Article

Results of pregnancy control before and during the covid-19 pandemic: a comparison of two cohorts

Javier Llorca1,2*, Carolina Lechosa-Muñiz1,3*, Pelayo Frank de Zulueta3, Sonia López-Gómez3, Victoria Orallo3, Jéssica Alonso-Molero1,2,4, Barbara Arozamena-Llano3, Yolanda Jubete3, María Paz-Zulueta1,3,4**, María J Cabero1,3,4** and the MOACC-19 group.

*Equal contribution. ** Share senior authorship.

Members of the MOACC-19 group:

Bárbara Arozamena, Laura Conde-Gil, Elsa Cornejo del Río, Rocío Cuesta-González, Trinidad Dierssen-Sotos, María Fernández-Ortiz, Inés Gómez-Acebo, Pilar Gortázar, Coral Llano-Ruiz, Lorena Lasarte-Oria, Sonia Mateo-Sota, Rosa Pardo, Daniel Pérez-González, María Sáez de Adana Herrero.

- ¹ Universidad de Cantabria, Santander, Spain
- ² CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
- ³ Hospital Universitario Marqués de Valdecilla, Santander, Spain
- ⁴ IDIVAL, Santander, Spain
- * Correspondence: javier.llorca@unican.es

Abstract: COVID-19 pandemic put pregnant women in high risk, but behavioural changes has also led to lower rates of preterm births in high-income countries. The main goal in this article is to study the impact that COVID-19 pandemic is having on pregnancy control and outcomes. This is a joint analysis of two cohorts. A pre-pandemic one includes 969 pregnant women recruited in 2018. The pandemic cohort comprises 1168 pregnant women recruited in 2020. Information on demographic and socio-economic characteristics, reproductive history, characteristics of the current pregnancy and its outcome were obtained from medical records. Caesarean section was more frequent in the pre-pandemic cohort (24% vs. 18%, p = 0.004). Birth with less than 37 weeks of gestational age was more frequent in the pre-pandemic cohort (6% vs. 5%, p = 0.04). Weight at birth lower than 2500 grams occurred more frequently in the pre-pandemic cohort (9% vs. 6%, p = 0.001). Exclusive breastfeeding at hospital discharge was more frequent in the pandemic cohort than in the pre-pandemic one (60% vs. 54%, p = 0.005). We are reporting reductions in Caesarean section and preterm birth during the pandemic in a hospital located Northern of Spain. Further analysis would clarify if these lessening are related to changes in health-related behaviour or health-care functioning.

Keywords: COVID19; pregnant; cohort

1. Introduction

Infection by SARS-CoV-2 put pregnant women in high risk [1], as previously found in other highly pathogenic coronavirus, as SARS and MERS. COVID-19 pandemic, however, can affect pregnancy not only via maternal infection, but also because of its impact on societal functioning -e.g., national lockdowns and stay-at-home orders-, health-related behaviour -such as working-at-home- and health care disruption -including tele-medicine, curtailed provision of obstetric services and weakened health-care-seeking behaviour.

While some effects of COVID-19 pandemic on pregnancy are deleterious, as it is the case for higher maternal morbidity and mortality, it has been described that preterm births

were decreased in high-income countries, although a meta-analysis found important heterogeneity among studies [2].

Spain has been one of the European countries more mercilessly hit by COVID-19. Partial lockdown was declared by 14th March 2020 and complete lockdown -including halting of non-essential activity- from 29th March to 12th April 2020. After 21st June 2020, regional -rather than national- restrictions applied [3].

To further study the impact that COVID-19 pandemic is having on pregnancy control and outcomes, we compare two cohorts of pregnant women recruited in 2018 and 2020 at the University Hospital Marqués de Valdecilla (HUMV), in Santander, Northern of Spain.

