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Maternal hemoglobin concentration and pregnancy outcome : a study of the effects of elevation in El Alto, Bolivia

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Maternal Hemoglobin Concentration of Pregnancy Outcome: A Study of the Effects of Elevation in El Alto, Bolivia

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INTRODUCTION

Iron-deficiency anemia is a health problem that often goes untreated, especially in developing countries, where it can be most dangerous. Many severe health complications of iron-deficiency anemia are evident in pregnancy. The World Health Organization (WHO) estimates that an average of 56% of pregnant women in developing countries are anemic. This percentage ranges from 35% to 75% in specific areas, and is much higher than the 18% of anemic pregnant women in developed countries (1). Iron deficiency during pregnancy is known to be caused by combination of factors such as previously decreased iron supply, the iron requirements of the growing fetus, and expansion of maternal plasma volume (2). While plasma volume and red cell mass are both known to expand during pregnancy, plasma volume swells to a greater extent, therefore diluting the maternal hemoglobin concentration (Hb) (3). It is necessary to take this into consideration when diagnosing anemia in pregnant women. Effective diagnosis has been achieved by accurate laboratory tests of hemoglobin and hematocrit levels. However, it is also necessary to identify precise cut-offs for anemia according to sex, age, and pregnancy trimester of the patient in consideration. Research has found that hemoglobin and hematocrit concentrations typically decrease during the first trimester and reach the lowest levels at the end of the second trimester. These levels tend to increase again during the third trimester of pregnancy (4). The Center for Disease Control (CDC) has used this research to establish trimester-specific Hb concentration cut-off adjustments for diagnosing anemia (Table 1). Unknown trimester hemoglobin adjustments have been developed by the WHO (5).

TABLE 1

Hemoglobin adjustments for pregnancy in women at sea level.

Trimester of Pregnancy	Hemoglobin Adjustment (g/dL)
First	-1.0 g/dL
Second	-1.5 g/dL
Third	-1.0 g/dL
Unknown Trimester	-1.0 g/dL

Hemoglobin levels have also been known to vary in response to altitude. Elevations of over 1000 meters have demonstrated influences of increasing patient Hb levels. This is known as an adaptation response to the lower partial pressure of oxygen, which causes reduced oxygen concentration in the blood. The body responds to this change by increasing Hb concentration in order to make certain that oxygen transport is sufficient for the needs of its tissues (3). This Hb increase is known as hypoxia, which can ultimately mask anemia if it is not carefully considered (6). In order to determine Hb concentration cut-off levels for anemia at varying altitudes, the CDC Pediatric Nutrition Surveillance System has used data from a study of children with little or no iron deficiency. Using this data, they developed a curve of Hb concentrations as altitude changed, demonstrating the following association between altitude and Hb:

$$Hb = -.32 * (\text{altitude in meters} * 0.0033) + 0.22 * (\text{altitude in meters} * 0.0033)^2$$

Another study of hemoglobin altitude correction values by Dirren et al. found that a different equation demonstrated this association. Their equation was as follows:

$$Hb = 6.83 * \exp[0.000445 * \text{altitude in meters}] + 113.3)$$

Dirren et al.'s equation demonstrated differences of 2 to 3 g/dL from the CDC in the recommended necessary adjustment of anemic Hb cut-off level. According to Nestel, the CDC adjustment values were declared more fitting. Research by Cohen and Hass at various altitudes in Bolivia also addresses this adjustment factor. Although their research accounts for gaps in previous data (i.e. curves created with child data instead of that of pregnant women, assumptions of linear relationship, and assuming data is

proportional at higher and lower altitudes (2),) they did assume that plasma volume expansion is similar at varying altitudes, which may not be accurate (3). The adjustment values determined by Cohen and Hass were very similar to those determined by the CDC, causing Nestel to reconfirm recommendation for usage of the CDC's adjustment values.

It is evident that knowledge of the effects of maternal anemia on the outcome of pregnancy is not completely understood (1). The relationships that have been demonstrated have been challenged, and various interpretations have been made on pregnancy outcomes and their association with maternal health. A U-shaped association has been found between the maternal Hb level and the birth weight of the infant. High Hb concentration has been associated with inadequate plasma volume expansion, often leading to a lower birth weight (7) or other adverse pregnancy outcomes (8). Low birth weight can also be associated with maternal anemia, or low Hb levels, as an outcome of preterm labor induced by these levels (1). Finally, there has been observed correlation between higher Apgar scores and increasing maternal Hb concentrations, as well as treatment with iron supplements (9, 10). Multiple pregnancies and low socioeconomic class have been found to be risk indicators for iron-deficiency anemia (8). In order to better prenatal health and preparation, additional research is necessary to confirm previous associations and to discover additional relationships.

