

# Clinical Outcome of Self-administered Vaginal Isonicotinic Acid Hydrazide (INH) Before T380A Copper Intrauterine Device Insertion in Adolescent and Young Women: A Double-Blind Randomized Controlled Study

Nahla W. Shady<sup>1</sup> , Hassan A. Farouk<sup>2</sup>, Hany F. Sallam<sup>1</sup>

1. Department of Obstetrics and Gynecology, Aswan Faculty of Medicine, Aswan University, Aswan Governorate, Egypt
2. Mansoura Insurance Hospital, Mansoura, Egypt



## Article Info

 [10.30699/jogcr.7.5.391](https://doi.org/10.30699/jogcr.7.5.391)

**Received:** 2021/10/31;

**Accepted:** 2021/12/28;

**Published Online:** 07 July 2022;

Use your device to scan and read the article online



## Corresponding Information:

Nahla W. Shady,

Department of Obstetrics and Gynecology,  
Aswan Faculty of Medicine, Aswan  
University, Aswan Governorate, Egypt

Email: [nahlagyn@yahoo.com](mailto:nahlagyn@yahoo.com)

## ABSTRACT

**Background & Objective:** To see if 900 mg of vaginal isonicotinic acid hydrazide (INH) given 12 hours before insertion of a T380A copper intrauterine device (IUD) was more effective than placebo in increasing insertion ease and reducing insertion discomfort in nulliparous ladies.

**Materials & Methods:** A double-blind, randomized controlled study recruited nulliparous women who wanted to use the Copper IUD for contraception. Women who were WHO-eligible for IUD implantation were recruited and randomly assigned (1:1) to vaginal INH 900 mg or placebo (n=100 in each group), 12 hours before the IUD was placed. The primary endpoint was the ease of insertion for the providers. The number of unsuccessful IUD insertions was also recorded.

**Results:** The groups had similar baseline characteristics. The ease of insertion score in the INH group was lower than in the placebo group (3 (2-5).5 vs. 6 (3-8);  $P=0.01$ ), indicating that physicians in the INH group had an easier time inserting the device. The INH group had a reduced mean pain score during the procedure ( $3.97 \pm 0.991$  vs.  $6.42 \pm 0.66$ ;  $P=0.001$ ). In the INH group, two incidences of failed IUD insertion occurred (2%) compared to four cases in the control group (4 percent). 0.594 is the p-value.

**Conclusion:** Self-administered INH 900 mg vaginally 12 hours before a copper T380A IUD insertion successfully reduced discomfort during insertion and improved women's satisfaction and ease of insertion as measured by physicians in nulliparous teenagers and young ladies.

**Keywords:** Intrauterine device, Isonicotinic Acid Hydrazide, Nullipara, Pain



Copyright © 2022. This is an original open-access article distributed under the terms of the Creative Commons Attribution-noncommercial 4.0 International License which permits copy and redistribution of the material just in noncommercial usages with proper citation.

## Introduction

Long-acting reversible contraceptives, such as intrauterine devices, can dramatically reduce the risk of unwanted births (1). Unintended pregnancy is most common among adolescents and young women (2). A copper intrauterine device IUD is recommended as a first-line contraceptive treatment for sexually active teenagers (3). One of the most significant hurdles to IUD use in adolescents and young women is the fear of painful insertion (4).

Furthermore, clinicians' misunderstandings about the suitability of IUD usage in teenagers and young nulliparous women hinder this very effective method of contraception from being recommended. (5) IUDs, on the other hand, can be implanted in both parous nulliparous and nulliparous women (6). Intrauterine contraception with copper is an appealing choice for teenagers who want long-term, continuous contraception with fast fertility recovery (7).

Many authorities suggest IUDs as first-line choices for teenagers (8, 9).

According to one research, nulliparous women's uterine cavities are narrow, and conventional-framed IUDs do not fit well (10), which might lead to increased discomfort during insertion, restricting IUD use in nulliparas (10, 11).