2. Materials and Methods

Setting and patients

This is a joint analysis of two cohorts recruited at the HUMV, Santander, Spain. A prepandemic cohort was recruited from 1st January to 31st August 2018 and included 969 pregnant women and their children. Its main characteristics have been described elsewhere [4].

The pandemic cohort was recruited in 2020. Its profile has been already reported [3]. Recruitment began on 26th May and finished on 22nd October. This cohort was composed by three sub-cohorts. Sub-cohort 1 was retrospectively recruited and includes women delivering at HUMV between 23rd March (the first date the hospital introduced routinely SARS-CoV-2 infection test via PCR for all women admitted for delivery) and 25th May, 2020. Sub-cohort 2 was prospectively recruited and includes women delivering at HUMV from 26th May on. Sub-cohort 3 was prospectively recruited and includes women attended at HUMV for their routine 12-week of pregnancy consultation; many of their pregnancies are still ongoing when carrying on this analysis. The rationale for these three sub-cohorts is to differentiate the pandemic consequences in pregnancy according to the period of risk for each woman, which was as follows: women in the first sub-cohort were neither exposed to nor aware of SARS-CoV-2 for most of their pregnancy, and their exposition was limited to the last trimester of pregnancy, which mostly coincided with the first pandemic wave. Women in the second sub-cohort could have been both exposed to and aware of the pandemic from their second trimester of pregnancy, which coincided with the first pandemic wave, while their third trimester was concurrent with the lower levels of covid-19 incidence between the first and the second waves. Finally, women in the third sub-cohort were aware of the pandemic all throughout their pregnancy and their exposition was higher in the second and posterior waves.

Gathered information

Information on maternal age, educational level (classified as primary school, secondary school, 3 and university), occupational situation (classified as employed, unemployed or inactive, student), number of previous children, length of pregnancy (later classified as less than 34 weeks, 34-36 weeks + 6 days, 37 weeds or more), type of delivery (eutocic, instrumental or Caesarean section), weight at birth (later classified as less than 2500 grams, 2500 – 4000 grams and more than 4000 grams) and type of feeding at hospital discharge (exclusive breastfeeding, mixed -breastfeeding and artificial formula-, and formula) were obtained from medical records.

Statistical analysis

In this article, we compare the pre-pandemic and the pandemic cohorts with each other. We also carry on the same comparisons between all three sub-cohorts in the pandemic cohort.

Association between smoking and cohort according to woman, pregnancy or child characteristics was tested using Chi-square test and association between the average daily number of cigarettes and cohort according to the same characteristics was tested using the Student's t test. Results are provided as number with percentage or mean with standard deviation. All p values are two-tailed. The statistical analysis was carried out with the package Stata 16/SE (StataCorp, College Station, Tx, US).

3. Results

In this study, 2137 pregnant women were included; 969 belonging to the pre-pandemic cohort and 1168 to the pandemic one. Among the pandemic cohort, 270 women were retrospectively recruited and had delivered a bay before 26th May, 2020 (sub-cohort 1); 350 were prospectively recruited at delivery from 26th May, 2020 on (sub-cohort 2), and 548 were prospectively recruited at week 12 of pregnancy (sub-cohort 3). Only 53 women in sub-cohort 3 had already delivered a baby by the time of this analysis, so this sub-cohort was excluded regarding variables related to delivery.

Table 1 provides the description of the participants. About 80% women were aged 28-40 years, without differences between pre-pandemic and pandemic cohorts (p = 0.47) or among pandemic sub-cohorts (p = 0.43). Women in the pre-pandemic cohort had lower educational attainment, 34% having secondary schooling or lower vs. 21% in the pandemic cohort (p < 0.001). Pregnant women in the pre-pandemic cohort were more frequently unemployed or inactive (30%) than in the pandemic cohort (24%) (p = 0.009). There were no differences between both cohorts regarding current pregnancy order of birth (p = 0.42). Gestational age at maternal leave of work was not recorded in the prepandemic cohort. Women in the pandemic sub-cohort 2 leaved about 2 weeks before than women in the pandemic sub-cohort 1 (23.5 vs. 25.3, p = 0.06).

