

## BIOMEDICAL FACTORS ASSOCIATED TO HIGH FERTILITY AT HIGH ALTITUDE<sup>1</sup>

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**SUMMARY.** The present study has been designed to analyze information from the National Peruvian Census, 1993, and the Demographic Survey, 1991-1992 carried out in Peru (Peru, 1994; Endes, 1992) to determine population size at high altitude and Global Fertility Rate. The study has been also designed to investigate in populations living at sea level and at high altitude, age at menarche and age at menopause, the prevalence of pregnancies in adolescents, the percentage of pregnancies during breast feeding in women who never use modern contraceptives, and the serum prolactin levels during first three post partum months in women during breast feeding. Length of reproductive life (years) was significantly higher at sea level than at high altitude. The highest the altitude of residence, the lowest the reproductive life span. The administrative regions located at high altitude, except Arequipa, have high Global Fertility Rates than populations living at the coast of Peru (La Libertad, Grau and Lima). The three regions located at the jungle of Peru have also high GFR. The GFR according natural geographical regions were 2.1 children per woman in Metropolitan Lima, 3.3 in the rest of the coast, 4.9 in altitude, and 5.1 in the jungle. In 224 mothers who never used modern contraceptive methods, interval between births was significantly lower at Cerro de Pasco ( $2.7 \pm 0.15$  years) than at Cusco ( $3.1 \pm 0.29$  years) or Lima ( $3.8 \pm 0.36$  years).

The percentage of women who got pregnant during breastfeeding increased as it increased the altitude of residence. Serum prolactin levels were significantly higher in women natives at sea level than at high altitude ( $P < 0.01$ ).

In conclusion our data suggest that women at high altitude have more reproductive efficiency.

**Key words:** Altitude, Global Fecundity Rate, Prolactin, Breastfeeding, Reproductive life, Fertilization.

## INTRODUCTION

In different populations in the world, number of children is determined by social and religious factors. Demographic analysis have demonstrated that in populations without access to modern forms

**RESUMEN** El presente estudio ha sido diseñado para analizar la información del Censo Nacional del Perú, 1993 y la Encuesta Demográfica de Población, 1991-1992 realizada en el Perú (Perú, 1994; Endes, 1992) para determinar la población que habita en las alturas del Perú y la Tasa Global de Fecundidad (TGF). El estudio ha sido diseñado para investigar en poblaciones que viven a nivel del mar y en la altura, la edad de menarquia, la edad de menopausia, la prevalencia de embarazos en la adolescencia, el porcentaje de embarazos durante la lactancia materna en mujeres que nunca utilizaron contraceptivos, y los niveles de prolactina sérica durante los tres primeros meses posteriores al parto en mujeres que dan lactancia materna exclusiva. La duración de la vida reproductiva fue mayor a nivel del mar que en la altura, donde a mayor altitud de residencia menor es la duración de la vida reproductiva. Exceptuando a Arequipa, las poblaciones de las regiones administrativas ubicadas en la altura tienen una mayor TGF que las localizadas en la costa del Perú (La Libertad, Grau y Lima). Las tres regiones localizadas en la selva tienen también una alta TGF. La TGF según regiones naturales fue de 2.1 niños por mujer en Lima Metropolitana, 3.3 en el resto de la costa, 4.9 en la altura, y 5.1 en la selva. En 224 madres que nunca usaron métodos contraceptivos, el intervalo entre hijos fue menor en Cerro de Pasco ( $2.7 \pm 0.15$  años) que en Cusco ( $3.1 \pm 0.29$  años) o Lima ( $3.8 \pm 0.36$  años).

El porcentaje de mujeres que se embarazaron durante la lactancia aumentó conforme aumentó la altitud de residencia. Los niveles de prolactina sérica fueron significativamente mayores en las lactantes de nivel del mar que en la altura ( $P < 0.01$ ).

En conclusión nuestros datos sugieren que en la altura hay más eficiencia reproductiva.

**Palabras claves:** Altura, Tasa Global de Fecundidad, Prolactina, Lactancia, Vida reproductiva, Fertilización.

of contraception, birth intervals are determined principally by the duration of breastfeeding (Bongaarts and Potter, 1983). Breastfeeding controls fertility not only during amenorrhea period but also beyond the resumption of menses (Singh et al, 1993).

Received December 20, 1994; revised and accepted March 22, 1995

Presented at the First World Congress on High Altitude Medicine and Physiology. La Paz, Bolivia, September 11 to 16, 1994.

