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Review Article

Examining the role and relevance of the critical analysis and comparison of cesarean section rates in a changing world

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ABSTRACT

Cesarean section (CS) is one of the most commonly performed surgical operations in the world and has resulted in improved maternal and neonatal morbidity and mortality rates internationally. However, concerns have been raised regarding the ever increasing CS rates to what has been described as 'epidemic' proportions. Global CS rates have increased from 6.7% in 1990 to 19.1% in 2014. However, there is a vast variation in the CS rates between countries with CS rates of 44.3% reported across Latin America & the Caribbean and CS rates as low as 4.1% in central and West Africa. There is much controversy regarding the optimal figure for CS in a population. The optimal CS rates for a population have been recommend in various studies, ranging from 10% to 19%, above which no reported improvement in maternal and neonatal mortality rates is observed. This review examines the evolution of the changing indications for CS and increasing CS rates in a world where family sizes are reducing and maternal age at first pregnancy is increasing. Efforts must be made to agree on an appropriate classification system whereby CS rates can be compared accurately between units and countries as a useful tool to audit and monitor our practice. Obstetricians should consider the indications for each CS performed, be conscious of the CS rate in our own countries and institutions and most importantly, be cognizant of how the CS rate impacts the maternal and perinatal morbidity and mortality rates and adjust our practice accordingly, to minimize harm.

Introduction

It is well established that cesarean section (CS) rates are rising globally and this persistent increase has resulted in worldwide concern. Both the World Health Organization (WHO) and the International Federation of Obstetrics and Gynecology (FIGO) have expressed alarm at this continuous increase, describing this troubling trend as an 'epidemic' [1,2]. In 1990 the international CS rate was approximately 6.7%, increasing to 19.1% in 2014, with an annual increase at a rate of 4.4% [3]. This increase was particularly notable in Eastern European and South Asian countries, with CS rates increasing at an annual rate of 5.5% and 6.1% respectively [4].

In 1985, the WHO declared that the optimal CS rate for a country was in the range of 10–15% [2]. They also reported that there was no improvement in the maternal and neonatal mortality rates when CS rates were greater than this figure [2]. Given the unprecedented increase in CS rates from then to now, the relevance and accuracy of this statement was questioned by leading professionals in the field [5]. However, more recent studies conducted in 2014 and 2015, have since corroborated the statement made by WHO in 1985, illustrating that there is no significant change in neonatal and maternal mortality when the CS rate is in excess of 15% [6,7].

Leading organizations and professionals in the field have called for the need to reduce CS rates globally [1,5]. Professor Gerard H.A. Visser, Chair of FIGO's Committee for Safe Motherhood and

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Newborn Health in 2018 stated that, "*Unnecessary cesarean sections cause more harm than good. Awareness must be raised both among doctors but also among patients who should be informed of the negative aspects of C-sections*" [8]. A statement made by Catherine Spong from the Institute of Child Health and Human Development, USA echoed this same concern; *"Given the major complications associated with multiple cesareans, to both mother and baby, women should carefully evaluate the immediate risks in the current pregnancy with the longer-term risks of multiple cesareans"* [9]. With the above statements in mind, this paper looks to examine the history of CS, the evolution of the changing indications for CS and examine the increasing CS rates in a world where family sizes are reducing and maternal age at first pregnancy is increasing [10,11].

Evolution of the caesarean section

CS is reported in ancient texts from around the world including Hindu, Egyptian, Grecian, Roman and European records and was originally performed only when the mother was either dead or dying [12]. Preceding the advent of anesthesia and antisepsis, the procedure was considered barbaric with associated high rates of pain and infection. The mortality rate associated with CS was over 50% worldwide in the 19th century [13]. Advances in anesthetics at the end of the 19th century resulted in improved surgical techniques, better record keeping and recording of previous procedures [12]. Alongside the development of improved anesthetic techniques, advances in antisepsis and sepsis treatments allowed obstetricians to enhance CS delivery [12,13]. This in turn led to the investigation of various methods that would result in both reduced infection and control of obstetric hemorrhage [12,13]. This continued evolution and advancement in the technique of CS has resulted in a significant reduction in complication rates and improvements in maternal and neonatal morbidity and mortality, which will be discussed in more detail below.

