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**Original Research Article**

# Effectiveness of innovator dydrogesterone versus generic dydrogesterone in early pregnancy: a real-world analysis

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## ABSTRACT

**Background:** Miscarriage is the most common complication of early pregnancy. Dydrogesterone, a retro-steroid with high oral bioavailability and receptor selectivity, is widely prescribed to support and maintain pregnancy *via* its novel immunomodulation mechanism. There is a lack of comparative data on the miscarriage rate for pregnant females prescribed innovator, generic, and no dydrogesterone in early pregnancy. This study aimed to evaluate this comparative rate in real-world settings.
**Methods:** A real-world, retrospective, observational study was conducted using anonymized and aggregated medical records from January 2017 to October 2024. Early pregnancy females (18-45 years) who consulted gynecologists were included. These were categorized into three arms: innovator dydrogesterone (Arm 1), generic dydrogesterone (Arm 2), and no dydrogesterone (Arm 3). These arms were balanced by propensity score matching (PSM), and miscarriage rates were compared using the Chi-square test.
**Results:** The incidence of miscarriage was significantly lower in the innovator arm (4.10%) compared to Arm 2 (5.54%, p=0.040) and arm 3 (12.46%, p<0.001). No event of miscarriage was reported among women who switched from generic to innovator dydrogesterone. However, one of the females who shifted from innovator to generic experienced a loss of pregnancy.
**Conclusions:** Innovator dydrogesterone was associated with the lowest rate of miscarriage compared to generic and no dydrogesterone. This suggests its potential clinical benefits in early pregnancy.

**Keywords:** Early pregnancy, Miscarriage, Innovator dydrogesterone, Generic dydrogesterone, Real-world evidence

## INTRODUCTION

Miscarriage, a common complication of pregnancy, is defined as the spontaneous loss of pregnancy before 20 weeks of gestation. It affects an estimated 12-15% of pregnant females worldwide.[1] Approximately 23 million miscarriages occur globally every year, equating to nearly 44 pregnancy losses every minute.[2] According to the national family health survey (NFHS-5), 2019-21, conducted by the government of India, approximately 7% of the pregnancies ended in miscarriage.[3]

Pregnancy loss is typically classified into varied categories based on clinical presentation and specificity, including biochemical, asymptomatic (missed), threatened, inevitable, incomplete, complete, recurrent, and septic loss. Over 60% of pregnancy losses occur between 6 and 10 weeks of gestation, with fetal chromosomal abnormalities like monosomy trisomies and polyploidy being the prominent etiological factors.[4]

Advanced maternal age is directly associated with an increased risk of miscarriage, primarily due to a higher

incidence of fetal chromosomal abnormalities. Similarly, advanced paternal age has also been implicated in elevated miscarriage risk, attributed to genetic and epigenetic abnormalities in sperm.[5] Additional risk factors include the extremes of body mass index (BMI), history of miscarriages, smoking, alcohol consumption, tobacco smoke, psychological stress, air pollution, exposure to pesticides, and chronic conditions such as hypertension and thyroid disorder.[2,6]

Recurrent pregnancy loss (RPL), characterized by the loss of two or more pregnancies, affects approximately 5% of women. The consensus meeting report by the federation of obstetric and gynecological societies of India (FOGSI) recommends a multifactorial treatment approach involving anticoagulation, immunological, surgical, and progesterone therapy in addition to lifestyle modification and psychological support.[7]

Progesterone, an endogenous hormone produced by the corpus luteum and by the placenta during pregnancy, has a pivotal role in maintaining endometrial receptivity and supporting the continuation of a successful pregnancy.[8] Through its immunomodulatory capabilities, progesterone modulates the maternal immune response to prevent embryonic rejection, promotes uterine quiescence, and prevents the onset of uterine contractions.[9] Insufficient levels of progesterone during the luteal phase of the menstrual cycle and early pregnancy are associated with increased risk of pregnancy loss.[10,11] Exogenous progestogen supplementation is recommended to combat insufficiency. These agents bind to the progesterone receptors with varying degrees of affinity and selectivity and activate them to exert their therapeutic effectiveness.[12] Commonly prescribed progestogens during pregnancy include dydrogesterone, natural progesterone, and 17α-hydroxyprogesterone caproate.[13]

