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REVIEW

Association of DAZL polymorphisms and DAZ deletion with male infertility: a systematic review and meta-analysis

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Abstract

Background Various populations have been investigated for the occurrence of two key DAZL polymorphisms, 260A > G (rs11710967) and 386A > G (rs121918346), as well as complete DAZ cluster deletion, with conflicting results.

Objective The purpose of the current meta-analysis was to investigate if there is an association between DAZL polymorphisms and complete deletion of the DAZ cluster gene with male infertility.

Methods Up until September 2022, a thorough search was conducted in the Pubmed and Google scholar databases. For 260A > G polymorphism, 8 studies with 2077 cases and 1398 controls, 13 studies for 386A > G polymorphism (4343 cases and 3727 controls) and 17 studies of DAZ deletion (2820 cases and 1589 controls) were included in the pooled analysis. All of the studies were statistically analysed by Review Manager 5.4, and publication bias was evaluated with JASP 0.16.2.0 software utilising funnel plots and Egger's linear regression test.

Results The meta analysis result for pooled data indicated no association between 260A > G and 386A > G polymorphisms and male infertility in any of the genetic models or ethnicities. However, there was a definite correlation between complete deletion of the DAZ gene cluster and male infertility, with an OR = 13.23, 95% confidence interval (6.63–26.39), and $p < 0.00001$. In the stratified analysis by ethnicity, Caucasians and Asian ethnic groups showed the similar relationship.

Conclusion In order to arrive at more definitive conclusions, further study should be conducted, including studies from a larger range of nations and nationalities.

Keywords 260A > G · 386A > G · DAZ deletion · Male infertility · Polymorphism

Introduction

Infertility is growing at an unprecedented rate over the world, and has therefore become a significant public health concern. Male-related anomalies are thought to be implicated in the aetiology of infertility in around half of infertile couples (Singh et al. 2015). Male infertility is a multifactorial disorder with a wide range of phenotypic manifestations (Krausz et al.2015). Since spermatogenesis is such an intricate process with so many genes involved, it's likely that a major amount of male infertility phenotypes are genetic in nature (Aston and Carell 2009). Male factor infertility is thought to be caused by genetic defects in 15–30% of cases and the majority of these characteristics have a genetic basis that involves many genes and gene products (O'Brien et al. 2010). Microdeletions of the long arm of the Y chromosome are one of the most common pathogenetic abnormalities related to male infertility (McLachlan et al. 1998). Most genes on the Y chromosome are thought to be important in the regulation of male sexual differentiation, and abnormalities will be phenotypic unless the gene has autosomal homologues, such as DAZ (Hargreave 2000).

DAZL/ DAZLA and DAZ are members of the "DAZ (Deleted in AZoospermia) family," a conserved gene family that has a role in in male and female gametogenesis. DAZL initially occurs in early vertebrates, and DAZ eventually appears in the Y chromosome in primates at 30- 40 million

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years ago, by translocation and amplification of autosomal Dazl (Fu et al. 2015). DAZLA is a single-copy gene on human chromosome 3 that is highly similar to the DAZ gene (Saxena et al. 2000). Both genes have a highly conserved RNA binding domain and a DAZ repeat for translational regulation throughout germ cell development (Brook et al. 2009). DAZLA is important for human spermatogenesis and could function as a translational activator by regulating mRNA expression (Zhang et al. 2014). It regulates spermatogenesis by regulating the mRNA and protein targets that can generate mature male germ cells, as well as their generation, migration, and localization (Fu et al. 2015). In the animal model study, male DAZLA knockout mice were shown to have entirely blocked meiosis in their developing germ cells (Saunders et al. 2003). When the human DAZ gene was introduced into male DAZL knockout mice, it led to the recovery of some of the lost germ cells. This demonstrates that the human DAZ and DAZL genes may function similarly (Slee et al. 1999). Interestingly, study from Taiwan identified two novel polymorphisms in the DAZLA gene, 260A > G (exon 2) and 386A > G (exon 3), with SNP 386A > G being associated to spermatogenic failure including hypospermatogenesis, maturation arrest, and Sertoli cell Only Syndrome among infertile Taiwanese men (Teng et al. 2002). These SNPs in the DAZL gene resulted in non-synonymous amino acid substitutions at codon positions 12 and 54, replacing Threonine with Alanine, respectively within the RNA Recognition motif which falicitate the binding of target RNA sequences during translation process (Teng et al. 2002). The mutation in exon 3 may have functional repercussions, such as decreased RNA binding capacity, because it is located within the highly conserved RNA recognition motif domain of the DAZLA protein (Becherini et al. 2004).

Early primary spermatocytes and spermatogonia express DAZ genes, demonstrating their involvement in the earliest phases of spermatogenesis and their contribution to the maintenance of spermatogonial stem cell populations that possibly explain the impairments in spermatogenesis caused by DAZ deletions (Saxena et al. 1996). In roughly 13% of cases of non-obstructive azoospermia and oligospermia, DAZ gene cluster deletion was reported (Seboun et al. 1996). According to some research, sperm production persists following complete deletion of the DAZ genes, although at extremely low levels, with only a few spontaneous conceptions. This could be due to some functional overlap between DAZ and DAZL (Fu et al. 2015).

Polymorphisms or deletions in the DAZLA and DAZ genes are a significant risk factor since they are considered candidate genes for male infertility. Several studies have been done to investigate the association between DAZL polymorphisms and DAZ deletion with male infertility in various populations, although the results are conflicting. As a result, the current meta-analysis aimed to establish a relation between DAZL polymorphisms and complete deletion of the DAZ cluster gene with male infertility.

Materials and methods

Search strategy

Up until September 2022, a thorough search of the National Library of Medicine's Pubmed and Google Scholar databases for case control studies evaluating the connection of the 260A > G, 386A > G polymorphism, and DAZ deletion with the risk of male infertility was conducted. "A260G," "T12A," "A386G," "T54A," "Human DAZL," "DAZL polymorphisms/SNPs," "Human DAZ deletion," "male infertility," and "AZFc deletion" were some of the key search terms used individually or in combination. Before screening, we also checked for duplicate studies and assessed the relevancy of the studies by examining at the research titles.

Inclusion criteria

We included all case control or cohort studies that investigated at the correlation of 260A > G and 386A > G polymorphisms in the DAZL gene, as well as complete deletion of the DAZ gene by using STS marker sY254 and sY255, with male infertility in humans in the meta-analysis. We chose full-text publications with enough data to calculate the Odds Ratio and the 95 percent Confidence Interval.

Exclusion criteria

Duplicate database entries, studies that looked for unrelated polymorphisms, articles without full texts, review articles or systematic reviews, articles published in languages other than English, animal model or in-vitro research, and case reports were also eliminated.

Data extraction

The first author's name, year of publication, country, ethnicity, allele and genotype frequency in cases and controls, method of genotype testing for DAZL polymorphism, and number of individuals with complete DAZ deletion in cases and controls, as well as the DAZ deletion study's methods of detection, were all extracted. Ethnicities were classified into Caucasians, Chinese, other Asians, and Caucasians, Asians, Latina, Arabs for the DAZL polymorphism and DAZ deletion meta-analyses.