Risks and benefits of CS

Risks

It is well established that CS is associated with increased maternal morbidity and mortality compared to vaginal delivery including post-partum hemorrhage, transfusion, hysterectomy, complications of anesthesia, venous thromboembolism and post-partum infections [14]. The burden of maternal mortality is disproportionately high in low-income and middle-income countries (LMICs). A 2019 systematic review and metanalysis reported that the risk of maternal death was significantly higher in LMICs, with the highest risk of death observed in women from sub-Saharan Africa [15]. This study also observed that women undergoing emergency CS in LMICs were twice as likely to die than those delivering by elective CS [15].

CS also confers increased risks in a subsequent pregnancy. Pregnancy after CS is associated with increased rates of miscarriage, stillbirth, placenta previa, placenta accreta, and placental abruption [16]. Additionally, vaginal birth after CS (VBAC) has a rare but devastating risk of uterine rupture - 1/200 women [17]. This risk increases with the number of CS performed, a shorter interval since last CS and induction/augmentation of labor. The risk of placenta accreta spectrum disorders similarly increases with the number of prior CS performed; with the incidence of placenta accreta approximately 0.24% after one CS compared to 2.33% in women after four previous CS procedures [18]. This results in an increased risk of peripartum hysterectomy [19].

CS has been linked to the risk of additional complications not only in the mother but also in the neonate. Repeat CS has been associated with an increased risk of respiratory complications, including transient tachypnoea of the newborn and respiratory distress syndrome, which corresponds with an increased rate of admission to neonatal intensive care units [20]. In LMICs a concerning proportion of stillbirths and perinatal deaths were reported in association with CS births, particularly in the sub-Saharan region where up to one in ten babies delivered by caesarean section were stillborn [15]. Further studies have raised additional concerns regarding the association between CS and other childhood conditions, including an increased risk of obesity up to 5 years and increased risk of asthma up to 12 years in children delivered by CS [16], though these associations need further investigation.

Benefits

Despite the numerous complications alluded to above, CS has several benefits when utilized appropriately. Arguably, the most important benefit of CS has been to reduce perinatal mortality rates [2]. Further reported benefits include reduced rates of urinary incontinence and pelvic organ prolapse, cerebral palsy in the neonate, and adverse neonatal outcomes in breech presentations [14,16,21].

One of the primary aims of CS is to offer a safe alternative to vaginal birth with an ensuing decrease in maternal and neonatal morbidity and mortality. However, it must also be acknowledged that advances in antenatal care, labor ward practice and improvements in neonatal care have all contributed to the improvements in these figures. Several studies have shown a direct correlation between CS rates and improved maternal and neonatal mortality, with data suggesting improved maternal and neonatal mortality up to a certain threshold which has been reported as CS rates ranging from 10% to 19% [22,23]. It is important to note that all of these studies found no correlation between maternal and neonatal mortality beyond a certain threshold, which is to say the mortality rate was not increased by increasing CS rates, nor was it reduced.

It was with this in mind that the WHO recommended the optimal CS rates for a population should be in the range of 10–15% [2]. A further study by Molina G et al. that included 97.6% of all live births in the world, proposed an optimal CS rate of below 19%, which suggests that previous targets sets by the WHO were lower than necessary [23]. Moreover, when considering the suggested CS rates described above, it is alarming to see CS rates of 44.3% reported across Latin America and the Caribbean and equally disconcerting to see CS rates as low as 4.1% in central and West Africa [4]. The corresponding neonatal mortality rates for the same period in both regions was 9.8 per 1000 live births and 29.3 per 1000 live births respectively [24]. The low CS and high neonatal mortality rates raises concerns regarding lack of access to safe CS in LMICs.

