

## Relation between Drug Use And Age-Related Cataract

Alaa Mohammed Ali Alshahrani<sup>1</sup>, Fahd B. Altherwi<sup>2</sup>, Rakan Mosa Algorinees<sup>3</sup>,  
Lujain Abdulaziz A Alrajhi<sup>2</sup>, Anas Hassan Saeed Alzahrani<sup>2</sup>, Nouf Mohammed Alrefay<sup>2</sup>,  
Moath Jamaan Al-Ghamdi<sup>4</sup>, Baraah Marwan Mohammed Lutfi AlSawaf<sup>2</sup>,  
Lujain Ahmed Ali Asiri<sup>1</sup>, Rawan Mohammad A AlMuhanna<sup>2</sup>

1- King Khalid University, 2- King Abdulaziz University,  
3- King Khalid eye Specialist Hospital-Riyadh, 4- Intern, Albaha University

### ABSTRACT

**Background:** A small number of studies have described the role of antidepressants as cataractogenic in humans, nevertheless, it remains unclear whether this possibility also prevails with the utilization of antidepressants.

**Methods:** We conducted this meta-analysis using a comprehensive search of PubMed, MEDLINE, Cochrane Database of Systematic Reviews, EMBASE and Cochrane Central Register of Controlled Trials till 01 February 2018 for studies that evaluated the relation between drug use and age-related cataract.

**Results:** Six studies were recognized with a total of 240,145 cases. The results for serotonin noradrenalin reuptake inhibitors (OR 1.32; 95% CI: 1.14–1.31)  $P = 0.026$ ,  $I^2 = 65.2\%$ , and selective serotonin reuptake inhibitors (OR 1.42; 95% CI: 1.19–1.21)  $P < 0.001$ ,  $I^2 = 89.4\%$ , tricyclic antidepressants (OR 1.41; 95% CI: 1.19–1.42)  $P = 0.08$ ,  $I^2 = 55.3\%$

**Conclusion:** There is a possible risk of the relation between drug use and age-related cataract. The utilization of antidepressants for more than 1 year or longer had increased risk for development of cataract.

**Keywords:** Age-related cataract, drug utilization, tricyclic antidepressant.

### INTRODUCTION

Cataracts are one of the primary reasons of vision loss worldwide, and are a main public health problem<sup>1</sup>. Oral and inhaled steroids increase risk of cataract<sup>2</sup>. Beaver Dam Eye Study suggested the relationship of amitriptyline with increased risk of cortical cataract<sup>3</sup>. Lately, beta blockers are found to be cataractogenic. The risk of cataract with newer generation antidepressants is unclear. Selective serotonin reuptake inhibitors (SSRIs) are the third most suggested class of medication in the world and are related with cataract gastrointestinal bleeding and fractures<sup>4,5</sup>.

The genuine component of cataract advancement stays obscure, however, numerous hazard factors, for example, age, gender, corticosteroid utilize, diabetes mellitus, hypertension, intraocular surgery, visual injury, uveitis, and smoking have been distinguished. As of late, various examinations have concentrated on the potential cataractogenic danger of professionally prescribed medications<sup>6,7</sup>. Selective serotonin reuptake inhibitors (SSRIs), extensively professionally prescribed medications for the treatment of bulimia, depression, anorexia nervosa, obsessive-compulsive disorder, anxiety, social phobia, and panic disorder, have a high therapeutic to toxicity ratio. Nevertheless, while selective serotonin reuptake inhibitors are related with less toxicity than tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors are frequently complicated in co-ingestions that can precipitate the potentially lethal serotonin syndrome. As of late, a few epidemiological examinations have concentrated on the danger of cataractogenic impacts of antidepressants, and a few sorts of antidepressants

have been observed to be related with expanded danger of cataract advancement. An examination establish an expanded danger of future cataract diagnosis in present users of venlafaxine and fluvoxamine, and additionally an expanded rate of surgery in present users of paroxetine in those matured 65 years<sup>8</sup>. In the Beaver Dam Eye study, amitriptyline, a tricyclic antidepressant, was found to be associated with an increased risk of cortical cataracts<sup>3</sup>. Another examination discovered that selective serotonin reuptake inhibitor (SSRI) use for more than 1 year was related with an expanded danger of cataract surgery in individuals matured 50 years<sup>9</sup>.

