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Socio-demographic factors of Caesarean births in Nha Trang city, Vietnam: A community-based survey --Manuscript Draft--

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Funding Information:	Japan Agency for Medical Research and Development (JP19fm0108001)	Dr. Lay Myint Yoshida
Abstract:	<p>Background: The Caesarean section rate in Vietnam has been increasing especially in urban area. However, limited evidence identified regarding socio-demographic factors of the Caesarean section birth. The objective of this study was to determine the current Caesarean birth rate and the associated socio-demographic factors among mothers in Nha Trang city, south-central Vietnam.</p> <p>Methods: A community-based cross-sectional study was conducted between October and November in 2016 as part of a <i>Streptococcus pneumoniae</i> carriage survey conducted in 27 communes of Nha Trang city. From each commune, 120 mothers and their children less than two years old were randomly selected. Mothers were asked to answer standardized questions regarding socio-demographic information and mode of birth. Multivariate logistic regression was adopted to examine associations between socio-demographic variables and mode of birth.</p> <p>Results: Of 3148 participants, the number of Caesarean births was 1396 (44.3 %). Older maternal age (≥ 30 years old), having another child going to school or kindergarten, monthly income more than 644 USD, gestational weeks at birth over 42 weeks, and low (< 2500g) or high (≥ 3500 g) birth weight were associated with higher likelihood of Caesarean births.</p> <p>Conclusion: The CS rate obtained in this study was more than twice of what is recommended by the World Health Organization, which is consistent with the previous nation-wide study in Viet Nam. Further monitoring is suggested to examine the non-medical reason for the increased CS rate.</p> <p>Keywords: Caesarean birth rate, community-based mothers, socio-demographic factors, urban city, Vietnam.</p>	
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Response to Reviewers:	<p>Response to the reviewer's comment Thank you for giving me the opportunity to submit a revised draft of my manuscript titled Demographic factors of Caesarean births in Nha Trang city, Vietnam: A community based survey. We are grateful to the reviewer 1 for giving his/her additional comment on our paper.</p> <p>Reviewer #1: My guess would be that people reluctant to have their children undergoing nasolaryngeal swab would be those less exposed to medicalization and therefore to cesarean section. This indicate that the CS rate in this study may be higher than that in the general population.</p> <p>We thank the reviewer for giving us the insightful comment. However, it might be the opposite as rich people may be less likely to participate in research activity but will seek proper health care when necessary. Nevertheless, we considered about the possible selection bias. There is also no supporting evidence that mothers, who are willing to have their child examined by nasopharyngeal swab, are also in favor of medicalized childbirth including CS. In addition, the CS rate in our study (43%) was consistent to that of urban area (2014: 43%) in the previous MICU survey. Hence, our conclusion is that it is unlikely to consider that the CS rate in our study is biased due to the refusal rate.</p> <p>Following was added; P18.292-293 Richer people may be less likely to participate in this research activity regardless of financial incentives.</p> <p>Thank you very much.</p>
Additional Information:	
Question	Response
Is this study a clinical trial?<hr><i>A clinical trial is defined by the World Health Organisation as 'any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes'.</i>	No
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Prevalence and characteristics of Caesarean births in south-central Vietnam

