

The Effect Red Betel Leaves (*Piper Crocatum*) On Pregnancy Gingivitis

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Abstract: Gingivitis is a periodontal disease that easily occurs in pregnant women, such as inflammation of the gums (3). The decrease in pH in the mouth, the influence of the hormones estrogen and progesterone during pregnancy causes gum inflammation (4), so safe therapy is needed such as boiled water from red betel leaves which can improve the oral hygiene status of gingivitis sufferers (11) and the inhibitory power of red betel leaf extract is very potently inhibits microorganisms that cause periodontal disease (12). The aim of this study was to determine whether there is an effect of boiled water from red betel leaves (*piper crocatum*) on pregnancy gingivitis. The method used in this research is quasi experimental with a pretest-posttest with control group design. The sample studied was 60 pregnant women, consisting of 30 pregnant women in the treatment group and 30 pregnant women in the control group. Data analysis used the Independent T-test. The results of the case group research in the pretest were 15 people (50%) of pregnant women with gingivitis and 13 people (43.6%) in the moderate category, 6 people (20%) in the post test results after intervention without gingivitis and 21 people (70%) in the mild category, while in the control group in the pretest, 19 people (63.3%) had mild category of pregnant women with gingivitis, 9 people (30%) in the moderate category, 17 people (56.7%) in the post test after intervention in the mild category, moderate category 11 people (36.7%), as well as the influence of boiled water from red betel leaves (*piper crocatum*) on pregnancy gingivitis (p value $0.000 < 0.05$). The conclusion is that boiled water from red betel leaves can reduce gingivitis so it can be used as a safe medicine to reduce gingivitis in pregnant women while maintaining oral and dental hygiene.

Keywords: Gingivitis; *Piper crocatum*; Pregnancy; Pregnant mother

Introduction

In Indonesia, dental and oral disease is a disease that attacks 90% of the population and ranks first in the top ten common diseases in society. Dental and oral disease consists of dental caries, gingivitis or gum inflammation which is the beginning of periodontal disease (Notohartojo I, 2020) including oral and dental problems that often occur in pregnant women, namely

gingivitis, where 5%-10% experience swollen gums (Alyfianita & Sarwo Edi, 2021).

Gingivitis is a periodontal disease that can easily occur in pregnant women if they cannot care for their teeth and mouth. Gingivitis is inflammation of the gums with signs of swelling, redness, bleeding and changes in the shape of the gums. Inflammation occurs in one or two teeth and can even occur in all teeth. Bleeding of the gums can occur due to mild stimulation such as

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gargling, or without any stimulation and bleeding can occur at any time (Sibuea A, 2022).

During pregnancy, acid levels in the mouth increase due to physiological nausea and vomiting that occurs in pregnant women. Feelings of nausea during pregnancy can cause changes in behavior in maintaining oral hygiene or brushing teeth because it will cause an increase in nausea and vomiting. Tooth decay can occur during pregnancy due to a decrease in pH in the mouth of pregnant women. The hormones estrogen and progesterone during pregnancy can also cause gum inflammation. An increase in the hormones estrogen and progesterone causes the release of histamine and proteolytic enzymes which cause an increased inflammatory response. If the gum inflammation gets worse, the gums become enlarged and swollen (inflammation), and the connective tissue in the gums slowly loosens so that the teeth become loose easily. Enlargement of the gums during pregnancy is called gingivitis gravidarum/pregnancy gingivitis. This problem usually occurs in the first trimester and reaches its peak in the second and third trimesters, and usually decreases in the ninth month of pregnancy. This gingivitis is a susceptible disease (Senjaya et al., 2020).

