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Association between deworming during pregnancy and low birth weight

A secondary analysis of Pakistan Demographic Health Survey 2017-18 data

Munazzah Ali

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Supervisor: Syed Moshfiq Rahman

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Abstract

It is estimated that about 22% of all births in Pakistan are low birth weight (<2500g), representing approximately 198,000 births per year. One of the major causes of low birth weight is maternal anemia. In Pakistan approximately 52% of pregnant women are anemic and one of the most common cause of maternal anemia is soil-transmitted helminthic infection. Soil-transmitted helminthiasis is endemic in Pakistan carries the highest burden of infection in Eastern Mediterranean region. Despite the recommendations deworming the mother during pregnancy is not being commonly practiced in routine antenatal care.

We hypothesized that there is an association between deworming during pregnancy and low birth weight. For this study, cross sectional analysis of secondary data from the latest Pakistan Demographic Health Survey (PDHS conducted in 2017-18 and released in 2019) was done. Total N=1403 mother and child were included, logistic regression was used to determine the association between deworming during pregnancy and low birth weight after adjusting for potential confounders.

We found no statistically significant association [aOR 0.63, 95% CI (0.21-1.83)] between deworming during pregnancy and low birth weight. Moreover the mothers who belonged to higher socioeconomic status [aOR 0.41, 95% CI (0.22- .76)] and attained higher education [aOR 0.55, 95% CI (0.34- .87)] had reduced odds of having a new born with low birth weight compared to newborn of the women from low socioeconomic status and had no education, respectively. Further research is needed to explore effectiveness of deworming during pregnancy at population level.

Abbreviations

aOR	Adjusted Odds Ratio
ANC	Antenatal Care
BMI	Body Mass Index
CI	Confidence Interval
DHS	Demographic Health Survey
PDHS	Pakistan Demographic Health Survey
FOAD	Fetal Origin of Adult Disease
GBD	Global Burden of Disease
HIV	Human Immune deficiency Syndrome
IQ	Intelligence Quotient
LBW	Low Birth Weight
OR	Odds Ratio
SES	Socio Economic Status
SDGs	Sustainable Development Goals
SPSS	Statistical Package for Social Sciences
STHs	Soil-Transmitted Helminthes
UNICEF	United Nation Children's Fund
USAID	United States Agency for International Development
WHO	World Health Organization
WHA	World Health Assembly

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1. Introduction

1.1Low birth weight and global prevalence

According to World Health Organization (WHO) low birth weight is defined as weight of a newborn less than 2500 grams or 5.5 pounds (1). Globally approximately 1 in 7 newborns have low birth weight. The major causes of low birth weight are preterm births (neonates born less than 37 weeks of gestations), small for gestation at term (growth restricted) and both early and small for gestational age. Low birth weight is a major public health concern. It is a major risk factor for neonatal morbidity and mortality with short and long term consequences for the infant (1–3).

It has been estimated that globally 15 to 20% of newborns are low birth weight, constituting more than 20 million births per year. In-addition, more than half of these births occur in South Asia. The regional distribution of low birth weight prevalence is, Asia 17.3% with 12.8 million births, Africa 13.7% with 5.7 million births, 9.9% in Oceania with 1.4 million births and 7.2% in other regions of the world with 1 million births (4) (5). The statistics reveal that large distinctions exist further within the regions. Indeed Southern Asia carries the highest burden in the world with a prevalence of 26.4% low birth weight infants (4).

Even though large burden exists in low and middle income countries, there are disparities in prevalence of low birth weight within the countries and populations at risk. It is worth noting that the above mentioned estimates do not include the percentage of infants who are not weighed at birth. The data is limited due to home deliveries and births at health care facilities that are not reported at official level. According to the estimation the region of South Asia has the highest percentage of around 66 % of infants that are not weighed at birth, Sub-Saharan Africa 54% and Latin America 10%. Therefore it is important to note that in spite of the high prevalence of low birth weight the rates might be underestimated (1,5)

According to report by UNICEF (United Nations Children's Fund) and WHO (World Health Organization) on low birth weight estimates, it has been evaluated that since the year 2000 to 2015, globally there has not been a progressive decline in the overall burden of low birth weight. In the past 15 years around the world no region has progressed significantly in reducing the prevalence of low birth weight among infants (6).

1.1.1 Causes and consequences of Low birth weight

Low birth weight in infants is multifactorial and is closely associated with neonatal morbidity and mortality (1). Preterm births, growth retardation and a combination of both are the most frequent causes of low birth weight in infants. Various factors affect the duration of gestation, the growth of fetus and consequently the weight of the newborn (7). The determinants involved are grouped in accordance with the causes related to the mother, the fetus, the physical environment or a combination of these (8,9) as shown in the figure 1. It has been evident that hereditary and constitutional factors undermine the fetal growth. It is anticipated that 40% hereditary and 60% environmental factors are involved in determining the birth weight of the infant (10).

Several factors related to the mother influence the weight of the new born. The socio-demographic factors contributing to birth weight of infant involve maternal age, ethnicity, marital status, education level and socioeconomic status (10). Maternal medical conditions affecting placenta-fetal circulation such as hypertension, diabetes, anemia malnutrition and infections have a significant impact on birth weight of the infant (7,11). Environmental and behavioral factors comprise of maternal work and stress, smoking and alcohol consumption and exposure to toxins (7). Genetic factors that influence fetal development include mother's own fetal growth, nutrition and congenital fetal anomalies. At the time of pregnancy the nutritional status, health and lifestyle of the mother (e.g. alcohol, smoking, and drug abuse) primarily determine the growth and development of the fetus as well as the duration of gestation (10). Mothers with low socioeconomic conditions also have an increased risk of having low birth weight infants due to poor nutrition, high prevalence of infections which are complicated due to poverty and limited access to health facilities (1,12). It has been evident that maternal under-nutrition during prenatal and neonatal period is substantially involved in the development and growth of the fetus (10).

Low birth weight is significant public health concern since it has serious consequences for the infant during perinatal period, infancy and adulthood (1). The importance is well understood by the concept of Fetal Origin of Disease (FOAD) also known as Barker's hypothesis. According to Barker's hypothesis the incidents that occur during early development of fetus have an influence on the fetus's risk for developing future adult disease (13).

During perinatal period it is the second most common cause of death (5). The low birth weight infants have 20% increased risk of dying as compared to an infant with normal birth weight (14). Apart from increased mortality among the neonates, low birth weight infants are also at a potential risk of poor cognitive development. It has been anticipated that the intelligence quotient (IQ) is lower among the infants born with low birth weight as compared to infants with normal birth weight, at the same time depending on the cause of growth restriction, the duration of impairment and the time of occurrence. Studies have demonstrated that intelligence quotient (IQ) of infants who were growth restricted and infants who were preterm along with growth restriction had 3.3 points and 6.7 points lower IQ respectively than infants born with normal weight (15).

Furthermore in adulthood these individuals have increased odds of developing long term illnesses latter as described in Barker's hypothesis (13). Epidemiological studies have illustrated a striking link between low birth weight and chronic diseases subsequently in life. These individuals are more likely to acquire medical conditions such as type II diabetes, hypertension and cardiovascular diseases in adulthood. It is noteworthy that intergenerational impact of low birth weight has been highlighted in several studies. The intergenerational cycle demonstrates that females infants born with low birth weight are consequently at risk of giving birth to smaller infants at the time of pregnancy and the cycle goes on (3, 10).

