PROF. JUN ZHANG (Orcid ID : 0000-0002-9926-5986)

DR. NAHO MORISAKI (Orcid ID : 0000-0001-6151-4513)

Article type : Original Article

Title page

**Increases in caesarean section rates and change of perinatal outcomes
in low- and middle-income countries: a hospital-level analysis of two
WHO surveys**

YanJun Zhao,^{1,2} Jun Zhang,¹ Javier Zamora,³ Joshua Peter Vogel,⁴ João Paulo Souza,⁵ Kapila Jayaratne,⁶ Togoobaatar Ganchimeg,⁷ Eduardo Ortiz-Panoso,⁸ Bernardo Hernandez,⁹ Olufemi Taiwo Oladapo,⁴ Maria Regina Torloni,¹⁰ Naho Morisaki,¹¹ Rintaro Mori,¹² Cynthia Pileggi-Castro,¹³ Özge Tunçalp,⁴ Xiaoming Shen,¹ Ana Pilar Betrán⁴

¹MOE-Shanghai Key Laboratory of Children's Environmental Health, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Email: 13524813362@163.com (YanJun Zhao); zhangjunjim@gmail.com (Jun Zhang); xmshen@shsmu.edu.cn (Xiaoming Shen)

² Department of Child Health Care, Shanghai Children's Hospital, Shanghai Jiao Tong University, Shanghai, China

³Clinical Biostatistics Unit, Hospital Ramon y Cajal, CIBER Epidemiology and

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ppe.12363

This article is protected by copyright. All rights reserved

Public Health, Madrid, Spain. Women Health Research Unit, Centre for Primary Care
and Public Health, Queen Mary University, London, UK

Email:javier.zamora@hrc.es

⁴UNDP • UNFPA • UNICEF • WHO • World Bank Special Programme of Research,
Development and Research Training in Human Reproduction (HRP), Department of
Reproductive Health and Research, World Health Organization, Geneva, Switzerland

Email:betrana@who.int (Ana Pilar Betrán); vogeljo@who.int (Joshua Peter Vogel);
oladapoo@who.int (Olufemi Taiwo Oladapo); tuncalpo@who.int (Özge Tunçalp)

⁵Department of Social Medicine, Ribeirão Preto Medical School, University of São
Paulo, Ribeirão Preto, SP, Brazil

Email:jpsouza@fmrp.usp.br

⁶Family Health Bureau, Ministry of Health, Colombo, Sri Lanka

Email:kapjay613@gmail.com

⁷Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

Email:ganchimeg.tb@gmail.com

⁸Center for Population Health Research, National Institute of Public Health,
Cuernavaca, Mexico

Email:eduardo.ortiz@insp.mx

⁹Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA,
USA

Email:bhp3@uw.edu

¹⁰Evidence Based Health Care Post Graduate Program, Department of Medicine, Sao
Paulo Federal University, Sao Paulo, Brazil.

Email:torlonimr@gmail.com

¹¹Division of Lifecourse Epidemiology, Department of Social Medicine, National
Center for Child Health and Development, Tokyo, Japan

Email:morisaki-n@ncchd.go.jp

¹² Department of Health Policy, National Center for Child Health and
Development, Tokyo, Japan

Email:rintaromori@gmail.com

This article is protected by copyright. All rights reserved

¹³Department of Pediatrics, Ribeirão Preto Medical School, University of São Paulo,
Ribeirão Preto, SP, Brazil
Email: cynthiaileggi@gmail.com

Correspondence to:

Dr Jun Zhang,
Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, 1665 Kong
Jiang Road, Shanghai, China
Email: zhangjunjim@gmail.com
Telephone: +86-21-2507-8871
Fax: +86-21-2507-8875

Abstract

Background

Maternal and neonatal outcomes have improved substantially. During the same period, the caesarean section (CS) rate soared. The aim of this analysis was to determine whether an increase in CS rate was associated with an improvement in perinatal outcome at an institutional level in low- and middle-income countries.

Methods

The WHO Global Survey on Maternal and Perinatal Health (WHOGS) and the WHO Multi-country Survey on Maternal and Newborn Health (WHOMCS) were two multi-country, facility-based cross-sectional surveys conducted in 2004–2008 and 2010–2011, respectively. The increase in CS rate and the change of incidence of adverse perinatal outcomes were calculated using a two-point estimator of percent change annualized (PCA) method. Perinatal, maternal and neonatal composite indexes were used as the outcomes. A linear mixed model was used to assess the association between the change of CS rate and the change of perinatal outcome.

Results

This article is protected by copyright. All rights reserved

A total of 259 facilities in 20 countries participated in both surveys, with 217844 women in WHOGS and 227734 women in WHOMCS. The CS rate in these facilities increased by 3.99% annually, on average, while the incidence of adverse perinatal outcomes decreased by 4.59% annually. However, after we adjusted for potential confounders, no significant association was found between the increase in CS rate and the change of adverse outcome index, regardless of whether starting CS rates were already high (above 10%) or not.

Conclusions

In low- and middle-income countries, the increases in CS rates were not associated with better perinatal outcomes regardless of whether the starting CS rate was already high or not.