Efforts to improve dental and oral health are to support a better quality of life, we can use medicines for both prevention and healing. These medicines can be made from synthetic chemical drugs or those made from traditional medicinal plants or herbs (Rahayu & Salikun, 2020). The red betel plant is a traditional medicinal plant that belongs to the piperaceae family. As a mouthwash for oral and dental hygiene, red betel leaves contain flavonoids, alkaloids, polyphenolic compounds, tannins and essential oils (Putri et al., 2020). Red betel leaves have antimicrobial and antiseptic power that is 2 (two) times higher than green betel leaves, because red betel leaves contain alkaloids which green betel leaves do not. Not only that, red betel leaves (*piper crocatum*) also contain carvacrol which functions as a disinfectant and anti-fungal (Rachman et al., 2024) and has the advantage of being an immunomodulator by suppressing or increasing the immune system against infections (Nurmeida, 2021).

Based on research results that the severity of gingivitis in pregnant women in the moderate category is 60%, mild and severe categories are 20% each (Sibuea A, 2022), the results of research analysis show that boiled betel leaves are able to inhibit the growth of streptococcus or staphylococcus aureus bacteria thereby reducing dental plaque (Silaban H, 2021), and the effectiveness of red betel leaves is 90% effective in cleaning teeth and mouth after gargling with boiled betel leaves so that the benefits can be used in gingivitis (Sayekti et al., 2022), besides that, betel leaves are useful for strengthening teeth, curing canker sores, eliminating

bad breath and stopping gum bleeding. As a mouthwash, it does not irritate the mucous membranes of the oral cavity, overcomes plaque and bad breath, because betel leaves contain kavikol which is 5 times stronger as an antimicrobial than other ingredients (Makrifah L, Susilowati H, 2014).

So from the above background, there is a need for natural medicinal ingredients for pregnant women that are safe in preventing periodontal disease, namely gingivitis, and this research is used as a scientific update, where what differentiates this research from previous research is that in previous research, red betel leaves were used for oral hygiene, whereas in this research This is the effect of red betel leaves on pregnant women with gingivitis. The government in Indonesia created a movement program to accelerate nutritional improvement, namely the First 1000 Days of Life (HPK) Movement. Efforts to improve nutrition through the First 1,000 Days of Life (HPK) Movement, starting from pregnancy until the child is two years old, are intended to achieve optimal child growth. The 1,000 HPK Movement steps are implemented through two approaches, namely through specific nutrition interventions and sensitive nutrition interventions (Notohartojo, 2020). This study aims to determine the effect of gargling boiled red betel leaves (*piper crocatum*) on gingivitis in pregnant women.

Method

The method used in this research was quasi experimental with a pretest-posttest with control group design. the samples studied were 60 pregnant women. This consisted of 30 pregnant women in the treatment group who gargled with boiled water from betel leaves, and 30 pregnant women in the control group who gargled with mineral water. This research was conducted at several Independent Midwife Practices in the Serang City area. The types of data in this research are primary and secondary data. Primary data was carried out by carrying out an intra-oral clinical examination using the gingival index, which was assessed by the level of inflammation which was given a score of 0-3 with categories (Arina et al., 2017) of mild inflation (score: 0.1-1), moderate inflammation (score: 1.1-2) , and severe inflammation (score: 2.1-3) (Fatimah S, Widodo, 2017), apart from using an interview method using a questionnaire to determine the characteristics of pregnant women, namely education, trimester of pregnancy (trimester I, II, III), and dental and oral hygiene behavior. Secondary data in this study looked at medical records or KIA book records, namely anemia status. Making boiled water from betel leaves is done using the infusion method by boiling at a temperature of 120° C for 15 minutes, 6 grams of betel leaves in 120 ml

of water, after the boiled water has cooled it is then filtered and put into bottles (Notoatmodjo, 2018). The gargling activity was carried out after the pre-test, then gargling for 30 seconds once a day after brushing your teeth, gargling 15 ml for 30 seconds, and after that you did not eat or drink for 30 minutes, then the post-test was carried out on the 8th day. Data analysis used in this research uses univariate and bivariate analysis. Univariate analysis is used to describe the distribution and percentage of each variable. In this study, bivariate analysis was carried out using the independent t-test.