Although most cases of anemia in pregnancy are caused by iron deficiency (11), it must also be considered in the diagnosis that many types of anemia are prevalent. These include iron-deficiency anemia, pure red cell aplasia, aplastic anemia, paroxysomal nocturnal hemoglobulinemia, and myelodysplastic syndrome (11). The classification of various types of anemia is based upon origin and morphology of red blood cells. Origin is classified based on bleeding, increasing destruction of blood cells, and decreased production of cells. Morphology is classified by cell size, shape and color. Based on these classifications, anemias are placed in categories of macrocytic or nomochromic anemias (B_{12} deficiency or folate deficiency), microcyic of hypochromic anemias (iron deficiency, sideroblastic, or thalassemia anemia), or normocytic or normochromic anemias (aplastic, hemolytic, chronic disease, or sickle cell) (12).

There are many women with iron-deficiency anemia that are not aware of it. Iron-deficiency ranges from iron depletion, which causes no physiological harm to the patient, to iron-deficiency anemia, which can cause damage to the function of organs. According to studies, iron-deficiency anemia can be diagnosed accurately if the Hb concentration of the patient rises after routine iron supplementation (8). These various types of anemia, along with multiple others, must be considered when diagnosing a patient with iron-deficiency anemia.

Iron supplementation during pregnancy has been implicated around the world in hopes of increasing the iron supply of otherwise anemic patients. Studies with large numbers of subjects have demonstrated that these supplements can increase the infant's birth weight (13, 14). A Nigerian study on supplementation in pregnancy found that iron supplements could increase Apgar scores of infants (1). Other studies show that supplements do not consistently decrease the incidence of iron-deficiency anemia in women that have entered pregnancy with low Hb levels and low iron stores. Regardless of varying study outcomes, many share the opinion that we should practice routine iron supplementation during pregnancy, most importantly to anemic pregnant women (1).

The purpose of this study was to incorporate current pregnancy and altitude Hb parameters for diagnosing anemia and evaluate the effects of adjusted Hb concentration on pregnancy outcome. Although research has demonstrated the effects of altitude on Hb concentrations, many patients in developing countries still remain undiagnosed of anemia due to the lack of application of these Hb adjustments. In this study we provide data that supports previous research on the effects of maternal Hb level on various pregnancy outcomes. Our work demonstrates that the application of altitude-specific Hb adjustments for anemia is useful in the prediction of pregnancy outcome. Finally, we determine which specific aspects of pregnancy outcome are most clearly affected by maternal Hb concentration. We also use this study to look specifically at the health of the population of El Alto, Bolivia.

METHODS

This study was carried out in El Alto, Bolivia, at the Los Andes Hospital, during the month of May, 2006. This institution is a small hospital with services specifically for mothers and children. El Alto is a growing city of over 500,000 people, found at an altitude of 4018 meters above sea-level (15). The protocols of the study were approved by Northeastern University's Director of Research Integrity. Review by the FDA's Institutional Review Board was waived by Northeastern, as work was done under the direction of Dra. Cecilia Uribe de Chavez, the Medical Director of Child and Family Health International. Consent to review patient charts was given by Dra. Uribe, who works in the Medical Cabinet of the Bolivian Air Force and is currently the Secretary General of the Committee of Adolescents for the Bolivian Society of Pediatrics. Subjects were randomly chosen as they gave birth in the hospital, and charts were reviewed after verbal consent by patients. All charts were reviewed after consent, although not all chart data was utilized. Many subjects had incomplete data and were not used in this study at all, while others had inconsistent data, and were used for applicable portions of the study.

There were 98 patient charts reviewed that were applicable to the study. Data collection took place in the weekday mornings, throughout the month of May, 2006. After receiving informed consent, an interviewer knowledgeable in the Spanish language reviewed the patient chart. Patient information was transcribed to a prepared data collection sheet, which included patient sociodemographic information, parity, weight, height, hemoglobin and hematocrit levels, infant birth weight, length, head circumference, gestational age, Apgar scores, and any other complications in pregnancy. Sociodemographic information was inconsistently available from charts and was not used in this study. All patient measurements were taken by medical professionals staffing the hospital. Gestational age was quantified as the number of weeks between the patients' last recalled menstrual period and the day of delivery.

STATISTICAL ANALYSIS

Hemoglobin levels were categorized as "anemic" and "non-anemic," according to The World Health Organization's accepted values to define anemia, along with the adjustments provided by the CDC to determine anemia during pregnancy. Averages of collected data for pregnancy number, gestational age, birth weight, birth length, head circumference and Apgar scores at 1 and 5 minutes were calculated for both "anemic" and "non-anemic" patients. These averages were analyzed for statistically significant relationships with Hb levels using the t-TEST in Microsoft Excel Data Analysis Toolpack.

Multiple linear regression analysis was also used to determine the effect of Hb levels on factors of pregnancy outcome, considering any confounding variables that may influence both Hb levels and outcomes. Pregnancy outcome factors analyzed by this regression included gestation age, Apgar scores at 1 and 5 minutes following birth, and birth weight of infant. Parity was also examined as a possible determinant of Hb concentration using this analysis. Regression was applied using Microsoft Excel Data Analysis Toolpack.

