SHORT COMMUNICATION

1. Obstetrician and gynecologist, Department of Obstetrics and Gynecology, Hospital Regional Docente de Cajamarca, Peru
2. Obstetrician and gynecologist, Department of Obstetrics and Gynecology, Simón Bolívar COVID-19 Hospital, Cajamarca, Peru
3. Obstetrician and gynecologist, Department of Obstetrics and Gynecology, Medimagen, Cajamarca, Peru
4. Obstetrician and gynecologist, Department of Obstetrics and Gynecology, Complejo Hospitalario Dr. Arnulfo Arias Madrid Hospital, Caja del Seguro Social, Panama
5. National Institute of Allergy and Infectious Diseases, Maryland, EE UU

Correspondence:
Jorge Arturo Collantes Cubas
♀ Mz H lote 15 Brisas de Villa, Santiago de Surco
☎ 965008273
✉ Dinaayala29@gmail.com

Clinical characteristics of pregnant women in labor with SARS-CoV-2 infection at high altitude: A case series

Características clínicas de gestantes en trabajo de parto con infección SARS-CoV-2 en la altura: serie de casos

Jorge Arturo Collantes Cubas[1], Segundo Alberto Pérez Ventura[1], Oscar Eduardo Morillo Montes[1], Galo Terrones Julcamoro[2], Gilmer Antonio Huancahuire Aguilar[2], Jorge Martín Benites Pajares[3], Paulino Vigil-De Gracia[4], Francisco José Leyva[5]

ABSTRACT

Introduction: Fewer COVID-19 cases and less lethality have been observed at high altitude compared to cases reported at sea level. There are currently no publications reporting clinical behavior of pregnant women with COVID-19 at high altitude. **Methods:** This is a retrospective study with review of medical records between March 6, 2020 and June 15, 2020. The first thirteen cases of pregnant women with COVID-19 who were attended at Simón Bolívar COVID-19 Hospital, located at 2 750 meters above sea level, are described. The cases came from altitudes between 2 035 and 3 502 meters above sea level (masl). Statistical analysis used SPSS, version 19.0. **Results:** Thirteen cases of pregnant women with COVID-19 confirmed by IgM for SARS-CoV-2 were attended at 2 750 masl (9 022.31 feet) in the Peruvian Andes. Delivery by cesarean section occurred in eight cases (61.5%) and five (38.5%) delivered vaginally. There were two cases (15.4%) of preeclampsia, one with diagnosis of HELLP syndrome, prematurity and fetal death. Three cases (23.1%) developed uterine hypotonia that required Hayman or B-Lynch suture. Two cases (15.38%) were complicated with oligohydramnios and two with urinary infection. Hemoglobin levels were between 11.1 and 16 g/dL. Only one case (7.7%) was symptomatic, with mild pharyngeal pain. No vertical transmission was detected by IgM/IgG for SARS-CoV-2. Clinical evolution was favorable in the thirteen cases and they were discharged after 2 to 4 days hospitalization to continue home quarantine. **Conclusions:** Results in this short study show pregnant women in labor with COVID-19 by rapid IgM test for SARS-CoV-2 at high altitude were mostly asymptomatic; there was no vertical transmission, but high presence of other obstetrical complications.
Key words: Pregnancy, Coronavirus infections, COVID-19, SARS CoV-2, High Altitude, Preeclampsia, Cajamarca, Peru.