As a result of the irregularity, we aimed to conduct the current meta-analysis to evaluate the relation between drug use and age-related cataract.

### METHODS

#### • Search methodology

A comprehensive search of PubMed, MEDLINE, Cochrane Database of Systematic Reviews, EMBASE and Cochrane Central Register of Controlled Trials till 01 February 2018 was done for studies that evaluated the relation between drug use and age-related cataract.

#### • Data collection

Two reviewers screened abstracts according to predefined study inclusion criteria. Full text articles were retrieved and reviewed if a decision on inclusion could not be made solely based on the abstract. Any disagreements were resolved by consensus between the two reviewers.

• **Study selection**

Studies were included in this meta-analysis if they fulfilled the following criteria:

The study was a case-control, cohort study, or randomized controlled trials (RCTs); cataracts and/or cataract surgery was an outcome; the association between antidepressants utilization and cataracts was investigated; risk estimates of morbidity and 95% CIs were reported or the information required to calculate them was available.

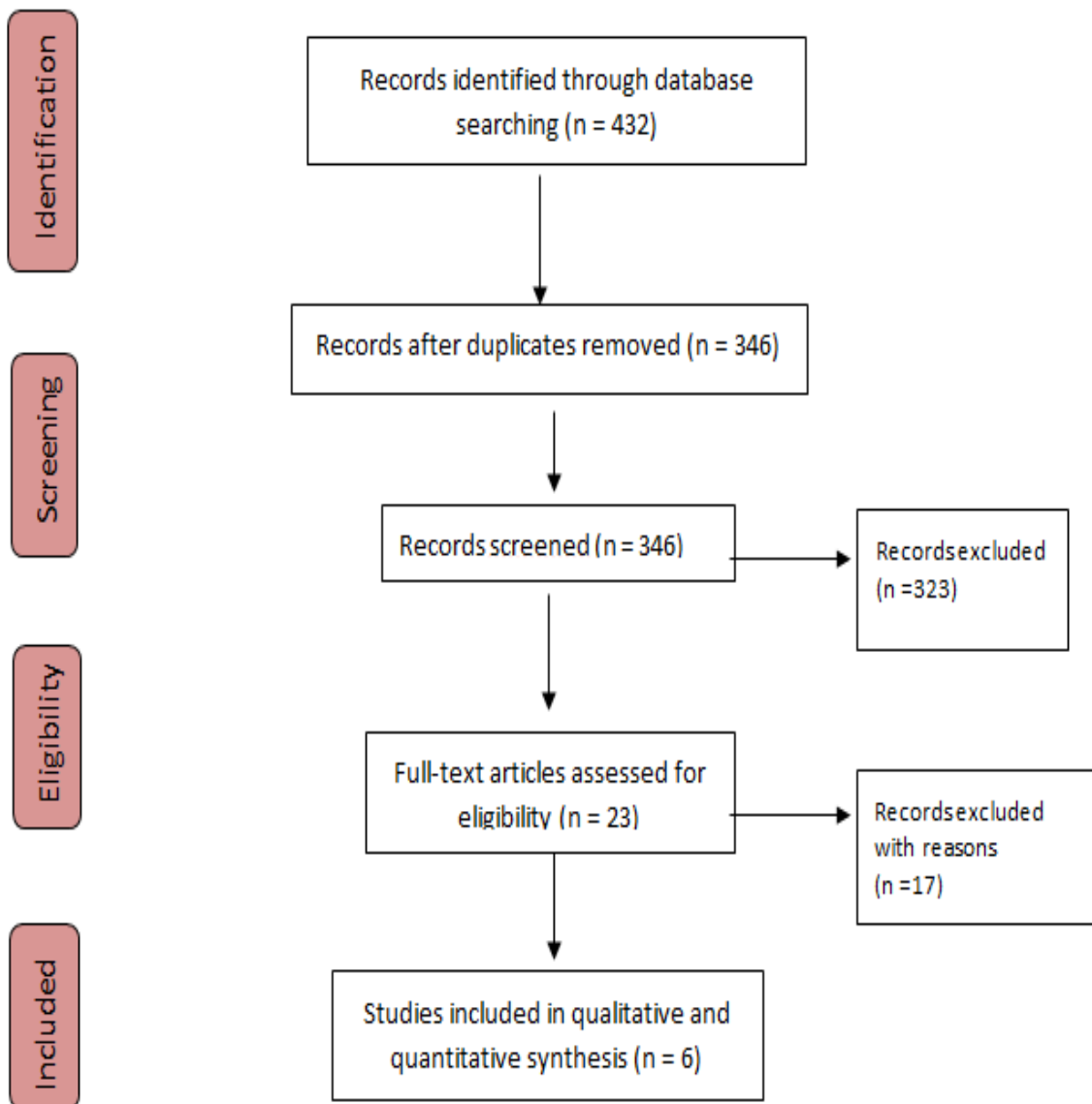
• **Data analysis**

The present meta-analysis utilized Stata version 12.0 software for statistical analysis. The significance levels were set to  $P < 0.05$  or  $P < 0.01$ , except for heterogeneity. The OR/RR values with corresponding 95% CI served as the valid estimates for all qualified studies to obtain a pooled OR/RR. Potential heterogeneity between the individual

studies was assessed by means of Cochran's Q statistic and  $I^2$  index score, with a significance set at the  $P$ -value  $< 0.10$  or  $I^2$  score  $> 50\%$  [10]. Flow diagram showing the selection criteria of assessed studies [11]. In studies reporting OR/RR of at least two subtypes, the process of Jan Hamling [12] was utilized for assessing the adjusted overall OR/RR.