Finding an effective pain reliever might boost IUD use and reduce the incidence of unplanned births among teenagers and young women, which can have negative social, economic, and physical health consequences (12).

In obstetrics, INH is utilized for cervical ripening and labor induction. According to research, INH is as good as or better than misoprostol for cervical softening during labor induction (13). Before diagnostic and operative hysteroscopic procedures, INH was also utilized for cervical ripening and priming in

nulliparous women. It was effective and safe in terms of hysteroscope entrance ease, procedure discomfort, and side effects (14, 15).

The role of INH administration prior to IUD implantation has never been investigated, especially in adolescents and young women under the age of 22, for whom analgesia is considered vital. In this trial, we evaluated the effectiveness and safety of self-administered INH 900 mg vaginally to placebo in decreasing discomfort during a copper T380A IUD implantation in adolescents and young nulliparous women.

## Methods

We performed a randomized controlled study at the Family planning clinic of the Obstetrics and Gynecology department at a tertiary university hospital from March 2020 to September 2020. The scientific departmental committee granted us ethical permission in advance. All ladies who decided to participate completed a written informed consent form after getting a detailed overview of the procedure, potential side effects, and complications.

Patients who desired copper T 380A intrauterine contraception were eligible for the trial if they were 18-22 years old, had a negative pregnancy test, didn't take any analgesics in the 48 hours preceding up to the IUD insertion, and had no previous pregnancies longer than 13 6/7 weeks.

Women who had a recent diagnosis of pelvic inflammatory illness, active vaginitis, or cervicitis, were presently pregnant or were pregnant within six weeks of study admission, or had a history of cervical surgery were excluded. The study excluded women with undiagnosed abnormal uterine bleeding, World Health Organization Medical Eligibility Criteria category 3 or 4 precautions to a copper IUD, a prior attempted or successful IUD insertion, fibroids, or other uterine abnormalities distorting the uterine cavity, and a known allergy or contraindication to INH.

We followed standard clinic procedures for pre-procedural counseling and evaluation: we took a full medical history and performed abdominal and vaginal exams. Participants filled out a demographics form on the day of their copper IUD insertion, and the research nurse gave everyone a urine pregnancy test.

We used a 1:1 allocation ratio and a computer-generated random numbers table to divide women into two groups. The computerized randomization list was created by a statistician who was not directly engaged in the investigation and kept the key for group allocation hidden from investigators until the trial was completed. 12 hours before the surgery, the first group received 900 mg vaginal INH. The second group got a placebo designed by the department of pharmaceutical chemistry at Aswan University's Faculty of Pharmacy to be identical to INH pills in form, size, and color.

Tablets of INH and placebo were placed in opaque, sealed envelopes with consecutive serial numbers.

They were utilized in the sequence in which the women were present. The allocation was kept a secret from the participants, study personnel, and suppliers.

The clinic nurse then booked all the participants for a second IUD installation appointment, advising them to keep the study medicines refrigerated and implant them as deeply as feasible in the posterior vaginal fornix 12 hours before their T380A IUD placement appointment. We sent automated reminders to participants' phones at the time of study medication delivery. Furthermore, one of the study's investigators called all participants to remind them about the study and verify that they took their medications on schedule.

The doctors implanted intrauterine contraceptive devices from the third to the fifth day of the menstrual cycle. The IUD utilized was Copper T380A (Pregna Copper T 380A, Pragma, Egypt), and all of the providers employed the manufacturer's recommended procedure for IUD insertion (16). After placing a speculum, cleaning the cervix with antiseptic, applying a single-toothed tenaculum, and sounding the uterus to measure its length, the inserting physicians inserted the IUD without ultrasound guidance. We tested whether Hegar dilators with a diameter of four millimeters or less could pass through the internal cervical os without resistance before copper IUD placement to assess the degree of cervical dilatation. Patients were not in any pain or discomfort since the physicians placed Hegar dilators softly and without force.