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Studies on populations living at high altitude of Hymalayas have revealed that fertility is reduced. This has been confronted by recent studies carried out in Peruvian Andean populations (Gonzales, 1993).

Prevalence of use of modern contraceptives in populations living at high altitude is still lower (Alarcón and Gonzales, 1993). However, when social factors and use of modern contraceptives is controlled, a high fertility is still observed at high altitude (Gonzales et al, 1993) suggesting that fertility in populations living at high altitude may be also determined by biomedical factors as a mechanism of adaptation to high altitude. For instance, diseases like hyperprolactinemia, which is a common cause of infertility in women living at sea level, has low prevalence at high altitude (Gonzales and Carrillo, 1993).

High fertility in any population is determined by long lenght of reproductive life based on the onset of menses (age at menarche) and the end of menses (age at menopause), high prevalence of pregnancies in adolescent ages, shorter intergenetic interval, which depends from length of post-partum sexual abstinence, and lenght of breastfeeding.

The present study has been designed to analyze information from the National Peruvian Census, 1993 and the Demographic Survey, 1991-1992 carried out in Peru (Peru, 1994; ENDES, 1992) to determine population size at high altitude and Global Fecundity Rate. The study has been also designed to investigate in populations living at sea level and at high altitude, age at menarche and age at menopause, the prevalence of pregnancies in adolescents, the percentage of pregnancies during breastfeeding in women who never use modern contraceptives, and the serum prolactin levels before three months after parturition in women during breastfeeding.

## MATERIAL AND METHODS.

The basic data used here come from the Demographic survey carried out in Peru during 1991-1992 and the National Peruvian Census carried out

in July 1993 under the auspices of the National Institute of Statistics and Informatic, Peru. The main objective of the study was to determine the effects of biomedical factors present in women at high altitude on fertility. Data from the National Peruvian Census were analyzed on departments basis (24 in 1993), whereas data from the Demographic survey was recorded by Administrative Regions. In Perú, during 1991-1992, it was defined 13 administrative regions. The following regions have populations living mainly at altitude: Andres Cáceres (70.6%), Arequipa (83.9%), Inka (85.9%), Mariátegui (75.5%).

Age at menarche was assessed in 296 women residing at Lima (150 m), Cusco (3400 m) and Cerro de Pasco (4340 m). Age of menarche was recorded by the Recall Method in women from 20-30 years old. Data were calculated as mean  $\pm$  SEM.

Age at menopause was assessed in 128 women residing at Lima (150 m), Cusco (3400 m) and Cerro de Pasco (4340 m). Data were obtained from women aged over 50 years. Age at menopause was recorded by the Recall Method, and data were calculated as mean  $\pm$  SEM.

Prevalence of women who got pregnancies during breast feeding was obtained after a survey carried out in Lima at two public hospitals, Cayetano Heredia Hospital and Arzobispo Loayza Hospital, and in Cerro de Pasco at one public hospital, Daniel A Carrión Hospital. The study was done in women who never used modern contraceptives methods. This study was carried out in Lima (150 m), Tarma (3000 m), Cusco (3400 m) and Cerro de Pasco (4340 m). Data were referred as percentage of women who got pregnancies before the last parturition despite of breastfeeding. In these women intergenetic interval was calculated indirectly by calculating interval between two births.

Serum prolactin levels were determined in 33 women from Lima (150 m) and 12 from Cerro de Pasco (4340 m) with exclusive lactation between 1-3 months of post-partum. Between 08.00-10.00 h a venous blood sample was obtained from each

women after fastnight and during 30-60 minutes after last suckling. Blood sample was centrifuged at 3000 RPM and serum was removed and kept frozen at -20°C until assayed for prolactin.

Serum prolactin concentration was measured by radioimmunoassay (RIA) using reagents provided by the World Health Organization. <sup>125</sup>Iodine-prolactin was used as reactive marker for the RIA. Data are referred as mIU/ml.

Data were analyzed using parametric and non parametric statistics. Differences among mean age at menarche or mean age at menopause were analyzed by analysis of variance and the multiple range test. Differences among prevalence of pregnancies during breast feeding were analyzed by chi square test. Differences between serum

prolactin levels in Lima and Cerro de Pasco were assessed by Student t test. A difference was considered as significant when p was below 0.05.

## RESULTS.

### Populations with >1x10<sup>6</sup> inhabitants in Peru

The population in Peru during 1993 was 22'128,466 inhabitants. These were distributed in the 24 departments, seven of them having >1 million inhabitants (Table 1). From these, four of them were located at altitudes over 2000 meter.

