

Prescribing antidepressants and anxiolytic medications to pregnant women: The perception of risk of foetal teratogenicity amongst Australian specialists and trainees

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Abstract

Background: The decision of whether to prescribe antidepressants (AD) and anxiolytics (AX) to pregnant women is complex, with serious potential ramifications. Clinicians' perception of the risk of teratogenicity significantly influences their prescribing decisions and in turn impacts maternal decision making. Our study sought to discern differences in perceived risk between Obstetricians and Gynaecologists (O&Gs) and General Practitioners (GPs) when prescribing these medications in pregnancy. Furthermore, we investigated factors impacting perception, clinicians' willingness to prescribe and their approach to provision of patient information.

Methods: This study was conducted via a nation-wide online SurveyMonkey extended to Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) database-derived affiliates: GP diplomates, fellows and trainees (5409 survey invitations: 545 respondents). Descriptive statistics were used to present responses for clinicians overall and separately for GPs and O&Gs.

Results: GPs reported higher rates of being aware of up-to-date medication prescription recommendations (57.6%) compared with O&Gs (44.2%). GPs also reported higher rates of training adequacy in psychotropic prescription (56.1% versus 29.0%). There was evidence to suggest GPs level of confidence in knowledge base, initiation and prescription of antidepressants and anxiolytics was higher than those of O&Gs. The mean perception of patient non-compliance was similar between clinician groups (approximately 35%), but GPs perceived the extent of patient anxiety as higher (mean 73.7% (SD 21.3) compared to O&Gs (mean 63.1% (SD 24.1))). Both groups showed a strong preference for improved training rather than patient-focused technology (above 70% for both groups).

Conclusion: Further development of clinician training in perinatal psychotropic prescription is warranted. **Keywords :** psychotropics, teratogenicity, pregnant, prescribing, foetal, perception

Background

Depression and anxiety are common disorders however their occurrence during pregnancy has the potential to significantly impact the health and wellbeing of both mother and child [1, 2]. Negative

outcomes include a variety of serious complications. Inadequately treated depression is associated with a significant risk of morbidity and mortality (suicide being the second largest cause of indirect maternal mortality in the perinatal period in Australian women) [1].

Unclear messages contribute to pregnant women being reluctant to take psychotropic medication, including antidepressants and anxiolytics [3-6] with many fearing foetal harm and seeking guidance outside the orthodox medical realm. Medical personnel including O&Gs and GPs form an important part of a pregnant woman's network of information sources during pregnancy and can impact patient decision-making around medications in pregnancy [5-7]. The Australian clinicians' own perception of teratogenicity of antidepressants (AD) and anxiolytics (AX) may influence counselling and care of vulnerable women and is largely unexplored. It is, however, likely to align with the international community where perceived teratogenicity is overestimated by physicians of all medical specialties, except psychiatrists [8-10].

Professional bodies such as the RANZCOG publish statements and recommendations to provide advice on management of perinatal anxiety and depression, serious mental illness and bipolar disorder. The target audience is all health professionals who are engaged in providing maternity and mental health care to these patients [11].

This study hypothesised that differences exist in the perception of risk of teratogenicity of AD and AX medication commonly prescribed to pregnant women, by differing clinicians, namely O&Gs and GPs. It also explored medication counselling and prescription practices, clinician resources and base knowledge of risk of AD and AX when used in pregnancy.

Methods

Setting and participants

Utilising the RANZCOG database, current Obstetrics and Gynaecology fellows, trainees and GP diplomats were invited to participate in a nation-wide cross-sectional observational study of practices relating to prescription of AD and AX in pregnancy and provided a link to an anonymous ten-minute online questionnaire (www.surveymonkey.com). Participation was voluntary and consent was implied with completion of the questionnaire and responses de-identified. GP affiliates from New Zealand

were virtually unrepresented, as they do not undertake the Diploma and were therefore not captured by this survey.

