28 to 32 weeks of gestation). Nearly half of respondents (45.5 %) were moderately preterm while only 4.8 % were found severe preterm birth.

Table 3 Status of preterm birth infant (N = 42)

Status of preterm birth infant	***n***	**%**
Extremely preterm birth (<28 to 32 weeks)	2	4.8
Very preterm birth (33-36 weeks)	21	50
Moderate preterm birth (< 37 weeks)	19	45.2

Part 2 Consumption of folic acid supplement and dietary folate in preconception and during pregnancy

1. Consumption of folic acid supplements in preconception

The Fisher exact test was done to determine the consumption of folic acid supplements in preconception period with preterm birth. Since there were more than 20 % of the cells had frequency 0. As presented in the table 4, test resulted consuming folic acid supplement in preconception significantly associated with preterm birth (p-value = .00).

Table 4 Consumption of folic acid supplement in preconception (N = 84)

FAS in preconception	**Preterm birth (*n* = 42)**		**Full term (*n* = 42)**		***p*-value**
	n	**%**	***n***	**%**	
Not used	42	56	33	44	.00
Used	0	.00	9	100	

FAS= folic acid supplement

2. Consumption of dietary folate in preconception

Result from independent t-test was found low score (M = 20.26, SD = 2.97) of consumption of dietary folate before pregnancy by women who delivered preterm birth in preconception compared with women delivered full term birth. The possible

range of consumption of dietary folate in preconception among women who delivered preterm infant was found 16 to 26 out of 0 to 28, which was less than women delivered full-term birth had range of dietary folate consumption in preconception was 20-28. Result showed that consumption of dietary folate in preconception with preterm birth. (t = 8.11) and (p-value = .00),

Table 5 Consumption of dietary folate in preconception (N = 84)

Dietary folate in PC	***n***	**Range**		***M***	***SD***	***t***	***p*-value**
		Possible	**Actual**				
Preterm	42	0-28	16-26	20.26	2.97	8.11	.00
Full term	42	0-28	20-28	24.60	1.78		

PC = preconception

3. Consumption of folic acid supplements during pregnancy

Independent *t*-test found there were statistically significant difference between the mean score was 4.59 in women who delivered preterm and 6.45 in women who delivered full term baby in terms of consumption of folic acid supplements during pregnancy. As presented in the table 6, folic acid supplements during first trimester (t = 3.01) and (p-value = .04), second trimester had (t = 9.61) and (p-value = .00) and third trimester had (t = 8.31) and (p-value = .00) as they were found to have significantly associated with preterm birth. Thus, overall (t = 8.19) and (p-value = .00). The possible range of consuming folic acid supplements among women delivered preterm baby during pregnancy were 4-9 out of 0-9 in overall pregnancy period.

Table 6 Consumption of folic acid supplements during pregnancy (N = 84)

Consumption of FAS during pregnancy	*n*	Range		*M*	*SD*	*t*	*p*-value
		Possible	Actual				
First trimester							
Preterm	42	0-1	0-3	0.02	1.06	3.01	.04
Full term	42	0-3	0-3	0.52			
Second trimester							
Preterm	42	3-Feb	0-3	2.24	0.43	9.61	.00
Full term	42	3-Feb	0-3	2.95	0.22		
Third trimester							
Preterm	42	3-Feb	0-3	2.33	0.48	8.31	.00
Full term	42	3-Feb	0-3	2.98	0.15		
Consumption of FAS throughout the pregnancy							
Preterm	42	9-Apr	0-9	4.59	0.91	8.19	.00
Full term	42	9-Apr	0-9	6.45	1.15		

FAS = folic acid supplement

4. Consumption of dietary folate during pregnancy

Independent *t*-test was used for this analysis and the results were presented in table 7. The result found low mean score that was 21.10 in women who delivered preterm birth in terms of consumption of dietary folate during pregnancy. Results found (t = 6.16) and (p-value = .00) of the consumption of dietary folate with preterm birth.

Table 7 Consumption of dietary folate during pregnancy (N = 84)

Dietary folate during pregnancy	***n***	**Range**		***M***	***SD***	***t***	***p*-value**
		Possible	**Actual**				
Preterm	42	0-28	13-25	21.10	2.66	6.16	.000
Full term	42	0-28	20-25	23.88	1.23		

Part 3 Factor predicting preterm birth

The result of multiple binary logistics regression was performed to examine predictors of folic acid supplement and dietary folate among women who delivered preterm and full-term birth using significant factors from the analysis including consumption of folic acid supplement in preconception, consumption of dietary folate in preconception, consumption of folic acid supplement during pregnancy and consumption of dietary folate. The Omnibus tests of model coefficients indicates that *p*-value of this model was less than .05. That means at 5 % level of significance the overall model coefficients are statistically significant ($\chi 2 = 75.32$, *p*-value = .00).

The result in table 8 revealed, the consumption of dietary folate in preconception was found to have significant association with preterm birth, result shows that women who had high consumption folate diet before pregnancy were .60 times less likely to have preterm birth to compare with women who had less consumption of dietary folate (OR = .60, 95 % CI = .42-.88). Result also indicates, that odds of having preterm birth among women who had irregular consumption of folic acid supplement was (OR = .20, 95 % CI = .06-.67) that indicates women who consumed folic acid supplement regularly during pregnancy were .20 times less likely to have preterm birth with compare to women who does not take folic acid supplement regularly during pregnancy. Additionally, it was found women who had high consumption of dietary folate throughout the pregnancy were .53 times less likely to have preterm birth (OR = .53, 95 % CI = .32-.92) compared with the women who do not had high consumption of dietary folate.

