

Knowledge, Information Sources, and Institutional Trust of Patients Regarding Medication Use in Pregnancy: A Systematic Review

Abirami Kirubarajan; M.D.^{1,2}, Andrew Lam; M.D.¹, Amy Yu B.Sc.³, Cameron Taheri; M.D.¹, Shawn Khan; B.H.Sc.¹, Claire Sethuram; B.Sc.¹, Vikita Mehta; B.Sc.⁴, Nancy Olivieri; M.D.^{3,5}

1 Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

2 Institute of Health Policy Management and Evaluation, University of Toronto, Toronto, Ontario, Canada

3 Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

4 Arts and Sciences, McMaster University, Hamilton, Ontario, Canada

5 Division of Pediatrics, University of Toronto, Toronto, Ontario, Canada

Received March 2021; Revised and accepted June 2021

Abstract

Objective: The objective of our study is to characterize the knowledge, information sources, and institutional trust of patients regarding medication use in pregnancy.

Materials and methods: We conducted a review of three databases: MEDLINE, EMBASE, and CINAHL. We included observational studies and knowledge assessments that examined the knowledge, attitudes, beliefs or information sources of pregnant patients related to medication use during pregnancy. Extraction was completed by two independent reviewers, outcomes were summarized descriptively, and appraisal was conducted.

Results: Of the 1359 search results, 34 studies met inclusion criteria. Thus, our systematic review encompasses the beliefs of 11,757 pregnant participants. In most studies, participants described apprehension regarding potential risks to the fetus and the inadequacy of safety information. Across the 23 knowledge assessments, the majority of studies reported patient misconceptions about prescription medication in pregnancy. The most preferred information source was a healthcare provider. However, many participants expressed frustration, mistrust, and skepticism regarding physician knowledge. A common source of mistrust was due to perceived physician self-interest as well as a lack of education tailored to pregnancy. Consequently, informal sources of information were also popular.

Conclusion: There is a need to improve the health literacy and trust among pregnant patients regarding drug prescribing. There are modifiable risk factors for mistrust that require further attention.

Keywords: Health Literacy; Pregnancy; Drug Safety

Introduction

The prescription of medications during pregnancy is a controversial subject for both patients and providers.

Medications can impose significant safety risks for both the pregnant individual and their child, and thus require a high level of caution. Since the thalidomide epidemic in 1961, there have been numerous examples of uncertain prescribing practices (1, 2). In 1977, the Food and Drug Administration (FDA)

Correspondence:

Abirami Kirubarajan

Email: abi.kirubarajan@mail.utoronto.ca

Copyright © 2021 Tehran University of Medical Sciences. Published by Tehran University of Medical Sciences.



This work is licensed under a Creative Commons Attribution-Noncommercial 4.0 International license (<https://creativecommons.org/licenses/by-nc/4.0/>). Noncommercial uses of the work are permitted, provided the original work is properly cited.

banned childbearing individuals of reproductive age from participating in clinical trials (3). Though initially posed as a method to prevent teratogenic effects, many medications were consequently understudied in pregnant populations with their long-term safety unknown (3). The FDA later revised its policies, although most clinical trials continue to be biased towards a heavily male population group (4-6). In addition, many medications lack appropriate labelling regarding safety in pregnancy (7). As a result, many physicians and pharmacists feel uncomfortable in appropriately counselling pregnant patients regarding pharmaceutical use (8-10).

However, medication use by pregnant patients during the first trimester has significantly increased over the last decade. Over 50% of pregnant individuals report taking at least one medication in their first trimester, which is the most critical window for fetal development (11). Moreover, polypharmacy (i.e., the use of four or more medications) during pregnancy has more than tripled in North America (11). Self-medication is particularly common during pregnancy, with many individual's taking over-the-counter (OTC) medications during all trimesters (12, 13).

As the practice of obstetrics moves towards shared decision-making, many patients consult their own information sources and support circles regarding best practices (14, 15). In addition, many pregnant people do not trust the medical system to provide impartial answers, which may also be influenced by lobbying from the pharmaceutical industry and conflicts of interest (16-18). While there are numerous editorials and media pieces on the topic, there has not yet been a systematic review conducted on this topic assessing patient beliefs. Thus, the objective of our systematic review is to characterize the beliefs of pregnant patients regarding medication use during their pregnancy. Specifically, we aim to systematically assess pregnant patients' knowledge, information sources, and trust of the medical system

related to prescribing.

Materials and methods

This systematic review consists of a review of original, peer-reviewed published literature. It was conducted according to the standards and guidelines established in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines, in addition to the fourth edition of the Joanna Briggs Institute Reviewer's Manual (19, 20).

Search Strategy: On March 18, 2020, we conducted a systematic literature search of three academic databases: MEDLINE, EMBASE, and CINAHL. In order to maximize sensitivity, the search criteria remained broad. The search strategy is included in Appendix A. Titles published from database inception to March 18, 2020 in any language were included. We did not limit our search by country of study. Published conference posters, papers, and abstracts were not eligible for inclusion.

After searches of the databases, a hand-search of the included articles' references as well as citing articles was conducted using the Scopus database. Eligible studies were added from the hand-search via group consensus.

Inclusion Criteria: Articles were included if they reported on any group of pregnant patients; described an observational survey of knowledge, attitudes, beliefs, or information sources related to taking any medication in pregnancy; and reported on any outcome (qualitative or quantitative). Details of inclusion criteria are outlined in Table 1.

Table 1: Eligibility criteria

Subject	Criteria
Population	Any group of pregnant patients
Comparator	N/A
Outcome	Any outcome reported in the literature (qualitative or quantitative), including but not limited to: knowledge, information sources, attitudes, beliefs, and trust of the medical system

Appendix A: Search Strategy (Search Strategy for MEDLINE-Ovid: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®)

Search	Search term
1	exp Pregnancy/ or Pregnant people/ or pregnan*.ti.
2	(Knowledge* or understand* or educat* or view* or attitude* or perspective* or percept* or belief* or inform* or comfort* or trust* or literacy*).ti.
3	Health knowledge, attitudes, practice/
4	(prescri* or drug* or medicat* or pharm*).ti.
5	2 or 3
6	1 and 4 and 5

The search strategy was adapted for the other databases, EMBASE and CINAHL.

