

# Recovery of uterine and ovarian function in patients with complete placenta previa after caesarean delivery

## A retrospective study

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### Abstract

This retrospective study was designed to explore the recovery of uterine and ovarian function in patients with complete placenta previa (PP) after caesarean delivery (CD). 136 complete placenta previa patients (group completed placenta previa) and 140 patients without complete PP (group non-PP, control group) were included in this study from Jan 2016 to Dec 2018. Subgroup analysis of patients with complete PP was made to determine the impact of different hemostatic methods used during CD on the recovery of uterine function. There were no statistically significant differences between the 2 groups in postpartum menstrual cycle changes, ovarian hormone, and uterine vascular supply as measured by pulsatility index and systolic/diastolic ratio ( $P > .05$ ). However, the group with complete PP had a reduced endometrial thickness ( $0.47 \pm 0.11$  vs  $0.50 \pm 0.12$ ,  $P < .001$ ), a lower uterine resistance index at 42nd days ( $0.84 \pm 0.03$  vs  $0.90 \pm 0.03$ ,  $P < .001$ ), and a delayed resumption menstruation ( $7.07 \pm 2.61$  vs  $5.31 \pm 2.16$ ,  $P < .001$ ) when compared with control group. Subgroup analysis showed that RI index of all subgroups in completed PP group was lower, endometrial thickness was thinner and the time to menstrual recovery was longer than that of non-PP group. In conclusion, the endometrial thickness and blood supply at 42nd days, not ovarian function, maybe affected after CD in patients with complete PP.

**Abbreviations:** AMH = anti-mullerian hormone, BTL = bilateral tubal ligation, CD = cesarean delivery, CPP = completed placenta previa, EBL = estimated blood loss, FSH = follicle stimulating hormone, RI = resistance index, UAE = uterine artery embolization.

**Keywords:** caesarean delivery, menstrual cycle, ovarian hormones, placenta previa

Editor: Daryle Wane.

XL and PM contributed equally to this work.

This work was supported by the National Natural Science Foundation of China (#81471544, #81871311) and the National Key Research and Development Program (2018YFC 1002104).

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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How to cite this article: Li X, Musoba PM, Zhou X, Lai S, Yang W, Wang LN, Chantholleng DD, Zhao J. Recovery of uterine and ovarian function in patients with complete placenta previa after caesarean delivery: a retrospective study. *Medicine* 2021;100:2(e24196).

Received: 12 April 2020 / Received in final form: 11 December 2020 / Accepted: 15 December 2020

<http://dx.doi.org/10.1097/MD.00000000000024196>

## 1. Introduction

The rates of caesarean delivery (CD) have been rising dramatically around the world, with 1 study showing a global rise from 6.7% in 1990 to 19.1% in 2014.<sup>[1]</sup> A much higher CD rate, reaching 46.2% in 2007 to 2008, was reported in China,<sup>[2]</sup> which inadvertently led to increased complications affecting subsequent pregnancy.<sup>[3]</sup> Placenta previa (PP), the most dangerous complication of CD, has a prevalence of approximately 5.2 cases per 1000 pregnancies.<sup>[4]</sup> A study published in 2016 showed that China has a total PP prevalence of 1.24%, of which complete PP accounted for 0.48%.<sup>[5]</sup> It is known that the history of abortion or CD, multiple births and advanced maternal age are associated with the occurrence of PP.<sup>[6]</sup> Patients with complete PP are at higher risk of hemorrhage during and after CD than non PP patients and it is the main cause of postpartum hemorrhage in Chinese women.<sup>[5]</sup> The management and treatment of patients with complete PP has been the focus during pregnancy. However, few researches reported the recovery of women in postpartum.