Survey instruments

Our questionnaire (attachment 1) was developed after researching questionnaire design and a directed literature search. Feedback was obtained from professional peers on the content and relevance of questions. A small pilot group of doctors (n = 10) tested the coherence of the questions, and time frame to complete the questionnaire. The 34 questions were designed to elicit clinician attitudes about AD and AX prescription AD and AX medication counselling practice, perceptions of level of patient concern regarding AD and AX use in pregnancy and the risk perceptions of the stakeholders who influenced a pregnant woman's decision making. Demographic data was collected about the clinicians aligned specialty including their proportion of public and private practice, age, training, experience, interest in mental health and educational exposure. Clinician confidence in prescribing, managing adherence issues and perceived adequacy of training to manage depression and anxiety in pregnancy were surveyed. Questions relating to attitudes and confidence were measured using Likert scales. Similar to other published literature, we included a series of questions to gauge basic AD and AX knowledge [2].

Survey administration

A reminder email was sent out by the RANZCOG, four weeks after the initial invitation, reminding clinicians of the survey closure date.

Statistical analysis

All data was analysed using the SPSS version 23. Data was summarised for clinicians overall and separately for GPs and O&Gs, as frequency and percentage for categorical responses and by mean and standard deviation for the continuous responses. To aid with interpretation of the questionnaire results, the following collapse of the Likert scale was made for Questions 21, 24 and 34: Agree = agree, strongly agree and Disagree = Strongly disagree, disagree and neutral.

Results

Overall, the RANZCOG database identified 5409 eligible clinicians, all of whom received a standardised invitation email. This comprised of 2120 Fellows, 769 FRANZCOG trainees and 2520

Diplomates. A total of 545 valid responses were received and submitted for analysis (10.1%), less than the predicted response rate for medical personnel (32.8%) [12]. The response rate for O&G affiliates (12.9%) was consistent with gynaecologist rates from a similar risk perception study by Csajka et al (13%) [2]. The response rate for GP affiliates was 6.8%.

Demographics

Three hundred and seventy-three clinicians aligned with RANZCOG (68.4%) and 172 aligned with RACGP (31.6%). 97.8% of the clinicians saw pregnant women regularly in their clinical practice, with similar proportions of O&Gs (97.3%) and GPs (98.8%). More than half of the responders in both groups were 50 years or younger but there was a higher proportion of responders 61 and above year-old amongst O&Gs (15.6%) compared to GPs (6.4%). The demographic characteristics of the respondents are shown in Table 1.

Table 1
Comparison of survey respondent demographics by clinical affiliation

Question	Overall (n (%), n = 545)	Obstetrician Gynaecologist (n (%), n = 373)	General Practitioner (n (%), n = 172)
Age (years, n = 543)			
23 to 30	47 (8.7%)	34 (9.2%)	13 (7.6%)
31 to 40	182 (33.5%)	121 (32.6%)	61 (35.5%)
41 to 50	116 (21.4%)	81 (21.8%)	35 (20.3%)
51 to 60	129 (23.8%)	77 (20.8%)	52 (30.2%)
61 or above	69 (12.7%)	58 (15.6%)	11 (6.4%)
Years in specialty (including training) (n = 542)			
<10	212 (39.1%)	142 (38.4%)	70 (40.7%)
10 or more	330 (60.9%)	228 (61.6%)	102 (59.3%)
Where was medical student training completed? (n = 541)			
Australia	391 (72.3%)	244 (65.9%)	147 (86.0%)
New Zealand	46 (8.5%)	45 (12.2%)	1 (0.6%)
Other	104 (19.2%)	81 (21.9%)	23 (13.5%)
How long ago were the Fellowship training requirements completed? (n = 543)			
Not yet completed	118 (21.7%)	97 (26.1%)	21 (12.3%)
< 5	119 (21.98%)	79 (21.2%)	40 (23.4%)
5 to 10	72 (13.3%)	43 (11.6%)	29 (17.0%)
> 10	234 (43.1%)	153 (41.1%)	81 (47.4%)
Working capacity? (n = 543)			
Full time	407 (75.0%)	306 (82.5%)	101 (58.7%)
Part time	132 (24.3%)	61 (16.4%)	71 (41.3%)
No longer clinically active	4 (0.7%)	4 (1.1%)	0 (0.0%)
You practice in a... (n = 543)			
Public health facility	198 (36.5%)	182 (49.1%)	16 (9.3%)
Private health facility	160 (29.5%)	72 (19.4%)	88 (51.2%)
Both	185 (34.1%)	117 (31.5%)	68 (39.5%)
Hours working with pregnant women per week (n = 541)			
Up to 10	222 (41.0%)	83 (22.4%)	139 (81.3%)
11 or more	319 (59.0%)	287 (77.6%)	32 (18.7%)