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33 29 Keywords: Caesarean birth rate, community-based mothers, socio-demographic factors,
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3 33 **ABSTRACT**
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6 34 **Background:** The Caesarean section rate in Vietnam has been increasing especially in
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10 35 urban area. However, limited evidence identified regarding socio-demographic factors
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12 36 of the Caesarean section birth. The objective of this study was to determine the current
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16 37 Caesarean birth rate and the associated socio-demographic factors among mothers in
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19 38 Nha Trang city, south-central Vietnam.
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22 39 **Methods:** A community-based cross-sectional study was conducted between October
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25 40 and November in 2016 as part of a *Streptococcus pneumoniae* carriage survey
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29 41 conducted in 27 communes of Nha Trang city. From each commune, 120 mothers and
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32 42 their children less than two years old were randomly selected. Mothers were asked to
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35 43 answer standardized questions regarding socio-demographic information and mode of
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38 44 birth. Multivariate logistic regression was adopted to examine associations between
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41 45 socio-demographic variables and mode of birth.
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44 46 **Results:** Of 3148 participants, the number of Caesarean births was 1396 (44.3 %).
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47 47 Older maternal age (≥ 30 years old), having another child going to school or
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51 48 kindergarten, monthly income more than 644 USD, gestational weeks at birth over 42
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54 49 weeks, and low (< 2500 g) or high (≥ 3500 g) birth weight were associated with higher
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57 50 likelihood of Caesarean births.
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51 **Conclusion:** The CS rate obtained in this study was more than twice of what is
52 recommended by the World Health Organization, which is consistent with the previous
53 nation-wide study in Viet Nam. Further monitoring is suggested to examine the non-
54 medical reason for the increased CS rate.

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3 56 **BACKGROUND**
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6 57 Rates of Caesarean section (CS) have increased dramatically over the last thirty years,
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9 58 especially in middle- and high-income countries [1-3]. Although deciding on what should
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13 59 be considered an acceptable CS rate has been controversial, there is no evidence that CS
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16 60 rates higher than 10% decrease maternal or neonatal mortality [4]. Nevertheless, the
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19 61 World Health Organization (WHO) has recommended an optimal CS rate between 10%
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22 62 and 15% [5]. Although there is little evidence to support this rate recommended by the
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25 63 WHO, a systematic review by Betran *et al.*[6] revealed that rates of CS higher than the
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28 64 threshold do not reduce mortality. However, many countries have CS rates much higher
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32 65 than this recommended threshold [1, 2]. Several studies have suggested that unnecessary
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35 66 CS could increase maternal and neonatal morbidity [4, 7], including postpartum
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38 67 complications [7], pregnancy complications [7], and neonatal risks [7, 8]. A recent meta-
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41 68 analysis has shown that children born by CS had an increased risk of asthma up to the age
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44 69 of 12 years and obesity up to the age of five years [8].

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48 70 Betran *et al.* [2] compared the CS rates among 150 countries and reported that
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51 71 the highest CS rates were found in Latin America and the Caribbean region (40.5%),
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54 72 followed by North America (32.3%), Oceania (31.1 %), Europe (25%), Asia (19%), and
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57 73 Africa (7.3%). CS rates in Asia are rapidly increasing with an annual rise of between
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3 74 4.4% and 8.5% [2]. In Asia, Vietnam has the fifth-highest CS rate (2014: 28%) after China
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6 75 (2013: 41%), Republic of Korea (2007: 37%), Thailand (2015: 33%), and Sri Lanka
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9 76 (2014: 32%) according to a Multiple Indicator Cluster Survey (MICS) [9]. A rapid
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12 77 increase in CS rates has also been observed in Vietnam: from 10% in 2002 to 28% in
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16 78 2014 [9]. This increase in CS rates has been especially high in urban areas (2014: 43%).
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19 79 Previous studies have investigated the determinants of increased CS rates in
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22 80 several Asian countries, such as China [10], Bangladesh [11], India [12], Nepal [13], and
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25 81 Cambodia [14]. The determinants of CS have included various dimensions related to the
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28 82 physical, social, cultural, and psychological characteristics of women and their families
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32 83 as well as factors relating to the health system in the study area. Physical characteristics
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35 84 included older maternal age [1, 10, 13] and primiparity [10]. Socio-demographic factors
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38 85 included higher education and higher economic status of mothers and their families [1,
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41 86 10, 13]. The parental or maternal request for CS without a medical indication has been
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44 87 reported in China [15], Cambodia [14], and Nepal [13]. In addition, pregnancies with a
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47 88 male fetus, access to full-insurance payments, and pregnancies after infertility treatment
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51 89 were associated with CS in China [15].
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54 90 A few studies have been conducted that have examined the determinants of CS
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57 91 in Vietnam. For example, Loezenien *et al.*[16] conducted a secondary analysis using
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3 92 country-wide data of 1350 participants in a 2014 MICS survey. The authors claimed that
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6 93 there was a large gap in CS rates between urban (42.4%) and rural areas (22.9%) and that
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9 94 factors associated with CS rates included maternal age at delivery over 35 years and
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13 95 higher economic background [16].