The changing indications for caesarean delivery

With the advances in surgical technique, there has been a resultant change in the various indications for CS, which in many respects are strongly associated with corresponding improvements in antenatal care and labor ward practice internationally. Leading medical indications for CS include previous CS, non-reassuring fetal heart rate, malpresentation, labor dystocia and suspected macrosomia [25]. With the advent of cardiotocography (CTG), continuous monitoring of fetal heart rate (FHR) has become the standard of care in labor wards [26]. A Cochrane review comparing continuous FHR monitoring versus intermittent auscultation observed that healthy parturients who had continuous FHR monitoring had a higher rate of CS compared to those who had intermittent auscultation [27]. A further leading indication for CS includes malpresentation, particularly breech presentation. The Term Breech Trial

published in 2000, concluded that planned CS was safer compared to planned vaginal delivery in a term breech presentation [21].

Furthermore, several studies have observed 'previous CS' as the most common indication for CS, with rates ranging from 26% to 30% of all CS indications [25,28]. The reasons for this are multifactorial but have been strongly associated with the declining VBAC rates internationally. The reasons for declining VBAC rates are multiple and complex and include inadequate resources, litigation concerns, as well as a lack of knowledge amongst both providers and patients [29]. Ambiguous statements by the ACOG regarding VBAC have raised concern among providers about litigation [30] and a 2009 study estimated that a $10,000 decrease in insurance premiums would be associated with a 1.45% increase in VBAC rates and associated decrease in CS performed due to previous CS [31]. This data combined with the study showing a power imbalance in the favor of the physician during mode of delivery decisions [32], suggests that physician associated factors are as important as patient associated ones and in turn have added to the increase in global CS rates.

Moreover, there has been an increase in CS rates performed for non-medical reasons. A study published in the NEJM in 1989, demonstrated a changing culture in the indications for CS from medical to non-medical indications [33]. The study found that rates of primary CS vary directly with socioeconomic status and that these differences are not accounted for by medical reasons, such as complications of pregnancy or childbirth, maternal age, parity and birth weight [33]. Similarly, there has been a rise in CS for maternal request/patient preference [34]. Studies have shown a link between a lack of positive anticipation of childbirth and increased CS rates as well as the increased perception of CS as a more convenient mode of birth [35]. A 2012 American study showed a positive correlation between cesarean delivery on maternal request (CDMR) and concern about delivery-related birth injuries to the neonate [36]. Additional reasons for CDMR were fear of urinary incontinence, pelvic floor/vaginal trauma, suggestion from a healthcare professional, and a prior experience of a traumatic delivery [37]. Various other non-medical factors have contributed to increasing incidence of CS. A study in China showed a correlation between higher CS rates and type of medical payment [38]. In countries where patients are charged more for a CS than a vaginal delivery, concerns have also been raised that doctors may be performing CS which are not medically indicated in an effort to earn more. FIGO therefore has recommended averaging cost and permitting the same fee to be paid to obstetricians irrespective of mode of delivery to negate this perception [1]. Another study from Turkey observed that women of higher socioeconomic status were more likely to accept CS than women of lower socioeconomic status, emphasizing that factors other than medical indications are associated with the increasing CS rates [39].

The impact of changing maternal demographics and assisted fertility on the CS rates

A 2017 report published by the United Nations observed a fall in the average household size almost everywhere in the world with a concurrent decline in fertility rates; in France the fertility rate reduced from 2.6 to 2.0 between 1968 and 2011 [40]. Similarly, in Kenya the fertility rates reduced from 8.1 to 4.4 between 1969 and 2014 [40]. The fall in fertility rates in these countries, both vastly different from each other from a socio-economic and health perspective, displays the global trend towards families having fewer children. Additionally, the mean age at first pregnancy is also increasing [11]. However significant differences have been observed in this statistic between countries. In 2015 the mean age at first birth was 19.9 years in Afghanistan compared to 30.7 years in Ireland [41]. In the USA, between 1990 and 2012, there was a substantial increase in the number of nulliparous women aged 35–39 years [42]. With this increasing age at first pregnancy, comes a decrease in fertility; without medical intervention. Women trying to conceive at an older age have a greater chance of infertility and hence form a growing cohort of women who attend fertility clinics for assisted reproductive technology (ART). This increase in the mean age at first pregnancy along with the increased use of ART have led to a dramatic increase in the twinning rate-from 18.9/1000 to 33.2/1000 between 1980 and 2009 [43], with further increased CS rates. It is clear that more women are having fewer children and at a later age. Care providers should in turn consider if these changing demographics reduce the relevance of CS complications in a subsequent pregnancy and is something that should be discussed with patients on an individualized basis.