Research Flow Chart

The flow diagram of this research is shown in Figure 1.

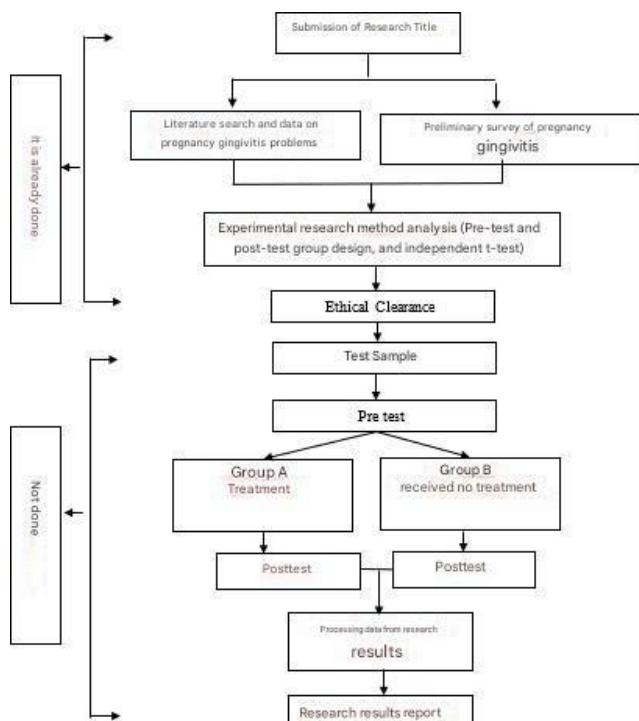


Figure 1. Research Flow Diagram

Result and Discussion

a) *Respondent characteristics*

Table 1. Frequency Distribution of Respondent Characteristics

| Variable | Group | | | Total | | |
|------------------|-------|------|---------|-------|----|------|
| | Case | % | Control | % | N | % |
| Education | | | | | | |
| High (SMA, PT) | 17 | 56.7 | 21 | 70 | 38 | 63.3 |
| Low (SMP, SD, | 13 | 43.3 | 9 | 30 | 22 | 36.7 |
| No School) | | | | | | |
| Trimester | | | | | | |
| Frist | 10 | 33.3 | 13 | 43.3 | 23 | 38.3 |
| Second | 8 | 26.7 | 9 | 30 | 17 | 28.3 |
| Third | 12 | 40 | 8 | 26.7 | 20 | 33.4 |

| Variable | Group | | Total | | | |
|----------------------------------|-------|------|---------|------|----|------|
| | Case | % | Control | % | N | % |
| Dental & Oral Hygiene | | | | | | |
| Good | 13 | 43.3 | 11 | 36.7 | 24 | 40 |
| Not Good | 17 | 56.7 | 19 | 63.3 | 36 | 60 |
| Anemia Status | | | | | | |
| No | 18 | 60 | 20 | 66.7 | 38 | 63,3 |
| Ya | 12 | 40 | 10 | 33.3 | 22 | 36.7 |
| Total | 30 | 100 | 30 | 100 | 60 | 100 |

Based on table 1 above, it shows that of the 60 pregnant women respondents, in the Case group there were 17 people (56.7%) with a higher education level equivalent to SMA and PT, pregnant women in the 3rd trimester, namely 12 people (40%) and 10 people (33.3%) trimester 1, dental and oral hygiene was in the poor category as many as 17 people (56.7%) and anemia status as many as 12 people (40%) had anemia. In the control group there were 21 people (70%) with a high level of education equivalent to high school and PT, some of the respondents were in the 1st trimester, namely 13 people (43.3%), in the 2nd trimester there were 9 people (30%), in the 3rd trimester there were 8 people. (26.7%), dental and oral hygiene was in the poor category as many as 19 people (63.3%) and anemia status as many as 10 people (33.3%) had anemia.