Sixty-one percent of clinicians had over 10 years' experience in their area of specialty. Predominantly, respondents had trained in Australian medical colleges (72.3%) with fewer trained in New Zealand (8.5%) and 19.2% trained elsewhere. Only one GP (0.6%) trained in New Zealand compared with 12.2% of O&G. 21.7% of O&Gs had not yet attained their fellowship with 43.1% of clinicians overall having been fully qualified specialist O&Gs for over 10 years. In the previous 12 months, O&Gs were more likely to have been working in a full-time capacity (82.5%) compared with GPs (58.7%). Overall O&Gs were more likely (49.1%) to have practiced in the public sector whereas GPs predominantly worked in private practice (51.2%). Unsurprisingly, 77.6% of O&Gs spent greater than 11 hours per week caring for pregnant women versus only 18.7% of GPs. The majority of the GPs (57.9%) spent

less than 5 hours per week with pregnant women.

Table 1 goes here

Interest

In general, respondents had no particular interest in perinatal mental health disorders (only 36.7%), however more GPs (46.7%) were interested than O&Gs (32.1%). The vast majority of clinicians (96.9%) had not conducted any perinatal mental health research in the last five years. Also, fewer than half (46.4%) of all clinicians had attended a conference or read a journal article where AD or AX medication use in pregnancy had been reviewed. In general, only a small proportion of clinicians (15.3%) were involved in the provision of education to trainees about psychotropic prescription during pregnancy.

Perception

Figure 1 shows clinician self-reported perception of concern prescribing AD or AX medications, with O&Gs apportioning a mean score of 3.7 (SD 2.3) and GPs 3.9 (SD 2.4), indicating a relatively low level of concern. (Likert scale 0 = no concerns and 10 = extremely concerned). Likewise, there was a similar perception of the mean percentage of patient compliance between GPs and O&Gs with both groups believing that over a third of patients were not compliant with their treatment: O&Gs mean 34.8% (SD 18.7) and GPs 36.4% (SD 19.3). When asked to share their perceptions, GPs estimated their patients' anxiety regarding AD and AX medication decision making in pregnancy as higher -mean 73.7% (SD 21.3) compared with O&Gs -mean 63.1% (SD 24.1).

Figure 1 goes here

Practice

Only 10.5% of all clinicians "very often" provided pregnant women with written information about the intended prescription AD or AX. Only 8.6% of O&G provided information "very often" compared to 14.5% of GPs.

Sources of written information were varied and the overall numbers were small. For O&Gs, most sourced UpToDate (32.2%), followed by MIMS (26.8%) and MotherRisk (13.4%). For GPs, the most commonly used resource was MIMS (27.9%) followed by "other" (19.2%) and Drug Company leaflets (15.1%). Less than 10% of all clinicians had their own practice pamphlets or relied on the pharmacists

as their main source of written information. 31.9% of O&Gs provided no written information, compared with 16.4% of GPs.

If seeing a pregnant patient with mental health illness for the first time, more than half of GPs (52.6%) reported spending 15 minutes discussing potential maternal and foetal side effects of AD or AX treatment. Nearly 18% of GPs spent “most” of the consultation time discussing side effects.

Comparatively, the O&Gs mostly reported spending less than five minutes on the subject (48.6%).

There was a statistically significant difference in prescription practice where AD or AX initiation was surveyed: 84.8% of GP initiated these medications, compared to 52.2% of O&G.

The GPs ranked “prior response to the medicine” as being an influential reason (60.5%) for prescribing a particular AD or AX. O&Gs on the other hand, were more influenced by a medication “a mental health practitioner has previously prescribed” (50.5%). This preponderance for O&Gs to rank a specialist mental health clinicians’ opinion highly was also demonstrated later in the questionnaire, where 55.7% of O&G would rely on the original prescriber’s management plan whereas only 11.7% GPs would.

