

Continuity of Care for Mrs. "R" At The Al Islam HM Mawardi General Hospital

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Abstract. The Maternal Mortality Rate (MMR) in East Java Province was significantly reduced in 2020 but is still far from the SDGs target. Continuity of Care is a healthcare approach continuously starting from pregnancy, childbirth, postpartum, newborns, and family planning. The purpose of this case study is to describe the implementation of CoC at Al Islam HM Mawardi Hospital during pregnancy to postpartum. Method : midwifery descriptive method, Mrs. R was given care from the third trimester of pregnancy up to family planning method. Result : The implementation of CoC on Mrs. R was in accordance with the standards of physiological midwifery care and the treatment went well without any pathological conditions. Low back pain is a frequent condition in pregnancy, Mrs. R was given accupressur on hegu point to relieve the pain. Conclusion : The care provided to the research subjects has been adjusted to the standards of midwifery care and the condition of the mother and baby and it worked physiologically.

Highlights:

1. Continuity of Care (CoC): The implementation of CoC from pregnancy to family planning at Al Islam H.M. Mawardi Hospital followed standard physiological midwifery practices.
2. Effective Pain Management: Mrs. R experienced low back pain during pregnancy, which was relieved through acupressure on the hegu point.
3. Physiological Care Success: The care provided aligned with midwifery standards, ensuring the well-being of both the mother and baby without complications.

Keywords: Pregnancy, Childbirth, Postpartum, Newborn, Contraception

Introduction

Maternal Mortality Rate (MMR) and Infant Mortality Rate (IMR) are one of the benchmarks used to see the level of welfare of a country and the health conditions of the community. Based on data obtained from the Central Statistics Agency (BPS), in Indonesia the infant mortality rate (IMR) has reached 16.9 per 1,000 live births. This figure has decreased by 1.74% compared to the previous year, which was recorded at 17.2 out of every 1,000 live births.[1]. In addition, according to the latest data from the

East Java Provincial Health Office, the maternal mortality rate in 2020 for every 100,000 live births reached 98.39. The data shows an increase from the previous year, which reached 89.81 out of every 100,000 live births. This condition is still far from achieving the Sustainable Development Goals (SDGs) target in Goal 3.1 which aims to reduce the maternal mortality ratio, which is less than 70 out of every 100,000 live births and Goal 3.2 which targets a reduction in the Neonatal Mortality Rate to 12 per 1,000 live births by 2030[2].

The implementation of maternal and neonatal health services should have a comprehensive service capacity, in accordance with culture, and be able to provide a positive response to the needs of mothers during the reproductive period and their families. Comprehensive services need to be supported by appropriate policies, adequate service facility capacity, development of necessary tools, competent health workers, relevant research, and effective health promotion programs.[3].

AKI and AKB can be reduced by providing continuous midwifery care or Continuity of Care (COC) delivered to the mother/client. In the implementation of COC, a midwife plays a very important role, namely conducting continuous examinations, which include examinations during pregnancy, childbirth, newborns, and postpartum[4]. The importance of implementing Continuity of Care is to reduce the level of anxiety and also the mother's worries during the perinatal period.[5]. This relationship is also known as 'relational continuity' and is defined as "care during pregnancy, labour and birth, and the postnatal period by a midwife of her choice."[6].

Management of maternal health problems requires the implementation of a continuous midwifery care approach. This approach includes a series of integrative and comprehensive service activities, starting from pregnancy, childbirth, postpartum period, newborn care, to family planning programs. This approach aims to establish a link between women's health needs and the personal conditions of each individual, as well as building a therapeutic relationship between women and health workers, especially midwives, in dealing with the health problems they face.

Methods

This final report was prepared using a comprehensive case study approach (Continuity of Care) which is in line with the authority of midwifery in providing midwifery care to pregnant women, starting in the third trimester of pregnancy, covering the labor process, postpartum period, newborn care, to contraceptive planning. The case study research was conducted at RSU Al Islam HM Mawardi by implementing the Continuity of Care approach.