Table 8 Factors predicting preterm birth

Predictors	B	SE	Wald	*p*-value	OR	95 % CI for OR
FAS in PC	18.573	11327.65	0	.99	0	0
Dietary folate in PC	-0.504	.19	7.01	.08	.60	(.42-.88)
FAS in pregnancy	-1.59	.6	6.94	.08	.20	(.06-.67)
Dietary folate in pregnancy	-0.633	.28	5.14	.02	.53	(.32-.92)

FAS= folic acid supplement, PC= preconception

CHAPTER 5
CONCLUSION AND DISCUSSION

This chapter provides the summary of the study findings, interpretation and explanation of the study results. Study findings are discussed according to the framework of the study and previous evidences on consumption of folic acid supplements and dietary folate in preconception and during pregnancy. In addition, to this implication of the study findings to nursing practice, future research, and education are being discussed. This chapter will also address some of the limitation of the study.

Summary of the study findings

Good maternal health and complications from preterm birth has become alarming issues all over the world. Women's are becoming more aware about the importance of nutrition from diet before and throughout the pregnancy period. Several factors have been studied to identify the associated cause of preterm birth, among them importance of folic acid supplement and dietary folate were found to have strong relationship with maternal health and preterm birth. Consumption of dietary folate and folic acid supplement were low in developing countries. Thus, the current study guided by literature examined the consumption of folic acid supplements and dietary folate in preconception and during pregnancy and its association with preterm birth among Nepalese women residing in Kathmandu, Nepal.

Eighty-four women who delivered preterm and full-term birth in Paropakar Maternity and Women's Hospital Kathmandu, Nepal were selected as a sample of this study. The study design was case control which have 1:1 ratio. The sample was 84 postpartum women, who gave birth to preterm baby and who delivered full-term baby. Non-probability sampling technique was using to collect the data. Data was collected by self-administered questionnaires and review of medical records. The questionnaires for this study were developed by the researcher based on the empirical review of literatures. Cronbach alpha coefficient for the consumption of folic acid supplement and dietary folate in preconception and during pregnancy was 0.83, 0.82

and 0.77 respectively. Data was analyzed using the; descriptive commands of frequency, percentage, mean and standard deviation; independent *t*-test, Pearson chi-square test, Fisher exact test were used to determine the consumption of the folic acid supplement and dietary folate in preconception and during pregnancy. Binary logistic regression was used to examine the influence of folic acid supplements and dietary folate in preconception and during pregnancy with preterm birth.

The result of the study presented as follows:

1. The participants were women from 18 to 45 years aged with mean age of 29.71 for preterm and 25.1 for full term birth. From the samples, mean number of pregnancy in preterm birth mothers was 1.88 and mean number of live birth was 1.55.

2. Half of them who gave preterm birth (47.22 %) and (52.8 %) of full term birth were married. The highest education attained by respondents was master's degree and bachelor's degree which is accounted for (31 %) among women who delivered preterm birth. Similar number of women from both group work outside of home which were 10 from preterm birth and 12 from full-term birth. Among the preterm birth mother participants (75 %) had experience of miscarriage and (38 %) had history of the previous preterm birth. More than half (73.9 %) of participant of preterm birth mothers smoked before pregnancy and majority (82.1 %) of the women who delivered preterm birth were found to have experienced anemia before pregnancy, whereas, (69.2 %), had a history of stillbirth. Women who delivered preterm birth had previous history of low birth weight baby which was < 2.5 kg were (75 %). Interestingly it was found that only women who were having preterm birth were found to have history of congenital anomalies (100 %).

3. Status of the preterm birth infant were also analyzed which resulted half (50 %) of the preterm baby who were found under the very preterm birth according to WHO.

4. From the analysis of Fisher exact, it showed that consumption of folic acid supplement in preconception period showed positive significance with preterm birth (*p*-value = .00). Similarly, from the independent *t*-test it was found that consumption of dietary folate in preconception period was also found significantly associated ($t = 1.15$) and (*p*-value = .00) with preterm birth. It also found that consumption of the folic acid supplement during pregnancy has strong association

with preterm birth (t = 8.19) and (p-value = .00) and dietary intake during pregnancy strongly associated with preterm birth (t = 6.16) and (p-value = .00).

5. While predicting the factor that mostly influence the preterm birth from the framework were folic acid supplement during pregnancy (OR = .20, 95 % CI = .06-.67), dietary folate during pregnancy (OR = .53, 95 % CI = .32-.92) and dietary folate in preconception (OR = .60, 95 % CI = .42-.88) which indicated the adequate consumption of folic acid supplements and consumption of dietary folate throughout the pregnancy period and preconception period could reduce the risk of preterm birth.

Discussion

This part was focused on discussing the research objectives, firstly, to determine the consumption of folic acid supplement and dietary folate in preconception and during pregnancy among Nepalese women and secondly, to examine the influence of folic acid supplement and dietary folate in preconception and during pregnancy among Nepalese women.

Factors predicting preterm birth

1. Consumption of folic acid supplement in preconception

The objectives to examine the influence of consumption of folic acid supplement and dietary folate by women before pregnancy can predict the preterm birth. Odd ratio from the logistic regression did not show any significant relation with consumption of folic acid supplement in preconception with preterm birth and (OR = .00, 95 % CI = .00-∞, p-value = .99). This finding is in contrast with the prospective cohort conducted in China which has found that women consuming folic acid in preconception had 8 % less chance to have preterm birth (RR = .81, 95 % CI = .70-.95, p-value = .08) compared to non-users (Zheng et al., 2016). It is also in contrast to the study done in China which shows that women taking folic acid supplement in preconception were .58 times less likely to have preterm (OR = .58, 95 % CI = .56-.61, p-value = .01) than non-users (Wang et al., 2015). The reason for this result might be because of the study setting that is the capital of country which is highly urban area and women are more aware about their health status.