Dydrogesterone, a retro-steroid with a bent molecular structure with 5.6 times higher oral bioavailability and selectivity, has been used for managing female reproductive health for more than six decades now.[11,14] Dydrogesterone and its active metabolites exhibit high receptor specificity and selectivity without cross-activation of the steroid-hormone receptor, and demonstrate minimal to no activity at androgenic, estrogenic, glucocorticoid, and mineralocorticoid receptors.[14] It prevents pregnancy loss via its novel immunomodulation mechanism. It positively regulates the synthesis and expression of progesterone-induced blocking factor (PIBF), natural killer (NK) cells, HOX-10, and trophoblast human leukocyte antigens (HLA) genes, resulting in a favorable shift towards T helper-2 (Th-2) anti-inflammatory response. Dydrogesterone supplementation during pregnancy helps maintain adequate serum PIBF levels, facilitating the production of antibodies that contribute to pregnancy maintenance.[15,16]

Manufacturing and prescription of generic medications are highly preferred in emerging economies like India. However, concerns have been raised regarding a higher incidence of serious adverse events associated with the generic drugs manufactured in India compared to equivalent drugs manufactured in the United States.[17] This underscores the significance of having generic switching policies in place. While prescribing generics, it should be ensured that they meet the quality, efficacy, and safety standards of the innovator.[18] In certain therapeutic contexts, generic products may compromise the effectiveness of treatment and safety.[19] Dydrogesterone, known for improving pregnancy outcomes and reducing the risk of miscarriages, exemplifies a condition that requires careful selection between innovator and generics. Currently, there is a lack of data comparing rates of miscarriage in females prescribed innovator dydrogesterone, generic dydrogesterone, and no dydrogesterone. The current study was planned to address the gap by assessing miscarriage rate across these groups. The findings are anticipated to support prescribing decisions for females requiring dydrogesterone during early pregnancy.

## METHODS

This study was a retrospective, real-world, observational analysis based on electronic medical records (EMRs). Anonymized and aggregated data from January 2017 and October 2024 were retrieved from the EMR database of HealthPlix Technologies Private Limited (https://www.healthplix.com/). Patient confidentiality was maintained throughout the study. Ethics approval for conducting the study was granted by the Central Independent Ethics Committee (CIEC370325) on 24th March 2025.

The study population consisted of pregnant females aged 18 to 45 years who consulted gynecologists and had a mention of early pregnancy in their prescriptions at the baseline, visit of first mention of early pregnancy on the platform. Exclusion criteria included conception via *in vitro* fertilization (IVF), ectopic pregnancy, documentation of miscarriage at the visit when dydrogesterone was prescribed, or medical termination of pregnancy due to genetic reasons. Based on the prescribed treatment, females were categorized into three groups: “arm 1” included the ones recommended innovator dydrogesterone (Duphaston), “arm 2” comprised of the pregnant women prescribed generic dydrogesterone (all brands other than Duphaston were categorized as generics) and “arm 3” included the ones who were not prescribed dydrogesterone at all.

The journey of the females was longitudinally followed and tracked to evaluate the occurrence of miscarriage, the primary endpoint of the study. For females in arms 1 and 2, the journey on the platform was followed until either a miscarriage was reported or dydrogesterone was removed from the prescription. In Arm 3, visits of pregnant females were tracked until a visit at which a miscarriage was recorded. The event of miscarriage was identified by the

mention of terms like spontaneous abortion, early pregnancy failure, pregnancy failure, dilation and evacuation (D and E), complete abortion, urine pregnancy test (UPT) negative and related terms in the 'Diagnosis' section of the EMR at the follow-up visits. Secondary endpoints of the study included assessment of demographic characteristics, clinical information, and prescription patterns, including dose strength, daily recommended frequency, and mean duration of prescription of dydrogesterone for pregnant women in arms 1 and 2. Additionally, the study examined the miscarriage rates among females who had a switch from innovator to generic dydrogesterone and vice versa.

To assess the rate of miscarriage across the three study arms, PSM was employed to balance the number of females in each group, with age used as the matching variable. A logistic regression was first conducted to create the initial base model, from which propensity scores were estimated. PSM was then performed using the "MatchIt" package in R (version 4.4.3), employing the "optimal" method algorithm. Propensity scores were used as the distance measure between observations for matching, with a 1:1 matching ratio. Missing data was not imputed, and the sample size was adjusted accordingly. All other statistical analyses were performed using STATA 15.1 SE. Miscarriage rates were calculated as proportions (n) and percentages (%), and the statistical significance for the same was evaluated using the Chi-square test. A predefined significance level of $p<0.05$ was used.