This case study on Continuity of Care uses Mrs. R as the subject observed from pregnancy to childbirth, postpartum period, and the planning phase of contraceptive use and newborn care. The compilation of this study uses a data collection method that includes subjective and objective data sources. Subjective data is obtained through anamnesis conducted on patients, families, and health workers, while objective data is collected from the results of physical examinations and supporting examinations according to the required data.

After the data is collected, the next stage is to conduct an analysis by managing midwifery care using the SOAP method, which will be implemented through the following steps:

1. The data will be separated, then grouped into subjective data and objective data.
2. Data will be analyzed to determine the diagnosis and problems.
3. Carry out management and evaluation based on identified cases
4. Analyze cases and midwifery care that has been implemented by referring to related theories.

Result and Discussion

A. Result

1. Midwifery Care for Pregnant Women

On July 1, 2024, Mrs. R GIIP0A1 underwent an antenatal care examination at the obstetrics and gynecology polyclinic of RSU Al Islam HM Mawardi. It is known that the first day of Mrs. R's last menstrual period (HPHT) was October 5, 2023, so the estimated date of birth (HPL) is predicted to fall on July 12, 2024.

Currently, the mother's pregnancy has entered the third trimester with a gestational age of 39 weeks. Antenatal care (ANC) visits carried out by Mrs. R are carried out routinely every month, namely three times in the first trimester, three times in the second trimester and four times in the third trimester.

Data were obtained directly during the care of Mrs. R and then compiled comprehensively. During the third trimester visit, the results of the examination showed that the weight before pregnancy was 50 kg, the current weight was recorded as 58 kg, height 149 cm, body mass index (BMI) 26.1. Vital signs were within normal limits, namely BP 118/71 mmHg, N 78 times/minute, RR 17 times/minute, temperature 36.2°C. On obstetric examination, the abdomen was found to be enlarged longitudinally, fetal movement was visible, Leopold I felt the fetal buttocks with a fundus uterine height (TFU) of 29 cm, Leopold II felt the fetal back on the left side of the mother's abdomen and a small part of the fetus on the right side of the mother's abdomen, Leopold III felt the fetal head that had entered the upper pelvic inlet, Leopold IV was parallel, and the fetal heart rate (FHR) was 151 times/minute using ultrasonography (USG). In the supporting examination, the results of complete blood and urine examination were obtained, namely WBC 9.8 HGB 11.8 HCT 34.7 PLT 340, urine trace protein, HbsAG screening, HIV and non-reactive syphilis. The upper and lower extremities did not appear swollen and there were no varicose veins.

The discomfort experienced by the mother related to her pregnancy was back pain. It is known that the mother always walks when going to work because the location is close to her residence, this continues to be done by the mother even though her pregnancy age is approaching delivery. In relation to this complaint, acupuncture therapy was given at the hegu point to reduce the pain felt and the mother felt that her complaints had decreased. The education given to the mother focused on the signs of the onset of labor and preparation for labor.

2. Midwifery Care for Mothers Giving Birth

Mrs. R came to the Emergency Room of Al Islam HM Mawardi Hospital on the morning of July 6, 2024 at 05.00 WIB, 39-40 weeks of pregnancy with complaints of stomach cramps since midnight and discharge of blood mucus.

Examination of the mother showed blood pressure of 122/78 mmHg, pulse 89 times/minute, respiration 16 times/minute, body temperature 36.6°C, fetal heart rate 135 times/minute, and contractions that occurred 3 times with a duration of 35 seconds in 10 minutes. Internal examination showed the results of cervical dilation of 6 cm, effacement of 50%, and intact amniotic membranes, presentation of the back of the head, small fontanel left front, descent of H-II, no small part palpable beside the lowest part of the fetus, and infiltration of 0. Furthermore, observation of the first stage of labor was carried out with recommendations for the mother to lie on her left side, consume food and drinks, give massage to the back area during contractions, and create a comfortable atmosphere.