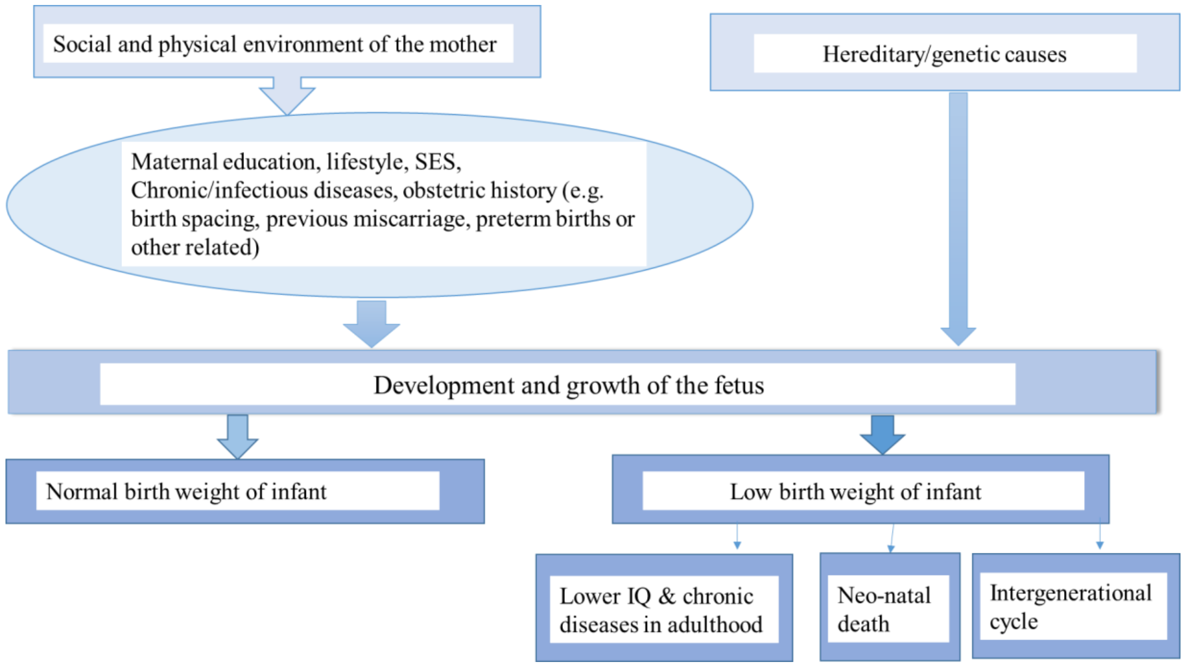

Fig 1- Brief description of determinants of birth weight of infant and consequences of LBW.

In the context of the widespread and prevailing malnutrition, in 2012 at 65th World Health Assembly a resolution "Comprehensive implementation plan on maternal, infant and young child nutrition" was introduced. Taking into consideration the interlinked drivers of malnutrition six global nutrition targets were established to be achieved by year 2025 (16). Among the six global nutrition targets, 2nd target focuses on 50% reduction of anemia in women of reproductive age and 3rd target focuses on 30% reduction in low birth weight. In order to accomplish these targets by the year 2025 and ultimately attaining Sustainable development goals (SDGs) by 2030, World health organization (WHO) came up with policy briefs for all the nutrition targets. These policy briefs comprise of evidence-based interventions and recommendations compassing from national to individual level (1,17). Furthermore for the reduction in prevalence of anemia among pregnant women apart from iron and folic acid supplementation, deworming medication was identified as an effective intervention (preventive chemotherapy) during second or third trimester of pregnancy to control and prevent maternal anemia during pregnancy in regions with high prevalence of Soil Transmitted Helminthes infection (17).

1.1.2 Treatment and prevention of low birth weight infants

Low birth weight contributes to an overall 60-80% of neonatal deaths globally (5). These neonatal deaths owing to low birth weight and pre-term births can be prevented by interventions focusing on care of the newborn. These measures comprise of appropriate feeding of newborn, maintenance of body temperature, hygienic cord and skin care, prompt detection and treatment of infections. All these interventions are considered to significantly reduce the neonatal mortality. However unfortunately the risk of developing chronic diseases and associated morbidity cannot be reversed (18).

The best possible strategy to reduce prevalence of low birth weight and its consequences is by the primary prevention (7). This involves identification and averting the risk factors involved in the hindrance of development and growth of the fetus and consequently improving the birth weight among infants. Majority of the causes and risk factors mentioned above are related to the mother and are constitutional in nature where a cause proceeds to an effect (7). Therefore in order to give birth to healthy child, the mother needs to be healthy. A comprehensive approach towards improving maternal nutritional status along with social support. Besides providing adequate and quality antenatal care which comprises of dietary advice, nutritional supplementation as per need and early detection of high risk pregnancies is essential. Similarly appropriate postnatal care plays an important role in growth and development of children (1).

1.2 Anemia during pregnancy

Anemia during pregnancy is a major problem encountered worldwide (19). Anemia is defined as a condition in which the number of red blood cells or their oxygen-carrying capacity is insufficient to meet the physiologic needs, which vary by age, sex, altitude, smoking, and physiological status of the body (17). Anemia in pregnant women is crucial because it enhances the risk of poor pregnancy outcomes and increases neonatal morbidity and mortality (17,20). Some of the major causes of anemia include nutritional deficiencies, chronic infections, and genetic disorders such as thalassemia and sickle cell anemia (21). Maternal anemia during pregnancy can easily remain undiagnosed during pregnancy due other obstetric priorities and busy antenatal clinics. Clinical assessments such as skin and mucosal pallor usually remain non-specific. The recommended cutoff for hemoglobin concentration of 110g/l has been set with the purpose to identify and target the population at risk. However current guidelines suggest 110g/l as non-anemic state, 100-109g/l as mild anemia, 70-99g/l as moderate anemia and less than 70g/l as severe anemia (22).

Anemia during pregnancy has adverse outcomes for both mother and the newborn (23). In pregnant woman it reduces the productivity and work capacity. It is also recognized as one of the major cause of post-partum hemorrhage which is consequently the foremost cause of maternal mortality (24,25). Globally anemia among pregnant women contributes to be a direct cause of 20% maternal deaths (17). Anemia in pregnancy also contributes to perinatal morbidity and mortality. Anemic pregnant women are likely at a risk of having preterm births, low birth weight infants and small for gestational age babies. Furthermore the studies also show that maternal anemia during pregnancy and at the time of birth was also strongly associated with child anemia (26).

1.2.1 Relation between anemia during pregnancy and low birth weight

Maternal anemia during pregnancy is a major risk factor for intrauterine growth restriction, preterm births and consequently low birth weight (27). Studies provide the evidence that U-shaped association exists between maternal hemoglobin concentration during pregnancy and birth weight of the newborn. This manifests that severe anemia and abnormally high hemoglobin concentrations during pregnancy both have an impact on birth weight of the newborn (11).

Several studies in middle and low income countries have found an association between maternal anemia during pregnancy and low birth weight. Evidence have revealed that the risk of having low birth weight babies was 1.6 times higher in moderate and 4.8 times higher in severely anemic women as compared to non-anemic pregnant women (28,29). A systematic review analysis evaluated that 12% of low birth weight and 19% of preterm births were attributable to maternal anemia during pregnancy in low and middle income countries. The percentage is much higher specially in low income countries where anemia in pregnant women resulted in 44% preterm births and 25% of low birth weight babies (23).

1.2.2 Iron deficiency anemia during pregnancy

Iron deficiency anemia is the most common cause of maternal anemia during pregnancy accounting for approximately 75-90% cases (23). Iron is an important trace element which is primarily involved in the transportation of oxygen and is required for the normal body functions.

During pregnancy in fetus it is significantly involved in the development of the central nervous system (30). Pregnancy is a state of high iron demand in the body. On average the pregnant woman requires 1000mg of additional iron throughout pregnancy (31,32). Iron demand and absorption is reduced during first trimester but increases to about 4-6mg per day during the second and third trimester of pregnancy. To meet the increasing demand during pregnancy a women should have additional 300mg of iron stores prior to conception (31–33). Therefore suboptimal or reduced iron stores prior to conception is associated with an increased risk of anemia during latter half of pregnancy with adverse maternal and perinatal outcomes (28,31).

1.2.3 Causes and management of iron deficiency anemia during pregnancy

Iron deficiency anemia is the most common cause of maternal anemia during pregnancy accounting for approximately 75-90% cases. The most common causes of iron deficiency anemia include blood loss, infections such as malaria and diet poor in nutrients and malabsorption (32). The most prevalent causes of blood loss include excessive bleeding during menstruation, hemorrhage, and hookworm infections (28,34).

For the control and prevention of maternal anemia during pregnancy several interventions have been recommended according to the context and individual needs. These interventions included intermittent iron and folic acid supplementation, improved dietary habits, food fortification, control of infections such as malaria and deworming medication after first trimester (17).