Variable		Pandemic cohort (recruited in 2020) n = 1168							
	Pre-pandemic cohort (recruited in 2018) n = 969	Total	p value between pre- pandemic and pandemic cohorts	Sub-cohort 1 (delivery before 26th May) n = 270	Sub-cohort 2 (recruited at delivery from 26th May) n = 350	Sub-cohort 3 (recruited at 12^{th} week consultation from 26^{th} May) $n = 548$	p value between pandemic sub- cohorts		
Age at delivery									
<24 years	36 (4)	38 (3)	0.47	7 (3)	18 (5)	13 (2)	0.43		
24-27 years	85 (9)	113 (10)		26 (10)	34 (10)	53 (10)			
28-34 years	411 (42)	476 (41)		102 (38)	147 (42)	227 (41)			
35-40 years	363 (37)	468 (40)		115 (43)	130 (37)	223 (41)			
>40 years	74 (8)	73 (6)		16 (6)	25 (7)	32 (6)			
Educational level									
Primary school	215 (22)	175 (15)	< 0.001	33 (12)	50 (14)	92 (17)	0.004		
Secondary school	114 (12)	73 (6)		18 (7)	34 (10)	21 (4)			
Vocational training	281 (29)	369 (32)		99 (37)	98 (28)	172 (31)			
University	359 (37)	544 (47)		116 (44)	166 (48)	262 (48)			
Occupational situation									
Employed	673 (69)	865 (75)	0.009	205 (78)	256 (73)	404 (74)	0.55		
Unemployed/inactive	286 (30)	277 (24)		56 (21)	89 (26)	132 (24)			
Student	10 (1)	18 (2)		3 (1)	4 (1)	11 (2)			
Order of birth									
First	507 (52)	335 (54)	0.42	132 (50)	203 (58)	-	0.04		
Other	462 (48)	281 (46)		134 (50)	147 (42)	-			
Gestational age at leave of work (weeks)	-	-	-	25.3±93	23.5±10.1	-	0.06		

Table 2 displays results regarding delivery. Caesarean section was more frequent (24%) and, thus, eutocic delivery less frequent (67%) in the pre-pandemic cohort, compared to 18% Caesarean section rate and 75% eutocic deliveries in the pandemic cohort (p = 0.004). Preterm birth, defined as pregnancy shorter than 37 weeks, was slightly more frequent in the pre-pandemic cohort (6%) than in the pandemic one (5%) (p = 0.04), as was low weight at birth -defined as less than 2500 g- (9% pre-pandemic, 6% pandemic; p = 0.001). Finally, new-borns fed with exclusive breastfeeding at hospital discharge were 60% in the pandemic cohort, compared to only 54% in the pre-pandemic cohort (p = 0.005). We found no differences in variables related to delivery between pandemic subcohorts 1 and 2.

Table 2. Type of delivery, length of pregnancy and weight at birth in the two cohorts. In the pandemic cohort, only sub-cohorts 1 and 2 are included as most pregnancies in sub-cohort 3 are still ongoing.