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16 96 Most previous studies have focused on the northern part of Vietnam. Two
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19 97 population studies [17, 18] conducted in Quang Ninh province close to the border of
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22 98 China found that mothers of a male child were more likely to receive CS surgery than
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25 99 mothers giving birth to a female child [17]. This finding likely stems from the enactment
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29 100 of the One-or-Two Child Policy in Vietnam in the late 1980s [17, 19]. Another two
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32 101 population studies [20, 21] conducted in urban and suburban areas of Hanoi also reported
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35 102 a difference in the CS rate between male and female children. Hence, these authors
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38 103 concluded that high income and differences in the CS rates between the sexes might be
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41 104 related to requests made for CS without medical needs [16, 17].

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44 105 Fewer studies have been conducted in the central or southern regions of Vietnam
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48 106 compared with the northern region. Giang *et al.* [22] investigated CS rates and their
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51 107 determinants in 10 hospitals in Da Nang city, an urban area in central Vietnam. The
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54 108 overall CS rate was 58.6%, and private hospitals had a much higher rate of CS (70.6%).
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57 109 CS rates were higher in women that were older than 30 years, had a history of abortion,
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3 110 worked an office job, were pregnant with a male child, or gave birth to a baby of heavier
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6 111 birth weight.
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9 112 Given that a preference for CS for male children might be influenced in the northern part
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12 113 of Vietnam by the culture of ‘Confucianism’, which originated in China, compared with
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15 114 the southern part of the country, geographical differences in several factors might
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18 115 contribute to variation in CS rates. In addition, more data in urban settings are needed to
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21 116 assess the consistency of a previous analysis of MICS data and confirm the pattern that
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24 117 CS rates are higher in urban settings compared with rural ones [9].
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28 118 The objective of this study was to identify the socio-demographic factors and
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31 119 delivery characteristics associated with CS among mothers living in Nha Trang city,
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41 122 **METHODS**
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44 123 This study was conducted in Nha Trang city, the capital of Khánh Hòa province, which
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47 124 is located 445 km north of Ho Chi Minh City in Vietnam. The estimated population in
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50 125 2020 was 329,373 [23]. Nha Trang city has become one of the main holiday
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53 126 destinations in Vietnam and has been experiencing economic growth. There is one
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57 127 public tertiary hospital and three private hospitals where CS can be performed.
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3 128 This study was completed as a part of a *Streptococcus pneumoniae* carriage
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6 129 survey conducted in Nha Trang city across 27 communes: 8 (30%) suburban and 19
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9 130 (70%) urban communes. We conducted a cross-sectional survey in the 27 communes in
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12 131 October and November 2016. First, each community health center made a list of all
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16 132 children aged 4 to 11 months and 14 to 23 months and their mothers living in the
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19 133 commune. All newborn baby must register at CHC for free national health insurance to
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22 134 receive national immunization program vaccines. We used this data since this newborn
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25 135 children data at CHC is the most representative data for number of deliveries in Nha
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28 136 Trang city. Because this survey originally aimed to investigate the carriage rate of
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31 137 *Streptococcus pneumococcus* among participants, we excluded children that were born
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35 138 with a cleft lip or cleft palate and their mothers due to the difficulty of collecting
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38 139 nasopharyngeal samples. Second, children and their mothers were randomly selected
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41 140 from this list and invited to participate in the pneumococcal carriage survey until 120
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44 141 participants per commune had been recruited. Because of the ubiquity of cell phone use
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47 142 in urban areas of Vietnam, trained staff from community health centers made a phone
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51 143 call to the candidates and invited them to participate. Home visit was made and
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54 144 requested to participate in the study for those who do not have mobile phone. One or
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57 145 two staff members visited interested mothers, explained the study, and obtained written
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3 146 informed consent. Upon agreement, the mother was then interviewed using a structured
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6 147 questionnaire requesting socio-demographic information.
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10 148 In terms of sample size calculation, we assumed the true proportion of children
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12 149 aged <24 months who have S. pneumoniae in the nasopharynx in the study area to be 0.5,
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16 150 to obtain the largest sample size, and required the estimate to be within 0.04 of the true
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19 151 value (precision) within the 95% confidence interval (CI). Based on this, the minimum
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22 152 sample size was calculated to be 600 for each introduction arm (6 communes). As there was
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25 153 six communes (clusters) in each arm, we decided to recruit 120 per communes resulting in
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28 154 720 per arm, and 3240 for 27 communes.