Standardizing comparison of caesarean section rates

A discussion regarding global CS rates is incomplete without discussing a standardized method to classify and thus compare CS rates between different countries. A 2011 systematic review by the WHO examined several classification methods including indication-based classifications, urgency-based classifications and women-based classifications. It noted that the most common classification system was indication-based, however the categories in these classes were not mutually exclusive, there were contrasting definitions of the indications, and the indications could only be identified retrospectively, making implementation difficult. Similar problems were noted with urgency-based classifications, although these seemed to have greater clinical applicability and potential to improve communications between healthcare professionals and thus outcomes, compared to indications-based classifications. Women-based classification were deemed to be the most superior approach, as these classification systems allowed prospective determination into mutually exclusive, completely inclusive categories, and had high reproducibility. The highest rated women-based classification system in the review was the Robson 10 group classification system and the Denk 8 group classification. Between these two classification system, the Robson 10 group classification system was determined to be the most suitable to fulfil local and international needs of the obstetric community [44].

The use of the Robson 10 group classification is increasing rapidly globally [45]. In 2015, the WHO endorsed the Robson 10 group classification as a global standard for monitoring, assessing and comparing CS rates [46]. The classification system comprises of 10 mutually exclusive and completely inclusive groups based on parity, number of fetuses, prior CS, onset of labor (spontaneous vs induced), gestational age and fetal presentation. This method of analyzing CS rates between and within countries would help eliminate differences caused by variations in the obstetric population. Stratifying the CS rates in such a way would also allow identification of the various subgroups where the CS rates could be deemed disproportionally high. For example, it has been suggested that reducing the CS rate in nulliparous women in spontaneous labor at greater than 37 weeks is a means to reducing overall section rate in subsequent pregnancies.

The variance in obstetric populations globally also brings into question the optimal CS rate determined by the WHO of 10–15% [2], and raises the question of whether we should be aiming for a blanket CS rate across the globe or varying it based on the underlying obstetric population of the country. The question remains as to whether comparing CS rates based on obstetrics classifications (e.g. the Robson groups) or other various maternal characteristics is more appropriate, rather than a single, summative figure.

Conclusion

The disparity in studies looking at an optimal CS rate, suggests an underlying flaw in the concept of a universally applicable 'optimal CS rate'. Firstly, as obstetricians we should be constantly critical of our own practice and the underlying indications when performing CS procedures, particularly a first CS procedure in a nulliparous woman. Secondly, we should be aware of our own population of parturients and the demographics of women attending our maternity services and be conscious of the broader CS rate in our own countries. Thirdly, efforts must be made to agree on an appropriate classification system whereby CS rates can be compared accurately between units and countries as a useful tool to both audit and monitor our practice. Finally, and most importantly, we must be cognizant of how the CS rate in our individual populations impacts the maternal and perinatal morbidity and mortality rates and aim to adjust our practice accordingly to minimize harm.

Declaration of competing interest

The authors report no conflict of interest.

References

[1] Visser GHA, Ayres-de-Campos D, Barnea ER, de Bernis L, Di Renzo GC, Vidarte MFE, et al. FIGO position paper: how to stop the caesarean section epidemic. Lancet 2018;392(10155):1286–7.

[2] WHO. WHO statement on caesarean section rates Geneva 2015 [Available from: https://www.who.int/reproductivehealth/publications/maternal_perinatal_health/cs-statement/en/.