Demographic variables such as age, body weight, and body mass index were summarized using descriptive statistics (mean, standard deviation [SD]). Clinical conditions were reported as frequency counts (n) and percentages (%). Prescription patterns, including dose strength, daily dosing frequency, were summarized for the females in arms 1 and 2 using counts and percentages. Duration of prescription across visits was depicted as the mean duration and SD. Additionally, the miscarriage rates for females who shifted from innovator to generics and vice versa were reported as proportions, and % of females, and statistical significance was evaluated using the Chi-square. test.

## RESULTS

### *Patient disposition*

A total of 32,730 females aged 18-45 years who consulted gynecologists and had documentation of early pregnancy or related terms in their prescriptions were identified on the platform. Based on the prescribed treatment, pregnant females were categorized into arm 1 (innovator dydrogesterone), arm 2 (generic dydrogesterone), and arm 3 (No dydrogesterone). Of those prescribed innovator dydrogesterone, 1878 females met the eligibility criteria and were included in the analysis. Subsequently, the number of females in arms 2 and 3 was balanced using PSM, and the matched cohorts were used for comparative analysis (Figure 1).

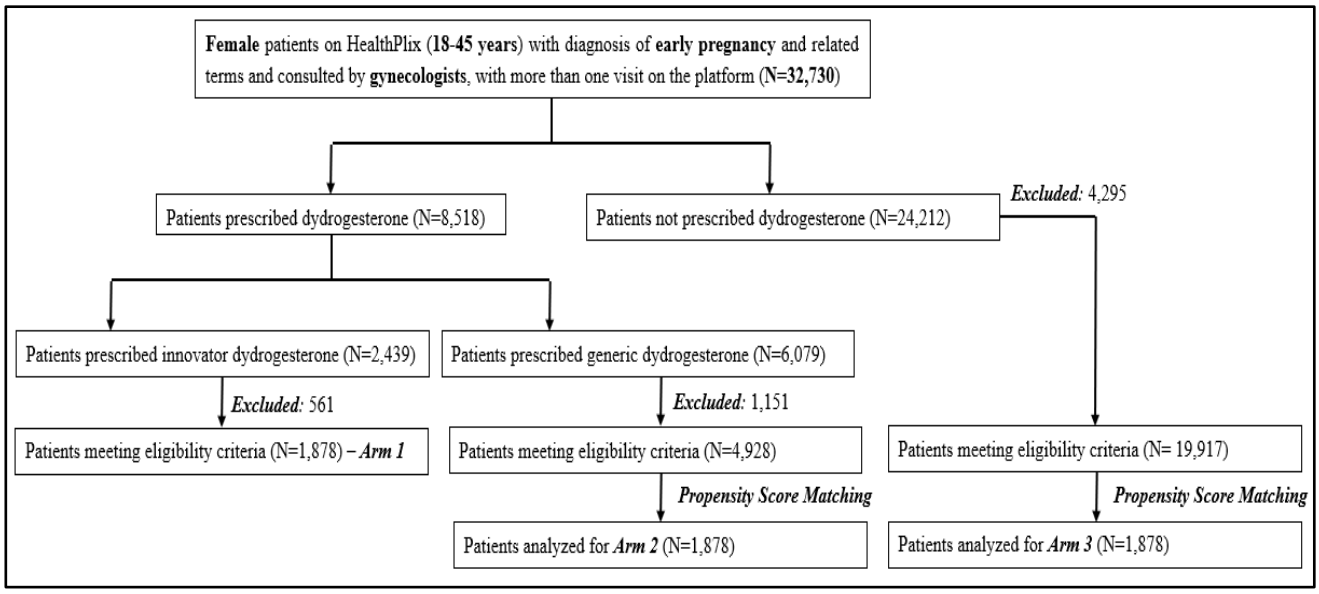


**Figure 1: Study flow diagram.**

### *Demographic characteristics*

The average age of pregnant females in arms 1, 2, and 3 was 28.84±4.53, 28.97±4.61, and 28.56±4.50 years, respectively. Over half of the study population for arms 1 and 2 had BMI outside normal range, with classification falling into underweight, overweight, or obese categories. In arm 3, this proportion was 50%.