Responses to the question relating to discontinuation of fluoxetine in a hypothetical pregnant patient signified varying practices between clinician groups. 59.1% of GPs indicated they initiate a patient consultation compared with only 18.0% O&Gs. Furthermore, response of O&Gs suggested that they would seek referral to a mental health specialist (48.8%), twelve times more often than GPs (5.3%).

Confidence

The questionnaire revealed that, overall, clinicians’ main concerns regarding AD and AX medication prescription to women of reproductive age are, in order of perceived influence medical safety profile including teratogenicity (86.9%), medical efficacy (75.2%), neonatal adaption syndrome (70.0%), and medication addiction potential (48.6%). Of note, 57.6% of GPs were concerned about maternal side effects compared to 47.3% of O&Gs.

There were differences in levels of reported confidence in medication recommendations and safety profile with 57.6% of GPs feeling confident compared to 44.2% of O&Gs. Figure 2 shows that in general, GPs consider themselves to be more confident in their knowledge and ability to manage and

prescribe AD and AX medications.

Figure 2 goes here

Knowledge

Respondents were tested on their knowledge of five well-known antidepressant and anxiolytic medications and their potential teratogenicity. As demonstrated in Table 2, GPs knowledge was similar to that of O&Gs, with the majority of respondents recognising that these medications had no significant proven teratogenicity. However, up to 22.3% respondents in both clinician groups incorrectly ascribed recognised teratogenicity to a commonly used AD or AX. 12.2% of O&Gs considered “Sertraline” teratogenic, compared to 3.5% of GPs.

Table 2
Correct knowledge of teratogenicity of common AD and AX by clinical affiliation

Medication	Overall (n = 545)	Obstetrician/Gynaecologist (n = 373)	General Practitioner (n = 172)
Sertraline	90.6%	87.8%	96.5%
Venlafaxine	87.1%	86.7%	87.8%
Amitriptyline	77.7%	77.9%	77.1%
Mirtazapine	82.5%	82.8%	81.8%
Diazepam	85.2%	84.6%	86.6%

Table 2 goes here

Training adequacy

GP were more likely to agree that training and education had been adequate for them to feel confident in prescribing AD and AX to pregnant women (56.1%) compared to only a third of O&Gs (29.0%). When asked what would be more useful to daily practice of caring for pregnant patients, 71% of all respondents chose increased clinician education and training (equal numbers of O&Gs and GPs) over increased technological supports such as apps for smart phones. Interestingly, 67.4% of clinicians overall agreed that completion of the study questionnaire had increased their interest in pursuing more information regarding AD and AX use in pregnancy.

Discussion

To our knowledge, this is the largest Australian survey of clinicians’ attitudes and practices, with regards AD and AX prescription in pregnancy. It explores the differences between the two groups of medical practitioners, most frequently engaged in counselling pregnant women. This is an important area of clinical practice with potentially grave outcomes including increased risk of maternal suicide and pregnancy termination if not properly addressed [1]. Given that this cohort of patients tend to

have a higher rate of unplanned pregnancies, clinician's confidence and competent practice in this area is vital.

Considerable uncertainty in prescribing AD and AX in pregnancy exists, even amongst clinicians with expertise in antenatal health care provision [2, 7, 9]. Women in general also express extreme reluctance to take medication in pregnancy [5, 6]. Our results suggest that clinicians are keenly aware of that reluctance and despite their best intentions, prescribed medication adherence rates are likely affected. Both groups in this study felt that training had not been adequate to instil confidence in medication prescription, even though many health professionals had trained for over 10 years. Both groups advocated for improved training to address this need.

This study suggests there may be differences in perception, confidence and practice between clinician groups. GPs perceived higher rates of patient anxiety regarding AD and AX use in pregnancy, and felt that they had the most influence upon a women's use of AD or AX in pregnancy. Even though they saw pregnant women less frequently, they reported their consults apportioned more time to medication risk discussions. GPs also indicated an intent to refer back to a mental health specialist far less often than O&G when trouble-shooting medication dosing. They also ranked the influence of their psychiatric colleagues lower than O&Gs and the impact of the internet. GPs reported higher rates of confidence in managing mental health in pregnant patients at a community-level compared to their O&G counterparts, is perhaps due to their familiarity with medication manipulation and more frequent provision of mental health advice for general patients [10].