2. Consumption of dietary folate in preconception

The finding of this study showed that women who have high consumption of folate from diet before pregnancy was significantly associated with preterm birth (*p*-value = .08). Likewise, women who consume high folate diet in preconception were .60 times less likely to have a preterm birth (OR = .60, 95 % CI = .42-.88) in comparison to mother who have low consumption of dietary folate in preconception. The finding was consistent with the study conducted by Liu et al. (2016 b), which found that women who consume high folate diet before conception were .68 times less likely to have a preterm birth compared to those who consume less dietary folate in preconception (OR = .68, 95 % CI = .56-.83). Similar study in Australia concluded that women who follow healthy dietary patterns before 12 month of pregnancy can lower the risk of preterm birth by .31 times (OR = .31, 95 % CI = .31-.73, *p*-value = .011) compared to mother who do not follow healthy dietary pattern in pregnancy (Grieger, Grzeskowick, & Clifton., 2014). The reason for less consumption of dietary folate in preconception period could be because of lack of sufficient awareness of preconception care and less awareness regarding the importance of consuming proper nutritious diet among Nepalese women.

3. Consumption of folic acid supplement during pregnancy

Consumption of the folic acid supplement during pregnancy is highly recommended by WHO and many other studies (WHO, 2012, Liu et al., 2016 b). According to the objective of the present study, consumption of folic acid supplement during pregnancy was assessed in three different trimesters. The odds ratio of the study indicates that women who had regular consumption of folic acid supplement throughout the pregnancy were .20 times less likely to have preterm birth (OR = 0.204, 95 % CI = .06-.67) in comparison to women who have less consumption of folic acid throughout the pregnancy. From the study it was found that women who delivered preterm baby started taking folic acid supplement from the second trimester (*M* = 2.24, *SD* = 0.43) compared to first trimester (*M* = .02, *SD* = .15). This statistic shows that women were not consuming folic acid supplement as per the recommendation set by WHO (2012). This is consistent with result of the study conducted in Pakistan where it was found that intake of folic acid supplements in first three month of pregnancy can reduce (33 %) the risk of preterm birth and other

neonatal risk (Nisar et al., 2015). Similarly, the study conducted in China by Wang et al. (2015), showed that women consuming folic acid supplement in pregnancy were .61 times less likely to have preterm birth then women who do not consume folic acid supplement in pregnancy (OR = .61, 95 % CI = .58-.65).

The result from the present study could explain that level of awareness about importance of consumption of folic acid supplement and distribution of folic acid supplement in Nepal are not sufficient and reachable to the all women. As women in this study reported that they were prescribed and advised to take folic acid supplement from the health personnel right from the second trimester and throughout the pregnancy. However, they did not use supplement regularly because they thought it was not important for the fetal health.

4. Consumption of dietary folate during pregnancy

Appropriate maternal diet and nutrition plays important role for the pregnancy outcomes. Assessment for dietary folate was determined by the seven questions and investigated the diet folate consumed by women in whole pregnancy period, which contain highly folate diet, such as dark green vegetables, lentils, beans, chicken, grains and organ meat. The odds ratio of study shows that women who consume high folate diet during pregnancy were .53 times less likely to have preterm birth then women who consume less folate diet during pregnancy (OR = .53, 95 % CI = .32-.92). Similar result was found in previous study conducted in China where women consuming adequate dietary folate during pregnancy were .61 times less likely to reduce the risk of preterm birth (OR = .61, 95 % CI = .43-.87) then women who had less consumption of dietary folate during pregnancy (Liu et al., 2016 b). Another study conducted in United States also supports that having low dietary intake during pregnancy is 1.44 times more likely to increase the risk (OR = 1.44, 95 % CI = 1.01-2.04) of preterm delivery (Shaw et al., 2011). Respondents of present study agreed that they had information about the diet and other issues of pregnancy during their antenatal visit, but they were not well informed about the importance of dietary folate during pregnancy. Most of the respondent said that they do not have information about the particular food which contains high folate.

In conclusion, the findings of the study found significant relationship between consuming folic acid and preterm birth before and throughout the pregnancy.

There was a lack of knowledge about consuming folic acid and awareness about identifying the food that contain high folate in preconception and during pregnancy among Nepalese women. Therefore, future intervention should be aimed to create awareness to encourage and practice regarding importance of consuming dietary folate from preconception to throughout the pregnancy along with regular consumption of folic acid supplement from first trimester to throughout the pregnancy in addition to complication of preterm birth.

Implication of the study

In terms of implications, this study provides better understanding about the importance of folic acid in preconception and during pregnancy with preterm birth. So intervention should be focused on emphasizing the dietary pattern of the women from the preconception period to throughout the pregnancy via health education campaign. Nurse can provide education about complications of preterm birth and its effect in different stage of life during antenatal visits. Education program should emphasize on the food which contain high folate and help to identify them from local available resources.

Limitations of the study

This is the first study conducted in Nepal determining the consumption of folic acid supplements and dietary folate in preconception and during pregnancy among women delivered preterm and full-term birth. It can provide baseline information for future studies. It is expected to create the importance and benefits of consuming folic acid and dietary folate in different stages of pregnancy and help to lower the risk of preterm birth in Nepal. But, however, it was not free from the limitations. Firstly, though data collection was done on a small sample size, so it has limitation of generalization. Secondly, this is a case control study and researcher collected the retrospective information from the respondent so there could be a chance to have recall bias on the information they provided.

Recommendation

1. Future research in this subject should be done in more type of food that contain high folate and which are locally available in different parts of the country. Large sample size can give good concept for promoting dietary folate from grass root level.

2. Nurse and midwives should provide effective educational intervention program regarding importance of consuming dietary folate and regular use of folic acid supplements and its association with preterm birth and complications of preterm birth to women and her family members in antenatal visit.

3. The findings of the study regarding folic acid supplement during pregnancy strongly advocates the need for free supply of folic acid supplement by government from beginning of the first trimester of pregnancy.