The main outcome measure was the difference in IUD insertion ease scores between study groups (as reported by physicians responsible for IUD insertion). On a 10-cm VAS scale, this score ranges from 0 to 10, with 0 indicating very simple insertion and 10 indicating exceedingly difficult insertion.

Secondary outcomes were the proportion of women with cervical dilatation less than four millimeters and the level of patient-perceived pain at the moment of IUD insertion, as determined by a visual analog scale. The VAS scale is evaluated from 0 to 10, with 0 signifying no discomfort and 10 indicating the most excruciating pain.

On a VAS sheet, the participant was asked to select the point that corresponded to the level of pain she had experienced. At the completion of the procedure, the providers reported the ease of insertion using the ease of insertion score (ES).

We asked for fever (oral temperature 38°C), nausea, vomiting, shivering, diarrhea, and cramps, all of which were documented shortly before IUD implantation, to confirm that they were caused by the medicine rather than the insertion procedure. As mentioned by the patients, we also recorded postprocedural bleeding five minutes after the

procedure, vasovagal reaction, uterine perforation, failed insertions, and insertion time.

The lowest clinically meaningful difference in ease of insertion scores was determined at 0.76 (i.e., the ease of insertion score for the INH group should be lower than the placebo group by 0.76).

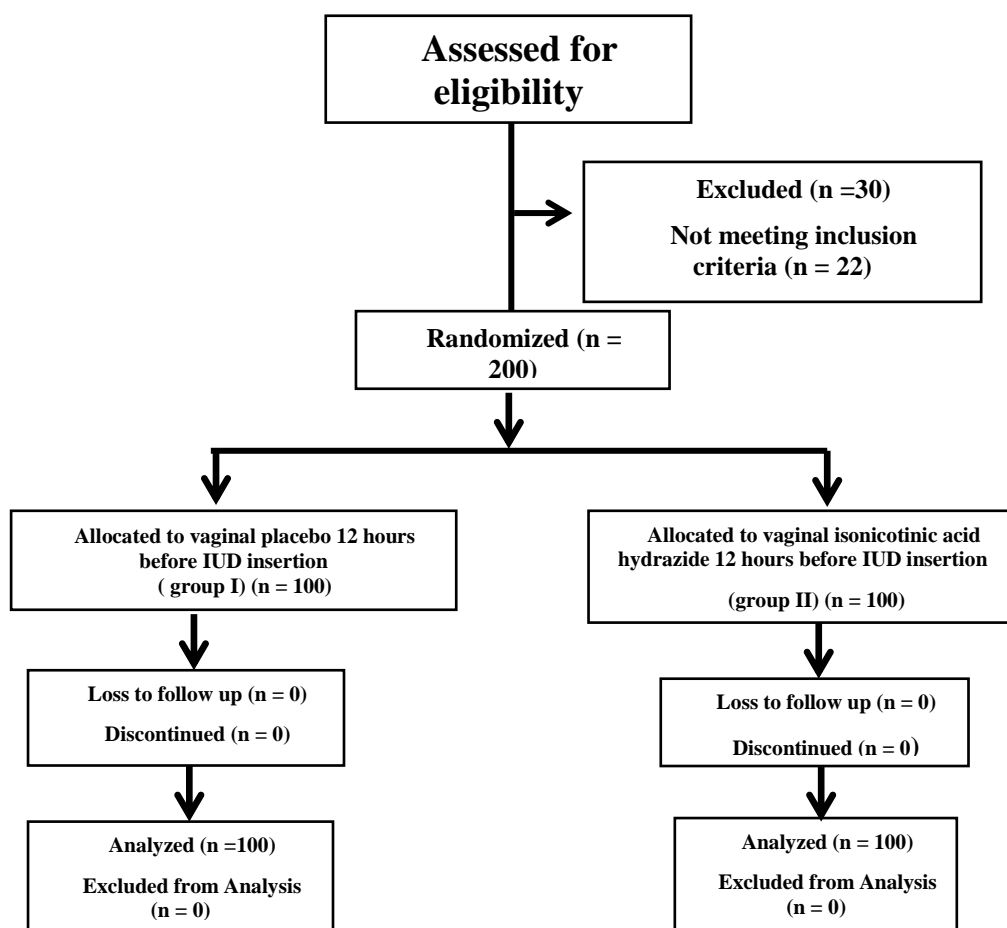
Each study group needed at least 90 people to detect this difference with 90% power and a 0.05 alpha level. To accommodate for attrition or disqualification of participants, we raised the expected sample size by 10%. A total of 200 persons were included in the study (100 patients in each group) (16).