1.3 Deworming during pregnancy

Deworming is giving anthelmintic drugs to treat worm infestation in the body. Soil transmitted helminthiasis (STH) are the result of intestinal worms Ascaris lumbricoides (roundworm), Trichuris trichiura (whipworm), Necator americanus and Ancylostoma duodenale (hookworm) (32). These worm eggs or larvae enter the human body by oral-fecal route (when an individual comes in contact with contaminated food, water or fecal matter containing worm eggs) or penetrate through skin (35). The worm grows and attaches itself to the intestines and feeds on the host tissue. These intestinal worms also release an anti-coagulant at the site of attachment which results in loss of blood from the host body of around 0.3-0.5 ml per day. With the exception of feeding on host tissue and causing anemia, helminthic infection has also been found to have an immune-modulatory effect on the host. Chronic helminthic infections are considered to inhibit, modify or alter the immunologic responses of the body (36,37).

Helminthic infections affect around one third of the world's population with high burden of disease particularly in low and middle income countries. Globally the impact of worm infection is estimated to cause 30 million disability adjusted life years (DALYs) almost equivalent to worldwide impact of malaria or tuberculosis (38). Pregnant women are identified as a risk group for the helminthic infections due to altered immune regulation during pregnancy and increasing the susceptibility to infections. It has been estimated that globally around 10% of pregnant women are at risk of STH infection and around 26.7 million pregnant women live in areas where prevalence of worm infection is >20% and more than 5 million pregnant women require preventive deworming medication (39).

Chronic blood loss from soil transmitted helminthes is one of the major reason for persistent anemia in pregnant women and has been one of the most common cause of iron deficiency anemia in poor communities with lack of proper sanitation and hygiene facilities (40). Apart from being fatigued and reduced work capacity due to iron loss, the infected individual usually remains asymptomatic. However in case of heavy infestations the complications such as intestinal obstruction and biliary ascariasis may occur (34,41).

With the exception of feeding on host tissue and causing anemia, helminthic infection have also been found to have an immune-modulatory effect on the host. Chronic helminthic infections are considered to inhibit, modify or alter the immunologic responses of the body. The worm infection during pregnancy alter the immune response and thus increase the susceptibility of pregnant women to infections (42,43). A study in Nigeria among children and pregnant women resulted in altered cytokines expression among worm (helminthic) infected group as compared to control group. These results also raise the concern regarding impaired immune function and vaccine responsiveness in children and pregnant women (44). In addition a randomized control trial conducted among Human Immune-deficiency Virus (HIV) infected pregnant women estimated the viral load and helminthic infections in Uganda. The study showed worm infection increased the HIV viral load during pregnancy and a decline in viral load was observed when treated with anthelmintic medication (45). In Rwanda another study was conducted among pregnant HIV positive women having worm infection. The findings showed an improved CD4 count, hemoglobin concentration and reduced viral load among the pregnant women treated for helminthic infection (46). Hence more research is required to explore further interactions of helminthes and human immune responses.

Moreover a study in China suggested the vertical transmission of Ancylostoma duodenale (round worm) from mother to child. The eggs of the worms were examined in the feces of infants following 1-26 days after birth. These finding illustrated a transmission from mother via placenta or breast milk (47,48). Therefore the evidence of possible vertical transmission of STH infection from mother to child highlight the significance of antihelminthic (deworming) during pregnancy.

An effective drug for worm infestation was discovered long ago in 1980s but due to the fear of teratogenic effect its role during pregnancy could not be analyzed. Globally maternal hookworm infections complicate around 44 million pregnancies (49). The complications occur due to risk factor of anemia that is a consequence of the blood loss due to worm infection. Deworming during pregnancy has been influential in reducing the worm infection which subsequently is considered to reduce maternal anemia and related morbidity and mortality (50). Deworming medication has been recommended by WHO as an intervention to control and prevent anemia among pregnant women particularly those living in regions endemic for STHs.

Deworming during pregnancy has been practiced in research projects in some countries. For example in Cambodia the non-government organizations are providing deworming among the plantation workers in adjunct to malaria control activities. The deworming coverage among women of reproductive age is estimated to increase from 30-50%. The inclusion of deworming pregnant women on a national level is being practiced in a few countries. In 2013 the Ministry of health Peru recommended inclusion of deworming medication during pregnancy in endemic areas. Indian Ministry of Health and Family Welfare are focusing on also implementing deworming program for pregnant women. National guidelines suggest deworming along with safe water and sanitation, and nutritional interventions (39). Besides Sri Lanka and Nepal have included deworming in routine antenatal care packages (51).

Various studies reveal that deworming during the second trimester of pregnancy has proved to be beneficial in improving the maternal hemoglobin concentration. In a community based study in rural Nepal, pregnant women were given deworming medication twice during second trimester along with multivitamin supplementation throughout pregnancy. The results showed an increase in hemoglobin concentration from <70 g/L towards 90-110g/L in women who took deworming medication during pregnancy (52). Similarly in Sri Lanka deworming during pregnancy resulted in improved hemoglobin concentration in pregnant women (53). In Pakistan a study conducted to estimate the efficacy of multivitamins and enhanced deworming medication (mebendazole) in severely anemic pregnant women. The analysis revealed that increase in hemoglobin concentration was more pronounced among women who were given enhanced medication (54). Experimental studies have shown that deworming pre-conceptually and during pregnancy along with iron supplementation was also beneficial for improving maternal hemoglobin concentration (40,55,56).

Furthermore there has been beneficial impact of deworming during pregnancy on birth outcomes as well. The understanding of deworming in relation to birth outcomes is through the phenomenon of reduction in anemia which in turn results in healthy growth and development of the fetus. Mothers who are dewormed during pregnancy tend to have an improved birth weight of their babies (50,57). Additionally the proportion of very low birth infants (birth weight <1500grams) has found to be low in mothers who were dewormed during pregnancy (58).

In Nepal a study estimated the differences in birth weight and survival of infants born to mothers who received deworming medication twice and those who were not dewormed during pregnancy. The results illustrated an increase of 59grams in birth weight of infant born to mothers who were dewormed during pregnancy. Additionally the infant survival also improved and resulted in 41% reduction in infant mortality at 6 months (52). While on the other hand in Uganda a study determined that deworming medication during pregnancy had no effect on the birth weight of the newborn. However it was concluded that the results might vary due to the fact that the prevalence of worm infection was high in the region but the intensity of infection was low (59). These evidence suggest that effect of deworming on birth outcomes is context specific depending on the disease intensity and treatment schedule.

The deworming medication during pregnancy has no adverse effects on mother and infant. The mothers who received deworming medication during pregnancy did not show symptoms of any adverse reaction or worsening of any symptoms. There has been no increase in frequency of miscarriage, prematurity or still birth in association to deworming drugs (50,58,60). During pregnancy deworming medication is also considered safe for the fetus, no reported increase in perinatal and infant mortality has been reported as a result of deworming medication. No congenital abnormality have been associated when deworming medication is given after first trimester. However deworming medication is contraindicated during first trimester of pregnancy due to the fear of birth defects in developing fetus (60,61). Furthermore there is no association of incidence of malaria, diarrhea and pneumonia among infants when mother receives deworming drugs during pregnancy (62).

1.4 Burden of Low birth weight in Pakistan

According to UNICEF it has been evaluated that 83% of live births in Pakistan lack the recorded birth weight (63). There has been a problem for estimating the magnitude of the problem in low and middle income countries. In low and middle income countries due to less number of institutional births it is difficult to give an estimate of the low birth weight in these countries. Meanwhile Demographic and Health Survey (DHS) have child birth size as perceived by the mother to get an estimation of weight of babies delivered at home. For the reason to get an estimate of low birth weight infants, the very small size and smaller than average are grouped as one to get an idea about infants below normal weight at birth (17).

In PDHS 1990-91 it was estimated that 88% of births were not delivered at health facility indicating that 9 in 10 children were born at home. Only 8% of total births were weighed at birth. Out of those 8% infants weighed at birth, 1.2% were low birth weight. In addition to that 24 % infants were reported to have small size at birth (64).

According to PDHS 2006-07, of the total infants weighed at birth, 26% were low birth weight. Besides of the total live births, 31% children had small size at birth (65). The infants weighed at birth improved to 12.2 % in 2012-13. Out of total weighed at birth, 25% were low birth weight. Furthermore according to latest PDHS 2017-18 report, of the total live births 16% are weighed at birth and 22% of those are low birth weight. Further to among the total live birth 18.8% had small size at birth. These estimates reflect the burden of the problem (66).