Studies were excluded if they did not describe patient beliefs, were not relevant to pregnancy, or did not report on outcomes or evaluation data. Articles related to breastfeeding and conception were also excluded. Finally, we excluded articles related to herbal remedies, supplements, vitamins, or vaccinations.

Study Selection, Extraction, and Analysis: Study selection was completed by two independent, parallel reviewers (AL, AY). Study selection was done in two separate stages: (1) title/abstract screening, followed by (2) full-text screening. Data extraction was performed by two investigators (AL, AY), with a third reviewer (AK) resolving discrepancies via consensus. Items identified via hand-search were included using a consensus-based approach between the three reviewers (AL, AY, AK).

Due to study heterogeneity, it was decided *a priori* that outcomes of all studies would be summarized descriptively.

Finally, eligible studies were assessed for risk of bias using a modified tool based on the Risk of Bias Instrument for Cross-Sectional Surveys of Attitudes and Practices. For the risk of bias assessment, articles were graded on the basis of representativeness of population, response rate, missing data, clinical sensibility, and reliability and validity of the survey instrument. For each criterion, a score of “1” indicated low risk, “2” indicated medium/unclear risk, and “3” indicated high risk. A score of 7 or lower was noted as low risk, a score of 8-10 was medium risk, and a score of 11 or higher was noted as high risk.

Results

The electronic search of the three databases yielded

1359 citations, of which 319 were duplicates and were subsequently removed. After title and abstract screening, 96 articles were eligible for full-text review. After a hand-search of relevant citations, a single article was added via consensus after translation into English. Of the 96 full-text articles identified, a total of 34 were eligible for data extraction and included in this systematic review (21-54). Results of the study screening process are shown in Figure 1.

Inter-rater agreement for study screening for titles and abstracts was 94.13% with a κ of 0.66. Inter-rater agreement for full-text database screening was 89.6% with a κ of 0.78, indicating substantial agreement.

Article Characteristics: Across the 34 included studies, there was a total sample size of 11,757 female participants (21-54). Details of the included studies are available in Appendix B.

The years of publication ranged from 1993 to 2020. The majority of included studies were conducted in Asia (n=11) or Europe (n=11), with the remainder set in Africa (n=5), North America (n=2), Australia (n=2) or South America (n=1). One study involved participants from multiple countries, while another analyzed comments online. The majority of included studies (n=32) were entirely observational study design. One netnographic study (i.e. qualitative study design that is similar to ethnography but examines digital) analyzed data from comments on an international web forum. The study design of included articles was mostly survey or questionnaire (n=28), and the remainder (n=5) were interviews or focus groups. Most of the studies (n=23) also included a knowledge assessment of the participants, in order to test their knowledge formally rather than self-assess.

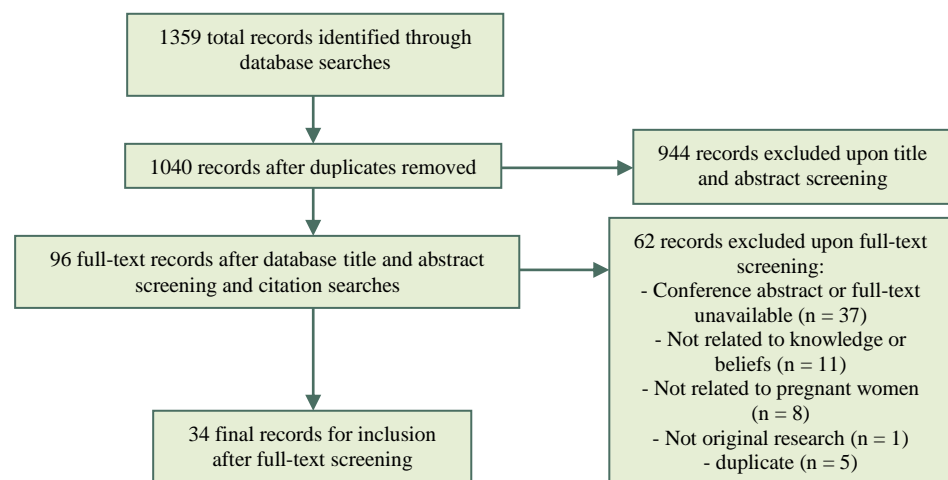


Figure 1: PRISMA Diagram showing study selection and reasons for exclusion

Appendix B: Characteristics of Included Studies (n=34)

