**Inhaler Adherence and Its Associated Factors Among Pregnant Women with Controlled Asthma Attending Selected Primary Care Clinics in Malaysia**

ABSTRACT

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| **Inhaler adherence particularly inhaled Corticosteroid (ICS) is essential among pregnant women with asthma to improve maternal and fetal outcome. This study identified factors associated with inhaler adherence among pregnant women with controlled asthma. Data from self-administered questionnaires and clinical audits were sampled among 369 pregnant women with controlled asthma attending 16 government primary care clinics in the four states in Malaysia between December 2023 to March 2024. Binary logistic regression was used to determine the association between sociodemographic characteristics, clinical parameters, organizational support and patients’ knowledge, perception and practices with inhaler adherence during pregnancy. Factors associated with increased likelihood of inhaler adherence were controlled asthma without depression (OR=3.73, 95%CI 2.78-7.79) and referral to pharmacists (OR=5.82, 95%CI 1.88-11.31). Factors associated with reduced inhaler adherence were; wrong inhaler techniques (OR=0.77, 95%CI 0.30-0.96), unable to differentiate between ICS and short-acting beta-agonists (OR=0.60, 95%CI 1.19-1.41), explanation not given on asthma action plan (OR=0.43, 95%CI 0.26-0.49), explanation not given on asthma diary (OR=0.70, 95%CI 0.21-0.95), not referred to primary care physicians (OR=0.55, 95%CI 0.33-0.70), did not practice trigger avoidance (OR=0.20, 95%CI 0.05-0.79), lacking confidence in using the asthma action plan (OR=0.62, 95%CI 0.33-0.58), and not using asthma diaries (OR=0.58, 95%CI 0.37-0.79). Consultation on self-management skills, asthma action plan, asthma diary and correct inhaler technique with a multidisciplinary team approach is needed to ensure inhaler adherence among pregnant women with controlled asthma.** |

***Keywords:*** pregnancy, asthma, Inhaled Corticosteroid (ICS), adherence, primary

1. INTRODUCTION

**Global prevalence of bronchial asthma among pregnant women ranges from 3% to 6%, with 19% of these women experiencing severe asthma and 16% having poorly controlled asthma(1). The estimated prevalence of asthma among adult Malaysians is 6.8% with recent studies indicating a mere 37% have controlled asthma(2). However, data on asthma control among pregnant women in Malaysia remains sparse.**

**A meta-analysis on studies done before 1990 assessing changes in asthma throughout pregnancy found that one-third of pregnant asthmatic women experience symptomatic improvement, one third experience worsening symptoms and one third remain the same(3). Nevertheless recent meta- analysis show a much lower percentage of asthma worsening during pregnancy at 18.8% (4). Guidelines recommend managing asthma actively during pregnancy with 4 weekly review, including prescribing inhaled corticosteroids (ICS) if indicated, and stepping up the regimen as necessary with the goal to maintain asthma control and avoid exacerbations. In addition, comorbidities such as rhinitis or gastro-oesophageal reflux, which can contribute to worsening asthma, should be identified and managed(5-7).**

**A significant proportion of pregnant women with asthma stop or decrease their ICS usage in pregnancy diminishing their asthma control(8) . Up to 23% to 36 % asthmatic women stop their ICS in the first and second trimester despite numerous studies indicating none adverse effects with the usage of ICS in pregnancy(9, 10).Studies suggest that negative perceptions and fear of corticosteroid use during pregnancy, particularly concerns about teratogenic risks, contribute to poor adherence. Additionally, a preference for alternative therapies and a lack of proper education on the importance of inhaler use and the dangers of uncontrolled asthma during pregnancy further exacerbate the issue (11, 12). Self-management skills and being provided asthma action plan remain low with no improvement in the past decade among pregnant women with asthma (13). Non adherence to ICS and poor self-management skills often leading to exacerbation with negative maternal and fetal outcome like pre-eclampsia, pregnancy induced hypertension, low birth weight, pre term and elevated risk of asthma and pneumonia in the first five years of life (14).**

**In Malaysia, postnatal depression affects 12.7% to 20.7% of women, with unipolar depressive disorders being a leading cause of disability among women of childbearing age, reducing productivity and increasing healthcare costs. The lack of perinatal mental health integration into primary care creates a critical gap, depriving mothers of essential care, worsening long-term health outcomes, and impacting child development and family well-being. At the time of this research, the Ministry of Health Malaysia was planning to implement universal screening for anxiety and depression among all pregnant women. This initiative would help address mental health issues in pregnant women with asthma, improving overall well-being, treatment adherence, and pregnancy outcomes(15).**

**In Malaysia, pregnant women with asthma are managed at primary care setting with significant opportunity to assess, educate and optimize management throughout the pregnancy. They are often managed by a team of doctors, nurses and pharmacist. Diagnosis are often made clinically by the treating doctor due to limited access to confirmatory test like spirometry(2). Limited data exist on the inhaler adherence, perception and self- management skills of pregnant women in Malaysia especially among those controlled asthma.**

**The preliminary finding of this study indicated that most pregnant women with asthma had controlled disease. Hence, we aimed to examine the factors influencing inhaler adherence within this population and identify potential gaps in care. Despite the assumption that asthma control is achieved through adherence, further investigation was necessary to determine whether challenges in asthma management persist in this group.**