1.5 Conceptual Framework

Owing to the complex and multi factorial causes of low birth weight, a conceptual framework has been developed to demonstrate the role of deworming during pregnancy and its association to low birth weight. This framework suggests that worm infestation causes anemia among pregnant women and which in turn effects the birth weight of the infant as shown in figure 2. However taking into account the fact that the socioeconomic status of the mother, access to clean water and sanitation facilities, environmental conditions, maternal health and nutrition have a possible impact on anemia and other health related problems may ultimately have an effect on birth weight of infants. Meanwhile for the purpose of this thesis we will focus only on deworming and low birth weight. A comprehensive list of variables will included and can be found under the heading of "co-variants" in the methods section.

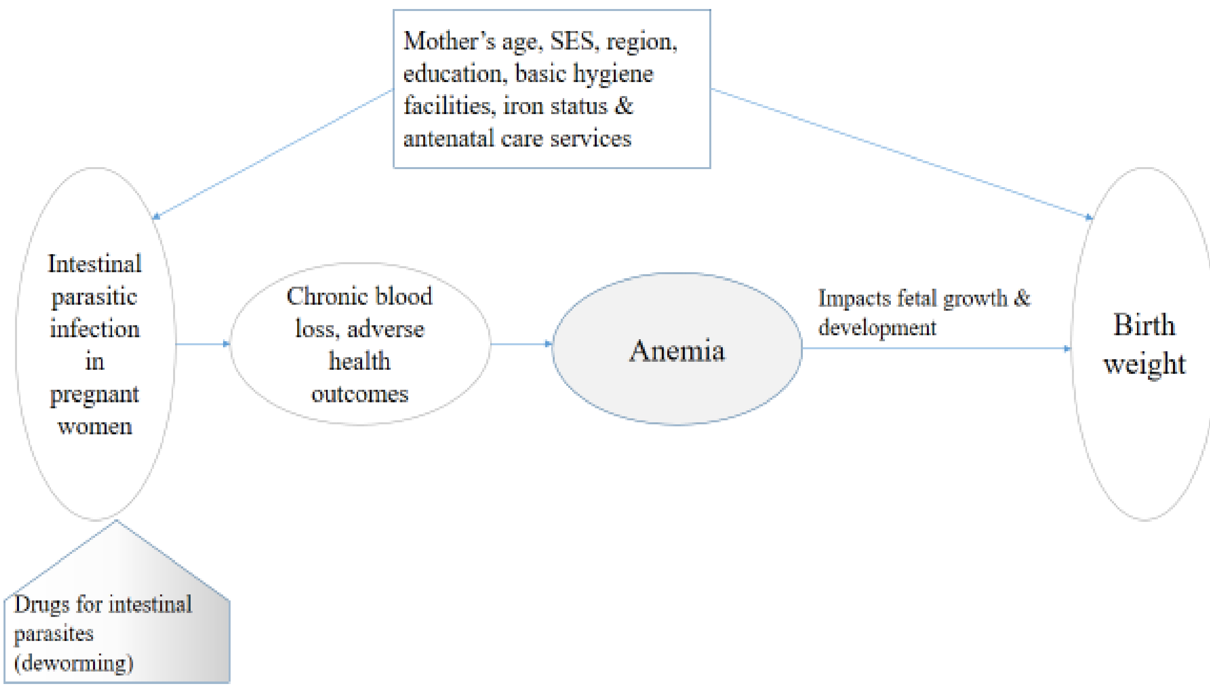

Fig 2- Flow chart illustration of the conceptual framework

1.6 Justification

After independence of Pakistan in 1947, the country has experienced a surge of illiteracy, poverty and malnutrition which has been further enhanced by political instability and conflict in the country. Despite the circumstances Pakistan has made progress in improving public health. However impoverishment and related health consequences remain prevalent (67).

The major determinants of low birth weight in Pakistan include maternal age, maternal anemia and previous obstetric history (68). Anemia during pregnancy is significant public health concern in the country. The prevalence of anemia in pregnant women is estimated to be 52% and has remained stagnant for the last two decades (69). Among anemic pregnant women iron deficiency anemia was found in approximately 90.5% of the pregnant women (70,71).

According to World Bank classification Pakistan is a lower middle income country. Approximately 60% of the population lives in rural areas and 30% of the population lives below the country's poverty line and around 12 million people currently live on less than $1,90USD per day. As a consequence malnutrition and increasing maternal and infant morbidity and mortality remains widespread (72,73). In 2013 an estimate of Global Burden of Disease (GBD) survey stated Pakistan among the top 10 countries in regards to high number of Neglected Tropical Disease (NTD). Among the NTD, soil transmitted helminthic infections are found to be the most prevalent NTDs in Pakistan (74).

According to WHO, Pakistan has the highest burden of soil-transmitted helminthic (STHs) infection in the Eastern Medeterrain region (75). Around 13% of the population is infected with worm infection and approximately 32 million children are at risk and require deworming medication (67). It is interesting to mark that the prevalence of infection among the population has remained almost the same over the last 25 years (67,74).

Despite the high burden of disease and recommendations for deworming women during pregnancy in endemic countries, anti-helminthic are not included in antenatal care packages and not practiced as routine during antenatal care. Keeping in mind the close interaction of mother and child, deworming programs and preventive medication for worm infection are only targeted towards children. Currently the government efforts in combating malnutrition are more focused towards fortification of staple food. Very few programs are focusing on improving anemia among pregnant women mainly by multi-vitamin supplementation during pregnancy. (76).

A positive association between antenatal care and birth outcome exists. It has been evident that good quality antenatal care results in better birth outcomes. Quality antenatal care is more focused towards the individual needs of the women and promptly addressing the high risk pregnancies. It also involves educating the women regarding consumption of nutritious diet during pregnancy and lactation and also informing women about the danger signs throughout pregnancy (77). Since the year 1990 antenatal care coverage in Pakistan has improved. Nearly 9 in 10 women receive antenatal care by a skilled health care provider. In-addition 86% women have at least one contact with antenatal care facility during antenatal period and 51% have 4 or more visits during antenatal period (66).

Owing to the increased antenatal coverage in the country this would be an opportunity for policy makers to review the inclusion of anti-helminthic - a low cost intervention in routine antenatal care packages in Pakistan. Whereas current estimates reveal that around 2% of the women receive deworming medication during pregnancy (66). This low cost intervention has proven to be effective in resource constrained settings. A pilot study in Vietnam involving women aged 15-45 years were given iron supplementation along with deworming medication. This resulted in reduction of the prevalence of anemia from 40%- 24% among all women of reproductive age. In Nepal deworming during pregnancy along with iron supplementation has resulted in improved anemia among mothers and increased the birth weight among newborn (17,78).

In the view of the above mentioned concern regarding prevailing anemia among pregnant women and burden of low birth weight in Pakistan this study hypothesized that the high prevalence of helminthic infection might be a contributing factor to iron deficiency anemia among pregnant women in Pakistan. Hence deworming medication as a treatment for helminthic infection might help improve anemia and consequently reducing the low birth weight among newborn.

1.7Aim of the study

The overall aim of this study is to evaluate the birth outcome mainly the birth weight of infants born to mothers that were given deworming medication during pregnancy. The hypothesis is that the mothers receiving deworming medication during pregnancy will be less likely to have infants with low birth weight.

The main objectives of the study will be

1. To evaluate the association of deworming during pregnancy and low birth weight.
2. To describe and analyze the prevalence of low birth weight, and its distribution by socio-demographic variables and selected maternal characteristics.

2. Methods

2.1Study Design

This is a cross-sectional study based on secondary analysis of data available from Pakistan Demographic Health Survey (PDHS) 2017-18. The data collection was done during November 2017 to April 2018. The survey was done in co-operation with the Pakistan bureau of statistics funded by Unites States Agency for International Development (USAID). The sole purpose of the survey was generating information on the current health status indicators of the population in the country.

2.2 Study setting

Pakistan is located in South-Asia covering a land mass of 881,913 square kilometers. Pakistan is bordered in South by Arabian Sea, India in East, Afghanistan in West, China in North-East, and Iran in South-West as shown in figure 3. The country is subdivided into administrative divisions which are further sub-divided into districts, tehsils and ending to union councils.