At 06.00 WIB the mother expressed her desire to push, cramps as if she wanted to defecate. After evaluation, the cervix had opened completely 10 cm, effacement was 100%, and the amniotic membrane had ruptured, was clear in color and had a distinctive fishy odor. The position of the baby's head was observed to be in the left front fontanel position, without infiltration, and the head was on D-IV. The midwife then provided delivery assistance to the mother by following the 60-step APN procedure, so that the baby was born spontaneously at exactly 06.13 WIB. The baby's APGAR score was recorded as 8-9, the baby cried loudly, muscle tone was active, the baby's skin color was reddish, the baby's genitals were female with a weight of 2700 grams, and a body length of 49 cm. After cutting the umbilical cord, the baby was immediately handed over to the mother to initiate early breastfeeding (IMD). In the third stage, the placenta was born spontaneously and there was a second-degree rupture in the perineum. After the perineum was sutured, observation of the fourth stage was carried out for up to two hours postpartum and it was found that the mother's condition was good, uterine contractions were strong, the bladder was empty and bleeding was ± 10 cc. Furthermore, the mother was given antibiotic therapy, painkillers and vitamins.

3. Midwifery Care for Mothers Postpartum

Postpartum care for Mrs. R was carried out in three visits. The first visit was carried out six hours after delivery, precisely on July 6, 2024 at 12.30 WIB. The mother reported pain in the stitches, but was able to walk and start learning to breastfeed her baby. The mother's vital signs were normal, showing blood pressure of 120/83 mmHg, pulse 90 beats/minute, respiration 19 times/minute, temperature 36.6°C. The height of the uterine fundus was measured three fingers below the navel, uterine contractions were felt hard, and her bladder was empty. The mother had urinated smoothly twice, lochia rubra of ± 20 cc and breast milk had come out smoothly from both breasts. The mother was allowed to go home the next day after 24 hours postpartum.

The second postpartum visit was carried out on the seventh day, which was on July 13, 2024. The mother reported that she had no complaints. The baby seemed to be able to suckle well, the mother breastfed the baby every 2-3 hours during the day and only woke up 3-4 times at night to breastfeed. The results of the examination on the mother showed blood pressure of 125/78mmHg, N 81 times/minute, RR 20 times/minute, temperature 36.2 °C. The height of the uterine fundus was not palpable, lochia sanguinolenta, and breast milk flowed smoothly, and the mother started pumping to store breast milk. The mother's extremities showed no signs of swelling. The third postpartum visit was carried out on the 14th day, which was July 20, 2024. The mother again reported that she had no problems during her postpartum period, her breast milk continued to flow smoothly, and the mother routinely exposed her baby to the sun in the morning.

4. Midwifery Care for Newborns

When the baby was born, IMD was immediately performed for one hour, and the baby successfully found the nipple. The baby was then given an injection of Vitamin K in the left thigh as much as 0.5 mg intramuscularly and eye ointment was applied to both eyes. The first neonatal visit was carried out six hours after birth. The baby was born full-term spontaneously, vital signs were N 140 times/minute, RR 45 times/minute, S 36.2°C, the baby's weight was 2700 grams, his body length was 49 cm, head circumference 33 cm, chest circumference 31

cm. The baby cried loudly, muscle tone moved actively, the baby's skin was reddish, the baby's gender was female. No abnormalities or birth defects were found, the baby had defecated and urinated, the baby's sucking reflex was strong, Mrs. R's breast milk had come out smoothly from both breasts, the umbilical cord was still wet. Mrs. R's baby was given newborn care, which included keeping the baby warm, caring for the umbilical cord and ensuring that the baby could breastfeed properly. Before going home, the baby received the first immunization, namely Hepatitis B (HB0) on the upper right thigh with a dose of 0.5 ml intramuscularly and congenital hypothyroid screening was carried out which resulted in negative results. Education provided to the mother and family included baby care at home, immunization schedules and danger signs in newborns.

On the second visit conducted on July 13, 2024, the mother said that the baby could breastfeed well and the umbilical cord had fallen off without any signs of infection in the navel. The examination results showed the baby's weight was 2600 grams, body length 49 cm, and heart rate 139 times/minute, breathing 49 times/minute, body temperature 36.6 °C. In addition, the baby's skin showed no signs of yellowing. On the third visit conducted on July 27, 2024, the baby's weight was recorded at 2900 grams, body length remained 49 cm, and all vital signs were within normal limits. The baby also received BCG immunization in the upper left arm of 0.05 cc and the first polio immunization of 2 drops. Based on the results of the examination, it was concluded that the baby was in normal condition.