2. material and methods

**2.1 Study design, Setting and Participants**

**This cross-sectional study was conducted in Malaysia’s government primary care clinics providing antenatal care in the states of Selangor, Wilayah Persekutuan, Perak and Johor derived from the purposive sampling method, a non-probability sampling method. Sixteen clinics were purposely selected considering their large antenatal attendee from a diverse ethnicity and socioeconomic group. This study was conducted from December 2023 to March 2024 (four months).**

**All Malaysian adult pregnant women age 18 years old and above with a doctor’s diagnosis of asthma and Asthma Control Test (ACT) score >19 (controlled asthma) attending government primary healthcare clinics between 17 weeks of gestation until 45 days postpartum were included in the study. Those illiterate in the Malay language or with poor cognition and with an ACT score of lesser than 19 were excluded.**

**2.2 Sample size and Sampling**

**We determined the sample size of the study using a single sample proportion for the dependent variable, and the derived formula is as below:**

**n = Z2 1-α/2 P1 (1-P1) /(d2)**

**Z 1-α/2 = 1.96 for α = 0.05**

**d = absolute precision (at 95% CI or based on the width of the confidence interval)**

**P1 = anticipated sample or population proportion derived Asthma knowledge, care, and outcome during pregnancy: The QAKCOP study(16).**

**This study was chosen as it closely matched this study in terms of sociodemographic factors and the level of asthma control. The item yielded the largest sample size was used to determine the sample size.**

**The calculated sample size for this study was 378 pregnant women. To account for a potential 20% non-response rate, the final desired sample size was increased to 454 pregnant women.**

**A total of 454 pregnant women with asthma were selected using systematic random sampling from 16 government primary care clinics in Malaysia. Following selection, their asthma control status was assessed, and only those with controlled asthma were included in the final analysis.**

**2.3 Study Instrument**

**Bilingual questionnaires were used in this study; a Malay version for the participants and an English version for the attending doctor. Each section is briefly described below.**

**The Malay version questionnaire for the participants consists of four sections; Section one consists of; sociodemographic characteristics of the participants while section two consists of participants antenatal history including screening questions for anxiety using Generalized Anxiety Disorder scale-2 (GAD-2), depression using Patient Health Questionnaire-2 (PHQ-2), history of Covid-19 infection and vaccination against Covid-19 and influenza history. Section three and four were developed by the researcher and each section is described below.**

**In section three participants were asked during each antenatal visit if they had been asked about their asthma controlled, provided counselling and education on asthma care, asked and provided education and education or none at all. Their experience with three categories of staff (doctor, nurses, pharmacist) were surveyed. Participants were also asked if they had been explained on asthma action plan, asthma diary and be referred to a primary care physician. In Section four participants perception and practices in managing asthma is pregnancy were explored.**

**The English questionnaire was filled by the attending doctor, section five involves assessment by the doctors on the participants’ clinical parameters, inhaler technique, ability to differentiate between controller and reliever inhaler, asthma control, exacerbation during pregnancy whether it required admission, was treated outpatient and if escalation of treatment occurred. Overall, the internal consistency Cronbach Alpha was good and acceptable with factors ranging from 0.700 to 0.759 in the perception and practices domain**

**2.4 Variables**

**The main outcome variable is the adherence to inhaler among pregnant women with controlled asthma. Pregnant women with controlled asthma in this study used a reliever inhaler for symptom relief, while their preventer medication varies. It may include an inhaled corticosteroid alone, a combination of a corticosteroid and a long-acting bronchodilator alongside a reliever, or a combination inhaler used as both maintenance and reliever therapy (MART). A participant was considered adherent if they had used their inhalers exactly as prescribed by the doctor in their clinical notes, including the correct dosage and frequency.**

**Asthma control was assessed using the ACT score; a validated tool with good internal consistency with scores ranging from 5 (*poor control of asthma*) to 25 (*complete control of asthma*). An ACT score > 19 indicates controlled asthma (17). Significant associations between asthma control during pregnancy by the Global Initiative for Asthma (GINA) classification and ACT has also been demonstrated (17, 18).**

**GAD-2 and PHQ-2 scores range from 0 to 6 and a score of 3 or greater is suggestive of major depressive disorder and anxiety disorder (19).**

**Inter-rater reliability on inhaler technique was ensured by establishing a standardized assessment. All researchers reached a consensus on the specific steps required for correct inhaler use, and doctors were trained to assess patients consistently based on these agreed-upon criteria. All 5 steps must be performed correctly for metered dose inhaler and all 4 steps must be performed correctly for dry powder inhalers (20). Patients were requested to demonstrate their inhaler technique to their doctors using their own inhalers and a patients was ascertained to have correct inhaler technique**

**For the clinical audit, site investigators reviewed key clinical parameters, including weight, height, BMI, and GDM screening in pregnancy. For asthma management, they assessed inhaler technique, patients’ ability to differentiate between controller and reliever inhalers, and documentation of asthma risk factors at each visit. Additionally, they audited documentation of asthma control, exacerbation history, treatment history, and inhaler usage to optimize management**

**2.5 Data collection method**

**Researchers obtained permission from the State and District Health Department and data collection was coordinated by site investigators. Participants were approached by the researchers while waiting to see their doctors and explained the purpose of the study. Participants were informed that this study aimed to identify factors associated with inhaler adherence among pregnant women with controlled asthma. Participants were provided with the patient information sheet which contained further details of the study and consent form were presented before proceeding to the questionnaire. Participants were allowed to agree or decline to participate in the study after reading the participant information sheet. Consented participants answered the questionnaire in the clinic. Section five of the questionnaire was completed by the attending doctor and all the answered questionnaires were collected by the site investigator. Missing data were checked by researchers. If any data were found to be missing, the site investigator rechecked the records and followed up to ensure completeness before data entry into SPSS.**