RESUMEN

Introducción. A gran altitud, se ha observado menos casos y menos letalidad de COVID-19 en comparación con cifras reportadas a nivel del mar. Actualmente no hay publicaciones que informen el comportamiento clínico de COVID-19 en mujeres embarazadas adaptadas a la altura e hipoxia crónica en el Perú. **Métodos.** Estudio retrospectivo mediante revisión de historias clínicas del 6 de marzo de 2020 al 15 de junio de 2020. Se describe los primeros trece casos de gestantes con COVID-19 atendidos en el Hospital COVID-19 Simón Bolívar, ubicado a 2 750 msnm. Los casos procedían de altitudes entre 2 035 msnm y 3 502 msnm. El análisis estadístico se realizó con SPSS, versión 19.0. **Resultados.** Trece casos de gestantes con COVID-19 confirmado por IgM para SARS-CoV-2, fueron tratadas a 2 750 msnm (9 022,31 pies), en los Andes peruanos. El parto fue por cesárea en ocho casos (61,5%) y por vía vaginal en cinco (38,5%). Hubo dos casos (15,4%) de preeclampsia, uno de ellos diagnosticado como síndrome HELLP, prematuridad y muerte fetal. Tres casos (23,1%) desarrollaron hipotonía uterina posparto y requirieron sutura de Hayman o B-Lynch. Dos casos (15,4%) se complicaron con oligohidramnios y otros dos casos con infección urinaria. Los niveles de hemoglobina variaron entre 11,1 y 16 g/dL. Solo un caso (7,7%) presentó sintomatología, con dolor faríngeo leve. No se observó transmisión vertical detectada por IgM/IgG para SARS-CoV-2. La evolución clínica fue favorable en los trece casos y el alta fue a los 2 a 4 días, para continuar la cuarentena en domicilio. **Conclusiones.** En el presente estudio preliminar, las gestantes en trabajo de parto con COVID-19 por prueba rápida IgM para SARS-CoV-2 en la altura fueron generalmente asintomáticas; no hubo transmisión vertical. Se presentó alto porcentaje de otras complicaciones obstétricas.
Palabras clave. Embarazo, Infecciones por coronavirus, COVID-19, SARS CoV-2, Altura, Preeclampsia, Cajamarca, Perú.

Jorge Arturo Collantes Cubas, Segundo Alberto Pérez Ventura, Oscar Eduardo Morillo Montes, Galo Terrones Julcamoro, Gilmer Antonio Huancahuire Aguilar, Jorge Martín Benites Pajares, Paulino Vigil-De Gracia, Francisco José Leyva

INTRODUCTION

Fewer cases and less lethality from COVID-19 have been seen at high altitudes compared with the numbers reported at sea levels[1]. Climatological and demographic factors could explain this observation[2,3]. At high altitude, chronic hypoxia has resulted in the genetic adaptation of man to a reduced amount of oxygen[4-8]. The association between hypoxia and a decreased expression of angiotensin-converting enzyme 2 (ACE2) is known[1]. ACE2 is the main receptor of the SARS-CoV-2 virus[9]. In addition, an increase in the activity and expression of ACE2 during pregnancy has been reported in experimental studies[10]. In Spain, the seroprevalence for SARS-CoV-2 during pregnancy has been published in 14%[11].

For diagnosis, viral RNA detection tests and serology tests that detect IgG/IgM antibodies are used[12].

Clinically, the majority of pregnant women are asymptomatic (87.9%)[13], and as for pregnant women with symptoms, they have mild (86%), severe (9.3%) and critical (4.7%) illness[14]. The most frequent symptoms in pregnant women with SARS-CoV-2 are cough (76%) and fever (38%)[15].

Complications from COVID-19 mostly occur in the third trimester, including 4.2% of patients who suffer from pneumonia[11]. Obstetric complications are observed in 45% of cases[15]. Clinical findings resembling preeclampsia have been reported[16-18]. Regarding the mode of delivery, 88% is via cesarean section[15].

Vertical transmission during pregnancy, childbirth and the puerperium is very low, despite being SARS-CoV-2 found in the placenta, not so in cord blood or breast milk[19,20].

At present, no publications have been found that indicate the clinical behavior of COVID-19 in pregnant women adapted to altitude and chronic hypoxia.

Our objective is to describe the maternal and neonatal clinical characteristics of the first cases of women in labor seen in the highlands of Peru infected with COVID-19 and diagnosed by rapid IgM or IgM/IgG antibodies tests.

METHODS

The present is a retrospective study of a series of cases of pregnant women treated in a single center located in the altitude between March 6, 2020 and June 15, 2020. It was approved by the institutional board of directors and informed consent was obtained from the pregnant women. We analyzed the clinical charts of 13 pregnant women admitted for labor in the city of Cajamarca, Peru, at 2 750 masl.