Citation; Country	Sample size and population	Study Design	Medications Assessed	Purpose of the study
Aviv 1993; South Africa (21)	236 pregnant people	Interview	All	To determine prevalence of medication use by pregnant people in a sample population in western Cape Town
Henry 2000; Australia (22)	140 pregnant people	Interview	All	To determine sources of medication advice during pregnancy and reasons for medication uptake and cessation
Rashmi 2006; India (23)	405 pregnant people	Survey	All	To examine knowledge, attitude and practice of self-medication among pregnant people living in the city of Zabol
Damase-Michel 2009; France (24)	250 pregnant people	Survey	NSAIDs	To determine pregnant people's knowledge of drugs used for pain, evaluate perception of the risk of NSAIDs in pregnancy, and describe the sources of drug information being used by pregnant people
Nordeng 2010; Norway (25)	866 pregnant people	Survey	All	To study pregnant people's beliefs about medication and factors that determine those beliefs
Nordeng 2010; Norway (26)	866 pregnant people and 927 mothers of children <5 years old	Survey	All	To evaluate the perception of risk of 17 commonly used drugs and other substances by pregnant people; to investigate which sources of information regarding exposures during pregnancy were most commonly used by women
Antolic 2011; Slovenia (27)	259 pregnant people	Survey	All	To establish medication interest for acute, chronic, iron and preventative drug intake in a group of pregnant people
Kamuhabwa 2011; Tanzania (28)	200 pregnant people	Survey	Artemether-lumefantrine, valproate, captopril, and tetracycline	To assess the knowledge of drug dispensers and pregnant people on the harmful effects of drug use during pregnancy
Ekama 2012; Nigeria (29)	170 pregnant people	Survey	Antiretrovirals	To determine the level and factors that influence adherence to antiretroviral drugs among HIV-positive pregnant people accessing PMTCT services in Lagos, Nigeria
Kassaw 2012; Ethiopia (30)	224 pregnant people	Survey	NSAIDs	To determine the consumption pattern of NSAIDs, knowledge of drugs, perception of risk of NSAIDs, and determine the sources of drug information on risk in pregnancy
Baghianimoghadam 2013; Iran (31)	180 pregnant people	Survey	All	To determine the knowledge, attitude, and practice of pregnant people in terms of self-medication
Kureshee 2013; India (32)	501 pregnant people	Survey	All	To assess the pattern of drug utilization during pregnancy and explore the knowledge, attitude, and awareness on drug use by the antenatal mother in a tertiary care hospital setup in western India
Pons 2014; Brazil (33)	144 pregnant people	Survey, focus group	All	To analyze women's concepts and perceptions concerning teratogenic risk from medicines and exposure to radiotherapy during pregnancy, in the context of a developing country
Walton 2014; Canada (34)	40 pregnant people	Survey, interview	Antidepressants	To quantify the level of decision-making difficulty among a clinical population of depressed pregnant people recommended antidepressant medication; and to characterize barriers and facilitators of decision-making among women with moderate to high decision-making difficulty
Zaki 2014; Saudi Arabia (35)	760 pregnant people	Survey	All	To assess medication use, knowledge and beliefs about medications among pregnant people in Saudi Arabia
Norby 2015; Sweden (36)	275 pregnant people	Survey	All	To verify the results from our pilot study and to further explore potential risks in order to clarify whether the database Drugs and Birth Defects is valuable to, and could be recommended to, pregnant people
Bohio 2016; Pakistan (37)	351 pregnant people	Interview	OTC drugs	To determine the frequency, type, and motivation for self-medication with OTC medicines among pregnant people

Appendix B: Characteristics of Included Studies (n=34) (continue)

Citation; Country	Sample size and population	Study Design	Medications Assessed	Purpose of the study
Juch 2016; Europe and Australia (38)	229 pregnant people	Survey	Hypothyroid medications	To characterize women who are nonadherent to hypothyroidism treatment during pregnancy and explore the socio-demographic, lifestyle, and medical characteristics as well as their beliefs about medication
Sarani 2016; Iran (39)	350 pregnant people	Survey, interview	OTC drugs	To understand how pregnant people in Mali perceive and experience multi-drug regimens in ANC in order to reveal factors that may influence uptake and adherence
Abduelkarem 2017, United Arab Emirates (40)	140 pregnant people	Survey	OTC drugs	To explore the awareness and assessing the usage of OTC medications among pregnant people in Sharjah, UAE
Cabut 2017; France (41)	68 pregnant people	Survey	OTC drugs and medications kept in family medicine cabinet	To determine the proportion of pregnant people self-administering medication and using alternative products
Devkota 2017; Nepal (42)	229 pregnant people	Survey, counselling intervention	All	To assess the knowledge, attitude and practice (KAP) of pregnant people towards their medications, to provide counseling regarding their understanding of medication use during pregnancy and evaluate the impacts of such counseling
Raheel 2017; Saudi Arabia (43)	354 pregnant people	Survey	Antibiotics and OTC drugs	To assess the use of OTC medications by pregnant people and the associated factors associated
Byatt 2018; United States (44)	25 pregnant people and postpartum women up to 2 years	Interview	Bipolar pharmacotherapy	To identify barriers women with bipolar disorder face in accessing pharmacotherapy during pregnancy and describe potential strategies to overcome barriers
Denton 2018; International (45)	NR (1728 comments)	Other (analysis of comments on website)	Psychotropic medications	To examine the type of feedback women receive on a popular internet message board about psychotropic medication use during pregnancy
Navaro 2018; Italy (46)	503 pregnant people	Survey	All	To characterize knowledge, attitudes, and medication use during pregnancy and to investigate which characteristics are associated with these outcomes
Sinclair 2018; United Kingdom (47)	284 pregnant people and postpartum women up to 1 year	Survey	All	To assess pregnant people's Internet searching activity about medication safety, knowledge and perceptions of medication risk and willingness to take prescribed and non-prescribed medication or make online medication purchases
Sverrisdottir 2018; Iceland (48)	213 pregnant people	Questionnaire	All	To assess attitudes of drug, vitamin, mineral, fatty acid, and natural product use during pregnancy along with knowledge
Yakuwa 2018; Japan (49)	681 pregnant people	Survey, counselling intervention	All	To confirm the current state of Japanese women's perception of the teratogenic risk of medication exposure during pregnancy, and to assess the effect of counseling by Japan Drug Information Institute in Pregnancy
Kothari 2019; Australia (50)	503 pregnant people	Survey	Antidepressant and anxiolytic medications	To explore attitudes and decision-making by pregnant people regarding antidepressant and anxiolytic use during pregnancy
Wolgast 2019; Sweden (51)	850 pregnant people	Survey	All	To examine pregnant people's perception of medication use, including herbal medicines, during pregnancy and breastfeeding
Atmadani 2020; Indonesia (52)	333 pregnant people	Survey	OTC drugs	To determine the prevalence, factors influencing, and knowledge of self-medication with OTC of pregnant people
Munoz 2020; Europe (53)	1219 pregnant people or mothers of children <1 year old	Survey	Medications for chronic diseases	To assess whether medication beliefs differ between women who use or do not use medication for their somatic chronic diseases during pregnancy and whether this association varies across diseases
Searle 2020; Mali (54)	49 pregnant people	Interview, focus group	Iron supplements, sulfadoxine-pyrimethamin, and antiretroviral therapy	To evaluate the drug utilization pattern during pregnancy and to evaluate the effect of the educational and economic status

NSAIDs: non-steroidal anti-inflammatory drugs; OTC: over-the-counter

Two studies provided a counselling intervention after completion of a survey (21, 22). In the two studies, the counselling was provided either by a healthcare provider (21), or by a national drug information institute (22).