The Statistical Package for Social Sciences (SPSS) version 16 was used to enter data and perform statistical analysis. Numbers and percentages were used to describe qualitative data. The Fisher's exact test and the Chi square test were employed to compare groups, if needed.

After checking for normality using the Kolmogorov-Smirnov test, quantitative data were presented as means (SD) or medians. The independent samples t-test was used to compare groups with normally distributed data, whereas the Mann-Whitney U test was used to compare groups with non-normally distributed variables. We estimated odds ratios and their 95% confidence intervals. Statistical significance was defined as  $P\text{-value} < 0.05$ .

## Results

We addressed 230 people who requested T380A copper IUD installation as part of our study; 30 patients were ruled out, 22 patients failed to meet the inclusion requirements, and 8 patients were rejected. As a result, the remaining 200 patients were split into two groups of 100 each. (Figure 1)



**Figure 1.** Consort flowchart showing enrollment of participants

In terms of age, weight, height, BMI, gravidity, location, education, prior IUD insertion history, time since last birth, and uterine position, there were no

significant variations between the two groups. (Table 1)

**Table 1.** Baseline Characteristics of adolescent women in the study groups

Parameters	Group I (n = 100)	Group II (n = 100)	95% confidence interval		Significance
			Lower	upper	
Age (year)	20.74 ± 2.21	20.68 ± 2.13	- 0.72194	0.75831	0.953
Weight (kg)	66.84 ± 5.34	66.09 ± 5.92	-2.22753	1.26389	0.761
Height (cm)	162.22 ± 4.34	161.98 ± 4.78	-1.06364	1.13637	0.543
Residence (%):					
Urban	52 (52)	54 (54)	1.474	0.501	0.542
Rural	48 (48)	46 (46)			
Education (%):					
Primary	42 (42)	40 (40)			0.866
Secondary	38 (38)	39 (39)			
University	20(20)	21 (21)			
Position of uterus (%):					
AVF	77 (77)	80 (80)			0.866
RVF	14 (14)	12 (12)			
Mid position	9 (9)	8 (8)			

# Variables are presented as mean and standard deviation, and number (percentage).

Furthermore, group II had a considerably higher ease of insertion score than group I while inserting the T380A copper IUD, as evidenced by the ease of insertion score. ( $P=0.0001$ ).

In addition, there was no statistically significant difference in the meantime of IUD implantation between the two groups ( $P=0.0.891$ ) (Table2).

During each phase of T380A copper IUD, we used the visual analog scale (VAS) to quantify pain in both groups. During 1- tenaculum placement ( $P=0.0001$ ), 2- sound insertion ( $P=0.0001$ ), 3- Mirena insertion

( $P=0.0001$ ), and 4- (10) minutes following the procedure ( $P= 0.0001$ ), there was a significant reduction in (VAS) for group II compared to group I ( $P=0. 0001$ ).

When compared to group I, group II had a significantly greater degree of satisfaction ( $P=0.0001$ ). In addition, as compared to group I, the requirement for additional analgesics was significantly reduced in group II ( $P=0.0001$ ) (Table 2).