Variable		Pandemic cohort (recruited in 2020)							
Variable	Pre-pandemic cohort (recruited in 2018) n = 969	n = 620							
		Total	p value between pre-pandemic	Sub-cohort 1 (delivery before	Sub-cohort 2 (recruited at delivery from 26 th May)	p value between pandemic sub-cohorts			
			and pandemic cohorts	26th May)					
				n = 270	n = 350				
Type of delivery			Conorts	11 270	11 000				
Eutocic	653 (67)	455 (75)	0.004	195 (74)	260 (76)	0.78			
Instrumental	80 (8)	40 (7)		19 (7)	21 (6)				
Caesarean section	236 (24)	110 (18)		50 (19)	6 (18)				
Length of pregnancy									
<34 weeks	20 (2)	3 (1)	0.04	2 (1)	1 (0)	0.65			
34-36 ⁶ weeks	39 (4)	23 (4)		11 (4)	12 (4)				
≥37 weeks	910 (94)	573 (96)		247 (95)	326 (96)				
Weight at birth									
<2500 g	83 (9)	34 (6)	0.001	17 (6)	17 (5)	0.50			
2500 – 4000 g	808 (83)	550 (90)		236 (89)	314 (92)				
>4000 g	78 (8)	25 (4)		13 (5)	12 (4)				
Feeding at hospital									
discharge									
Exclusive breastfeeding	521 (54)	359 (60)	0.005	156 (60)	203 (61)	0.67			
Mixed breastfeeding	280 (29)	128 (22)		54 (21)	74 (22)				
and artificial formula	200 (29)	140 (44)		9 4 (21)	74 (22)				
Artificial formula	168 (17)	107 (18)		51 (20)	56 (17)				

4. Discussion

According to our results, Caesarean section was less frequent in the pandemic year than two years before. Birth at term was more frequent and low weight at birth less frequent in the pandemic cohort. It is noteworthy that the previously reported trend of low birth weight in Spain throughout the 21st century was towards fast increase [5]. Explanations of these results could be related with changes in health care during the pandemic, more self-protective behaviour by pregnant women and stay-at-home orders.

Previous studies have reported contradictory results regarding preterm birth or low weight at birth in developed countries. Dramatic decreases in extremely premature (i.e., gestational age at birth lower than 28 weeks) in a Danish population [6] and in very low birth weight and extremely low birth weight in Ireland [7] have been reported. In Italy, however, a small decrease was only found in late preterm births [8], a result that is in agreement with ours. Handley et al (2021) [9], by the other hand did not find changes in preterm rates in Philadelphia, and Main et al (2020) [10] described a small increase in preterm births between 28 and 31+6 weeks in California, but no changes in other gestational ages. Most of that increase appeared in Hispanic/Latino populations. It is noteworthy that European studies tend to describe declines in preterm rates, while American studies portray no changes or even small increments. Pandemic-associated factors that could explain differences between studies could include changes in health care and pregnant woman self-protective behaviour.

Changes in health care functioning during the pandemic have included reductions in antenatal maternity consultations, a rise in remote appointments and, also, a diminution in emergency antenatal presentations [11]. Western-Europe health care services are usually of public instead of private funding and they have universal coverage. Further information is required to ascertain if attendance to pregnancy in European countries changed during the pandemic in different ways than in the US, including access to health care.

Pregnant women could have changed their health-related behaviour in a more protective way as response to the perceived risk covid-19 would put on them. For instance, less social activity and lower physical demands -including among others earlier maternal leave of work, more time expended at home- would have led to lower foetal stress. On this subject, studies on the putative connection between work and prematurity are contradictory [12]. National lockdowns and stay-at-home orders would have also contributed to changes in woman health-related behaviour, but their contribution may vary with how restricted they were and how the authorities enforced them [10].

Reported changes in Caesarean section rates seem to be of small amount and unpredictable direction. Thus, a small increase has been reported in England (from 28.3 to 29.7%) [13], a small non-significant decrease in Italy (from 36.2 to 35.5%) [8] and no relevant changes in New York (from 31.7 to 31.3%) [14]. In our results, Caesarean section rates hugely cutdown from 24 to 18% in just two years. This decrease could not be wholly attributed to changes in the pandemic period. Actually, two factors would have played a role in it: Firstly, to diminish Caesarean rates was an institutional target before the pandemic began. Secondly, women infected of covid-19 had been considered to have high surgical risk; therefore, they have been closely followed and induction was used early to avoid Caesarean section. We have no data to evaluate the relative contribution of these two factors to the Caesarean section rate stepdown.