Half of the included studies (n=17) included any drug class in their assessment, while the remainder (n=17) specifically studied antidepressants (n=3), non-steroidal anti-inflammatory medications (n=2), over-the-counter medications (n=4), antiretroviral treatment (n=1), antimalarial (n=1), and chronic disease medication (n=2).

The majority of studies (n=19) stated explicitly that they did not have competing interests, while others (n=14) did not disclose any information. One study was found to have a financial conflict of interest related to authors advising pharmaceutical companies (23).

Risk of Bias Assessment: The risk of bias assessment displayed large variation, with an even spread of studies graded as low (n=13), medium (n=13), and high (n=8) risk of bias. Details of the individual Risks of Bias assessments for each included study are found in Appendix C.

Appendix C: Risk of Bias Assessment (n=34) (score of “1” indicates low risk, “2” indicates medium/unclear risk, and “3” is high risk.)

Citation; Country	1. Representative Population	2. Response Rate	3. Missing Data	4. Clinical Sensibility	5. Reliability and validity of the survey instrument
Aviv 1993; South Africa (21)	2	2	2	3	3
Henry 2000; Australia (22)	1	2	2	2	2
Rashmi 2006; India (23)	1	3	3	1	1
Damase-Michel 2009; France (24)	2	1	1	1	1
Nordeng 2010; Norway (25)	1	3	3	2	3
Nordeng 2010; Norway (26)	2	1	3	2	1
Antolic 2011; Slovenia (27)	2	1	1	1	2
Kamuhabwa 2011; Tanzania (28)	1	2	2	3	3
Ekama 2012; Nigeria (29)	2	1	1	3	3
Kassaw 2012; Ethiopia (30)	1	1	1	1	1
Baghianimoghadam 2013; Iran (31)	1	2	2	1	1
Kureshee 2013; India (32)	2	1	1	1	1
Pons 2014; Brazil (33)	1	2	2	2	2
Walton 2014; Canada (34)	2	1	2	1	1
Zaki 2014; Saudi Arabia (35)	2	1	2	1	1
Norby 2015; Sweden (36)	2	2	3	1	2
Bohio 2016; Pakistan (37)	2	2	2	3	3
Juch 2016; Europe and Australia (38)	1	1	1	1	1
Sarani 2016; Iran (39)	1	2	2	2	2
Abduelkarem 2017, United Arab Emirates (40)	1	1	1	1	1
Cabut 2017; France (41)	1	2	2	2	2
Devkota 2017; Nepal (42)	2	1	1	1	1
Raheel 2017; Saudi Arabia (43)	2	1	3	1	3
Byatt 2018; United States (44)	1	2	2	2	2
Denton 2018; International (45)	1	2	2	2	2
Navaro 2018; Italy (46)	1	1	3	1	2
Sinclair 2018; United Kingdom (47)	3	3	3	1	1
Sverrisdottir 2018; Iceland (48)	1	1	1	1	2
Yakuwa 2018; Japan (49)	2	1	3	1	3
Kothari 2019; Australia (50)	2	3	1	3	3
Wolgast 2019; Sweden (51)	1	1	1	1	1
Atmadani 2020; Indonesia (52)	1	1	1	1	1
Munoz 2020; Europe (53)	1	3	1	1	2
Searle 2020; Mali (54)	2	3	3	2	2

Knowledge and Information Sources: A total of 15 studies analyzed the self-perception of pregnant patients related to their knowledge of pharmaceutical medications. A dominant theme emerged in 14 (93.3%) of these surveys, where participants did not believe that they knew enough about pharmaceutical medication use in pregnancy or wished to learn more about the safety profiles of these medications.

The results of the 23 knowledge assessments largely found that the majority of women had information gaps regarding prescription medication, regardless of country of origin. Many women were unaware that commonly prescribed medications could be harmful to their fetus, especially if the medications were also available over-the-counter (24, 37, 52). In addition, women who were taking over-the-counter medications were more likely to incorrectly answer knowledge-based questions (52). In one study, some women also had the misconception that the second and third trimesters are the most important for fetal development and carry the greatest risk of teratogenicity (40), however, another survey noted high knowledge of the fact that the first trimester is the most significant (35). One study noted the misconception that 4.39% of women believed that all medications are safe in pregnancy (32).

Knowledge related to teratogenicity significantly increased after counselling in both interventional studies (42, 49). Devkota et al (2017) noted that this knowledge translated into changes in practice, as women significantly decreased their self-medication, inquired about medication safety, and adhered to safety guidelines (42). In addition, Yakuwa et al (2018) noted that pregnant people were more likely to continue their medication use once adequately counselled regarding medication teratogenicity and addressing misconceptions (49).

The studies also reported on the numerous information sources regarding medication use during pregnancy that were accessed by the pregnant people. Details of these information sources are included in

Table 2. The most commonly cited sources were drug stores or formal healthcare providers, including general practitioners, obstetricians, midwives, and pharmacists (21, 24, 35-37, 41, 43, 46, 50). Others used the guidance of their friends and family (21, 24, 33, 43, 50). The internet (26, 33, 36, 43, 45, 47, 48, 50) and magazines (21, 50) were other information sources accessed by this population. Health service websites and telephone advisory services were rated to be highly trustworthy and helpful (45, 47). Information provided directly from pharmaceutical companies was also used, including package inserts (33) and product leaflets (26, 35, 43, 51).

Five studies noted that patients believed there was insufficient information provided by physicians (33-35, 38, 50, 38). One study found that even when patient education was provided, patients sometimes had difficulty understanding the information, which they found unclear (50). Zaki (2014) reported that patients relied on pamphlets or brochures to receive information as a direct result of the lack of information given by providers (35). Another study noted that pregnant people chose to take medication sparingly due to the lack of available safety information (53).

Attitudes and Trust of Providers: In most of the observational studies (n=22, 69%), patients were afraid of adverse effects of medications on the fetus. Despite most studies discussing that patients wanted additional information, one study noted that more information about potential effects of medications made women feel more anxious (36). Walton (2014) reported that women felt reassured if the clinic frequently treated pregnant people (34). In one study, women's beliefs about the prescribed medication was found to be the most important determinant of medication adherence to prescription (38). Finally, one study found that concerns related to adverse effects during pregnancy resulted in women refraining from taking necessary medication (e.g., for epilepsy) or medication that was strongly recommended by their physician (51).