[3] 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.

[4] Boerma T, Ronsmans C, Melesse DY, Barros AJD, Barros FC, Juan L, et al. Global epidemiology of use of and disparities in caesarean sections. Lancet 2018;392(10155):1341–8.

[5] Purandare CN. Caesarean section rates going up. In: Naik DS, editor. 61st all India congress of obstetrics and gynaecology. FIGO; 2018.

[6] Ye J, Betrán AP, Guerrero Vela M, Souza JP, Zhang J. Searching for the optimal rate of medically necessary cesarean delivery. Birth 2014;41(3):237–44.

[7] Betran 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. Reprod Health 2015;12:57.

[8] FIGO. C-Sections: How to stop the epidemic. FIGO; 2018. Available from: https://www.figo.org/c-sections-how-stop-epidemic.

[9] Spong C. Uterine rupture more likely with repeated C-sections. FIGO; 2012. Available from: https://www.figo.org/uterine-rupture-more-likely-repeated-c-sections.

[10] Division UDoEaSAP. Population facts: United Nations. 2017 [2017/2:[Available from: https://www.un.org/en/development/desa/population/publications/pdf/popfacts/PopFacts_2017-2.pdf.

[11] CDC. CDC. In: Births: Final data for 2013. USA: CDC; 2015.

[12] Sewell JE. Cesarean section - a brief history National Library of Medicine - National Institutes of Health. 1995. Available from: https://www.nlm.nih.gov/exhibition/cesarean/index.html.

[13] Peleg D, Burke YZ, Solt I, Fisher M. The history of the low transverse cesarean section: the Pivotal Role of Munro Kerr. Isr Med Assoc J 2018;20(5):316–9.

[14] Gupta Mamta, Saini Vandana. Caesarean section: mortality and morbidity. J Clin Diagn Res 2018;12(9):QE01–6.

[15] Sobhy S, Arroyo-Manzano D, Murugesu N, Karthikeyan G, Kumar V, Kaur I, et al. Maternal and perinatal mortality and complications associated with caesarean section in low-income and middle-income countries: a systematic review and meta-analysis. Lancet 2019;393(10184):1973–82.

[16] Keag OE, Norman JE, Stock SJ. Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: systematic review and meta-analysis. PLoS Med 2018;15(1). e1002494-e.

[17] Gupta JK, Smith GCS, Chodankar RR. Birth after previous caesarean birth. UK: Royal College of Obstetricians and Gynaecologists; 2015.

[18] Silver RM, Landon MB, Rouse DJ, Leveno KJ, Spong CY, Thom EA, et al. Maternal morbidity associated with multiple repeat cesarean deliveries. Obstet Gynecol 2006;107(6):1226–32.

[19] Knight M, Kurinczuk JJ, Spark P, Brocklehurst P. Cesarean delivery and peripartum hysterectomy. Obstet Gynecol 2008;111(1):97–105.

[20] Morrison JJ, Rennie JM, Milton PJ. Neonatal respiratory morbidity and mode of delivery at term: influence of timing of elective caesarean section. BJOG An Int J Obstet Gynaecol 1995;102(2):101–6.

[21] Hannah ME, Hannah WJ, Hewson SA, Hodnett ED, Saigal S, Willan AR. Planned caesarean section versus planned vaginal birth for breech presentation at term: a randomised multicentre trial. Term Breech Trial Collaborative Group Lancet 2000;356(9239):1375–83.

[22] McClure EM, Goldenberg RL, Bann CM. Maternal mortality, stillbirth and measures of obstetric care in developing and developed countries. Int J Gynecol Obstet 2007;96(2):139–46.

[23] 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(21):2263–70.

[24] Bank TW. Mortality rate, neonatal (per 1,000 live births). The World Bank; 2015. Available from: https://data.worldbank.org/indicator/SH.DYN.NMRT?end=2015&start=1990&view=chart.