Statistical analysis

Odds ratios and their corresponding 95% confidence intervals were calculated to analyse the extent of the correlation between DAZL polymorphisms and complete DAZ deletion with male infertility. The DAZL polymorphism was tested using the dominant (AA vs AG + GG), codominant (AA vs AG; AA vs GG; AG vs GG), and recessive (AA + AG vs GG) models. Hardy Weinberg Equillibrium test for the control group was performed by chi square goodness of fit using SPSS 20. Heterogeneity was assessed for each ethnicity in different countries using Cochran's Q statistical test. When I^2 is ≥ 50% with p value < 0.1, the random effect model was applied, otherwise, if I^2 is ≤ 50% with p value > 0.1 the fixed effect model of Mantel Hanaenszel method was to used to pooled ORs. The Z test was used to establish the statistical significance of pooled ORs, and $p < 0.05$ was considered statistically significant. Review Manager 5.4 was used to perform statistical analysis on all of the studies, and sensitivity analysis was used to see how each study affected the pooled ORs by deleting one study at a time. Funnel plots and Egger's linear regression test were used to evaluate potential publication bias using the JASP 0.16.2.0 software.

Results

Study characteristic

After searching the Pubmed and Google scholar databases uptil September 2022, a total of 502 records were found. The most recent study relevant to our investigation was found to have been published in August 2021. After removing all articles that did not meet the inclusion criteria, the current meta analysis of 260A > G SNP (rs11710967), 386A > G SNP (rs121918346), and DAZ deletion contained 8, 13, and 17 case control studies (9240 cases and 6714 controls). Figures 1 and 2 show the flowchart for selecting studies for inclusion in this meta

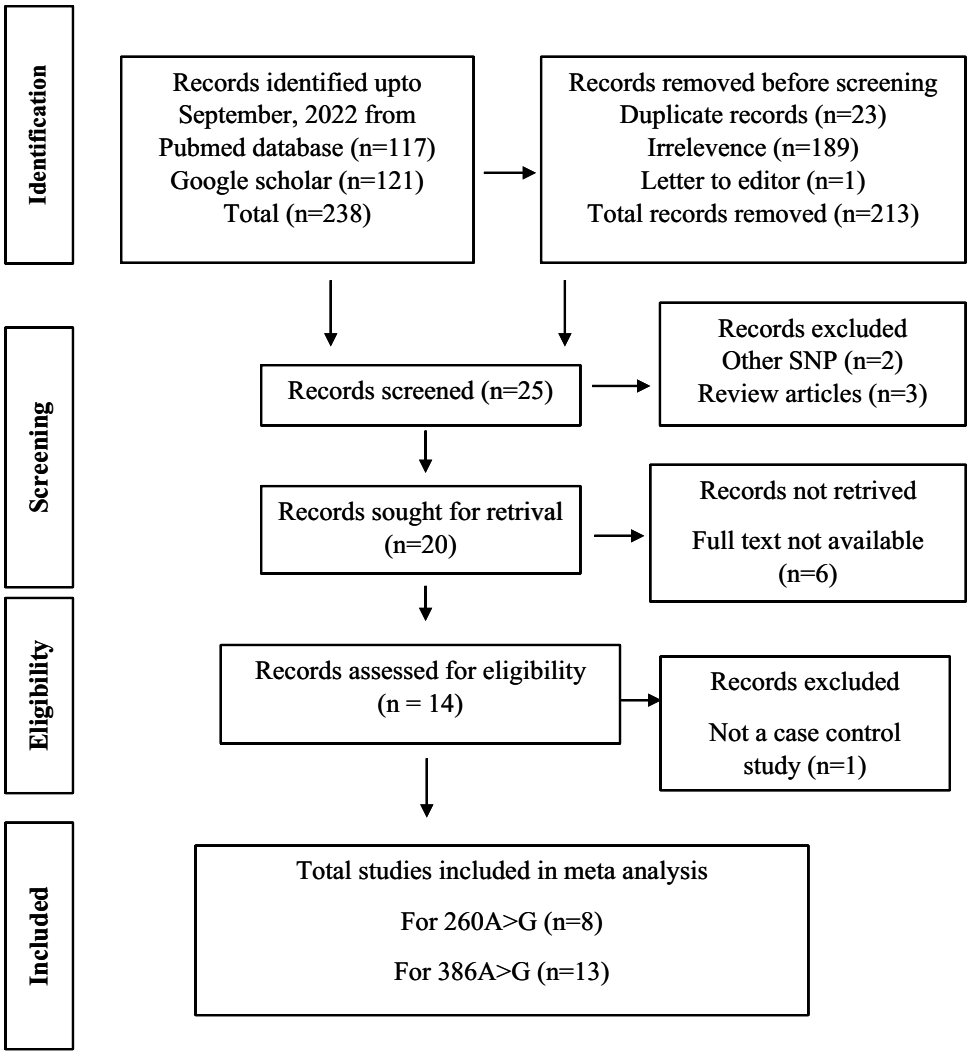
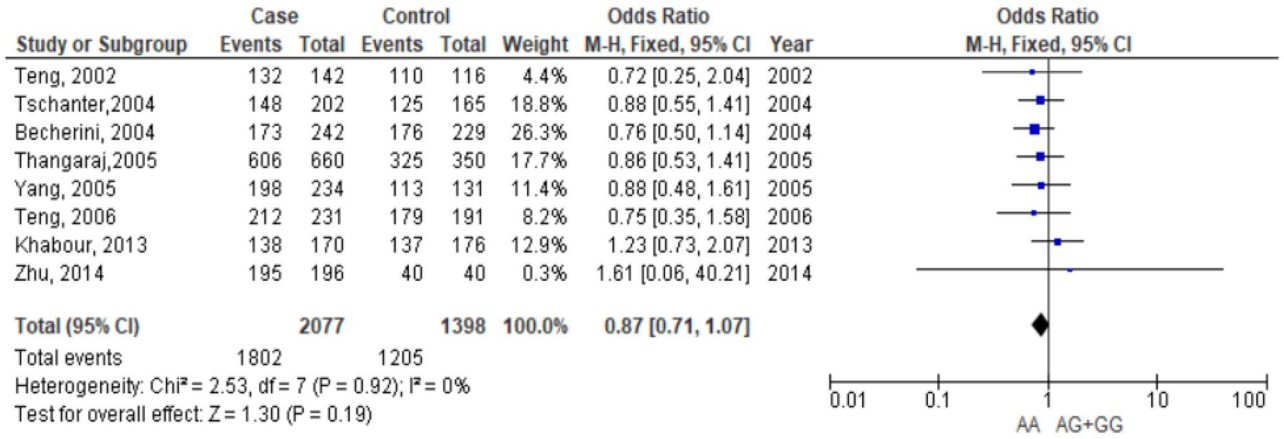
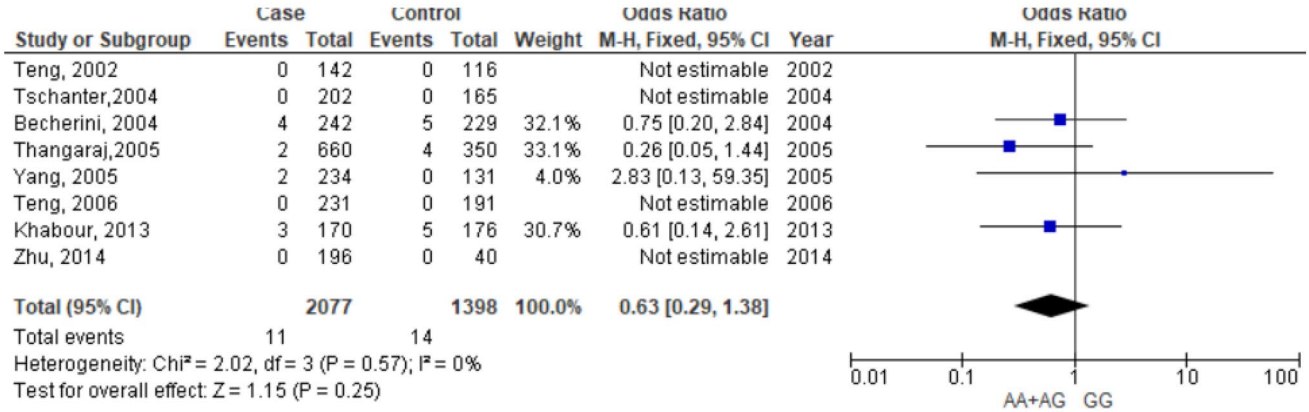