Keywords

Caesarean section rate, perinatal, adverse outcomes, low and middle income countries

Introduction

Maternal health has undergone a dramatic improvement worldwide in the past two to three decades. The latest report shows that globally there were an estimated 303 000 maternal deaths in 2015, a decline of 43.9% from 1990 levels.¹ Global perinatal mortality statistics have also improved.²⁻⁴ Neonatal and infant mortality rate declined by 36% and 46% in low-income countries, and 43% and 58% in high-income countries from 1990 to 2012.⁵ Meanwhile, caesarean section (CS) rates have increased substantially, even tripled or quadrupled, in many parts of the world.⁶

Have increased CS rates contributed to better maternal and neonatal outcomes, and if so by how much? Studies of the relationship between CS rate and mortality have yielded inconsistent results.⁷ A recent cross-sectional, ecological study estimating annual CS rates from data collected during 2005 to 2012 for all 194 World Health Organization(WHO) member states, suggested that national CS rates of up to approximately 19 per 100 live births were associated with lower maternal or neonatal

mortality among WHO member states. Higher CS rates were not correlated with maternal or neonatal mortality at a country level.⁸ Some other population-based ecological studies suggest that when a national CS rate is below 10%, an increase in the CS rate is associated with a decrease in maternal and neonatal mortality.⁹ Further increases in national CS rates beyond 10% are not associated with further reductions in mortality, when socioeconomic conditions are adjusted for.⁹ This phenomenon has been consistently demonstrated with data from both high and low-income countries, and in cross-sectional and longitudinal analyses.^{9,10}

These ecological studies have been limited to using national rates of CS and maternal and neonatal mortality, as these measures are routinely reported in civil vital registration systems and readily available for analysis. Although mortality rates are generally good indicators for overall maternal and neonatal health at a country level, other outcomes such as maternal and neonatal severe morbidity,¹¹⁻¹³ and quality of life are also important, particularly as maternal and newborn outcomes are improving^{14,15} (i.e., mortality decreased substantially, morbidity become more sensitive indicator). Unfortunately, morbidity data are generally unavailable at a national level, as are data on potential confounders. Where such data exist, comparisons are often not possible due to the lack of standardized definitions and outcomes. More evidence is needed to examine whether CS rate is associated with less severe maternal and neonatal outcomes. The aim of this analysis is to determine whether an increase in CS rate was associated with an improvement in maternal and neonatal morbidity and mortality outcomes at an institutional level in 20 low- and middle-income countries that participated in two consecutive WHO surveys.¹⁶⁻¹⁸

Methods

Design and setting

Data for this secondary analysis were derived from two large, cross-sectional, facility-based surveys of maternal and perinatal health: the WHO Global Survey of Maternal and Perinatal Health (WHOGS) and the WHO Multi-Country Survey of Maternal and Newborn Health (WHOMCS). Detailed descriptions of these studies are

available elsewhere.¹⁶⁻¹⁸ Briefly, the WHOGS was conducted to examine the association of the mode of delivery and maternal and perinatal outcomes in 373 health facilities in 24 countries from Africa and Latin America (2004–2005) and Asia (2007–2008). A stratified, multistage cluster sampling strategy was applied to select the countries, provinces and health facilities.¹⁶ According to this scheme, the first stage of sampling consisted of countries. This selection was stratified by the WHO regions and the levels of under-five child and adult mortality. Fourteen sub-regions were used to frame the first stage of sampling. From each sub-region, a total of four countries were selected at random for participation in the study, with probability proportional to the country population. When the total number of countries was less than four in any sub-region, all the countries were included. This process resulted in 12 sub-regions having four countries each and two sub-regions having three countries each. A total of 54 countries were initially pre-selected, but, due to operational and budgetary reasons, the WHOGS was implemented in 24 countries from Africa, Asia and Latin America plus Canada. The second sampling stage consisted of randomly selection of two provinces/states (with probability also proportional to the population size), in addition to the country capital city in these 24 countries. A tertiary sampling stage (below the province/state level) was used for very large provinces/states. For the latter (e.g. Mexico City and Beijing), a fourth sampling stage was implemented. Once the geographical areas were selected, seven health facilities with a minimum of 1,000 deliveries per year were randomly selected from each of these areas. If there were less than 7 facilities, all facilities of that area were selected. Within each selected facility, detailed information on all births during a specified period was collected before death, hospital discharge or up to seven days postpartum (whichever came first) by trained health professional staff, with a total number of 287036 women (290610 births). Since there was no individual follow-up of women or newborns after hospital discharge, data on newborn and maternal status were only collected from the hospital medical records or staff during the early postpartum period or intensive care units.

In 2010–2011, WHOMCS was conducted as a subsequent survey based on the WHOGS settings and added seven new countries using the same sampling

methodology. WHOGS countries were invited to participate in the WHOMCS. Two countries were unable to join. In total, 359 facilities across 29 countries from Africa, Asia, Latin America, and the Middle East participated. WHOMCS aimed to examine severe maternal and newborn outcomes and maternal near miss cases and deaths regardless of gestational age and mode of delivery (i.e., abortion, ectopic pregnancies). The study included 314623 women (318534 births). Data collection was conducted in each facility for a period of 2–4 months, and the study was conducted between May 2010 and December 2011. In addition, in both surveys, institutional information on the availability of obstetric and newborn services, laboratory tests, and human and training resources were also collected.

The technical content of both protocols was reviewed by specialist panels at the UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction. The Specialist Panel on Epidemiological Research reviewed and approved the WHOGS study protocol for technical content; the Research Project Review Panel (name of panel was changed in 2010) reviewed and approved the technical content of the WHOMCS. Both surveys had ethical approval by the WHO Ethics Review Committee, and the relevant authorities and institutional review boards in all participating countries.

Data quality

In both studies, a data form was developed and pilot tested. In addition, a Manual of Operations was developed to guide a structured medical record data abstraction process by data collectors. This manual minimized the need for judgment and interpretation by the data collectors. Where incomplete data were identified, data collectors could verify with medical staff. Validity and random cross-checks were conducted to ensure quality of entered data.