**Table 2.** The principal outcomes during IUD insertion in the study groups: -

Parameters	Group I (n = 100)	Group II (n = 100)	95% confidence interval		Significance
			Lower	upper	
Duration of the procedure	4.64 ± 0.83	4.71 ± 0.62	-0.20293	0.18474	0.891
VAS tenaculum insertion	5 (3-6)	3 (1-4)			0.0001*
VAS sound insertion	6.08 ± 0.75	3.12 ± 0.68			0.0001*
VAS IUD insertion	6.42 ± 0.66	3.97 ± 0.991	1.98968	2.42850	0.0001*
VAS 5 minutes post insertion	4 (3-5)	2 (1-3)	1.82545	2.24728	0.0001*
Ease of insertion score	6 (3-8)	3 (2-5)			0.0001*
Female satisfaction score	6.03 ± 0.59	8.74 ± 0.89	-2.79103	-2.40897	0.0001*
Need for additional analgesia (%)	25 (25)	7 (7)	0,083	0,438	0.0001*

Parameters	Group I (n = 100)	Group II (n = 100)	95% confidence interval		Significance
			Lower	upper	

VAS (visual analog scale). \*Statistically Significant Difference

# Variables are presented as mean and standard deviation, median (minimum-maximum), and number (percentage).

There were no significant differences related to the complication of the insertion procedure as tenaculum site bleeding, abdominal cramps, fever, nausea, chills,

and failure of insertion ( $P=0.885, 0.639, 1.000, 0.517, 1.000$  and  $0.372$ ) respectively. No reported cases of diarrhea or vomiting. (Table 3).

**Table 3. Insertion complications in the study groups: -**

parameters	Group I (n = 100)	Group II (n = 100)	95% confidence interval		Significance
			Lower	upper	
Tenaculum site bleeding (%)	6 (6)	5 (5)			0.885
Abdominal cramp (%)	18 (18)	15 (15)	0.422	3.062	0.639
Fever (%)	0	1 (1)	0.372	1.1710	1.000
Chills (%)	0	1(1)			1.000
Nausea (%)	3 (3)	2 (2)	0.365	4.362	0.893
Vomiting (%)	0	0			----
Diarrhea (%)	0	0			----
Failure of IUD insertion (%)	4 (4)	2 (2)	0.034	3.195	0.594

# Variables are presented as numbers (percentage).

## Discussion

This is the first study to examine the effectiveness of vaginal INH 900 mg vs. placebo in enhancing copper T380A IUD insertion ease and lowering insertion discomfort in nulliparous women.

We evaluated insertion pain in women who received vaginal INH 900 mg vs. placebo 12 hours before insertion and found a difference in insertion pain between the two treatment groups. The INH 900 mg group had less resistance at the internal cervical os level and less insertion discomfort. INH is a low-cost, widely available, and well-tolerated method of facilitating the insertion of copper T380A IUDs.

In our study, the difference in ease of insertion between the INH and placebo groups was greater than 1.6, which was clinically significant.

In several randomized studies utilizing NO donors, the force required to expand the cervix prior to a first-trimester abortion is lowered even when the cervical width is less than 6 mm (17-19).

Two investigations looked at the impact of NO donors on the ease of installation of IUDs and the need for further installation procedures (20, 21).

In 24 nulliparous women, the effects of nitroprusside gel given intracervical shortly before IUD implantation were studied. There were no significant differences in provider assessment of ease of installation among all



women randomized between the research groups (mean=32.4 versus 26.5, respectively) (20). It's possible that this study and our experiment aren't the same. It's possible that the time between nitroglycerin and IUD implantation was too short, or the medication dose was too high for cervical remodeling to occur. Furthermore, the authors of this study state that pain levels following IUD implantation vary greatly across women and that a larger sample size may have revealed considerably different outcomes.

The effects of nitroglycerin gel administered vaginally prior to IUD implantation on 24 nulliparous women were evaluated in the second study (21). The study failed to show the difference as regards the ease of insertion (mean=29.4 versus 22.8) or the need for cervical dilatation between the groups among all women randomized. Participants were given analgesia prior to IUCD insertion, which may have altered the pain score obtained during IUCD insertion.