Pakistan is a lower-middle income country with a rapidly increasing population. In 2017 national population census revealed a population of 207 million with a growth rate of 2.4% considering it the fifth most populous country in the World. The median age among population in Pakistan is 22.5 years with a sex ratio (female proportion) of 48.6%. Pakistan is an agricultural country with major by-product of cotton, textile, and rice. Approximately 42.02% of the population is involved in agriculture labor (79,80). The Pakistan Demographic Health Survey (PDHS) 2017-18 was conducted in all the provinces of the country including Azad Jammu Kashmir (AJK) and former Federally Administered Tribal Areas (FATA).

Fig 3- A Picture showing the map of Pakistan (66).

2.3 Study Population

The total 11,869 number of households were interviewed in (PDHS) 2017-18. Of the total participants women had a response rate of 95.3% and men had a response rate of 86.5%. All the men and women included were aged 15-49 years and ever married (66).

Inclusion criteria for this study were ever married female, age- 15-49 years, minimum one birth at the time of data collection or in the past five years, single pregnancy, history of drug for intestinal parasite (deworming) during pregnancy and the birth weight of the child born (written record or mother's recall).

Women who were currently pregnant at the time of data collection and women with no birth in the last five years and had twin child or multiple pregnancy were excluded. Children with no birth weight information were also excluded. Missing and incomplete data was also excluded as shown in figure 4.

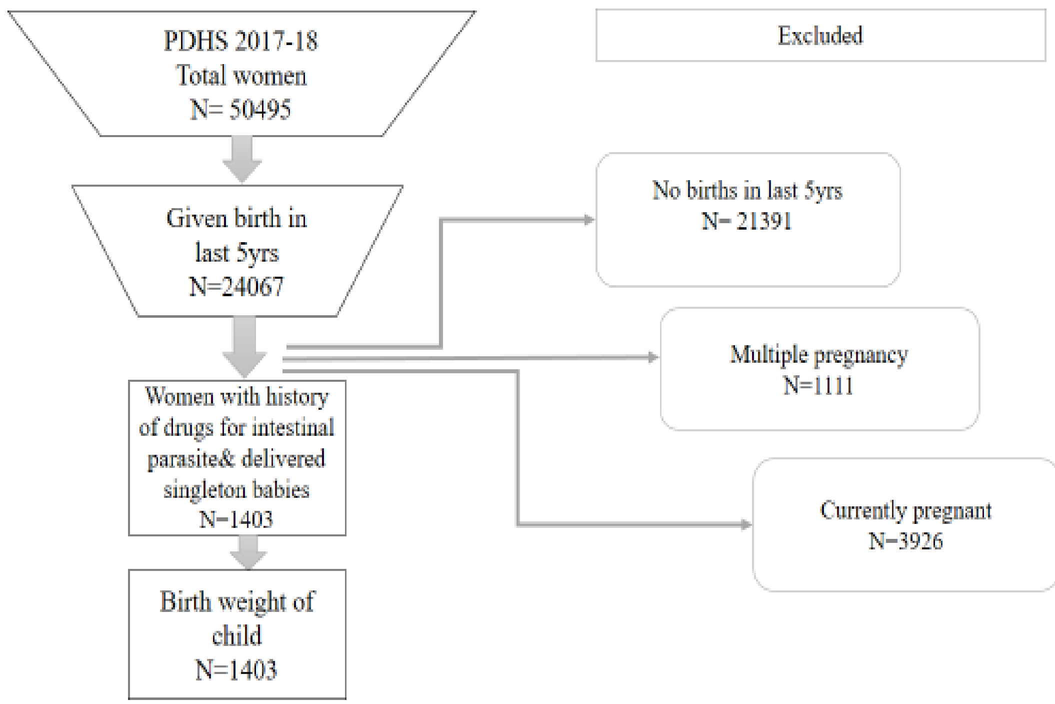

Fig 4- Flow chart demonstrating that participants of the study from the data available from PDHS 2017-18.

2.4 Sample Size

The selection process for this study is illustrated in the figure 4. Among the total sample women who did not give birth in the last 5 years, had twin child or multiple pregnancy and those women who were currently pregnant were excluded. Accordingly the women who gave birth during the last 5 years were separated. Based on the data available from PDHS 2017-18 the women who took deworming drugs (yes/no) during pregnancy N=6691. Furthermore among those, women with a child not weighed at birth N=4139 and birth weight of infant not known N= 1449. Thus the women who took drugs for intestinal parasites (yes/no) during pregnancy and had (written record or mother’s recall) weight at birth (normal/low birth weight). This yielded the sample size N= 1403.

In-addition the women who had missing response or a response of “don’t know” for drug of intestinal parasite during pregnancy was also excluded. The women with the child birth weight response was “don’t know”, missing or “not weighed at birth” were also excluded.

2.5 Data collection

The information comes from participants interviewed according to the standardized women's questionnaire of Demographic Health Survey (DHS) which is to be used in secondary analysis of the data. The interviews were conducted by the fieldworkers in Pakistan. Interviewing is done according to the interviews manual provided by DHS program and the interviewers belong to different regions of the country with knowledge of different languages. Therefore use of interpreters is usually discouraged and third party is involved in case the problem of language cannot be solved otherwise (66).

2.6 Methods and Variables

The Statistical Package for Social Sciences (SPSS) software 25th trial version has been used for descriptive statistics and statistical analysis. After being granted access to data for PDHS-2017-18 by submitting a request from dhsprogram.com, the variables of interest were selected from birth recode data file of PDHS 2017-18.

2.6.1 Exposure variable

The main exposure variable deworming was assessed by from mother's response to the question "During this (last) pregnancy, did you take any drug to get rid of worms in your intestines?" Here a dichotomous variable was developed to inquire the presence and absence of drugs for intestinal parasite (treatment and control respectively). The variable was assigned a value of 1 if women took deworming medication during pregnancy and a value of 0 if she did not have deworming medication during pregnancy. In-addition the name of deworming drug used was not mentioned neither in data available nor in the final report for PDHS 2017-18.

2.6.2 Outcome variable

The outcome variable (birth weight of the infant) was only the numerical birth weight data attained from written record on birth cards and in few cases mother's recall. Data for birth weight of infants born in last five years to mothers with a history of deworming medication (yes/no) preceding the DHS 2017-18 survey in Pakistan. The outcome variable were used to measure the birth weight assessed by the question "how much did (infant) weight?" The answer was recorded as birth weight (3 decimals) in grams. This birth weight was converted to kilograms by dividing by 1000. Meanwhile a dichotomous variable was created to assess the low birth weight. The infants weighing 2.49kg and lower were given the value of 1(low birth weight) and the infants weighing 2.50kg and above were given the value of 0 (normal birth weight).

2.6.3 Co-variants

The variables identified as co-variants were among individual characteristics included mother's age, women and husband's education, location, socioeconomic status (SES), height and Body Mass Index (BMI) of mother and occupation of mother. Among the individual characteristics women age and height were included as continuous variables.

Education level

The education level of mother and husband were originally categorized into 4 groups as no education with a value of 0, primary education value 1 refers to completing classes 1-8, and secondary value 2 refers to completing classes 9-10 and high education value 3 refers to completing class 11 or more. Here no education is the reference category.

Location

Mother's location was also categorized into urban and rural. Mother's residing in urban areas were given a value of 0 and those residing in rural areas were given a value of 1. Reference category was women residing in rural areas.

Socioeconomic status

The socioeconomic status (SES) of mother is the wealth index originally presented in five quintiles as poorest, poorer, middle, richer and richest in the data available from PDHS 2017-18. This categorization was done according to the score given according to the household economic status and goods they possess. These goods range from television to a vehicle and housing characteristics such as water and sanitation facilities, house construction material. These scores are calculated according to the principle component analysis. The poorest SES is the reference category.

Occupation of mother

The occupation of mother was categorized in two groups as not working given a value of 0 and working with a given value 1. Mothers were asked what work they do and nine responses were recorded which included professional, clerical, sales, agriculture (employed and self-employed), household/domestic, services, unskilled/skilled manual workers. All these responses were categorized as working. Not working is defined as the reference group.

Body Mass Index of mother

The Body Mass Index (BMI) of the mother was recorded as two decimal. The BMI value was divided 100 and then categorized into four groups according to the standardized BMI classification. Mothers with BMI less than 18.5 was given a value of 0, BMI between 18.5-24.9 was given a value of 1, BMI between 25-29.9 were given a value of 2, and BMI 30 or more was given a value of 3. BMI less than 18.5 is the reference category.