**2.6 Data analysis**

**The data was analyzed using the IBM SPSS statistic version 26.0. Descriptive statistics were computed as proportions, mean and standard deviation for nominal and continuous variables, respectively. In this study (Variation Inflation Factor) VIF values ranged from 1.000 - 1.013 for all independent variables suggesting a reliable regression result. The actual Goodness-Of-Fit was 0.737 for this study, Cook’s distance <1, Leverage value 0-1, Studentized and Standardized residual < 3, DFBeta <1. Therefore, the regression model fits all the observed data**

**To examine the associated factors with the inhaler adherence bivariate analysis was used. From the bivariate analysis, a p-value cut-off point of 0.25 from simple logistic regression will be taken as the clinical significance and selected for the multivariate analysis given more traditional levels such as 0.05 can fail in identifying variables known to be significant. In the final model, the statistical significance will be accepted at p-values equal to or less than 0.05 (21).**

1. results and discussion
   1. results

**A total of 454 pregnant women with asthma were approached for this study. We had a good response rate of 98.2% (446/454) among approached participants. 81.3% (369/454) of pregnant asthmatic women in this study had controlled asthma. The sociodemographic factors of the participants are shown in Table 1. Majority of participants with controlled asthma (78.6%) were below 35 years with more than 80% participants being Malay. Descriptive analysis of pregnant women with controlled asthma attending primary care clinics in Malaysia reveals that the mean age of the participants was 30 years. The average gestational age at the time of booking was 11 weeks of amenorrhea (POA), and the mean gestational age during the study was 26 weeks period of amenorrhea. The above descriptive analysis is shown in Table 2. Results show a balanced distribution of smoking status among spouses, where 53% (196/369) were identified as active smokers. Most participants reported to have atopy (269/369 ,72.9%) and those with any form of comorbidities were almost two thirds of the total study participants, (263/ 369, 71,2%).**

**Table 1: Sociodemographic characteristics, clinical parameters, organizational support, knowledge, perception and practices among pregnant women with good asthma control attending primary healthcare clinics in Malaysia**

|  |  |  |
| --- | --- | --- |
|  | **N (369)** | **%** |
| **Sociodemographic** | | |
| **Age (years)**  < 35  ≥35 | 290  79 | 78.6  21.4 |
| **Ethnicity**  Malay  Chinese  Indian  Others | 301  22  38  8 | 81.6  6.0  10.3  2.1 |
| **Education**  Secondary School and below  Tertiary Education and above | 200  169 | 54.2  45.8 |
| **Occupation**  Employed  Unemployed | 217  152 | 58.8  41.2 |
| **Income per-month**  <RM3000  ≥RM3000 and above | 188  181 | 50.9  49.1 |
| **Marital status**  Married  Single | 362  7 | 98.1  1.9 |
| **Smoking status**  Smoker  Non-Smoker | 1  368 | 0.3  99.7 |
| **Spouse smoking status**  Smoker  Non-smoker | 196  173 | 53.1  46.9 |
| **History of Atopy**  Yes  No | 269  100 | 72.9  27.1 |
| **Clinical Parameters** | | |
| **Grand multipara (≥Para 5)**  Yes  No | 56  313 | 15.2  84.8 |
| **Comorbidities \***  None  One comorbid  Two comorbidities  Three comorbidities | 106  208  38  17 | 28.7  56.4  10.3  4.6 |
| **BMI (kg/m2)**  < 24.9  25-29.9  30 and above | 133  109  127 | 36.0  29.5  34.4 |
| **GDM in the current pregnancy**  Yes  No | 73  296 | 19.8  80.2 |
| **Depression PHQ-2 Screen**  Yes  No | 30  339 | 8.1  91.9 |
| **Anxiety GAD-2 Screen**  Yes  No | 14  355 | 3.8  96.2 |
| **History of Covid -19 infection**  Yes  No | 231  138 | 62.6  37.4 |
| **Vaccination Status**  Covid 19  Influenza  Covid 19 & Influenza  Not Vaccinated | 311  3  50  5 | 84.3  0.8  13.5  1.4 |
| **Correct inhaler technique**  Yes  No | 260  109 | 70.5  29.5 |
| **Able to different between ICS and SABA**  Yes  No | 298  71 | 80.8  19.2 |
| **Exacerbation-required hospital admission**  Yes  No | 20  349 | 5.4  94.6 |
| **Exacerbation-required outpatient visits other than routine antenatal care**  Yes  No | 50  319 | 13.6  86.4 |
| **Escalation of treatment during pregnancy**  Yes  No | 85  284 | 23.0  77.0 |
| **Organizational support** | | |
| **Documentation of asthma risk factor**  Yes  no | 262  107 | 71.0  29.0 |
| **Documentation of asthma control**  Yes  No | 301  68 | 81.6  18.4 |
| **Doctor**  None  Provided asthma education and counselling  Asked asthma control  Both above | 18  15  83  253 | 4.9  4.1  22.5  68.5 |
| **Nurse**  None  Provided asthma education and counselling  Asked asthma control  Both above | 43  19  96  211 | 11.7  5.1  26.0  57.2 |
| **Pharmacist**  None  Provided asthma education& counselling  Asked asthma control  Both above | 168  49  27  125 | 45.5  13.3  7.3  33.9 |
| **Inhaler usage during pregnancy**  SABA PRN  Daily ICS and PRN (MART)  Daily ICS and SABA PRN  Not using inhaler | 66  138  100  65 | 16.8  35.1  25.4  16.5 |
| **Explained on Asthma Action Plan**  Yes  No | 275  94 | 74.5  25.5 |
| **Explained on Asthma Diary**  Yes  No | 215  154 | 58.3  41.7 |
| **Referred to Primary care Physician**  Yes  No | 369  0 | 100  0 |
| **Referred to pharmacist**  Yes  No | 126  243 | 34.1  65.9 |
| **Availability of Smart Therapy**  Yes  No | 348  21 | 94.3  5.7 |
| **Patient’s knowledge of asthma during pregnancy** | | |
| **Asthma can affect baby**  Yes  No | 168  201 | 68.8  31.2 |
| **Inhaled corticosteroids are more harmful than asthma to babies than asthma**  Yes  No | 105  264 | 28.5  71.5 |
| **Uncontrolled Asthma is more harmful than inhaled corticosteroids to the baby**  Yes  No | 223  146 | 60.4  39.6 |
| **Patient’s perception of asthma control** | | |
| **Pre-pregnancy**  Controlled  Uncontrolled | 353  16 | 95.7  4.3 |
| **During pregnancy**  Controlled  Uncontrolled | 340  29 | 92.1  7.9 |
| **Patient’s practices in managing asthma during pregnancy** | | |
| I**nitiative to improve knowledge on asthma during pregnancy**  Yes  No | 297  72 | 80.5  19.5 |
| **Trigger Avoidance**  Yes  No | 334  35 | 90.5  9.5 |
| **Adherence to inhaler as prescribed**  Yes  No | 279  90 | 75.6  24.4 |
| **Monitor symptoms during pregnancy**  Yes  No | 308  61 | 83.5  16.5 |
| **Confident in using the Asthma action plan**  Yes  No | 276  93 | 74.8  25.2 |
| **Uses Asthma diary**  Yes  No | 125  244 | 33.9  66.1 |