The tests used for the detection of antibodies against SARS-CoV-2 were subjected to immunochromatographic assay for the rapid, qualitative, and differential detection of IgG and IgM antibodies, with a sensitivity of 91.8% and specificity of 96.4%.

For the study, we used the CARE Guidelines: Consensus-based Clinical Case Reporting Guideline Development checklist. Statistical analysis was performed with SPSS software, version 19.0. Continuous variables were expressed directly as a range. Categorical variables were expressed as numbers (%).

RESULTS

The 13 pregnant women in labor were attended at Simón Bolívar COVID-19 Hospital in Cajamarca, Perú, located at 2 750 masl. They came from altitudes between 2 035 and 3 502 masl. All cases were positive for SARS-CoV-2 IgM or IgM/IgG. Age ranged from 19 to 41 years, gestational age from 33 to 41 weeks. One patient (7.7%) presented mild symptoms (pharyngeal pain) and twelve (92.3%) were asymptomatic. Type of delivery was cesarean section in 8 (61.5%) cases and vaginal in 5 (38.5%). Eight (61.5%) had other pregnancy complications and five (38.5%) did not; two (15.4%) had preeclampsia, one (7.7%) of them HELLP syndrome that resulted in prematurity and fetal death. Three (23.1%) were complicated by postpartum hemorrhage due to uterine hypotonia during cesarean section, which required Hayman or B-Lynch suture. Two (15.4%) had oligohydramnios and other two (15.4%) urinary tract infection (Table 1, Figure 1). No patient required admission to intensive care unit or received specific treatment for COVID-19.
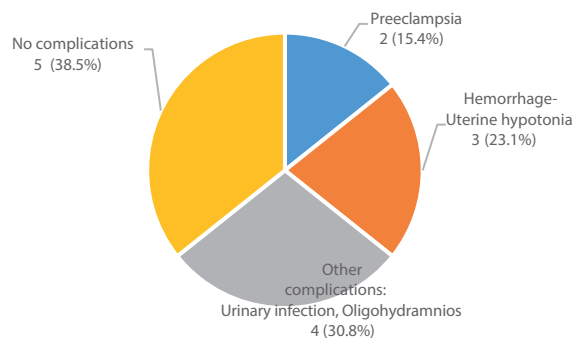
Table 1. Cities of origin, altitude and clinical characteristics.

Characteristics	1	2	3	4	5	6	7	8	9	10	11	12	13	n (13)
Date	Abr 21	Abr 21	Abr 22	Abr 24	Abr 30	May09	May20	May 23	May25	May27	Jun 03	Jun 05	Jun14	
Origin	Tacabamba	Cuyumalca	Chota	Chota	Cajamarca	Chota	Cajamarca	Hualgayoc	Bambamarca	Santa Cruz	Cutervo	Huasmin	Sucre	
Altitude in masl* (m)	2 035	2 780	2 388	2 388	2 750	2 388	2 750	3 502	2 526	2 035	2 649	2 550	2 612	2 566±371.9
Altitude in feet	6 677	9 121	7 835	7 835	9 022	7 835	9 022	11 490	8 287	6 677	8 691	8 366	8 590	8 417±1 220
Age (years)	28	38	37	41	31	36	23	19	39	21	41	23	21	30.6±8.4
Gestacional age (weeks)	38	40	40	37	40	39	40	39	33	41	35	39	37	38.3±2.3
Pregnancies	2	1	3	3	1	2	1	1	1	4	4	2	2	2.1±1.1
Days of hospitalization	3	3	2	3	4	2	2	2	4	2	2	2	2	2.1±1.1
Temperature (°C)	37.4	36.5	36.8	36.2	36	36.3	36.6	36.7	36.5	36	36.2	36.2	36.3	36.5±0.4
Systolic pressure (mmHg)	100	100	110	140	120	100	110	90	140	100	90	90	135	109.6±2
Diastolic pressure (mmHg)	60	60	79	80	80	70	80	60	100	70	60	60	60	70.7±12
Heart rate	88	72	78	101	76	88	72	84	110	79	80	76	63	82.1±12
Oxygen saturation		96		98	96	94		93		94			95	95.1±1.6
Weight (kg)	58			69	58			64					51	60±6.8
Height (m)	1.55			1.53	1.52				1.50	1.55	1.54	1.54	1.51	1.5±0.0
Complications	Hypotonia	UTI	No	Preeclampsia	Hypotonia	No	Oligohy-dramnios		Hypotonia Preeclampsia HELLP Sd.	No	No	UTI	Oligohy-dramnios	
Delivery data														
Cesarean (Cs) vs Vaginal delivery (Vd)	Cs + BTL + Hayman	Cs	Cs	Cs	Cs + Hayman	Vd	Cs	Vd	Cs + B-Lynch	Cs	Vd	Vd	Vd	61.5% 38.5%
Indications for Cs	Previous Cs and narrow pelvis	Previous Cs and narrow pelvis	Previous Cs and CPD	CPD	Disfunctio-nal labor	-	Oligohy-dramnios	-	Preeclamp-sia/HELLP	Previous Cs	-	-	Oligohy-dramnios	
Anesthesia	Spinal	Spinal	Spinal	Spinal	Spinal	-	Spinal	-		Spinal	-	-	-	
Surgical time (minutes)	80	50	50	30	45	-	50	-			-	-	-	