INH is a cervical ripening therapy that is still in the development phases. According to a study conducted by Highlight *et al.*, vaginal INH is an effective medication for cervical ripening prior to labor induction in term pregnancies (14). INH acts in the same manner that NO donors do when it comes to cervical dilatation. Many investigations have found that INH impacts cervical dilatation by causing NO production (15).

Initial cervical dilatation and dilatation length were higher with vaginal misoprostol than with a Foley catheter and vaginal isosorbide mononitrate, according to El-Khayat *et al* (22). Still, there was no significant difference in operation time or dilation problems between the two groups. It's conceivable that their lack of statistical significance stems from different sample sizes or methods than those used in the current study.

According to our findings, self-administering vaginal INH 900 mg 12 hours before a coper-IUS insertion reduced discomfort related to various phases of copper T380A IUD implantation.

Ladies who underwent INH insertion were happier than women in the placebo group when questioned about their satisfaction with copper T380A IUD implantation. In terms of side effects or procedure-related problems, there were no notable differences between the two groups. In our research, there were four unsuccessful insertions (two in the placebo group and two in the INH group), all due to a very tight cervical os. After the procedure, women in the placebo group required far more extra analgesics than women in the INH group, indicating the therapeutic utility and effects of INH administration.

The INH group required less cervical dilatation than the placebo group (7.3 percent vs. 16.5 percent;  $P=0.01$ ), suggesting that physicians in the INH group had an easier difficulty placing the device.

This research has several advantages. As previously noted, this is the first study to look at the impact of INH on pain following coper-IUS implantation in nulliparous and teenage women. We could minimize possible biases that an unblinded or observational study might have introduced by comparing the two treatment arms in a prospective, double-blinded, randomized control trial. Because we eliminated women who had taken other pain medications the day before, we were able to look at the effect of INH on pain following coper-IUD implantation. Finally, an adequate sample size with sufficient power to detect significant differences between groups was determined using CONSORT guidelines for clinical studies.

The likelihood that patient characteristics or anxiety levels influenced pain evaluation in our study reduced the subjective pain assessment. On the other hand, randomization and a proper research design were able to overcome this difficulty. Another issue was that we didn't keep track of how uncomfortable patients were at different periods following the operation. Several baseline factors, such as provider experience and time since the last birth, may have influenced pain and ease of insertion results. The substantial similarity of these features in the two groups ruled out this idea.

One of the study's drawbacks was the necessity for two visits for copper T380A IUD insertion. This is, however, standard protocol at our family planning clinic, and it helps us deliver better LNG-IUD contraceptive counseling and patient decision-making. In addition, the study's single-center design restricted IUD placement to skilled physicians.

INH can be used to make IUCD implantation go more smoothly. It's easy to get and doesn't look to be difficult. Cervical ripening's underlying mechanism, on the other hand, remains unknown. More study is needed to establish the mechanisms of action and clinical effectiveness of INH for cervix softening prior to IUCD implantation and the optimum dosage and timing.

## Conclusion

In nulliparous teens and young women, self-administered INH 900 mg vaginally 12 hours before a copper T380A IUD insertion successfully decreased discomfort during insertion and enhanced women's pleasure and ease of insertion, as assessed by physicians.

## Acknowledgments

None.

## Conflict of Interest

The authors declared no conflict of interest.

## Compliance with Ethical Standards

The study was in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

### Informed Consent:

Informed consent was obtained from all individual participants included in the study.

### Funding

No funding.