Hemoglobin concentrations were sorted into four categories of 1.99 g/dL per category, ranging from 7.00 g/dL to 14.99 g/dL. Categories were labeled based on the CDC's trimester-specific cutoff level for anemia in pregnancy as High-Normal (13.00-14.99 g/dL), Normal (11.00-12.99 g/dL), Mild Anemia (9.00-10.99 g/dL) and Moderate Anemia (7.00-8.99 g/dL). Severe Anemia would have been considered to be Hb values less than 7.00 g/dL. Hb levels above 14.99 g/dL and below 7.00 g/dL were considered extraneous and unusable in our study due to the few data points found in these ranges. Using this data in our analysis would have caused unequal group sizes. Averages of collected data for aforementioned pregnancy outcome factors were calculated for each category. Using SPSS 14.0.1 for Windows, ANOVA (ANalysis Of VAriance between groups) was applied to determine the statistically significant difference between the means of the four categories. Further post hoc Tukey honest significant difference (HSD) analysis ($P < 0.05$) was applied to all data analyzed in the ANOVA.

RESULTS

This study included 98 women in total (Table 2). It is recognized that there are various gaps in our data, as some of the subjects' charts did not provide all necessary information. Each descriptive variable of maternal health and each variable of pregnancy outcome was analyzed from the available data. The average age of the women evaluated was 27.2 years, while the median age was 26.0 years. The majority of

the women were from El Alto (82), while the others were documented to have come from the nearby areas of La Paz, Polochoco, Alto Lima, Challahuyo, Guayuyo, Yuayayo, Achacadi, Puerto de Gui Gui, and Brosil.

TABLE 2
Characteristics of the study population, El Alto, Bolivia.

Variable	n	Mean ± SD	Median
Age, *years*	98	27.2 ± 6.9	26.0
Height, *cm*	74	148.4 ± 6.2	148.0
Weight, *kg*	80	56.0 ± 9.8	55.1
Weight at Birth, *kg*	65	65.1 ± 9.6	64.5
BMI, kg/m^2	51	29.5 ± 4.4	30.1
Maternal Hb, *g/dL*	79	12.97 ± 2.07	13.40
Maternal Hb (altitude-adjusted) *g/dL*	79	12.61 ± 2.08	13.06
Infant Gestational Age, *weeks*	94	38.5 ± 2.1	39.0
Infant Birth Weight, *g*	97	3,200 ± 500	3,300
Infant Birth Length, *cm*	95	47.76 ± 4.3	49.0
Infant Head Circumference, *cm*	95	37.9 ± 31.9	34.8
Apgar Score, *1 min*	95	7.4 ± 1.3	8.0
Apgar Score, *5 min*	95	9.0 ± 1.4	9.0
Parity	75	1.8 ± 1.9	1.0

The average hemoglobin concentration of the subjects was 12.965 g/dL, which was adjusted to 12.609 g/dL using the Center for Disease Control and Prevention's anemia criteria and altitude adjustment (16). This adjustment was carried out by subtracting the adjustment value from the measured Hb concentration at the relevant altitude, to the nearest 500 meters, in order to obtain the comparative sea-level value. Previous research has determined that elevations about 1000 meters can cause Hb levels to increase as a response to lower atmospheric partial pressure (4). This lower pressure is known to cause reduced oxygen in the blood, which increases production of red blood cells in order to sustain adequate oxygen supply to the body. This increase in Hb concentration is often misinterpreted as a sign of sufficient iron status, while a patient in a high-altitude area may actually have iron-deficiency anemia. The questions we face are whether or not women are anemic despite these higher Hb concentrations, and whether or not these high Hb concentrations that result from increased altitude are themselves a risk factor for poor pregnancy outcome. Based on this research and suggested Hb adjustment values (4)**,** we have subtracted 0.34 g/dL from all patients' Hb concentrations in order to consider the effects of altitude.

In this study, anemia is defined as an Hb level lower than the "normal" Hb level at the defined altitude. This lower level corresponds to a decrease in number of erythrocytes. Hb concentrations during pregnancy are generally lower due to the maternal plasma expansion, along with the growing fetus's use of the maternal iron stores (2). For these reasons, data in this study were used only if maternal Hb concentrations were analyzed before the end of the first trimester of pregnancy. Studies have also concluded that Hb cutoff levels to define anemia in non-pregnant females above the age of fifteen should be 12.0 g/dL (3**).** The CDC has developed trimester-specific cutoff level adjustments for pregnant women. These can be calculated by subtracting 1.0 g/dL from the accepted cut-off level during the first trimester, 1.5 g/dL during the second trimester, and 1.0 g/dL during the third trimester, or if the trimester is unknown (4). The blood tested for this study was obtained during the first trimester of pregnancy, and therefore the cutoff level used for identifying anemia was 11.0 g/dL.

Based on the altitude-adjusted Hb concentrations and the above anemia criteria, 14 women were defined as anemic and 66 were without anemia (17.5% anemic). Excel was used to compare the means of various

factors of pregnancy outcome between anemic and non-anemic groups (Table 3), and statistically significant differences were assessed used Student's t-TEST. Maternal anemia was associated with lower infant Apgar scores at both 1 minute and 5 minutes after birth. The stronger relationship was observed in the effects of anemia on low Apgar scores at 1 minute (P = 0.006), while a slightly weaker relationship was seen between maternal anemia and scores at 5 minutes (P = 0.039).