Study population

In order to be included in this analysis, a facility must have participated in both WHOGS and WHOMCS and had more than 100 deliveries in each survey. We excluded women whose gestational age at delivery was less than 22 weeks or unknown, or with missing information on exposure and outcome variables of interest:

delivery mode, five-minute Apgar score, maternal blood transfusion, maternal admission to ICU/special care unit, newborn status at hospital discharge or on the seventh day of life (alive/dead), neonatal conditions at birth(alive/fresh stillbirth) and maternal status at hospital discharge or on the seventh day postpartum if still in hospital (alive/dead). Most countries participated in both surveys were low- and middle-income countries, except Japan. Because we were interested in low- and middle-income countries in this study, we excluded Japan for further analysis. In addition, the surgical capacity of participating facilities in Angola had a significant change between the two surveys, and the quality of gestational age data in the WHOGS was poor.¹⁹ Therefore, we excluded that country, leaving 259 facilities from 20 low- and middle-income countries which participated in both surveys for further analysis.

Variables and definitions

We used individual data on demographic characteristics, maternal risks, mode of delivery, pregnancy events and perinatal outcomes. The main exposure of interest in our study was CS as final mode of delivery. We used the following information as the main potential confounders: maternal age (< 20, 20-34, > 34 years), gestational age(< 37, 37-41, > 41 weeks), years of education(0, 1-6, 7-9, 10-12, >12 years), marital status (without partner, with partner), parity (0, 1-2, > 2), previous CS (none, one or more), fetal presentation (vertex, breech and other), onset of labour (spontaneous, induced, no labour), birthweight (< 2500, 2500-3999, $\geq$ 4000 g), number of neonates (singleton, multiple), chronic hypertension, preeclampsia and data collection year. Level of facility was classified as primary and secondary, tertiary and other referral level. We used gross domestic product (GDP) that were reported by the World Bank as a proxy for the socioeconomic condition for each country.

The main outcomes of this study included one primary and two secondary outcomes. Since severe maternal and neonatal morbidity and mortality are rare, we used a weighted perinatal adverse outcome index proposed by Mann et al.²⁰ as the primary outcome (Appendix Table 1). Several adverse outcomes listed in the Appendix Table 1 were not available in both surveys. Thus, our composite outcome

included Apgar score at five minutes < 7, maternal and/or neonatal death at hospital discharge or on the seventh day of life (alive/dead), maternal blood transfusion, admission of the mother to ICU/special care unit and neonatal conditions at birth (alive/fresh stillbirth). We calculated the perinatal adverse outcome index as the sum of weighted adverse outcome scores divided by the number of deliveries for each facility. Maternal and neonatal adverse outcome indexes were also created as the secondary outcomes. The maternal index was composed of maternal death at hospital discharge or on the seventh day of life (alive/dead), maternal blood transfusion, and admission of the mother to ICU/special care unit, while the neonatal index included Apgar score at five minutes < 7, neonatal death at hospital discharge or on the seventh day of life (alive/dead), and neonatal conditions at birth (alive/fresh stillbirth).

Statistical analysis

In the current analysis, the facility was the unit of analysis. The exposure and covariates are all calculated as a rate or proportion in each facility. The covariates included the proportion of women in the facility aged 19 years or younger, 35 years or older, education less than seven years, more than 12 years, marital status, parity, previous caesarean delivery, fetal presentation, gestational age less than 37 weeks, more than 41 weeks, birthweight less than 2500 g, more than 4000 g, multiple births, chronic hypertension, preeclampsia, level of facility, and GDP.

Since the interval between the two surveys varied from country to country, we used a two-point estimator of Percent Change Annualized (PCA)²¹ to examine how the annual rate of change in CS rate was associated with the annual rate of change in the incidence of adverse perinatal outcomes at the facility level between two surveys, where

$$PCA = \left[\left(\frac{WHOMCS \text{ CS rate}}{WHOGS \text{ CS rate}} \right)^{\frac{1}{\text{time difference (year)}}} - 1 \right] \times 100$$

A similar equation was used by WHO in calculating maternal mortality trends.^{6,22} With the underlying assumption that the CS rate changed linearly, the statistical model was as follows:

PCA of adverse perinatal outcome composite index = PCA of CS rate + PCA of

covariates.

However, the PCA function became undefined when a zero rate was observed at either survey. To avoid this, we used a continuity correction by adding a small amount (0.0001) to facilities with a zero rate. This was particularly important for those variables with zero prevalence. All covariates and outcomes were aggregated and reported at "facility" level as described above, and then put into a linear mixed model where "country" was also considered as a level. The analyses were weighted by the average number of women of the two surveys for each facility. We also conducted stratified analyses according to the facility CS rate ($\leq 10\%$ vs. $>10\%$). To be more statistically conservative, the latter was calculated as the geometric mean of the CS rates (the square root of the CS rates) of the two surveys. All analyses were carried out with the statistical software SAS 9.1 (SAS Institute, Cary, NC, USA). $P < 0.05$ was considered statistically significant.

Results

Figure 1 illustrates our selection process of the study population. In total, 217 844 women in WHOGS and 227 734 women in WHOMCS from 259 facilities in 20 low- and middle-income countries were included in the following analysis. Appendix Table 2 provides detailed information of the facilities by country.