Among those with available body weight data, most females' body weight was in range of 51.0 to 60.9 kg. the demographic characteristics of the study population are summarized in Table 1.

***Clinical conditions***

The diagnosis section of the females included in the study across the study arms was analyzed to gain insights into the clinical conditions. A substantial proportion of the females were primigravid. Among these, a subset reported symptoms such as spotting or bleeding at the time of clinical presentation. A considerable proportion of the study population had a history of abortion, with a higher prevalence observed in arms 1 and 2.

Additionally, more cases of RPL were prescribed innovator dydrogesterone compared to generic formulations. Other clinical conditions observed across the study arms included spotting/bleeding, history of infertility, bad obstetric history, delayed conception, threatened abortion, and others, summarized in Table 2.

***Miscarriage rates***

The rates of miscarriage across the three study arms are presented in Table 3. Arm 1 demonstrated the lowest incidence of miscarriage (n=77, 4.10%) in comparison to 5.54% in arm 2, and 12.46% in arm 3. The difference in rates of miscarriage for arm 1 was statistically significant when compared to arms 2 (p=0.040) and 3 (p<0.001).

***Treatment pattern-innovator and generic dydrogesterone***

Dydrogesterone 10 mg was commonly prescribed as a twice a day (BID) regimen, a pattern observed consistently in arm 1 and 2 Table 4).

The mean duration of dydrogesterone prescription across visits on the platform was 24.74±8.46 weeks for arm 1 and 25.17±8.05 weeks for arm 2.

***Miscarriage rates: switch from innovator to generic dydrogesterone and vice versa***

In the study cohort, no events of miscarriage were reported among females who transitioned from generic formulations of dydrogesterone to innovator dydrogesterone. Conversely, a single case of pregnancy loss was documented following the switch from innovator to generic dydrogesterone (Table 5).

**Table 1: Demographic characteristics.**

| Parameter | Categories | Arm 1 | | | Arm 2 | | | Arm 3 | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | N | % | Mean (SD) | N | % | Mean (SD) | N | % | Mean (SD) |
| Age (in years) | Overall | 1878 | 100 | 28.84 (4.53) | 1878 | 100 | 28.97 (4.61) | 1878 | 100 | 28.56 (4.50) |
| | 18-25 | 460 | 24.49 | 23.04 (1.80) | 460 | 24.49 | 23.14 (1.79) | 460 | 24.49 | 22.75 (1.93) |
| | 26-30 | 606 | 32.27 | 27.66 (1.10) | 756 | 40.26 | 28.14 (1.33) | 606 | 32.27 | 27.40 (1.11) |
| | >30 | 812 | 43.24 | 33.00 (2.70) | 662 | 35.25 | 33.97 (2.57) | 812 | 43.24 | 32.71 (2.53) |
| BMI (kg/m$^2$) | Overall | 382 | 20.34 | 24.95 (4.67) | 303 | 16.13 | 24.84 (4.80) | 256 | 13.63 | 24.63 (4.59) |
| | Underweight (<18.50) | 28 | 7.33 | 16.87 (2.85) | 30 | 9.90 | 16.69 (1.34) | 16 | 6.25 | 16.57 (1.49) |
| | Normal (18.50-24.99) | 179 | 46.86 | 22.43 (1.72) | 127 | 41.91 | 22.33 (1.87) | 128 | 50.00 | 22.02 (1.73) |
| | Overweight (25.00-29.99) | 125 | 32.72 | 27.09 (1.37) | 106 | 34.98 | 27.09 (1.39) | 80 | 31.25 | 26.99 (1.29) |
| | Obese (≥30.00) | 30 | 13.09 | 33.14 (3.03) | 40 | 13.20 | 32.95 (2.78) | 32 | 12.50 | 33.17 (2.17) |
| Weight (kg) | Overall | 1363 | 72.58 | 61.70 (11.35) | 1446 | 77.00 | 58.41 (11.86) | 1339 | 71.30 | 59.50 (11.65) |
| | ≤50.9 | 222 | 16.29 | 46.34 (2.88) | 396 | 27.39 | 44.54 (4.43) | 324 | 24.20 | 45.43 (4.33) |
| | 51.0 - 60.9 | 454 | 33.31 | 55.94 (2.88) | 474 | 32.78 | 56.07 (2.78) | 441 | 32.94 | 55.95 (2.79) |
| | 61.0 - 70.9 | 430 | 31.55 | 65.23 (2.80) | 378 | 26.14 | 65.07 (2.83) | 356 | 26.59 | 65.09 (2.78) |
| | ≥71.0 | 257 | 18.86 | 79.22 (7.56) | 198 | 13.69 | 79.04 (6.77) | 218 | 16.28 | 78.45 (6.89) |