[25] Lurie S, Shalev A, Sadan O, Golan A. The changing indications and rates of cesarean section in one academic center over a 16-year period (1997–2012). Taiwan J Obstet Gynecol 2016;55(4):499–502.

[26] Stout MJ, Cahill AG. Electronic fetal monitoring: past, present, and future. Clin Perinatol 2011;38(1):127–42.

[27] Devane D, Lalor JG, Daly S, McGuire W, Cuthbert A, Smith V. Cardiotocography versus intermittent auscultation of fetal heart on admission to labour ward for assessment of fetal wellbeing. Cochrane Database Syst Rev 2017;(1).

[28] Ryan GA, Nicholson SM, Morrison JJ. Vaginal birth after caesarean section: current status and where to from here? Eur J Obstet Gynecol Reprod Biol 2018;224:52–7.

[29] Sargent J, Caughey AB. Vaginal birth after cesarean trends: which way is the pendulum swinging? Obstet Gynecol Clin N Am 2017;44(4):655–66.

[30] Niino Y. The increasing cesarean rate globally and what we can do about it. BioScience Trends 2011;5(4):139–50.

[31] Yang YT, Mello MM, Subramanian SV, Studdert DM. Relationship between malpractice litigation pressure and rates of cesarean section and vaginal birth after cesarean section. Med Care 2009;47(2):234–42.

[32] Gamble J, Creedy DK, McCourt C, Weaver J, Beake S. A critique of the literature on women's request for cesarean section. Birth 2007;34(4):331–40.

[33] Gould JB, Davey B, Stafford RS. Socioeconomic differences in rates of cesarean section. N Engl J Med 1989;321(4):233–9.

[34] Florica M, Stephansson O, Nordström L. Indications associated with increased cesarean section rates in a Swedish hospital. Int J Gynecol Obstet 2006;92(2):181–5.

[35] Ryding EL, Lukasse M, Parys A-SV, Wangel A-M, Karro H, Kristjansdottir H, et al. Fear of childbirth and risk of cesarean delivery: a cohort study in six European countries. Birth 2015;42(1):48–55.

[36] Romero ST, Coulson CC, Galvin SL. Cesarean delivery on maternal request: a western North Carolina perspective. Matern Child Health J 2012;16(3):725–34.

[37] Jenabi E, Khazaei S, Bashirian S, Aghababaei S, Matinnia N. Reasons for elective cesarean section on maternal request: a systematic review. J Matern Fetal Neonatal Med 2019:1–6.

[38] Cai WW, Marks JS, Chen CH, Zhuang YX, Morris L, Harris JR. Increased cesarean section rates and emerging patterns of health insurance in Shanghai, China. Am J Publ Health 1998;88(5):777–80.

[39] Koc I. Increased cesarean section rates in Turkey. Eur J Contracept Reprod Health Care 2003;8(1):1–10.

[40] Nations U. Division DoEaSAP. In: Household size and composition around the world. United Nations; 2017.

[41] Agency CI. Mother's mean age at first birth: central Intelligence Agency; [Available from: https://www.cia.gov/library/publications/the-world-factbook/fields/352.html.

[42] Mathews TJ, Hamilton BE. First birthds to older women continue to rise. In: Control CfD. USA: CDC; 2014.

[43] Martin Joyce A, Hamilton BE. Births: final data for 2018. In: Control CfD. USA: CDC; 2018. Available from: https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_13-508.pdf.

[44] Torloni MR, Betran AP, Souza JP, Widmer M, Allen T, Gulmezoglu M, et al. Classifications for cesarean section: a systematic review. PloS One 2011;6(1):e14566.

[45] Betrán AP, Vindevoghel N, Souza JP, Gülmezoglu AM, Torloni MR. A systematic review of the Robson classification for caesarean section: what works, doesn't work and how to improve it. PloS One 2014;9(6):e97769.

[46] WHO. WHO statement on caesarean section rates: human reproduction programme. 2015. Available from: https://apps.who.int/iris/bitstream/handle/10665/161442/WHO_RHR_15.02_eng.pdf?sequence=1.