Table 1 presents the characteristics of women at the individual level. These characteristics were reported because they were included in both surveys. More facilities became tertiary hospitals, increased from 31.1% (WHOGS) to 55.9% (WHOMCS). Women over 34 years changed from 9.9% to 10.7%. The proportion of education more than 12 years changed from 13.4% to 17.0%. In the WHOGS and WHOMCS surveys 43.7% and 45.5% of women were nulliparas, respectively. The proportion of women with previous CS changed from 10.5% to 12.9%. The prevalence of preeclampsia decreased from 2.8% to 2.1%, and chronic hypertension from 0.5% to 0.4%. Women with spontaneous onset of labor changed from 80.7% to 77.6%. The overall CS rate increased from 27.0% to 31.7% between the two surveys. Multiple births had a reduction from 2.3% to 1.5%. Birthweight less than 2500g was from 10.5% in WHOGS to 11.1% in WHOMCS. In WHOGS, 95.0% had cephalic

fetal presentation compared with 95.5% in WHOMCS.

Table 2 presents the characteristics of the facilities in each survey. Due to a skewed distribution of most variables, we used median and interquartile range (Q1 and Q3). The median CS rate by facility increased from 24.7% in WHOGS to 30.5% in WHOMCS.

During that period, the CS rate in these facilities increased by 3.99% annually, on average, while the incidence of adverse perinatal outcomes decreased by 4.59% annually. Figure 2 illustrates the relationship between PCA of CS rate and PCA of perinatal, maternal and neonatal adverse outcome indices at the facility level. The scatter plot shows no association between PCA of CS rate and PCA of adverse outcome. Table 3 quantitatively summarizes the crude and adjusted associations. An increase in CS rate was not significantly associated with a change in perinatal adverse outcome index in the crude analysis. When adjusted for a set of confounding variables, the results were similar ($\beta=0.11$, 95% CI: -0.71, 0.94, $p=0.78$). Again, there was no significant association between PCA of CS rate and PCA of maternal and neonatal adverse outcomes ($\beta=0.53$, 95% CI: -0.06, 1.12, $p=0.08$ for maternal adverse outcome index; $\beta=-1.00$, 95% CI: -8.23, 6.25, $p=0.79$ for neonatal adverse outcome index). Furthermore, we stratified the CS rates by less or more than 10%. This stratification was based on our previous findings that when CS rate was below 10%, an increase in CS rate was associated with a decrease in mortality rates, but when CS rate was above 10%, this association virtually disappeared. However, the current analysis failed to show any significant association regardless whether the CS rate was below or above 10% or 19% in both multiparous and nulliparous women (also see Appendix Table 3 and 4).

Discussion

Our study found that at the hospital level, increases in CS rates in low- and middle-income countries were not associated with changes in perinatal adverse outcome index irrespective of the baseline CS rate. This finding remained the same when we looked at the maternal and neonatal adverse outcome indexes separately.

As more and more developing countries have improved economic conditions in recent years, maternal and newborn mortality has decreased. Despite that mortality is considered to be a powerful socio-economic and health indicator within a population, death is a rare event and the isolated cases may not reflect the quality of obstetrical assistance.^{20,23} Morbidity has been suggested as an alternative measure²⁴ Preventing morbidity and improving quality of care have become more important. Would a higher CS rate be necessary to achieve this goal? And how high should it be? Unfortunately, little is known in this regard.

Some European countries²⁵ and Japan²⁶ have maintained a CS rate below 20% at country level in the past two decades while continuing to improve perinatal outcomes. As these countries have some of the lowest perinatal mortality rates in the world, it may be assumed that generally speaking, CS rates may not have to go beyond 20% in order to achieve excellent perinatal outcomes.

In fact, the mode of delivery may play a less important role in improving perinatal outcomes at a population level. The CS rate is usually already much higher in the high risk pregnancies.²⁷ For example, in China, the CS rate in women with severe preeclampsia was 80% in comparison to 46.2% in the general population.^{27,28} Will an even higher CS rate be necessary in these pregnancies? Probably not.

Ample evidence indicates that a high CS rate in some developing countries is due to CS without clear medical indication.^{29,30} In our data, 85% of the facilities had a CS rate over 10%. It is likely that some of these CS were not medically indicated. A previous WHOGS analysis³¹ showed that a total of 1.0 percent of all deliveries had CS without medical indications, and the overall proportion of women delivering by CS

without medical indication ranged from 0.01 to 2.10%. In the Chinese institutions participating in WHOOGS this figure was exceptionally higher at 11.6%.³¹ The previous study demonstrated that CS without medical indication was associated with an increased risk of short-term adverse maternal outcomes.³¹ Not only will it increase perinatal morbidity and mortality,^{32,33} but also contribute to health care costs.³⁴ In UK, each additional vaginal birth instead of CS saves more than £1200.³⁵ For a lower-income country like Chile, the difference in cost between a vaginal delivery and a CS is about US\$350.³⁶ If unnecessary CS can be reduced, financial and human resources could be used in other parts of the health system.

It is worth mentioning that PCA was used as the main metrics of interest in this study. PCA is often used to measure trends in disease or mortality rates. For making comparisons or studying associations between very different rates, the absolute change in rates may not be appropriate. Thus, a relative change like PCA is better suited for such comparisons. This measure is often used in epidemiological literature and well recognized as a robust way of comparing rates.³⁷

The current study is unique in that it linked the records of two large sequential WHO multi-country surveys to examine changes in CS rate and the changes in adverse maternal and perinatal outcomes in 20 low- and middle-income countries. A very large sample size in both surveys made the analysis possible, and results could potentially shed important light on changes in CS usage in those countries.