Note: Data for BMI and weight was available for 382 and 1363 females, respectively. Percentage calculation was done based on the respective numbers.
Note: Data for BMI and weight was available for 303 and 1446 females, respectively. Percentage calculation was done based on the respective numbers.
Note: Data for BMI and weight was available for 256 and 1339 females, respectively. Percentage calculation was done based on the respective numbers.

**Table 2: Baseline clinical conditions.**

| Diagnosis | Arm 1 | | Arm 2 | | Arm 3 | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| **Primigravida** | 498 | 26.52 | 424 | 22.58 | 477 | 25.40 |
| Primigravida with spotting or bleeding | 51 | 10.24 | 42 | 9.91 | 58 | 12.16 |
| **History of abortion** | 373 | 19.68 | 405 | 21.57 | 316 | 16.83 |
| Abortion (one) | 259 | 69.44 | 288 | 71.11 | 190 | 60.13 |
| Recurrent pregnancy loss (two or more) | 103 | 27.61 | 95 | 23.46 | 113 | 35.76 |
| Death of previous child | 6 | 1.61 | 16 | 3.95 | 4 | 1.27 |
| Ectopic pregnancy | 3 | 0.80 | 3 | 0.74 | 4 | 1.27 |
| Medical termination of pregnancy | 1 | 0.27 | 2 | 0.49 | 4 | 1.27 |
| Chemical pregnancy/biochemical pregnancy | 1 | 0.27 | 0 | 0.00 | 1 | 0.32 |
| Mid trimester delivery | 0 | 0.00 | 1 | 0.25 | 0 | 0.00 |
| **Nausea/vomiting/hyperemesis gravidarum** | 209 | 11.13 | 253 | 13.47 | 207 | 11.02 |
| **Spotting or bleeding** | 165 | 8.79 | 155 | 8.25 | 202 | 10.76 |
| **History of infertility** | 79 | 4.21 | 56 | 2.98 | 24 | 1.28 |
| Infertility (type not specified) | 61 | 77.22 | 10 | 17.86 | 8 | 33.33 |
| Primary infertility | 12 | 15.19 | 23 | 41.07 | 9 | 37.50 |
| Secondary infertility | 6 | 7.59 | 23 | 41.07 | 7 | 29.17 |
| **Multiple gestation** | 44 | 2.34 | 18 | 0.96 | 19 | 1.01 |
| Twin pregnancy | 41 | 93.18 | 17 | 94.44 | 17 | 89.47 |
| Triplet pregnancy | 1 | 2.27 | 0 | 0.00 | 0 | 0.00 |
| Quadruple pregnancy | 2 | 4.55 | 1 | 5.56 | 2 | 10.53 |
| **Precious pregnancy** | 24 | 1.28 | 13 | 0.69 | 14 | 0.75 |
| Elderly | 21 | 87.50 | 8 | 61.54 | 11 | 78.57 |
| Precious | 3 | 12.50 | 3 | 23.08 | 3 | 21.43 |
| High risk | 0 | 0.00 | 1 | 7.69 | 0 | 0.00 |
| Low BMI | 0 | 0.00 | 1 | 7.69 | 0 | 0.00 |
| **Uterine fibroid** | 27 | 1.44 | 12 | 0.64 | 18 | 0.96 |
| **Bad obstetric history** | 20 | 1.06 | 10 | 0.53 | 22 | 1.17 |
| **Delayed conception** | 19 | 1.01 | 25 | 1.33 | 14 | 0.75 |
| **Threatened abortion** | 16 | 0.85 | 24 | 1.28 | 59 | 3.14 |
| **Conception by assisted reproductive technology** | 10 | 0.53 | 8 | 0.43 | 3 | 0.16 |
| Conception after fertility treatment | 7 | 70.00 | 8 | 100.00 | 2 | 66.67 |
| Conception after ovulation induction | 3 | 30.00 | 0 | 0.00 | 1 | 50.00 |
| **Related conditions** | 372 | 19.81 | 291 | 15.50 | 259 | 13.79 |
| Abdominal pain | 149 | 40.05 | 144 | 49.48 | 128 | 49.42 |
| Hypothyroidism | 89 | 23.92 | 50 | 17.18 | 49 | 18.92 |
| Backache | 45 | 12.10 | 53 | 18.21 | 37 | 14.29 |
| Subchorionic hematoma/bleed | 50 | 13.44 | 19 | 6.53 | 10 | 3.86 |
| PCOD/PCOS | 14 | 3.76 | 9 | 3.09 | 17 | 6.56 |
| Herpes Simplex virus | 12 | 3.23 | 2 | 0.69 | 0 | 0.00 |
| Vaginal discharge | 9 | 2.42 | 13 | 4.47 | 18 | 6.95 |
| Endometriosis | 2 | 0.54 | 1 | 0.34 | 0 | 0.00 |
| Bicornuate uterus | 2 | 0.54 | 0 | 0.00 | 0 | 0.00 |