Both groups, in practice, recommended close doctor-patient relationships to nurture clear communication and support during the pregnancy, and no groups ill-advisedly recommended ceasing AD or AX upon pregnancy or for lactation. Both groups perceived women's fear about foetal malformation when AD or AX use in pregnancy was raised. However, it is concerning that 9.4-22.3% of clinicians incorrectly labelled commonly used AD or AX medication as having recognised teratogenicity. This highlights the need for ready access to updated, evidence-based sources of medication advice for clinicians.

Provision of written information has a solid evidence base supporting benefit for patient decision

making [13], especially in a population group where anxiety or concentration may cause impairment. Our study shows that this resource is infrequently used ~ 10%. There was no universal patient and clinician-friendly source from where information was obtained.. This likely reflects the difficulty of sourcing robust evidence regarding medication use in pregnancy. Due to ethical limitations, there is a paucity of randomised controlled trials and safety data is based on observational studies or medication registries [14].

The onus is on the clinicians to update themselves with latest available data. The doctors who responded to the survey admitted only a modest interest in mental health disorders in pregnancy. They also admitted to not being actively involved in research, nor had their knowledge of treatments challenged often by new data at conferences or journal articles. In addition, they were infrequently involved in passing on that knowledge to trainees. This lack of familiarity may lead to both clinical affiliates overestimating perceived teratogenicity of psychotropic medications.

Limitations

Although there was a significant number of participants in each clinician group, generalisability of results is limited by the low response rate and bias of GP responders with a special interest in pregnant women. The results of this study are purely descriptive because of these limitations and to exercise caution in over interpretation of statistically significant study findings. The number of responders is however not trivial and their perceptions around the prescription of AX an AD during pregnancy clearly hints at the need for further research in this very important area of medicine.

Conclusion

In pregnancies complicated by mental health conditions requiring AD or AX treatment, GPs are potentially more confident discussing these medications with patients and more comfortable prescribing and managing this patient population than their O&G counterparts. Nevertheless, with over 22% clinicians overall overestimating the teratogenicity of a commonly used AD, training could be improved for both GPs and O&G affiliates. Training may improve clinicians' perception of risk, and by doing so, inform optimal pharmaceutical management of anxiety and depression in pregnancy for the benefit of the mother and unborn child.