\*Comorbidities – allergic rhinitis, gastroesophageal reflux disease, allergy

**Table 2: Descriptive statistics of pregnant women with controlled asthma attending primary healthcare clinics in Malaysia**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **Median (\*IQR)** | **Min** | **Max** |
| Age (years) | 31 (39) | 27 | 34 |
| Booking gestation (weeks) | 11 (29) | 9 | 12.5 |
| Current gestation (weeks) | 26 (30) | 20 | 31 |

\*IQR interquartile range

**Factors associated with inhaler adherence among good asthma control in pregnant women attending primary healthcare clinics by binary regression in Table 3. Although participants in this study exhibited good asthma control with treatment adherence, a substantial number still demonstrated improper inhaler technique (OR=0.77, 95% CI 0.30–0.96, p=0.041) and were unable to differentiate inhalers (OR= 0.60, CI 0.49- 0.91, p=0.006). Among all the major ethnicities, Chinese ethnicity demonstrates significantly higher odds of treatment adherence (OR=2.41, 95% CI 2.03-6.06, p=0.033) compared to Malay ethnicity. Unemployment is associated with a 70% lower likelihood of treatment adherence (OR=0.30, 95% CI 0.12-0.75, p=0.012) compared to employment.**

**Pregnant women without depression show 3.73 times higher odds of treatment adherence (OR=3.73, 95% CI 2.78-7.79, p=0.048) compared to those with depression, however anxiety was not significant in determining treatment adherence among controlled asthma (OR=0.111, CI 0.84-1.67, P=0.624. Organisational support exploring on the three major categories of health care workers, highlighted that role of pharmacist in ensuring treatment adherence is significant when referral to pharmacists for education and assessment increases odds of adherence (OR=5.82, 95% CI 1.88-11.31, p=0.031) compared to no referral. Similarly, participants with controlled asthma despite having good treatment adherence, a significant number did not receive specialist input, (OR=0.55, CI 0.33-0.70, p=<0.001)**

**Lack of explanation on the asthma action plan reduces adherence by 57% (OR=0.43, 95% CI 0.26-0.49, p<0.001) compared to explained plans. Non-use of the asthma diary is associated with a 42% decrease in adherence (OR=0.58, 95% CI 0.37-0.79, p<0.001) compared to diary users. Failure to practice trigger avoidance results in an 80% decrease in adherence (OR=0.20, 95% CI 0.05-0.79, p<0.001) compared to those who do. Lack of confidence in using the asthma action plan leads to a 58% reduction in adherence (OR=0.42, 95% CI 0.33-0.58, p<0.001) compared to confident users. Non-use of the asthma diary is associated with a 42% decrease in adherence (OR=0.58, 95% CI 0.37-0.79, p<0.001) compared to diary users.**