## References

- Lu S, Lin J, Zhang Z, Xiao L, Jiang Z, Chen J, Hu C, Luo S. Alert for non-respiratory symptoms of coronavirus disease 2019 patients in epidemic period: A case report of familial cluster with three asymptomatic COVID-19 patients. *J Med Virol.* 2021;93(1):518-21. [[DOI:10.1002/jmv.25776](https://doi.org/10.1002/jmv.25776)] [[PMID](#)]
- Zeng JH, Liu YX, Yuan J, Wang FX, Wu WB, Li JX, et al. First case of COVID-19 complicated with fulminant myocarditis: a case report and insights. *Infection.* 2020;48(5):773-7. [[PMCID](#)] [[DOI:10.1007/s15010-020-01424-5](https://doi.org/10.1007/s15010-020-01424-5)] [[PMID](#)]
- Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet.* 2020;395(10223):514-23. [[DOI:10.1016/S0140-6736\(20\)30154-9](https://doi.org/10.1016/S0140-6736(20)30154-9)]
- Han C, Duan C, Zhang S, Spiegel B, Shi H, Wang W, Zhang L, Lin R, Liu J, Ding Z, Hou X. Digestive symptoms in COVID-19 patients with mild disease severity: clinical presentation, stool viral RNA testing, and outcomes. *Am J Gastroenterol.* 2020; 115(6):916-23. [[PMCID](#)] [[DOI:10.14309/ajg.0000000000000664](https://doi.org/10.14309/ajg.0000000000000664)] [[PMID](#)]
- Puntmann VO, Carerj ML, Wieters I, Fahim M, Arendt C, Hoffmann J, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). *JAMA Cardiol.* 2020;5(11):1265-73. [[PMCID](#)] [[DOI:10.1001/jamacardio.2020.3557](https://doi.org/10.1001/jamacardio.2020.3557)] [[PMID](#)]
- Huang L, Zhao P, Tang D, Zhu T, Han R, Zhan C, et al. Cardiac involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging. *Cardiovasc Imag.* 2020;13(11):2330-9. [[PMCID](#)] [[DOI:10.1016/j.jcmg.2020.05.004](https://doi.org/10.1016/j.jcmg.2020.05.004)] [[PMID](#)]
- Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. *Radiology.* 2020;296(2):E32-40. [[PMCID](#)] [[DOI:10.1148/radiol.2020200642](https://doi.org/10.1148/radiol.2020200642)] [[PMID](#)]
- Liu D, Li L, Wu X, Zheng D, Wang J, Yang L, et al. Pregnancy and Perinatal Outcomes of Women With Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis. *AJR Am J Roentgenol.* 2020;215(1):127-32. [[DOI:10.2214/AJR.20.23072](https://doi.org/10.2214/AJR.20.23072)] [[PMID](#)]
- Liu H, Liu F, Li J, Zhang T, Wang D, Lan W. Clinical and CT imaging features of the COVID-19 pneumonia: Focus on pregnant women and children. *J Infect.* 2020;80(5):e7-13. [[PMCID](#)] [[DOI:10.1016/j.jinf.2020.03.007](https://doi.org/10.1016/j.jinf.2020.03.007)] [[PMID](#)]
- Long C, Xu H, Shen Q, Zhang X, Fan B, Wang C, et al. Diagnosis of the Coronavirus disease (COVID-19): rRT-PCR or CT?. *Eur J Radiol.* 2020;126:108961. [[PMCID](#)] [[DOI:10.1016/j.ejrad.2020.108961](https://doi.org/10.1016/j.ejrad.2020.108961)] [[PMID](#)]
- Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet.* 2020;395(10226):809-15. [[DOI:10.1016/S0140-6736\(20\)30360-3](https://doi.org/10.1016/S0140-6736(20)30360-3)]
- Liu W, Wang Q, Zhang Q, Chen L, Chen J, Zhang B, et al. Coronavirus disease 2019 (COVID-19) during pregnancy: a case series.
- Yu N, Li W, Kang Q, Xiong Z, Wang S, Lin X, Liu Y, Xiao J, Liu H, Deng D, Chen S. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *Lancet Infect Dis.* 2020;20(5):559-64. [[DOI:10.1016/S1473-3099\(20\)30176-6](https://doi.org/10.1016/S1473-3099(20)30176-6)]
- Schwartz DA. An analysis of 38 pregnant women with COVID-19, their newborn infants, and maternal-fetal transmission of SARS-CoV-2: maternal coronavirus infections and pregnancy outcomes. *Arch Pathol Lab Med.* 2020;144(7):799-805. [[DOI:10.5858/arpa.2020-0901-SA](https://doi.org/10.5858/arpa.2020-0901-SA)] [[PMID](#)]
- World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance, 13 March 2020. World Health Organization; 2020. [[DOI:10.15557/PiMR.2020.0003](https://doi.org/10.15557/PiMR.2020.0003)]