In the past decades, advancements in surgical technique have greatly reduced bleeding and hysterectomy. Bakri balloons was put in the bleeding lower uterine segment during the cesarean section for pressing hemostasis 24 to 74 hours;<sup>[7]</sup> Uterine compression sutures make the uterus in a stress state by binding and pressing the uterus for better squeezing the blood vessels in the uterine wall.<sup>[8]</sup> Uterine cervical multi-position spiral sutures were used to directly suture the cervical bleeding site for shrinking and compressing lower uterine cavity.<sup>[9,10]</sup> Artery ligation, including internal iliac ligation and uterine artery ligation, were used to block the blood supply to the uterus to stop severe

bleeding.<sup>[11]</sup> All these operational approaches were reported to be effective way to reduce the maternal mortality.<sup>[10]</sup> Previous research suggested that uterine artery embolization should not be performed routinely in women of childbearing age because it was liable to damage the endometrium or even induce endometrial adhesion. And it might be detrimental to ovarian function, resulting in infertility.<sup>[12–15]</sup> For now, few studies focused on the recovery of the uterine and ovarian reserve after surgery. These may be significant concerns for patients who want to conceive babies in the future.

Thus, the aim of this retrospective study is to investigate the recovery of the uterine and ovarian reserve between patients with and without complete PP, and explore the impact of different hemostatic methods used during CD on the resumption of uterine hemodynamics and ovarian function in patients with complete PP.

## 2. Materials and methods

### 2.1. Study design and patients

This was a retrospective, single-center study of patients who delivered by CD in department of obstetrics and gynaecology of Tongji Hospital affiliated to Tongji Medical College of Huazhong University of Science and Technology from January 2016 to December 2018. The department of obstetrics and gynaecology is intensive care center, mainly dealing with high-risk pregnancies. The study was approved by the Ethics Committee of Tongji Medical College in accordance with the Declaration of Helsinki (IORG No: IORG0001089).

In this study, complete PP referred to a placenta totally overlapping the cervical os confirmed by ultrasound. The inclusion criteria for all patients are as follows:

- (1) 20 to 40 years old before pregnancy<sup>[16]</sup>;
- (2) regular menstrual cycles before pregnancy (defined as once every 21–35 days, with menstrual flow lasting 3–7 days);

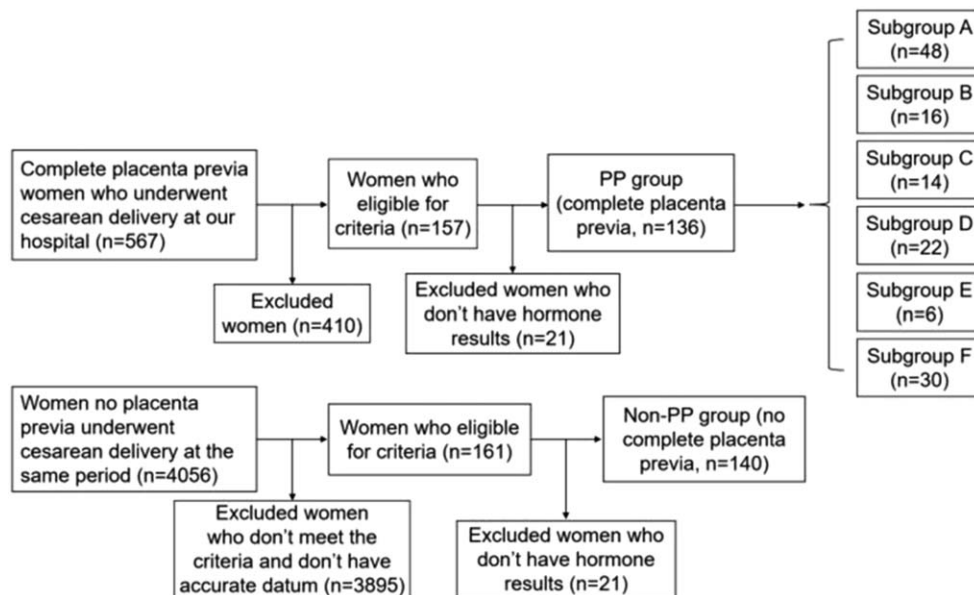
- (3) has an CD at 28 to 42 weeks;
- (4) lactation;
- (5) hemoglobin levels  $\geq 9.0$ g/dL 1 week after CD; 6) contraception by condom after CD.

The exclusion criteria included:

- (1)  $\geq 40$  is excluded accord to the Bologna criteria;
- (2) diminished ovarian reserve (basal follicle-stimulating hormone (FSH)  $>10$  and antral follicles  $<5$ );
- (3) chronic disease, especially hematological disorders, renal failure, cardiac or thyroid disease;
- (4) conception prior to resumption of menstruation;
- (5) hysterectomy;
- (6) uterine artery embolization used before, during or after CD;
- (7) incomplete PP.