Fig. 1 PRISMA (2020) flow diagram for study selection included in meta analysis for the association of 260A > G and 386A > G polymorphisms with male infertility

Dominant model: AA vs AG+GG



Recessive model: AA+AG vs GG



Codominant model: AA vs AG

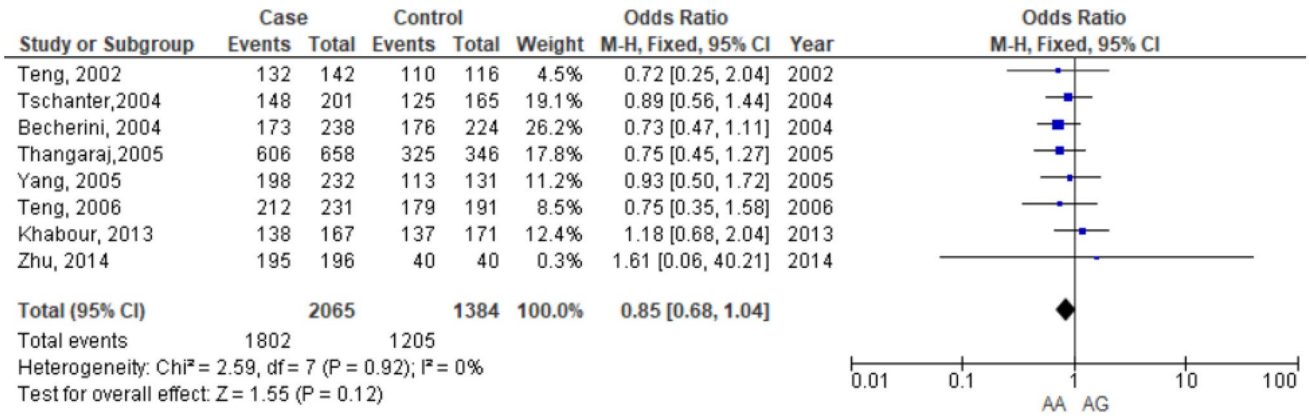
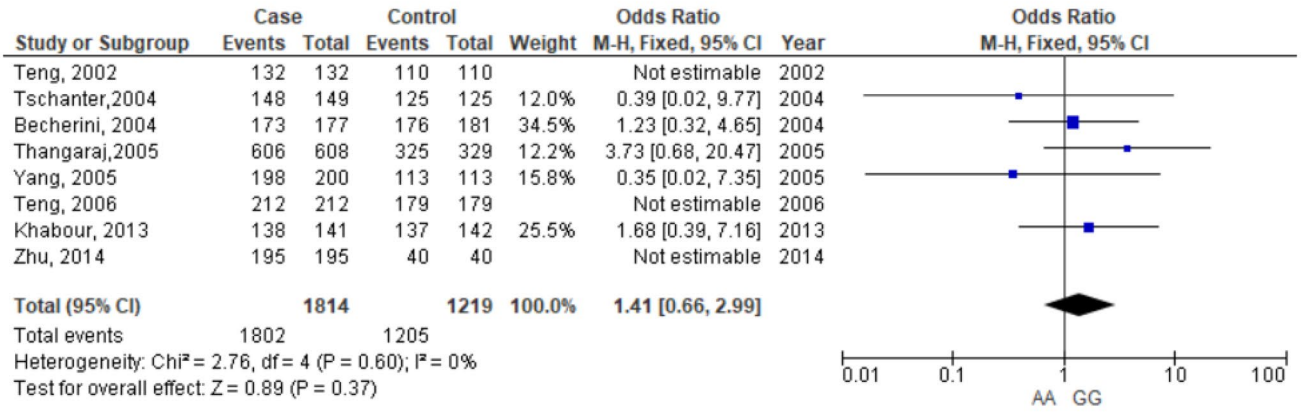


Fig. 2 PRISMA (2020) flow diagram for study selection included in meta analysis for the association of complete deletion of DAZ genes in Y chromosome with male infertility



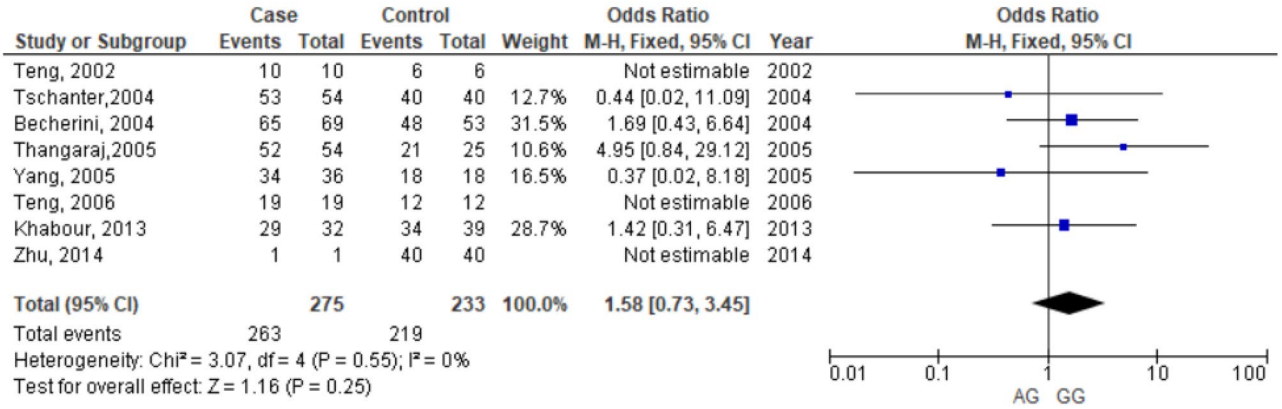


Fig. 2 (continued)

Table 1 Characteristics of DAZL 260A > G polymorphism studies included in the meta analysis