*masl=meters above sea level; UTI=urinary tract infection; BTL=bilateral tubal ligation; CPD=cephalopelvic disproportion

Jorge Arturo Collantes Cubas, Segundo Alberto Pérez Ventura, Oscar Eduardo Morillo Montes, Galo Terrones Julcamoro, Gilmer Antonio Huancahuire Aguilar, Jorge Martín Benites Pajares, Paulino Vigil-De Gracia, Francisco José Leyva

FIGURE 1. OBSTETRIC COMPLICATIONS IN PREGNANT WOMEN WITH IGM (+) FOR SARS-COV-2 AT ALTITUDE.

Regarding the laboratory characteristics (Table 2), hemoglobin was reported between 11.1 g/dL and 16 g/dL, leucocytes between 8 720 /mL and 19 800 /mL, lymphocytes 1 188/mL to 2 814/mL, and platelets between 80 000/mL and 249 000/mL.

All newborns had a negative rapid test for SARS-CoV-2 IgM/IgG. The stillborn was not tested. All newborns were breastfed. The weights of the newborns ranged between 2 600 and 3 600 g. There were two cases of prematurity (15.4%) and one case of fetal death (7.7%) (Table 3).

DISCUSSION

92.3% of pregnant women evaluated in labor coming from altitudes between 2 035 and 3 502 masl, with positive IgM antibodies by rapid test for SARS-Cov-2 had asymptomatic or mild disease, and 61.5% suffered obstetric complications. There were 15.4% prematurity and 7.7% fetal deaths. No vertical transmission was found.

In altitude, most of the pregnant women studied had asymptomatic or mild disease, similar to studies from the USA, i.e., approximately 87%[13,14]. The cesarean delivery rate was lower than worldwide, i.e. 61.5% instead of 88%[15]. However, the high percentage of other obstetrical complications associated to the COVID-19 virus stands out, as it surmounts to 61,5% instead of the 45% published in a systematic review[15]. Preeclampsia (15.4%) and uterine atony (23.0%) were the complications found. There was no vertical transmission detected by IgG/IgM in neonates, data that coincides with the report by Chen, who found no vertical transmission[19].

Limitations of this study are having few cases, being retrospective, not having carried out molecular tests and having only evaluated patients during the third trimester; reasons for which the conclusions should be considered in context.

These results show that pregnant women in labor with a rapid test for SARS-CoV-2 in a highland region of Peru were generally asymptomatic or had mild disease. No vertical intrauterine transmission was found and there was a high percentage of other obstetric complications.