**Table 3:** **Binary logistic regression: Independent Factors Influencing Inhaler Adherence Among Pregnant Women with Good Asthma Control Attending Primary Healthcare Clinics in Malaysia**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **Preliminary model** | | | | **Final model** | | | |
|  | **Simple logistic regression** | | | | **Multiple logistic regression** | | | |
|  | **\*COR** | **95% CI** | | ¶**p-value** | **\*AOR** | **95% CI** | | ¶**p-value** |
|  |  | **Upper** | **Lower** |  |  | **Upper** | **Lower** |  |
| **Sociodemographic characteristics:** |  |  |  |  |  |  |  |  |
| **Age** |  |  |  |  |  |  |  |  |
| < 35 years | 1.00 |  |  |  |  |  |  |  |
| ≥ 35 years | 0.83 | 0.49 | 1.61 | 0.708 |  |  |  |  |
| **Ethnicity** |  |  |  |  |  |  |  |  |
| Malay | 1.00 |  |  |  | 1.00 |  |  |  |
| Chinese | 5.24 | 2.18 | 12.81 | **<0.001** | 4.41 | 4.92 | 21.13 | **0.033** |
| Indian | 1.28 | 0.60 | 2.81 | 0.510 | 1.13 | 0.29 | 4.34 | 0.849 |
| Others | 1.21 | 0.24 | 6.14 | 0.818 | 0.19 | 0.46 | 8.46 | 0.925 |
| **Education** |  |  |  |  |  |  |  |  |
| Secondary School and below | 1.00 |  |  |  | 1.00 |  |  |  |
| Tertiary Education and above | 1.33 | 0.82 | 2.13 | **0.245** | 1.52 | 0.67 | 3.49 | 0.506 |
| **Occupation** |  |  |  |  |  |  |  |  |
| Employed | 1.00 |  |  |  | 1.00 |  |  |  |
| Unemployed | 0.63 | 0.36 | 0.99 | **0.048** | 0.30 | 0.12 | 0.75 | **0.012** |
| **Income per month** |  |  |  |  |  |  |  |  |
| <RM3000 | 1.00 |  |  |  |  |  |  |  |
| ≥RM3000 and above | 0.83 | 0.52 | 1.34 | 0.446 |  |  |  |  |
| **Marital status**  Married  Single | 1.00  2.83 | 0.81 | 9.93 | **0.060** | 1.00  3.12 | 0.51 | 7.80 | 0.462 |
| **Spouse smoking status**  Smoker  Non-smoker | 1.00  0.65 | 0.40 | 1.05 | **0.082** | 1.00  0.57 | 0.25 | 1.31 | 0.181 |
| **History of Atopy**  Yes  No | 1.00  1.99 | 0.77 | 2.19 | 0.326 |  |  |  |  |
| **Clinical Parameters** |  |  |  |  |  |  |  |  |
| **Grand multipara (≥Para 5)**  Yes  No | 1.00  0.96 | 0.49 | 1.86 | 0.908 |  |  |  |  |
| **Comorbidities \***  None  One comorbid  Two comorbidities  Three comorbidities | 1.00  0.83  0.71  0.57 | 0.49  0.29  0.15 | 1.43  1.72  2.12 | 0.522  0.447  0.402 |  |  |  |  |
| **BMI (kg/m2)**  < 24.9  25-29.9  30 and above | 1.00  1.70  1.06 | 0.95  0.59 | 3.04  1.92 | 0.704  0.845 |  |  |  |  |
| **GDM in the current pregnancy**  Yes  No | 1.00  1.46 | 0.77 | 2.76 | **0.249** | 1.00  1.89 | 0.28 | 2.78 | 0.826 |
| **Depression PHQ-2 Screen**  Yes  No | 1.00  2.23 | 1.03 | 4.83 | **0.035** | 1.00  3.73 | 2.78 | 7.79 | **0.048** |
| **Anxiety GAD-2 Screen**  Yes  No | 1.00  2.42 | 0.82 | 7.71 | **0.111** | 1.00  1.69 | 0.84 | 1.67 | 0.624 |
| **History of Covid -19 infection**  Yes  No | 1.00  1.02 | 0.63 | 1.67 | 0.932 |  |  |  |  |
| **Vaccination Status**  Covid 19  Influenza  Covid 19 & Influenza  Not Vaccinated | 1.00  2.04  0.54  0.71 | 0.72  0.24  0.08 | 19.88  1.20  6.44 | 0.999  **0.131**  0.761 | 1.00  3.11  0.57  0.84 | 0.89  0.71  0.38 | 21.98  1.87  7.88 | 0.999  0.368  0.178 |
| **Correct inhaler technique**  Yes  No | 1.00  0.50 | 0.30 | 0.82 | **0.006** | 1.00  0.77 | 0.30 | 0.96 | **0.041** |
| **Able to different between ICS and SABA**  Yes  No | 1.00  0.47 | 1.32 | 3.98 | **0.003** | 1.00  0.60 | 1.19 | 1.41 | **0.007** |
| **Exacerbation- required hospital admission**  Yes  No | 1.00  3.03 | 0.69 | 13.64 | **0.124** | 1.00  1.41 | 0.90 | 15.28 | 0.781 |
| **Exacerbation- required outpatient visits other than routine antenatal care**  Yes  No | 1.00  1.17 | 0.57 | 2.39 | 0.672 |  |  |  |  |
| **Escalation of treatment during pregnancy**  Yes  No | 1.00  1.85 | 0.99 | 3.48 | **0.055** | 1.00  1.46 | 0.79 | 1.34 | 0.167 |
| **Organizational support** |  |  |  |  |  |  |  |  |
| **Documentation of asthma risk factor**  Yes  No | 1.00  0.58 | 0.35 | 1.97 | **0.236** | 1.00  0.26 | 0.26 | 1.68 | 0.218 |
| **Documentation of asthma control**  Yes  No | 1.00  0.44 | 0.25 | 0.77 | **0.004** | 1.00  0.77 | 0.30 | 2.16 | 0.062 |
| **Doctor**  None  Asked asthma control  Provided asthma education & counselling  Both above | 1.00  0.68  2.00  0.68 | 0.21  0.49  0.21 | 2.21  8.24  2.21 | 0.518  1.337  0.518 |  |  |  |  |
| **Nurse**  None  Asked asthma control  Provided asthma education &counselling  Both above | 1.00  0.61  1.75  0.66 | 0.21  0.33  0.24 | 1.79  3.33  1.82 | 0.365  0.939  0.416 |  |  |  |  |
| **Pharmacist**  None  Provided asthma education & counselling  Asked asthma control  Both above | 1.00  1.25  1.29  4.08 | 0.32  0.48  1.64 | 4.87  3.43  10.15 | 0.751  0.618  **0.002** | 1.00  5.20  6.32  5.82 | 0.68  0.74  1.88 | 6.88  5.47  11.31 | 0.881  0.910  **0.031** |
| **Inhaler usage during pregnancy**  SABA PRN  Daily ICS and PRN (MART)  Daily ICS and SABA PRN  Not using inhaler | 1.00  0.90  0.40  0.10 | 0.04  0.01  0.05 | 1.18  2.31  3.42 | 0.301  0.411  0.516 |  |  |  |  |
| **Explained on Asthma Action Plan**  Yes  No | 1.00  0.23 | 0.14 | 0.38 | **<0.001** | 1.00  0.43 | 0.26 | 0.49 | **<0.001** |
| **Explained on Asthma Diary**  Yes  No | 1.00  0.22 | 0.16 | 0.85 | **<0.001** | 1.00  0.70 | 0.21 | 0.95 | **<0.001** |
| **Referred to Primary care Physician**  Yes  No | 1.00  0.42 | 0.25 | 0.69 | **0.001** | 1.00  0.55 | 0.33 | 0.70 | **<0.001** |
| **Referred to pharmacist**  Yes  No | 1.00  0.36 | 0.20 | 0.65 | **0.040** | 1.00  0.71 | 0.26 | 1.93 | 0.055 |
| **Availability of Smart Therapy**  Yes  No | 1.00  0.96 | 0.34 | 2.71 | 0.949 |  |  |  |  |
| **Patient’s knowledge of asthma during pregnancy** |  |  |  |  |  |  |  |  |
| **Asthma can affect baby**  Yes  No | 1.00  0.72 | 0.44 | 1.89 | **0.196** | 1.00  0.97 | 0.68 | 2.01 | 0.501 |
| **Inhaled corticosteroids are more harmful than asthma to babies than asthma**  Yes  No | 1.00  0.79 | 0.47 | 1.32 | 0.363 |  |  |  |  |
| **Uncontrolled Asthma is more harmful than inhaled corticosteroids to the baby**  Yes  No | 1.00  1.66 | 0.47 | 2.68 | **0.038** | 1.00  1.78 | 0.53 | 3.09 | 0.074 |
| **Patient’s perception of asthma control** |  |  |  |  |  |  |  |  |
| **Pre-pregnancy**  Controlled  Uncontrolled | 1.00  1.42 | 0.39 | 5.09 | 0.593 |  |  |  |  |
| **Patient’s perception of asthma control**  **During pregnancy**  Controlled  Uncontrolled | 1.00  2.98 | 0.88 | 10.09 | **0.079** | 1.00  3.74 | 0.99 | 11.69 | 0.091 |
| **Patient’s practices in managing asthma during pregnancy** |  |  |  |  |  |  |  |  |
| I**nitiative to improve knowledge on asthma during pregnancy**  Yes  No | 1.00  0.20 | 0.11 | 0.33 | **0.031** | 1.00  0.34 | 0.44 | 0.67 | 0.061 |
| **Trigger Avoidance**  Yes  No | 1.00  0.08 | 0.04 | 0.59 | **<0.001** | 1.00  0.20 | 0.05 | 0.79 | **0.023** |
| **Monitor symptoms during pregnancy**  Yes  No | 1.00  0.19 | 0.12 | 0.34 | **0.021** | 1.00  0.49 | 0.55 | 0.74 | 0.078 |
| **Confident in using the Asthma action plan**  Yes  No | 1.00  0.21 | 0.12 | 1.35 | **<0.001** | 1.00  0.62 | 0.33 | 0.58 | **<0.001** |
| **Uses Asthma diary**  Yes  No | 1.00  0.42 | 0.26 | 0.68 | **<0.001** | 1.00  0.58 | 0.37 | 0.79 | **<0.001** |