Table 2: Information sources of pregnant people

Information Sources (ordered from most to least frequently mentioned)	Studies
Healthcare providers, including physicians and midwives	Avviv 1993, Bohio 2016, Cabut 2017, Damase-Michel 2009, Kothari 2019, Navaro 2018, Norby 2015, Raheel 2017, Zaki 2014, Sverrisdóttir 2019
Internet, including health service websites	Denton 2018, Kothari 2019, Navaro 2018, Norby 2015, Pons 2014, Raheel 2017, Sinclair 2018, Sverrisdóttir 2019
Friends and family	Aviv 1993, Damase-Michel 2009, Kothari 2019, Pons 2014, Raheel 2017
Information from pharmaceutical companies, including package inserts and product leaflets	Pons 2014, Nordeng 2010, Raheel 2017, Wolgast 2019, Zaki 2014
Drug stores, pharmacies	Bohio 2016, Nordeng 2010B, Pons 2014
Telephone advisory services	Henry 2000

Table 3: Reasons for mistrust of physicians

Reasons for Mistrust	Studies
Perception that physicians overly prescribe medications	Nordeng 2010B, Antolic 2011
Concern of self-interest of physicians	Damase-Michel 2009
Lack of time spent with patients	Nordeng 2010B
Lack of consensus among physicians	Pons 2014, Bohio 2016

A total of fifteen studies measured the trust of pregnant people towards prescribing practices of physicians. There were contrasting results, as eight studies (53.3%) reported that patients trust their physician, while the remaining seven studies (46.7%) described patients' skepticism and apprehension. In one study, the participants noted that they would not take a medication during pregnancy without explicitly being told to do so by their physician (44). This is consistent with other studies in which participants noted that their preferred source of information was healthcare providers (22, 51). However, in six studies, participants outlined reasons they mistrust physicians regarding medication use during pregnancy (Table 3).

For example, in two studies, participants believed that physicians were not vigilant enough regarding safety, and that physicians were too trusting of external sources of information (21, 29).

Furthermore, two studied groups believed that physicians were too quick to prescribe medication during pregnancy (26, 27). There was a concern among pregnant patients of physicians primarily considering their own self-interests, with one participant noting "doctors want to avoid any risk to themselves" (24). One study noted that over 70% of women agreed that if physicians spent more time with patients, they would not prescribe as many medications (26). In particular, two studies noted that patients were concerned when physicians from different specialties had contrasting opinions and could not reach consensus (33, 37).

Discussion

Our systematic review assessed the knowledge, information sources, and beliefs of 11,757 participants represented in 34 studies. The majority of studies were observational in nature and aimed to assess the comfort levels regarding medication use during pregnancy. Many participants described apprehension regarding potential risks to the fetus and safety information. In all studied countries, there were notable knowledge gaps among patients regarding teratogenicity and potential side effects. The most preferred source of information was a

physician or healthcare provider. However, many participants self-reported frustration and skepticism regarding physician knowledge. Reasons for mistrust included the lack of consensus between different providers, the lack of available information, and potential self-interest of physicians. As such, internet sources and support circles were also highly valued. Moreover, the counselling interventions evaluated in two studies were effective in significantly increasing patient knowledge.

This systematic study is particularly relevant due to the increased use of medications during pregnancy. There are several reasons for this phenomenon. Firstly, cultural attitudes may have been influenced by the increasingly medicalized practice of pregnancy in North America and Europe (5557). In addition, the average maternal age has been increasing, and older individuals are more likely to require prescription medication than younger individuals (58, 59). The incidence of gestational diabetes has also increased, due to changes in screening guidelines as well as the rising rate of obesity, necessitating that more women are placed on medication (60, 61).

It is important to highlight that the expansion of the pharmaceutical industry may also be a reason for this growth (62). There is a large market for medications that reduce side effects related to pregnancy, such as morning sickness, as well as antidepressants and anxiolytics (63, 64). Both pregnant people and their providers are faced with advertisements related to prescription medication, which may contain biased and incomplete information (65). Many of these advertisements exist on social media or come directly from celebrities. In our systematic review, we found that many participants obtained safety information directly from drug packaging, even though this information is often inconsistently labelled. Physicians, including obstetricians and gynecologists, may also receive financial incentives and samples from pharmaceutical representatives and may not adequately disclose these conflicts of interest (66, 67). For this reason, it is not surprising that many participants described feelings of mistrust in the medical system. One of the potential consequences of

this mistrust is the increasing prevalence of home births, complementary herbal remedies, and unassisted births (68-70). Many participants are wary of the medicalization of pregnancy and are increasingly preferring non-medical options for their care. As such, there is increasing pressure on physicians to disclose financial conflicts of interest and avoid relationships with pharmaceutical industries, in order to regain public trust for various aspects of medical care extending beyond prescribing.

Our systematic review aligns well with the current literature base. Overall, there is a lack of health literacy among all patient groups regarding both over-the-counter and prescription medications (71, 72). Patients often lack an understanding of side effects related to medication use, particularly overuse, and many patients experience unnecessary polypharmacy (73, 74). This tends to be an issue when healthcare providers are rushed for time (75, 76). Direct-to-consumer advertisements are also linked to misinformation among patients (77, 78). There is increasing interest to improve health literacy among all patients, including prescribing clinics, counselling activities, and impartial education sources (79-81). These interventions may be particularly useful in pregnant populations and warrant future study.

Strengths of this systematic review include the rigorous and broad scope of the search of three databases. To our knowledge, ours is the first review to examine the beliefs of patients regarding medication use during pregnancy, and with a total patient population of 11,757 pregnant people worldwide. There were no exclusions based on country of origin, language of study, or studied drug class, which allowed for a comprehensive understanding of the current literature. In addition, our two reviewers had strong inter-rater reliability and agreement. All abstracts and full-texts were screened by two independent reviewers in parallel, which minimized the risk of excluding relevant studies. Limitations of our review include the heterogeneous nature of the literature, which precluded the ability to perform a meta-analysis. In addition, most studies did not use well-validated questionnaires in their methodology, and thus the studies are not easily comparable.