b) Frequency distribution of pregnancy gingivitis in the Case group

Table 2. Frequency Distribution of Pregnancy Gingivitis in Case Groups

| Pregnancy gingivitis | n | % | Pre-Test N | Post-Test % |
|-------------------------|----|------|---------------|----------------|
| Normal | - | - | 6 | 20 |
| Light | 15 | 50 | 21 | 70 |
| Currently | 13 | 43.3 | 3 | 10 |
| Heavy | 2 | 6.7 | - | - |
| Amount | 30 | 100 | 30 | 100 |

Based on table 2 above, it shows that of the 30 pregnant women respondents in the Case group, there were pregnant women in the pretest before being given boiled water from red betel leaves (*piper crocatum*), there were 15 pregnant women in the light category (50%), 13 people in the currently category (43.6%) and the heavy category 2 people (6.7%), and the post test results after the intervention was carried out by giving boiled water from red betel leaves (*piper crocatum*) there were 6 pregnant women without gingivitis (20%), category 21 people (70%) in the light category and 3 people (10%) in the currently category.

c) *Frequency distribution of pregnancy gingivitis in the Control group*

Table 3. Frequency Distribution of Pregnancy Gingivitis in the Control Group

| Pregnancy gingivitis | n | Pre-Test % | Post-Test N | Post-Test % |
|----------------------|----|------------|-------------|-------------|
| Light | 19 | 63.3 | 17 | 56.6 |
| Currently | 9 | 30 | 11 | 36.7 |
| Heavy | 2 | 6.7 | 2 | 6.7 |
| Amount | 30 | 100 | 30 | 100 |

Based on table 3 above, it shows that of the 30 pregnant women respondents in the Control group, the pre-test results showed that 19 people were in the light category (63.3%), 9 people in the moderate category (30%) and 2 people in the heavy category (6.7%), and the post-test results showed that there were 17 pregnant women with gingivitis in the mild category (56.6%), 11 people in the moderate category (36.7%) and 2 people in the severe category (6.7%).

d) *The effect red betel leaves (*piper crocatum*) on pregnancy gingivitis*

Table 4. The effect red betel leaves (*piper crocatum*) on pregnancy gingivitis

| Variabel | Negative Ranks | Positive Ranks | Mean Rank | p-value |
|-----------|----------------|----------------|-----------|---------|
| Case | | | | |
| Pre-Test- | 19 | 0 | 10 | |
| Post-Test | | | | 0.000 |
| Control | | | | |
| Pre-Test- | 1 | 3 | 2,5 | |
| Post-Test | | | | |

Based on table 4, it shows that in the Case group the results were negative rank or the difference between the pre-test and post-test which showed a decrease in gingivitis between the pre-test and post-test as many as 19 people, the results of the positive rank or difference for the pre-test and post -test showed no increase in gingivitis, the mean rank or average increase was 10. In the Control group it showed negative rank results or a decrease in gingivitis between pre-test and post-test by 1 person, positive rank or difference for pre-test and post -test showed that there were 3 people with increased gingivitis, and the mean rank or average increase was 2.5. The p-value (sig. 2-tailed) is 0.000 (p-value < 0.05) so that H0 in this study is rejected and H1 is accepted, meaning that there is an effect of red betel leaf (*piper crocatum*) boiled water on gingivitis pregnancy.

Description of respondent characteristics

Based on the results of this research, there were 60 pregnant women respondents who were divided into 2

groups, namely the case and control groups. The educational level of respondents in the case group was 17 people (56.7%) and in the control group there were 21 people (70%) with a high level of education equivalent to high school and university, where education in health is an effort to persuade with the aim of helping society get learning to take action to either maintain or improve their health. (16) In line with the results of previous research where pregnant women with a high level of education experienced gingivitis as many as 28 (39.4%) respondents. The level of education has an influence on the knowledge, behavior or attitudes of pregnant women in maintaining oral health. Pregnant women who have studied at high school level or equivalent and PT will usually have better knowledge and attitudes regarding their health behavior. Differences in educational levels will influence the determination of attitudes and behavior in determining health services (16), but good behavior in health requires self-awareness to have a healthy lifestyle, whether for pregnant women with high or low education, a healthy standard of living occurs because of healthy living habits.