Distributed as natural geographic regions, 11'558,204 inhabitants were at the coast, 7'904,-711 at altitude, and 2'665,551 inhabitants at the jungle of Peru.

Table 1.- Departments with higher 1 million inhabitants during 1993 and place of location

Departments	Inhabitants	Location
Cajamarca	1'273,596	Altitude
Cusco	1'016,954	Altitude
Junín	1'026,946	Altitude
La Libertad	1'279,472	Sea level
Lima	6'483,901	Sea level
Piura	1'437,675	Sea level
Puno	1'057,606	Altitude

Source: National Population Survey. Peru, 1993.

Table 2 shows that, excepting Arequipa, all the administrative regions located at high altitude have high Global Fecundity Rates than populations living at the coast of Peru (La Libertad, Grau and Lima).

The three regions located at the jungle of Peru (Loreto, Ucayali and San Martín) have also high GFR ranging from 4.6 to 5.5 children per woman.

The GFR according natural geographical regions were 2.1 children per woman in Metropolitan Lima, 3.3 in the rest of the coast, 4.9 in altitude, and 5.1 in the jungle.

### Rate of fertilization

Interval between births (months) were lowest at highland places than at the coast or jungle. This low interval (29.2 months) compared with that observed at jungle (29.4 months) was lower despite of higher use of contraceptives (49.5% vs 48.3%) and low sexual activity (70.5% at altitude vs 76.4% at jungle) (Table 3).

Analysis of 224 mothers who never use modern contraceptive methods having the second child demonstrated that interval between children was significantly lower at Cerro de Pasco ( $2.7 \pm 0.15$  years) than at Cusco ( $3.1 \pm 0.29$  years) and Lima ( $3.8 \pm 0.36$  years).



Table 2. Global Fecundity Rate (per thousand of women) in women according administrative regions in Peru

Administrative region	GFR (Children per woman)	Percent of population living at altitude	Number of live children
Inka	5.2	85.9	6.2
Arequipa	3.0	83.9	4.0
Mariátegui	4.4	75.5	5.6
A. Cáceres	4.6	70.6	6.1
Chavín	4.2	52.5	5.9
Libertadores	5.2	51.6	6.7
Nor-Oriental	4.1	43.4	5.7
La Libertad	3.9	21.4	5.9
Grau	3.9	10.8	6.5
Lima	2.3	1.1	3.8
Loreto	5.5*	0.0	6.5
Ucayali	5.0*	0.0	7.0
San Martín	4.6*	0.0	6.5

\*Located at the jungle of Peru. GFR: Global Fertility Rate.

Table 3. Interval between births according natural geographical regions in Peru and prevalence of use of contraceptives

Natural Region	Median of interval between births (months)	Use of any contraceptive methods (%)	Sexually active during the last 4 weeks of the survey (%)
Metropolitan Lima	39.9	72.7	73.0
Rest of coast	31.6	63.9	74.6
Altitude	29.2	49.5	70.5
Jungle	29.4	48.3	76.4

Source: Endes, 1992

Table 4. Length of reproductive life at Lima (150 m), Cusco (3400 m) and Cerro de Pasco (4340 m).

Place	Altitude (m)	Age at menarche (yrs)	Age at menopause (yrs)	Length of reproductive life (yrs)
Lima	150	12.94 ± 0.21	48.4 ± 0.75	35.5
Cusco	3400	14.12 ± 0.25*	45.5 ± 0.67**	31.4
Cerro de Pasco	4340	14.65 ± 0.20*	42.6 ± 0.39*	28.0

Data are mean ± SEM. \*P < 0.01; \*\*P < 0.05 with respect to values at Lima.

### Reproductive life span

Length of reproductive life (years) was significantly higher at sea level than at high altitude (Table 4). The highest the altitude of residence, the lowest the reproductive life span.

### Age of mother at first child.

Age of mother at first child at coast region was 21.5 years for women actually ranging 25-49 years of age; age at first child at highland region was 21 years, and at jungle, it was 19.7 years (ENDES, 1992).

### Percentage of Women who got pregnancies during exclusive breastfeeding

The percentage of women who got pregnancies during breastfeeding increased as it increased the altitude of residence (Table 5).

### Serum Prolactin levels in women during first three months of exclusive breastfeeding

As it was shown in Table 6, serum prolactin levels were significantly higher in native women at sea level than at high altitude ( $P < 0.01$ ).