Source of drinking water

The variable source of drinking water was categorized into unimproved source given a value 0, improved source as value 1 and other source a value of 2. The source division was done according to the standards set by WHO for unimproved and improved sources. Unimproved source of drinking water is considered the reference category.

The other co-variants related to antenatal care included were iron supplements during pregnancy, number of ANC visits during pregnancy, place of delivery, and sex of the child born.

Iron supplementation

A dichotomous variable identified mothers who did not take iron tablets or syrup during pregnancy with a value 0 and those who took iron supplements given a value 1. Here mothers who did not take iron as the reference group.

Number of antenatal care visits

The number of antenatal care ANC visits was defined by the number of times mother received ANC during pregnancy. This was categorized as no visit with a value of 0, 1-3 visits with a value

1 and 4 or more than 4 visits given a value of 2. The mothers who had no visit were considered as the reference category.

Place of delivery

Regarding place of delivery the mother was asked "where did you give birth?" Thirteen responses were recorded. The responses were respondent's home, other home, public sector, government hospital, rural mother and child health center, government basic health unit, community midwife, other government facility, private sector, private hospital, private clinic and other private facility and other. These response were further categorized into three categories, home delivery with included home and other and given a value of 0, delivery at public health facility including all the delivery at public sector and given a value of 1 and delivery at private health facility including all delivery at private sector was given a value of 2. Home delivery was the reference category.

Sex of child

The sex of the child born was categorized as male value 0 and female value of 1.

The variable of mother's weight was considered but not included as a co-variant. The data available for mother's weight in PDHS 2017-18 was the weight measured at time of interview which might not be relevant for this study. Other variables such as mother's dietary routine during pregnancy, hemoglobin concentration of the mother, timing and frequency of deworming medication were considered but could not be included in analysis as the data was not available for these variables in PDHS 2017-18.

2.7 Statistical analysis

The SPSS- software 25th trail version has been used for descriptive statistics and statistical analysis. The p-value of <0.01 was set for bivariate analysis and p-value of < 0.05 for multivariate analysis. 95% Confidence Interval (CI) was described for both crude and adjusted odds ratios.

2.7.1 Descriptive statistics

To illustrate the characteristics of participants and the distribution of dependent and independent variables, the frequency and count was used. Although most of the variables were categorical for analysis yet some variables such as mother's age, height and BMI were used as numerical variable for descriptive analysis. Mean, standard deviation, and histograms were used to describe and understand the numerical variable summaries.

2.7.2 Inferential statistics

In order to assess the association of outcome (low birth weight) with the independent variable and other predictor variables, bi-variate analysis was done. Bivariate associations between exposures (Deworming medication), outcome (LBW), and potential confounders were assessed using Spearman's rank correlation coefficient ($r_{s,}$), by One-way ANOVA by One-way ANOVA, or χ^2 tests depending on the type of data analyzed.

2.7.3 Multivariate analysis

Binary logistic regression was considered as the most appropriate for multivariate statistical analysis. Initially the exposure variable was assessed for its association to the outcome variable. Predictor variables that were identified to be significant to the outcome were included in regression models. Moreover variables that were found to be non-significant but were significant in previous studies were included in crude analysis. Next in multivariable adjusted model (final model) only those variables were added which showed significant association to the outcome in crude analysis and the adjusted odds ratios and 95% Confidence Intervals (CI) are presented. Goodness of fit for the models is assessed by the Hosmer and Lemeshow test, depicting how well the model fits the data. If the significance value is >0.05 then the model is a good fit.

2.8 Ethical consideration

The data for this study was provided by the DHS Program after receiving a brief description of the study to be done. The Pakistan Demographic Health Survey (PDHS) 2017-18 was implemented by the National Institute of Population studies (NIPS) under the supervision of Ministry of National Health Services, Regulation and Coordination. International ethical standards are assured for the survey. All the participants gave written informed consent and were informed regarding confidentiality. The consent form described all the objectives of the survey and the participation being voluntary and the right to withdraw at any point. In case the participant did not want to answer a question was allowed to skip to next question and stop the interview at any time (66). Appropriate measures were undertaken for the purpose of privacy and confidentiality of the participant. To maintain confidentiality and anonymity, basic identity information of the participants was converted into codes in DHS data set files. All the data set files received from PDHS 2017-18 were stored in a computer secured with password (66).

3. Results

3.1 Descriptive statistics of the study population

The descriptive statistics of the characteristics of the mother and child (N= 1403) are given in table 1. More than 61% of the mothers resided in urban areas and 38% in rural areas. The mean age of mother was 30.1year's and 23 % women had BMI $\geq$30 kg/m^2. Approximately 88% of the mothers was using improved source of drinking water. Around 40% of the mothers had attained high education and more 41% of the husband/partner had earned high education as the highest level of education. Moreover, about 85% of the mothers were not currently working.

During the antenatal period about 78% of the mothers had first antenatal care (ANC) visit during first trimester of pregnancy and more than 80% of mothers had 4 or more than 4 antenatal care visits during pregnancy. Furthermore 81% of the mothers took iron supplements and 2.5% took drugs for intestinal parasites (deworming medication) during pregnancy. The mean birth weight was 2.97 kg (range= 0.59 – 6.0 kg), and 18.6 % of the newborns weighted <2.5 kg (LBW).

Table 1- Background characteristics of mother and child with the data available from PDHS 2017-18

Characteristics	**Number**	**Frequency %**	**Mean+-S.D**
Age of mother	1403	-	30.1$\pm$ 5.80
Height of mother	536	-	171.3 $\pm$ 114.4
BMI of mother	515		
• <18.5	26	5.0	
• 18.4-24.9	215	41.0	
• 25-29.9	164	31.2	
• 30 or >30	120	22.9	
Mother's education			
• No Education	226	16.1	

• Primary	168	12.0	
• Secondary	446	31.8	
• Higher	563	40.1	
Mother's occupation			
• Not working	1196	85.2	
• Working	207	14.8	
Husband's education			
• No education	161	11.5	
• Primary	128	9.1	
• Secondary	526	37.5	
• Higher	588	41.9	
No. of ANC visits			
• No visit	12	0.9	
• 1-3 visits	255	18.2	
• 4 or more visits	1136	81.0	
Iron supplementation			
• No	261	18.6	
• Yes	1142	81.4	
Deworming medication			
• No	1371	97.7	
• Yes	32	2.3	
Place of delivery			
• Home	66	4.7	
• Public health facility	516	36.8	
• Private health facility	821	58.5	
Source of drinking water			
• Unimproved	158	11.3	
• Improved	1245	88.7	
Location			
• Urban	868	61.9	
• Rural	535	38.1	
Newborn			
Sex of child			
• Male	733	52.2	
• Female	670	47.8	
Birth weight of child			
• Normal weight	1142	81.4	
• Low birth weight	261	18.6	

3.1.1 Bi-variate analysis for the association of background characteristics with deworming during pregnancy and with low birth weight

In bi-variant analysis as described in table 2 the factors such as mother's occupation, source of drinking water, deworming medication, place of delivery and sex of child were not associated with the low birth weight. The mothers residing in rural areas had higher prevalence of low birth weight estimated to be (21.1%) in comparison to (17.1%) of the mothers living in urban areas. Among SES, the mothers belonging to poorest SES had highest prevalence (34.8%) of low birth weight as compared to mothers belonging to richest SES as shown in figure 5. About (23.0%) low birth weight was found in group of mothers who had no formal education and much lower in mothers with higher education i-e (11.2%). Similarly the prevalence of low birth weight was (25.5%) among husbands having no formal education.