16. Dashraath P, Wong JL, Lim MX, Lim LM, Li S, Biswas A, et al. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. *Am J Obstet Gynecol.* 2020;222(6):521-31. [PMCID] [DOI:10.1016/j.ajog.2020.03.021] [PMID]
17. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr.* 2020;9(1):51. [DOI:10.21037/tp.2020.02.06] [PMID] [PMCID]
18. de Souza Santos D, de Oliveira Menezes M, Andreucci CB, Nakamura-Pereira M, Knobel R, et al. Disproportionate impact of coronavirus disease 2019 (COVID-19) among pregnant and postpartum black women in Brazil through structural racism lens. *Clin Infect Dis.* 2021;72(11):2068-9. [DOI:10.1093/cid/ciaa1066] [PMID] [PMCID]
19. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: a systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand.* 2020;99(7):823-9.
20. Ashraf MA, Keshavarz P, Hosseinpour P, Erfani A, Roshanshad A, Pourdast A, et al. Coronavirus disease 2019 (COVID-19): a systematic review of pregnancy and the possibility of vertical transmission. *J Reprod Infertil.* 2020;21(3):157.
21. Blitz MJ, Rochelson B, Minkoff H, Meirowitz N, Prasannan L, London V, et al. Maternal mortality among women with coronavirus disease 2019 admitted to the intensive care unit. *Am J Obstet Gynecol.* 2020;223(4):595-9. [PMCID] [DOI:10.1016/j.ajog.2020.06.020] [PMID]
22. Cheng SO, Khan S, Alsafi Z. Maternal death in pregnancy due to COVID-19. *Ultrasound Obstet Gynecol.* 2020;56(1):122. [DOI:10.1002/uog.22111] [PMID] [PMCID]
23. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, Seferovic MD, Aski SK, et al. Maternal death due to COVID-19. *Am J Obstetrics Gynecol.* 2020;223(1):109-e1. [PMCID] [DOI:10.1016/j.ajog.2020.04.030] [PMID]
24. Takemoto ML, Menezes MO, Andreucci CB, Knobel R, Sousa LA, Katz L, et al. Maternal mortality and COVID-19. *J Matern Fetal Neonatal Med.* 2020:1-7. [DOI:10.1080/14767058.2020.1786056] [PMID]
25. Reinhard G, Noll A, Schlebusch H, Mallmann P, Ruecker AV. Shifts in the TH1/TH2 balance during human pregnancy correlate with apoptotic changes. *Biochem Biophys Res Commun.* 1998;245(3):933-8. [DOI:10.1006/bbrc.1998.8549] [PMID]
26. Gujski M, Humeniuk E, Bojar I. Current state of knowledge about SARS-CoV-2 and COVID-19 disease in pregnant women. *Med Sci Monit.* 2020;26:e924725-1. [DOI:10.12659/MSM.924725]

#### How to Cite This Article:

Shady N W, Farouk H A, Sallam H F. Clinical Outcome of Self-administered Vaginal Isonicotinic Acid Hydrazide (INH) Before T380A Copper Intrauterine Device Insertion in Adolescent and Young Women: A Double-Blind Randomized Controlled Study. *J Obstet Gynecol Cancer Res.* 2022; 7(5):391-8.

#### Download citation:

[BibTeX](#) | [RIS](#) | [EndNote](#) | [Medlars](#) | [ProCite](#) | [Reference Manager](#) | [RefWorks](#)