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31 155 Appendix figure 1 shows a flow chart of participants. Out of 5533 pairs listed
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34 156 in 27 commune health centers, 5348 were invited to the study by means of a phone call
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38 157 from community health center staff. Around one out of five candidates (n = 1219,
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41 158 22.8%) refused to participate in this study, and 17% (n = 952) could not be contacted. In
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44 159 addition, 29 pairs were not eligible (duplicate participants or out of the eligible age
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47 160 range) based on the participant criteria. A total of 3148 pairs of mothers and their
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50 161 children participated in the survey: 1562 children were aged 4 to 11 months, and 1586
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53 162 were aged 14 to 23 months.

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57 163 The questionnaire included socio-demographic variables, such as maternal age,
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3 164 educational background of the mother and the head of household, name of the commune
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6 165 of residence, household income in the previous month (Vietnamese don, VND), whether
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9 166 the mother has another child going to school or kindergarten, and the total number of
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12 167 household members. Household income in the previous month (VND) was converted into
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15 168 US dollars (1 dollar = 23,291 VND, Sep 17th, 2019). Living in suburban or urban areas
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19 169 was coded based on the administrative definition of the communes. Delivery information
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22 170 included the mode of delivery, the child's sex and birth weight (g), gestational weeks at
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25 171 birth, and the date of birth. The day of delivery was calculated from the birth date of the
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28 172 child. Matshidze *et al.* [24] observed that the CS rate was much higher during weekdays
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32 173 than during the weekends in private settings, whereas CS rates in public facilities did not
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35 174 vary throughout the week, suggesting that there is an institutional effect related to the
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38 175 scheduling of planned CS at convenient times for obstetricians.

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41 176 Binary logistic regression was performed to examine associations between
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44 177 socio-demographic variables and the mode of delivery. The adjusted model included
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47 178 variables that were independently associated with CS births in the crude analysis ($p < 0.05$).
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51 179 To assess the multicollinearity of independent variables, variables that showed moderate
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54 180 correlations with others ($r \geq 0.4$) were excluded from the final model [25]. Analyses were
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57 181 conducted in STATA version 14.0 (Stata Corp., College Station, TX, US).
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3 182 This study was approved by the ethical review boards of the Institute of Tropical
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6 183 Medicine, Nagasaki University, Japan and the National Institute of Hygiene and
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9 184 Epidemiology, Hanoi, Vietnam.
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16 186 **RESULTS**
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19 187 A total of 1396 out of 3148 births were completed by CS, resulting in a CS rate of
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22 188 44.3% (Table 1). Of the 1752 mothers that gave birth vaginally, 227 (12.9%) reported
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25 189 that they had received a medical intervention, such as forceps, vacuum, or oxytocin
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28 190 induction. Of the 1396 CS births, 603 (43.1%) were planned during pregnancy and 777
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32 191 (55.6%) were decided during labour. Previous CS was the most common indication (n =
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35 192 420, 30.1%) followed by cephalo-pelvic disproportion (CPD) (n = 157, 11.2 %),
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38 193 oligohydramnios (n = 147, 10.5%), and malposition (n = 128, 9.1%).
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41 194 Table 2 shows the characteristics of the participants and the CS birth rates in
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44 195 each group. Few mothers were younger than 20 years old (n = 70, 2.2%), and 517
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48 196 (16.4%) were older than 35. A small number of mothers (n = 167, 5.3%) had not
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51 197 completed primary school, while 1207 (38.3 %) had received post-secondary education.
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54 198 Approximately one-fifth of mothers (n = 707, 22.4 %) reported a monthly household
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57 199 income in the previous month higher than 644 USD. Few mothers (n = 85, 2.7%) gave
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3 200 birth post-term (≥ 42 gestational weeks). Approximately one-third of babies ($n = 1116$,
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6 201 35.4 %) were born weighing over 3500 g at birth, while the number of babies weighing
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9 202 less than 2500 g at birth was 69 (2.1%). The percentages of CS births were similar
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12 203 among each day of the week (ranging from 13.1 to 15.2%). The number of male babies
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15 204 ($n = 1660$, 53.7%) was slightly higher than the number of female babies ($n = 1448$,
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19 205 47.2%).