5. Midwifery Care for Contraceptive Acceptors

On July 20, 2024, the third postpartum visit was conducted while providing midwifery care related to family planning. Given that Mrs. R and her husband had never used contraception before, the midwife was present to provide education and counseling on various contraceptive methods. The goal was for Mrs. R to have sufficient understanding to discuss with her husband in choosing the appropriate contraception. Mrs. R and her husband had planned to use condoms as a contraceptive method. This was because both of them worked

in different cities, Mrs. R's husband came home once a month so they rarely met. They chose the condom method because it was more efficient and did not interfere with their activities. In the counseling session, the midwife explained in detail about the use and effectiveness of the condom contraception that had been chosen by the couple.

B. Discussion

1. Midwifery Care for Pregnant Women

One of the recommendations from WHO states that pregnant women with normal pregnancies should undergo ANC at least eight times. After making adjustments with related professions and programs, in Indonesia it has been agreed to stipulate that ANC is carried out at least six times. In this case, there are at least two contacts with doctors to conduct screening for risk factors or pregnancy complications in the first trimester, and one screening for risk factors for childbirth in the third trimester.[7]. Mrs. R has met the minimum standards, which are carried out nine times, which are carried out routinely every month.

Complaints of back pain in the third trimester of pregnancy are common and are often considered a normal part of pregnancy discomfort. This is due in part to the morphological and biomechanical changes that occur in pregnant women. Skeletal muscles can adapt their structure/function in response to increasing abdominal size, and variations in the maternal hormonal environment. These adaptations can alter trunk segment kinematics, posture, balance, dynamic stability, flexibility, and muscle fatigue resistance.[8]. Mothers are advised to reduce heavy activities, get enough rest and wear loose and comfortable clothing.

To overcome the discomfort caused by back pain experienced by pregnant women, we recommend a safe and easy therapy, namely acupressure at the hegu point. This point is located on the back of the hand, right between the base of the thumb and index finger. Through acupressure at the hegu point, endorphin hormone levels can increase. The endorphin hormone naturally functions as a pain reliever.[9].

2. Midwifery Care for Women in Labor

Childbirth is a natural process experienced by every mother, where the baby and placenta are removed from the uterus. In order for vaginal delivery to be successful, several factors are needed, such as thinning and dilation of the cervix, progressive and effective uterine contractions and the match between the diameter of the lowest part of the fetus and the size of the mother's pelvis.[10].

During the first period of labor, Mrs. R arrived in the active phase, mAccording to the author, the opening process in the mother is fast because the mother often walks regularly, and the size of the fetus is not too large so that the presentation of the fetus will drop faster. According to the results of a study by Shojaei entitled The effect of walking during late pregnancy on the outcomes of labor and delivery: A randomized clinical trial, walking during late pregnancy can be an effective, safe, and acceptable method to achieve cervical ripening and spontaneous labor.[11]. From full opening to the baby, the process took place quickly, in the second stage the mother only needed 13 minutes to give birth. The mother showed a very cooperative attitude and was able to push effectively.

The different things in the theory of cervical opening in primigravida and multigravida include physical factors, hormonal factors, maternal experience history, and support. With in-depth knowledge of these characteristics, the medical team can provide appropriate care, thus supporting a safe and comfortable birthing process for the mother. Although there are variations, the average duration of labor can be estimated through studies involving records from several thousand primiparas and multiparas. For example, the average duration of labor for primiparas is around 14 hours, where the first stage lasts around 13 hours and the second stage ranges from 5 minutes to 1 hour. Meanwhile, the average duration of labor for multiparas is around 7 hours 20 minutes in the first stage, 15 to 30 minutes in the second stage, and around 10 minutes in the third stage.[12].

3. Midwifery Care for Postpartum Mothers

The postpartum period is the period experienced by a woman after giving birth, lasting from the birth of the baby and placenta until six weeks after giving birth. There are several stages in this postpartum period. First, the immediate

postpartum stage which takes place within the first 24 hours after delivery. Second, the early postpartum stage which covers the time from 24 hours after delivery until the end of the first week. And third, the late postpartum stage which occurs in the second week to the sixth week after delivery.[13].