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APPENDICES

APPENDIX A

Questionnaires of English version

QUESTIONNAIRES

STUDY TITLE: CONSUMPTION OF FOLIC ACID IN PRECONCEPTION AND DURING PREGNANCY AND ITS ASSOCIATION WITH PRETERM BIRTH AMONG NEPALESE WOMEN: A CASE CONTROL STUDY

Identification code:

Date of interview……. Start time……. Finish time

Part I. Personal Demographic Information Questionnaire

Instructions: *Answer to the following questions by filling in the blanks or marking (✓)" in the box.*

1. Age……. (Years)
2. What is your marital status?
   a. Married ☐ Widowed ☐
   b. Single ☐ Divorced ☐
   c. Other……. (Specify)
3. What is your highest education level achieved?
   a. No formal education ☐ Secondary ☐
   b. Primary ☐ Tertiary (degree and above) ☐
4. Occupation
   a. Housewife ☐ Private employee ☐
   b. Farmer ☐ Student ☐
   c. Government employee ☐ Own business ☐
   d. Others (Specify……)
5. Gravida……
6. Parity……...
7. Have you had any pregnancies that were ……Miscarriage?
   a. No ☐
   b. Yes ☐ (……. times)

8. Do you have any history of premature birth (< 37 weeks of gestation)?
   a. No ☐
   b. Yes ☐ (……. times)
9. Do you have any history of stillbirth (i.e. birth of baby that is not alive, past 24 weeks pregnancy)?
   a. No ☐
   b. Yes ☐ (……..times)
10. Do you have any history of anemia before pregnancy?
   a. No ☐
   b. Yes ☐ (…….times)
11. Do you smoke during pregnancy?
   a. No ☐
   b. Yes ☐ (…….times)
12. Did you deliver a child with any of medical conditions mentioned below? *(Can have more than one answer)*
   12.1 Low birth weight (less than 2.5 kg)
      a. Yes ☐
      b. No ☐
   12.2 Cleft lip or Palate
      a. Yes ☐
      b. No ☐
   12.3 Neural tube defects
      a. Yes ☐
      b. No ☐

Others (please specify) ……..

Part II: Information from Medical Records

Instructions: *please tick* (✓) the correct answer in the box, which you think is appropriate. This section is the review of the medical record of the mother about the gestational age of the baby

1: Preterm birth

1.1 What is the gestational age of the baby?

a) < 28 weeks ☐

b) 28 to 32 weeks ☐

c) < 37 weeks ☐

d) 37 to 42 weeks ☐

Part III: Consumptions of folic acid supplements in preconception (CFASP)

Instructions: *please tick* (✓) the correct answer in the box appropriate to your practice. The following questions are about the consumption of folic acid supplements before one month you become pregnant

1. Did you take folic acid one month before you get pregnant?

   Yes ☐

   No ☐

2. If yes how often did you take folic acid?

   Everyday ☐

   Sometime ☐

Part IV: Consumptions of folic acid supplements during pregnancy (CFSDP)

Instructions: *please tick* (✓) the correct answer in the box appropriate to your practice. The following questions are about the consumption of folic acid supplements when you become pregnant

1. How often did you take folic acid from conception to three months of pregnancy?
   a) Everyday ☐ b) About 3 days a week ☐ c) once a week ☐
   d) Not taken ☐

2. How often did you take folic acid from first three to six months of pregnancy?
   a) Everyday ☐ b) About 3 days a week ☐ c) once a week ☐
   d) Not taken ☐

3. How often did you take folic acid from six to nine months of pregnancy?
   a) Everyday ☐ b) About 3 days a week ☐ c) once a week ☐
   d) Not taken ☐

Part V: Consumption of dietary folate in preconception (CDFP) (please put ✓ in every line)

Instructions: *please tick* (✓) the correct answer in the box appropriate to your practice. The following questions are about the consumption of dietary folate three month before you get pregnant

SN	Items of food	Average consumption of dietary folate in preconception				
		Never	<½ cup/day	½ cup cup/ day	1 cup/day	2-5 cup
1.	How much did you eat cooked dark green vegetables (such as spinach, mustard green, turnip green, and all type of dark green leafy vegetables)?					
2.	How often did you eat cooked vegetables (such as Okra, Turnip, Potato)?					
3.	How much did you eat grains products (such as Pasta, noodles, bread)?					
4	How much did you eat Beans/Peas/Lentils (such as, black beans, Navy beans, Kidney beans, Nima beans, Green peas, split peas and lentils)?					
5	How much did you eat fruits (orange and grapes)?					
6	How much did you eat and meat alternatives such as Chicken, fish?					
7.	How much did you eat organ meat (liver of lamb and pork)?					

Part VI: Consumption of dietary folate during pregnancy (CDFDP) (please put ✓in every line)

Instructions: *please tick* (✓) the correct answer in the box appropriate to your practice. The following questions are about the consumption of dietary folate during your pregnancy

SN	Items of food	Average consumption of dietary folate during pregnancy				
		Never	<½ cup/day	½ cup cup/ day	1 cup/day	2-5 cup
1.	How much did you eat cooked dark green vegetables (such as spinach, mustard green, turnip green, and all type of dark green leafy vegetables)?					
2.	How often did you eat cooked vegetables (such as Okra, Turnip, Potato)?					
3.	How much did you eat grains products (such as Pasta, noodles, bread)?					
4	How much did you eat Beans/Peas/Lentils (such as, black beans, Navy beans, Kidney beans, Nima beans, Green peas, split peas and lentils)?					
5	How much did you eat fruits (orange and grapes)?					
6	How much did you eat and meat alternatives such as Chicken, fish?					
7.	How much did you eat organ meat (liver of lamb and pork)?					

APPENDIX B

Questionnaires of Nepali version

प्रश्नावली

अध्ययन अनुसन्धान विषयः

"नेपाली महिलाहरुमा गर्भवती हुनअघि र गर्भवती अवस्थामा फोलिक एसिड खाने अभ्यास र समय अगाडी जन्मेका शिशुहरुसँगको सम्बन्ध"

पहिचान कोडः

अर्न्तवार्ताको मिति : ..... शुरु भएको समय : .....सकिएको समयः.....