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22 206 Rates of CS were high among women older than 35 years (59.0%), those that
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25 207 had completed post-secondary education (49.8%), those that had a monthly income
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28 208 greater than 644 USD (50.1%), and those with babies weighing over 3500 g (3500–
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31 209 3999 g: 49.8%, 4000–4499 g: 59.4%, > 4500 g: 80.8%) or under 2500 g (55.1%). The
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35 210 CS rate varied depending on the day of the week (ranging from 39.3 to 48.3%), but the
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38 211 sex of the child had no effect on the CS rate.

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41 212 A moderate correlation was observed between the educational backgrounds of
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44 213 the mother and the head of household ($r = 0.57$), which was assumed to be a
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47 214 multicollinear factor. After adjustment for potential confounding factors, CS rates were
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51 215 higher among older women (30–34 years: adjusted odds ratio [AOR] = 1.18, 95%
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54 216 confidence interval [CI] (1.43, 2.31); ≥ 35 years: AOR 2.90, 95% CI (2.22, 3.79)); those
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57 217 with a monthly income of 644 USD or more (AOR = 1.43, 95% CI = 1.14, 1.80), those

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3 218 giving birth after 42 weeks of gestation (AOR = 2.62, 95% CI = 1.63, 4.21), those with
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6 219 babies weighing less than 2500 g at birth (AOR = 1.87, 95% CI = 1.09, 3.26), and those
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9 220 with babies weighing 3500 g or more at birth (3500–3999 g: AOR = 1.50, 95% CI =
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12 221 1.18, 1.91, 4000–4499 g: AOR = 2.04, 95% CI = 1.42, 2.95, \geq 4500 g: AOR = 5.57,
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16 222 95% CI = 2.02, 15.34).

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20 21 22 224 **DISCUSSION**

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25 225 The CS rate in Nha Trang city in Vietnam was 44.3%. The rate of CS was particularly
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28 226 high among women over the age of 30 years, those with a monthly income of more than
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31 227 644 USD, those giving birth after 42 weeks of gestation, and those with either a low (<
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35 228 2500 g) or high (\geq 3500 g) birth weight baby.