**RESULTS**

We recognized 432 citations using the search strategy. Of these, we excluded 323 after examining the title and abstract including removal of duplicates. We retrieved and evaluated 23 articles in more detail, of which 17 articles were excluded, leaving 6 studies [3,8,9,13-15] that were eligible for inclusion (Figure 1). Major characteristics of included studies have been summarized in Table 1.



**Figure 1:** Flow diagram showing the selection criteria of assessed studies [11].

**Table 1.** Characteristics of 6 studies included in the Meta-Analysis

Author	Year	Age	Sample size	CataractDefinition	Adjusted variables	Drug type
Raj et al. <sup>15</sup>	2017	50 >	39	Diagnosed by an ophthalmologist	Duration, dose, Episodes of depression per year, and gender	SSRI and SNRI
Klein et al. <sup>3</sup>	2001	50 <	716	Diagnosed by an ophthalmologist	Age and gender	TCA
Becker et al. <sup>14</sup>	2017	≥40	206,931	Computer records (CPRD)	age, sex, general practice, BMI, smoking, diabetes, and hypertension.	SSRI,SNRI, and TCA
Erie et al. <sup>9</sup>	2014	50 <	6024	Medical records	Age, sex, and date of surgery	SSRI
Chou et al. <sup>13</sup>	2017	50 <	7651	Computer records (NHIRD)	Age, sex, index date, patient's demographics, and mental illness characteristics.	SSRI,SNRI, and TCA
Etminan et al. <sup>8</sup>	2010	≥65	18,784	Medical records	Age, cohort entry, gender, statins, hypertension, and antihypertensive.	SSRI and SNRI

SSRI=selective serotonin reuptake inhibitor, SNRI=serotonin noradrenalin reuptake inhibitor, TCA=tricyclic antidepressant

The results for serotonin noradrenalin reuptake inhibitors (OR 1.32; 95% CI: 1.14–1.31)  $P = 0.026$ ,  $I^2 = 65.2\%$ , and selective serotonin reuptake inhibitors (OR 1.42; 95% CI: 1.19–1.21)  $P < 0.001$ ,  $I^2 = 89.4\%$ , tricyclic antidepressants (OR 1.41; 95% CI: 1.19–1.42)  $P = 0.08$ ,  $I^2 = 55.3\%$