Abbreviations

AD Antidepressants

AX Anxiolytics

O&G Obstetrician and Gynaecologist

GP General Practitioner

RANZCOG Royal Australian College of Obstetricians and Gynaecologists

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Figures

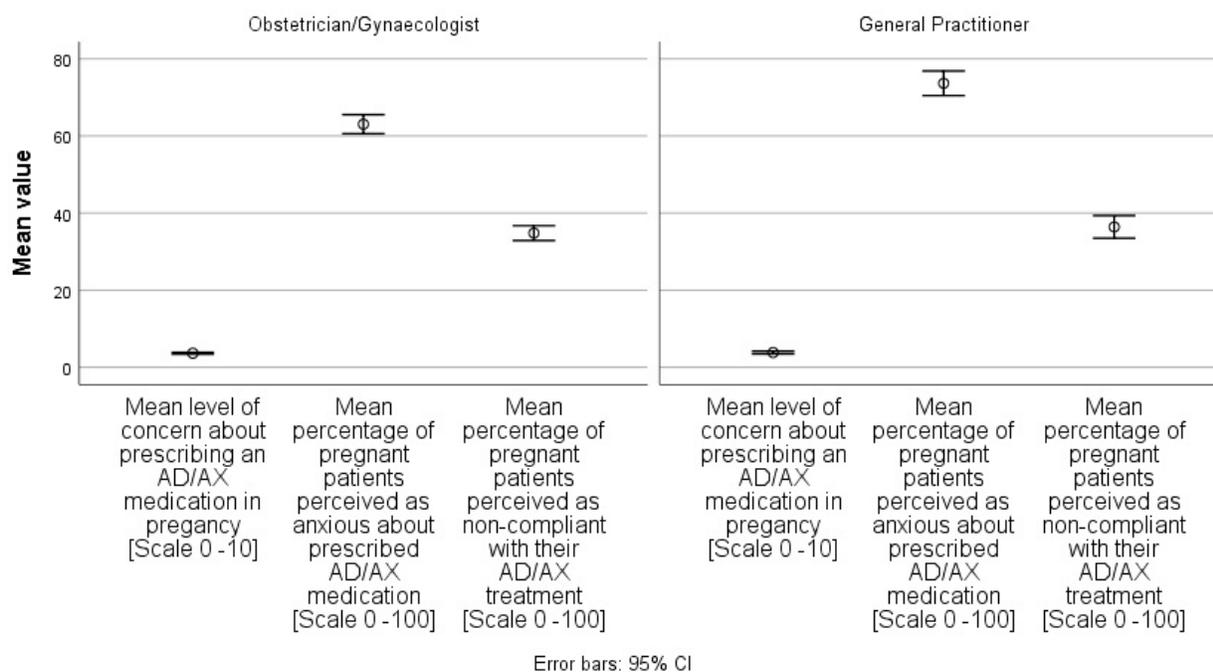


Figure 1

Comparison of self-reported perception of concern in prescribing AD and AX medications by clinical affiliation.

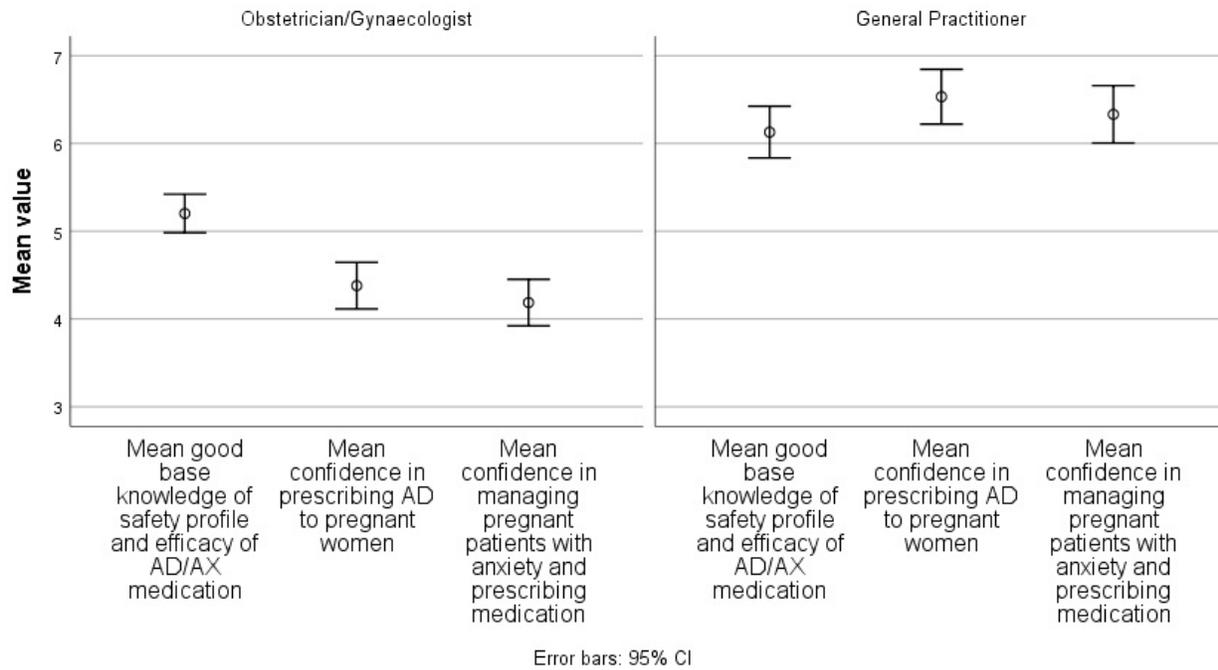


Figure 2

Comparison of clinician perception of confidence by clinical affiliation

Supplementary Files

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