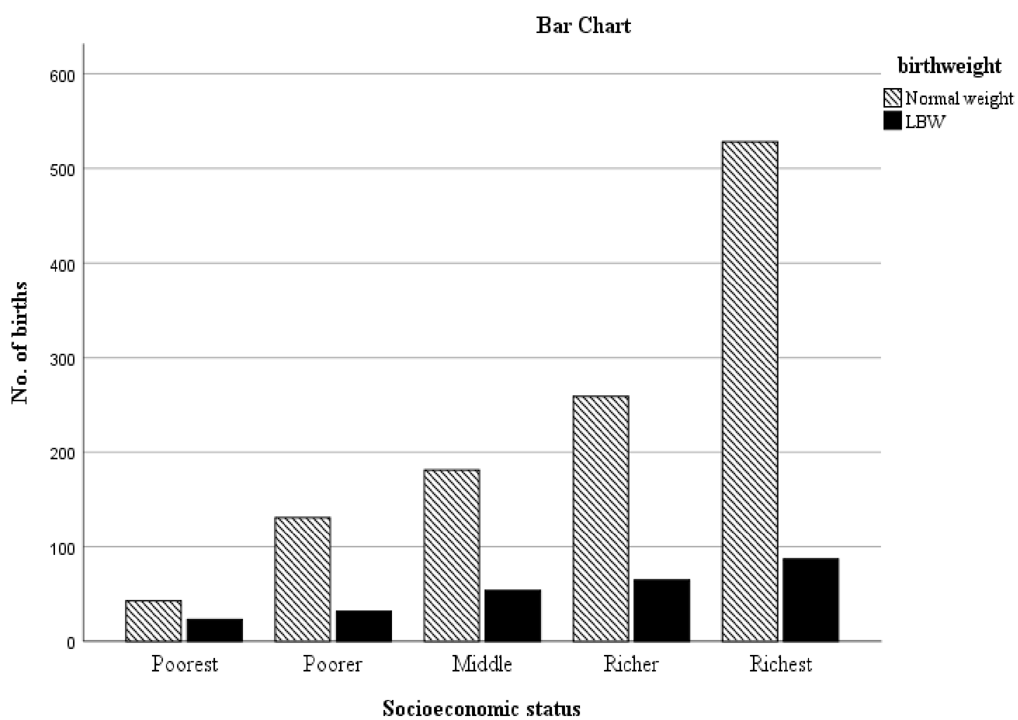

Fig 5- Cluster bar chart showing distribution of birth weight of infant by socioeconomic status.

During the antenatal time period disparities exist between the birth weights of infants where the mothers attended antenatal care and those who did not. About (16.8%) of low birth weight among mothers who attended more than 4 ANC visits and (41.7%) among those with no history of ANC visits through-out pregnancy. The prevalence of low birth weight (12.5%) among the mothers who received deworming medication during pregnancy and was lower as compared to mothers who were not given deworming medication during pregnancy.

The factors associated with low birth weight were mother's age and height of mother, education level of mother and husband, socioeconomic status, number of ANC visits during pregnancy, and iron supplementation during pregnancy. However, there was no association between deworming medication and background characteristics of the mother such as occupation, place of delivery in bivariate analysis.

Table 2- Bi-variate association between background characteristics and birth weight (low birth weight and normal birth weight) of infants

Variables [a]	**Number**	**Low birth weight (mean± SD or %)**	**Normal birth weight (mean ± SD or%)**	***p*-value[b]**
Mothers				
Age (years)	1403	29.3± 6.1	30.2± 5.7	.035
Height (cm)	536	162.0 ± 82.3	173.6 ± 121.1	.003
BMI (kg/m^2)				.873
<18.5	26	15.4	84.6	
18.5-24.9	215	19.1	80.9	
25-29.9	164	21.3	78.7	
30 or >30	120	20.8	79.2	
Mother's education				.000
No education	226	23	77.0	
Primary	168	22.6	77.4	
Secondary	446	24.2	75.8	
Higher	563	11.2	88.8	
Socioeconomic status (SES)				.000
Poorest	66	34.8	65.2	
Poorer	163	19.6	80.4	
Middle	235	23.0	77.0	
Richer	324	20.1	79.9	
Richest	615	14.1	85.9	
Occupation				.288
Not working	1196	18.1	81.9	

Working	207	21.3	78.7	
No. of ANC visit				.000
No visit	12	41.7	58.3	
1-3 visit	255	25.9	74.1	
4 or more visit	1136	16.7	83.3	
Iron Supplementation				.00
No	261	27.2	72.8	
Yes	1142	16.0	83.4	
Deworming medication				.369
Yes	32	12.5	87.5	
No	1371	18.7	81.3	
Place of delivery				.288
Home	66	22.7	77.3	
Public health facilities	516	20.2	79.8	
Private health facilities	821	17.3	82.7	
Source of drinking water				.152
Unimproved	158	22.8	77.2	
Improved	1245	18.1	81.9	
Location of residence				.057
Urban	868	17.1	82.9	
Rural	535	21.1	78.9	
Husband's education				.001
No education	161	25.5	74.5	
Primary	128	25.8	74.2	
Secondary	526	19.6	80.4	
Higher	588	14.3	85.7	
Newborns				
Sex				.930
Male	733	18.7	81.3	
Female	670	18.5	81.5	

3.1.2 Association between deworming and low birth weight

In crude and adjusted logistics regression models, we included variables that are known risk factors for low birth weight, or that were significantly associated with the deworming medication during pregnancy and LBW in the bivariate analyses. However, the variables that are statistically significant with LBW in multivariable adjusted model, were included in the final model. The result of crude and adjusted analysis are presented in table 3.

Initially, deworming medication and age of mother were added together and no change in significance values was observed. Then location of the residence was added along other variables. Next education level of women was added along. Here the age of mother and location became non-significant to the low birth weight (LBW). In-addition the odds ratios of deworming medication had changed slightly but remained non-significant to LBW. Next on addition of SES along with other variables, higher education of mother had a slight change in odds ratios but remained significant to LBW. Upon addition of no. of ANC visits along with other variables, the no. of ANC visits became non-significant to the low birth weight. In the final model those variables which were not statistically significant to low birth weight were excluded. However it was tested that after excluding mother's age, location and no. of antenatal care visits from the model, the estimate for the association of deworming medication to low birth weight did not change. Therefore we excluded those variables from the final model. The adjusted odds ratios (aOR) along with 95% confidence interval (CI) are given in table 3 multivariable adjusted model.

In multivariable adjusted logistic model, there was no significant association between deworming medication during pregnancy and low birth weight, aOR 0.63, 95%CI (0.21-1.83). Furthermore mother's education and wealth index, showed significant association to the low birth weight. Mother's with higher education aOR 0.55, 95% CI (0.34-0.87) had 45% reduced odds of having LBW infant in reference to the mothers with no formal education. Similarly mothers belonging to richer socioeconomic status (SES) had aOR 0.52, 95% CI (0.28-0.96) and mother belonging to richest SES had aOR 0.41, 95%CI (0.22-0.76). The mothers from richer SES had 48% and mothers from richest SES had 59% reduced odds of having low birth weight infant as compared to mothers from poorest SES.

Table 3- Crude and multivariable adjusted analysis for low birth weight with data available from PDHS 2017-18.

Variables	**Crude analysis OR, (95%CI)**	**Multivariable adjusted model Adjusted OR, (95%CI) µ**
Deworming medication		
No	Ref	Ref
Yes	0.61 (0.21-1.78)	0.63 (0.21-1.83)
Age of mother	**0.97 (0.95-0.99)**	-
Location of mother		-
Rural	Ref	
Urban	0.76 (0.58-1.00)	
Mother's education		
No education	Ref	Ref
Primary	0.97 (0.60-1.57)	1.10 (0.67-1.80)
Secondary	1.06 (0.73-1.56)	1.26 (0.84-1.91)
Higher	**0.42 (0.28-0.63)**	**0.55 (0.34-0.87)**
Socioeconomic status		
Poorest	Ref	Ref
Poorer	**0.45 (0.24-0.86)**	**0.49 (0.25-0.93)**
Middle	0.55 (0.30-1.00)	0.59 (0.32-1.08)
Richer	**0.46 (0.26-0.83)**	**0.52 (0.28-0.96)**
Richest	**0.30 (0.17-0.53)**	**0.41 (0.22-0.76)**
No. of ANC visits		-
No visit	Ref	
1-4 visits	0.48 (0.15-1.59)	
>4 visits	**0.28 (0.88-0.89)**	

µ : Final model adjusted for maternal education and SES

4. Discussion

This study did not find any statistically significant association between deworming medication during pregnancy and low birth weight within the study population. The data showed that the mothers who had attained higher education had reduced odds of having low birth weight infant as compared to mothers with no education. The mothers belonging to higher SES also had reduced odds of having low birth weight infant as compared to the mothers from poorest SES. These findings are similar to the results of previous studies (81,82). The importance is well understood as the mothers with high education have more knowledge and are more aware regarding the factors significant for the fetal growth. These mothers are more likely to take care of themselves. While the mothers with no education and having lower SES are prone to late start of prenatal care and less likely to avail antenatal care services (83,84).