TABLE 3

Comparison of Mean Between Anemic and Non-Anemic Pregnant Women (n = 79).

	ANEMIC	**NON-ANEMIC**	**P VALUE**
Hb, *g/dL*	9.31	13.73	$1.16e^{-08}$
Hb (altitude-adjusted), *g/dL*	8.97	13.38	$1.19e^{-09}$
Gestation Length, *weeks*	37.1	38.9	0.059
Birth Weight, *g*	3,100	3,300	0.213
Birth Length, *cm*	47.8	47.5	0.431
Head Circumference, *cm*	34.2	39.5	0.137
Apgar, *1 minute*	5.9	7.6	0.006
Apgar, *5 minute*	7.8	9.2	0.039
Parity	4.1	1.5	0.010
Birth Complications	64.3% with complications	15.4% with complications	0.002

Birth complications were more prevalent in anemic women than in non-anemic women. In this study, any major deviation from normal, healthy labor was considered a "complication." A patient was considered positive for birth complications if she underwent a forced cesarean birth or experienced preeclampsia, or if the infant needed oxygen through a facemask to be revived, or was not moving when born. Women who experienced a birth complication were assigned the categorical value of "1," and a woman with no complications a value of "0," and a t-TEST was run to assess the effect of maternal anemic on this specific outcome. While 64.3% of anemic subjects experienced some type of birth complications, only 15.4% of non-anemic subjects faced these problems. The t-TEST showed a strong correlation between maternal anemia and complications in birth (P = 0.002).

Higher parity was also associated with anemia, with 4.1 previous pregnancies observed in anemic women compared to just 1.5 previous pregnancies number in non-anemic women (P = 0.010). Although the average gestational age of infants born to anemic women was nearly two weeks less than that of infants born to non-anemic women, this difference failed to reach statistical significance (P = 0.059). Average birth weight of infants of anemic patients was 210 g less than the average birth weight of those of non-anemic patients, however, insignificant statistical significance was also observed in this analysis (P = 0.213).

Complete data for both Hb concentrations and all pregnancy outcome factors that we desired to evaluate were available for a total of 56 woman-infant pairs. Multiple linear regression was used to assess the relationship between maternal Hb levels and pregnancy outcomes. The association between Hb level and gestation age was statistically significant (P = 0.0284), and the Hb level and the Apgar score at 1 minute were also found to be meaningfully related (P = 0.00039). Apgar score at 5 minutes showed a clear statistical significance in relation to maternal Hb level (P = 0.018). Finally, a statistically significant correlation was determined between Hb level and parity (P = 0.00082), which may suggest that women with higher parity are more likely to become anemic.

TABLE 4

Categorical Hb levels and associated averages of various pregnancy outcome factors

Hb, *g/dL*	**n**	**AVERAGES OF PREGNANCY OUTCOME FACTORS**					
		Hb, *g/dL*	**Birth Weight, *g***	**Apgar, *1 min***	**Apgar, *5 min***	**Gestation, *weeks***	**Parity**

7.00-8.99	7	8.25	2,950	4.75	6.5	37.6	3.65
9.00-10.99	6	10.26	3,006	6.875	8.75	36.5	5.75
11.00-12.99	20	11.97	3,231	7.357	9.048	38.399	1.85
13.00-14.99	41	13.99	3,208	7.761	9.349	39.135	1.27
15.00-16.99	2	15.21	3,500	7.5	8.5	39	3
17.00-18.99	1	17.66	2,635	8	10	40	4

Subjects were divided into six groups based on their maternal Hb level (Table 4). The means of various pregnancy outcomes were calculated for each Hb category. In further analysis, only data from subjects with Hb concentrations between 7.00 g/dL and 14.99 g/dL were used, as there was not enough data in the upper categories to make statistically significant conclusions. When mean Apgar score recorded at 1 minute is plotted against Hb ranges of the subjects, a gradually increasing trend is observed (Figure 1). At lower Hb levels, Apgar score increases significantly as maternal Hb levels increase. At higher maternal Hb levels, Apgar scores tend to increase less drastically and the trend curve levels off. When plotting Hb ranges against Apgar scores at 5 minutes after birth, a similar trend is observed (Figure 2). However, the curve formed from this data includes a point that falls off the apparent trend line (at Hb concentrations of 15.21 g/dL.) Average birth weight of the infants also showed a slight increase as Hb concentrations increased (Figure 3). The point on this plot referring to mean Hb of 17.66 g/dL demonstrates that the aforementioned U-shaped association between Hb concentration and birth weight may be weakly present within our data.