Our study has some limitations. Firstly, it has been carried out in a single hospital. This is a double-edge characteristic: by one hand, it makes it difficult to generalize our results; by the other hand, it allows us to collect data in a reliable, standardized way.

Secondly, most data we are reporting on the pandemic cohort belong to women already pregnant when the pandemic was declared. The ongoing sub-cohort 3, comprised of women who became pregnant after the pandemic began, would contribute to clarify some remaining questions, including the relevance of health-care changes throughout the whole pregnancy. Thirdly, the sample size of our cohorts is limited to ascertain rare pregnancy outcomes, such as extreme prematurity.

.5. Conclusions

In conclusion, we are reporting reductions in Caesarean section and preterm birth during the pandemic in a hospital located Northern of Spain. Further analysis would clarify if these lessening are related to changes in health-related behaviour or health-care functioning

Author Contributions: Conceptualization, J.LL. and C.LM.; methodology, J.LL. and C.LM.; validation, P.FZ. and S.LG.; formal analysis, J.LL. and C.LM.; investigation, J.LL., C.LM., V.O.; data curation, V.O., M.P.Z. and J.AM.; writing—original draft preparation, J.LL. and C.LM.; writing—review and editing, J.LL., C.LM., and J.A.M; visualization, J.AM., B.ALL. and Y.J.; supervision, J.LL. and M.JC.; project administration, MOACC-10 group; funding acquisition, MOACC-19 group. All authors have read and agreed to the published version of the manuscript." Please turn to the CRediT taxonomy for the term explanation. Authorship must be limited to those who have contributed substantially to the work reported.

Funding: This research was funded by the Spanish Instituto de Salud Carlos III (ISCIII), grant number COV20/00923

Institutional Review Board Statement: The study was approved by the Clinical Research Ethics Committee of Cantabria (reference: 2020.174).

Informed Consent Statement: Two different written informed consents -one for the mother and one for the child- have to be signed by the mother before being admitted in the study. The study is conducted according to the Declaration of Helsinki (last update of Fortaleza) and the European Union regulation 2016/679 on the protection of natural persons with regard to the processing of personal data

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to patient's privacy.

Acknowledgments: In this section, you can acknowledge any support given which is not covered by the author contribution or funding sections. This may include administrative and technical support, or donations in kind (e.g., materials used for experiments).

Conflicts of Interest: The authors declare no conflict of interest

References

- 1. Knight, M.; Bunch, K.; Vousden, N.; Morris, E.; Simpson, N.; Gale, C.; O'Brien, P.; Quigley, M.; Brocklehurst, P.; Kurinczuk, J.J. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. BMJ 2020, 369, m2107, doi:10.1136/bmj.m2107.
- 2. Chmielewska, B.; Barratt, I.; Townsend, R.; Kalafat, E.; van der Meulen, J.; Gurol-Urganci, I.; O'Brien, P.; Morris, E.; Draycott, T.; Thangaratinam, S.; et al. Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis. Lancet Glob. Heal. 2021, 9, e759–e772, doi:10.1016/S2214-109X(21)00079-6.
- 3. Llorca, J.; Lechosa-Muñiz, C.; Gortazar, P.; Fernández-Ortiz, M.; Jubete, Y.; Cabero, M.J. COVID-19 in a cohort of pregnant women and their descendants, the MOACC-19 study. BMJ Open 2021, 11, e044224, doi:10.1136/bmjopen-2020-044224.
- 4. Lechosa-Muñiz, C.; Paz-Zulueta, M.; Herrero, M.S. de A.; Rio, E.C. Del; Sota, S.M.; Llorca, J.; Cabero-Perez, M.J. Health care costs associated to type of feeding in the first year of life. Int. J. Environ. Res. Public Health 2020, 17, 1–9, doi:10.3390/ijerph17134719.
- 5. Erasun, D.; Alonso-Molero, J.; Gómez-Acebo, I.; Dierssen-Sotos, T.; Llorca, J.; Schneider, J. Low birth weight trends in Organisation for Economic Co-operation and Development countries, 2000–2015: economic, health system and demographic conditionings. BMC Pregnancy Childbirth 2021, 21, 13, doi:10.1186/s12884-020-03484-9.
- 6. Hedermann, G.; Hedley, P.L.; Bækvad-Hansen, M.; Hjalgrim, H.; Rostgaard, K.; Poorisrisak, P.; Breindahl, M.; Melbye, M.;