However, our study had several limitations. First, some additional variables that may be potential confounders for the association between CS rate and perinatal outcomes were included in only one survey but not both, precluding their use in the present study. Thus, potential residual confounding is possible. However, since our result is already negative, adjustments for more potential confounders would unlikely change our conclusion. Second, the number of facilities with a CS rate lower than 10% was small. The stratified analysis in this subgroup may have been underpowered. Third, the weighted adverse perinatal outcome index used in this study²¹ lumped intrapartum fetal and neonatal deaths together. Given that the intrapartum stillbirth rate is considered as a good indicator for quality of intrapartum care, of which CS is

an important component, future studies are worth exploring “fresh stillbirth” rates in relation to CS.

Finally, it is important to point out that we used the Weighted Perinatal Adverse Outcome Index as our primary outcome but information on uterine rupture, birth trauma, return to the operating/labor and delivery room, admission to NICU (in neonates greater than 2500 g for over 24 hours), and third or fourth degree perineal tear was not available in both surveys. Thus, our index was based on 5 maternal and neonatal outcomes only. Nonetheless, we tried three different composite outcomes – severe maternal outcome, severe neonatal outcome and combined maternal and neonatal outcome. We also tested models using un-weighted adverse outcome indexes. The results were similar(not shown),reassuring the validity of our conclusion.

Conclusions

Our facility-based ecological analysis indicates that in low- and middle-income countries, the increases in CS rates were not associated with better perinatal outcomes regardless of whether the starting CS rate was already high or not.

Authors’ contributions

JZ conceived this study. YJ Zhao analysed the data. YJ Zhao and JZ co-drafted the article. J Zamora and JZ supervised the data analysis. JP Vogel, JP Souza, K Jayaratne, T Ganchimeg, E Ortiz-Panozo, B Hernandez, OT Oladapo, MR Torloni, N Morisaki, R Mori, C Pileggi-Castro, Ö Tunçalp, XM Shen, AP Betrán provided critical feedback on the interpretation of the results, helped with the writing of the article, and approved the final report. JZ is the guarantor.

Funding

The current analysis was partially funded by a grant from UNDP • UNFPA • UNICEF • WHO • World Bank Special Programme of Research, Development and Research Training in Human Reproduction, Department of Reproductive Health and Research, World Health Organization, Geneva, Switzerland and by the National Natural Science Foundation of China (Grant No. 81273091).The funder had no role in any aspect of the study. The authors have independence of research from the funders and have not

This article is protected by copyright. All rights reserved

been paid to write this article.

Competing interests

The authors declare that they have no competing interests.

Ethical approval

The WHOGS and WHOMCS were approved by the WHO Ethical Review Committee and the relevant ethical clearance bodies in participating countries and facilities.

Written consent from individual women was not needed because there was no contact between the data collectors (who extracted routine medical record data) and individual women.

Acknowledgments

This article represents the views of the named authors only, and does not represent the views of the World Health Organization. This work was supported by the National Natural Science Foundation of China (Grant No. 81273091) and the Department of Reproductive Health and Research, WHO, Geneva. The WHO Global Survey on Maternal and Perinatal Health was financially supported by the UNDP • UNFPA • UNICEF • WHO • World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), Department of Reproductive Health and Research, World Health Organization, Geneva, Switzerland; WHO; the Governments of China, India, and Japan; and the United States Agency for International Development (USAID). The WHO Multi-Country Survey on Maternal and Newborn Health was financially supported by the UNDP • UNFPA • UNICEF • WHO • World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), Department of Reproductive Health and Research, World Health Organization, Geneva, Switzerland; WHO; USAID; the Ministry of Health, Labour and Welfare of Japan; and Gynuity Health Projects. We thank all members of the WHO Global Survey on Maternal and Perinatal Health Research Network and the WHO Multi-Country Survey on Maternal and Newborn

This article is protected by copyright. All rights reserved

Health Research Network, including regional and country coordinators, data collection coordinators, facility coordinators, data collectors, and all staff of the participating facilities who made the surveys possible.

References

- 1 Alkema L, Chou D, Hogan D, et al. Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group. *Lancet* 2015. DOI: [http://dx.doi.org/10.1016/S0140-6736\(15\)00838-7](http://dx.doi.org/10.1016/S0140-6736(15)00838-7)
- 2 WHO, Neonatal and perinatal mortality, 2004: country, regional and global estimates. Geneva: World Health Organization; 2007.
- 3 WHO. Perinatal and neonatal mortality for the year 2000: Country, regional and global estimates. Geneva: World Health Organization; 2006.
- 4 Cousens S, Blencowe H, Stanton C, et al. National, regional and worldwide estimates of stillbirth rates in 2009 with trends since 1995: a systematic analysis. *Lancet* 2011; **377**:1319-1330.
- 5 World health statistics 2014 Part 3 Global health indicators.
- 6 Betrán AP, Ye J, Moller AB, Zhang J, Gülmezoglu AM, Torloni MR. The increasing trend in caesarean section rates: global, regional and national estimates: 1990-2014. *PLoS One* 2016; 11(2):e0148343. doi: 10.1371/journal.pone.0148343
- 7 Betrán AP, Torloni MR, Zhang J, Ye J, Mikolajczyk R, Deneux-Tharaux C, et al. What is the optimal rate of caesarean section at population level? A systematic review of ecologic studies. *Reproductive Health* 2015;12:57.
- 8 Molina G, Weiser TG, Lipsitz SR, Esquivel MM, Uribe-Leitz T, Azad T, et al. Relationship Between Cesarean Delivery Rate and Maternal and Neonatal Mortality. *JAMA* 2015;314:2263-2270.
- 9 Ye J, Betrán AP, Guerrero VM, Souza JP, Zhang J. Searching for the optimal rate of medically necessary cesarean delivery. *Birth* 2014;**41**:237-244.
- 10 Ye J, Zhang J, Mikolajczyk, et al. Association between rates of caesarean section and maternal and neonatal mortality in the 21st century: a worldwide