भाग एकः (व्यक्तिगत तथा आधारभूत सूचना तथा विवरण)

निर्देशनः हरेक प्रश्नको खाली ठाउँमा उचित उत्तरमा (√) चिन्ह लगाउनुहोस् ।

१. तपाईको उमेर .....कति हो ?

क) .....वर्ष

२. तपाईको वैवाहिक स्थिती के हो ?

क) विवाहित ☐ ख) विधवा ☐

ग) अविवाहित ☐ घ) पारपाचुके भएको ☐

अरु कुनै .....(खुलाउनुहोस्)

३. तपाईको अहिले सम्मको उच्च शिक्षा कति हो ?

क) कहिले पनि स्कूल नगएको ☐ ख) प्राथमिक ☐

ग) बाह्र कक्षा ☐ घ) स्नातक वा माथि ☐

४. तपाईको पेशा के हो ?

क) गृहिणी ☐ ख) निजी कम्पनीमा काम ☐ ग) कृषि ☐

घ) विद्यार्थी ☐ ङ) सरकारी नोकरी ☐ च) व्यवसाय ☐

(अन्य कुनै भए खुलाउनुहोस् .....)

५. तपाई अहिले सम्म कति पटक गर्भवती हुनुभएको छ ?

.....पटक

६. तपाईका कतिवटा जिउँदा बच्चाहरु छन् ?

.....वटा

७. तपाईको कुनै गर्भ खेर गएको थियो ?

क) थियो ☐ ख) थिएन ☐ (.....पटक)

८. तपाईको कहिल्यै २४ हप्ता भन्दा बढीको गर्भ खेर गएको छ ?

क) छ ☐ ख) छैन ☐ (.....पटक)

९. तपाईलाई कहिल्यै गर्भवती हुनु अगाडी रक्तअल्पता भएको छ ?

क) छ ☐ ख) छैन ☐ (.....पटक)

१०. तपाईले गर्भवती हुनुअघि धुम्रपान गर्नुभएको थियो ?

क) छ ☐ ख) छैन ☐ (.....पटक)

११. तपाईले कहिल्यै शिशुको अस्वस्थताको कारणले गर्दा गर्भ तुहाउनु भएको छ ?

क) छ ☐ ख) छैन ☐ (.....पटक)

१२. तपाईले कहिल्यै तल उल्लेखित कुनै मेडिकल अवस्थामा बच्चा जन्माउनु भएको छ ? (एक भन्दा बढी उत्तर आउनु सक्छ)

१२.१. तौल नपुगिकन बच्चा जन्मेको थियो ? (२.५ के.जी. भन्दा कम)

क) थियो ☐ ख) थिएन ☐

१२.२. खुडे ओठ भएको बच्चा जन्मेको थियो ?

क) थियो ☐ ख) थिएन ☐

१२.३. न्यूरल ट्युब डिफेक्ट भएको थियो ?

क) थियो ☐ ख) थिएन ☐

भाग २: मेडिकल रेकर्डबाट सूचना

निर्देशन: कृपया सही उत्तरमा (√) चिन्ह लगाउनुहोस् (यो भाग शिशुहरुको गर्भावधिको बारेमा हो ।)

१. तपाईको शिशुको गर्भावधि कति हो ?

क) २८ हप्ताभन्दा कम ☐

ख) २८-३६ हप्ता ☐

ग) ३७ हप्ता पूरा नभएको ☐

घ) ३७ देखि ४२ हप्ता ☐

भाग ३: गर्भवती हुन अगाडी फोलिक एसिड ट्याब्लेट खाने अभ्यास

निर्देशनः कृपया सही उत्तरमा √) चिन्ह लगाउनुहोस् ।यो भाग आइमाईहरुले गर्भवती हुनु अगाडी फोलिक एसिड ट्याब्लेट खाने बारेमा सम्बन्धित छ ।

१. तपाईले गर्भवती हुन अगाडी फोलिक एसिड ट्याब्लेट खानु भएको थियो ?

क) थियो ☐ ख) थिएन ☐

२. तपाईले फोलिक एसिड कति पटक खानुभयो ?

क) हरेक दिन ☐

ख) कहिलेकाहीँ ☐

ग) कहिले पनि नखाएको ☐

भाग ४: गर्भवती हुँदा फोलिक एसिड ट्याब्लेट खाएको अभ्यास ।

निर्देशन: कृपया सहि उत्तरमा (√) चिन्ह लगाउनुहोस् ।

(यो भाग तपाई गर्भवती हुँदा खाएको फोलिक एसिड ट्याब्लेटको बारेमा सम्बन्धित छ ।)

१. गर्भवती भएको शुरुका तीन महिना तपाईले कति पटक फोलिक एसिड ट्याब्लेट खानुभयो ?

क) हरेक दिन ☐ ख) हप्तामा २ दिन ☐

ग) हप्तामा १ दिन ☐ घ) कहिले पनि खाइन ☐

२. गर्भवती भएको पहिलो ३ महिना देखि ६ महिना सम्म कति पटक फोलिक एसिड ट्याब्लेट खानुभयो ?

क) हरेक दिन ☐ ख) हप्तामा ३ दिन ☐

ग) हप्तामा १ दिन ☐ घ) कहिले पनि खाइन ☐

३. गर्भवती भएको ६ महिना देखि नौ महिना सम्म पटक फोलिक एसिड खानुभयो ?