In this study, there were 12 people in the case group of pregnant women in the 3rd trimester (40%) and 10 people (33.3%) in the 1st trimester, and in the control group of pregnant women in the 1st trimester, namely 13 people (43.3%), in the 2nd trimester. as many as 9 people (30%), in the third trimester there were 8 people (26.7%). Based on the results of previous research, 21 (29.6%) pregnant women experienced gingivitis in the first trimester. Pregnant women in the 2nd and 3rd trimesters of pregnancy with gingivitis were 39 (34.6%) and those who did not experience gingivitis were 2 (6.4%) respondents. The hormones estrogen and progesterone will increase as pregnancy occurs, thus affecting gingivitis in pregnant women due to the presence of plaque bacteria. Those who maintain good oral and dental hygiene will reduce the risk of gingivitis in pregnant women (Nataris & Santik, 2017).

The results of other research showed that those most affected were 33 people (66%) in the 3rd trimester, and 8 people (16%) in the 1st trimester, 9 people (18%) in the 2nd trimester. In the first trimester of pregnancy, the health of the gingival tissue tends to remain good, while in the second trimester, the health of the gingiva tends to get worse and in the third trimester, the health of the gingival tissue tends to increase towards good status, although the condition is not as good as in the first trimester (Salifiyadi et al., 2022). Gingiva shiny and stiff on the surface occurred in respondents who experienced gingivitis. In the first, second and third trimesters, spontaneous bleeding will begin to occur due to gingiva (Gürsoy et al., 2013) so pregnancy factors can influence the increase in gingivitis.

During pregnancy, physiological and psychological changes occur, where the hormones estrogen and progesterone increase, causing changes in the 1st, 2nd and 3rd trimesters, starting from changes in body shape and increased anxiety levels, which causes excessive worry, including problems maintaining oral and dental hygiene. So this causes health problems in the oral cavity. The main factor in the occurrence of gingivitis is not only caused by pregnancy but also by maintaining proper and good oral and dental hygiene (Arina et al., 2017).

In the case group of pregnant women with poor dental and oral hygiene category, there were 17 people (56.7%) and in the control group of pregnant women with poor category, there were 19 people, 63.3%), maintaining dental and oral hygiene during pregnancy can reduce risk of gingivitis. Increased secretion of pregnancy hormones causes many complaints such as nausea, vomiting, problems absorbing stomach acid, including increased problems with the oral cavity and teeth of pregnant women. Cleaning your teeth regularly and correctly every morning and evening after eating, then rinsing your mouth after vomiting to remove oral acid is one way to maintain healthy teeth and mouth (Salfiyadi et al., 2022).

Oral and dental hygiene behaviors during pregnancy such as oral hygiene and brushing teeth, consuming sweet foods have a significant impact on the oral and dental health of pregnant women. Not all pregnant women brush their teeth twice a day, because brushing their teeth is the wrong way. Health behavior and use of health services are related to the level of community education. The determining factor for the occurrence of gingivitis in pregnant women is the presence of certain bacteria on the teeth, which influences the oral hygiene behavior of pregnant women. Inconsistent oral and dental hygiene habits are caused by the behavior of pregnant women, which may be caused by the attitudes and behavior of pregnant women who pay less attention to maintaining dental health and verbally who do not understand the importance of maintaining dental and oral health during pregnancy (Alyfianita & Sarwo Edi, 2021).

In the Case group, 12 pregnant women (40%) were anemic and in the control group 10 pregnant women (33.3%) were anemic. Based on previous research, pregnant women with anemia have a 1.3 times greater risk of developing gingivitis than pregnant women without anemia, with the distribution of respondents from pregnant women with anemia being higher than the distribution of respondents from pregnant women without anemia. Some respondents have weak immune systems, this is proven by the many complaints from pregnant women during the survey which can lead to other diseases, including dental and oral health.