-
- population-based ecological study with longitudinal data. *BJOG* 2015 Aug 24. doi: 10.1111/1471-0528.13592.
- 11 World Health Organization: Evaluating the quality of care for severe pregnancy complications. The WHO near-miss approach for maternal health. World Health Organization; 2011.
- 12 Pileggi-Castro C, Camelo JS Jr, Perdoná GC, et al. Development of criteria for identifying neonatal near-miss cases: analysis of two WHO multicountry cross-sectional studies. *BJOG* 2014; Suppl 1:110-8. doi: 10.1111/1471-0528.12637.
- 13 Firoz T, Chou D, von Dadelszen P, et al. Measuring maternal health: focus on maternal morbidity. *Bulletin of the World Health Organization* 2013; 91:794-796. doi: 10.2471/BLT.13.117564
- 14 ChavesSda C, Cecatti JG, Carroli G, et al. Obstetric transition in the World Health Organization Multicountry Survey on Maternal and Newborn Health: exploring pathways for maternal mortality reduction. *Rev Panam Salud Publica* 2015;37: 203-210.
- 15 Souza JP, Tunçalp Ö, Vogel JP, et al. Obstetric transition: the pathway towards ending preventable maternal deaths. *BJOG* 2014; Suppl 1:1-4. doi: 10.1111/ 1471-0528.12735.
- 16 Shah A, Faundes A, Machoki M, et al. Methodological considerations in implementing the WHO Global Survey for Monitoring Maternal and Perinatal Health. *Bulletin of the World Health Organization* 2008; **86**: 126–131.
- 17 Souza JP, Gulmezoglu AM, Vogel J, et al. Moving beyond essential interventions for reduction of maternal mortality (the WHO Multicountry Survey on Maternal and Newborn Health): a cross-sectional study. *Lancet* 2013;**381**:1747–1755.
- 18 Souza JP, Gulmezoglu AM, Carroli G, Lumbiganon P, Qureshi Z,WHOMCS Research Group. The World Health Organization multicountry survey on maternal and newborn health: study protocol. *BMC Health Services Research* 2011;**11**:286.
- 19 Vogel JP, Betrán AP, Vindevoghel N, et al. Use of the Robson classification to

-
- 494 assess caesarean section trends in 21 countries: a secondary analysis of two WHO
495 multicountry surveys. *Lancet Global Health* 2015;**3**: e260–270.
- 496 20 Mann S, Pratt S, Gluck P, et al. Assessing quality in obstetrical care: development
497 of standardized measures. *Joint Commission Journal on Quality and Patient*
498 *Safety* 2006;**32**:497–505.
- 499 21 Fay MP, Tiwari RC, Feuer EJ, et al. Estimating Average Annual Percent Change
500 for Disease Rates without Assuming Constant Change. *Biometrics* 2006; 62:
501 847–854.
- 502 22 Kassebaum NJ, Bertozzi-Villa A, CoggeshallMS, et al. Global, regional, and
503 national levels and causes of maternal mortality during 1990–2013: a systematic
504 analysis for the Global Burden of Disease Study 2013. *Lancet* 2014; **384**:
505 980–1004.
- 506 23 de Moraes AP, Barreto SM, Passos VM, et al. Severe maternal morbidity:
507 a case-control study in Maranhao, Brazil. *Reprod Health* 2013;**10**:11. doi:
508 10.1186/1742-4755-10-11.
- 509 24 World Health Organization: Beyond the numbers: reviewing maternal deaths
510 and complications to make pregnancy safer. Geneva: WHO; 2004.
- 511 25 EURO-PERISTAT Project with SCPE and EUROCAT. European Perinatal Health
512 Report. The health and care of pregnant women and babies in Europe in 2010.
- 513 26 Survey of Medical Institutions, Ministry of Health, Labour and Welfare and
514 Survey of all the hospitals in Japan on patients, health care professionals and
515 clinical practice in one month (September). Accessed August 7, 2015. Available
516 at: <http://www.mhlw.go.jp/toukei/list/79-1a.html#01>.
- 517 27 Zhang YL, Li W, Xiao J & Chen SH. The complication and mode of delivery in
518 Chinese women with severe preeclampsia: a retrospective study. *Hypertens*
519 *Pregnancy* 2014;**33**:283–290.
- 520 28 Lumbiganon P, Laopaiboon M, Gülmezoglu AM, et al. Method of delivery and
521 pregnancy outcomes in Asia: the WHO global survey on maternal and perinatal
522 health 2007–08. *Lancet* 2010; **375**: 490–499.
- 523 29 Zhang J, Liu Y, Meikle S, Zheng J, Sun W, Li Z. Cesarean delivery on

maternal request in southeast China. *Obstetrics and Gynecology* 2008; **111**:
1077–1082.

30 Ramires de Jesus G1, Ramires de Jesus N, Peixoto-Filho FM, Lobato G.

Caesarean rates in Brazil: what is involved? *BJOG* 2015; **122**: 606-609.

31 Souza JP, Gülmezoglu A, Lumbiganon P, et al. Caesarean section without
medical indications is associated with an increased risk of adverse short-term
maternal outcomes: the 2004-2008 WHO Global Survey on Maternal and
Perinatal Health. *BMC Medicine* 2010; **8**:71-80.

32 Villar J, Valladares E, Wojdyla D, et al. Caesarean delivery rates and pregnancy
outcomes: the 2005 WHO global survey on maternal and perinatal health in Latin
America. *Lancet* 2006; **367**:1819–1829.