\*Comorbidities – allergic rhinitis, gastroesophageal reflux disease, allergy

¶p-value <0.05

\*COR crude odds ratio

\*AOR adjusted odds ratio

**3.2 Discussion and Conclusion**

**Our findings from this study shows that there are factors that increase and decrease inhaler adherence among pregnant women with controlled asthma. Being not depressed and being referred to a pharmacist and primary care physician improves inhaler adherences while poor inhaler knowledge and self-management skills hinders inhaler adherences. Our study findings also reveal even among pregnant women with controlled asthma there are still presence of concern with the use of corticosteroids. This could have contributed the fraction of pregnant women who were not adherent to their inhalers.**

**Depression is a extrapulmonary treatable trait that affects asthma outcome and quality of life, it is detectable via screening questionnaire such as PHQ -2 and it is treatable (22,23). Studies showed pregnant women with poorly controlled asthma with depression were non adherent to their inhalers (24). Our findings were similar where those women with controlled and not depressed were more likely to be adherent to their inhaler. At present, treatable traits approach has been in use in tertiary hospital with the focus on patients with severe asthma (22). Our finding added that even in well controlled asthma pregnant women, these treatable traits were present. With availability of screening tools, antidepressants and psychologist services at primary care clinics, asthma care among pregnant women with controlled asthma should include screening of depression with the use of PHQ- 2 (25) and treatment to help ensure inhaler adherence to ensure a continued controlled asthma (22).**