First author, year	Country	Control						Cases					
		AA	AG	AA + AG	GG	AG + GG	Total	AA	AG	AA + AG	GG	AG + GG	Total
Teng et al. 2002	Taiwan	110	6	116	0	6	116	132	10	142	0	10	142
Becherini et al. 2004	Italy	176	48	224	5	53	229	173	65	238	4	69	242
Tschanter et al. 2004	Germany	125	40	165	0	40	165	148	53	201	1	54	202
Thangaraj 2005	India	325	21	346	4	25	350	606	52	658	2	54	660
Yang et al. 2005	Japan	113	18	131	0	18	131	198	34	232	2	36	234
Teng et al. 2006	Taiwan	179	12	191	0	12	191	212	19	231	0	19	231
Khabour et al. 2013	Jordan	137	34	171	5	39	176	138	29	167	3	32	170
Zhu et al. 2014	China	40	0	40	0	0	40	195	1	196	0	1	196

analysis, while Tables 1, 2 and 3 indicate the characteristics of each study, including genotype frequency in cases and controls, and country of origin. In order to have a better understanding of the actual prevalence of these polymorphisms, people from China and Taiwan were pooled as Chinese ethnicity and population from other Asian countries as Other Asians for the meta analysis of DAZL polymorphisms. Except for one study in 260A > G polymorphism analysis, all of the investigations complied with Hardy Weinberg Equilibrium.

Table 2 Characteristics of DAZL 386A > G polymorphism studies included in the meta analysis

First author, year	Country	Control						Cases					
		AA	AG	AA + AG	GG	AG + GG	Total	AA	AG	AA + AG	GG	AG + GG	Total
Teng et al. 2002	Taiwan	116	0	116	0	0	116	121	21	142	0	21	142
Bartolini et al. 2004	Italy	63	0	63	0	0	63	95	0	95	0	0	95
Becherini et al. 2004	Italy	229	0	229	0	0	229	242	0	242	0	0	242
Tschanter et al. 2004	Germany	165	0	165	0	0	165	202	0	202	0	0	202
Thangaraj et al.2005	India	350	0	350	0	0	350	660	0	660	0	0	660
Yang et al. 2005	Japan	131	0	131	0	0	131	234	0	234	0	0	234
Teng et al. 2006	Taiwan	189	2	191	0	2	191	205	25	230	1	26	231
Poongathai et al. 2008	India	140	0	140	0	0	140	147	0	147	0	0	147
Singh and Raman 2009	India	199	1	200	0	1	200	165	0	165	0	0	165
Khabour et al. 2013	Jordan	176	0	176	0	0	176	170	0	170	0	0	170
Zhu et al. 2014	China	36	4	40	0	4	40	190	6	196	0	6	196
Nejati and Karimian 2016	Iran	100	0	100	0	0	100	97	2	99	1	3	100
Wang et al. 2017	China	1634	190	1824	2	192	1826	1607	152	1759	0	152	1759

Table 3 Characteristics of complete DAZ deletion studies included in the meta analysis

First author, year	Country	Control		Cases	
		DAZ deletion	Total	DAZ deletion	Total
Kent-First et al. 1996	US	0	200	1	32
Simoni et al. 1997	Italy	0	86	5	168
Vereb et al. 1997	US	0	55	6	168
Liow et al. 1998	China	0	101	6	202
Foresta et al. 1999	Italy	0	100	16	230
Kim et al. 1999	Korea	0	14	7	40
Fu et al. 2002	China	0	60	12	101
SãoPedro et al. 2003	Brazil	0	12	4	60
Ferrás et al. 2004	Portugal	0	114	16	91
Yang et al. 2006	China	0	236	42	485
Mau Kai et al. 2008	Denmark	0	168	1	264
Vijesh et al. 2015	India	0	125	11	354
Shafae et al. 2018	Egypt	0	30	3	64
Akbarzadeh Khiavi et al. 2020	Iran	0	100	20	100
Elsaid et al. 2021	Sudan	0	4	4	51
Sharma et al. 2021	India	0	100	22	292
Dutta et al. 2021	India	0	84	8	118

Meta-analysis of 260A > G DAZL polymorphism

A total of 8 studies were included in the meta analysis for SNP 260A > G (rs11710967), including 2077 cases and 1398 controls. We found studies on Chinese (3), Caucasian (2), and Other Asians among these (3). Figure 3 depicts the meta analysis in various analysis models: Dominant model (AA vs AG + GG); Recessive model (AA + AG vs GG); and Codominant models (AA vs AG), (AA vs GG) and (AG vs GG). Table 4 summarises the major findings of the meta-analysis for pooled studies and ethnicity in various genetic models. With the exception of a 15% heterogeneity in the other Asians group in the codominant mode (AG vs GG), no heterogeneity ($I^2 = 0\%$) was detected in any of the genetic models or ethnic groups. The pooled ORs and 95% confidence intervals from the fixed effect analysis were as follows: Dominant model, AA vs AG + GG (OR = 0.87; 95% CI = 0.71–1.07, $p = 0.19$); Codominant model AA vs AG (OR = 0.85; 95% CI = 0.68–1.04, $p = 0.12$); Codominant model AA vs GG (OR = 1.41; 95% CI = 0.66–2.99, $p = 0.37$); Codominant model AG vs GG (OR = 1.58; 95% CI = 0.73–3.45, $p = 0.25$); recessive model AA + AG vs GG