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38 229 The CS rate (44.3%) observed in our study is consistent with the rate observed
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41 230 in a national survey of urban areas in Vietnam in 2014 [9]. In addition, the rate is much
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44 231 higher than the CS rate recommended by the WHO (10–15%) [5], suggesting that there
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47 232 may be a substantial number of unnecessary CS births that are not based on medical
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51 233 need. The CS rate in urban areas of Vietnam has increased dramatically over the last 20
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54 234 years from 12% in 1997 (Demographic Health Survey [DHS] 1997) to 23%, 31%, and
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57 235 43% in 2002, 2010, and 2014, respectively (DHS 2002, MICS 2010–2011, MICS 2014)

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3 236 [9]. Giang *et al.* [22] noted that the CS rate at private hospitals (70.6%) was much
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6 237 higher than that at public hospitals (57.9%). After the economic reform in the late
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9 238 1980s, private health facilities have increased in number dramatically in metropolitan
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12 239 areas, attracting wealthier people that expect better quality care in private hospitals. The
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15 240 link between the mode of delivery at private hospitals and the risk for CS has been
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18 241 widely documented in other countries [1]. One of the limitations of our study is that we
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21 242 did not ask mothers whether they gave birth at private or public hospitals; nevertheless,
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24 243 our sample covered three private hospitals. Thus, the high rate of CS may have reflected
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27 244 the increased use of CS associated with private hospitals.

31 Mothers with higher economic status were more likely to receive CS births.

32 245 The health care system was organised by the Vietnamese government in the late 1980s
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35 246 [26]. Currently, health insurance covers a variety of health care services, including from
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38 247 80 to 100% of the total cost of antenatal checkups and both normal and abnormal
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41 248 childbirths. The introduction of user fees for service in the late 1980s has increased the
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44 249 number of service options [26] as well as the out-of-pocket expenses of patients.
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47 250 Mothers that undergo CS sometimes need to pay out-of-pocket expenses for additional
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50 251 services, such as a single room charge for hospitalization; therefore, mothers with a low
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53 252 economic status may not be able to afford medical expenses for CS [27]. Another reason
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3 254 for the association between higher economic status and CS birth may be a difference in
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6 255 access to antenatal care services between women with higher and lower socio-economic
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9 256 status. Wealthier pregnant women receive more frequent and qualified antenatal care,
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12 257 including ultrasonographic examinations, that can aid the identification of medical
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16 258 conditions requiring CS [27].
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19 259 Contrary to a previous study reporting higher CS rates in urban areas (43%)
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22 260 than in suburban areas (21%) [9], place of residence was not significantly associated
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25 261 with CS rates in our final adjusted model. This discrepancy may stem from the greater
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28 262 proximity between urban and suburban regions inside Nha Trang city. As several studies
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31 263 have indicated [1, 13], one of the reasons for higher CS rates in urban areas is increased
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35 264 accessibility to maternity health care facilities that are well equipped and well-staffed.
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38 265 Another reason is that patients with higher socio-economic status who are able to
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41 266 receive CS often live in urban areas [3, 27]. However, only a weak association of
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44 267 education and economic status with residential areas was observed in our study. Thus,
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47 268 the higher geographical proximity among the study areas likely explained the negligible
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51 269 difference in the CS rate between urban and suburban areas.
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54 270 Child sex was not associated with the CS rate in our study in contrast to findings
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57 271 from previous studies in Vietnam [17, 22]. Giang *et al.* [22] suggested that some families
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3 272 under the traditional culture of ‘Confucianism’ may request a CS when they find out by
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6 273 ultrasonography that the child is a male. The sex ratio at birth was higher in northern areas
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9 274 (> 120 male births to 100 female births) than in central or southern areas of Vietnam (<
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12 275 110 male births to 100 female births) [29]. Da Nang city is located approximately 500 km
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16 276 north of Nha Trang city. Therefore, the association between child sex and CS may be
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19 277 influenced by cultural differences between regions.

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22 278 Older maternal age (≥ 30 years old), low birth weight (< 2500 g), and high birth
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25 279 weight (≥ 3500 g) resulted in higher CS rates. Although we did not take data on birth
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28 280 parity in our study, CS rates were lower for mothers that reported ‘having another child
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31 281 going to school or kindergarten’. These findings are consistent with previous studies that
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35 282 have been conducted in other countries [30]. Older age, primiparity, low birth weight, and
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38 283 high birth weight may be associated with a higher risk of pregnancy and birth
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41 284 complications and a greater need for CS [27]. However, given that the CS rates in younger
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44 285 age groups (20–29 years old) were over 30%, CS for a substantial number of patients
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47 286 might not have been medically required.