REFERENCES

1. Arias-Reyes C, Zubieta-DeUrioste N, Poma-Machicao L, Aliaga-Raudan F, Carvajal-Rodríguez F, Durschmann M, et al. Does the pathogenesis of SARS-CoV-2 virus decrease at high-altitude? Respir Physiol Neurobiol. 2020 Apr;277:103443. doi:10.1016/j.resp.2020.103443

2. Ahmadi MF, Sharifi A, Dorosti S, Jafarzadeh Ghoushchi S, Ghanbari N. Investigation of effective climatology parameters on COVID-19 outbreak in Iran [published online ahead of print 2020]. Sci Total Environ. 2020;729:138705. doi:10.1016/j.scitotenv.2020.138705

3. Bashir MF, Ma B, Bilal, Komal B, Mashir MA, Tan D, Bashir M. Correlation between climate indicators and COVID-19 pandemic in New York, USA. Sci Total Environ. 2020;728:138835. doi:10.1016/j.scitotenv.2020.138835

4. Julian CG, Moore LG. Human genetic adaptation to high altitude: Evidence from the Andes. Genes. 2019;10(2):1-20. doi: 10.3390/genes10020150

5. Moore LG. Measuring high-altitude adaptation. J Appl Physiol 2017 Nov 1;123(5):1371-85. doi: 10.1152/japplphysiol.00321.2017

6. Hamming I, Cooper ME, Haagmans BL, Hooper NM, Korstanje R, Osterhaus ASME, et al. The emerging role of ACE2 in physiology and disease. J Pathol. 2007 May;212(1):1-11. doi: 10.1002/path.2162

7. Bigham AW, Kiyamu M, León-Velarde F, Parra E, Rivera-Ch M, Shriver M, Brutsaert T. Angiotensin-converting enzyme genotype and arterial oxygen saturation at high altitude in Peruvian Quechua. High Alt Med Biol. 2008;9(2):167-78.

8. Vargas M, Vargas E, Julian CG, Armaza JF, Rodriguez A, Tellez W, mNiermeyer S, et al. Determinants of blood oxygenation during pregnancy in Andean and European residents of high altitude. Am J Physiol Regul Integr Comp Physiol. 2007 Sep;293(3):R1303-12. DOI: 10.1152/ajpregu.00805.2006

9. Li Y, Zhou W, Yang L, You R. Physiological and pathological regulation of ACE2, the SARS-CoV-2 receptor. Pharmacol Res. 2020;157:104833. doi:10.1016/j.phrs.2020.104833

10. Levy A, Yagil Y, Bursztyn M, Barkalifa R, Scharf S, Yagil C. ACE2 expression and activity are enhanced during pregnancy. Am J Physiol Regul Integr Comp Physiol. 2008;295:R1953–R1961.

11. Crovetto F, Crispi F, Llurba E, Figueras F, Gómez-Roig MD, Gratacós E. Seroprevalence and presentation of SARS-CoV-2 in pregnancy [published online ahead of print, 2020 Aug 6]. Lancet. 2020;S0140-6736(20)31714-1. doi:10.1016/S0140-6736(20)31714-1

12. Ravi N, Cortade DL, Ng E, Wang SX. Diagnostics for SARS-CoV-2 detection: A comprehensive review of the FDA-EUA COVID-19 testing landscape [published online ahead of print, 2020 Jul 18]. Biosens Bioelectron. 2020;165:112454. doi:10.1016/j.bios.2020.112454

13. Sutton D, Fuchs K, D'Alton M, Goffman D. Universal screening for SARS-CoV-2 in women admitted for delivery. N Engl J Med. 2020 May 28;382(22):2163-4. DOI: 10.1056/NEJMc2009316.

14. Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, et al. COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals. Am J Obstet Gynecol MFM. 2020 May;2(2):100118. doi: 10.1016/j.ajogmf.2020.100118

15. Capobianco G, Saderi L, Aliberti S, Mondoni M, Piana A, Dessole F, et al. COVID-19 in pregnant women: A systematic review and meta-analysis [published online ahead of print, 2020 Jul 16]. Eur J Obstet Gynecol Reprod Biol. 2020 Jul 16;S0301-2115(20)30446-2. doi:10.1016/j.ejogrb.2020.07.006

16. Mendoza M, Garcia-Ruiz I, Maiz N, et al. Pre-eclampsia-like syndrome induced by severe COVID-19: a prospective observational study [published online ahead of print, 2020 Jun 1]. BJOG. 2020 Jun 1;10.1111/1471-0528.16339. doi:10.1111/1471-0528.16339

17. Abbas AM, Ahmed OA, Shaltout AS. COVID-19 and maternal pre-eclampsia: A synopsis [published online ahead of print, 2020 Jun 15]. Scand J Immunol. 2020;e12918. doi:10.1111/sji.12918

18. Rolnik DL. Can COVID-19 in pregnancy cause pre-eclampsia? [published online ahead of print, 2020 Jun 22]. BJOG. 2020;10.1111/1471-0528.16369. doi:10.1111/1471-0528.16369

19. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet. 2020;395(10226):809-815. DOI:https://doi.org/10.1016/S0140-6736(20)30360-3

20. Lackey KA, Pace RM, Williams JE, Bode L, Donovan SM, Järvinen KM, et al. SARS-CoV-2 and human milk: What is the evidence? [published online ahead of print, 2020 May 30]. Matern Child Nutr. 2020;e13032. doi:10.1111/mcn.13032

Jorge Arturo Collantes Cubas, Segundo Alberto Pérez Ventura, Oscar Eduardo Morillo Montes, Galo Terrones Julcamoro, Gilmer Antonio Huancahuire Aguilar, Jorge Martín Benites Pajares, Paulino Vigil-De Gracia, Francisco José Leyva

Table 2. Laboratory results.

	Cases													N (13)
	1	2	3	4	5	6	7	8	9	10	11	12	13	
Hemoglobin (g/dL)	12.2	12.5	16	13.6	14.7		13.7	13.3	11	11.4	12.4	13.1	11.6	12.9±1.4
Blood type	A+	O+	O+	O+	A+		O+	O+	O+	O+	O+	O+	O+	
Leucocytes (cel/L)	13 900	11 100	19 800	10 100	9 500		8 720	13 400	15 800	11 900	10 800	15 600		12 783.6±3 315.6.
Lymphocytes (cel/L)	2 085	2 331	1 188	2 525	1 330		1 850	2 814	2 686	1 785	1 620	1 716		1 993.6±541.0
Creatinine (mg/dL)	0.6	0.57	0.55	0.62	0.61		0.8	0.67	1.14	0.45		0.67	0.73	0.7±0.2
Platelets (cel/L)	125 000	153 000	17 000	241 000	249 000		217 000	220 000	80 000	176 000		205 000	233 000	174 181.8±74 061.9
Elevated transaminases ALT (>45U/L) or AST (>35U/L)	No	No	No	No	No		No	No	Yes	No	No	No	No	1 (7.7%)

Table 3. Neonatal outcome

	Cases													n (13)
	1	2	3	4	5	6	7	8	9	10	11	12	13	
Birth weight (g)	2 650	3 600	2 600	2 600	3 000	3 600	3 000	2 600		3 300	2 750	3 100	2 700	2 958.3+-375.9
Low weight (<2 500 g)	No	No	No	No	No	No	No	No		No	No	No	No	
Apgar	8/9	8/9	8/9	8/9	8/9	9/9	8/9	7/9	0/0	8/9	7/8	9/10	8/9	
Prematurity	No	No	No	No	No	No	No	No	Yes	No	Yes	No	No	2 (15.4)
IgG/IgM	Negative	Negative	Negative	Negative	Negative		Negative	Negative	Yes	Negative	Negative	Negative	Negative	
Fetal demise	No	No	No	No	No	No	No	No	Yes	No	No	No	No	1 (7.7%)
Neonatal death	No	No	No	No	No	No	No	No		No	No	No	No	0