33 Villar J, Carroli G, Zavaleta N, et al. Maternal and neonatal individual risks and
benefits associated with caesarean delivery: multicentre prospective study. *BMJ*
2007;**335**:1025.

34 Henderson J, McCandlish R, Kumiega L, Petrou S. Systematic review of
economic aspects of alternative modes of delivery. *BJOG* 2001;**108**:149–157.

35 The National Collaborating Centre for Women's and Children's Health.
Caesarean section clinical guideline. *London: RCOG Press*, 2004.

36 Bonilla E. Scholarship report: midwife in Chile. *Jordemodern*1990; **103**:24–27.

37 Clegg LX, Hankey BF, Tiwari R, et al. Estimating average annual per cent change
in trend analysis. *Statist Med* 2009; **28**:3670–3682.

Table 1. Characteristics of women in the World Health Organization Global Survey and Multi-Country Survey

		World Health Organization Global Survey N = 217 844		World Health Organization Multi-Country Survey N = 227 734	
		n	%	n	%
Level of facility					
	Primary and secondary	148 965	68.4%	94 219	41.4%
	Tertiary and other referral level	67 638	31.1%	127 344	55.9%
	Missing	1 241	0.6%	6 171	2.7%
Maternal age					
	<20 years	26 110	12.0%	24 987	11.0%
	20 – 34 years	169 813	78.0%	177 864	78.1%
	>34 years	21 585	9.9%	24 433	10.7%
	Missing	336	0.2%	450	0.2%
Years of education					
	0 year	17366	8.0%	23107	10.2%
	1 – 6 years	41639	19.1%	29 343	12.9%
	7 – 9 years	49351	22.7%	47153	20.7%
	10 – 12 years	69787	32.0%	72723	32.0%
	>12years	29 079	13.4%	38750	17.0%
	Missing	10 622	4.9%	16 658	7.3%
Marital status					
	Without partner	24 114	11.1%	23 273	10.2%
	With partner	193 232	88.7%	202 839	89.1%
	Missing	498	0.2%	1 622	0.7%
Parity					
	0	95 169	43.7%	103 588	45.5%
	1 – 2	92 954	42.7%	96 886	42.6%

	>2	28 986	13.3%	26 973	11.8%
	Missing	735	0.3%	287	0.1%
Previous caesarean delivery					
	No	194 200	89.2%	196 758	86.4%
	Yes	22 840	10.5%	29 373	12.9%
	Missing	804	0.4%	1 603	0.7%
Preeclampsia					
	No	211 290	97.0%	223 046	97.9%
	Yes	6 195	2.8%	4 688	2.1%
	Missing	359	0.2%	0	0%
Chronic hypertension					
	No	216 388	99.3%	226 811	99.6%
	Yes	1 011	0.5%	923	0.4%
	Missing	355	0.2%	0	0%
Onset of labour					
	Spontaneous	175 826	80.7%	176 660	77.6%
	Induced	19 153	8.8%	22 891	10.1%
	No labour	22 779	10.5%	28 069	12.3%
	Missing	86	0%	114	0.1%
Mode of delivery					
	Vaginal	159 082	73.0%	155 466	68.3%
	Caesarean	58 762	27.0%	72 268	31.7%
Number of neonates					
	Singleton	212 880	97.7%	224 374	98.5%
	Multiple	4 964	2.3%	3 342	1.5%
	Missing	0	0%	18	0%
Birthweight					
	< 2500 gr	22 892	10.5%	25 314	11.1%
	2500 – 3999gr	189 423	87.0%	196 264	86.2%

	> 3999gr	5 529	2.5%	6 156	2.7%
Gestational age					
	<37 weeks	20 798	9.6%	15 865	7.0%
	37 – 41 weeks	192 149	88.2%	208 010	91.3%
	>41 weeks	4 897	2.3%	3 859	1.7%
Fetal presentation					
	Cephalic	207 046	95.0%	217 510	95.5%
	Non- Cephalic	10 603	4.9%	9 983	4.4%
	Missing	195	0.1%	241	0.1%
Apgar score at five minutes					
	<4	2 373	1.1%	1755	0.8%
	4 – 6	4 163	1.9%	3 242	1.4%
	> 6	211 308	97.0%	222 737	97.8%

Note: all differences were statistically significant by chi-square test.

Table 2. Characteristics of 259 facilities participating in both the World Health Organization Global Survey and Multi-Country Survey

	World Health Organization	World Health Organization	P value
	Global Survey	Multi-Country Survey	
	Median (Q1, Q3)	Median (Q1, Q3)	
Number of deliveries	632 (356, 1 070)	701 (397, 1 157)	<0.001
Maternal age			
< 20 years	11.3 (3.1, 18.2)	10.8 (3.5, 17.6)	<0.001
> 34 years	10.7 (7.2, 14.6)	11.4 (8.3, 15.0)	<0.001
Years of education			
0–6 years	23.4 (7.7, 44.9)	16.7 (6.0, 38.7)	<0.001
> 12 years	6.6 (2.5, 23.3)	11.9 (3.6, 25.8)	<0.001
Marital status			
Without partner	5.0 (0.9, 17.1)	5.3 (1.0, 16.1)	<0.001
Nulliparous	42.1 (34.4, 49.1)	44.1 (34.6, 52.3)	<0.001
Previous caesarean delivery	9.3 (4.0, 14.0)	11.8 (6.4, 16.9)	<0.001
Preeclampsia	1.4 (0.4, 3.4)	1.1 (0.1, 2.6)	<0.001
Chronic hypertension	0.2 (0, 0.5)	0.1 (0, 0.4)	<0.001
Onset of labour			
Induced	4.4 (1.6, 10.2)	3.7 (0.9, 9.6)	<0.001
No labour	6.5 (1.4, 16.8)	9.0 (1.9, 19.8)	<0.001
Caesarean delivery	24.7 (12.8, 38.3)	30.5 (19.9, 43.4)	<0.001
Multiple births	2.1 (1.1, 3.3)	1.2 (0.7, 1.9)	<0.001
Birth weight			
< 2500 gr	9.0 (6.1, 12.5)	7.8 (5.1, 12.1)	<0.001
> 4000 gr	2.0 (0.8, 3.6)	2.1 (1.0, 4.9)	<0.001
Gestational age			
< 37 weeks	7.1 (3.9, 10.9)	5.7 (2.9, 8.3)	<0.001