**Our study showed despite controlled asthma, the knowledge on inhalers and self-management is still suboptimal. One of the reason could be due to the patients’ perception such as worries about the necessity of medication when symptoms are absent especially in cases with controlled asthma, worries about potential side effects of corticosteroids, influences by family and friends and poor knowledge of the importance of maintaining controlled asthma leading to inhaler non adherence (26,27) .Evidence showed that majority of patients have poor asthma self-management skills regardless of their asthma severity (28). Our study showed despite controlled asthma there is still lack of confidence in asthma self-management skills particularly in the use of asthma action plan and asthma diary. Asthma diary and asthma action plan play an integral part in tracking potential triggers, monitoring symptoms and deciding on asthma treatment (28). Therefore, there is a need for health care providers to not only provide asthma education but also to ensure that patients are empowered in their asthma self-management skills. This involves tailoring asthma self- management to suit community’s cultural norm with practical demonstrations, addressing concerns, and ongoing support by health care provider to build their confidence and self-efficacy in managing their asthma (5, 27).**

**Evidence supporting the effectiveness of pharmacist-led interventions in improving inhaler adherence is well-established globally (29, 30). Similarly, our study reaffirms the role of pharmacist in the management of pregnant women with asthma. Currently, most clinics do not have a dedicated pharmacist for asthma management. Even in clinics where a pharmacist is available, their role is primarily in the outpatient setting or during dedicated asthma clinics. In certain antenatal clinics, only an assistant pharmacist is present, and referrals to a pharmacist often require patients to visit another clinic, which can pose logistical challenges. The involvement of pharmacist in asthma care can improve outcome in asthma patients given their clinical expertise in patient management and their ability to educate patient on asthma medication, training of inhaler usage, address patients’ concern around the side effects of corticosteroids in particular in the period of pregnancy (31,32). Findings from our study suggest there is a need of pharmacist involvement that has the expertise to provide a comprehensive asthma education among pregnant women with controlled asthma.**

**Recommendation:**

All pregnant women with controlled asthma should be screen and treated for depression. A standardize evidence-based management protocol with a multidisciplinary team care that focus on asthma self-management skills and inhaler adherence among women with controlled asthma to ensure continued asthma control throughout pregnancy. Development of a pregnancy specific asthma management protocol and patient education should be considered.

**Strength and Limitations**

This study is the first to provide insight on process of care received and provided from the participants perspective and clinical audit notes. One limitation of this study is that while it includes a large sample of pregnant women with controlled asthma across Malaysia, the findings may be limited to patients attending public primary healthcare facilities. A larger sample size, including participants from private clinics and east Malaysia should be included. In addition, this study was conducted in Malay language where findings from participants who were not well verse in Malay language might not be captured. We were unable to determine whether depression was a consequence of asthma or an underlying condition coexisting with asthma in this study

**POLICY IMPLICATIONS**

The governments’ maternal health goals for managing asthma using pregnancy should focus on comprehensive policies and program that ensure the well-being of pregnant women throughout their pregnancy. We recommend the development of a standardize evidence- based management protocol with asthma checklist in managing asthma women in pregnancy targeting guideline adherence, training and education for health care providers. Measures should be taken via community-based approach to enhance asthma education particularly on the safety of inhalers, lifestyle and environmental control during pregnancy. Integrating pharmacist into antenatal care should be considered to enhance inhaler adherence and assisting in patient education and empowerment.

Ethical approval:

Ethical approval to conduct this study was obtained from the Medical Research Ethics Committee of Malaysia. (RSCH ID-23-03493) and followed current regulations on the protection of personal data where no personal data was collected from medical records.

**Consent:**

As per international standards or university standards, Participants’ written consent has been collected and preserved by the author(s).

**Disclaimer (Artificial intelligence)**

The authors hereby declare that no generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

References

1. Bravo-Solarte DC, Garcia-Guaqueta DP, Chiarella SE, editors. Asthma in pregnancy. Allergy and asthma proceedings; 2023: OceanSide Publications.

2. Hussein N, Ramli R, Liew SM, Hanafi NS, Lee PY, Cheong AT, et al. Healthcare resources, organisational support and practice in asthma in six public health clinics in Malaysia. NPJ Primary Care Respiratory Medicine. 2023;33(1):13.

3. Juniper E, Newhouse M. Effect of pregnancy on asthma: systematic review and meta-analysis. Schatz M, Zeiger R, Claman H, editors. New York: Marcel Dekker; 1993.

4. Grosso A, Locatelli F, Gini E, Albicini F, Tirelli C, Cerveri I, et al. The course of asthma during pregnancy in a recent, multicase–control study on respiratory health. Allergy, Asthma & Clinical Immunology. 2018;14:1-5.

5. Popa M, Peltecu G, Gica N, Ciobanu AM, Botezatu R, Gica C, et al. Asthma in Pregnancy. Review of Current Literature and Recommendations. Maedica-a Journal of Clinical Medicine. 2021;16(1).

6. Couillard S, Connolly C, Borg C, Pavord I. Asthma in pregnancy: an update. Obstetric Medicine. 2021;14(3):135-44.

7. Vieira AC, Pité H, Morais-Almeida M. Asthma and pregnancy in the 2020 decade: still a matter of concern. The Journal of Maternal-Fetal & Neonatal Medicine. 2022;35(25):6498-504.