Figure 1. Hemoglobin Concentration vs. Apgar 1 minute Score

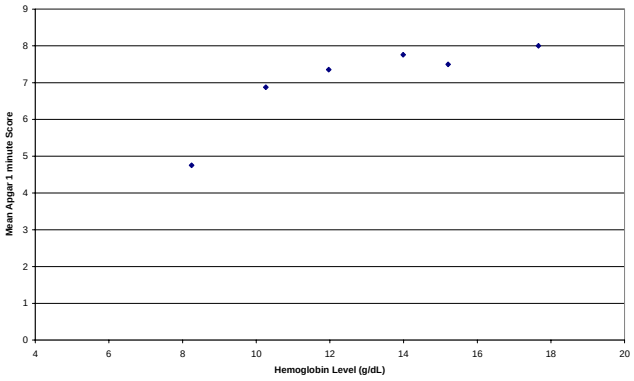
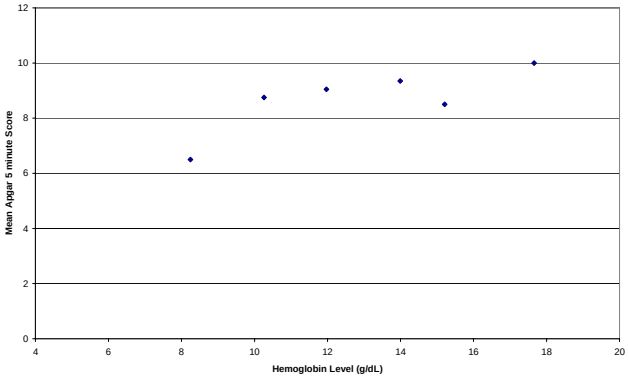
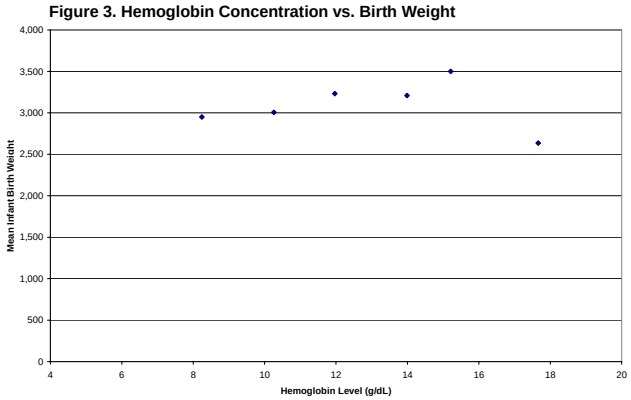


Figure 2. Hemoglobin Concentration vs. Apgar 5 minute Score





ANOVA analysis was used to evaluate the statistical significance of these observed trends. As previously mentioned, subjects with Hb concentrations below 7.00 g/dL and above 14.99 g/dL were not included in the ANOVA. The analysis confirmed that correlations between differences in increasing Hb concentrations and gestation length were statistically significant ($P = 0.007$). When this method was used to evaluate the relationship between increasing Hb levels and infant birth weight, no statistically significant differences were present ($P = 0.458$). However, infant Apgar scores at 1 minute following birth were found to be statistically different as Hb levels changed ($P = 0.000$), as well as Apgar scores at 5 minutes following birth ($P = 0.002$). Finally, parity also demonstrated significant differences according to Hb level ($P = 0.000$). Using the same data and same Hb groups (7.00-8.99 g/dL, 9.00-10.99 g/dL, 11.00-12.99 g/dL, and 13.00-14.99 g/dL), the ANOVA analysis was further developed with an additional post hoc Tukey HSD analysis. When examining gestation length as a dependent variable, Mild Anemia (Hb 9.00-10.99 g/dL) subjects were observed to have significantly lower gestational lengths ($P < 0.05$) than groups those of the Normal (11.00-12.99 g/dL) and High-Normal (13.00 – 14.99 g/dL) groups, which are statistically equal to the Moderate Anemia group (7.00-8.99 g/dL.)

In comparing these Hb groups with respect to the infants' Apgar scores at 1 minute following birth, the Moderate Anemia group had correspondingly lower scores than the Normal and High-Normal groups, which were statistically equal to the Mild Anemia group. When Tukey's HSD analysis was repeated with Apgar scores at 5 minutes following birth, the same relationships were observed as in Apgar scores at 1 minute. Finally, parity in the Mild and Moderate Anemia subjects were found to be significantly greater than parity in subjects from the Normal and High-Normal subjects.

DISCUSSION

Our study demonstrated that 17.5% of the subjects could be diagnosed with maternal anemia in pregnancy. Based on previous research, this proportion is lower than estimates of some areas, where 35%-75% of the population are thought to be anemic (1). However, this study only incorporated pregnant subjects and does not reflect the anemic population of the area in general. If 17.5% of the 66 women providing maternal Hb concentrations were anemic, this could easily translate into a large number of women in El Alto experiencing anemia in pregnancy.

Previous studies have demonstrated a relationship between maternal Hb and birth weight of the infant (7), as well as gestation age (1). Agpar scores have also been associated with maternal Hb in multiple studies (9, 10). Our study can be used as an evaluation of multiple factors of pregnancy outcome in relation to maternal Hb. Maternal anemia was significantly associated with the health of the infant at birth. The current study's results demonstrated that anemic pregnant women gave birth to infants with lower Apgar scores at 1 minute following birth than healthy pregnant women. There was also a strong relationship between anemia in pregnancy and lower infant Apgar scores at 5 minutes following birth.