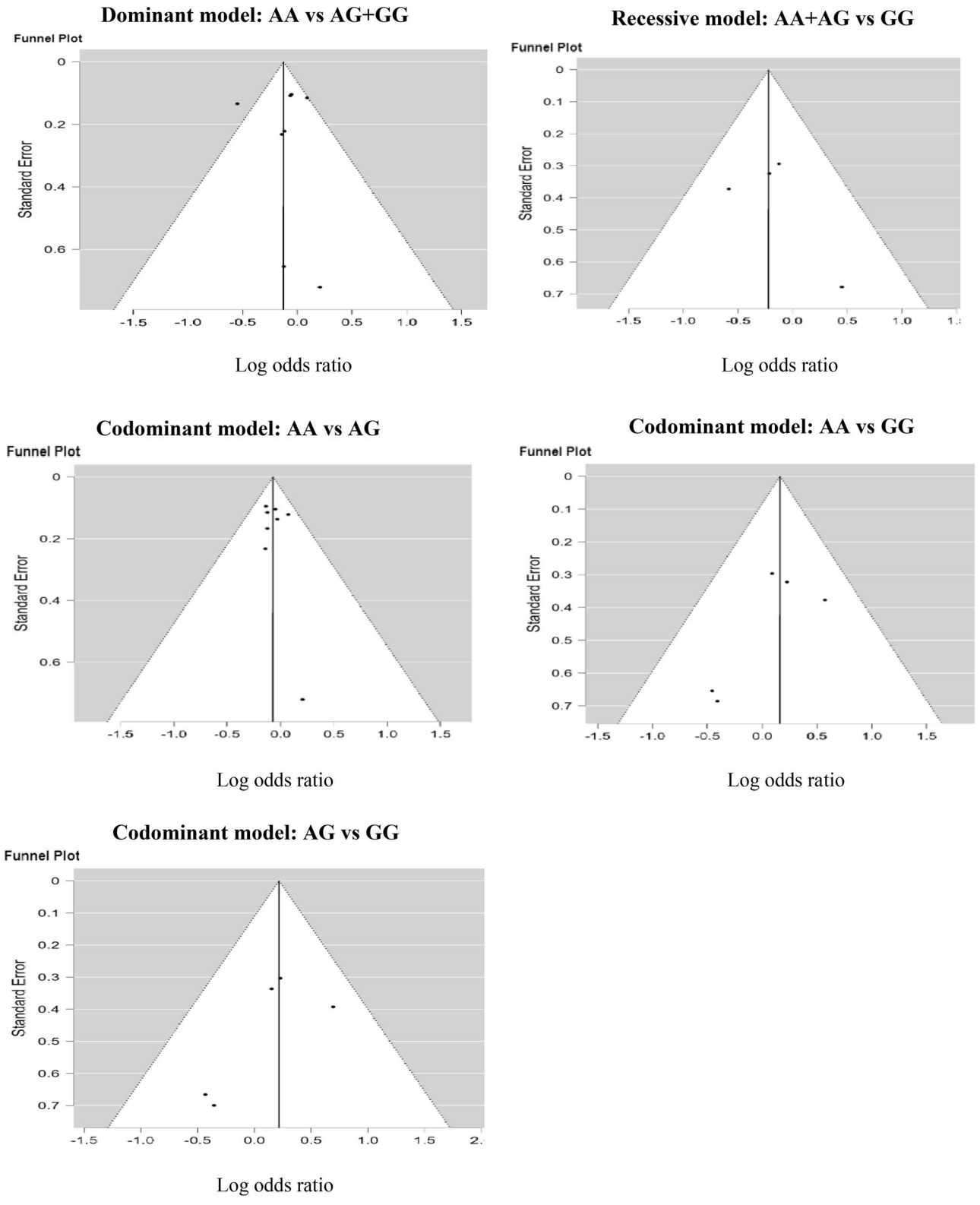


Fig. 3 Forest plot depicting the analysis of 260A > G polymorphism in different genetic models

Table 4 Meta analysis result of 260A > G polymorphism in different genetic analysis models and their ethnic subgroups

Analysis model		Ethnic groups	Heterogeneity		Fixed effect	
			I^2	p Q test	OR (95% CI)	p Z test
Dominant	AA vs (AG + GG)	Total	0%	0.92	0.87 (0.71–1.07)	0.19
		Chinese	0%	0.90	0.76 (0.42–1.38)	0.36
		Caucasian	0%	0.64	081 (0.59–1.10)	0.17
		Other Asian	0%	0.58	0.98 (0.72–1.33)	0.89
Codominant	AA vs GG	Total	0%	0.92	0.85 (0.68–1.04)	0.12
		Chinese	0%	0.90	0.76 (0.42–1.38)	0.36
		Caucasian	0%	0.52	0.8 (0.58–1.09)	0.16
		Other Asian	0%	0.51	0.93 (0.67–1.28)	0.65
	AA vs GG	Total	0%	0.60	1.41 (0.66–2.99)	0.37
		Chinese	–	–	–	–
		Caucasian	0%	0.52	1.01 (0.31–3.37)	0.98
		Other Asian	0%	0.40	1.75 (0.66–4.46)	0.26
	AG vs GG	Total	0%	0.55	1.58 (073–3.45)	0.25
		Chinese	–	–	–	–
		Caucasian	0%	0.45	1.33 (0.39–4.52)	0.64
		Other Asian	15%	0.31	1.78 (0.65–4.9)	0.26
Recessive	(AA + AG) vs GG	Total	0%	0.57	0.63 (0.29–1.38)	0.25
		Chinese	–	–	–	–
		Caucasian	–	–	–	–
		Other Asian	0%	0.39	0.57 (0.22–1.52)	0.26

(OR = 0.63; 95% CI = 0.29–1.38, $p = 0.25$). This suggested that the DAZL 260A > G polymorphism has no association to male infertility. The symmetrical distribution was revealed by funnel plots in Fig. 4, and Egger's test with p values of 0.87; 0.5; 0.772; 0.287; 0.284 respectively revealed no indication of publication bias for all genetic models.

Meta-analysis of 386A > G DAZL polymorphism

For the 386A > G polymorphism study, a total of 4343 cases and 3727 controls from 13 investigations were used. There were four studies in the Chinese ethnic group, three in the Caucasian ethnic group, and six in the Other Asian ethnic group. Figure 5 depicts the meta analysis in different analysis models. In the dominant (AA vs AG + GG) and codominant models (AA vs AG), respectively, there was 82% and 81% heterogeneity, with the ethnic Chinese group scoring 88 percent heterogeneity in both models ($p < 0.0001$). As a result, for these models and subgroups, the random effect test was used, while for the remaining groups in various models, the fixed effect test was used. All investigations from Taiwan, China, and Iran found the 386A > G polymorphism, but none from other nations. According to Table 5, the Z test indicated no significant correlation between the 386A > G polymorphism and male infertility in any of the genetic models or ethnic subgroups. The funnel plots (Fig. 6) revealed that all of the studies had a symmetrical distribution and that none of the genetic models had a publication bias.The Egger's test values for the dominant model (AA vs AG + GG) were $p = 0.662$, $p = 0.183$ for the recessive model (AA + AG vs GG), and $p = 0.322$ and $p = 0.180$ for the codominant model (AA vs GG) and (AA vs AG) respectively.

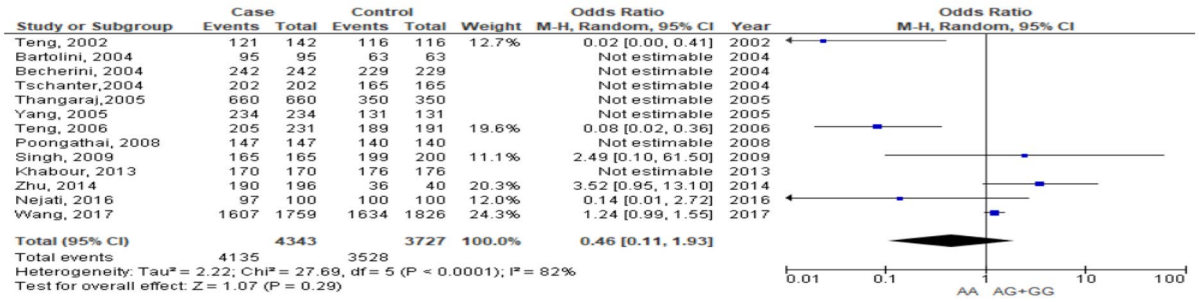
Meta-analysis of DAZ deletion

The complete DAZ deletion analysis included 17 studies with 2820 cases and 1589 controls and Caucasians (6), Asians (8), Latinos (1), and Arabs (2) were the ethnic groups studied. Figure 7 shows the pooled ORs and their 95 percent confidence intervals for each study. Heterogeneity ($I^2 = 0\%$) was absolutely absent in both the general population and various ethnic subgroups. As shown in Table 6, the overall impact of the Z test demonstrated an association between complete deletion of the DAZ cluster and male infertility. The same relation was observed in Caucasian and Asian ethnic groups ($p < 0.00001$). With a $p = 0.065$ from Egger's test, no publication bias was found in the meta analysis study (Fig. 8).