According to the Ministry of Health, health services for mothers for 42 days after giving birth consists of four visits. The first visit was carried out within a time span of six hours to two days after delivery. The second visit is carried out between three days to seven days after delivery. The third visit takes place between eight and 28 days after delivery. Finally, the fourth visit is scheduled between 29 days and 42 days after the delivery process.[14].

Postpartum care is very important for maternal and child health. The main goal of this service is to maintain the physical and mental well-being of the mother and baby. In addition, this service also focuses on early detection of postpartum problems, diseases, and complications. Providing information and education to mothers and families regarding maternal and infant care, nutrition, use of contraceptives, breastfeeding, and immunization is very important. The involvement of husbands and other family members in maintaining the health of mothers and newborns is also no less crucial. In addition, Family Planning (KB) services need to be provided immediately after giving birth[15]. Mrs. R has fulfilled the minimum number of postpartum visits, which is three times.

4. Midwifery Care for Newborns

Newborns, or known as neonates, refer to the early life period (0–28 days), which is a time when significant changes occur from life in the womb to life outside the womb. During this phase, almost all organ systems undergo a maturation process. Babies who are less than one month old are included in the age group that has the highest risk of health disorders. Various health problems can arise, and without proper treatment, these conditions can be fatal.[7].

Early initiation of breastfeeding (EIB) has been recognized for its health benefits for both mother and newborn. IB is defined as initiation of breastfeeding within the first hour after birth. The World Health Organization (WHO) recommends supporting mothers to initiate breastfeeding after birth.[16]. Current evidence suggests that IMD reduces neonatal mortality and early infant

mortality.[17]. Mrs. R's baby had undergone IMD for one hour according to the theory.

Neonatal visits should be carried out three times, namely at 6-48 hours, 3-7 days, and 8-28 days.[18]. Based on the existing theory, Mrs. R's baby has undergone three neonatal visits and no abnormal conditions were found.

5. Midwifery Care for Contraceptive Acceptors

The effectiveness of contraception is influenced by several factors, including the effectiveness of the drug or device used, the individual's fertility level, the frequency of sexual intercourse, and the acceptor's compliance and commitment. [19]. Condoms act as a barrier contraceptive that prevents contact between sperm and the genitals. Consistent or perfect (correct) condom use provides effective contraception. With correct condom use in the first year of use, the pregnancy rate is two out of every 100 women. This is a 98% success rate.[20]. The mother and husband stated their commitment to comply with condom use.

Conclusions

After implementing the Continuity of Care (CoC) model of midwifery care with a comprehensive approach and documentation using the SOAP system on Mrs. R, which includes the periods of pregnancy, childbirth, postpartum, and newborn care, and family planning from June 11, 2024 to July 27, 2024, it can be concluded that the midwifery care process was physiological.

References

- [1] Central Statistics Agency, Neonatal Mortality Rate (NAR) and Infant Mortality Rate per 1000 Births by Province. Jakarta, Indonesia: BPS, 2022.
- [2] Bappenas, "3 Healthy and Prosperous Lives," Sustainable Development Goals (SDGs) Indonesia, Oct. 22, 2024. [Online]. Available: <https://sdgs.bappenas.go.id/17-goals/goal-3/>
- [3] S. Prawirohardjo, Midwifery, 4th ed. Jakarta, Indonesia: PT Bina Pustaka Sarwono Prawirohardjo, 2016.