Ultimately, further research is required to understand which interventions are most beneficial in counselling pregnant patients. Based on the findings of our systematic review, we recommend that physicians take additional time with pregnant patients to improve

appropriate counselling. Physicians should avoid advertisements and marketing in their decision-making, and instead rely on impartial and transparent sources of information. We also recommend that patients' informal sources of information, such as social support circles and online forums, be investigated in order to determine their quality and accuracy. Finally, we encourage initiatives to ethically include childbearing individuals, particularly pregnant people, in clinical trials. Inclusive research is required to properly advise patients about both maternal and fetal risks of medication use during pregnancy.

Conclusion

In conclusion, the evidence from this systematic review suggests that there are numerous knowledge gaps for patients regarding medication use in pregnancy. There was a common theme of fear of teratogenicity in all studied countries. While many pregnant patients prefer physicians to be their source of information, others do not trust the medical system to provide the most accurate recommendations. Further research is required to improve health literacy and trust among pregnant patients, as well as improve safety-related information.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

None.

References

1. Vargesson N. Thalidomide- induced teratogenesis: History and mechanisms. *Birth Defects Res C Embryo Today* 2015; 105: 140-56.
2. Potts JM, Nelson-Piercy C. Prescribing in pregnancy. *Obstetrics, Gynaecology & Reproductive Medicine* 2013; 23: 137-45
3. Sherman LA, Temple R, Merkatz RB. Women in clinical trials: an FDA perspective. *Science* 1995; 269: 793-5.
4. Holdcroft A. Gender bias in research: how does it affect evidence based medicine?. *J R Soc Med* 2007; 100: 2-3.
5. Meinert CL, Gilpin AK. Estimation of gender bias in clinical trials. *Stat Med* 2001; 20: 1153-64.
6. Shields KE, Lysterly AD. Exclusion of pregnant people from industry-sponsored clinical trials. *Obstet Gynecol* 2013; 122: 1077-81.

7. Mazer-Amirshahi M, Samiee-Zafarghandy S, Gray G, van den Anker JN. Trends in pregnancy labeling and data quality for US-approved pharmaceuticals. *Am J Obstet Gynecol* 2014; 211: 690-e1.
8. Bakkebø T, Widnes SF, Aamlid SS, Schjøtt J. Physicians' perception of teratogenic risk and confidence in prescribing drugs in pregnancy— influence of Norwegian drug information centers. *Clin Ther* 2016; 38: 1102-8.
9. Baldon JP, Correr CJ, Melchior AC, Rossignoli P, Fernandez-Llimos F, Pontarolo R. Community pharmacists' attitudes and knowledge on dispensing drugs to pregnant people. *Pharm Pract* 2006; 4: 38-43.
10. Hutchinson S, Mitchell K, Hansford D, Stewart D. Community pharmacists' views and experiences of counter- prescribing in pregnancy. *Int J Pharm Pract* 2001; 9: 15-21.
11. Mitchell AA, Gilboa SM, Werler MM, Kelley KE, Louik C, Hernández-Díaz S, et al. Medication use during pregnancy, with particular focus on prescription drugs: 1976-2008. *Am J Obstet Gynecol* 2011; 205: 51-e1-8.
12. Werler MM, Mitchell AA, Hernandez-Diaz S, Honein MA. Use of over-the-counter medications during pregnancy. *Am J Obstet Gynecol* 2005; 193: 771-7.
13. Tillett J, Kostich LM, VandeVusse L. Use of over-the-counter medications during pregnancy. *J Perinat Neonatal Nurs* 2003; 17: 3-18.
14. Tucker Edmonds B. Shared decision-making and decision support: their role in obstetrics and gynecology. *Curr Opin Obstet Gynecol* 2014; 26: 523-30.
15. Say R, Robson S, Thomson R. Helping pregnant people make better decisions: a systematic review of the benefits of patient decision aids in obstetrics. *BMJ Open* 2011; 1: e000261.
16. Prather C, Fuller TR, Marshall KJ, Jeffries WL. The impact of racism on the sexual and reproductive health of African American women. *J Womens Health (Larchmt)* 2016; 25: 664-71.
17. Grande D, Shea JA, Armstrong K. Pharmaceutical industry gifts to physicians: patient beliefs and trust in physicians and the health care system. *J Gen Intern Med* 2012; 27: 274-9.
18. Boucher D, Bennett C, McFarlin B, Freeze R. Staying home to give birth: why women in the United States choose home birth. *J Midwifery Womens Health* 2009; 54: 119-26.
19. Moher D, Liberati A, Tetzlaff J, Altman DG, Prisma Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; 6: e1000097.
20. Peters MD, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. *Int J Evid Based Healthc* 2015; 13:141-6.
21. Aviv RI, Chubb K, Lindow SW. The prevalence of maternal medication ingestion in the antenatal period. *S Afr Med J* 1993; 83: 657-60.
22. Henry A, Crowther C. Sources of advice on medication use in pregnancy and reasons for medication uptake and cessation during pregnancy. *Aust N Z J Obstet Gynaecol* 2000; 40: 173-5.
23. Sharma R, Kapoor B, Verma U. Drug utilization pattern during pregnancy in North India. *Indian J Med Sci* 2006; 60: 277-87.
24. Damase- Michel C, Christaud J, Berrebi A, Lacroix I, Montastruc JL. What do pregnant people know about non- steroidal anti- inflammatory drugs? *Pharmacoepidemiol Drug Saf* 2009; 18: 1034-8.
25. Nordeng H, Koren G, Einarson A. Pregnant people's beliefs about medications-a study among 866 Norwegian women. *Ann Pharmacother* 2010; 44: 1478-84.
26. Nordeng H, Ystrøm E, Einarson A. Perception of risk regarding the use of medications and other exposures during pregnancy. *Eur J Clin Pharmacol* 2010; 66: 207-14.
27. Antolič R, Polič M, Stanovnik L, Antolič ŽN. Medication interest in pregnant people. *Zdravniški vestnik* 2011; 80: 897-904.
28. Kamuhabwa A, Jalal R. Drug use in pregnancy: Knowledge of drug dispensers and pregnant people in Dar es Salaam, Tanzania. *Indian J Pharmacol* 2011; 43: 345-9.
29. Ekama SO, Herbertson EC, Addeh EJ, Gab-Okafor CV, Onwujekwe DI, Tayo F, et al. Pattern and determinants of antiretroviral drug adherence among Nigerian pregnant people. *J Pregnancy* 2012; 2012: 851810.
30. Kassaw C, Wabe NT. Pregnant people and non-steroidal anti-inflammatory drugs: knowledge, perception and drug consumption pattern during pregnancy in Ethiopia. *N Am J Med Sci* 2012; 4: 72-6.
31. Baghianimoghadam MH, Mojahed S, Baghianimoghadam M, Yousefi N, Zolghadr R. Attitude and practice of pregnant women regarding self-medication in Yazd, Iran. *Arch Iran Med* 2013; 16: 580-3.
32. Kureshee NI, Dhande PP. Awareness of mothers and doctors about drug utilization pattern for illnesses encountered during pregnancy. *J Clin Diagn Res* 2013; 7: 2470-4.
33. Pons Eda S, Pizzol Tda S, Knauth DR. Perceptions by pregnant and childbearing-age women in southern Brazil towards teratogenic risk from medicines and