Gingivitis in pregnant women causes bleeding in the gums so that pregnant women suffer from anemia (Nataris & Santik, 2017).

Pregnancy gingivitis in the Case group

In the Case group, there were pregnant women in the pretest before being given boiled water from red betel leaves (*piper crocatum*), there were 15 pregnant women in the light category (50%), 13 people in the moderate category (43.6%) and 2 people in the heavy category. (6.7%), and post test results after intervention with the provision of boiled water from red betel leaves (*piper crocatum*) showed that there were 6 pregnant women without gingivitis (20%), 21 people (70%) in the mild category and 21 people in the moderate category. as many as 3 people (10%). The difference in reducing gingivitis before and after gargling boiled water with red betel leaves is because betel leaves contain five times stronger antibacterial power, contain phenol and cavitol with bactericidal power, and the essential oils in betel leaves can prevent periodontal disease, so this can reduce plaque formation, this is what causes the difference in index scores in the treatment group who gargled with boiled betel leaf water (Fatimah S, Widodo, 2017).

In line with previous research, there is a difference in the final results before and after gargling boiled betel leaf water on the gingival index, this is because plaque caused by lack of cleanliness on the respondents' teeth can be removed after gargling boiled betel leaf water, plaque is the cause of the onset. If gingivitis occurs, plaque is prevented through mechanical and chemical methods such as brushing teeth and gargling with safe natural ingredients, namely betel leaf decoction. (Nurmeida, 2021).

Pregnancy gingivitis in the Control group

The results of this study showed that of the 30 pregnant women respondents in the Control group, the pre-test results showed that there were 19 respondents in the light category (63.3%), 9 people in the moderate category (30%) and 2 people in the heavy category (6.7%), and the post-test results showed that there were 17 pregnant women with gingivitis in the mild category (56.7%), 11 people in the moderate category (36.7%) and 2 people in the severe category (6.7%). %).

In line with the results of other studies, the mean initial plaque index scores for the treatment group and control group were almost the same as the initial plaque index scores of 3.55 and 3.61. The mean final plaque index score of the treatment group and control group was much different from the score (Nurmeida, 2021).

The reduction in gingivitis in the control group showed that there was no difference in gingival index scores because the bottled mineral water used as a

substitute for mouthwash only contained Ca^{2+} and Mg^{2+} , bottled water with high mineralization often contains up to half of the daily Na^+ intake (Azoulay et al., 2001) Meanwhile, reducing gingivitis requires antibacterial power, such as the content in red betel leaves (*pipper crocatum*).

*The effect of red betel leaves (*piper crocatum*) on pregnancy gingivitis*

The results of this study showed that in the Case group the results were negative rank or the difference between the pre-test and post-test which showed a decrease in gingivitis between the pre-test and post-test by 19 people, the results of the positive rank or difference for the pre-test and post -test showed no increase in gingivitis, the mean rank or average increase was 10, but this was different in the control group which showed negative rank results or a decrease in gingivitis between pre-test and post-test of only 1 person, apart from that the positive rank or The difference between the pre-test and post-test showed an increase in gingivitis of 3 people. The p-value (sig. 2-tailed) is 0.000 (p-value < 0.05) so that there is an influence of boiled water from red betel leaves (*pipper crocatum*) on pregnancy gingivitis.

Red betel leaves have antibacterial properties because they contain active compounds, namely flavonoids, phenols, alkaloids, saponins and tannins. By reducing cell surface tension and protein denaturation as an antibacterial power possessed by phenol and its derivatives. The function of flavonoids has lipophilic properties as anti-inflammatory which can damage bacterial cells. As an antimicrobial, the role of alkaloids and ethanol extract of betel leaves is also able to inhibit bacterial growth (Pasil & Okasari, 2020).