क) हरेक दिन ☐ ख) हप्तामा ३ दिन ☐

ग) हप्तामा १ दिन ☐ घ) कहिले पनि खाइन ☐

भाग ५: गर्भवती हुनुभन्दा ३ महिना अगाडी आइमाईहरुमा खानेकुराबाट पाउने फोलेट खाने अभ्यास ।

निर्देशन : कृपया हरेक लाईनको उत्तरमा (√) चिन्ह लगाउनुहोस् ।

क्र.सं.	खानेकुराको नाम	गर्भवती हुनुभन्दा ३ महिना अगाडी आइमाइहरुले खानेकुराबाट पाउने औसत फोलेट				
		कहिल्यै नखाएको	< आधा कप (प्रतिदिन)	आधा कप (प्रतिदिन)	एक कप (प्रति दिन)	२-५ कप (प्रतिदिन)
१.	तपाइले पकाएको गाढा हरियो साग (जस्तै पालुङ्गो, चम्सुर, सलगमको साग, रायो साग वा अन्य सबै सागहरु) खाँदा प्राय जसो कति खानु हुन्थ्यो ?					
२.	तपाइले पकाएको तरकारीहरु (जस्तै भिण्डी, ब्रोकाउली, सलगम, आलु) खाँदा प्राय जसो कति खानु हुन्थ्यो ?					
३.	तपाईले गहुँबाट बनेका खानेकुरा (चाउचाउ, रोटी) खाँदा प्राय जसो कति खानु हुन्थ्यो ?					
४.	तपाइले पकाएको गेडागुडी (जस्तै दाल, कालो सिमी, भटमास, बोडी, मुसुरी दाल, हरियो केराउ) खाँदा प्राय जसो कति खानु हुन्थ्यो ?					
५.	तपाईले फलफूल (जस्तै सुन्तला, अंगुर) खाँदा प्राय जसो कति खानु हुन्थ्यो ?					
६.	तपाईले कति पटक कुखुराको मासु वा माछा खानुहुन्थ्यो ?					
७.	तपाईले कति पटक खसी वा बङ्गुरको कलेजो खानुहुन्थ्यो ?					

भाग ६: गर्भवती भएपछि आइमाईहरुमा खानेकुराबाट पाउने फोलेट खाने अभ्यास ।

निर्देशन : कृपया हरेक लाईनको उत्तरमा (√) चिन्ह लगाउनुहोस् ।

क्र.सं.	खानेकुराको नाम	गर्भवती हुनुभन्दा ३ महिना अगाडी आइमाइहरुले खानेकुराबाट पाउने औसत फोलेट				
		कहिल्यै नखाएको	< आधा कप (प्रतिदिन)	आधा कप (प्रतिदिन)	एक कप (प्रति दिन)	२-५ कप (प्रतिदिन)
१.	तपाइले पकाएको गाढा हरियो साग (जस्तै पालुङ्गो, चम्सुर, सलगमको साग, रायो साग वा अन्य सबै सागहरु) खाँदा प्राय जसो कति खानु हुन्थ्यो ?					
२.	तपाइले पकाएको तरकारीहरु (जस्तै भिण्डी, ब्रोकाउली, सलगम, आलु) खाँदा प्राय जसो कति खानु हुन्थ्यो ?					
३.	तपाईले गहुँबाट बनेका खानेकुरा (चाउचाउ, रोटी) खाँदा प्राय जसो कति खानु हुन्थ्यो ?					
४.	तपाइले पकाएको गेडागुडी (जस्तै दाल, कालो सिमी, भटमास, बोडी, मुसुरी दाल, हरियो केराउ) खाँदा प्राय जसो कति खानु हुन्थ्यो ?					
५.	तपाईले फलफूल (जस्तै सुन्तला, अंगुर) खाँदा प्राय जसो कति खानु हुन्थ्यो ?					
६.	तपाईले कति पटक कुखुराको मासु वा माछा खानुहुन्थ्यो ?					
७.	तपाईले कति पटक खसी वा बङ्गुरको कलेजो खानुहुन्थ्यो ?					

APPENDIX C

IRB approvals, Hospital permission and informed consent forms

THE INSTITUTIONAL REVIEW BOARD (IRB) FOR GRADUATE STUDIES
FACULTY OF NURSING, BURAPHA UNIVERSITY, THAILAND

Thesis Title Consumption of Folic Acid in Preconception and During Pregnancy and Its Association with Preterm Birth among Nepalese Women: A Case Control Study

Name Ms. Binita Puri
ID: 59910040
Master of Nursing Science Program, Pathway of Maternity Nursing and Midwifery (International Program)

Number of the IRB approval **02 – 02 – 2561**

The Institutional Review Board (IRB) for graduate studies of Faculty of Nursing, Burapha University reviewed your submitted proposal. The contingencies have been addressed and the IRB **approves** the protocol. Work on this project may begin. This approval is for a period of one year from the date of this letter and will require continuation approval if the research project extends beyond **February 13rd, 2019**.

If you make any changes to the protocol during the period of this approval, you must submit a revised protocol to the IRB committee for approval before implementing the changes.

Date of Approval February **13rd**, 2018

Chintana Wacharasin, R.N., Ph.D.

Chairperson of the IRB
Faculty of Nursing, Burapha University, THAILAND

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Government of Nepal
Ministry of Health and Population
Paropakar Maternity and Women's Hospital
Development Board

Phone No.
Director- 4260405
Office- 4260231
Reception- 4253276
4253277
Fax No.- 4260274
P.O. BOX No.- 5307
Thapathali, Kathmandu

58-11ka-1516

Ministry of Health
Paropakar Maternity & Women's Hospital
Development Board

To,

09/12/2074

Ms. Binita Puri

Subject: Approval for data collection

Dear Madam

The research proposal **"Consumption of folic acid in preconception and during pregnancy and its association with preterm birth among Nepalese women: a case control study"** has been approved for the data collection. The study will be conducted under the supervision of the incharge of the concerned department.

The researcher has to submit the final report to the research committee.