Demographic and obstetric characteristics retrieved included: maternal age, previous pregnancies, parity, previous CD and vaginal deliveries, previous abortions, gestational age at CD, estimated blood loss (EBL), hemostatic methods used during CD, menstrual changes, resumption of menstruation and duration of lactation. Ultrasound examination were performed routinely at 42 days post-delivery by 2 experienced operators using the voluson 3-dimensional doppler transvaginal scan machine, with a multi-frequency transvaginal probe (5 to 9 megahertz). Endometrial thickness and uterine artery characteristics were recorded. Hormones examination would be routinely tested during day 2 to day 4 of the first recovered menstrual cycle after CD. Hormones items included serum levels of FSH, luteinizing hormone, estradiol (E2) and anti-Mullerian hormone (AMH). FSH $>25$ U/L was defined as premature ovarian insufficiency (POI).<sup>[16]</sup> All these data were obtained from hospitalization records, outpatient records, follow-up visits or phone calls.

The enrollment and classification of patients were presented in Figure 1. 567 patients underwent CD were diagnosed completed PP and 4056 patients underwent CD had no abnormal placenta



**Figure 1.** Flow diagram of the study. Subgroup A: patients underwent lower segment cesarean section only; subgroup B: patients were applied uterine compression suture; subgroup C: patients were applied uterine and/or iliac artery ligation; subgroup D: patients were applied cervical procedures; subgroup E: patients were applied balloon insertion; subgroup F: patients were applied 2 or more hemostatic techniques applied. PP: placenta previa.

position. 157 patients diagnosed with completed PP and 161 patients without abnormal placenta position matched the criteria. But 21 completed PP patients and 21 control patients were excluded because of lacking accurate datum in feeding period or hormone results after operation. At last, a total of 276 patients were enrolled in the study (group completed placenta previa [CPP], n=136, group non-PP, i.e. control group, n=140). For analyzing the effects of different hemostatic methods used during the process of CD on the recovery of uterine and ovarian function, we classified CPP patients into 6 subgroups (group A to F). The subgroups in our study were divided according to the hemostasis methods adopted by the patients in the operation record. Patients in group A (n=48) underwent lower segment cesarean section only. Patients in group B (n=16) were applied uterine compression suture in the process of CD. Patients in group C (n=14) were applied uterine and/or iliac artery ligation in the process of CD. Patients in group D (n=22) were used cervical procedures (cervicoplasty or multifaceted spiral suture of the lower uterine segment) during the CD. Patients in group E (n=6) were applied balloon insertion during the CD. And patients in group F (n=30) were applied 2 or more hemostatic techniques during the CD.

**2.2. Statistical analysis**

All statistical analyses were performed using the SPSS Statistical Software Package (version 19.0, SPSS Inc., Chicago, IL). Continuous variables were presented by mean ± standard deviation. Student T test was used to compare 2 groups when variables were normal distribution and non-parametric test was used when variables were not normal distribution. Categorical variables were presented by frequency and percentage. Chi-square test or Fischer exact test were performed to compare categorical variables. The statistical level for rejection of the null hypothesis was set as *P* < .05.

**3. Results**

There were 136 patients in CPP group and 140 in non-PP group. As shown in Table 1, there were no significant difference in the age, gravidity, parity and the number of previous abortion between 2 groups. The number of previous CD was significantly higher in the CPP group (0.81 ± 0.60 vs 0.38 ± 0.51, *P* < .001). For the times of pregnancy termination, elective surgery was performed at 36.65 ± 1.78 weeks in the CPP group and at 38.19 ± 1.93 weeks in the non-PP group (*P* < .001). Moreover, the EBL

**Table 1**  
Characteristics of the 2 groups.

| Variable                      | PP (n=136)        | Non-PP (n=140)  | P-value |
|-------------------------------|-------------------|-----------------|---------|
| Age (yr)                      | 30.04 ± 4.90      | 29.95 ± 4.82    | .88     |
| Gravidity                     | 2.35 ± 1.41       | 2.29 ± 1.34     | .71     |
| Parity                        | 1.45 ± 0.61       | 1.44 ± 0.40     | .87     |
| Previous CDs                  | 0.81 ± 0.60       | 0.38 ± 0.51     | <.001*  |
| Previous Vaginal deliveries   | 0.24 ± 0.40       | 0.41 ± 0.30     | <.001*  |
| Induced abortions             | 0.65 ± 1.11       | 0.61 ± 1.10     | .76     |
| Gestational age at CD (weeks) | 36.65 ± 1.78      | 38.19 ± 1.93    | <.001*  |
| EBL (ml)                      | 1206.56 ± 1052.52 | 784.67 ± 174.24 | <.001*  |

CD=Cesarean delivery, EBL=Estimated blood loss, PP=placenta previa. *P* < .05 was considered statistically significant difference.