- radiotherapy. *Cad Saude Publica* 2014; 30: 1965-76.
34. Walton GD, Ross LE, Stewart DE, Grigoriadis S, Dennis CL, Vigod S. Decisional conflict among women considering antidepressant medication use in pregnancy. *Arch Womens Ment Health* 2014; 17: 493-501.
 35. Zaki NM, Albarraq AA. Use, attitudes and knowledge of medications among pregnant people: A Saudi study. *Saudi Pharm J* 2014; 22: 419-28.
 36. Nörby U, Källén K, Shemeikka T, Korkmaz S, Winbladh B. Pregnant people's view on the Swedish internet resource Drugs and Birth Defects intended for health care professionals. *Acta Obstet Gynecol Scand* 2015; 94: 960-8.
 37. Bohio R, Brohi ZP, Bohio F. Utilization of over the counter medication among pregnant people; a cross-sectional study conducted at Isra University Hospital, Hyderabad. *J Pak Med Assoc* 2016; 66: 68-71.
 38. Juch H, Lupattelli A, Ystrom E, Verheyen S, Nordeng H. Medication adherence among pregnant people with hypothyroidism—missed opportunities to improve reproductive health? A cross-sectional, web-based study. *Patient Educ Couns* 2016; 99: 1699-707.
 39. Sarani M, Saravani S. Knowledge, attitude and practice of self-medication among pregnant people in the city of zabol. *International Journal of Pharmacy & Technology* 2016; 8: 21588-99.
 40. Abdulqareem AR, Mustafa H. Use of over-the-counter medication among pregnant people in Sharjah, United Arab Emirates. *J Pregnancy* 2017; 2017: 4503793.
 41. Cabut S, Marie C, Vendittelli F, Sauvart-Rochat MP. Intended and actual use of self-medication and alternative products during pregnancy by French women. *J Gynecol Obstet Hum Reprod* 2017; 46: 167-73.
 42. Devkota R, Khan GM, Alam K, Sapkota B, Devkota D. Impacts of counseling on knowledge, attitude and practice of medication use during pregnancy. *BMC Pregnancy Childbirth* 2017; 17: 131.
 43. Raheel H, Alsakran S, Alghamdi A, Ajarem M, Alsulami S, Mahmood A. Antibiotics and over the counter medication use and its correlates among Arab pregnant people visiting a tertiary care hospital in Riyadh, Saudi Arabia. *Pak J Med Sci* 2017; 33: 452-6.
 44. Byatt N, Cox L, Moore Simas TA, Biebel K, Sankaran P, Swartz HA, et al. Access to Pharmacotherapy Amongst Women with Bipolar Disorder during Pregnancy: a Preliminary Study. *Psychiatr Q* 2018; 89: 183-90.
 45. Denton LK, Creeley CE, Stavola B, Hall K, Foltz BD. An analysis of online pregnancy message boards: Mother-to-mother advice on medication use. *Women Birth* 2020; 33: e48-e58.
 46. Navaro M, Vezzosi L, Santagati G, Angelillo IF, Collaborative Working Group. Knowledge, attitudes, and practice regarding medication use in pregnant people in Southern Italy. *PloS One* 2018; 13: e0198618.
 47. Sinclair M, Lagan BM, Dolk H, McCullough JEM. An assessment of pregnant people's knowledge and use of the Internet for medication safety information and purchase. *J Adv Nurs* 2018; 74: 137-47.
 48. Sverrisdóttir U, Jónsdóttir F, Gunnarsdóttir AI, Harðardóttir H, Bjarnadóttir RI. Use of medication, supplements and natural products during pregnancy. *Laeknabladid* 2019; 105: 11-6.
 49. Yakuwa N, Nakajima K, Koinuma S, Goto M, Suzuki T, Ito N, et al. Perception of pregnant Japanese women regarding the teratogenic risk of medication exposure during pregnancy and the effect of counseling through the Japan drug information institute in pregnancy. *Reprod Toxicol* 2018; 79: 66-71.
 50. Kothari A, de Laat J, Dulhunty JM, Bruxner G. Perceptions of pregnant people regarding antidepressant and anxiolytic medication use during pregnancy. *Australas Psychiatry* 2019; 27: 117-20.
 51. Wolgast E, Lindh- Åstrand L, Lilliecreutz C. Women's perceptions of medication use during pregnancy and breastfeeding—A Swedish cross-sectional questionnaire study. *Acta Obstet Gynecol Scand* 2019; 98: 856-64.
 52. Atmadani RN, Nkoka O, Yunita SL, Chen YH. Self-medication and knowledge among pregnant people attending primary healthcare services in Malang, Indonesia: a cross-sectional study. *BMC Pregnancy Childbirth* 2020; 20: 42.
 53. Munoz SR, Lupattelli A, de Vries ST, Mol PG, Nordeng H. Differences in medication beliefs between pregnant people using medication, or not, for chronic diseases: a cross-sectional, multinational, web-based study. *BMJ Open* 2020; 10: e034529.
 54. Searle AR, Hurley EA, Doumbia SO, Winch PJ. “They Merely Prescribe and I Merely Swallow”: Perceptions of Antenatal Pharmaceuticals and Nutritional Supplements Among Pregnant people in Bamako, Mali. *Matern Child Health J* 2020; 24: 110-20.
 55. Araújo DD, Leal MM, Santos EJ, Leal LB. Consumption of medicines in high-risk pregnancy: evaluation of determinants related to the use of prescription drugs and self-medication. *Brazilian Journal of Pharmaceutical Science* 2013; 49: 491-9.
 56. Parry DC. “We wanted a birth experience, not a medical experience”: exploring Canadian women's use of midwifery. *Health Care Women Int* 2008; 29: 784-806.
 57. Shaw JC. The medicalization of birth and midwifery as resistance. *Health Care Women Int* 2013; 34: 522-36.