In addition to Apgar scores in determining infant health, birth complications were also used as a method of evaluation. For this study, birth complications were defined as mentioned in the preceding section. The

prevalence of difficulties in pregnancy in women with maternal anemia was significantly higher than in non-anemic women. According to t-TEST analysis, gestation age of the infants was not significantly different between anemic and non-anemic mothers. However, the average gestation age of women with anemia was about two weeks less than the average gestation of non-anemic women. The average infant birth weight of women with maternal anemia was 210 grams less than that of women without maternal anemia; however, no statistical significance was determined between the two.

In addition to correlations observed between maternal Hb concentrations and various pregnancy outcome factors, there were also relationships found between the latter and parity. A t-TEST determined that parity was a statistically significant determinant of maternal Hb concentrations. Higher parity was associated with lower maternal Hb. Anemic patients demonstrated a greater number of prior pregnancies than non-anemic patients. In addition to the idea that pregnancy outcome factors may be affected by maternal Hb concentrations, parity number may in fact affect these concentrations themselves. In past studies, the rate of anemia was found to increase with increasing parity (18, 19, and 20). In a study of Mexican American women, subjects with parity greater than 2 were 2.7 times more prone to be anemic **(**19). In this same study, non-Hispanic white subjects with parities greater than 2 were also associated with a higher incidence of iron deficiency anemia. The results of this research are once more confirmed in our study. When multiple linear regression is applied to our data, parity is again observed to be a determinant of maternal hemoglobin level. However, within this same regression analysis, Apgar scores at 1 and 5 minutes after birth, as well as gestational age, also demonstrate a significant correlation with maternal Hb concentration. This multiple linear regression confirms that the increase in parity associated with the lower Hb levels does not also affect the trends in the aforementioned pregnancy outcome factors.

When ANOVA was used to evaluate significant differences in between the four Hb groups (7.00-8.99 g/dL, 9.00-10.99 g/dL, 11.00-12.99 g/dL, and 13.00-14.99 g/dL), similar significances were determined as were when multiple regression was applied. ANOVA Oneway analysis determined differences in gestation length, parity and Apgar scores at 1 and 5 minutes following birth to be associated with changes in Hb levels. Similar to multiple regression analysis, variance in infant birth weight did not correlate with change in Hb level.

Post hoc analysis using the Tukey HSD test confirmed specific differences between the four particular Hb groups. In all dependent variables, at least one of the lower two Hb groups, 7.00-8.99 g/dL and 9.00-10.99 g/dL demonstrated significant differences from both of the higher two Hb groups, 11.00-12.99 g/dL and 13.00-14.99 g/dL. When parity was compared with Hb, the two lower groups were found to be statistically significant in their difference from the two higher Hb groups.

In a population of non-pregnant women, an anemic rate of 17.5% is relatively low when compared to other developing regions. However, this percentage is not characteristic of a healthy population, and is not acceptable for women in pregnancy. According to our research, iron-deficiency anemia can not only cause problems in the health of the mother, but can also carry serious complications to the condition of the infant. In our study, and in general observation in the hospitals of La Paz and El Alto, Bolivia, many birth complications were witnessed. While 31.8% of all women in our study experienced some type of birth complication, 64.3% of anemic women were found to have complications in pregnancy.

In a supplementary investigation at the Los Andes Hospital in El Alto, a separate group of 83 women were interviewed regarding their past pregnancies and knowledge of hemoglobin, hematocrit and anemia. When surveyed about complications in their past pregnancies, fifty-nine of the women (71.1%) claimed to have experienced no known complications. Fifteen women (18.1%) reported complications in one or more of their pregnancies. Forced cesarean births were included in these complications. Knowledge of hemoglobin and hematocrit levels and their effects on pregnancy outcome varied within the survey population. Seventy-one women claimed to have no knowledge of the levels and their affects. Eight women provided responses of both symptoms of anemia, as well as believed causes of variation of Hb concentration. Responses included explanations of “sugar in the blood,” or conditions “when you have a lot of blood.” Others responded that these levels had to do “with red blood cells.” In addition, one subject described that “the altitude makes these levels higher than normal.” Some women also referred to the effects on

pregnancy outcome with descriptions such as “infants are born with deformities or are not able to talk,” or “the baby can be born with complications and can’t see.”

Women were asked to describe any perceptions they held about the conditions of anemia. Approximately half of the women (53.0%) were not at all familiar with the term. Of those who recognized the condition, many identified causes of anemia as “bad nutrition, “bad blood,” and “lack of red blood cells,” as well as a general association with food consumption. Other knowledge was based upon symptoms of the disease. These responses included both eating less than usual and inability to eat at all, as well as increased fatigue and “sleeping a lot.” Weight loss and lowered immune system defense were thought to be physical effects of the condition. Several women also described their perceptions of anemia as effects on pregnancy outcome. One subject described that the infant may have a low birth weight and recognized that the mother should be “taking tablets to receive better nutrition during pregnancy,” referring to iron supplements. Another woman also mentioned that anemia may “kill the child” during the pregnancy.