Table 5.- Percentage of women who got pregnancies during exclusive breastfeeding at sea level and at high altitude.

Place	Altitude (m)	Number	% of pregnant women
Lima	150	92	6.4
Tarma	3000	24	25.0*
Cusco	3400	62	24.2*
Cerro de Pasco	4340	82	37.8*

\* $P < 0.05$  with respect to Lima (150 m).

Table 6.- Serum prolactin levels (mIU/ml) during first three months of exclusive breastfeeding.

Place, altitude	Prolactin (mIU/ml)
Lima, 150 m (33)	2473.56 $\pm$ 211.97
Cerro de Pasco, 4340 m (12)	1353.33 $\pm$ 331.61*

Data are mean  $\pm$  SEM. Between parentheses are number of data. \* $P < 0.01$  with respect with values in Lima.

## DISCUSSION

Data from the present study revealed that reproductive life span as defined as by age at menarche and age at menopause is shorter at high altitude populations than at sea level, as a consequence of later age at menarche and earlier onset of menopause at high altitude, as reported previously (Gonzales, 1994; Gonzales and Ortíz, 1994). However, despite of this shorter reproductive life span, Global Fecundity Rate (GFR) was higher in Peruvian high altitude populations than those living at the coast. A high GFR was also observed at

populations living at jungle of Peru. The high GFR at jungle was explained due to a high prevalence of pregnancies at adolescent ages (Wilhelm et al, 1991). However, this is not the case for women living at high altitude. In fact, at the coast, age of mother at first child was 21.5 years for women actually ranging 25-49 years of age; at highland places age at first child was 21 years, and at jungle was 19.7 years (ENDES, 1992).

This high GFR at high altitude results in high population growth. As, it is observed in the data of the present study, from seven departments with



higher 1 million inhabitants, four are located at high altitude. If we except Lima, with about 6 millions inhabitants, which is the capital of the country where industry, commerce, and seat of government is concentrated, and the number of migrant people is extremely high, we have that from six departments with high population, 66% of them are at highlands.

Use of contraceptives is an important mechanism to explain differences in population size. For instance, in Peru use of contraceptives is still lower in populations from high altitude and jungle, being lowest in the last group. However, interval between births (months) were lowest at highland places than at the coast or jungle. This low interval (29.2 months) compared with that observed at jungle (29.4 months) was lower despite of higher use of contraceptives (49.5% vs 48.3%) and low sexual activity (70.5% at altitude vs 76.4% at jungle) as it is shown in Table 3. If we select women who never use contraceptive methods, and we analyze the birth interval between first and second child, we found that this interval is lower at high altitude than at sea level suggesting a more reproductive efficiency at high altitude (Gonzales, 1993).

Birth interval and intergenesic interval depends of several factors, as use of contraceptives after parturition, post-partum sexual abstinence, maternal breastfeeding.

Controlling use of modern contraceptive methods, we have observed that interval between first and second child was significantly lower at Cerro de Pasco (4340 m) than at Cusco (3400 m) and Lima (150 m). As sexual abstinence duration after parturition was similar at sea level and at high altitude, it was suggested that differences in rate of fertilization between sea level and high altitude population must be in maternal breastfeeding habits.

Previously we have demonstrated that exclusive maternal lactancy is more frequent at high altitude than at sea level populations, and that frequency of suckling was similar between both population groups (Gonzales, 1994a). This situa-

tion should produce a high protection to women living at high altitude against a pregnancy during lactation, since exclusive breastfeeding is an effective contraceptive method (Díaz et al, 1989), however, our data demonstrate that maternal breastfeeding is not protecting against a new pregnancy at high altitude as well as at sea level.

Amenorrhea produced by lactancy prolongs the interval between births (Rosner and Schulman, 1990), but variation in the duration of post-partum infertility by lactancy between populations has been reported (Díaz et al, 1982; 1991; Shaaban et al, 1990; van Look 1988). No studies has been carried out about prevalence of returned menses after parturition during exclusive breastfeeding at high altitude.

Prolactin, a glycoprotein hormone, which when it is anormally increased is associated with infertility (Gonzales and Carrillo, 1993), may be the hormone associated to lactational amenorrhea (McNeilly, 1988). Our study demonstrated that serum prolactin levels were lower during first three months of breastfeeding at high altitude than at low altitude.

In conclusion our data suggest that women at high altitude have more reproductive efficiency.

#### ACKNOWLEDGMENT

This study was supported in part by the Long Institutional Development Grant from the Human Reproduction Programme, World Health Organization.

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