58. Ziadeh S, Yahaya A. Pregnancy outcome at age 40 and older. *Arch Gynecol Obstet* 2001; 265: 30-3.
59. Mills, TA, Lavender T. Advanced maternal age. *Obstet Gynaecol Reprod Med* 2011; 21: 107-11
60. Ferrara A, Kahn HS, Quesenberry CP, Riley C, Hedderson MM. An increase in the incidence of gestational diabetes mellitus: Northern California, 1991–2000. *Obstet Gynecol* 2004; 103: 526-33.
61. Ferraiolo A, Bordone C, Ramone A, Sala P, Gorlero F, Gustavino C, et al. Universal versus risk factor screening for gestational diabetes mellitus. *Clinical and Experimental Obstetrics & Gynecology* 2018; 45: 53-7.
62. Sufrin CB, Ross JS. Pharmaceutical industry marketing: Understanding its impact on women's health. *Obstet Gynecol Surv* 2008; 63: 585-96.
63. Badell ML, Ramin SM, Smith JA. Treatment options for nausea and vomiting during pregnancy. *Pharmacotherapy* 2006; 26: 1273-87.
64. Cooper WO, Willy ME, Pont SJ, Ray WA. Increasing use of antidepressants in pregnancy. *Am J Obstet Gynecol* 2007; 196: 544.e1-5.
65. Korenstein D, Keyhani S, Mendelson A, Ross JS. Adherence of pharmaceutical advertisements in medical journals to FDA guidelines and content for safe prescribing. *PLoS One* 2011; 6: e23336.
66. Taheri C, Kirubarajan A, Li X, Lam ACL, Taheri S, Olivieri NF. Discrepancies in self-reported financial conflicts of interest disclosures by physicians: a systematic review. *BMJ Open* 2021; 11: e045306.
67. Muffly TM, Giamberardino WL, Guido J, Weterings R, Bastow B, Sheeder J. Industry payments to obstetricians and gynecologists under the Sunshine Act. *Obstet Gynecol* 2018; 132: 9-17.
68. Dahlen HG, Jackson M, Stevens J. Homebirth, freebirth and doulas: casualty and consequences of a broken maternity system. *Women Birth* 2011; 24: 47-50.
69. Benyamini Y, Molcho ML, Dan U, Gozlan M, Preis H. Women's attitudes towards the medicalization of childbirth and their associations with planned and actual modes of birth. *Women Birth* 2017; 30: 424-30.
70. Brubaker SJ, Dillaway HE. Medicalization, natural childbirth and birthing experiences. *Sociology Compass* 2009; 3: 31-48.
71. Berkman ND, Sheridan SL, Donahue KE, Halpern DJ, Crotty K. Low health literacy and health outcomes: an updated systematic review. *Ann Intern Med* 2011; 155: 97-107.
72. Mullan J, Weston KM, Bonney A, Burns P, Mullan J, Rudd R. Consumer knowledge about over-the-counter NSAIDs: they don't know what they don't know. *Aust N Z J Public Health* 2017; 41: 210-4.
73. Lyles A, Culver N, Ivester J, Potter T. Effects of health literacy and polypharmacy on medication adherence. *Consult Pharm* 2013; 28: 793-9.
74. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. *Am J Geriatr Pharmacother* 2007; 5: 345-51.
75. Davidson W, Molloy DW, Somers G, Bedard M. Relation between physician characteristics and prescribing for elderly people in New Brunswick. *CMAJ* 1994; 150: 917–21.
76. Tamblyn R, Berkson L, Dauphinee WD, Gayton D, Grad R, Huang A, et al. Unnecessary prescribing of NSAIDs and the management of NSAID-related gastropathy in medical practice. *Ann Intern Med* 1997; 127: 429–38.
77. Gilbody S, Wilson P, Watt I. Benefits and harms of direct to consumer advertising: a systematic review. *Qual Saf Health Care* 2005; 14: 246-50.
78. Ventola CL. Direct-to-consumer pharmaceutical advertising: therapeutic or toxic? *P T* 2011; 36: 669-84.
79. Mudge A, Radnedge K, Kasper K, Mullins R, Adsett J, Rofail S, et al. Effects of a pilot multidisciplinary clinic for frequent attending elderly patients on deprescribing. *Aust Health Rev* 2016; 40: 86-91.
80. Taggart J, Williams A, Dennis S, Newall A, Shortus T, Zwar N, et al. A systematic review of interventions in primary care to improve health literacy for chronic disease behavioral risk factors. *BMC Fam Pract* 2012; 13: 49.
81. Collins S, Barber A, Sahn LJ. Pharmacist's counselling improves patient knowledge regarding warfarin, irrespective of health literacy level. *Pharmacy* 2014; 2: 114-23.

Citation: Kirubarajan A, Lam A, Yu A, Taheri C, Khan S, Sethuram C, et al. **Knowledge, Information Sources, and Institutional Trust of Patients Regarding Medication Use in Pregnancy: A Systematic Review.** *J Family Reprod Health* 2021; 15(3): 160-71.