Iron supplementation has been an important approach in battling iron-deficiency anemia in pregnancy, both in developed and developing countries. During pregnancy, iron requirements are significantly higher than normal. Requirements have been known to increase by 0.8 to 7.5 milligrams of absorbed iron per day (21). Although it has been discussed as to whether or not pregnant women can naturally maintain necessary iron stores, research regarding anemia has demonstrated that a normal dietary intake of iron is not sufficient for pregnant patients (22). Various techniques have been implemented to meet iron requirements in pregnancy, such as increasing consumption of foods that are fortified with iron (23). Genetic engineering of foods by removing iron absorption inhibitors or boosting nutrient stores in certain products has also been recently developed (24). A clinical approach that has been widely practiced to prevent iron-deficiency anemia in pregnancy is the distribution of oral iron supplements. Data shows that these supplements are successful in achieving increased iron stores in pregnancy (25, 26, 27). However, regardless of its success in increasing iron stores, supplementation has not noticeably improved the prevalence of iron-deficiency anemia. It has been discussed that this lack of progress may be caused by low compliance to supplementation, or side effects of the tablets (28, 29). There has been suggestion of using an intermediate dosage for supplementation to avoid side effects while still improving iron status of patients (30, 31).

Although the women interviewed seemed to be aware of the iron supplements available to them during pregnancy, not all utilized this resource. While 42 women (56.8%) had regularly self-administered iron supplements during their previous pregnancies, 32 women (43.2%) had not. Most women who had not administered these supplements did not seek prenatal care.

The lack of sought prenatal care in Bolivia is surprising because of the country’s advantageous health insurance system for pregnant women and young children. On January 1, 2003, Bolivia passed the Bolivian Universal Mother and Infant Health Insurance (SUMI) Law to provide free medical attention to pregnant women beginning at the start of pregnancy and ending six months after the infant’s birth (32). The health insurance also covers the infant from birth until five years of age. SUMI covers hospitalization, all diagnostic procedures, treatment, surgery, provisions and medications. This health insurance is extremely valuable to the impoverished populations of Bolivia, but is not always utilized. There are numerous Bolivian women who do not seek prenatal care during pregnancy. These women rely on their personal knowledge alone regarding the prenatal growth of the infant, and preparing for the birth. In many situations, the nutrients needed during pregnancy are not obtained, and the nutrition of the food consumed by the mother is not sufficient. Information about the benefits of this free health insurance should be promoted in Bolivia so that more of the population may use it to their advantage.

It is imperative that additional research is done to determine ways to decrease maternal and infant mortality rates. The public’s awareness of iron-deficiency anemia and its adverse effects must be increased in developing countries. Prenatal care and education from medical professionals may be crucial in improving the health of the mother and the developing fetus during pregnancy. Women in all regions of the world must be taught the importance of this medical care, as well as the value of adherence to vitamin supplementation.

Using current knowledge and additional studies, as well as effective implementation, public understanding is achievable. Public information sessions and education programs regarding health care during pregnancy and infancy may improve knowledge in El Alto. Given the results of our study, there are still major gaps to bridge in regards to the awareness and treatment of anemia and other health conditions during pregnancy.

CONCLUSIONS

The application of altitude-specific hemoglobin adjustments for anemia was useful in the prediction of pregnancy outcome. Maternal anemia was strongly associated with lower infant Apgar scores at both 1 and 5 minutes following birth, as well as shorter gestational length and higher parity.

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LITERATURE CITED

1. Allen LH. “Anemia and iron deficiency: effects on pregnancy outcome.” The American Journal of Clinical Nutrition. April 2000; 71(suppl):1280S-4S.

2. Cohen JH, Haas JD. “Hemoglobin correction factors for estimating the prevalence of iron deficiency anemia in pregnant women residing at high altitudes in Bolivia.” Pan American Journal of Public Health. December 1999; 6.6:392-399.

3. Nestel, Penelope. “Adjusting Hemoglobin Values in Program Surveys.” International Nutritional Anemia Consultative Group. June 2002.

4. Center for Disease Control. “Current Trends CDC Criteria for Anemia in Children and Childbearing-Aged Women.” Morbidity and Mortality Weekly Report. June 9, 1989; 38(22); 400-404.

5. WHO/UNICEF/UNU, ed. “Iron deficiency anaemia, assessment, prevention and control: a guide for programme managers.” WHO. 2001.

6. Hinderaker SG, Olsen BE, Bergsjo P, Lie RT, Gasheka P, Kvale G. “Anemia in pregnancy in the highlands of Tanzania.” Acta Obstretricia et Gynecologia Scandinavica. 2001; 80:18-26.

7. Murphy JF, O’Riordan J, Newcombe RG, Coles EC, Pearson JF. “Relation of haemoglobin levels in first and second trimesters to outcome of pregnancy.” Lancet. May 1986;1(8488):992-995.