**Table 2.** Effect of serotonin noradrenalin reuptake inhibitors

Study	OR	95% CI
Raj et al. <sup>15</sup>	1.85	0.44-7.79
Etminan et al. <sup>8</sup>	1.23	1.08-1.40
Becker et al. <sup>14</sup>	1.06	1.01-1.11
Erie et al. <sup>9</sup>	1.37	1.11-1.70
Chou et al. <sup>13</sup>	1.07	0.98-1.17

**Table 3.** Effect of selective serotonin reuptake inhibitors

Study	OR	95% CI
Raj et al. <sup>15</sup>	1.98	0.49-7.94
Etminan et al. <sup>8</sup>	1.12	1.06-1.18
Becker et al. <sup>14</sup>	1.02	1.00-1.04
Erie et al. <sup>9</sup>	1.36	1.23-1.51
Chou et al. <sup>13</sup>	1.20	1.11-1.31

**Table 4.** Effect of tricyclic antidepressants

Study	OR	95% CI
Klein et al. <sup>3</sup>	1.33	0.87-2.14
Becker et al. <sup>14</sup>	1.15	1.13-1.17
Chou et al. <sup>13</sup>	1.25	1.15-1.34

**DISCUSSION**

The present analysis showed a significant positive association of serotonin noradrenalin reuptake inhibitors, selective serotonin reuptake inhibitors, and tricyclic antidepressants use with risk of cataract. The frequency of antidepressant utilization has risen 63% between 1999 and 2010<sup>16</sup>. The increase in antidepressant utilization has been decidedly connected with a reduction in the practice of psychotherapy<sup>17</sup>. Nevertheless, numerous antidepressants are prescribed to patients who do not have a psychiatric diagnosis<sup>18</sup>. Coexisting with the current increase in selective serotonin reuptake inhibitor prescription rates, we perceived accelerated growth in incident cataract surgery in women between 2005 and 2012 when contrasted to an earlier 7-year period<sup>19</sup>. A conceivable relationship amid the increased utilization of selective serotonin reuptake inhibitor and increasing rates of cataract in women is unclear.

Etminan et al.<sup>8</sup> found a relationship between the use of serotonin norepinephrine reuptake inhibitors, which upregulate the concentrations of serotonin and norepinephrine, and an increased risk of cataract surgery. Even though this relationship was statistically significant, the clinical importance can be marginal as the variance in serotonin norepinephrine reuptake inhibitor use between the 2 groups was <1%, and these medications were used by a very small proportion of the cohorts.

Numerous instruments might be engaged with the positive relationship of drug utilization with the risk of cataract. Chou et al.<sup>13</sup> found that constant utilization of other antidepressants for example; trazodone, fluoxetine, bupropion, moclobemide, and mirtazapine could likewise be connected with an increased risk of cataract development. In animal studies, serotonin has been shown to play a crucial role in lens transparency

<sup>20</sup>. Correspondingly, high levels of serotonin have been found in the aqueous humor of cataract and glaucoma patients<sup>21</sup>.

Furthermore, increased serotonin levels have been presented to cause lens opacity in rats, probable by reducing the creation of aqueous components<sup>22</sup>.

Tricyclic antidepressants utilize is accounted for to be connected with photosensitivity to ultraviolet or daylight. This last presentation has been recommended to be related with cortical cataract in Beaver Dam Eye Study<sup>23</sup>.

The present meta-analysis has numerous strengths. Most studies included in the meta-analysis containing a large number of cases and studies were based on the general population for more generalizable results. Furthermost of the studies edited a sequence of variables, which significantly decreased the probability of confounding bias.

Limitations of the present analysis would be reflected as the quantity of studies was limited, which could have an impact on the consistency of the outcomes and significant heterogeneity was perceived between the studies which could misrepresent the conclusion of our study.

**CONCLUSION**

There is a possible risk of the relation between drug use and age-related cataract. The utilization of antidepressants for more than 1 year or longer had increased risk for development of cataract.

To confirm these results, further studies should be made to make a better understanding of the potential biological mechanisms. Large-scale and long-term randomized controlled trials in various populations must be carried out in future studies to deliver more significant evidence.

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