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51 287 The major strength of our study was that we recruited a large number of
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54 288 participants (n = 3140) and followed a strict randomization enrollment technique. Our
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57 289 data included participants from urban and suburban areas across Nha Trang city.
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3 290 Our study has a few limitations that should be considered. First, 22.8 % of
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6 291 participants refused to participate in the *Streptococcus pneumococcus* carriage survey.
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9 292 The lack of participation by some participants might have reflected their fear of having
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12 293 a nasopharyngeal swab taken from their child. Richer people may be less likely to
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15 294 participate in this research activity regardless of financial incentives. In addition, we
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18 295 were unable to contact 17.9% of the candidates on the original candidate list, possibly
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21 296 because they had changed their mobile phones or moved to a different address. These
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24 297 facts might slightly influence the representativeness of participants. Second, we did not
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27 298 have information on parity and other clinical factors, such as pregnancy, delivery
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30 299 complications, and the number of antenatal checkups identified in a previous study [16],
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33 300 as this study was a part of a *Streptococcus pneumoniae* carriage survey. Third, our data
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36 301 were based on the ability of mothers to recall the requested information, but we were
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39 302 unable to confirm the information that they provided from medical charts. Although the
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42 303 medical reasons for CS in our study were similar to those provided by a previous study
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45 304 [22], data based on clinical indications for CS from hospital records would have been
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48 305 superior and of higher quality than the data that we collected. Women may have also
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51 306 misreported their age, income, gestational age, or the birth weight of their children.
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54 307 Misclassification of gestational age and birth weight may have been related to the mode
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308 of delivery, although it is difficult to predict in which direction this would have biased
309 the results.

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311 **CONCLUSIONS**

312 The CS birth rate in Nha Trang city was 44.3% in 2016. Older maternal age (≥ 30 years
313 old), having another child, monthly income greater than 644 USD, gestational weeks at
314 birth over 42 weeks, and low (< 2500 g) and high (≥ 3500 g) birth weight were
315 associated with a higher likelihood of CS birth.

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6 319 **Abbreviations**

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9 320 AOR: Adjusted Odds Ratio, CI: Confidential Interval; CPD: Cephalo Pelvic

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12 321 Disproportion; CS: Caesarean Section; DHS: Demographic Health Surveys; MICS:

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15 322 Multiple Indicator Cluster Surveys; N: Number; WHO: World Health Organization;

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18 323 USD: US dollar; VND: Vietnamese don.

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29
30
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33
34 328 MT(1st) and LMY contributed to the conception and design of this study, acquired,

35
36
37 329 analyzed and interpreted the data, drafted original manuscript, and revised

38
39
40 330 the manuscript. HATN, NK, CI, and DAD contributed to the investigation, collecting

41
42
43 331 information, data entry and data-cleaning. M.T (5th) and H.M contributed to supervision

44
45
46 332 of the manuscript regarding analysis and draft and revision of the manuscript. CR

47
48
49 333 contributed to the overall contribution regarding analysis, draft of the manuscript and

50
51
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4
5
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10
11
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16 340 The database used for this study is part of an ongoing PCV reduced dosing schedule
17
18
19 341 trial in Nha Trang, Vietnam. The data can be assessed by contacting Prof. Lay Myint
20
21
22 342 Yoshida (lmyoshi@nagasaki-u.ac.jp) who is the PI of the project.

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24
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28
29 344 This study was approved by the ethical review boards of the Institute of Tropical
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32 345 Medicine, Nagasaki University, Japan and the National Institute of Hygiene and
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38 347 informed consent prior to participation into the study.

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41 348 **Consent for publication**

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44 349 Not applicable

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47 350 **Competing interests**

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51 351 The authors declare that they have no competing interests.

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54 352 **Author details**

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