As far as we know this is the first study looking into deworming mothers during pregnancy and its effect on birth weight of infant in Pakistan. Besides similar studies looking into the association of deworming during pregnancy and its effect on birth weight have been done in different regions. Our study did not find an association between mothers receiving deworming medication and low birth weight. Similarly in Uganda, a trial conducted in 2003-2005 reported that there was no effect on the birth weight of infants born to mothers who were given deworming medication in second or third trimester of pregnancy (59). The trial in Uganda gave iron and folic acid supplementation to all the pregnant women and similarly our data showed that more than 81% of the women took iron supplementation during pregnancy. Here iron supplementation might have influenced the effect of deworming medication by improving the anemia status of the mother. The results of study in Uganda also showed that the prevalence of helminthic infection among the pregnant women was high but the intensity of infection was low. In contrast in our study setting perhaps the prevalence of infection might be high among pregnant women but the intensity of infection could be low. There is lack of literature which specifically evaluates the prevalence and intensity of helminthic infection among pregnant women in Pakistan. This could also illustrate here that inadequately addressing the problem might be the result of the low utilization of deworming medication during pregnancy in Pakistan which is ultimately reflected in our study where the women receiving deworming medication was quite low.

While in contrary a study in Nepal showed that there was an increase in birth weight of infants born to mothers who were given deworming medication during pregnancy (52). In this study the pregnant women were given multi-nutrient supplementation throughout pregnancy and deworming was given twice during pregnancy. In Peru, Larocque et al. stated that that the proportion of very low birth weight infants (<1500grams) was much lower in mothers who received deworming medication during pregnancy (85) and similar findings were revealed in Sri Lanka (58). These trials focused on the very low birth weight infants which is a rare outcome. The trail in Peru was done in poor community with including only the women residing in rural or peri-urban regions and these regions lacked the basic water and sanitation facilities. Similarly two studies India reported a positive impact of deworming during pregnancy with an increase in birth weight of the infant (86). The study in West Bengal, India analyzed the effect of deworming medication only in severely anemic pregnant women (87). Thus it is likely that the measures in above mentioned studies might have yielded a more precise estimate of effect of deworming medication during pregnancy on birth weight of the newborn.

Furthermore, keeping in mind maternal anemia a major contributor of low birth weight, for the past two decades the non-progressive decline in anemia among pregnant women in Pakistan might be explained by the high prevalence of STHs infection among the population. WHO recommends practicing anthelmintic medication as a preventive measure to control and prevent anemia among pregnant women in STHs endemic regions and regions with high burden of maternal anemia during pregnancy (39). Meanwhile Sri Lanka and Nepal are the only countries among endemic regions that are implementing deworming as routine in antenatal care. Moreover these countries have successfully reduced the prevalence of anemia among pregnant women since the inclusion of deworming in their antenatal care programs (51).

The integration of deworming in antenatal care requires more attention and further research to understand the role of deworming mother during pregnancy and its effect on birth outcomes in different regions of Pakistan. Other factors that subsidize the STH infections are contaminated source of drinking water, unhealthy living conditions and poor sanitation. These components generally require much more time and resources to meet the standards. Thus taking into consideration the recommendations and comparing the findings of previous studies it is evident that giving deworming medication during pregnancy has an impact on improving the birth weight in regions with high burden of STH infections. Therefore initiating research projects by incorporating the low cost intervention (deworming drug) in antenatal care across different regions of the country might be a favorable step in further understanding the role of deworming medication towards reducing the burden of anemia among pregnant women and low birth weight in Pakistan.

The data from this study suggests that deworming mother with anthelmintic medication during pregnancy had no significant impact on the birth weight. However more randomized control trials are required in order to provide evidence regarding the benefits of deworming during pregnancy and its effect on mother and child health. Some of the practical implications taken into consideration may include the prevalence and intensity of STHs infection among population. In-addition the frequency, dosage and schedule of giving deworming medication (during second or third trimester of pregnancy) may influence the pathway and perhaps could be taken into consideration.

4.1Strengths

This secondary analysis is from DHS 2017-18 in Pakistan. This is nationally representative and results are generalizable in the particular context. The DHS data is collected by highly trained and skilled professionals which has very less chance of errors and mistakes. The data available for the birth weight of infant used for this study is considered reliable as it was recorded from a birth card or mother's recall.

4.2 Limitations

The cross sectional study design is itself a limitation. In this study design we can only describe whether the association is present or not. It is not possible to determine how strong or weak the association is. The variable for deworming medication does not differentiate between the timing (during second or third trimester), dosage and frequency of receiving deworming medication. The number of women who took deworming medication was quite low and might be a contributing factor for no significant association to the low birth weight. The number of missing values and don't know as a response in the exposure and outcome variable further reduced the number of participants. All these factors might contribute to the underestimation of the effects.

In PDHS 2017-18 of the total births only 16% of the babies were weighed at birth and which significantly reduced the sample size. However it is noteworthy that the majority of the mothers giving birth to newborns that were weighed at birth belonged to richer and richest SES and majority of the mothers and husband's had higher education.

This problem has been discussed previously for the purpose of estimation of low birth weight in low income countries. In low income countries the majority of newborns are not weighed at birth and hence lack of valid birth weight data which is itself an under estimation of low birth weight infants. However the newborns weighed at birth in these countries are more likely to be born at medical facility and have parents with high education and belonging to rich SES. The infants not weighed at birth do not have access to health facility and are therefore more vulnerable to adverse health outcomes. Hence to summarize, the limitations of this study might have generated an underestimate of the association of deworming during pregnancy to low birth weight instead of an overestimate.

In PDHS 2017-18 the data for hemoglobin concentration of the mother during pregnancy was not available. In-addition the data of mother's current hemoglobin concentration was also not available. There was no data on mothers for the prevalence of worm infection. Also no data was available of data for dietary habit of mother currently or during pregnancy in PDHS 2017-18.

4.3 Internal validity

This study results have good internal validity as the data from DHS that is considered to be high-quality data with quite low possibility of random errors. However the estimates cannot be unbiased as descriptive statistics was not done using the sampling weights and complex sample packages for inferential statistics. The weighted sampling was not used for this study due to limited understanding.

4.4 External Validity

In our study the possibility of selection bias cannot be ruled out. Many mothers did not know whether they were given deworming medication or not and at the same time lacked the valid and reliable data for birth weight of infant. Majority of the women who did not have the recorded birth weight of infant were excluded. Missing record of birth weight represents the proportion of infants not born at health facility and are at risk of poor health outcomes. It might be possible that if those mother were included in our analysis the findings could have been different. Meanwhile generalizability of the findings is not appropriate. The external validity of the findings is not supported by other studies and might be due to study limitations.

The findings in our study reveal that deworming the mother during pregnancy reduces the chance of having low birth weight infant. The association of deworming and low birth weight might not be statistically significant owing to the fact that only 2.5% of the women took deworming drugs during pregnancy. The limitations of this study would have contributed to the absence of association between deworming during pregnancy and low birth weight. However the reduced risk of having low birth weight infant when dewormed during pregnancy in our study is in accordance to the findings of other studies.

5. Conclusion

In our study we hypothesized that deworming reduces the worm infection which in turn reduces anemia among pregnant women and consequently improving the birth weight of infant. While in this study the data depicts that there is no significant association between deworming during pregnancy and low birth weight. It is likely that the lack of association might be attributable to the small sample size in the group of mothers who took deworming medication during pregnancy. Meanwhile among the socioeconomic determinants, maternal education and SES of mother all independently influenced the low birth weight.

Furthermore as taking account of the previous evidence and the recommendations by WHO it is apparent that practicing deworming medication in routine antenatal care might be effective in controlling and prevention of anemia among pregnant women. In-addition there is no evidence of adverse health effects in mothers and child related to deworming medication when prescribed during second or third trimester of pregnancy. To reduce the prevalence and transmission of helminthes infection, prevention strategies targeting the source of helminthic infection requires further attention. Commencing awareness campaigns focusing on the methods to make drinking water safe before consumption. Initiation of programs that are aimed at improving living conditions by promoting hygienic practices and enhancing sanitation facilities.

Since there are concerns regarding varying findings in different contexts about the effects of deworming medication during pregnancy on the mother and infant. Hence more randomized controlled trials are needed to provide more evidence in relation to the health benefits of deworming during pregnancy for both mother and child.

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