In line with the results of other research, red betel leaf extract (*Piper crocatum*) has antibacterial power against *P gingivalis*. For moderate category gingivitis sufferers, gargling red betel leaf boiled water with a concentration of 10% can reduce the number of gingivitis bacteria. Apart from that, red betel leaf decoction has the same effect as 0.2% chlorhexidine gluconate in reducing the number of dental plaque bacteria in moderate category gingivitis sufferers. (Arnanda, 2015).

The buildup of plaque bacteria on the tooth surface is the main cause of periodontal disease. Gingivitis is a cause of periodontal disease, so early treatment is needed so that it cannot develop into periodontitis which causes tissue damage. *Porphyromonas gingivalis* is the main bacteria that causes periodontitis, of which 82% occurs at all ages and genders. Periodontitis cases can occur due to susceptibility such as in pregnant women. Red betel leaves contain antibacterial properties, in which there is essential oil as an alternative ingredient to prevent periodontal disease, the

compound kavicol which is a derivative of phenol which has 5 times greater bacterial killing power than the phenol in essential oils (Auliya, V., sendy, A., Oujiastuti, P., Ermawati, 2014).

Using mouthwash is an effort to reduce and prevent plaque and improve oral and dental health. Betel leaves in mouthwash are used to prevent plaque, mouthwash with antiseptic content can be used to prevent dental and oral disease to remove germs that cause plaque, gingivitis, swelling and bad breath. Boiled water from betel leaves can be used to reduce the dental plaque index and betel water made by boiling can reduce the risk of bacterial growth (Nurmeida, 2021).

Apart from the content of red betel leaves, a supporting factor that can influence gingivitis and improve dental and oral health is implementing a pattern of maintaining good and correct dental and oral hygiene. This is supported by previous research which shows that there is a relationship between dental and oral hygiene and gingivitis caused by Maintaining dental and oral health for pregnant women is not optimal, and lack of regular tooth brushing due to nausea and vomiting makes them reluctant to brush their teeth, this can cause plaque to form and even inflammation of the gums. Bacteria that cause gingivitis can occur in everyone, including those in pregnancy in all trimesters, therefore gingivitis in pregnancy can not only be caused by pregnancy hormones but also hygiene habits. The hormones estrogen and progesterone in pregnancy can cause an increase in the severity of gingivitis. (Salfiyadi1 et al., 2022).

Conclusion

Pregnant women's knowledge of the 1000 HPK nutrition movement, of the 60 respondents from pregnant women in the pretest before being given counseling, 34 people had knowledge in the poor category (56.7%), in the sufficient category there were 23 people (38.3%), after being given counseling there was a category 32 people (53.3%) were good and 25 people (41.7%) were in the fair category. The pretest before being given counseling had an attitude of 35 people (58.3%) in the poor category and 21 people (35%) in the sufficient category, after being given the counseling the results showed that the attitude of the respondents was in the good category as many as 32 people (53.3%) and in the sufficient category as many as 25 people (41.7%). The level of knowledge before counseling and after counseling (p-value: 0.000), meaning that nutritional counseling in the first 1000 days of life is effective on pregnant women's knowledge and attitudes before counseling and after counseling (p-value: 0.000), meaning that nutritional counseling in the first 1000 days of life is effective on attitude of pregnant women.

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Author Contributions

Each author has duties and responsibilities at each stage of the research, Sandy Nurlaela Rachman as the head researcher plays a role in conducting literature reviews, and compiling research, collecting first stage data (pretest), carrying out second stage data collection (posttest) and conducting experiments as well as compiling reports and publications, Fathiyati played a role in collecting the first stage of data (pretest), carrying out the second stage of data collection (posttest) and conducting experiments and compiling reports and publications, Ade Anwar played a role in submitting ethical clearance, processing and analyzing data, compiling reports and publications.

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Conflicts of Interest

The authors declare no conflict of interest

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