**Table 2**  
Comparison of endometrial thickness and uterine artery characteristics in the 2 groups.

| Variable                   | PP (n=136)  | Non-PP (n=140) | P-value |
|----------------------------|-------------|----------------|---------|
| Endometrial thickness (cm) | 0.47 ± 0.11 | 0.50 ± 0.12    | <.001*  |
| PI                         | 2.40 ± 0.20 | 2.41 ± 0.18    | .99     |
| S/D                        | 8.60 ± 1.18 | 8.70 ± 0.85    | .42     |
| RI                         | 0.84 ± 0.03 | 0.90 ± 0.03    | <.001*  |

PI=pulsatility index, PP=placenta previa, RI=resistance index, S/D=systolic and diastolic ratio. *P* < .05 was considered statistically significant difference.

was significantly higher in the CPP group (1206.56 ± 1052.52 vs 784.67 ± 174.24, *P* < .001).

As shown in Table 2, patients in CPP group had a thinner endometrium (0.47 cm) compared to those patients in non-PP group (0.50 cm) at the 42nd day after CD (*P* < .001). In addition, among the uterine hemodynamics indexes, only resistance index (RI) values between 2 groups were significantly different (0.84 ± 0.03 vs 0.90 ± 0.03, *P* < .001).

Comparison of menstrual changes between the 2 groups was presented in Table 3. The time to menstruation resumption was significantly longer in CPP group than non-PP group (7.07 ± 2.61 vs 5.31 ± 2.16, *P* < .001) and none of the patients experienced secondary menopause. The proportion of women who reported no change in menstruation was 86.03% (117/136) in the CPP group and 90% (126/140) in the non-PP group (*P* = .36). Specifically, a significantly higher proportion of women who had irregular cycles (4.41% vs 0.00%, *P* = .01) and a significantly lower proportion of women who had prolonged menses (1.47% vs 7.14%, *P* = .04) in CPP group than non-PP group. The duration of lactation between the 2 groups were similar (*P* > .05).

70.65% (n=195) of women were less than 35 years old, and 29.35% (n=81) were 35 or older. Comparison of ovarian function between the 2 groups was shown in Table 4, we found that the level of AMH was slightly higher in patients under 35 years old than in patients over 35 in both groups (*P* > .05). No statistically significant differences were observed in the levels of the ovarian hormones between the 2 groups (*P* > .05).

Subgroups analysis of CPP group was illustrated in Table 5. The EBL were significantly higher in patients in the subgroup B, C, D, F than non-PP group (*P* < .05). Patients in subgroup F who were applied 2 or more hemostatic methods during the CD had the most EBL (2338.90 ± 1029.50 mL). Overall, RI index of all

**Table 3**  
Comparison of menstrual changes between the 2 groups.

| Variable                              | PP (n=136)   | Non-PP (n=140) | P-value |
|---------------------------------------|--------------|----------------|---------|
| Duration of lactation (mo.)           | 4.79 ± 3.14  | 4.81 ± 2.52    | .95     |
| Time to menstruation resumption (mo.) | 7.07 ± 2.61  | 5.31 ± 2.16    | <.001*  |
| No menstrual changes, n (%)           | 117 (86.03%) | 126 (90.00%)   | .36     |
| Menstrual changes, n (%)              | 19 (13.97%)  | 14 (10.00%)    | .36     |
| Irregular cycles, n (%)               | 6 (4.41%)    | 0 (0.00%)      | .01*    |
| Lengthened cycle, n (%)               | 3 (2.21%)    | 0 (0.00%)      | .12*    |
| Prolonged menses, n (%)               | 2 (1.47%)    | 10 (7.14%)     | .04*    |
| Volume increase, n (%)                | 8 (5.88%)    | 3 (2.14%)      | .13     |
| Volume decrease, n (%)                | 0 (0.00%)    | 1 (0.83%)      | >.99    |

PP=placenta previa.