Thank you

Rijuta

Dr. Rijuta Joshi
Member Secretary
Research Committee

CC:

1. Research Unit
2. Administration
3. Account section

Government of Nepal
Nepal Health Research Council (NHRC)
Estd. 1991

Ref. No.: 2179.

13 March 2018

Ms. Binita Puri
Principal Investigator
Burpha University
Thailand

Ref: **Approval of thesis proposal** entitled **Consumption of folic acid in preconception and during pregnancy and its association with preterm birth among Nepalese women attending paropakar maternity and women's hospital: A Case Control Study**

Dear Ms. Puri,

It is my pleasure to inform you that the above-mentioned proposal submitted on **12 February 2018** (**Reg. no. 62/2018**) has been approved by Nepal Health Research Council (NHRC) National Ethical Guidelines for Health Research in Nepal, Standard Operating Procedures Section 'C' point no. 6.3 through Expedited Review Procedures.

As per NHRC rules and regulations, the investigator has to strictly follow the protocol stipulated in the proposal. Any change in objective(s), problem statement, research question or hypothesis, methodology, implementation procedure, data management and budget that may be necessary in course of the implementation of the research proposal can only be made so and implemented after prior approval from this council. Thus, it is compulsory to submit the detail of such changes intended or desired with justification prior to actual change in the protocol. Expiration date of this proposal is **August 2018.**

If the researcher requires transfer of the bio samples to other countries, the investigator should apply to the NHRC for the permission. The researchers will not be allowed to ship any raw/crude human biomaterial outside the country; only extracted and amplified samples can be taken to labs outside of Nepal for further study, as per the protocol submitted and approved by the NHRC. The remaining samples of the lab should be destroyed as per standard operating procedure, the process documented, and the NHRC informed.

Further, the researchers are directed to strictly abide by the National Ethical Guidelines published by NHRC during the implementation of their research proposal and **submit progress report in between and full or summary report upon completion.**

As per your thesis proposal, the total research budget is **NRs 1,50,000** and accordingly the processing fee amounts to **NRs 20,000.** It is acknowledged that the above-mentioned processing fee has been received at NHRC.

If you have any questions, please contact the Ethical Review M & E Section at NHRC.

Thanking you,

Prof. Dr. Anjani Kumar Jha
Executive Chairperson

Tel: +977 1 4254220, Fax: +977 1 4262469, Ramshah Path, PO Box: 7626, Kathmandu, Nepal
Website: http://www.nhrc.gov.np, E-mail: nhrc@nhrc.gov.np

Office of Graduate Studies
Faculty of Nursing, Burapha University
169 Longhad Bangsaen Rd., Chon Buri, THAILAND 20131
Tel : +66 38 102 836 Fax: +66 38 393 476

MOE 6206/ 0455

February 14th, 2018

Medical superintendent
Paropakar Maternity and Women's Hospital
Kathmandu, Nepal

Subject: Asking permission for data collection

Dear Medical superintendent:

Mrs. Binita Puri is a master degree student of Faculty of Nursing, Burapha University, Thailand. Presently, she is in the process of conducting her master thesis entitled "*Consumption of folic acid in preconception and during pregnancy and its association with preterm birth among Nepalese women: A case control study*" under supervision of Associate Professor Dr. Wannee Deoisres.

In this regard, I am writing to ask your permission to allow Mrs. Binita Puri to collect data from Paropakar Maternity and Women's Hospital, Nepal, the details are as follows:

1. Collecting data in order to test the reliability of research instruments from 20 postnatal mothers at postnatal ward during the period of March 11th – 17th, 2018.
2. Collecting data from 84 postnatal mothers at postnatal ward during the period of March 18th – April 22nd, 2018.

Participants will be interviewed and asked to complete questionnaires. Should you need further information of this research project, please contact Mrs. Binita Puri at binita.puri@gmail.com.

Your kind cooperation for this matter will be highly appreciated.

Yours sincerely,

Nujjaree Chaimongkol, RN, PhD, Associate Professor
Dean, Faculty of Nursing, Burapha University
Chon Buri, 20131, THAILAND
E-mail: nujjaree@buu.ac.th
Tel: 66 38 102 809
Fax: 66 38 393 476

PARTICIPANT'S INFORMATION SHEET

2561-02-Code: 02

Dear……

I am Binita Puri a graduate student at the faculty of Nursing, Burapha University Thailand. My study entitled "Consumption of folic acid in preconception and during pregnancy and its association with preterm birth among Nepalese women." The objective of this study is to examine the association between consumption of folic acid with preterm birth and determines the consumption of folic acid prior and during pregnancy among postnatal mothers.

This study will be hospital-based case-control study. If you agree to participate in this study, you will ask to come to the separate room along with postnatal ward during interview. Researcher will help to come to the separate room and will be offer a comfortable bed then will interview you. You will be asked to complete a set of questionnaires for 10-15 minutes. Participation in this study is completely voluntary there will not be any direct personal benefit but result of the study is expected to reduce the mortality and morbidity rate of maternal and child in near future. The result is expected to create awareness regarding consumption of folic acid prior and during pregnancy and its importance on fetal health. Your participation will not harm you and your baby in anyway.

You have right to end your participation in this study at any time without any penalty. You may refuse any specific questions, remain silent or leave this study anytime. Any information received from this study including your identity will be kept confidential. Findings from the study will be presented as a group of participants, no specific information from any individual participant.

The research will be carried out by Ms. Binita Puri under supervision of my major advisor Assoc. Prof. Dr. Wannee Deoisres. If you have any questions. Please contact me # 9851105974 or by email: binitapuri@gmail.com and/ or my advisor's email ID wannee@buu.ac.th. Your co-operation will be highly appreciated.