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- [4] Y. Yanti, M. Claramita, O. Emilia, and M. Hakimi, "Students' Understanding of 'Women-Centred Care Philosophy' in Midwifery Care Through Continuity of Care (CoC) Learning Model: A Quasi-Experimental Study," *BMC Nursing*, vol. 14, no. 1, p. 22, Dec. 2015, doi: 10.1186/s12912-015-0072-z.
- [5] S. Cibralic, M. Alderliesten, M. Caplice, A. Homer, M. Homer, and H. Sweet, "The Impact of Midwifery Continuity of Care on Maternal Mental Health: A Narrative Systematic Review," *Midwifery*, vol. 116, p. 103546, Jan. 2023, doi: 10.1016/j.midw.2022.103546.
- [6] C. Homer, P. Brodie, J. Sandall, and N. Leap, *Midwifery Continuity of Care*, 2nd ed. Sydney, Australia: Elsevier, 2019.
- [7] Ministry of Health of the Republic of Indonesia, *Guidelines for Antenatal, Childbirth, Postpartum, and Newborn Services in the Era of Adapting to New Habits*. Jakarta, Indonesia: Ministry of Health of the Republic of Indonesia, 2020.
- [8] C. Colla, LL Paiva, and RP Thomaz, "Therapeutic Exercise for Pregnancy Low Back and Pelvic Pain: A Systematic Review," *Fisioterapia em Movimento*, vol. 30, no. 2, pp. 399–411, Apr. 2017, doi: 10.1590/1980-5918.030.002.ar03.
- [9] F. Rahimi, S. Goli, N. Soltani, H. Rezaei, and Z. Amouzeschi, "Effects of Complementary Therapies on Labor Pain: A Literature Review," *Modern Care Journal*, vol. 15, no. 1, Jan. 2018, doi: 10.5812/modernc.69306.
- [10] J. M. Thornton, B. Browne, and M. Ramphul, "Mechanisms and Management of Normal Labor," *Obstetrics, Gynecology & Reproductive Medicine*, vol. 30, no. 3, pp. 84–90, March. 2020, doi: 10.1016/j.ogrm.2019.12.002.
- [11] B. Shojaei, M. Loripoor, M. Sheikhfathollahi, and F. Aminzadeh, "The Effect of Walking During Late Pregnancy on the Outcomes of Labor and Delivery: A Randomized Clinical Trial," *Journal of Education and Health Promotion*, vol. 10, no. 1, p. 277, 2021, doi: 10.4103/jehp.jehp_1437_20.
- [12] Halimatussakdiah, "The First and Second Stage Duration of Mother Multipara's Delivery with Newborn Apgar Score," *Journal of Midwifery and Traditional Health*, 2017.
- [13] N. Azizah and R. Rosyidah, *Textbook for Postpartum Midwifery Care and Breastfeeding Course*. Sidoarjo, Indonesia: Umsida Press, 2019, doi: 10.21070/2019/978-602-5914-78-2.
- [14] Ministry of Health of the Republic of Indonesia, *Guidelines for Antenatal, Childbirth, Postpartum, and Newborn Services*. Jakarta, Indonesia: Ministry of Health of the Republic of Indonesia, 2020.
- [15] R. Savita, H. Heryani, C. Jayanti, S. Suciana, T. Mursiti, and DN Fatmawati, *Postpartum Textbook for Diploma III Midwifery Volume II*. Jakarta, Indonesia: PT Mahakarya Citra Utama Group, 2022. [Online]. Available: www.mahakarya.academy

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- [16] World Health Organization, "Infant and Young Child Feeding," WHO Fact Sheets, Oct. 23, 2024. [Online]. Available: <https://www.who.int/news-room/fact-sheets/detail/infant-and-young-child-feeding>
- [17] Neovita Study Group, et al. "Timing of Initiation, Patterns of Breastfeeding, and Infant Survival: Prospective Analysis of Pooled Data from Three Randomized Trials," *The Lancet Global Health*, vol. 4, no. 4, pp. e266–e275, Apr. 2016, doi: 10.1016/S2214-109X(16)00040-1.
- [18] Ministry of Health of the Republic of Indonesia, *Indonesian Health Profile 2020*. Jakarta, Indonesia: Ministry of Health of the Republic of Indonesia, 2021.
- [19] S. Teal and A. Edelman, "Contraception Selection, Effectiveness, and Adverse Effects," *Journal of the American Medical Association (JAMA)*, vol. 326, no. 24, p. 2507, Dec. 2021, doi: 10.1001/jama.2021.21392.
- [20] H. Mahdy, A.D. Shaeffer, and D.M. McNabb, *Condoms*. Treasure Island, FL: StatPearls Publishing, 2024. [Online]. Available: <https://www.ncbi.nlm.nih.gov/books/NBK470385/>