\* *P* < .05 was considered statistically significant difference.

**Table 4**  
Comparison of ovarian function between the 2 groups.

| Hormone level | <35y (n = 195) |                 |         | ≥35y (n = 81) |                 |         |
|---------------|----------------|-----------------|---------|---------------|-----------------|---------|
|               | PP (n = 98)    | Non-PP (n = 97) | P-value | PP (n = 38)   | Non-PP (n = 43) | P-value |
| FSH (mIU/ml)  | 5.37 ± 1.16    | 5.29 ± 1.20     | .63     | 6.41 ± 1.63   | 6.35 ± 1.46     | .86     |
| LH (mIU/ml)   | 5.63 ± 1.25    | 5.41 ± 1.67     | .29     | 6.02 ± 2.01   | 6.24 ± 1.67     | .58     |
| E2 (pg/ml)    | 61.74 ± 30.15  | 63.89 ± 28.76   | .61     | 62.95 ± 29.67 | 65.23 ± 27.21   | .71     |
| AMH (ng/ml)   | 3.01 ± 0.56    | 3.29 ± 0.89     | .56     | 2.08 ± 0.41   | 2.45 ± 0.38     | .35     |

AMH = anti-mullerian hormone, FSH = follicle stimulating hormone, LH = luteinizing hormone, PP = placenta previa; \**P* < .05 was considered statistically significant difference.

subgroups in completed PP group was lower, endometrial thickness was thinner and the time to menstrual recovery was longer than that of non-PP group. Among the subgroups, patients in subgroup C who were applied uterine and/or iliac artery ligation during CD had the thinnest average endometrial thickness (0.42 ± 0.06 cm). Patients in subgroup E who applied balloon insertion during the CD needed the longest average time to recover menstruation (8.44 ± 1.78 months).

#### 4. Discussion

In our study, reduced endometrial thickness, lower uterine resistance index at 42nd days and delayed resumption menstruation were observed in CPP group compared with control group. The levels of FSH, luteinizing hormone, E2 and AMH during the first recovered menstruation were similar in the 2 groups. None of patient has intrauterine synechiae, amenorrhea and premature ovarian insufficiency after operation.

As the most dangerous obstetric complications, complete PP has been a research hotspot, especially its management and treatment during pregnancy. However, few researches reported the recovery of women after the pregnancy. Shamshirsaz et al suggested that a multidisciplinary team was very important in the successful resuscitation,<sup>[17]</sup> and proper operational treatment in cesarean section could shorten hemorrhage time and accelerate the recovery of menstruation.<sup>[18]</sup> Uterine artery embolization used during CD might have adverse effects on reproduction including intrauterine synechiae, amenorrhea, ovarian reserve or the decrease of endometrial volume for the long-term.<sup>[19–21]</sup>

Over the past twenty years, the rates of induced abortion and spontaneous abortion have increased dramatically because of family planning policies and sexual openness in China.<sup>[22]</sup> In our study, compared with the non-PP group, the CPP group had a significantly increased number of previous CDs and a thinner endometrium at 42 days after CD. Although our data are limited

for lack recording of the patients' endometrial thickness before pregnancy, and CPP group women have thinner endometrium. Endometrial thickness does not seem to influence the fertility outcome.<sup>[23–25]</sup>

The use of transvaginal 3D Doppler ultrasound enhanced our understanding of the cyclic changes in endometrial thickness and uterine hemodynamics during the menstrual cycle. An increase in uterine artery flow impedance had a negative effect on fertility and endometrial proliferation.<sup>[22,23]</sup> In our study, no significant differences were found in both pulsatility index and systolic and diastolic ratio indexes between the 2 groups. However, a statistically significant lower RI was observed in the CPP group. This may be associated with an increased vascularization and compliance of vessels around the placental implantation site at the cervix. In addition, patients in the CPP group had a thinner endometrium, which might not affect the pattern of menstrual cycle but might delay the time of menstruation resumption significantly. RI index of all subgroups in completed PP group was lower, endometrial thickness was thinner and the time to menstrual recovery was longer than that of non-PP group. We attributed this delay to many factors such as maternal age, history of dilation and curettage (D&C), previous uterine surgical history and previous CD.<sup>[26,27]</sup>