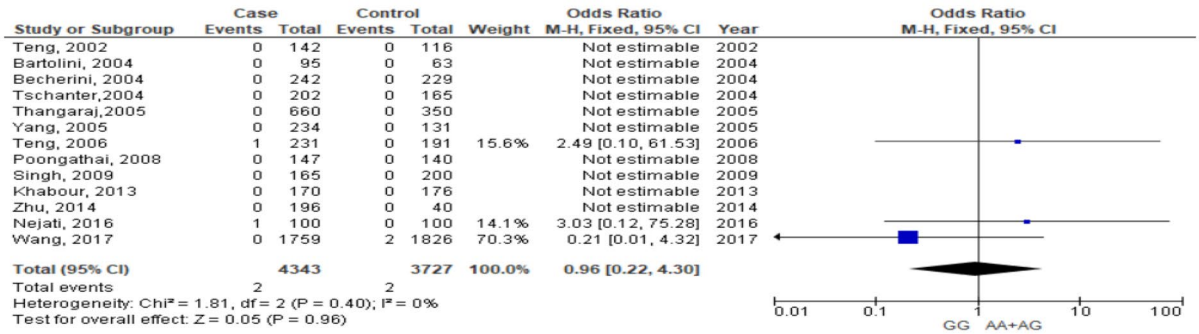
Discussion

The current meta-analysis examined into the association between DAZL polymorphisms and DAZ deletion and male infertility. We included 8 studies relating to 260A > G (rs11710967) polymorphism (2077 cases and 1398 controls), 13 studies for 386A > G (rs121918346) polymorphism (of 4343 cases and 3727 controls) and 17 studies of DAZ deletion (2820 cases and 1589 controls). In all of the genetic models or ethnicity, the meta analysis outcome for pooled

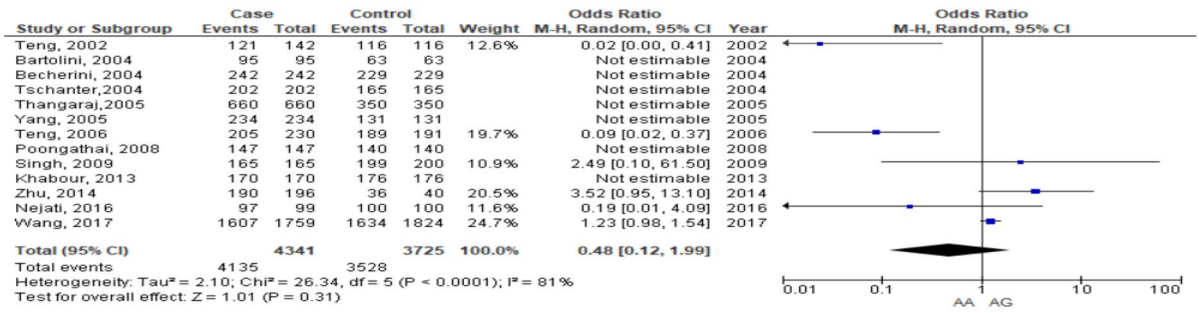
Dominant model: AA vs AG+GG



Recessive model: AA+AG vs GG



Codominant model:AA vs AG



Codominant model: AA vs GG

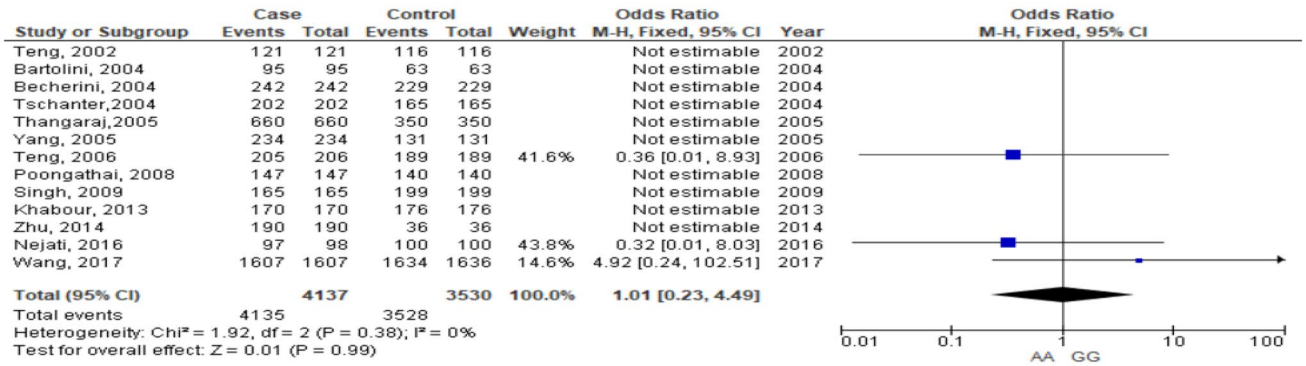


Fig. 4 Funnel plot (Log odds ratio verses Standard error) to check publication bias for the association of 260A > G polymorphism with male infertility