INFORMED CONSENT

Title: "CONSUMPTION OF FOLIC ACID IN PRECONCEPTION AND DURING PREGNANCY AND ITS ASSOCIATION WITH PRETERM BIRTH AMONG NEPALESE WOMEN: A CASE CONTROL STUDY

IRB approval number: 2561-02-02
Date of collection:
Date……..Month……Years……

Before I gave my signature in below, I already have informed and explained by Ms. Binita Puri, about purposes, method, procedures, and benefits of this study, and I understood all of that explanation. I agree to be as a participant of this study.
I am Binita puri, as a researcher I have explained all about purposes, method, procedures, and benefits of this study to the participants honestly: then, all of data/ information of the participants will only be used for purpose of this research study.

Name and signature of the Participants Date

बुराफा विश्वविद्यालय
नर्सिङ संकाय
चोन्बुरी, थाईल्याण्ड

सुसुचित मञ्जुरीनामा

नमस्कार, म विनिता पुरी, अनुसन्धानकर्ता, बुराफा विश्वविद्यालय, नर्सिङ संकाय, चोन्बुरी, थाईल्याण्डमा स्नातकोत्तर तह द्वितीय वर्षमा अध्ययनरत छात्रा हुँ । म यहाँ **"नेपाली महिलाहरुमा गर्भवती हुनुअघि र गर्भवती अवस्थामा फोलिक एसिड खाने अभ्यास र समय नपुगी जन्मेका शिशुहरूसँगको सम्बन्ध"** शिर्षकमा अनुसन्धानको लागी उपस्थित भएकी हुँ । यो अनुसन्धान नर्सिङ्ग विषयको स्नातकोत्तर तहको पाठ्यक्रमको आंशिक आवश्यकता पूरा गर्नको लागी गर्न लागिएको हो । यो अनुसन्धान गर्नका लागी बुराफा विश्वविद्यालय, नर्सिङ संकाय, चोन्बुरी, थाईल्याण्डको इन्स्टिच्युसनल् रिभ्यू बोर्डबाट अनुमति प्राप्त भइसकेको छ । यस अनुसन्धान बाट तपाइँलाई कुनै पनि क्षति हुनेछैन । तपाइँले आफ्ना अनुभवहरू भनेर यस अनुसन्धानमा योगदान गर्नसक्नु हुनेछ । तपाइँले भनेका जवाफहरु अनुसन्धानकर्ता द्वारा फारममा लेखिनेछ । यसका लागी तपाइँले १५ देखि २० मिनेट समय दिनुपर्नेछ । तपाइँका बहुमूल्य जवाफद्वारा सेवाप्रदायकलाई सेवालाई अझै राम्रो बनाउन मदत पुग्नेछ । यस अध्ययनमा तपाइँका सहभागिता पूर्ण स्वैच्छिक हुनेछ । यसका साथै यस अनुसन्धानमा तपाइँ आफ्नो ऐच्छिक सहभागिता रहनेछ ।

आफूले चाहेमा कुनैपनि समयमा विना कुनै शंकोच छोड्न सक्नु हुनेछ । अनुसन्धानकर्ता तपाइँलाई यो विश्वास दिलाउन चाहन्छ कि यहाँहरू बाट प्राप्त सम्पूर्ण विवरण गोपनिय ढंगले राखिनेछ र प्राप्त विवरण विशुद्ध यस अध्ययनको लागी मात्र प्रयोग गरिनेछ ।

यहाँका व्यक्तिगत विवरण कतैपनि उल्लेख गरिने छैन । यहाँ प्रस्तुत गरिएका प्रश्नहरूको उत्तर दिई अनुसन्धानमा सहयोग पुऱ्याइदिनु हुनेछ भन्ने आशा व्यक्त गरिएको छ ।

यहाँ उल्लेखित सम्पूर्ण जानकारीहरू बुझ्नुभयो र के तपाइँ यस अनुसन्धानमा सहभागी हुन चाहनुहुन्छ ?

मञ्जुरीनामा,

मैले यस मञ्जुरीनामा पूरै पढेको छु र यहाँ उल्लेखित सबै कुरा साथै यसको उदेश्य बुझेको छु । मैले मेरा सबै प्रश्नहरुको चित्त बुझ्ने गरि उत्तर पाइसकेको छु । तसर्थ यस अनुसन्धानमा मलाई सहभागी बनाउन म अनुमति दिन्छु । यस मञ्जुरीनामा सही गर्दा मैले आफ्नो कुनै पनि कानुनी अधिकार हनन् हुन दिएको छैन ।

दाँया	बाँया

सहभागीको लागि मात्र

सहभागीको सही

अनुसन्धानकर्ताको सही

मिति :

तपाइँको सहयोग र सहभागिताको लागी धन्यवाद

APPENDIX D

List of experts for content validity of the instruments

LIST OF EXPERTS FOR CONTENT VALIDITY OF THE INSTRUMENTS

1. Amit Rauniyar, MBBS, MD	Gynecologist Paropakar Maternity and Women's Hospital, Kathmandu, Nepal
2. Astha Tiwari, MBBS, MD	Obstetrician Paropakar Maternity and Women's Hospital, Kathmandu, Nepal
3. Elina Joshi, MN	Coordinator Tribhuvan University, Institute of Medicine, Nursing campus, Biratnagar, Nepal
4. Sheela Thapa, MN	Teaching Assistant Tribhuvan University, Institute of Medicine, Nursing campus, Biratnagar, Nepal
5. Bidhya Basnet, MN	Teaching Assistant Tribhuvan University, Institute of Medicine, Nursing campus, Biratnagar, Nepal

BIOGRAPHY

NAME	BINITA PURI
DATE OF BIRTH	09 August 1980
PLACE OF BIRTH	Chitwan, Nepal
POSITION HELD	Post basic bachelor of nursing, Chitwan Medical college, Nepal Master of nursing science, Burapha University, Thailand
HOME ADDRESS	Kalankisthan-14, Kathmandu, Nepal
INSTITUTIONS ATTENDED	Post basic bachelor of nursing, Chitwan Medical college, Nepal Master of nursing science, Burapha University, Thailand