In the study, 1 limitation is that the data were retrospectively analyzed in which selection bias may be not totally avoided. Doctor choose different hemostasis methods according to the amount of bleeding, the bleeding speed and the specific bleeding location of the patient during the operation. There was an inevitable selection bias in the hemostasis methods adopted by the patients in the subgroup analysis. Another important limitation was that we didn't follow up the prospectively results of the next pregnancy and the future pregnancy outcomes of CPP women after CD. Moreover, we didn't have data of endometrial thickness and intrauterine environment of CPP-patient before this pregnancy. And a low participant number was included. We

**Table 5**  
Surgical subgroups of the PP group.

| Group  | n   | EBL (ml)          | P-value | RI          | P-value | Endometrial thickness (cm) | P-value | Menstrual resumption time (mo) | P-value |
|--------|-----|-------------------|---------|-------------|---------|----------------------------|---------|--------------------------------|---------|
| A      | 48  | 770.78 ± 108.21   | .52     | 0.84 ± 0.01 | <.001*  | 0.44 ± 0.14                | .01*    | 7.04 ± 1.57                    | <.001*  |
| B      | 16  | 1060.45 ± 87.26   | <.001*  | 0.85 ± 0.05 | <.001*  | 0.47 ± 0.05                | .07     | 6.43 ± 1.04                    | <.001*  |
| C      | 14  | 888.91 ± 143.12   | .02*    | 0.84 ± 0.01 | <.001*  | 0.42 ± 0.06                | <.001*  | 6.74 ± 1.25                    | <.001*  |
| D      | 22  | 1400.35 ± 932.90  | .01*    | 0.86 ± 0.02 | <.001*  | 0.44 ± 0.10                | .02*    | 7.16 ± 2.08                    | <.001*  |
| E      | 6   | 733.32 ± 35.23    | .02*    | 0.85 ± 0.03 | .01*    | 0.43 ± 0.09                | .12     | 8.44 ± 1.78                    | <.001*  |
| F      | 30  | 2338.90 ± 1029.50 | <.001*  | 0.84 ± 0.02 | <.001*  | 0.45 ± 0.13                | .06     | 7.33 ± 1.98                    | <.001*  |
| Non-PP | 120 | 784.67 ± 174.20   |         | 0.90 ± 0.03 |         | 0.50 ± 0.12                |         | 5.31 ± 2.16                    |         |

A: lower segment cesarean section only; B: uterine compression suture; C: uterine and/or iliac artery ligation; D: cervical procedures; E: balloon insertion; F: two or more hemostatic techniques applied. EBL = Estimated blood loss, PP = placenta previa, RI = resistance index.

\* *P* < .05 were considered statistically significant. \* compared with non-PP group.

believe that the study provided a major supplementary advance in the PP field and references for the young women in childbearing age, as well as clinical researchers tackling obstetric complications.

## 5. Conclusion

In summary, our study concluded that CPP women undertaking CD had a delayed menstruation resumption and a thinner endometrium post-delivery, which may be associated with their history of previous caesarean deliveries, abnormal placenta location and degree of placenta adhesion in this pregnancy. Multicenter perspective researches are need in the future.

## Acknowledgments

The authors thank Dr. Feng Ling, Dr. Zeng Wanjiang and Dr. Deng Dongrui and all staffs worked in the Department of Obstetrics & Gynecology, Tongji Hospital, Tongji Medical College of Huazhong University of Science & Technology, for their contributions to the management and treatment of patients. We also thank Kunyu He, PhD of Computational Analysis and Public Policy, College of University of Chicago, for his statistical expertise which was invaluable during the analysis of the data and Yonghong Wan, a professor from department of Pathology and Molecular Medicine, McMaster Immunology Research Centre, McMaster University, Hamilton, Ontario, Canada, for his improving the English style of the manuscript. Last but not least, we would like thank Rong Zhong, an epidemiologist in Department of Epidemiology and Biostatistics in Huazhong University of Science and Technology, who offer constructive suggestion in the methodology. All of them agreed to be named here.

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