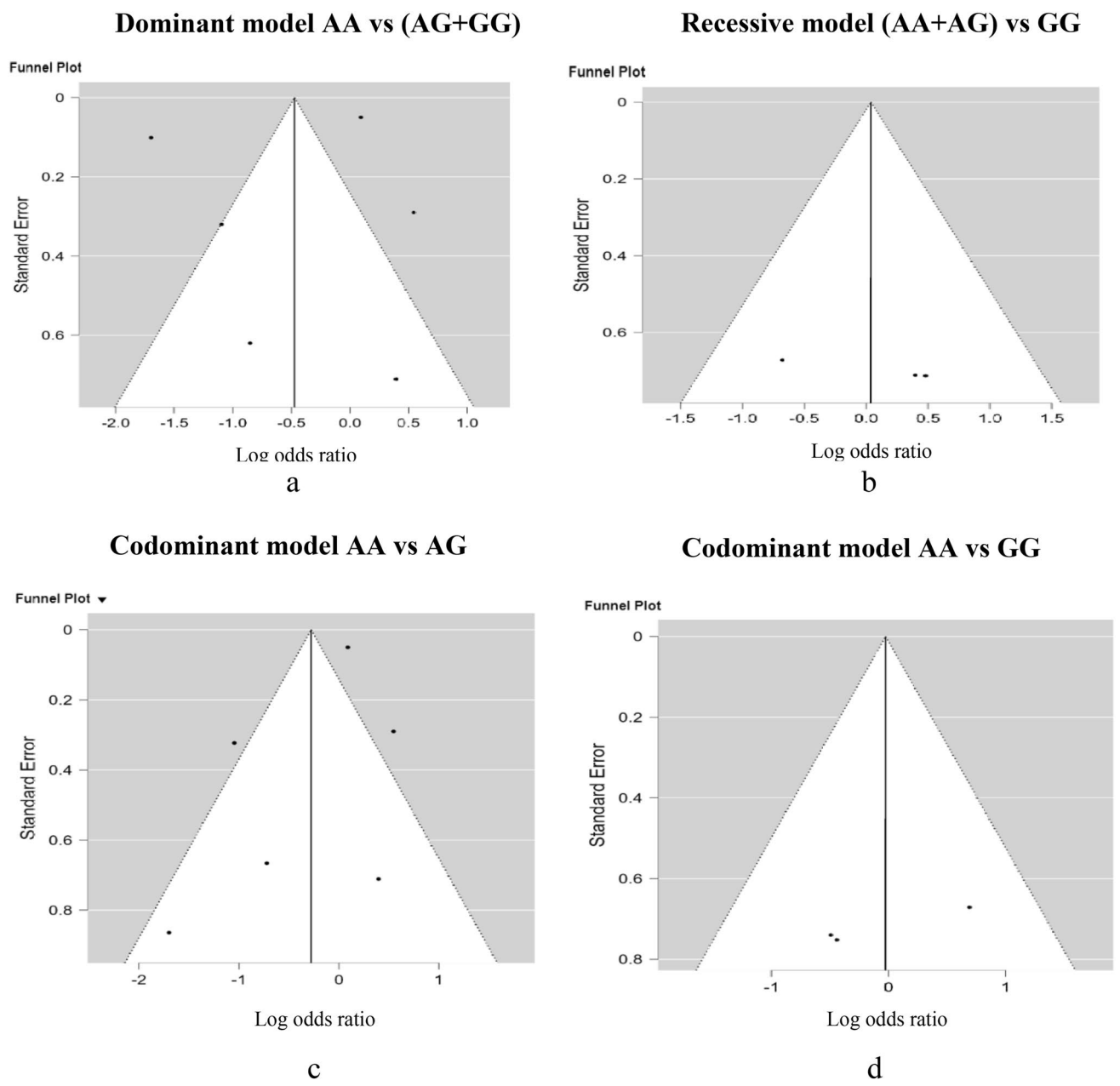


Fig. 5 Forest plot depicting the analysis of 386A > G polymorphism in different genetic models

data found no correlation of 260A > G and 386A > G polymorphisms with male infertility. This meta analysis result validates past findings in the case of the 260A > G polymorphism, but not in the case of the 386A > G SNP. Our findings contradict two previous meta-analyses, one by Zhang et al. 2014, and the other by Chen et al. 2016, both of which indicated a significant relationship between the 386A > G SNP and male infertility. In the study by Zhang et al. 2014, the aforementioned correlation was identified primarily in Asian ethnicity but not in Caucasian under codominant (AG vs AA) and dominant genetic models. There were 12 investigations in total, with 2456 cases and 1897 controls. Chen et al. 2016 identified a significant connection between the 386A > G polymorphism with male infertility in the Han Chinese population in a pooled study that included 11 studies with 2222 cases and 1677 controls. Additionally, in our study, when the heterogeneity was calculated for overall Asians including Chinese, Taiwanese and other Asians altogether, observed values were $I^2 = 82\%$, $p < 0.0001$, OR and 95% CI = 0.46 (0.11–1.93) and $p_z = 0.29$ for dominant model and $I^2 = 81\%$, $p < 0.0001$, OR and 95% CI = 0.48 (0.12–1.99) and $p_z = 0.31$ for codominant model (AA vs AG)

Table 5 Meta analysis result of 386A > G polymorphism in different genetic analysis models and their ethnic subgroups

Analysis model		Ethnic groups	Heterogeneity		Random/Fixed effect	
			I^2	p Q test	OR (95% CI)	p Z test
Dominant	AA vs (AG + GG)	Total	82%	< 0.0001	0.46 (0.11–1.93)	0.29
		Chinese	88%	< 0.0001	0.42 (0.07–2.40)	0.33
		Caucasian	–	–	–	–
		Other Asian	41%	0.19	0.46 (0.08–2.56)	0.37
Codominant	AA vs AG	Total	81%	< 0.0001	0.48 (0.12–1.99)	0.31
		Chinese	88%	< 0.0001	0.42 (0.07–2.38)	0.33
		Caucasian	–	–	–	–
		Other Asian	22%	0.26	0.6 (0.1–3.72)	0.59
	AA vs GG	Total	0%	0.38	1.01 (0.23–4.49)	0.99
		Chinese	26%	0.25	1.55 (0.25–9.41)	0.64
		Caucasian	–	–	–	–
		Other Asian	–	–	0.32 (0.01–8.03)	0.49
	AG vs GG	Total	0%	0.94	0.26 (0.02–2.76)	0.27
		Chinese	0%	0.94	0.26 (0.02–2.76)	0.27
		Caucasian	–	–	–	–
		Other Asian	–	–	–	–
Recessive	(AA + AG) vs GG	Total	0%	0.40	0.96 (0.22–4.3)	0.96
		Chinese	18%	0.27	0.62 (0.1–3.85)	0.61
		Caucasian	–	–	–	–
		Other Asian	–	–	3.03 (0.12–75.28)	0.5

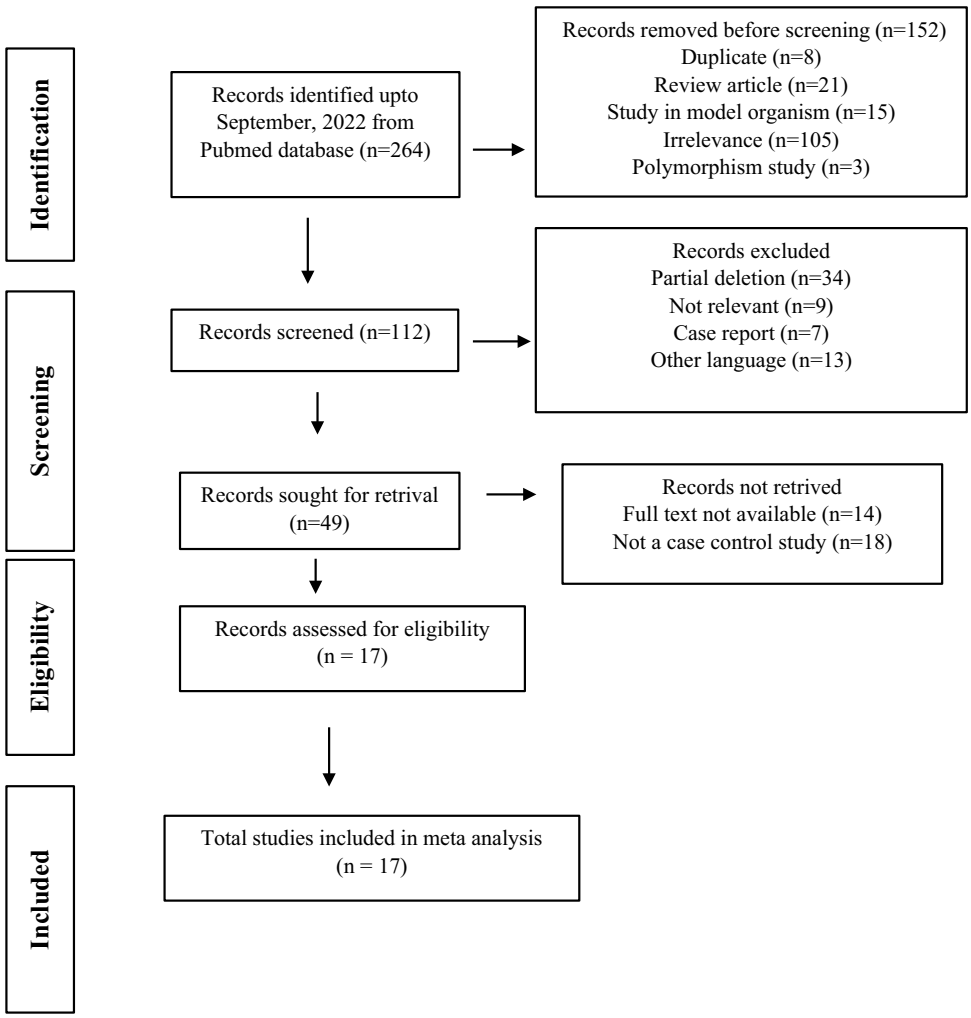


Fig. 6 Funnel plot (Log odds ratio verses Standard error) to check publication bias for the association of 386A > G polymorphism with male infertility