- Hougaard, D.M.; Christiansen, M.; et al. Danish premature birth rates during the COVID-19 lockdown. Arch. Dis. Child. Fetal Neonatal Ed. 2021, 106, 93–95, doi:10.1136/archdischild-2020-319990.
- 7. Morris, E.; Draycott, T.; O'Brien, P.; Thomso, A.; Ross-Davie, M.; Love, C.; Jardine, J.; Okano, S.; Shea, M.; Waite, L.; et al. Coronavirus (COVID-19) infection in pregnancy. Information for healthcare professionals. In Royal College of Obstetricians & Gynaecologists.; 2021.
- 8. De Curtis, M.; Villani, L.; Polo, A. Increase of stillbirth and decrease of late preterm infants during the COVID-19 pandemic lockdown. Arch. Dis. Child. Fetal Neonatal Ed. 2020, fetalneonatal-2020-320682, doi:10.1136/archdischild-2020-320682.
- 9. Main, E.K.; Chang, S.-C.; Carpenter, A.M.; Wise, P.H.; Stevenson, D.K.; Shaw, G.M.; Gould, J.B. Singleton preterm birth rates for racial and ethnic groups during the coronavirus disease 2019 pandemic in California. Am. J. Obstet. Gynecol. 2020, 224, 239–241, doi:10.1016/j.ajog.2020.10.033.
- 10. Handley, S.C.; Mullin, A.M.; Elovitz, M.A.; Gerson, K.D.; Montoya-Williams, D.; Lorch, S.A.; Burris, H.H. Changes in Preterm Birth Phenotypes and Stillbirth at 2 Philadelphia Hospitals During the SARS-CoV-2 Pandemic, March-June 2020. JAMA 2021, 325, 87, doi:10.1001/jama.2020.20991.
- 11. Jardine, J.; Relph, S.; Magee, L.; Dadelszen, P.; Morris, E.; Ross-Davie, M.; Draycott, T.; Khalil, A. Maternity services in the UK during the coronavirus disease 2019 pandemic: a national survey of modifications to standard care. BJOG An Int. J. Obstet. Gynaecol. 2021, 128, 880–889, doi:10.1111/1471-0528.16547.
- 12. Snijder, C.A.; Brand, T.; Jaddoe, V.; Hofman, A.; Mackenbach, J.P.; Steegers, E.A.P.; Burdorf, A. Physically demanding work, fetal growth and the risk of adverse birth outcomes. The Generation R Study. Occup. Environ. Med. 2012, 69, 543–550, doi:10.1136/oemed-2011-100615.
- 13. Bhatia, K.; Columb, M.; Bewlay, A.; Eccles, J.; Hulgur, M.; Jayan, N.; Lie, J.; Verma, D.; Parikh, R. The effect of COVID-19 on general anaesthesia rates for caesarean section. A cross-sectional analysis of six hospitals in the north-west of England. Anaesthesia 2021, 76, 312–319, doi:10.1111/anae.15313.
- 14. Bornstein, E.; Gulersen, M.; Husk, G.; Grunebaum, A.; Blitz, M.J.; Rafael, T.J.; Rochelson, B.L.; Schwartz, B.; Nimaroff, M.; Chervenak, F.A. Early postpartum discharge during the COVID-19 pandemic. J. Perinat. Med. 2020, 48, 1008–1012, doi:10.1515/jpm-2020-0337.