Females on each arm: 1878. Percentage calculation for categories has been done taking 1878 as denominator. Percentage for subcategories has been calculated numbers of respective categories as the denominator. Females can have more than one condition mentioned in the diagnosis. ART: Assisted reproductive technology, PCOD: Polycystic ovarian disease, PCOS: Polycystic ovarian syndrome.

**Table 3: Miscarriage rates across study arms.**

| Variables | Females without miscarriage | | Females with miscarriage | |
|---|---|---|---|---|
| | N | % | N | % |
| **Study arm** | | | | |
| Arm 1, (n=1,878) | 1801 | 95.90 | 77 | 4.10 |
| Arm 2, (n=1878) | 1774 | 94.46 | 104 | 5.54 |
| Arm 3, (n=1878) | 1644 | 87.54 | 234 | 12.46 |
| **Statistical comparison (p value)** | | | | |
| Arm 1 vs. arm 2 | 0.040* | | | |
| Arm 1 vs. arm 3 | <0.001*** | | | |
| Arm 2 vs. arm 3 | <0.001*** | | | |
| All arms | <0.001*** | | | |

P value calculated using Chi-Sq. test at 5% level of significance. *p value significant at 0.05 level of significance. **p-value significant at 0.01 level of significance. ***p-value significant at 0.001 level of significance, Abbreviations: N: Number of females.

**Table 4: Prescription pattern of dydrogesterone.**

| Variables | | Arm 1 | | Arm 2 | |
|---|---|---|---|---|---|
| **Dose strength** | **Daily recommendation** | **N** | **%** | **N** | **%** |
| **Dydrogesterone 10 mg** | OD | 272 | 14.48 | 655 | 35.25 |
| | BID | 1333 | 70.98 | 1111 | 59.80 |
| | TID | 223 | 11.87 | 78 | 4.20 |
| | QID | 3 | 0.16 | 0 | 0.00 |
| | Not mentioned | 47 | 2.50 | 14 | 0.75 |
| **Dydrogesterone 20 mg SR** | OD | NA | NA | 17 | 94.44 |
| | BID | NA | NA | 1 | 5.56 |
| **Dydrogesterone 30 mg SR** | OD | NA | NA | 2 | 100.00 |

Note: In case of arm 2 - Percentage of females for each frequency was calculated based on the females prescribed each dose strength.
Abbreviations: SR: Sustained release; OD: Once daily; BID: Twice daily; TID: Thrice daily; QID: Four times daily; NA: Not applicable.

**Table 5: Miscarriage rate post switch.**

| Study arms | Miscarriage events | After switching from innovator to generics | | While on innovator | | After switching from generics to innovator | | While on generics | |
|---|---|---|---|---|---|---|---|---|---|
| | | **N** | **%** | **N** | **%** | **N** | **%** | **N** | **%** |
| **Arm 1** | 77 | 1 | 1.30 | 76 | 98.70 | -- | -- | -- | -- |
| **Arm 2** | 104 | -- | -- | -- | -- | 0 | 0.00 | 104 | 100.00 |