> 41 weeks	1.5 (0.4, 3.5)	0.8 (0.2, 2.2)	<0.001
Non-cephalic fetal presentation	4.2 (3.1, 5.8)	4.0 (2.7, 5.4)	<0.001

Author Manuscript

Table 3. Crude and adjusted associations between Percent Change Annualized (PCA) of caesarean section rate and PCA of adverse outcome index by levels of caesarean rate at the facility level

Linear Mixed Model [#]	Perinatal adverse outcome		Maternal adverse outcome		Neonatal adverse outcome	
	index ^b		index ^c		index ^d	
	β [95%CI]	P	β [95%CI]	P	β [95%CI]	P
Overall Caesarean section rate	(n=259)		(n=259)		(n=259)	
Crude	0.29 [-0.49, 1.08]	0.46	0.54 [0.01, 1.06]	0.05	0.22 [-5.96, 6.40]	0.95
Adjusted ^a	0.11 [-0.71, 0.94]	0.78	0.53 [-0.06, 1.12]	0.08	-1.00 [-8.23, 6.25]	0.79
Caesarean section rate^{\$} ≤10%	(n=38)		(n=38)		(n=38)	
Crude	0.06 [-0.75, 0.87]	0.87	0.87 [-0.01, 1.76]	0.05	0.15 [-0.11, 0.42]	0.25
Adjusted ^a	-0.10 [-1.32, 1.43]	0.87	0.63 [-0.66, 1.92]	0.30	-0.10 [-0.43, 0.23]	0.56
Caesarean section rate^{\$} >10%	(n=221)		(n=221)		(n=221)	
Crude	0.77 [-0.73, 2.27]	0.31	-0.04 [-0.96, 0.88]	0.93	1.60 [-10.72, 13.91]	0.80
Adjusted ^a	-1.04 [-3.07, 0.99]	0.31	-0.90 [-2.27, 0.47]	0.20	-8.11 [-27.50, 11.28]	0.41

[#] In linear mixed model, the dependent variable is the PCA of adverse outcome index, weighted by the average number of women in two facilities. We added a small amount (0.0001) when a zero rate was observed

^{\$} geometric mean of CS rate of two surveys

^a Adjusted for PCA of women in the facility aged 19 years or younger, 35 years or older, education less than 7 years, education more than 12 years, marital status, parity, previous caesarean section, fetal presentation, year of survey, log gross domestic product, gestational age less than 37 weeks, gestational age more than 41 weeks, birthweight less than 2500g, birthweight more than 4000g, multiple births, chronic hypertension, preeclampsia and level of facility change (tertiary or other referral level) per year

^b Perinatal adverse outcome index: Apgar score at five minutes < 7, maternal and/or neonatal death at hospital discharge or on the seventh day of life (alive/dead), maternal blood transfusion, admission of the mother to ICU/special care unit, neonatal conditions at birth(alive/fresh stillbirth).

^c Maternal adverse outcome index: maternal death at hospital discharge or on the seventh day of life (alive/dead), maternal blood transfusion, admission of the mother to ICU/special care unit.

^d Neonatal adverse outcome index: Apgar score at five minutes < 7, neonatal death at hospital discharge or on the seventh day of life (alive/dead), neonatal conditions at birth (alive/fresh stillbirth).

ppe_12363_f1.tif

ppe_12363_f2a.tif

ppe_12363_f2b.tif

ppe_12363_f2c.tif

Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:

Zhao, Y;Zhang, J;Zamora, J;Vogel, JP;Souza, JP;Jayaratne, K;Ganchimeg, T;Ortiz-Panozo, E;Hernandez, B;Oladapo, OT;Torloni, MR;Morisaki, N;Mori, R;Pileggi-Castro, C;Tuncalp, O;Shen, X;Betran, AP

Title:

Increases in Caesarean Delivery Rates and Change of Perinatal Outcomes in Low- and Middle-Income Countries: A Hospital-Level Analysis of Two WHO Surveys

Date:

2017-07-01

Citation:

Zhao, Y., Zhang, J., Zamora, J., Vogel, J. P., Souza, J. P., Jayaratne, K., Ganchimeg, T., Ortiz-Panozo, E., Hernandez, B., Oladapo, O. T., Torloni, M. R., Morisaki, N., Mori, R., Pileggi-Castro, C., Tuncalp, O., Shen, X. & Betran, A. P. (2017). Increases in Caesarean Delivery Rates and Change of Perinatal Outcomes in Low- and Middle-Income Countries: A Hospital-Level Analysis of Two WHO Surveys. *PAEDIATRIC AND PERINATAL EPIDEMIOLOGY*, 31 (4), pp.251-262. <https://doi.org/10.1111/ppe.12363>.

Persistent Link:

<http://hdl.handle.net/11343/292870>