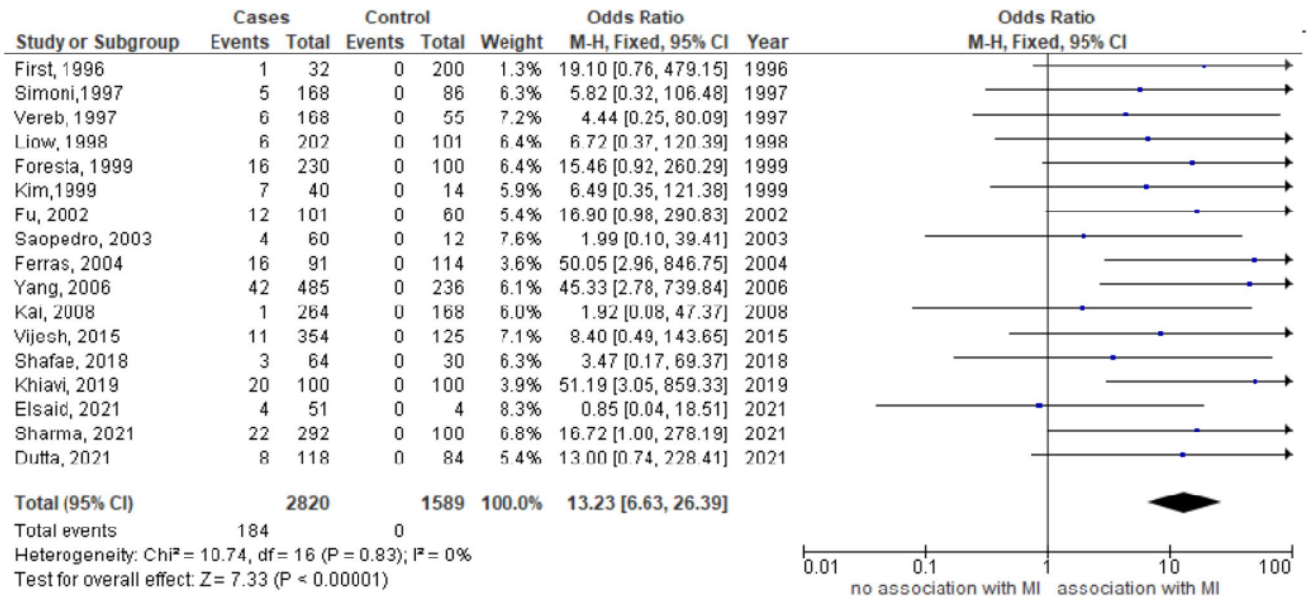


Fig. 7 Forest plot depicting the Odds Ratio, 95% Confidence Interval of the Cochran-Mantel- Haenszel fixed model test for the studies included in the meta-analysis

Table 6 Meta analysis result of DAZ deletion studies in different ethnic subgroups

Number of studies	Ethnic groups	Heterogeneity		Fixed effect	
		I^2	p Q test	OR (95% CI)	p Z test
17	Total	0%	0.83	13.23 (6.63–26.39)	< 0.00001
6	Caucasian	0%	0.69		< 0.0001
8	Asian	0%	0.94	12.49 (3.77–41.36)	< 0.00001
1	Latina	–	–		0.65
2	Arab	0%	0.51	19.01 (7.02–51.45)	0.52
				1.99 (0.10–39.41)	
				1.99 (0.24–16.61)	

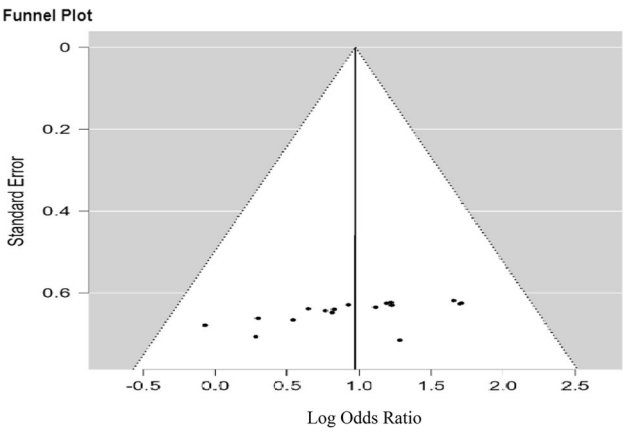


Fig. 8 Funnel plot (Log odds ratio verses Standard error) to check publication bias for the association of DAZ deletion with male infertility

that showed no obvious association in these models. The reason for this could be that the sample sizes in the above pooled studies were smaller, affecting the degree of association.The 386A > G polymorphism, however, is completely absent in Caucasian ethnic subgroups, according to our and other investigations. In terms of studying the relationship between DAZL polymorphisms and male infertility, the current meta analysis is the most comprehensive. This meta-analysis has been updated to include four new studies with larger sample sizes from other countries, making it more diverse and robust. More investigation into the relationship between the 386A > G polymorphism and male infertility in the Chinese ethnic group is needed, as the dominant and codominant models (AA vs AG) in this subgroup showed significant heterogeneity. On the other side, there was no heterogeneity in the 260A > G polymorphism, and neither polymorphism analysis revealed any publication bias. Furthermore, there was a substantial association between complete deletion of the DAZ gene cluster and male infertility in the pooled data. The stratified analysis by ethnicity based on country of origin of the investigated population revealed a similar relationship in Caucasians and Asians, but not in Latinas and Arabs, probably due to the inclusion of very less study for each ethnic category. In this investigation, the larger sample size employed to examine the correlation of DAZL polymorphisms and DAZ deletion with male infertility was a substantial benefit. Furthermore, the inclusion

of the English-language literature, as well as the relatively small number of articles included in the meta analysis in Caucasians for DAZL polymorphisms and Latinos and Arabs for DAZ deletion, are some of the limitations of our meta-analysis. Because all of the individual studies included in our meta analysis lacked information on other cofounding variables such as age, smoking and drinking status, existence of other diseases, exposure to environmental risks, and so on, findings were generated using unadjusted ORs. Finally, publication bias was not detected as well as the heterogeneity in the aggregate pooled data for the association of DAZ deletion with male infertility.

In conclusion, we revealed no association between DAZL polymorphisms 260A > G and 386A > G with male infertility in any ethnic group in our meta-analysis. However, male infertility has been associated to complete deletion of the DAZ gene cluster in Caucasian and Asian men. DAZL polymorphisms may therefore be ruled out as a biomarker for the diagnosis of male infertility. More research should be done, including studies from a wider range of countries and nationalities, in order to reach more conclusive results.

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Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest Puja Devi Nongthombam and Suttur S Malini declare that they have no conflicts of interest.

Ethical approval Not Applicable.

Consent to participate Not Applicable

Consent for publication Not Applicable

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