8. Yilmaz I, Erkekol FO, Celen S, Karaca MZ, Aydin O, Celik G, et al. Does drug compliance change in asthmatic patients during pregnancy? Multidisciplinary Respiratory Medicine. 2013;8:1-4.

9. Enriquez R, Wu P, Griffin MR, Gebretsadik T, Shintani A, Mitchel E, et al. Cessation of asthma medication in early pregnancy. American journal of obstetrics and gynecology. 2006;195(1):149-53.

10. Schatz M, Leibman C. Inhaled corticosteroid use and outcomes in pregnancy. Annals of Allergy, Asthma & Immunology. 2005;95(3):234-8.

11. Lim AS, Stewart K, Abramson MJ, Ryan K, George J. Asthma during pregnancy: the experiences, concerns and views of pregnant women with asthma. Journal of Asthma. 2012;49(5):474-9.

12. Chambers K. Asthma education and outcomes for women of childbearing age. The Case manager. 2003;14(6):58-61.

13. Robijn AL, Jensen ME, Gibson PG, Powell H, Giles WB, Clifton VL, et al. Trends in asthma self-management skills and inhaled corticosteroid use during pregnancy and postpartum from 2004 to 2017. Journal of Asthma. 2019;56(6):594-602.

14. Abdullah K, Zhu J, Gershon A, Dell S, To T. Effect of asthma exacerbation during pregnancy in women with asthma: a population-based cohort study. European Respiratory Journal. 2020;55(2).

15. Noor Ani A UAS, Fatanah I, Baizury B, Majdah M, Fazly Azry AA, Nik Adilah S, Sarah AD, Chan YY, Aznuddin AR, Noraida MK,. Screening for perinatal depression: should we do it? Institute for Public Health, Ministry of Health Malaysia.

16. Ibrahim WH, Rasul F, Ahmad M, Bajwa AS, Alamlih LI, El Arabi AM, et al. Asthma knowledge, care, and outcome during pregnancy: The QAKCOP study. Chronic Respiratory Disease. 2018;16:1479972318767719.

17. Palmsten K, Schatz M, Chan PH, Johnson DL, Chambers CD. Validation of the pregnancy asthma control test. The Journal of Allergy and Clinical Immunology: In Practice. 2016;4(2):310-5. e1.

18. de Araujo GV, Leite DF, Rizzo JA, Sarinho ES. Asthma in pregnancy: association between the Asthma Control Test and the Global Initiative for Asthma classification and comparisons with spirometry. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2016;203:25-9.

19. Staples LG, Dear BF, Gandy M, Fogliati V, Fogliati R, Karin E, et al. Psychometric properties and clinical utility of brief measures of depression, anxiety, and general distress: The PHQ-2, GAD-2, and K-6. General hospital psychiatry. 2019;56:13-8.

20. Medicine UoVHSNI. A Patient Guide: Northridge Internal Medicine, University of Virginia, Health System; 2001.

21. Chowdhury MZI, Turin TC. Variable selection strategies and its importance in clinical prediction modelling. Family medicine and community health. 2020;8(1).

22. Gibson PG, McDonald VM, Thomas D. Treatable traits, combination inhaler therapy and the future of asthma management. Respirology. 2023;28(9):828-40.

23. Joshi E, Gibson PG, McDonald VM, Murphy VE. Treatable traits in asthma during pregnancy: a call for a shift towards a precision-based management approach. European Respiratory Review. 2023;32(170).

24. Grzeskowiak LE, Smith B, Roy A, Schubert KO, Baune BT, Dekker GA, et al. Impact of a history of maternal depression and anxiety on asthma control during pregnancy. Journal of Asthma. 2017;54(7):706-13.

25. Gigantesco A, Palumbo G, Cena L, Camoni L, Trainini A, Stefana A, et al. A Brief Depression Screening Tool for Perinatal Clinical Practice: The Performance of the PHQ‐2 Compared with the PHQ‐9. Journal of Midwifery & Women's Health. 2022;67(5):586-92.

26. Horne R, Price D, Cleland J, Costa R, Covey D, Gruffydd-Jones K, et al. Can asthma control be improved by understanding the patient's perspective? BMC pulmonary medicine. 2007;7:1-11.

27. Koh WM, Abu Bakar AI, Hussein N, Pinnock H, Liew SM, Hanafi NS, et al. Sociocultural influences on asthma self‐management in a multicultural society: a qualitative study amongst Malaysian adults. Health Expectations. 2021;24(6):2078-86.

28. Murphy VE, Gibson PG, Talbot PI, Kessell C, Clifton VL. Asthma self-management skills and the use of asthma education during pregnancy. European Respiratory Journal. 2005;26(3):435-41.

29. Bhattarai A, Shakya R, Bista D. Impact of Pharmacist-Led Intervention on Adherence to Inhalers, Inhalation Technique, and Disease Control Among Asthma/COPD Patients in a Resource Limited Center: An Interventional Study. Patient preference and adherence. 2024:1395-408.

30. Mes MA, Katzer CB, Chan AHY, Wileman V, Taylor SJC, Horne R. Pharmacists and medication adherence in asthma: a systematic review and meta-analysis. European Respiratory Journal. 2018;52(2).

31. Mehuys E, Van Bortel L, De Bolle L, Van Tongelen I, Annemans L, Remon JP, et al. Effectiveness of pharmacist intervention for asthma control improvement. European Respiratory Journal. 2008;31(4):790-9.

32. Murphy VE. Managing asthma in pregnancy. Breathe. 2015;11(4):258-67.