8. Lee RL. “Iron Deficiency Anemia.” California Department of Health Services; Maternal Child and Adolescent Health Branch. January 2004.

9. Rusia U, Madan N, Agarwal N, Sikka M, Sood S. “Effect of maternal iron deficiency anaemia on foetal outcome.” Indian Journal of Pathology and Microbiology. 1995;38:273-279.

10. Preziosi P, Prual A, Galan P, Daouda H, Boureima H, Hercberg S. “Effect of iron supplementation on the iron status of pregnant women: consequences for newborns.” American Journal of Clinical Nutrition. 1997;66:1178-1182.

11. Dallman PR, Yip R, Johnson C. “Prevalence and causes of anemia in the United States, 1976 to 1980.” American Journal of Clinical Nutrition. 1984;39:437-445.

12. Erwin G. “Consultant Pharmacist-Driven Approach to Identification of Anemia of CKD in SNF Residents.” American Society of Consultant Pharmacists.

13. Agarwal KN, Agarwal DK, Mishra KP. “Impact of anaemia prophylaxis in pregnancy on maternal haemoglobin, serum ferritin & birth weight.” Indian Journal of Medical Research. August 1991;94:277-80.

14. Hemminki E, Starfield B. “Routine administration of iron and vitamins during pregnancy: Review of controlled clinical trials.” Blackwell Journal of Obstetrics & Gynaecology. June 1978;85(6):404.

15. Gamponia MJ, Babaali H, Yugar F, Gilman RH. “Reference values for pulse oximetry at high altitude.” Archives of Disease in Childhood. May 1998;78:461-465.

16. CDC (1995): Altitude, Hemoglobin Curve and CDC Anemia Criteria which uses the altitude adjustment. Centers for Disease Control and Prevention.

17. Medline Plus Medical Encyclopedia. Entries on Hematocrit, Hemoglobin, Iron deficiency anemia. Available at: http://www.nlm.nih.gov/medlineplus/. Accessed January 25, 2006.

18. Desalegn S. “Prevalence of anaemia in pregnancy in Jima town, southwestern Ethiopia.” Ethiopian Medical Journal. October 1993;31(4):251-258.

19. Frith-Terhune AL, Cogswell ME, Khan LK, Will JC, Ramakrishnan U. “Iron deficiency anemia: higher prevalence in Mexican American than in non-Hispanic white females in the third National Health and Nutrition Examination Survey, 1988–1994.” American Journal of Clinical Nutrition. October 2000;72(4):963-968.

20. Abyad A. “Routine Prenatal Screening Revisited.” Health Care For Women International. March 1999;20(2):137-145.

21. Viteri F. Iron supplementation for the control of iron deficiency anemia in populations at risk. Nutrition Review. 1997;55:189–203.

22. World Health Organization. The prevalence of anemia in women: a tabulation of available information. 2nd ed. Geneva: World Health Organization, 1992.

23. Institute of Medicine, Food and Nutrition Board. Iron deficiency anemia: recommended guidelines for the prevention, detection, and management among US children and women of child bearing age. Washington, DC: National Academy Press, 1993.

24. Theil EC, Burton JW, Beard JL. A sustainable solution for dietary iron deficiency through plant biotechnology and breeding to increase seed ferritin control. European Journal of Clinical Nutrition. 1997;51:S28–31.

25. Centers for Disease Control and Prevention. CDC report: recommendations to prevent and control iron deficiency in the United States. MMWR Morbidity and Mortality Weekly Report 1998;47:1–29.

26. Milman N, Agger AO, Nielsen OJ. Iron supplementation during pregnancy. Effect on iron status markers, serum EPO, and human placental lactogen. A placebo controlled study in 207 Danish women. Danish Medical Bulletin. 1991;38:471–6.

27. Sjostedt JE, Manner P, Nummi S, Ekenved G. Oral iron prophylaxis during pregnancy: a comparative study on different dosage regimens. Acta Obstetricia et Gynecologica Scandinavica Suppl 1975;48:87–108.

28. Galloway R, McGuire J. Determinants of compliance with iron supplementation; supplies, side effects, or psychology? Social Science & Medicine. 1994;39:381–90.

29. Yu SM, Keppel KG, Singh GK, Kessel W. Preconceptional and prenatal multivitamin mineral supplement use in the 1988 National Maternal and Infant Health Survey. American Journal of Public Health. 1996;86:240-242.

30. Chanarin I, Rothman D. Further observations on the relation between iron and folate status in pregnancy. British Medical Journal. 1971;2:81–4.

31. Hemminki E, Uski A, Koponen P, Rimpela U. Iron supplementation during pregnancy—experiences of a randomized trial relying on health service personnel. Control Clinical Trials. 1989;10:290–8.

32. Inter-American Parliamentary Group on Population and Development. “New legislation Universal Mother and Infant Health Insurance Law (SUMI) – Bolivia.” IAPG Parliamentary Dialogue. http://www.iapg.org/pdf/IAPG_NewsLetter.pdf.