## DISCUSSION

In this study, the average age of females in arms 1 and 2 was comparable to that reported in existing literature involving the prescription and use of dydrogesterone. Kuptarak and Phupong, in a randomized controlled trial assessing the effectiveness of oral dydrogesterone in averting miscarriage among females with threatened miscarriage, reported a mean age of 30.5±5.2 years for participants in the dydrogesterone group.[20] Similarly, real-world evidence conducted by Manickavasagam et al reported mean ages of 27.23±4.79 and 28.56±5.17 years for the ones prescribed dydrogesterone 20 mg sustained-release (SR), and dydrogesterone 30 mg SR, respectively.[11]

A systematic review and meta-analysis conducted by Ng et al. highlighted that both low BMI and BMI exceeding 25 kg/m$^2$ significantly increase the risk of pregnancy loss.[21] Similarly, Qu et al established a correlation between the pre-pregnancy BMI and the incidence of miscarriage in patients who conceived by assisted reproductive technology (ART). They concluded that the risk of miscarriage was higher in the obese group compared to the patients in the normal group.[22] These findings are consistent with the present study, where more than half of the pregnant females prescribed dydrogesterone (Arms 1 and 2) fell outside the normal BMI range.

Dydrogesterone is known to downregulate the production of T helper-1 (Th-1) cytokines and upregulate the production of Th-2 cytokines. This results in a shift towards a pregnancy-protective Th-2- dominated immune response, favorable for pregnancy maintenance.[23] It also helps maintain sufficient levels of PIBF, which plays a crucial role in supporting positive pregnancy outcomes.[16] This study demonstrated that pregnant women prescribed innovator dydrogesterone had a significantly lower rate of miscarriage when compared to those who were recommended generic dydrogesterone or no dydrogesterone. There was no miscarriage among the females who transitioned from generic to innovator dydrogesterone, while one of the patients who switched from innovator to generic dydrogesterone experienced miscarriage. The lower rate of miscarriage in arm 1 may be attributed to the existing literature that demonstrates that clinical effectiveness and safety of generic medications can differ from the innovator.[19] Hsu et al evaluated and compared the effectiveness of generic antidepressants against brand-name counterparts in the treatment of patients with depressive disorders. The findings reported that brand-name drugs elicited better protective effects.[24] Although the findings pertain to the different therapeutic areas, these highlight that there can be potential therapeutic variability between innovator and generic medications. These findings suggest that the innovator dydrogesterone may offer improved clinical outcomes in early gestation. This underscores careful consideration while prescribing innovator versus generics, specifically in high-risk pregnancies.

Manickavasagam et al reported the use of dydrogesterone in medical conditions like threatened abortion, early pregnancy, twin and precious pregnancy, as well as in patients with a history of infertility or prior miscarriage.[11] The reported indications are consistent with the ones observed in the present real-world study. Similarly, these align with the indications presented by Tank et al.[25]

Tank et al have reported twice daily (BID) as the most prescribed dosing regimen for dydrogesterone.[25] In a knowledge, attitude, and practice survey, Khanna et al documented dydrogesterone 10 mg BID as the most preferred dosage.[26] The dosing schedule reported in the

literature is in line with the schedule observed in this study, where BID was the most recommended.

The retrospective model for this study included an analysis of extensive patient records collected over the years. This helped in understanding the effectiveness and prescription trends of dydrogesterone in early pregnancy in the real world. Since this was an analysis of the retrospective data from electronic medical records, some variables may not have been recorded across the study population. The study data were retrieved from private practitioners using this EMR across the country for their routine practice. However, the data is limited to the practices using this specific platform. Additionally, the matching technique used for balancing the number of patients on each arm was done using a single variable (age), and the residual confounding factors may affect the interpretation of results. Despite these constraints, the present findings provide valuable insights into the real-world effectiveness of dydrogesterone in early gestation.

## CONCLUSION

This retrospective EMR-based analysis observed a statistically significant lower rate of miscarriage among patients prescribed innovator dydrogesterone (4.10%) compared to those prescribed generic dydrogesterone (5.54%, p=0.040) or no dydrogesterone (12.46%, p<0.001) during early pregnancy. Further investigation using more robust study designs and comprehensive data is warranted to confirm these observations and understand the comparative clinical effectiveness of innovator versus generic dydrogesterone in early pregnancy. These findings serve as an important reference for gynecologists when using dydrogesterone in early gestation.

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